

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

**Research on reproductive health at WHO—
pushing the frontiers of knowledge**

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Acronyms used in this report

AIDS	acquired immunodeficiency syndrome
ANRS	Agence nationale de recherches sur le SIDA
ARV	antiretroviral
CAC	comprehensive abortion care
CDC	Centers for Disease Control and Prevention
CONRAD	Contraceptive Research and Development Program
DHS	Demographic and Health Survey
DMPA	depot-medroxyprogesterone acetate
ERK	extracellular signal-related kinase
FGM	female genital mutilation
hCG	human chorionic gonadotropin
HIV	human immunodeficiency virus
HPV	human papilloma virus
HRP	UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction
ICPD	International Conference on Population and Development
IgA	immunoglobulin A
IgG	immunoglobulin G
IUD	intrauterine device
MTCT	mother-to-child transmission (of HIV)
NET-EN	norethisterone enantate
NGO	nongovernmental organization
NIH	National Institutes of Health
PAHO	Pan American Health Organization
ORC	Opinion Research Co-operation
RHR	WHO Department of Reproductive Health and Research
RTI	reproductive tract infection
STI	sexually transmitted infection
TU	testosterone undecanoate
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
USAID	United States Agency for International Development
VIA	visual inspection with acetic acid
WHO	World Health Organization

Preface

6

to



“HRP is a unique Programme and the international leader in reproductive health research. It needs to be supported further to enable it to continue its role effectively in response to evolving reproductive health problems and practices.”

(from the External Evaluation Report on HRP's work during 1990–2002, World Health Organization, 2003)

Sexual and reproductive health concerns everyone: men and women, young and old, rich and poor. In an ideal world, everyone would be able to decide for themselves whether and when to have children; everyone would have the knowledge and skills they need to avoid risky sexual behaviour; every woman would be able to obtain skilled help during pregnancy and childbirth. Unfortunately, we do not live in an ideal world. There are still too many women dying in childbirth, almost all of them in developing countries; there are still too many couples who do not have access to effective contraception and too many women who are compelled to resort to unsafe abortion when faced with an unintended pregnancy; and too many people—especially women and adolescents—are still unable to protect themselves against sexually transmitted infections, including the human immunodeficiency virus (HIV).

Over and above the individual suffering they cause, sexual and reproductive health problems have a broader impact on social and economic development. As the global community focuses on achieving the Millennium Development Goals, improvements in sexual and reproductive health will constitute an essential foundation for these efforts. Recognizing this, WHO has developed a new global strategy, approved by the WHO Executive Board in January 2004 and World Health Assembly in May 2004, to accelerate progress towards the achievement of international goals and targets in reproductive health.

The UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP) is uniquely placed to contribute to these efforts.

As the global community focuses on achieving the Millennium Development Goals, improvements in sexual and reproductive health will constitute an essential foundation for these efforts. Recognizing this, WHO has developed a new global strategy, approved by the WHO Executive Board in January 2004 and World Health Assembly in May 2004, to accelerate progress towards the achievement of international goals and targets in reproductive health.

By supporting basic, clinical, epidemiological, social science and operations research, and by conducting systematic reviews, it augments the evidence base for reproductive health practices and service delivery. In addition, through its capacity-building activities, it strengthens the ability of countries, not only to carry out research that responds to national and global priorities, but also to translate the results of that research into effective and locally appropriate programmes.

This report presents an overview of HRP's work over the biennium 2002–2003. Chapter 1 looks at activities in the area of family planning, a field in which HRP has been active since its inception in 1972. Over the past three decades, contraceptive prevalence has risen dramatically and fertility has fallen in almost every country of the world. Nevertheless, there are still an estimated 123 million couples, mainly in developing coun-

tries, who do not use contraception, despite wanting to space or limit the number of their children, and some 300 million who are dissatisfied with the methods they use. More recently, the pandemic of HIV infection has thrown into focus the broader issue of protection, not just against unwanted pregnancies but also against sexually transmitted infections. HRP's work addresses all these issues, seeking to develop new and more acceptable contraceptive methods, to assess the safety and effectiveness in use of existing methods, and to understand better the attitudes and perceptions of men and women to the methods available. In particular, a number of studies in Africa and Asia have looked at attitudes to use of condoms for dual protection against pregnancy and sexually transmitted infections. The findings of these studies have immediate implications for programmes seeking to reduce HIV transmission through increased use of condoms.

Chapter 2 outlines research activities carried out in the context of WHO's Making Pregnancy Safer initiative. Here, the focus has been on generating evidence for the development of acceptable and affordable maternal and newborn health programmes in developing countries. A new antenatal care model has been developed, comprising only components that have been scientifically validated as effective in reducing risks for the mother and her baby. More condition-specific studies have looked at potential treatments for pre-eclampsia and the underlying factors linked to preterm delivery.

Research on the control of sexually transmitted infections, including HIV, is described in Chapter 3. The development of the female condom offers women the possibility of a method of

protection against both pregnancy and sexually transmitted infection that is under their control. However, more information is needed on its effectiveness in this regard, and HRP is supporting a number of studies to elucidate the issues. Another area of vital interest is the prevention of mother-to-child transmission (MTCT) of HIV, which represents a growing concern in many developing countries. HRP is coordinating a multicentre study in several African countries aimed at optimizing the use of antiretroviral drugs, both to prevent MTCT and to preserve the health of the HIV-infected mother.

HRP's work on preventing unsafe abortion, which responds to the recommendations of the International Conference on Population and Development, is described in Chapter 4. In addition to documenting the magnitude of the problem of unsafe abortion and its associated mortality, HRP supports clinical research, which provides the high-quality scientific data needed for registration of drugs for medical abortion in countries where such a service is legally available.

Addressing the sexual and reproductive health needs of young people, particularly in developing countries, represents a considerable challenge. HRP's research in the field of adolescent health, outlined in Chapter 5, seeks to help meet this challenge by building the evidence base on the sexual and reproductive health needs of young people. Findings from social science studies in a number of countries have highlighted the extent, patterns and consequences of risky sexual behaviour, contraception and abortion in this age group, and have shed light on some of the underlying factors that can increase or decrease the risks. In addition, operations research in five African countries is seeking to evaluate and eventually improve reproductive health services for adolescents.

Finally, Chapter 6 describes how HRP works directly with countries to strengthen their capac-

Indeed, as demonstrated unequivocally by the report from the team that carried out an external evaluation of HRP's work during the last 12 years, the Programme has made important contributions "to global public goods through its cumulative impact on fertility regulation and on reproductive health, leading to significant public health benefit for women, couples and children throughout the world".

ity to undertake research in reproductive health. Working with and through a network of over 120 institutions, HRP provides financial and technical support for capacity development, focused on national and global priorities.

The various research projects reported here have produced a wealth of valuable information, much of which is already being used in policy development and programme delivery. Indeed, as demonstrated unequivocally by the report from the team that carried out an external evaluation of HRP's work during the last 12 years, the Programme has made important contributions "to global public goods through its cumulative impact on fertility regulation and on reproductive health, leading to significant public health benefit for women, couples and children throughout the world". We have every intention to continue on this path, building on our past achievements and comparative strengths in partnership with our worldwide network of collaborating organizations, institutions and concerned individuals. Our Medium-term Programme of Work for the period 2004–2009, that was crafted during the past two years and approved in 2003 by our Scientific and Technical Advisory Group and Policy and Coordination Committee, will be our road map in the years ahead.

The approval of the global reproductive health strategy and of our Medium-term Programme of Work 2004–2009, together with the very positive external evaluation of our work over the last 12 years, should make us feel happy and content. But, in fact, we are not. As shown in Annex I of this report, our income during the past biennium has dropped precipitously, necessitating substantial cutbacks in support to research projects and staffing. As the External Evaluation Team observed, "Productivity [of the Programme] has remained high in the face of declining budgets. However, there are limits to the ability to increase efficiency while maintaining the quality of work. HRP's agenda has reached a stage where additional resources are needed to maintain the same level of productivity." Without a dramatic upturn in funding the Programme will find it increasingly difficult to meet the high expectations of performance by both donors and beneficiaries. Indeed, its very existence could be threatened.

Ten years after the International Conference on Population and Development, when countries committed themselves to providing universal access to reproductive health services, we can look back and say that the world has made progress—but not enough. We have had fine words about the importance of reproductive health from national governments and the international community, but not enough action. There is an urgent need now to recognize the key role of reproductive health in underpinning sustainable development, and to increase our efforts, not only to build the evidence base for effective action, but also to put into practice what we already know. Only in this way can we move towards our ideal world.

Paul F.A. Van Look, M.D., Ph.D.
Director
April 2004

The Report

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to



Family planning

In recent decades, enormous strides have been made in the development of safer and more effective contraceptives. Yet still an estimated 123 million couples, mainly in developing countries, do not use contraceptives, despite wanting to space or limit their childbearing.

In recent decades, enormous strides have been made in the development of safer and more effective contraceptives, and in the provision of affordable and accessible family planning services. Yet still an estimated 123 million couples, mainly in developing countries, do not use contraceptives, despite wanting to space or limit their childbearing. In addition, there are up to 27 million unintended pregnancies each year among people who use contraceptives, and some 300 million couples are dissatisfied with the methods they use.

These figures raise a number of questions concerning the acceptability and efficacy of the methods available and the quality of family planning services. Clearly, there is a need to expand the choices available to couples who wish to regulate their fertility, and to continue to assess the safety and effectiveness of the choices already available. In addition, an understanding of the perspectives of users and potential users of family planning services is essential if those services are to respond effectively to their needs and preferences.

Since its inception in 1972, the Special Programme of Research, Development and Research Training in Human Reproduction (HRP)¹ has stimulated and funded research that addresses these issues. More recently, the pandemic of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) has thrown into focus the broader issue of protection, not just against unintended pregnancies, but also against sexually transmitted infections (STIs), including HIV.

In a pioneering attempt to assess the interactions between family planning and risk behaviour related to HIV/AIDS, a multicountry research project has been conducted in six Eastern and Southern African countries where HIV infection is particularly widespread.

This chapter provides a brief summary of selected aspects of the Programme's work in this field over the biennium 2002–2003.

The views of users

The attitudes of sexually active couples to contraception are shaped by various factors, perhaps most importantly the prevailing social and cultural norms. Beyond that, their views will be influenced by their contacts with providers, the quality of care they receive or perceive, the available reproductive health services and supplies, and their personal assessment of the risks of unintended pregnancy and sexually transmitted infections.

HRP's work in this area seeks to increase understanding of how these various factors affect people's behaviour, and to address aspects of quality of care that have an important bearing on access to and use of services. The work also covers selected issues related to infertility, an important but frequently neglected component of reproductive health.

Family planning in the era of HIV/AIDS

In a pioneering attempt to assess the interactions between family planning and risk behaviour related to HIV/AIDS, a multicountry research project has been conducted in six Eastern and Southern African countries where HIV infection is particularly widespread: Kenya, South Africa, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe. The study was designed to address three main objectives: (1) to determine the perspectives of sexually active individuals on the dual risks of STIs (including HIV/AIDS) and unintended pregnancy; (2) to develop strategies that sexually active individuals would consider appropriate, practical and effective in coping with these risks; and (3) to explore opportunities for, and constraints to, behavioural change.

One of the aspects explored by the study was the use of condoms, in particular within marriage and stable relationships. 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.

Findings from Kenya, South Africa, Uganda and Zimbabwe show that educated couples are more likely to use condoms than those with little education; in South Africa and Uganda, young people were more likely than older ones to use condoms with stable partners. These findings suggest that condom use could be increased in other social groups, since the young and

¹ The Special Programme of Research, Development and Research Training in Human Reproduction (HRP) became a cosponsored Special Programme in 1988, with the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA), the World Bank and WHO as its cosponsors. Since 1998 HRP has functioned within the WHO Department of Reproductive Health and Research (RHR). RHR includes a non-research component, namely Programme Development in Reproductive Health (PDRH), the work of which is the subject of a separate biennial report. The present report covers only the work of HRP.

the educated urban elites could be considered as trend-setters or role models for other social groups. Refocused social marketing campaigns, building on the progress already made, could do much to counter the stigma associated with condom use in stable relationships. The condom's association with STI/HIV has overtaken its family planning functions and this needs to be taken into account in policies and programmes.

Other work completed during the biennium reinforces this conclusion, through the finding—using Demographic and Health Survey (DHS) data from 16 developing countries—that a massive shift from the more effective oral contraceptive pills to the less effective condom would not jeopardize family planning goals, but would contribute to preventing HIV infections.

- **Cameroon.** A study in Central and West Cameroon compared condom use in two very different ethnic groups: the Beti, where sexual norms are relatively permissive, and the Bamileke, where more conservative mores prevail. Despite their differences, attitudes towards condom use and sexual behaviour in the two groups were broadly similar. In both groups, the probability of condom use increased with educational level of men and women. Other factors associated with condom use were: a small age difference between the man and the woman; a higher frequency of discussion about sexual matters; and greater decision-making power of the woman. These findings on the relationship between women's status and condom use have important implications for HIV prevention programmes.
- **China.** Further findings from a study on sexual behaviour and condom use in China became available in 2002. The study examined the effectiveness of a video-based reproductive health education intervention in increasing knowledge of STIs and improving attitudes to condom use among 2261 men attending an STI clinic in Shanghai. Video-based interventions were found to have a significant impact on both knowledge and attitudes, and could easily be integrated into different STI clinic settings.

Quality of care

In 2000, a research initiative on quality of care was launched focusing on research to assess the quality of reproductive health services from the perspectives of clients, potential clients, and providers, and in terms of objective standards of care. The initiative also sought proposals designed to assess the effects of improved service

HRP reviews existing evidence in order to build an evidence base on the safety and performance of contraceptives in developing countries. All the resulting evidence is used to generate norms and guidelines for use by countries in developing high quality family planning services.

quality on intermediate outcomes (e.g. provider behaviour, client knowledge, client satisfaction, and client behaviour, especially with regard to the continuation of contraceptive use).

New findings from the initiative became available in 2003. Studies have assessed barriers to access to family planning services in several African countries, and analysed provider perspectives on the provision of family planning services in several countries.

- In Mali and Senegal, family planning providers were reportedly refusing to provide contraceptives to some non-menstruating clients, in the belief that contraceptives may harm an unrecognized pregnancy. Providers from six clinics were therefore given training and a checklist of six questions to ask clients in order to rule out pregnancy. The intervention had significant impact in Senegal, where the percentage of new clients denied services because of fear of an unrecognized pregnancy declined from 10% to 4%. In Mali, researchers were surprised to find that, at least in the urban and periurban centres studied, menstruation requirements were not rigidly enforced. There was, thus, little room for improvement, and refusal rates remained flat at the low level of 4%.
- In Uganda, a study on provider perspectives on quality of family planning care 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 and provider motivation; and provider perceptions of their work environment. It was found 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 were concerned about the quality of family planning services. Providers felt constrained in their ability to provide quality family planning care by factors over which they had little control, for example, ensuring privacy. Other key findings includ-

ed the lack of a national policy for training family planning providers. However, almost all providers and supervisors felt that the recent introduction of the health subdistrict concept into Uganda's health care delivery system had contributed to improving the quality of family planning services.

Infertility

In collaboration with Opinion Research Cooperation (ORC) Macro, HRP worked on measuring infertility, using nationally representative DHS data collected between 1995 and 2000 from 47 developing countries. Data were available for 495 000 women aged 15–49 years. Overall, 2.5% of couples were found to experience primary involuntary infertility, but important regional, demographic and socioeconomic differentials were noted.

Safety and effectiveness of family planning methods

Much of the existing information on the safety and effectiveness of modern contraceptives comes from studies in developed countries, and is not necessarily applicable to developing regions with very different health, social and economic conditions. HRP seeks to bridge this gap in various ways. It reviews existing evidence in order to build an evidence base on the safety and performance of contraceptives in developing countries. It supports and coordinates clinical trials under carefully controlled conditions, with screened and monitored volunteers. And it is involved in observational epidemiological studies in developing countries to assess the safety and effectiveness of different methods under actual conditions of use. All the resulting evidence is used to generate norms and guidelines for use by countries in developing high quality family planning services.

Intrauterine devices

Since the appearance of the first intrauterine devices (IUDs) in the 1960s, research has led to various advances in materials and form, with the result that modern IUDs combine high effectiveness with a long duration of action. More than 147 million women currently use an IUD, making it the second most popular contraceptive method in the world, after sterilization.

Modern IUDs are of basically two types: copper-bearing devices, and hormone-releasing devices. Because IUDs are intended to be left in place for several years, demonstration of

their long-term safety and efficacy is of prime importance. HRP is involved in several long-term studies that have been following cohorts of women using IUDs.

Copper-bearing IUDs

Between 1989 and 1998, nearly 6000 women had a TCU-380A IUD inserted, as part of HRP-sponsored trials. Most of the insertions took place in 1990–1991, and the first large cohort of users completed 10 years of use at the end of 2001. Over 500 women completed 13 years of use by the end of 2003. Data from this research have already been used to support the progressive extension of the approved lifespan of the device from 3 to 10 years. Follow-up of users will continue for up to 15 years, and it is expected that the data will allow consideration of a further extension of the approved lifespan.

A randomized comparative study of the TCU-380A and the Multiload (ML) 375 copper-releasing devices was started in the early 1990s; the interim 10-year results are shown in Table 1.1. Both devices proved highly effective in preventing pregnancy and had similar continuation rates. However, the intrauterine pregnancy rate of the TCU-380A was about half that of the ML375.

Levonorgestrel-releasing IUD

The clinical performance of Mirena, a levonorgestrel-releasing device, is being compared with that of the TCU-380A IUD in a multicentre study involving over 3800 women. The interim results

HRP is sponsoring a multicentre study in Kenya, Thailand and Zimbabwe to investigate the impact of different contraceptive methods on the course of HIV infection in women.

after 6 years of use are shown in Table 1.2. The hormone-releasing device is associated with a significantly lower pregnancy rate, but has a higher rate of removal, mainly because of menstrual disturbances.

Hormonal contraceptives

Synthetic hormonal contraceptives first became available in the mid-twentieth century, with the development of the oral contraceptive pill, containing a progestogen and an estrogen. The pill is used today by some 76 million women, making it the third most popular means of contraception. It is highly effective, but has to be taken every day, which presents a difficulty for some women. As a result, other forms of delivering contraceptive hormones have been developed, such as implants and injectable products.

Almost from the beginning, hormonal contraceptives generated controversy regarding short-term and long-term side-effects, including possible links with cancer and, more recently, with the potential for increased susceptibility of the user to HIV infection. HRP is involved in a number of trials looking at different aspects of the safety of these contraceptives.

Hormonal contraceptives and cervical cancer

The possible link between use of hormonal contraceptives and cervical cancer has generated considerable debate over the years. In 1990, a WHO Scientific Group concluded that use of oral contraceptives for more than five years was associated with a modest (1.3–1.8-fold) increased risk of cervical cancer. However, the reasons for the increased risk were not clear. In 2002, a report in *The Lancet* showed that, among women who tested positive for human papilloma virus (HPV) infection, those who had used hormonal contraceptives for between 5 and 9 years had a 2.8-fold increased risk of cervical cancer, and those who had used hormonal contraception for more than 10 years had a 4-fold increased risk.

In March 2002, HRP convened a consultation to review these and other data. The consultation recommended no changes in contraceptive prescribing practice or use. The number of cervical cancers that result from hormonal contraceptive use is likely to be very small. For young healthy women who do not smoke, the health benefits far outweigh the risks. A systematic review of the subject confirmed that long-term use of oral contraceptives was associated with an increased risk of cervical cancer, but because of lack of data could draw no conclusions as to whether this risk might decrease once use was discontinued. Work is currently under way on an individual record meta-analysis from all relevant studies in an effort to address this question.

Hormonal contraceptives and HIV

HRP is sponsoring a multicentre study in Kenya, Thailand and Zimbabwe to investigate the im-

Table 1.1 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	

pect of different contraceptive methods on the course of HIV infection in women. The study is observational, with 6-monthly follow-up visits for four years. By December 2003, 626 women had been recruited to the study, most of whom were using hormonal contraception. In light of the increasing access to antiretroviral (ARV) therapy in the study sites, the protocol of the study has been modified to allow the introduction of these drugs in a structured way, in line with national and WHO guidelines. Initial results are expected in 2005.

Progestogen contraceptives and bone mineral density

Progestogen-only contraceptives include injectable products, implants, vaginal rings, IUDs and oral preparations. Concern has been raised that these preparations could decrease bone mineral density and thus increase the risk of subsequent osteoporotic fracture.

A study at the Reproductive Health Research Unit in Durban, South Africa, is looking at the impact of progestogen-only contraceptives on women aged 15–19 years, i.e. who are still acquiring bone mass, and older women of 42–49 years, i.e. who are nearing the menopause. At least 100 women in each age group have been recruited to each of four subgroups: those using depot-medroxyprogesterone acetate (DMPA); norethisterone enantate (NET-EN); combined oral contraceptives; and non-hormonal meth-

HRP has invested in research to develop new methods that are easier to use and to deliver, that are associated with fewer and less serious side-effects, and that respond to the needs of different users.

ods. All women are being seen at 6-monthly intervals for up to five years. Initial results are expected in 2004.

Performance of new implantable contraceptives

Two new implantable contraceptives have recently become available. Jadelle, developed by the Population Council, contains two rods that release levonorgestrel; Implanon is a single-rod system delivering etonogestrel. HRP has initiated a multinational randomized comparative trial of the two implants to determine differences in clinical performance and contraceptive efficacy. Primary endpoints for the study 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. In parallel, an age-matched cohort of 1000 women who choose the TCU-380A IUD will be used as controls for non-reproductive system complaints.

Ten sites in nine countries are participating: Ankara (Turkey), Bangkok (Thailand), Beijing and Shanghai (China), Campinas (Brazil), Harare (Zimbabwe), Ljubljana (Slovenia), Santiago (Chile), Santo Domingo (Dominican Republic) and Szeged (Hungary). Interim results are expected in 2005 and final results in 2007.

Developing new and better contraceptive methods

The contraceptive methods developed over the past 50 years have found wide acceptance in many parts of the world, so that today it is estimated that over 635 million couples regularly use some form of contraception. Nevertheless, the choice of methods is relatively limited, and each method has specific drawbacks, whether in terms of convenience of use, reliability, or side-effects. Nearly half of users of a reversible method discontinue its use within a year, for a variety of reasons. The availability of improved, or totally new, methods could therefore have a significant impact on public health by meeting the needs of millions of men and women for whom the current range of options is inadequate.

HRP has therefore invested in research to develop new methods that are easier to use and to deliver, that are associated with fewer and less serious side-effects, and that respond to the needs of different users.

Table 1.2 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	

Emergency contraception

Emergency, or postcoital, contraception has been available for over 30 years. The Yuzpe regimen, introduced in the 1970s, was for many years the standard regimen. It consisted of two doses of combined oral contraceptive pills containing an estrogen and a progestogen, taken 12 hours apart, with the first dose being taken within 72 hours of intercourse. The efficacy of this regimen, however, was limited and it was associated with a number of side-effects. In the late 1980s, therefore, HRP began a research effort aimed at developing new approaches to emergency contraception.

- ▶ Levonorgestrel. A landmark multinational HRP study, reported in 1998, clearly demonstrated the superiority of two 0.75 mg doses of levonorgestrel, taken at an interval of 12 hours with the first dose within 72 hours of intercourse, over the Yuzpe regimen, in terms of both efficacy and acceptability.

A randomized study, reported in 2002, compared the efficacy and side-effects of a single 1.5 mg dose of levonorgestrel given up to 120 hours after intercourse with the two-dose regimen, and with a single 10 mg dose of mifepristone (see below). Over

4000 women attending 15 family planning clinics in Europe and Asia were enrolled in the study, which found no difference in pregnancy rates in the different treatment groups. These findings are of considerable importance, since the now widely accepted levonorgestrel-only regimen will become even easier to use in a single dose.

The data on levonorgestrel from this trial were combined with results from a previous study comparing the two-dose levonorgestrel regimen with the Yuzpe regimen, in a meta-analysis to investigate the effect of delay in the administration of levonorgestrel on the efficacy of treatment. The analysis included data on 377 women, and found a significantly higher pregnancy rate among those who took levonorgestrel on the fifth day after intercourse than among those who were treated within 24 hours (4.8% vs 1.3%). The number of women receiving treatment on day 5 was, however, rather small, and further research is needed on the effectiveness of the levonorgestrel regimen after day 3. It is therefore planned to add the data from a double-blind, multicentre study carried out in Hong Kong, China, in a further meta-analysis. The results of this analysis will be published in 2004.

- ▶ Mifepristone. Mifepristone was originally developed in the 1980s for termination of pregnancy, but was shown in the 1990s to be effective as emergency contraception. HRP studies in recent years have found that a dose as low as 10 mg taken within 120 hours of intercourse is as effective in preventing pregnancy as 600 mg (the dose used in initial pilot studies), and is associated with very few side-effects. To test further this regimen, HRP has collaborated with investigators in China in a 3-year initiative funded by the Rockefeller Foundation, and including two large multicentre trials. Fourteen papers resulting from this collaboration were published in the December 2003 issue of *Contraception*.

Overall, the 10 mg dose was found to be as effective as a 25 mg dose. The pregnancy rates in the two trials were 1.1% and 1.4%. Risk of pregnancy was found to be higher among women who had no children.

A meta-analysis of data from 13 randomized trials found a sharp decline in efficacy when treatment was administered on day 5 compared with treatment on day 1 after intercourse.

Box 1.1 Basic research on male fertility regulation

As a complement to clinical research related to male fertility regulation, HRP 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 flagellum formation; the expression and function of sperm-specific proteins; and specific intracellular pathways or events required for sperm function.

A number of activities were under way during the biennium, including the following:

- ▶ 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 immunoglobulin G (IgG) and immunoglobulin A (IgA) do enter the rete testes and prostatic fluids of the mouse and rat. 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.
- ▶ Anti-spermatogenic effects of luteinizing and thyroid hormones. Data from this pilot study indicate that, in 3-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 relationship 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 continuing. Final results will be available in 2004.
- ▶ Human sperm mitogen-activated protein kinase cascades and their role in sperm functions. Natural and potential sperm ligands have been used to investigate the presence and role of a series of kinases in ligand-stimulated human sperm function in this study. Initial results demonstrated localization of human kinases and their upstream ligands in human sperm. Inhibitors of these enzymes seem to alter sperm motility and ligand-induced stimulation of the sperm acrosome reaction *in vitro*. In 2003, the investigators determined that extracellular signal-related kinase (ERK) is downstream from protein kinase C; they have 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.

Male hormonal contraceptives

The contraceptive methods available to men are currently limited to condoms, vasectomy and withdrawal, and for some years now researchers have sought to develop a hormonal method for use by men that would be as safe, convenient and effective as those available for women. HRP has played a major role in pursuing this goal, and has supported work on several testosterone derivatives, including testosterone enantate, testosterone buciclate and testosterone undecanoate (TU).

- Androgen alone. In 2000, a phase II study of TU in 6 centres in China gave very promising results. After one year of use by 290 couples, there were no pregnancies and only minor side-effects. Following up on this, a four-year phase III study, involving 1000 couples, is currently under way in 10 centres in China, to investigate the effects of a monthly injection of 500 mg of TU on fertility. Volunteers are monitored for sperm suppression for the first 6 months. If sperm concentrations are suppressed to fewer than 1 million per ml, the volunteers continue to receive monthly injections for 24 months. If sperm levels are not adequately suppressed, the volunteer is discontinued from the study. All men who discontinue early for any reason are followed until their sperm levels return to normal (20 million per ml or more). Preliminary results indicate that a higher than expected number of participants failed to respond adequately to the regimen, leading to a primary failure rate of 4.3 per 100 couple-years; this is still considered acceptable.

In a bid to develop safe, effective and convenient hormonal contraceptives for men, HRP has supported work on several testosterone derivatives, including testosterone enantate, testosterone buciclate and testosterone undecanoate (TU).

- Androgen/progestogen combination. A phase II trial was conducted in Indonesia to evaluate sperm suppression in men given TU every six weeks, either alone or in combination with DMPA every 12 weeks. The trial was completed in 2002, and the results analysed in 2003. The combination regimen proved to be more effective in rapidly and completely suppressing spermatogenesis (Fig. 1.1). It is planned to carry out an expanded study, using a new formulation of TU, to investigate the possibility of simplifying administration, by lowering the doses of both components and extending the interval between injections.

In conjunction with the completed clinical trial, a study was performed to assess users' perspectives and acceptability of the method. Generally, study participants and their wives found the regimens acceptable. Many men reported short-lived pain at the injection site, but on the other hand felt that they had higher levels of sexual activity and energy during the study.

HRP is also supporting a study in Italy to develop and pilot test instruments to assess mood and behavioural changes resulting

from the administration of hormonal contraceptives. The instruments have been validated, and data have been collected and are currently being analysed. It is anticipated that these instruments could become standard tools for use in clinical trials of male hormonal contraceptives.

Combined vaginal ring

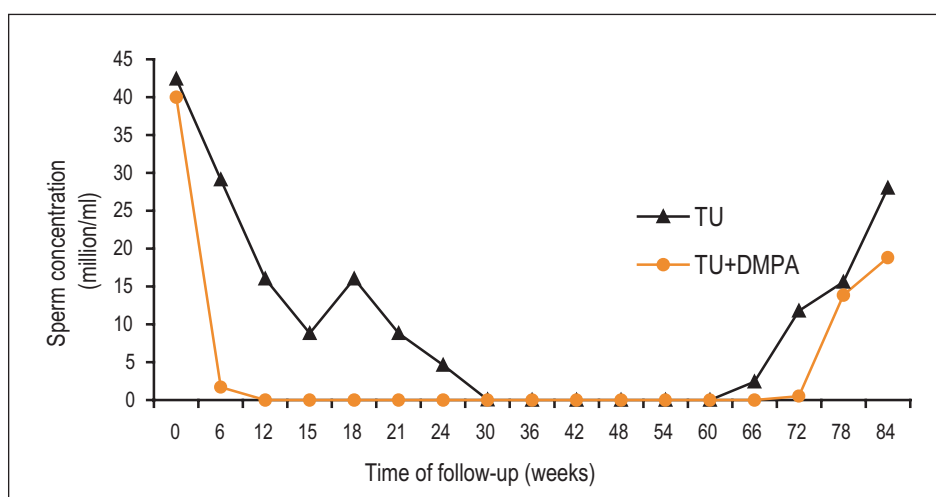
Many women express a need for a long-acting method of contraception that does not need daily interventions and is under the user's control. The vaginal ring is one approach that meets these needs. The Silastic ring is impregnated with hormones, which are absorbed through the vaginal wall. The ring can be left in place for several weeks and can be easily inserted and removed by the woman herself.

HRP is planning to provide support to two clinical research centres to take part in a phase III clinical trial of a contraceptive vaginal ring releasing 150 µg of nesterone and 15 µg of ethinyl estradiol daily over the course of a year. The trial will be coordinated by the Population Council, and will start once the performance profile of the rings has been verified in a pharmacokinetic study.

An immunocontraceptive for women

A number of agencies have been trying for some years to develop a totally new method of contraception—immunocontraception—based on the production of an immune response to specific molecules. HRP's work in this area is focused on the development of an immunocontraceptive based on, and directed against, human chorion-

Fig. 1.1 Average sperm concentrations in men receiving TU every 6 weeks, either alone or with DMPA every 12 weeks, for 48 weeks



ic gonadotrophin (hCG), a protein produced by the early embryo to allow successful implantation in the endometrium. A successful anti-hCG vaccine would theoretically provide long-lasting protection against pregnancy (approximately 6 months), without producing the endocrine and

other metabolic disturbances often associated with long-acting hormone preparations.

A candidate hCG immunocontraceptive has been developed, and a phase I clinical trial application submitted to the regulatory authorities

in Sweden. Pending approval of this application (which was, in fact granted in early 2004), work continued over the biennium to characterize the existing formulation in terms of immunogenicity, safety, and stability, and to explore alternative formulations.

Box 1.2 Basic research on implantation

An anti-implantation agent would be an attractive contraceptive for many women, since it would only need to be taken once a month, and then only on an as-needed basis or as a back-up method. Such a method could be expected to be free of the side-effects associated with many existing methods of family planning that need to be used on a continuing basis, and to be relatively inexpensive.

A five-year collaborative initiative to conduct basic research in this area, established by HRP and the Rockefeller Foundation, has just ended. The work, which was carried out in six centres in Australia, China, Germany, India, the United Kingdom, and the USA, has investigated various entities—genes, hormones, enzymes, etc.—to inhibit temporarily folliculogenesis, ovulation, development of the corpus luteum, and transport and implantation of the embryo.

A meeting was held in May 2003, at which the different teams presented their work. A number of pharmaceutical companies were also invited to attend, and as a result, several potential collaborative projects were identified and discussed.

It is planned to publish a journal supplement or special edition, containing reports from each centre of the work done over the past five years.

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Making pregnancy safer

In September 2000, WHO launched a *Making Pregnancy Safer* initiative, for which HRP is handling all research-related activities. HRP seeks to generate appropriate evidence for the development of acceptable and affordable maternal and newborn health programmes in developing countries.

The figures for maternal mortality are among the most striking examples of health disparity between developing and developed countries: of the half a million deaths each year that are related to pregnancy, fewer than 1% occur in the developed world. The average risk of dying from a pregnancy-related disorder in a developing country is about 250 times what it is in a developed country.

Many of the complications of pregnancy that cause death and disability among women also jeopardize the survival and health of newborn infants. Every year, nearly 4 million newborn babies die and millions more are disabled because of inadequately managed pregnancies and deliveries, or because of the mother's poor health and nutritional status.

In September 2000, WHO launched a *Making Pregnancy Safer* initiative, for which HRP is handling all research-related activities. Much of the research done in developed countries in the past has failed to address the needs and constraints of developing countries; indeed, programme interventions in developing countries based on such research may have introduced non-useful practices and wasted limited resources. HRP has therefore sought to generate appropriate evidence for the development of acceptable and affordable maternal and newborn health programmes in developing countries by: (1) evaluating the effectiveness of practices; (2) improving understanding of sociocultural and economic factors influencing maternal health care; (3) reviewing methods used in maternal health research; (4) conducting follow-up studies of populations included in pregnancy-related research; (5) evaluating strategies for implementing research results; (6) stimulating basic research on obstetric problems of global

In 2002, HRP, in collaboration with institutions in developing and developed countries, launched the Global Programme to Conquer Pre-Eclampsia/Eclampsia to increase understanding of the conditions in order to identify new preventive strategies.

importance; and (7) mapping the magnitude of maternal ill-health.

Selected highlights of HRP's work in this area in 2002–2003 are described below.

Preventing and treating pre-eclampsia

Pre-eclampsia is a little-understood disorder of pregnancy, characterized by high blood pressure, excessive protein in the urine, gastric pain, swollen limbs, headache and visual disturbances. In about one case in 200, pre-eclampsia progresses to eclampsia, which is marked by convulsions and can be fatal. Taken together, hypertensive conditions affect about 10% of all pregnancies and account for some 12% of maternal deaths. In addition, up to 12% of infants born to mothers with pre-eclampsia or eclampsia die within the first month of life. Those who survive may have an increased risk of impaired mental development, diabetes and cardiovascular disease later in life.

► In 1998, HRP joined an international effort to conduct the largest clinical study to date of any drug with the potential to treat pre-

eclampsia in order to prevent eclampsia. The so-called "Magpie trial" recruited 10 000 women with pre-eclampsia in 33 countries; half received magnesium sulfate and half a placebo. The results showed that magnesium sulfate reduced the risk of eclampsia by nearly half and, at the doses used in the study, had no harmful effects on the mothers or their babies. Long-term follow-up will be completed in 2004.

► In 2001, HRP launched a study to investigate the potential of calcium supplementation to prevent pre-eclampsia. A randomized, double-blind trial was conducted among women in populations with low calcium intake in Argentina, Egypt, India, Peru, South Africa and Viet Nam. A total of 8338 women were recruited to receive either 1.5 g of calcium a day or a placebo. Follow-up of the women was completed in 2003, and the results are expected in early 2004.

► In 2002, HRP, in collaboration with institutions in developing and developed countries, launched the Global Programme to Conquer Pre-Eclampsia/Eclampsia. This comprehensive service and research programme aims to increase understanding of the conditions in order to identify new preventive strategies. A systematic review was prepared on screening methods for pre-eclampsia, as well as reviews on promising etiological and pathophysiological leads to be tested in future research. These reviews are expected to be published in 2004. A large multicountry study of genetic factors involved in pre-eclampsia, intrauterine growth restriction and preterm delivery is planned, in order to gain insight into the pathological processes and, ultimately, to allow improved care for women at risk.

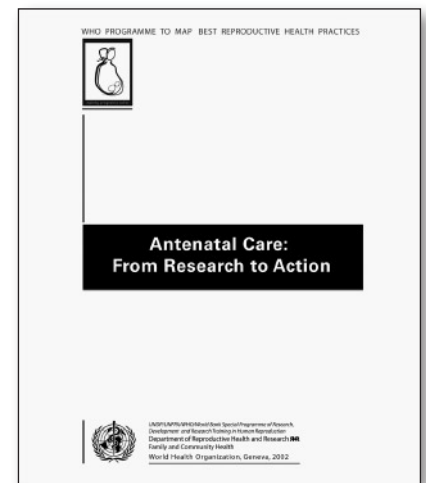
- Treatment of mild to moderate hypertension has been proposed as a strategy to prevent progression to pre-eclampsia. HRP therefore plans to implement a multicentre, randomized trial of labetalol for the treatment of moderate hypertension in pregnancy.
- Recently, pre-eclampsia has been linked to oxidative stress, which may potentially be reversed by giving antioxidants (vitamins C and E). HRP has initiated a randomized trial to determine whether giving 1000 mg of vitamin C and 400 IU of vitamin E daily to high-risk women, from the second trimester onwards, reduces the incidence of pre-eclampsia. The research is coordinated by the Maternal and Fetal Research Unit of St Thomas Hospital, London, United Kingdom.

HRP has developed a new model for antenatal care, comprising only the components that have been scientifically validated as effective in reducing the risks of ill-health for the mother and her baby.

The new WHO antenatal care model

HRP has developed a new model for antenatal care, comprising only the components that have been scientifically validated as effective in reducing the risks of ill-health for the mother and her baby. This model provides a leaner, more rational approach to antenatal care than the one generally used in developed countries. A large randomized trial of the new model found that it was as effective as the standard model, acceptable to women and to health providers, and could potentially reduce costs. Results of the economic evaluation of the model, which was done in collaboration with the University of East Anglia and the London School of Tropical Medicine and Hygiene, will be published in 2004.

In 2002–2003, an extensive effort was made to disseminate the results of the studies, and to promote use of the model. A manual on the implementation of the model was published in 2002, and has so far been distributed in over 2000 copies. During the biennium, a total of



17 presentations were made in 13 countries, including nine as part of training workshops.

Specific efforts to introduce the model were started in 2003 in 16 countries. Its use is currently being monitored and evaluated in Khon Kaen, Thailand, and in the Province of Corrientes, Argentina.

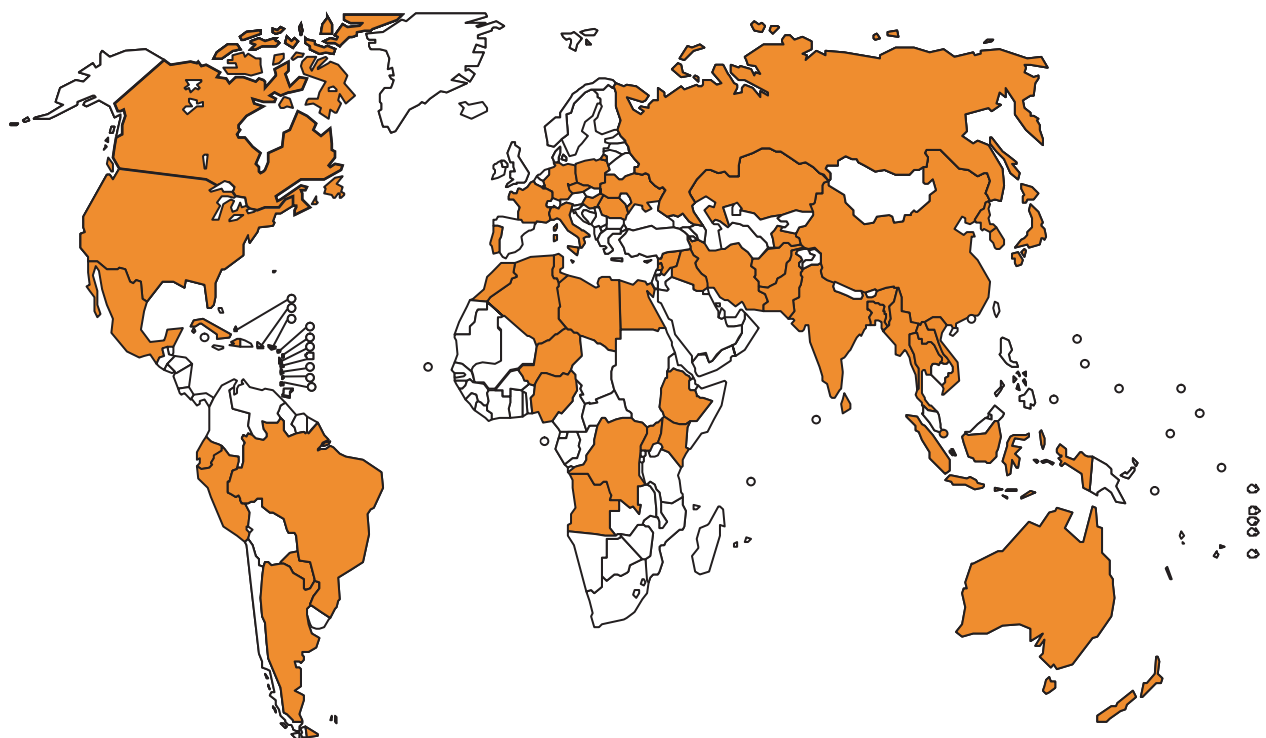
Nutrition in pregnancy

In 2003, HRP was invited by the Wellcome Trust and the United States Agency for International Development (USAID) to participate in an initiative on “Nutrition as prevention strategy against adverse maternal pregnancy outcomes”. As part of this initiative, HRP prepared two systematic reviews of the effectiveness of nutritional

Mapping maternal ill-health

A systematic review of epidemiological data from 1997–2002 on the incidence and prevalence of maternal morbidity was carried out during 2002–2003, and will be used as background information for the Global Survey for Maternal and Perinatal Health, which started in 2003. The survey is the first-ever global effort to assess the relationship between the burden of disease and the services provided in the area of maternal and perinatal health. A network of institutions throughout the world will collect data periodically, using a simple standard instrument. Data collection will begin in 2004 in eight countries in Africa and 11 in the Americas (Fig. 2.1).

Fig. 2.1 Countries participating in the Global Survey for Maternal and Perinatal Health



Box 2.1 New tool for strengthening laws, policies and standards in reproductive health

A new tool—entitled *Using human rights for maternal and neonatal health: a tool for strengthening laws, policies and standards of care*—has been developed in collaboration with the International Health and Human Rights Program, Francois-Xavier Bagnoud Center for Health and Human Rights, Harvard University School of Public Health, Boston MA, USA. This tool is designed to help countries to use a human rights framework to identify and address legal, policy and normative barriers to women's access to, and use of, maternal and newborn health care services, and to the provision of high-quality services. The use of human rights framework to complement the public health approach to health care and provision of services will allow countries: (1) to apply systematically the human rights principles (such as non-discrimination, participation and accountability) to all policies and programmes; and (2) to examine their laws and policies to ensure they are supportive of, rather than a barrier to, maternal and newborn health, as well as being in line with the government's human rights obligations. The principal component of the tool is a set of questionnaires for collecting information on the country's laws and policies. The tool also includes instructions for collecting and analysing the information through a participatory process involving various governmental and nongovernmental stakeholders. Field-testing of the tool started in Mozambique in 2003; there are plans to support its use of in two other countries with high maternal and neonatal mortality and morbidity.

interventions during pregnancy in preventing and treating maternal morbidity and mortality, preterm delivery, and intrauterine growth impairment. The two reviews, which were published in the *Journal of nutrition* in 2003, are being used by the Wellcome Trust and USAID in decision-making. They were also used as the basis for HRP's new guidelines on nutrition in pregnancy, which are part of a series of materials spe-

cifically designed to facilitate the translation of research results into clinical and public health practice.

Long-term follow-up of subjects involved in pregnancy-related research

There is an understandable concern that babies born to mothers who are given new treatments in clinical trials while pregnant may be affected—positively or negatively—by the interventions in later life. It is essential to improve understanding of the long-term effects on the fetus of treatment and preventive interventions during pregnancy.

HRP is currently conducting two major studies in this area.

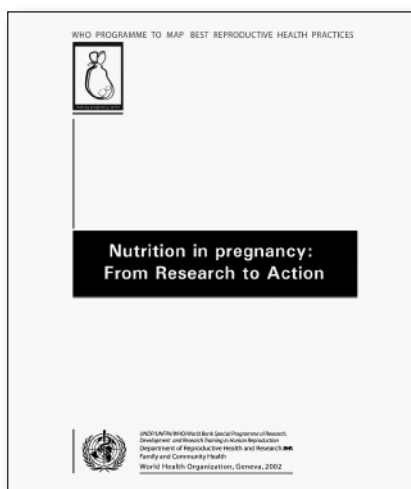
- Some 600 children born to women enrolled in the first trial of calcium supplementation during pregnancy were followed up for 13 years to determine whether the treatment had any protective effect on the child's blood

pressure. Contrary to previous results, the study found no effect on blood pressure.

- Children born to mothers enrolled in the "Magpie trial" (in which magnesium sulfate was given to pregnant women to prevent pre-eclampsia; see page 19) were followed up for two years. The study, which was conducted in Colombia, Cuba and Nigeria, was completed in 2003. It found no negative effects, on either the mothers or their children, in growth, development and morbidity.

Understanding preterm delivery

Preterm delivery is still the main cause of perinatal mortality throughout the world. HRP has initiated epidemiological research to understand better the heterogeneity of this condition, and identify specific underlying causes that are most likely to be preventable. A study of a cohort of over 40 000 women was completed during 2003, and demonstrated the differences in morbidity and mortality for subgroups of preterm delivery. The results will be published in 2004.



Box 2.2 Radiation and reproductive health

Radiation has the potential to influence reproductive health negatively in three ways. Direct irradiation of an embryo or fetus could influence the outcome of pregnancy and the health of the baby; it could also have carcinogenic effects that would become evident in later life. Irradiation of the gonads can have genetic effects, which could also affect the health of the offspring. Irradiation of the gonads can also affect fertility, through radiation-induced death of germinal cells. However, to date very few data are available on this topic.

In collaboration with the Institute for Cancer Research in the United Kingdom and the Scientific Research Institute for Radiation Medicine and Ecology in Kazakhstan, a research effort was launched in 2001 with UNFPA support to investigate the consequences for reproductive health of exposure to radiation in the area of Semipalatinsk in Kazakhstan. This area was a nuclear weapons testing site from 1947 to 1989, as a result of which the population in the area was exposed to high levels of radiation.

The study is focusing on three types of exposure that are of concern in relation to reproductive health: (1) exposure before or during reproductive age, and its effect on fertility and birth outcomes; (2) exposure in the womb and in early childhood, and its effect on infant and child mortality; and (3) exposure during adulthood and its effect on mortality of subsequent offspring. This study is one of the largest of its kind, and will eventually include some 50 000 subjects.

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Reproductive tract infections

In May 2002, the Department of Reproductive Health and Research (RHR) assumed responsibility for all WHO's work on sexually transmitted and reproductive tract infections. HRP is responsible for the research component, which involves conducting and advocating for research.

Reproductive tract infections (RTIs), which include sexually transmitted infections (STIs), are responsible for considerable ill-health throughout the world, both directly and by increasing the risk of transmission of human immunodeficiency virus (HIV). In addition to the 340 million curable STIs that are estimated to occur each year, there are many millions of incurable viral STIs, including an estimated 5 million new HIV infections. Moreover, some 600 000 children contract HIV infection every year, most of them from their mother during pregnancy or delivery, or while breastfeeding.

In May 2002, the Department of Reproductive Health and Research (RHR) assumed responsibility for all WHO's work on STIs and RTIs. This has provided an opportunity to take a coherent view of WHO's strategies and policies for STI prevention and management, including global advocacy, country support and technical issues (research, guideline development and normative functions). HRP is responsible for the research component, which involves conducting and advocating for research on: (1) new and improved control strategies for RTIs; (2) the prevention of mother-to-child transmission (MTCT) of HIV and other STIs; and (3) the development and deployment of safe and effective microbicides.

Prevalence of RTIs

The available data on the etiology and prevalence of RTIs are currently very limited, especially for developing countries. HRP is therefore supporting a number of studies in Asia to determine the prevalence of RTIs and STIs, both to

HRP is studying the contraceptive effectiveness of the female condom, compared with the male condom, in four centres: Chengdu (China), Durban (South Africa), Panama City (Panama), and Sagamu (Nigeria).

provide data for use by countries in programme planning and to strengthen the research capacity of scientists and institutes in the region.

Nine studies are being conducted or are planned, in China, Indonesia, Lao People's Democratic Republic, Myanmar, and Viet Nam, to investigate the prevalence of specific RTIs. In addition, two studies—in Mongolia and Myanmar—are looking into the association between *Chlamydia trachomatis* infection and ectopic pregnancy, while a study in Ulaanbaatar, Mongolia, is assessing clinical aspects of vaginal discharge in prepubertal girls. A further study in several sites in Mongolia is assessing the performance of syphilis screening in antenatal services.

Preventing RTIs

Condoms

Condoms are currently the only available means of protection against STIs, including HIV. The male condom is widely available and well known, but has a number of drawbacks, not

least the fact that it is under the control of the man. The female condom, which was introduced in the early 1990s, is gaining in popularity, and has the advantages that it can be inserted several hours before intercourse and is controlled by the woman.

More information is still needed on the effectiveness of the female condom in preventing both pregnancy and STIs.

► HRP is studying the contraceptive effectiveness of the female condom, compared with the male condom, in four centres: Chengdu (China), Durban (South Africa), Panama City (Panama), and Sagamu (Nigeria). Between August 2002 and November 2003, 1149 women were enrolled in the study; 63% chose to use the female condom and the remainder the male condom. So far, 359 women have stopped participating in the study, and 130 have switched groups (120 from female to male and 10 from male to female condoms). Eighteen pregnancies have been reported—nine in each group—and emergency contraception has been requested a total of 85 times. Participants will be followed up for a maximum of 12 months.

A study is planned among sex workers in Johannesburg, South Africa, to determine whether female condoms prevent exposure to sexually transmitted pathogens as effectively as male condoms.

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A second pilot study is comparing the performance of self-collected vaginal swabs with that of swabs collected by a clinician. So far, 398 self-collected swabs have been assessed; recruitment will continue to the planned number of 810 paired swabs.

Microbicides

Microbical gels or creams that can be applied in the vagina are new products that have the potential to protect both the woman and her partner against STIs, including HIV. Some products also have contraceptive effects. In collaboration with the Contraceptive Research and Development Program (CONRAD), HRP has just completed a three-centre trial of the safety and acceptability of one such product, cellulose sulfate gel. The trial was conducted in Kampala (Uganda), Mumbai (India), and Sagamu (Nigeria). A total of 180 women were enrolled; half were given 6% cellulose sulfate gel and half K-Y Jelly, to be applied twice daily. The women in both groups generally found the product easy to use, and no serious adverse events were reported. Almost all the women said that, if the product was proven to work, they would buy it or recommend it to others. There were no significant differences between the groups in terms of genital symptoms or colposcopy findings. Thus, cellulose sulfate appears to be as safe and well tolerated as K-Y Jelly. Further studies of the effectiveness of the product in preventing HIV transmission and pregnancy are planned.

Reducing mother-to-child transmission of HIV

Effectiveness of antiretroviral therapy

Rates of mother-to-child transmission of HIV remain persistently higher in developing than in

Microbical gels or creams that can be applied in the vagina are new products that have the potential to protect both the woman and her partner against STIs, including HIV. HRP has just completed a three-centre trial of the safety and acceptability of one such product, cellulose sulfate gel. The trial was conducted in Kampala (Uganda), Mumbai (India), and Sagamu (Nigeria).

developed countries, and HIV-related mortality is high. HRP is collaborating with the French *Agence nationale de Recherches sur le SIDA* (ANRS), the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) in the USA to conduct a multicentre study in several African countries, with the overall aim of optimizing the use of antiretroviral (ARV) drugs during the antepartum, intrapartum and postpartum periods, both to prevent MTCT and to preserve the health of the mother.

The study has two parts:

- ▶ Part I is a prospective cohort study of HIV-positive pregnant women and their children, followed for two years after childbirth. Those women who meet the WHO criteria for treatment, i.e. CD4+ count less than 200 cells per mm³, will be offered a triple regimen of zidovudine, lamivudine and nevirapine. Those who do not require treatment, or who have contraindications to the triple regimen, will be offered a short-course regimen for MTCT prevention, comprising zidovudine from 34–36 weeks of pregnancy until labour,

HRP is collaborating with researchers from France and the USA to conduct a multicentre study in several African countries, with the overall aim of optimizing the use of antiretroviral (ARV) drugs during the antepartum, intrapartum and postpartum periods, both to prevent MTCT and to preserve the health of the mother.

plus one dose of zidovudine and one dose of nevirapine at the onset of labour. All infants will receive one dose of nevirapine within 72 hours of birth. All mothers will be counselled on infant feeding choices. Those opting not to breastfeed will receive free formula milk; those choosing to breastfeed will be advised to stop after 6 months. The primary objectives of this part of the study are to assess the rates of AIDS-free maternal survival and HIV-free child survival, and to assess the acceptability and safety of ARV drugs.

- ▶ Part II is a nested randomized controlled trial of women enrolled in the cohort study, with CD4+ counts between 200 and 500 cells per mm³. These women will be assigned at random to receive one of two different regimens for the prevention of MTCT: either a triple ARV regimen, beginning at 34–36 weeks of gestation and continued for a maximum of six months postpartum unless breastfeeding is stopped earlier; or the short-course MTCT-prevention regimen described above. The efficacy and safety of the two regimens will be compared.

Five sites have been identified for the study in Burkina Faso, Kenya, Rwanda, and United Republic of Tanzania. A sixth site will be added as more funds become available. Study instruments and procedures have been developed and pre-pilot-tested during 2003. The study is expected to start in April–May 2004.

Safety of antiretroviral regimens

Transient emergence of resistant HIV strains has been reported following use of short-course prophylaxis in MTCT prevention, particularly with single-dose nevirapine. However, it is not known whether this has any impact on the efficacy of therapeutic ARV regimens given months or years later. To assess this possibility, HRP has developed a protocol for an observational study of women receiving ARV therapy, who had previously been exposed to low-dose nevirapine compared with women with no prior antiretroviral exposure. Due to financial constraints HRP is unable to support research in this area and the study will be implemented by the US Centers for Disease Control and Prevention, with WHO being represented in the study working group.

Pelvic infection following induced abortion

The incidence and risk factors for pelvic infection following surgical abortion are being examined in a multicentre case-control study in nine countries. The study will be nested within a study looking at the effect of administration of misoprostol before surgical abortion on the incidence of complications. The nested study will involve 11 sites and approximately 4000 women. By December 2003, recruitment had started at ten sites, and enrolment at all 11 sites is expected to be completed in 2004.

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Preventing unsafe abortion

HRP's work in the area of prevention of unsafe abortion has had a major impact, both on raising awareness of this public health problem and on medical practice.

WHO defines unsafe abortion 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. HRP's work on preventing unsafe abortion responds to recommendations of the International Conference on Population and Development (ICPD), which urged countries and organizations to address the health consequences of unsafe abortion and to ensure that, in circumstances where abortion is not against the law, it is provided safely. In 1999, at the five-year review of progress made since ICPD, governments agreed that, "in circumstances where abortion is not against the law, health systems should train and equip health-service providers and should take other measures to ensure that such abortion is safe and accessible".

HRP's work in this area over the years has had a major impact, both on raising awareness of this public health problem and on medical practice. HRP has continued to document the magnitude of the problem of unsafe abortion and its related mortality. HRP's clinical research also provides the high-quality scientific data needed for registration of drugs for medical abortion in countries where such a service is legally available. Furthermore, study teams often play a crucial role in improving the quality of care, introducing improved techniques and developing guidelines for services.

Incidence of unsafe abortion

HRP maintains a database on unsafe abortion and periodically produces updated estimates of numbers of unsafe abortions and related mortality. The most recent estimates, using information for the year 2000, suggest that some 19 million

Analysis of the available data on abortion by age shows that two-thirds of unsafe abortions are performed on women aged between 15 and 30 years.

unsafe abortions take place every year, leading to the deaths of about 68 000 women and to disability in a further 5 million. Unsafe abortion thus accounts for 13% of all maternal deaths (Table 4.1). Where maternal mortality is generally low, a small number of unsafe abortion-related deaths may account for a substantial percentage of maternal deaths, e.g. in Latin America.

Analysis of the available data on abortion by age shows that two-thirds of unsafe abortions are performed on women aged between 15 and

30 years. More importantly from a public health perspective, 14% of all unsafe abortions are performed in women under 20 years. The age pattern of unsafe abortion differs considerably between regions (Fig. 4.1). Knowledge of age patterns is essential to a better understanding of the local situation and to tailoring interventions to prevent unsafe abortion.

Unsafe abortion and contraception

Since contraception and abortion are two means of regulating fertility, it seems self-evident that increased use of contraception will lead to a decrease in induced abortion. However, in some countries rising levels of contraceptive prevalence have been accompanied by a rise in the number of abortions. To try to shed some light on this apparently contradictory situation, HRP supported a review of existing evidence on the relationship between abortion and contraceptive use. Careful analysis showed that, where fertility is relatively constant, increased contraceptive use is, indeed, associated with a fall in the incidence of abortion. However, where fertility is falling rapidly, both abortion and contraceptive use may rise in parallel initially, most probably because contraception alone is not sufficient to meet the demand for fertility regulation. However, in the long run, increased use of modern contraceptives leads to a decline in the incidence of induced abortion.

Abortion in a legally restricted context

HRP is supporting studies to determine the incidence of abortion in particular circumstances.

- ▶ A study in Sri Lanka, where abortion is permitted only to save the life of the woman, is

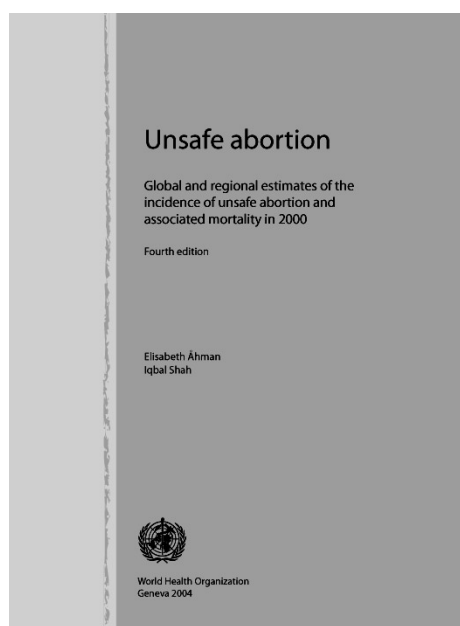
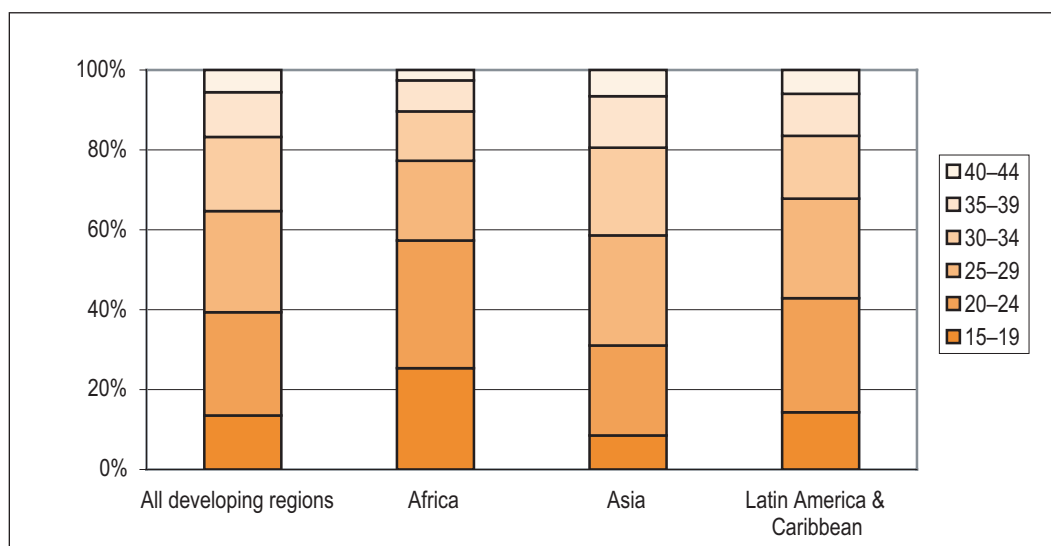


Fig. 4.1 Percentage distribution of unsafe abortion, by age



investigating the incidence of unsafe abortion from reports of health professionals. The study suggests a rate of 40 abortions per 1000 women of reproductive age in the Colombo District.

- In Togo, abortion is currently permitted only to save the life of the woman; despite this, it is believed that recourse to abortion is high. A study in the country is documenting the incidence of abortion and investigating pathways to abortion, using interviews with 4500 women of reproductive age and focus group discussions. The results of the study are expected at the end of 2004.

Medical abortion

Vacuum aspiration is one of the safest surgical procedures when performed by trained providers in hygienic conditions. In many countries

where the law permits abortion, these requirements cannot always be met and women have to resort to unsafe abortions. Even when safe, vacuum aspiration is an invasive procedure and many women prefer to avoid surgery. Medical, or drug-induced, abortion appears to offer an attractive alternative. Since the 1970s, HRP has supported numerous studies aimed at finding the optimum drug combination for medical termination of pregnancy. This research was crucial for the development of the sequential regimen of mifepristone followed 36–48 hours later by a prostaglandin analogue, such as misoprostol or gemeprost.

In 2003, HRP conducted a systematic review of 39 trials of first-trimester medical abortion. The major conclusions were as follows:

- Combined regimens are more effective than single agents.

- In the combined regimen, the dose of mifepristone can be lowered to 200 mg without significantly reducing method effectiveness.
- Misoprostol is more effective when taken vaginally than when taken orally.

Clinical trials

A number of clinical trials have recently been completed, or are still under way, to identify how far the doses of the drugs used for medical abortion can be reduced without affecting their efficacy, and to determine the best modes of administration.

- In 2003, results were published from a trial in Hong Kong, China, that compared sublingual and vaginal administration of misoprostol after treatment with 200 mg of mifepristone. Misoprostol is currently

Table 4.1 Global and regional estimates of maternal deaths due to unsafe abortion

Region	Maternal deaths due to unsafe abortion		
	No.	% of all maternal deaths	Per 100 000 live births
World	68 000	13	50
Africa	30 000	12	100
Asia ^a	34 000	13	40
Europe	340	20	5
Latin America and the Caribbean	4000	17	30
Oceania ^b	<100	7	20

^a Excluding Japan.

^b Excluding Australia and New Zealand.

registered only for oral use, and sublingual administration would be simpler and, possibly, more acceptable to some women than vaginal administration. The results of this relatively small trial were encouraging, and demonstrated a need for larger trials to test the effectiveness of sublingual administration and eventually to test a lower dose.

- ▶ A multicentre trial was conducted in China to evaluate the efficacy and side-effects of 150 mg of mifepristone followed two days later by 0.4 mg of misoprostol vaginally, for menstrual induction among women whose period was up to 7 days late. A total of 720 women were recruited, with a mean menstrual delay of 4.9 days. Retrospective serum analysis showed that 492 of the women were actually pregnant at the time of admission. Among the pregnant women, 455 (92.5%) had a complete abortion and 12 (2.4%) an incomplete abortion, while pregnancy continued in 25 women (5.1%). This rather high pregnancy rate is of concern, and further work is needed to assess this regimen.
- ▶ A further study of medical abortion is under way in 14 centres in 10 countries, to compare two doses of mifepristone (100 mg and 200 mg) followed by 0.8 mg of vaginal misoprostol 24 or 48 hours later. The target is to include a total of 2184 women; the clinical phase is expected to be completed by the end of 2004.
- ▶ Two studies to test the efficacy and safety of misoprostol-alone regimens have been undertaken. In the first study, over 2000 women requesting legal termination of early pregnancy in 11 centres were given three doses of 0.8 mg of misoprostol, either sublingually or vaginally, and at intervals of either 3 or 12 hours. The second study involved 684 women requesting legal termination during the second trimester. These women were given 0.4 mg of misoprostol either vaginally or sublingually every three hours for up to five doses. The results of these studies of misoprostol-alone regimens will be available by the end of 2004.

Mid-level providers and surgical abortion

A trial is under way in South Africa and Viet Nam to investigate the safety of surgical abortions performed by medically trained and government-certified mid-level providers (e.g. midwives) and physicians. The study sample com-

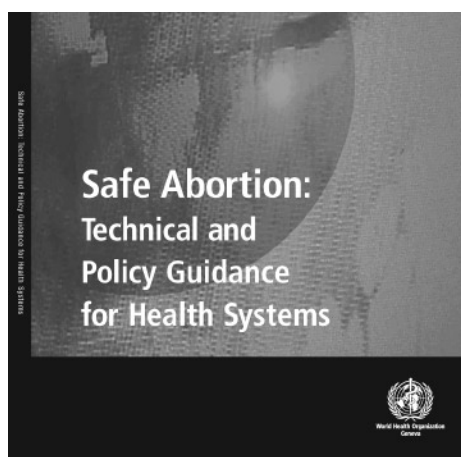
A trial is under way in South Africa and Viet Nam to investigate the safety of surgical abortions performed by medically trained and government-certified mid-level providers (e.g. midwives) and physicians.

prises about 1400 women, treated randomly by mid-level providers or physicians in four clinics in each country. In Viet Nam, 1690 women have already completed follow-up. Comparative results from the two countries are expected by the end of 2004.

Most complications during surgical termination of pregnancy occur during dilatation of the cervix. A large randomized trial is investigating the benefits and disadvantages of misoprostol when administered vaginally three hours prior to vacuum aspiration. The study is also comparing the rates of immediate and late complications between groups given misoprostol and a placebo. The clinical phase of this trial is expected to be completed by the end of 2004.

Technical and policy guidance

In order to provide guidance for Member States on how to implement the ICPD+5 agreement (noted in *Key actions for the further implementation of the Programme of Action of the International Conference on Population and Development*. New York, United Nations, 1999; paragraph 63.iii), HRP published *Safe abortion: technical and policy guidance for health systems* in English in 2003. The document provides a comprehensive overview of the many actions that can be taken to ensure access to good-quality abortion services as allowed by law. It covers the public health challenge of safe abortion services, clinical care for women undergoing abortion, putting services in place, and legal and policy considerations.



The document has been widely distributed to governments, professional associations, United Nations and other partner agencies, public health and research institutions, and nongovernmental organizations. French, Polish, Portuguese, Russian and Spanish translations of the document will be available in 2004.

Improving abortion care

As part of technical cooperation with countries, HRP assisted Mongolia, Romania and Viet Nam with assessing and improving the quality of abortion services, including counselling.

- ▶ In 2003, HRP assisted the Ministry of Health in Mongolia to conduct a strategic assessment (see also page 36) 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 findings and recommendations were presented in a national dissemination workshop in Ulaanbaatar in 2003.
- ▶ In 2001, HRP had assisted Romania in the conduct of 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 by Romania was the need to develop national standards and guidelines for abortion care. In 2003, guidelines prepared by staff from the Romanian Ministry of Health and Family, the national College of Physicians, and the Society of Obstetrics and Gynaecology were launched in a national meeting entitled "Family Planning in Romania: From Strategy to Best Practices".
- ▶ In Viet Nam, following the HRP-supported national strategic assessment of issues related to abortion and abortion services, a project was launched in late 2001 known as Comprehensive Abortion Care (CAC). In 2003, with technical support from HRP and Ipas, which included training of health care providers in advanced counselling, this project made major improvements in the quality of abortion services at two hospitals. This has led to all women being offered private counselling prior to abortion procedures. The project is now being expanded to the provincial level.

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Adolescent sexual and reproductive health

Addressing the needs of young people undoubtedly represents a considerable challenge. HRP's research in the field of adolescent health seeks to help meet this challenge by focusing on policy-relevant issues, as well as building the evidence base on the sexual and reproductive health needs and perspectives of young people.

The meaning of adolescence—the period from 10 to 19 years of age—is understood in different ways in different cultural contexts. Almost universally, however, it is seen as a time of transition between childhood and adulthood, a period of physical and psychological changes associated with puberty, and of preparation for the roles, privileges and responsibilities of adulthood. The nature and experience of adolescence vary tremendously by sex, marital status, educational level, socioeconomic class, region and cultural context. As a group, however, adolescents are increasingly recognized to have sexual and reproductive health needs that differ from those of adults, and which are still poorly understood and poorly served in much of the world.

Addressing the needs of young people—particularly in developing countries, which are often in the throes of rapid and profound social, economic, and political change—undoubtedly represents a considerable challenge. HRP's research in the field of adolescent health seeks to help meet this challenge by focusing on policy-relevant issues, as well as building the evidence base on the sexual and reproductive health needs and perspectives of young people. Most of the current work is supported by the social science research initiative on adolescent sexual and reproductive health, which includes some 43 studies in 28 countries. The following is a brief overview of some of the highlights of the biennium 2002–2003.

Attitudes and behaviour of adolescents

In 2002–2003, findings became available from a number of the social science studies. Many

A study in a low-income setting in New Delhi, India, found risky sexual behaviour among adolescent boys and girls. The findings highlighted the need to address the misperceptions of the parents, as well as to provide sexuality education for adolescents.

of them highlighted the extent, patterns and consequences of risky sexual behaviour, contraception, and abortion. They also shed light on underlying factors that can increase or decrease the risk of unsafe sexual and reproductive experiences for young people, such as young people's own skills, awareness, and attitudes, power imbalances between the sexes, access to sexuality education programmes, the roles and attitudes of parents and health care providers, quality of health services, and more generally, the broad sociocultural context, including in particular prevalent gender attitudes and roles.

Disadvantaged groups

A number of studies have looked at the sexual and reproductive health needs of disadvantaged groups, such as migrant and unemployed adolescents.

► A study in a slum setting in Jakarta, Indonesia, focused on young men aged 15–24 years, most of whom had some education but were not currently in school or employed. Premarital sex in this group was found to be common, and often involved sex workers. Condom use was largely

dismissed, and neither sexually transmitted infection, including HIV, nor unplanned pregnancy was considered problematic. These findings have several implications for local programmes, including the need to address misconceptions and lack of awareness about sexual risk behaviours, and to provide counselling and information on sexual and reproductive health.

- A study in a low-income setting in New Delhi, India, also found risky sexual behaviour among adolescent boys and girls; 5% of girls and 15% of boys reported sexual activity. The study findings underscored wide gender disparities, as well as a false confidence among parents that withholding information from adolescents, and closely regulating the activities of daughters, would protect them from risky sexual encounters. The findings highlighted the need to address the misperceptions of the parents, as well as to provide sexuality education for adolescents.
- A study of young female migrants in five cities in China found a high level of risky sexual behaviour. While the young women generally perceived premarital sex as acceptable, most had never used contraception, few knew where to obtain it, and many preferred to risk pregnancy rather than the embarrassment of having to disclose their sexual activity in order to obtain contraceptives. Providers reported that migrant women were more likely than non-migrants to delay seeking abortion, and to have multiple abortions. They were also more likely to resort to private—usually unqualified—providers in the belief that confidentiality would thereby be protected better.

Adolescents in Latin America

Thirteen studies in Latin America examined how gender disparities, shaped by the cultural context, influence adolescent sexuality and reproductive health.

► Four studies in Colombia, Mexico and Peru explored adolescents' perceptions of gender roles, sexual negotiation, risks, and pregnancy. 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 of proving their virility, fending off accusations of homosexuality, or enhancing their prestige among male peers. In contrast, young women who had casual sex or multiple partners were generally condemned, although attitudes varied somewhat by country, region, and socioeconomic class. In all study sites, adolescents described difficulties in communicating about sex with parents, and with sexual partners. Most adolescents did not use contraception, or relied on the rhythm method or withdrawal. 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. Thus, in many cases, young women did not feel free to initiate discussions about protection, while many young men were unwilling to do so since they considered contraception to be the responsibility of the woman. At the same time, for many young people in these settings, unplanned pregnancy was seen as a manageable event. Abortion was perceived as being relatively easily available, single motherhood was acceptable to many, and early motherhood or fatherhood was seen by many as a way to become an adult, create a life, or make a partnership more secure.

► In collaboration with the London School of Hygiene and Tropical Medicine, HRP recently completed a study to document trends in sexual activity, contraceptive use, and reproductive outcomes among young unmarried women in Colombia and Peru. Using data from successive Demographic and Health Surveys for the period 1985–1999, the study found an increase in sexual activity among unmarried women aged 15–24 years. Contraceptive use also increased, but by less than the increase in

Pioneering research in the Syrian Arab Republic explored the sexual and reproductive knowledge and attitudes of 4440 boys and girls aged 15–18 years. Results showed a general lack of knowledge about sexual and reproductive health.

sexual activity. The evident unmet need for contraception among these young women will pose a challenge for both countries, and will require programmes and policies to provide appropriate information and services. In addition, both the number of children born outside marriage and the number of abortions are increasing, as fewer single women are turning to marriage when faced with an unintended pregnancy.

Sexual and reproductive knowledge among students

► Pioneering research in the Syrian Arab Republic explored the sexual and reproductive knowledge and attitudes of 4440 boys and girls aged 15–18 years attending schools. Results, which became available in 2003, showed a general lack of knowledge about sexual and reproductive health: for example, 74% 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.

All the above studies point to a need to promote easier access to sexual and reproductive health information and services, and to encourage freer discussion of sexual issues.

Improving reproductive health services for adolescents in Africa

An operations research project to evaluate and improve reproductive health services for adolescents is being carried out in five French-speaking sub-Saharan countries. The project has three phases: (1) a baseline survey of adolescents using health services and of the quality of services offered; (2) 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 improve their “youth-friendliness”; and (3) a post-intervention survey to evaluate

the effectiveness of the intervention. HRP 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 2003 was as follows:

► Senegal. All three stages completed and final report available. Preliminary results show that reproductive health services, especially those in the public sector, are beyond the reach of most young people for a number of reasons, such as cost, negative attitudes of providers, and the prevailing societal values against sexual activity outside marriage.

► Guinea. Baseline study completed, interventions defined and carried out, but on a smaller scale than originally planned because of lack of funding; evaluation initiated.

► Côte d'Ivoire. Baseline study completed, interventions defined; progress halted because of lack of funding and political and socioeconomic instability.

► Benin. Baseline study completed, results currently being analysed.

► Cameroon. Baseline study completed in 2003.

In January 2003, an investigators' meeting was held in Bamako, Mali, to review progress and experience and to develop plans for future activities. Qualitative data are already available from interviews and focus group discussions carried out so far. These show that reproductive health services, especially those in the public sector, are not accessible to most young people for a number of reasons, such as cost, negative attitudes of providers, lack of privacy, and the prevailing societal values opposing sexual activity outside marriage.

Non-consensual sex

In September 2003, a global consultative meeting on non-consensual sex among young people in developing countries was held in New Delhi, India. The meeting, which was jointly co-sponsored by HRP, the Population Council (New Delhi), and Family Health International/YouthNet, included 35 invited papers and pre-

sentations by some 50 experts in this field. The 100 or so participants from all regions of the world included mainly researchers but also legal analysts, advocates, policy-makers, and young people themselves. Non-consensual sex was examined in terms of:

- ▶ experiences of young women and men: prevalence, forms, and contexts;

- ▶ youth perspectives (through a panel of seven young people);
- ▶ patterns of transactional sex;
- ▶ roles of the legal system;
- ▶ outcomes of coercion at the individual and community levels;

- ▶ interventions for prevention, support, and treatment; and
- ▶ research methodological issues.

The meeting identified several interventions and made a number of recommendations for needed research, which will be used as the basis for the development of a research initiative in 2004.

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Cooperating with countries

Since its establishment in 1972, HRP has worked with countries to strengthen their capacity to undertake research in reproductive health, both to respond to national needs and priorities and to contribute to the global research effort.

Since its establishment in 1972, HRP has worked with countries to strengthen their capacity to undertake research in reproductive health, both to respond to national needs and priorities and to contribute to the global research effort. Currently, HRP works with a network of over 120 institutions in 59 developing countries; 53 of these institutions are officially designated as WHO Collaborating Centres. During the biennium, 27 institutions (or national HRP research coordinating committees) were receiving support through either long-term institutional development grants or resource maintenance grants. Research training grants were also awarded to 24 scientists from these institutions, most of whom received their training within their own region. With support from HRP, 761 research projects were started or continued during 2002–2003, and 736 research articles were published or presented at national, regional or international scientific congresses.

In response to requests from countries, HRP organized in 2003 a consultation to develop guidelines on translating research findings into policy and programmes. These guidelines, which are expected to be finalized in 2004, are complementary to the existing HRP guidelines on developing research proposals.

Africa and the Eastern Mediterranean

In 2002–2003, HRP collaborated with 47 institutions or research groups in 28 countries in Africa and the Eastern Mediterranean. Seven institutions in these countries received long-term institutional development grants and three received resource maintenance grants. These ten centres were involved in 129 studies, 16 of which were supported by HRP. Some 42 studies

Currently, HRP works with a network of over 120 institutions in 59 developing countries. With support from HRP, 761 research projects were started or continued during 2002–2003, and 736 research articles were published or presented at national, regional or international scientific congresses.

of local or global relevance received support from other international agencies, which can be considered a direct result of HRP's efforts to strengthen the capacity of these centres to raise funds for research.

During the biennium, 45 research articles were published and 14 books or book chapters authored by staff from the HRP-supported centres. In addition, 40 presentations were made in national, regional or international scientific meetings.

Among its research training activities, HRP organized a number of workshops and short courses, covering research methodology, operations research, ethics, and semenology, as well as providing support to an MSc course in biostatistics at the University of Ibadan, Nigeria. Work continued on a training manual on

In 2002–2003, HRP collaborated with 47 institutions or research groups in 28 countries in Africa and the Eastern Mediterranean. During the biennium, 45 research articles were published and 14 books or book chapters authored by staff from the HRP-supported centres.

research methodologies in French, to be used to train trainers in French-speaking Africa. A meeting was held in March 2003 to elaborate a process for the further development of the material.

HRP also supported a workshop on electronic communication in Lomé, Togo, organized by the African Reproductive Health Research Network (RESAR). Twenty-two participants from Benin, Burkina Faso, Cameroon, Democratic Republic of Congo, Niger and Togo were trained in using electronic communication and databases, creating internet 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.

Regional research activities

- ▶ A multicentre prospective cohort study is being conducted in maternity units and obstetrics departments in 33 sites in 6 countries to estimate the incidence of obstetric complications among women with female genital mutilation (FGM) and to evaluate the relationship between FGM and such complications. A total of 29 700 women were enrolled in the study, and data collection was completed in May 2003. The data are currently being analysed and a report will be available in 2004.
- ▶ A study is under way in 7 centres in Nigeria to compare the efficacy and side-effects of two regimens of levonorgestrel for emergency contraception: (1) two doses of 0.75 mg given 24 hours apart; and (2) one dose of 1.5 mg. In addition, the project is being used to provide training in Good Clinical Practice and to develop a network of clini-

Box 6.1 Operations research training in French-speaking Africa

A special initiative was launched in 2002, in collaboration with the Population Council's FRONTIERS Project and the WHO Regional Office for Africa, to develop the Centre de Recherche sur la Population et le Développement in Bamako, Mali, as an operations research training centre for French-speaking Africa. A first workshop was held at the Centre in September 2003, attended by 17 policy-makers, programme managers and researchers from six French-speaking African countries. The participants agreed on three themes for operations research projects to be developed in future training workshops: maternal health (especially the low proportion of births attended by skilled health personnel); family planning (especially the low contraceptive prevalence rates in rural areas); and adolescent reproductive health (especially the high abortion mortality and prevalence of sexually transmitted infections).

Box 6.2 From research to action

In 2001 at a regional symposium for policy-makers, the Department of Obstetrics and Gynaecology of the University of Harare, Zimbabwe, presented the results of a field-based study that demonstrated that visual inspection with acetic acid (VIA) was a promising screening approach for identifying women with high-grade precancerous cervical lesions. A number of directors from collaborating centres in Africa expressed interest in conducting similar projects. A workshop was therefore held in October 2003 to train district hospital physicians in VIA and cryotherapy. Eight participants from Nigeria, Uganda, United Republic of Tanzania, Zambia and Zimbabwe attended the workshop. In addition to receiving training, the participants prepared draft proposals for demonstration projects to pilot-test the integration of VIA into existing reproductive health services in their hospitals.

cal research centres in Nigeria. As a side benefit, the project will contribute to making emergency contraception known in various areas of the country.

- ▶ A multicountry study is planned in Ethiopia, Nigeria, South Africa and Uganda to improve maternal and newborn health by identifying and implementing community- and health facility-based interventions that make it easier for pregnant women to obtain appropriate health care. The study will be conducted in three phases: pre-intervention assessment, intervention and evaluation. During the assessment phase, pregnant women and women who delivered within the previous 12 months, their 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 need for training to improve the skills of health care workers, and for equip-

ment, drugs and other supplies to ensure that women receive quality maternity care.

- ▶ Studies in the Islamic Republic of Iran, Oman, and the Syrian Arab Republic are exploring the reproductive health knowledge, attitudes and behaviour of adolescents.

The Americas

During 2002–2003, HRP collaborated with 18 institutions in 10 countries in the Region of the Americas. Seven centres received resource maintenance grants. These centres were involved in 187 studies addressing regional and national priorities, of which 28 were supported by HRP. Other international agencies provided funds for a further 62 of the projects. In this biennium, for the first time, epidemiological and social science projects accounted for over half of all these research studies.

Ongoing projects supported by long-term institutional development grants include basic research in the area of male fertility, an assessment to identify priority interventions that would improve access to and quality of family planning services, maternal and neonatal health care, and social science research in the area of male involvement in reproductive health. Maternal and 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.

Training grants were awarded to support postgraduate courses in reproductive biology (Mexico), reproductive epidemiology (Mexico), and social sciences (Argentina). Individual training grants were awarded to 19 scientists, of whom 15 were women. In addition, the seven supported centres provided individual training to 847 staff of other local institutions. Staff of these centres authored 299 research articles

Box 6.3 Using research findings

A national workshop on utilization of research findings was held in Buenos Aires, Argentina, aimed *inter alia* at promoting evidence-based interventions in sexual and reproductive health services and increasing use of research results by programmes and services by facilitating closer interactions between researchers, policy-makers and heads of maternal and child health services in hospitals. The workshop was attended by 58 participants, including health officers, directors of maternity hospitals, researchers from local WHO collaborating institutions, and representatives of WHO/PAHO. Discussions centred on the need to use evidence-based practices in the management of two of the main contributors to maternal mortality in the country—hypertensive disorders of pregnancy and postpartum haemorrhage. The need for a gender- and rights-based approach to providing services was also highlighted. The links established between the researchers and hospital directors at the workshop will form a basis for continuing exchange. An assessment will be conducted in eight months' time of the extent to which recommended practices have been adopted by the participants and the level of improvement of services offered to pregnant women.

Box 6.4 Information dissemination

A workshop was held in Buenos Aires, Argentina, with the aim of disseminating information on the results of the regional research initiative, "Reality and beliefs in the sexual and reproductive decision-making process: men's perceptions and behaviour". This initiative involved centres in Argentina, Bolivia, Cuba and Peru. For the workshop, a booklet was produced summarizing the project's findings and their interpretation, and containing specific recommendations for policies and programmes. The principal investigators made oral presentations, and extensive discussions were held with the audience of 106 people, which included researchers, teachers, social workers, and representatives of NGOs and international organizations. The workshop and the results of the study received good press coverage, with two articles in national newspapers and several television interviews.

and 77 books or book chapters. They also made 467 presentations in national, regional or international scientific meetings, and presented 43 official reports to national or international authorities and agencies.

Asia and the Western Pacific

This is the largest of HRP's four regional groupings, comprising 37 countries and nine territories, with a total population of over 3 billion. The sheer size of the population, coupled with the social, cultural and geographical diversity of the area, poses particular challenges. In 2002, the Regional Advisory Panel, while endorsing research capacity strengthening in the region, recommended a shift away from support for single-centre research in reproductive health to promotion of regional initiatives and networking among national centres.

During 2002–2003, 6 centres received long-term institutional development grants, and 4 countries were awarded resource maintenance grants (shared by 13 centres in the 4 countries). Some of the institutions that have received grants, notably those in China and India, have collaborated with HRP for a number of years and can be considered as "mature". They have demonstrated financial viability and programme sustainability, and many have been designated as WHO Collaborating Centres. These centres conduct training programmes in areas ranging from cellular and molecular biology, reproductive toxicology, reproductive endocrinology to laboratory techniques. Other centres, which can be considered as still developing their capacities, are in different stages.

During 2002, the centres in China published 182 original articles in national journals and 16 in international journals. A total of 64 papers were presented at seminars. The Indian National Institute for Research in Reproductive Health in Mumbai was also active in disseminating research results. Between 2001 and 2002, researchers at the Institute published 23 articles

HRP aims to strengthen national capacity for reproductive health research, with a particular focus on providing training opportunities, and to work with the WHO Regional Office for Europe in providing technical support to countries.

in national and international peer-reviewed journals, and made 53 presentations at national meetings and six at international meetings. Other centres in the region still need to expand their efforts to disseminate the results of their work: their combined output in 2002 was 11 original papers and 51 presentations.

Regional research initiatives

Regional research initiatives have been undertaken with the aim of fostering collaboration between centres, enhancing capacity-building in reproductive health, and promoting networking as a means of increasing the effectiveness and efficiency of the centres.

- ▶ A project on reproductive health of adolescent migrants 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 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.
- ▶ A project to determine patterns and predictors of caesarean section has been completed in nine out of thirteen centres, and a data analysis workshop is planned in 2004.

Eastern and Central Europe

This region includes the countries of Eastern and Central Europe, the Newly Independent States and the Central Asian Republics. HRP's work in this region is set against a background of: (1) relatively early marriage and childbearing (compared with women in Western Europe); (2) reliance on repeat abortions to limit or space births (although there has recently been a decline in this practice as use of modern contraception increases); (3) persistently high unmet needs for modern contraception; (4) levels of maternal deaths up to five times higher than in Western Europe despite universal coverage of care during pregnancy and childbirth; and (5) an emerging HIV/AIDS epidemic, linked to an explosion of sexually transmitted infections, intravenous drug use, increased sexual activity 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. Most countries have undertaken some policy reforms aimed at improving the responsiveness and stewardship of the health system, often by turning over parts of it to the private sector or to national insurance agencies. However, this has resulted in some population subgroups being left without insurance coverage or with minimum benefits. The impact of such measures on the effectiveness and quality of reproductive health services is under study.

In this context, HRP aims to strengthen national capacity for reproductive health research, with a particular focus on providing training opportunities, and to work with the WHO Regional Office for Europe in providing technical support to countries. A Regional Advisory Panel was established in 2001, and held its second and third meetings during 2002–2003. The Panel has highlighted the need to bridge the gap between researchers and policy-makers in the region, and to develop models for collaboration, as well as supporting research and research capacity building.

Operations research training

HRP is collaborating with the Population Council's FRONTIERS Project to build capacity in operations research in the region. As part of this initiative, and in collaboration with the WHO Regional Office for Europe, an operations research

training course for Russian-speaking countries was held in Almaty, Kazakhstan, in April 2003. Twenty participants came from ten countries; as part of the training, six research proposals were prepared. Three of these will be submitted for review by HRP for possible funding.

A second course is planned for 2004, after which the training will be evaluated for its effectiveness in shifting the approach to research. It is also planned to link this initiative to the application of the WHO Strategic Approach for strengthening reproductive health policies and programmes (see Box 6.5).

Box 6.5 The Strategic Approach

One of RHR's main areas of work is to review, develop, and test methodologies for the planning and implementation of reproductive health services and to assist countries in strengthening their reproductive health 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: (1) the needs and perspectives of current and potential users; (2) the extent of coverage, quality of care and capacity of the service delivery system; and (3) the mix of technologies and other reproductive health interventions.
- ▶ In Stage II, the recommendations coming from Stage I for policy change or other interventions are tested on a limited scale.
- ▶ Stage III applies the findings from Stage II to policy-making and planning for wider implementation.

While it was originally developed to address contraceptive introduction, the methodology has been, and is continuing to be, adapted for use with a range of reproductive health policy and programme issues.

Annex I

Financial overview for the biennium 2002–2003

In July 2001, the HRP Policy and Coordination Committee approved the Programme's budget (and work plan) for 2002–2003, totalling US\$ 40.3 million. However, income for the biennium reached only US\$ 26.5 million, representing a shortfall of almost US\$ 14 million. Fig. I.1 shows the historical trend in the approved HRP biennial budgets and the net income levels over the past seven biennia. As can be seen in the figure, HRP's income has declined considerably during this period. In light of the shortfall, a more focussed budget was implemented in 2002–2003, based on the priorities set by the Policy and Coordination Committee at its meeting in 2001.

Table I.1 shows the sources of contributions received by HRP during the 2002–2003 biennium as well as totals of contributions from each donor for the period 1970–2003. Three of the four HRP cosponsors, namely the United Nations Population Fund, The World Bank and WHO continued substantial support in 2002–2003. Income from WHO Member States was also strong, with contributions having been received from 13 of them, including a number of developing countries. This can be viewed as an important indicator that HRP is meeting the needs of the developing countries. However, the United States of America, which has been an important contributor for many years, declined to support the programme in 2002–2003 causing a major funding setback. Contributions were also received during the biennium from foundations, nongovernmental organizations, and civil society. The foundations included: The Bill and

Melinda Gates Foundation, The David and Lucile Packard Foundation, The Ford Foundation, The William and Flora Hewlett Foundation, The MacArthur Foundation and The Rockefeller Foundation. The Wellcome Trust, the Program for Appropriate Technology in Health (PATH), the United Nations Foundation Inc., and the Joint United Nations Programme on HIV/AIDS (UNAIDS) also contributed.

In order to strengthen its financial position and to expand into new and emerging areas of research in human reproduction, HRP is working actively to maintain its existing sources of income as well as to seek new ones.

Figure I.1 HRP income, 1996-2003

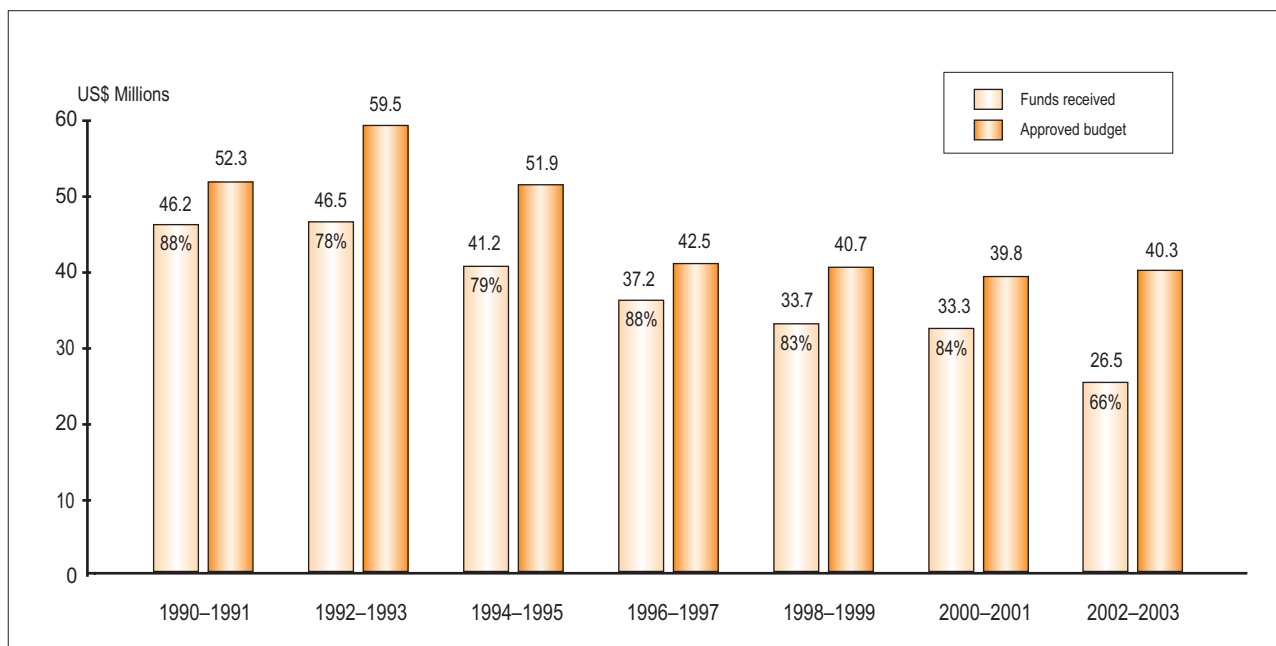


Table I.1 HRP income, 1987–2003 ⁽¹⁾ (US\$000)

Source	1970-1997	1998	1999	2000	2001	2002	2003	Grand Total
HRP Cosponsors⁽²⁾ and other UN system agencies								
Joint United Nations Programme on HIV/AIDS	-	12	-	405	150	338	338	1,243
United Nations Development Programme	1,695	-	-	-	-	-	-	1,695
United Nations Population Fund	55,040	3,000	3,000	1,000	2,000	2,653	228	66,921
United Nations Foundation for International Partnerships	-	-	131	105	89	-	-	325
The World Bank	24,258	2,500	2,250	2,000	2,000	1,000	2,000	36,008
World Health Organization ⁽³⁾	14,476	725	513	1,240	66	1,023	130	18,173
<i>Subtotal Cosponsors and other UN system agencies</i>	<i>95,469</i>	<i>6,237</i>	<i>5,894</i>	<i>4,750</i>	<i>4,305</i>	<i>5,014</i>	<i>2,696</i>	<i>124,365</i>
National governments								
Argentina	45	-	-	-	-	-	-	45
Australia	4,109	-	-	-	-	-	-	4,109
Bangladesh	5	-	-	-	-	-	-	5
Belgium	-	-	-	-	-	-	238	238
Canada	9,829	282	265	270	253	283	288	11,470
Chile	35	-	-	-	-	-	-	35
China	820	55	55	-	110	-	110	1,150
Cuba	25	-	-	-	-	-	-	25
Denmark	29,515	-	-	-	-	-	-	29,515
Finland	3,198	151	-	-	-	-	-	3,349
France	7	-	-	-	-	-	-	7
Germany	15,327	691	519	199	258	25	-	17,019
India	729	-	35	35	35	35	35	904
Italy	655	-	-	-	-	-	-	655
Japan	300	-	-	-	-	-	-	300
Kenya	1	-	-	-	-	-	-	1
Malaysia	1	-	-	-	-	-	-	1
Mexico	98	3	4	3	4	3	3	118
Netherlands	6,291	538	1,888	1,724	1,726	1,665	2,199	16,031
New Zealand	27	-	-	-	-	-	-	27
Nigeria	60	-	-	-	-	-	-	60
Norway	45,864	1,475	1,394	1,228	1,237	1,452	1,497	54,147
Pakistan	5	-	-	-	-	-	-	5
Russian Federation	99	-	-	-	-	-	-	99
Spain	-	-	20	-	20	22	-	62
Sweden	93,742	1,282	1,180	1,057	1,028	1,209	1,751	101,249
Switzerland	2,907	177	163	146	155	-	372	3,920
Thailand	159	40	19	-	-	-	75	293
United Kingdom ⁽⁴⁾	68,538	2,353	1,587	1,089	-	857	-	74,424
United States of America	15,221	2,000	2,250	2,250	2,750	-	-	24,471
<i>Subtotal national governments</i>	<i>297,612</i>	<i>9,047</i>	<i>9,379</i>	<i>8,001</i>	<i>7,576</i>	<i>5,551</i>	<i>6,568</i>	<i>343,734</i>
Foundations and other sources								
Commission of the European Communities	-	-	-	-	-	-	571	571
Contraceptive Research and Development Program	-	-	28	-	-	-	-	28
Family Health International	205	-	-	-	-	-	-	205
Ford Foundation	1,084	78	-	-	230	-	150	1,542
Bill & Melinda Gates Foundation	-	-	2,000	2,000	2,000	2,000	2,000	10,000
William and Flora Hewlett Foundation	-	-	150	-	150	150	-	450
International Development Research Centre	716	-	-	-	-	-	-	716
The John D. and Catherine T. MacArthur Foundation	-	15	-	30	20	250	-	315
The Andrew W. Mellon Foundation	360	-	-	-	-	-	-	360
Ortho-McNeil Pharmaceutical, Inc.	-	-	5	-	-	-	-	5
The David and Lucile Packard Foundation	20	-	20	2,020	-	-	-	2,060
Program for Appropriate Technology in Health	156	-	27	5	-	-	76	264
Reproductive Health Alliance Europe	-	-	-	41	-	-	-	41
The Rockefeller Foundation	3,518	20	143	220	-	36	50	3,987
The Wellcome Trust	21	18	-	-	25	-	-	64
Miscellaneous income	185	4	31	113	2	32	-	367
WHO Special Account for Servicing Costs	999	93	93	-	-	-	-	1,185
Royalties and licensing fees	225	243	271	354	511	422	97	2,123
Interest and adjustments ⁽⁵⁾	13,165	137	160	434	478	567	221	15,162
<i>Subtotal foundations and other income</i>	<i>20,654</i>	<i>608</i>	<i>2,928</i>	<i>5,217</i>	<i>3,416</i>	<i>3,457</i>	<i>3,165</i>	<i>39,445</i>
Grand Total	413,735	15,892	18,201	17,968	15,297	14,022	12,429	507,544

Notes

(1) Source: WHO accounting database.

(2) UNDP, UNFPA, WHO and The World Bank are the Cosponsors of HRP.

(3) The WHO Regular Budget income figure shown for 2002 is the amount allotted for the biennium 2002–2003. An additional \$130,000 was allotted in 2003.

(4) The contribution from the United Kingdom for 2001 of \$453,153, which was received in December 2001, was recorded in January 2002.

(5) Interest earnings for the biennium 2002–2003 totalled \$788,060, of which 2002 totalled \$567,240

Annex II

Centres collaborating with HRP in 2002–2003¹

WHO African Region

Benin

Centre for Research in Human Reproduction and Demography (CERRHUD),
Cotonou

Cameroon

Institute for Training and Research in Demography (IFORD), University of
Yaoundé, Yaoundé

Côte d'Ivoire

Reproductive Health Research Unit (CRESAR), Abidjan

Ethiopia

Addis Ababa University, Addis Ababa

Republic of Guinea

Reproductive Health Research Unit (CERREGUI), Conakry

Kenya

International Centre for Reproductive Health, Mombasa
African Population and Health Research Centre, Nairobi
Institute of Primate Research, Nairobi

Mali

Reproductive Health Research Unit (CRESAR), Bamako

Nigeria

University of Ibadan, Ibadan,
Teaching Hospital, Ogun State University, Sagamu

Senegal

Centre for Research and Training in Reproductive Health (CEFOREP), Dakar

South Africa

Reproductive Health Research Unit, Addington Hospital, Durban
Chris Hani Baragwanath Hospital, Johannesburg
National Health and Laboratory Service, University of Witwatersrand,
Johannesburg
University of Witwatersrand Coronation Hospital, Johannesburg

Uganda

Makerere University, Kampala

United Republic of Tanzania

Kilimanjaro Christian Medical Centre, Tumaini University, Moshi

Zimbabwe

University of Zimbabwe, Harare

WHO Region of the Americas

Argentina

Centre for Studies of the State and Society (CEDES), Buenos Aires
Centre for Population Studies (CENEP), Buenos Aires
Institute of Biology and Experimental Medicine, Buenos Aires
Rosario Centre for Perinatal Studies (CREP), National University of Rosario,
Rosario

Brazil

Campinas Research Centre for the Control of Maternal and Childhood Diseases
(CEMICAMP), Campinas
Institute of Collective Health (ISC), Federal University of Bahia, Salvador
Federal University of Juiz de Fora, Juiz de Fora

Chile

Catholic University of Chile, Santiago
Chilean Institute of Reproductive Medicine (ICMER), Santiago
Unit of Clinical and Epidemiological Investigation in Human Reproduction
(UNICEHR), Santiago
University of Chile, Santiago

Colombia

Foundation for Higher Education, Cali
SISMA - MUJER, Bogota

Cuba

National Institute of Endocrinology, "Cmdte. Fajardo" Hospital, Havana

Dominican Republic

Dominican Association for Family Welfare Inc., Profamilia, Santo Domingo

Guatemala

Epidemiologic Research Center in Sexual and Reproductive Health, "San Juan
de Dios" General Hospital, Guatemala City

Mexico

National Institute of Nutrition, Mexico City
National Institute of Public Health, Cuernavaca, Morelos

Panama

Centre for Research in Human Reproduction, Panama

¹ This list includes institutions with which the Programme entered into a technical services agreement, either for the conduct of research or for training activities.

Peru

National Research Institute, Lima

United States of America

The Ohio State University Research Foundation, Columbus, OH
Reproductive Health Technologies Inc., Galveston, TX
University of Texas, Galveston, TX

WHO Eastern Mediterranean Region

Egypt

Assiut University Hospital, Assiut
Egyptian Fertility Care Society, Cairo

Sudan

University of Khartoum, Khartoum

Tunisia

National Office for Family and Population, Tunis

WHO European Region

Armenia

Armenian Research Centre of Maternal and Child Health Protection, Yerevan

Georgia

Zhordania Institute of Human Reproduction, Tbilisi

Germany

Institute of Reproductive Medicine, University of Munster, Munster

Hungary

University Medical School of Debrecen, Debrecen
Albert Szent-Gyorgy Medical University, Szeged
University Medical School, Szeged

Italy

University of Bologna, Bologna

Latvia

Latvian Association for Family Planning and Sexual Health, Riga

Lithuania

Public Hospital of Panevezys, Panevezys

Poland

Institute of Philosophy and Sociology of the Polish Academy of Sciences (IFIS/PAN), Warsaw

Romania

East European Institute of Reproductive Health, Targu-Mures

Slovenia

University Medical Centre, Ljubljana

Turkey

Hacettepe University, Ankara
University of Istanbul, Istanbul

United Kingdom

Institute of Health Sciences, Magpie Trial Coordinating Centre, Headington
London School of Hygiene and Tropical Medicine, London
Institute of Cancer Research, Royal Cancer Hospital, Sutton

WHO South-East Asia Region

Bangladesh

Bangladesh Institute of Research for Promotion of Essential and Reproductive Health and Technologies, Dhaka

India

The Sangath Society for Child Development and Family Guidance, Goa
Government Medical College, Nagpur
All India Institute of Medical Sciences, New Delhi
MAMTA Health Institute for Mother and Child, New Delhi
S.A.T. Hospital, Trivandrum
Christian Medical College, Vellore

Indonesia

Airlangga University, Surabaya
National Family Planning Coordinating Board (BKKBN), Jakarta
Andalas University, Padang
West Indonesian Reproductive Health Development Centre (WIRHDC), Medan

Sri Lanka

University of Kelaniya, Ragama

Thailand

Chulalongkorn University, Bangkok
Siriraj Hospital, Bangkok
Chiang Mai University, Chiang Mai
Khon Kaen University, Khon Kaen
Mahidol University, Nakhon Pathom

WHO Region of the Western Pacific

Australia

Prince Henry's Institute of Medical Research, Clayton
University of Newcastle, Callaghan

China

Beijing Obstetrics and Gynaecology Hospital, Beijing
National Research Institute for Family Planning, Beijing
Peking University, Beijing
National Population and Family Planning Commission, Beijing
Family Planning Research Institute of Sichuan, Chengdu
University of Hong Kong, Hong Kong
Institute of Medical Biology, Chinese Academy of Sciences, Kunming
Jiangsu Family Health Institute, Nanjing
International Peace Maternity and Child Health Hospital (IPMCH), Shanghai
Renji Hospital, Shanghai Second Medical University, Shanghai
Shanghai Institute of Planned Parenthood Research, Shanghai
Shanghai Medical University, Zhong Shan Hospital, Shanghai
Tianjin Municipal Research Institute for Family Planning, Tianjin

Lao People's Democratic Republic

Ministry of Health Mother and Child Health Centre, Vientiane

Mongolia

State Research Centre for Maternal and Child Health and Human Reproduction, Ulaanbaatar

Myanmar

Ministry of Health, Yangon

Viet Nam

Hung Vuong Hospital, Ho Chi Minh City
Tu Du Hospital, Ho Chi Minh City
Institute for the Protection of the Mother and Newborn, Hanoi
Hanoi Obstetric and Gynaecology Hospital, Hanoi

Annex III

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Catherine Blanc, Secretary

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Margrit Kaufmann, Secretary

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Communication, Advocacy and Information Group

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