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Impact of HRP research in maternal and perinatal care: a case-study

Reviewer

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Executive summary

Background

The work of HRP on maternal and perinatal health between 2003 and 2007 included trials on the prevention and management of pre-eclampsia, an assessment of the maternal and neonatal consequences of female genital mutilation and scaling-up of a new approach to antenatal care. The last activity – the WHO antenatal care model for translating evidence-based interventions into policy and practice – combined work on best practices, safe motherhood and control of sexually transmitted infections, and is relevant for low-income countries in which maternal health must be improved [Millennium Development Goal 5 (MDG5)].

Methods

Publications, technical reports, 'grey' literature and a site visit to Thailand provided the basis for evaluating the new approach in operation. Meetings with policy-makers, health-care providers and mothers and an e-mail questionnaire to elicit expert opinion provided information on experiences, potential barriers and facilitators of use of the model.

Findings

Process

Between 1991 and 1998, HRP designed an evidence-based antenatal care model for low-risk women, which was integrated into a four-visit programme of screening, intervention and health promotion for delivery at the first visit and at 26, 32 and 38 weeks. A cluster – randomized trial was conducted to compare the clinical effectiveness and cost–effectiveness of the model with that of the commonly used standard model in Argentina, Cuba, Saudi Arabia and Thailand. On the basis of the results, published in 2001, HRP's maternal and perinatal health team of four persons supported a scaled-up approach in Khon Kaen Province, Thailand, between 2003 and 2006 by helping to prepare training material (WHO 2002a) and e-learning tools and by sponsoring training workshops.

Outputs

The new model was equivalent to the standard model in terms of perinatal outcome. Intervention clinics achieved more effective treatment of syphilis and a significant reduction in the number of visits (median, five versus nine). In a low-risk population, participating women had a higher rate of pre-eclampsia (prevalence, < 2%; odds ratio, 1.26; 95% confidence interval: 1.02–1.56) out of three maternal outcomes (pre-eclampsia/eclampsia, postpartum anaemia and urinary-tract infection); however, there was no difference in complication rates.

Policy and programme outcomes and collaborative arrangements

Thai Government support for research on public policy results in collaboration between academia and the State and creates an atmosphere receptive to evidence-based interventions. The provincial team modified the model to address psychosocial and logistical concerns and inefficiencies in the health promotion component. During the transformation, stakeholders (the public and health-care providers) were informed by various media about the new approach. Deficiencies in skills were addressed, and facilities were equipped to deliver new services. The programme will be extended to five additional provinces in 2008, to reach 12% of the population.

The study team from Centro Rosarino de Estudios Perinatales (CREP) – a WHO collaborating centre in Argentina – introduced the new model elsewhere

in Argentina and in Yap State, Federated States of Micronesia. The United States Agency for International Development promoted the model as 'focused antenatal care' in Ghana, Kenya and South Africa. The model is also in use in the United Republic of Tanzania and Zimbabwe. In 2007, HRP modified the model for the African setting, adding new components on the prevention of HIV infection and violence.

Cost-effectiveness and expected annual global benefits

The four-visit model is less expensive than the commonly used standard model, even with an additional visit. Women attending clinics under the new model spent less time and money for antenatal care, and the health-sector costs per pregnancy were lower. Globally, US$ 16.4 billion dollars could be saved annually by switching to the four-visit antenatal care model, including US$ 5.4 billion in countries with medium (50–500/100 000) and high (> 500/100 000) maternal mortality ratios.

Impact

Stanton et al. (2007) reported that, in Africa and Asia, antenatal care increases the rate of births with a skilled attendant, from 13% to 45% for women who make two or three visits to 73% for those who make four or more visits. The availability of high-quality antenatal care may encourage women to attend the recommended four visits and help increase skilled attendance, with the long-term potential of significantly reducing both maternal and perinatal mortality.

Conclusions

Strengths

HRP research has set the global standard for antenatal care. The framework for monitoring attainment of MDG5 now includes the HRP recommendation of using the proportion of pregnant women worldwide who attend for four antenatal visits as an indicator of antenatal care use.

The model should be seen as a blueprint, to be adapted to the local context and updated as new evidence becomes available. Its robustness is demonstrated by its capacity to yield equivalent results in four different developing country settings, whether delivered by midwives, general practitioners or obstetricians. It has also performed well in Africa, where antenatal care attendance has usually been less prevalent compared with other parts of the world.

Cost-effective interventions can be designed systematically and implemented on a wide scale, resulting in savings for both individuals and the health sector without compromising outcomes and at the same time, improving care, as health-care providers have more time to spend with women. A political environment receptive to evidence-based approaches eases the transition from research to practice. Leadership is critical, as an active change agent will be more effective in bringing new evidence into policy and practice.

Weaknesses

This new approach will require modification of basic obstetric and midwifery training programmes. Concern that too few visits during the third trimester could result in under-diagnosis of pre-eclampsia must be addressed, as this condition is a significant risk factor for maternal and perinatal morbidity and mortality, especially in countries with few resources.

Recommendations

As the HRP maternal and perinatal health team consists of only four persons, HRP should use collaborating centres, institutions and networks of health-care professionals to share its experience more widely, e.g. by sponsoring regional meetings and attendance at professional meetings. By working with local champions, HRP could more effectively reach policy-makers and health authorities to increase use of the model.

Future work

HRP could evaluate the impact of the new approach on health systems, especially in countries with few resources, where demand for maternal health care may increase. It could also design and test strategies for health promotion and behaviour change and draw up guidelines for women at high risk attending clinics as outpatients.

1. Introduction

1.1 Antenatal care: rationale and use

Antenatal care evolved as a model of preventive care, involving identifying and addressing health conditions in the mother or fetus that might threaten the pregnancy outcome, while preparing mothers for their parental role (Villar, Bergsjo, 1997). The expected benefits include greater awareness and positive health behaviour, especially with regard to infant health care, nutrition, immunization, family planning, control of sexually transmitted infections and use of skilled care at delivery for reducing maternal mortality (Stanton et al., 2007).

Utilization rates vary from almost universal coverage in developed regions to one in three mothers in least developed countries (HRP, 2007). Care can range from routine primary care to screening and intensive life-support during pregnancy up to delivery. Primary and first referral level care should be available to all pregnant women, including those referred due to complications of pregnancy (Carroli et al., 2001a).

Experts have reported (e.g. Lindmark, Cnattingius, 1991; Rosen et al., 1991) that antenatal care procedures and examinations have been accepted as standard practice without rigorous evaluation to determine their effectiveness in improving pregnancy outcome. The areas that require evaluation include the content, number and timing of visits and how the needs of women with different medical and social risks should be addressed (Villar et al., 1998).

Evaluation of the effectiveness of antenatal care requires large sample sizes, as the primary outcomes – maternal or perinatal death – are relatively rare events, even in developing countries. A valid, cost-effective model of antenatal care that is applicable in a wide range of sociodemographic settings would be a global public good.

1.2 Why did HRP become active in this field?

The mandate of HRP is to conduct or promote research on important questions in sexual and reproductive health. By being sited within a respected international body and due to the scope of the work of WHO in the field of health, HRP is ideally suited to tackle unresolved topics affecting large sections of the global population, which might not be initiated by institutions or countries.

The evaluation of HRP in 2002 identified several priorities for future research: adolescent reproductive health, preventing unsafe abortion, reproductive tract infections and sexually transmitted infections, best practices and safe motherhood. The means identified by WHO for improving the efficacy of antenatal care were: rationalizing the rituals of antenatal care, using antenatal care as a platform for other interventions, establishing more effective communication with women and avoiding over-medicalization (WHO, 2006).

HRP is uniquely qualified to evaluate routine antenatal care owing to its capacity to mobilize the human, technical and financial resources necessary for a large, multi-disciplinary study in many geographical areas.

1.3 Inclusion of this topic in the evaluation

The objectives of HRP's programme of work for improving maternal and perinatal health in 2006–2007 included (WHO 2005):

1. generating evidence of the effectiveness of interventions;

2. elucidating the etiology and pathophysiology of the main causes of adverse pregnancy outcomes and preterm delivery;

3. summarizing epidemiological evidence and evidence for effective interventions; and

4. monitoring the situation of maternal and perinatal health worldwide.

In evaluating the work of HRP, it was decided to focus on a selected number of global public goods that lend themselves to in-depth analysis of inputs, outputs, outcomes and, where possible, the impact on sexual and reproductive health and their contribution to achieving the MDGs, including poverty alleviation. HRP supported work in the field of maternal and perinatal health over the review period by:

- demonstrating the effectiveness of magnesium sulfate for the treatment (the eclampsia trial) and prevention (the MAGPIE trial) of eclampsia;

- evaluating calcium supplementation for prevention of pre-eclampsia in populations with inadequate dietary calcium intake;

- assessing the adverse impact of female genital mutilation on maternal and infant health outcomes; and

- formulating a rational approach to antenatal care, assessment of obstetric outcomes, acceptability by clients and providers, and cost.

The WHO antenatal care randomized trial combines investigations of best practices and safe motherhood, including control of sexually transmitted infections, and addressed objective 1 above in its initial conception and objectives 2 and 3 in follow-up activities supported by HRP since 2001. This intervention is of particular relevance to low-income countries where the quality of health care needs to be improved generally and maternal health care specifically, taking into account the funding required for social and economic development.

Given the public health importance of antenatal care and its relevance to achieving MDG4 and MDG5, the project provides tangible evidence of HRP's ability to provide a global public good, in the form of sexual and reproductive health research and capacity strengthening at country level, including attention to the cost-efficiency of the proposed strategies.

1.4 Method of evaluation

Data were collected at interviews with informants and clients, by observation of provider–client interactions and by reviews of peer-reviewed and 'grey' literature, including *The Reproductive Health Library* (WHO), the Cochrane Collaboration and the Internet. A site visit to Thailand made it possible to observe the transformation of research into practice by in-depth interviews with the principal investigator, personnel at the Ministry of Public Health and the Royal Thai College of Obstetricians and Gynaecologists and mothers, to document their experiences, satisfaction and concerns. International experts were canvassed by electronic mail to solicit their views on barriers to more widespread use of the model and how the Department of Reproductive Health and Research (RHR) could facilitate its use. The experts included researchers, project development experts and providers of 'Safe Motherhood' care at national and district levels in Belgium, Benin, Burkina Faso, Côte d'Ivoire, Jamaica, Mauritania, Morocco, Senegal, South Africa and the United Kingdom (see Annex 1).

2. Findings

2.1 Process

In November 1991, a randomized controlled trial was undertaken to evaluate the goal-oriented, evidence-based model of antenatal care. Five sites in Latin America, the Caribbean, Asia and sub-Saharan Africa were chosen; however, the site in Africa was excluded after a pilot study in 1996 showed a high rate of loss to follow-up at delivery. The four countries finally selected were Argentina, Chile, Saudi Arabia and Thailand; the first woman was enrolled in Thailand in May 1996 and the last in Argentina in April 1998. In May 2001, ten years after the project's conception, the findings were published in *The Lancet* (Villar et al., 2001a), with an updated systematic review of trials aimed at reducing the number of antenatal visits (Carroli et al., 2001b). The main steps are outlined below.

2.1.1 Systematic review of what works in antenatal care

The HRP team conducted systematic reviews mainly of randomized controlled trials of antenatal care to identify services that affect maternal (Villar, Bergsjo, 1997) and perinatal outcomes (Bergsjo, Villar, 1997), either positively or negatively. The strategies fell into four categories: process of care, screening, prophylaxis and disease treatment.

Important *processes of care* included risk scoring (to refer women selectively for a higher level of care), pelvic assessment for infection and cervical cancer, fundal height measurement to screen for growth retardation and external version for breech presentation. Fewer routine visits for low-risk women did not place their pregnancies at greater risk but might have lessened patient satisfaction.

Screening for urinary tract and sexually transmitted infections and pre-eclampsia reduced long-term morbidity, such as pyelonephritis.

Important *prophylactic interventions* included tetanus immunization and supplementation with iron and folate.

Treatment of medical conditions such as tuberculosis and malaria, identification of HIV-positive women for treatment and prevention of mother-to-child transmission of HIV, and protein–energy supplementation for severely undernourished women improved maternal and perinatal health.

A package of four evidence-based, goal-oriented visits was designed for delivery in the first trimester (preferably at or before 12 weeks) and at 26, 32 and 38 weeks. Women who did not deliver by 41 weeks of gestation were to be evaluated for possible induction of labour. A postpartum visit at the end of the first week (day 7) was also envisaged.

2.1.2 Eligibility criteria

Clear rules were established for the eligibility of countries and sites to participate (Piaggio et al., 1998). These included a well-defined antenatal care programme, a system for referring high-risk women to tertiary care, a perinatal data collection system capable of providing reliable data on primary maternal and neonatal outcomes and a regional epidemiological research unit with field experience in multicentre studies. HRP required written evidence that the programme was acceptable to local authorities and physicians and that the government would allow transmission of data to WHO headquarters for analysis.

Participating clinics (Donner et al., 1998) had to belong to a non fee-for-service public or semi-public antenatal care system that covered the same geographical area but served distinct neighbourhoods. Each site had to be able to recruit at least 300 new patients within 24 months,

have the capacity to trace all women at delivery and have sufficient staff to care for the patients, implement the new tests or activities required by the protocol and fund the new activities.

2.1.3 Ethics

The trial was approved by HRP's Scientific and Ethical Review Group and included two types of ethical consent: institutional consent before randomization by the institutional review boards of the selected health facilities and informed consent, but only from women in the intervention arm. The refusal rate was 1.3% (Piaggio et al., 2001).

2.1.4 Data and safety monitoring

A three-member committee for monitoring data and safety had adequate means to review the logistics, compliance with the protocol, efficacy, safety and other ethical issues (Bergsjø et al., 1998). The committee received monthly reports from each site of recruitment and risk factors in each arm and a list and individual case reports of maternal deaths, fetal deaths and cases of eclampsia.

2.1.5 Hypothesis and intervention

The hypothesis tested was that, among women with singleton pregnancies, the new antenatal care model was equivalent to the commonly used standard model of antenatal care with respect to the proportion of infants of low birth weight (< 2500 g) and women with severe maternal morbidity, and was not more expensive. The outcomes were surrogate measures of perinatal and maternal mortality, respectively, which would have required large samples if they had been used as primary outcomes.

The control clinics followed their exisiting guidelines. Ideally, a woman who attended a clinic early in pregnancy would make 12 visits. The routine included clinical activities, urine tests, screening for syphilis, haemoglobin measurement and blood group typing.

Women attending the intervention clinics were screened on the basis of predetermined risk criteria (WHO, 2002b). Women who gave a positive response to any question were classified as requiring further assessment or special care and were not eligible for the basic component of the new model; these high-risk women received care consistent with their condition. Low-risk women were invited to join the new programme. Those who refused to participate received care according to standard pre-trial procedures but were counted in the intention-to-treat analysis as having been assigned to the new model. Women who agreed to participate received a basic programme of activitites at four antenatal visits.

2.2 Inputs

2.2.1 Human resources

HRP brought together a large multidisciplinary team of investigators in statistics, economics, medicine and the social sciences. Six technical working groups were established (Villar et al., 2001a): the trial coordinating unit (head: J. Villar; five persons), the data coordinating unit (head: G. Piaggio; four persons), a health economics group (head: M. Mugford; three persons); a quality of care group (head: A. Langer; five persons), a data and safety monitoring group (head: P. Bergsjo; six persons) and the steering committee, which included country coordinators (chair: J. Villar; 12 persons).

Efforts were made to ensure that the trial had adequate power to test the study hypothesis. Academic discussions (Donner, 1998; Donner et al., 1998) on sample size calculation and data analysis were well documented and published (Annex 2).

The participating institutions assembled a team of 233 persons, including five country data coordinators and four field coordinators (country principal investigator in brackets), as follows:

- Centro Rosarino de Estudios Perinatales (CREP), Rosario, Argentina, 123 persons (J.M. Belizan)
- America Arias Hospital, Havana, Cuba, 36 persons (U. Farnot)
- King Abdulaziz University and Ministry of Health, Jeddah, Saudi Arabia, 30 persons (Y. Al-Mazrou)
- Faculty of Medicine, Khon Kaen University, Provincial Health Office and Health Promotion Centre, Khon Kaen Region, Thailand, 44 persons (P. Lumbiganon).

The principal health-care provider in Argentina was an obstetrician, those in Cuba and Saudi Arabia were general practitioners, and that in Thailand was a midwife. Obstetric specialists were available on site in Argentina and Cuba and at referral hospitals in Saudi Arabia and Thailand. A physician was available at all sites.

2.2.2 *Contributions of stakeholders*

HRP mobilized US$ 2.5 million dollars for the three-year research programme. The stakeholders that provided additional financial and human resources, facilities and equipment included: Municipal Government, City of Rosario, Argentina; Ministry of Health, Cuba; National Institute of Public Health, Mexico; The Population Council–Regional Office for Latin America and the Caribbean; Ministry of Health, Saudi Arabia; Swedish Agency for Research Cooperation with Developing Countries; Ministry of Public Health and Faculty of Medicine, Khon Kaen University, Thailand; Department for International Development, United Kingdom; Mother Care–John Snow Inc.; National Institute for Child Health and Human Development, National Institutes of Health (USA), and the World Bank. The following institutions supported the initial phase: University of Western Ontario, Department of Epidemiology and Biostatistics, Canada; National Institute of Public Health, Norway; University of Uppsala, Department of Obstetrics and Gynaecology, Sweden; and the United Nations Development Programme.

2.2.3 *Participating institutions and women recruited*

The trial was completed by 53 clinics (27 with the new antenatal care model, 26 with the standard model), recruiting 24 526 of the 24 678 women attending for antenatal care for the first time (12 568 new model, 11 958 standard model). After exclusion of abortions, multiple births and women lost to follow-up, data were available for analysis on 22 793 singleton births (11 672 new model, 11 121 standard model) (Villar et al., 2001a).

Piaggio et al. (1998) reported that the clinics were well equipped (sphygmomanometers, weighing scales, vaginal specula, fetal stethoscope, ultrasound) to provide the necessary services and conduct laboratory investigations. Some resources, such as urine dipsticks and iron and folate tablets, were supplied to ensure implementation of the new procedures. In order to standardize the intervention, all study sites were provided with a *Manual of clinical activities* translated into the local language.

2.3 Outputs

2.3.1 Local and regional outputs

The principal investigators in each country trained research teams, monitored implementation, presented findings at local meetings and wrote papers for national journals. The local meetings led to a decision to implement the findings in health facilities in Khon Kaen Province, Thailand (where the trial was conducted); Corrientes Province, Argentina (a province not initially associated with the trial); Yap State, Federated States of Micronesia (supported by HRP through the team at the Centro Rosarino de Estudios Perinatales, Argentina). The Ministry of Public Health, Thailand, will extend the project to five additional provinces in 2008, to cover 12% of the Thai population as part of a commitment to scale up the intervention nationally.

HRP supported implementation in Khon Kaen Province and the expansion of the new model in Thailand by facilitating production of a Thai version of the WHO *Antenatal care manual*, assisting in workshops to train staff in pelvic assessment (the most critical skill deficiency and a barrier to full implementation of the new approach), sponsoring use of electronic learning tools to re-train staff and supporting revision of these and other tools to assist national expansion through collaboration with Boston University and the Massachusetts Institute of Technology (USA).

2.3.2 International dissemination of data

The HRP team made significant efforts to document the research, from conception to findings (see Annex 2). Over 30 peer-reviewed publications and technical reports were published on conceptual issues and approaches, technical evidence, primary findings (Villar et al., 2001a) and secondary analyses of the data. A supplement of *Paediatric and Perinatal Epidemiology* in 1998 gave a comprehensive summary of methodological issues.

Other outputs at global level include:

- an updated meta-analysis of studies on reduced numbers of antenatal visits (Carroli et al., 2001b), which showed that fewer visits resulted in equivalent maternal and perinatal outcomes;
- an updated Cochrane Database of Systematic Reviews (2001) on routine care for low-risk women (see Villar et al., 2001b);
- a manual describing the trial (Villar et al., 2002), which can be downloaded free of charge from the WHO website;
- information in electronic form on compact disc, updated annually, in *The WHO Reproductive Health Library* and *The Cochrane Library* (*The WHO Reproductive Health Library* is disseminated free of charge to persons in developing countries); and
- publications on syphilis control (Lumbiganon et al., 2002), hypertensive disorders of pregnancy (Villar et al., 2006) and preterm birth (Villar et al., 2004).

2.3.3 Capacity-building

HRP's maternal and perinatal health team has been collaborating with Boston University to develop training materials not only for Thailand but for other research teams interested in implementing the WHO antenatal care model. The material includes a free, five-week Internet-based course (WHO, 2002b), set up in July 2005, for physicians and health planners. It describes the concepts

underlying the model, provides information about the randomized clinical trial and lists strategies for using the new model.

This course was revised for inclusion in the package for national implementation of the WHO antenatal care model in Thailand during 2008. It will target various audiences, including mid-level policy-makers responsible for organizing, changing and managing clinical systems and also obstetric care providers. This tool can also be used to adapt the model for use in other countries and includes new modules for dealing with complications during childbirth, such as eclampsia, bleeding in pregnancy and sepsis. Strategies are also included to assist professors who will monitor and mentor implementation in Thailand (personal communication, M. Merialdi, HRP).

Boston University, in collaboration with the Massachusetts Institute of Technology, will design a highly interactive, web-based pilot educational module for use in clinical and public-health training and for increasing awareness and encouraging action for improving sexual and reproductive health.

Investigators were invited to undertake secondary analyses of the data and write papers on topics of interest for publication. This contributed to building local capacity, as teams received guidance from the technical experts assembled by HRP (see Langer et al., 2002; Lumbiganon et al., 2002; Borghi et al., 2003; Nigenda et al., 2003; Lumbiganon et al., 2004).

2.3.4 Generation of new research questions

The trial and the meta-analysis suggested that the new model might increase the risk for undiagnosed pre-eclampsia by as much as 26%. The issue requires further examination. In settings with limited access to neonatal intensive care, this might increase perinatal and neonatal mortality. Guidelines for managing high-risk conditions might limit the risk for poor outcomes, especially in countries with limited resources, especially for tertiary care of high-risk newborns.

The experts considered that WHO or other bodies might explore and demonstrate the benefits of antenatal care (e.g. morbidity averted) quantitatively (by primary studies or modelling), to support and encourage changes in practice at policy and planning levels.

In December 2007, the maternal and perinatal health unit of HRP prepared a new intervention for three African countries in which antenatal care is used to integrate other services, such as prevention and treatment of malaria and counselling and testing for HIV (see 2.4.4).

2.4 Outcomes

2.4.1 Developments in trial countries: Thailand

An enabling environment

The Thai Govermment officially supports research for health policy formulation and programme implementation. Reform of the health system created opportunities for community participation in the administration of Government hospitals. This policy in turn creates a climate conducive to research into health systems, with benefits both domestically and internationally. This attitude made local health teams willing to collaborate and cooperate in research and to respond to the evidence, for transforming research into practice. Health teams reported that policy support, regular meetings to clarify and resolve problems in

implementation and feedback on progress helped smooth the transition.

Implementation strategy: from research to scale-up phase

HRP supported the scaling-up of the antenatal care model in Thailand by sponsoring four workshops for 155 health professionals. By May 2004, the model had been used in 24 hospitals. As primary care facilities are the responsibility of local government and not of the Ministry of Public Health, training has not yet been extended to primary care personnel.

The model was modified in accordance with local epidemiology (e.g. screening for thalassaemia) and evidence from the trial (re-screening for sexually transmitted infections during the third trimester) and included psychosocial factors (a visit added at 20 weeks, delaying of pelvic assessment beyond the first trimester) (see Annex 3). The Thai model now includes a minimum of six visits for women presenting in the first trimester. The value of the approach is that decisions about antenatal care practices are now based on evidence.

Behaviour change

To encourage behaviour change, the Thai research team from the outset involved key players, including the policy directorate in the Ministry of Public Health, the main professional group, represented by the Royal Thai College of Obstetricians and Gynaecologists, local health teams, mothers and their families. Health-care providers and policy-makers were involved through meetings, publications in professional newsletters in Thai, seminars and training workshops. Families were informed about the new approach through the media and by community volunteers, who routinely encourage early attendance for antenatal care. In 2005, information was integrated into the maternal and child health booklet given to pregnant women. At group education sessions, women were told about the new strategy, its components and the services provided at each visit.

Uptake by the private sector

Some private practitioners fear that clients might blame them if complications arise after a reduced number of visits, as fewer visits are perceived as less care. In Thailand, private doctors who also work in the public sector were trained and shown the improved quality of care that the reduced visit schedule allows. They expressed willingness to modify their private practice. Health-care providers were less willing to discuss the impact of a reduced visit schedule on their income. One solution is to market antenatal care as a package of services instead of charging for each visit. The insurance industry could be encouraged to support the new approach for low-risk women.

National commitment to scaling-up and coverage

The Ministry of Public Health supported the antenatal care trial and its extension because of its cost-effectiveness and its consistency with their strategic plan for maternal and child health. Phased implementation in five additional provinces (Chiangrai, Lopburi, Nakorn-Srithamarat, Kalsin and Maha-Sarakham) will begin in 2008, which will make the new service available to 7.3 million of the 62.8 million (11.7%) Thai population. During this phase, the Government will conduct new costing studies to verify the cost-effectiveness of the intervention, before implementing it nationwide.

Sustainability of the new model will depend on integration of the new guidelines into practice throughout the health system. The Royal Thai College of Obstetricians and Gynaecologists endorsed the strategy and published Thai versions

of the trial findings and guidelines for the new strategy in their monthly newsletter. They have also agreed to integrate questions about the new approach into specialty board examinations. This support is critical; one local health team reported that endorsement by the College influenced their department's willingness to use the approach in their sub-district.

2.4.2 Developments in trial countries: Argentina

In August 2002, the principal investigator in Argentina, who heads a WHO reproductive health collaborating centre, presented the new model and trial results to health personnel in the City of Corrientes. Encouraged by the efficiency and effectiveness of the model, the Maternal and Child Health Department, Ministry of Public Health decided to implement the new antenatal care approach in Corrientes Province. A planning committee informed stakeholders, including the Government, hospital obstetric teams and primary care personnel, about the change in approach. Other strategies included publications in medical journals, presentations at meetings and congresses and a participatory approach in the design of norms and guidelines for the intervention. They also designed a referral system and a monitoring and evaluation system. They trained a team of trainers, who subsequently ran workshops for physicians, paramedics, social workers and administrative staff. A public education campaign launched the programme in March 2004.

2.4.3 Developments in a country not in the trial: Federated States of Micronesia

The WHO antenatal care model has been institutionalized in Yap State in the Federated States of Micronesia (10% of the 107 000 population), guided by the Centro Rosarino de Estudios Perinatales, Argentina, with HRP support. All personnel involved in antenatal and postpartum care followed an on-line training course designed by WHO. Forms and procedures were revised and quality standards were defined in keeping with the new model, and formal transition to the new model was completed in August 2007. As in Thailand and Argentina, the success of this project depended on the commitment of the health services. The experience is being shared with other States in Micronesia and other jurisdictions in the Pacific.

2.4.4 Plans for the maternal and perinatal health unit of HRP: southern Africa

In December 2007, the maternal and perinatal health team completed a proposal to integrate the WHO antenatal care model into a project in Malawi, Mozambique and South Africa. They will adapt the model to the needs in these countries after an initial assessment. Country-specific WHO models of routine antenatal care will include additional components on HIV, violence against women and updated components for malaria, congenital syphilis and anaemia. Addition of the HIV component is particularly important, as HIV-associated diseases are a major cause of maternal mortality in southern Africa.

2.4.5 Use of the WHO model by other countries and stakeholders

An adaptation of the WHO antenatal care model has been reported in Zimbabwe (Munjanja et al., 1996; Majoko et al., 2007), and plans for its use have been reported in the United Republic of Tanzania (von Both et al., 2006). The results also stimulated research and discussion of the evidence base and strategies used in antenatal care policies and services in developed countries, such as Australia (e.g. Hunt, Lumley, 2002).

The experts surveyed reported that, in 2004, the Federal Knowledge Centre for Health Services (Belgium) reviewed the evidence base in the literature, including the paper by Villar et al. in *The Lancet* in 2001, and redefined their standards for antenatal care for a normal pregnancy to 10 visits for primiparae and seven for multiparae. They reported use of the basic WHO antenatal care programme in Benin, Burkina Faso, Côte d'Ivoire, Mauritania, Morocco, Niger, Senegal and South Africa, ranging from pilot projects to national level. While the actual number of visits for a normal pregnancy was usually three or four, this rate was still below 70% in some settings.

USAID published a 'Global Technical Brief' (Stephenson, 2005) which endorsed the new model and provided standards and guidelines that can be adapted to local conditions, including training modules and curricula to update providers' knowledge and skills. The Agency has promoted the approach in projects in Ghana, Kenya and South Africa (Population Council, 2007). In adapting the model, they added an extra visit in all three settings and included screening, counselling and treatment for HIV and other sexually transmitted infections, treatment of malaria and individual birth plans (Chege et al., 2005; Birungi, Onyango-Ouma, 2006; Nyarko et al., 2006).

Villar (2003) reported that interest in the method had been expressed in Brazil, Chile, El Salvador, Ethiopia, Haiti, Oman, the Syrian Arab Republic and Zambia after the results were published in the scientific literature. WHO has not, however, sponsored training workshops in countries other than Argentina, the Federated States of Micronesia and Thailand. A proposed update of electronic learning tools will broaden access to material for self-instruction by local teams.

2.4.6 Universal access to sexual and reproductive health: setting global standards for achieving MDG5

The framework for monitoring attainment of MDG5 has accepted HRP's recommendation to include a new indicator of universal access to sexual and reproductive health, which measures and reports the proportion of the world's women who attend for four antenatal visits. This is direct evidence that the results of research conducted by HRP contribute to setting the global standard for antenatal care.

2.5 Impact

2.5.1 Global antenatal care coverage

By 2000, 68% of women worldwide were making at least one antenatal visit and 60% made four or more visits, an improvement from 45% in 1990 (Stanton et al., 2007). For countries with limited resources and for both developed and developing countries that face rising health-care costs, the results of the trial show that high standards and reduced costs to both the health system and women seeking care can be achieved and can further improve antenatal care coverage.

2.5.2 Primary health outcomes

No difference in perinatal outcome was seen during the trial. The statistically significantly increased likelihood of undiagnosed pre-eclampsia was not associated with more hospital admissions or complications (Table 1). The results for postpartum anaemia differed by site (heterogeneity), as iron and folate supplementation was not standard practice in Argentina. Significantly higher levels of supplementation achieved in clinics in which the new model was used (85.6% versus 63.8%) led to a lower rate of severe postpartum anaemia in Argentina (8.8% versus 13.3%) and the observed differences (7.6% versus 8.7%) seen in Table 1 for

the pooled data. These results validate universal iron supplementation in pregnancy (Villar et al., 2001a).

2.5.3 Secondary health outcomes

The only difference noted among the secondary outcomes for maternal and perinatal morbidity and mortality explored was that more women in the intervention arm were treated for syphilis [133/12 470 (1.1%) versus 83/11 799 (0.7%); $p = 0.03$], confirming the usefulness of introducing rapid testing for this disease, with immediate results and initiation of treatment. The standard practice required women to return for results at their next visit, delaying treatment.

In Thailand, rapid testing for syphilis was discontinued to accommodate other laboratory tests at the first visit (for HIV infection, thalassaemia and ABO and rhesus grouping). Their laboratory system provided results within 1 week, and women (and their partners) with positive findings returned to the health facility the following week. If this visit was missed, they were seen at the visit added at 20 weeks' gestation (Lumbiganon et al., 2002). In countries where this is not logistically feasible, rapid testing remains the gold standard. The trial showed an incidence of pregnancy-acquired syphilis of 0.4% among women who were not treated for syphilis during pregnancy and tested at delivery. This led to a recommendation to re-screen all women during the third trimester or at delivery, and this has been added to the revised Thai model. Health staff in Thailand reported that screening for cervical cancer and vaginal infection was appreciated by both the health team and mothers.

2.5.4 Contribution to MDGs: reducing infant and maternal mortality

Stanton et al. (2007) reported that in sub-Saharan Africa and south, south-eastern and western Asia, one antenatal visit is associated with a large rise in the proportion of women who deliver with a skilled

Table 1. Primary maternal and perinatal outcomes, all clinics

Indicator	New model	Standard model	Adjusted odds ratio (95% confidence interval)[a]
Infants			
Low birth weight	886/11 534 (7.7%)	788/11 040 (7.1%)	1.06 (0.97–1.15)
Mothers			
Pre-eclampsia/eclampsia	197/11 672 (1.7%)	153/11 121 (1.4%)	1.26 (1.02–1.56)
Postpartum anaemia	814/10 720 (7.6%)	871/10 050 (8.7%)	1.01[b]
Treated urinary-tract infection	695/11 672 (6.0%)	824/11 121 (7.4%)	0.93 (0.79–1.10)

Source: Villar et al. (2001a)

[a] Adjustment for variables that were significantly different at the start of the trial: smoking during pregnancy, education less than primary, hospital admission during the preceding pregnancy for hypertension or pre-eclampsia/eclampsia, gynaecological surgery before the index pregnancy, previous low-birth-weight infant, first-trimester vaginal bleeding, late booking (> 28 weeks), maternal age, nulliparity.

[b] Effect heterogeneous across sites and strata; confidence interval not shown as computational method assumes homogeneity.

birth attendant. The average proportion of births with a skilled attendant in 54 countries increased from 13% of women with no antenatal care to 28% of those with one visit, 45% of those with two or three visits and 73% among those making four or more visits. Encouraging women to attend for four visits, as suggested in the WHO model, might therefore increase skilled attendance at birth and reduce maternal and perinatal mortality significantly in the long term.

At the demonstration Maternal and Child Health Promotion Hospital in Khon Kaen, Thailand, the proportion of women making four or more visits increased, and the rates of perinatal mortality and low birth weight decreased. One explanation may be better management of asymptomatic bacteriuria, which would reduce the number of preterm births.

In Argentina, implementation of the antenatal care model in Corrientes Province (2.5% of Argentina's population) in 2003 was most successful in the City of Corrientes. Table 2 shows that infant and maternal health outcomes improved between 2002 and 2006, especially in the City of Corrientes, where the rates have dropped to those of the Province as a whole. Maternal mortality decreased from 110/100 000 in 2002 to 75/100 000 in 2006.

2.5.5 Potentially harmful impacts

Lower rates of diagnosis of pre-eclampsia

Trials of reduced numbers of antenatal care visits raise questions about whether standard antenatal care contributes to so-called white coat hypertension (increased blood pressure due to anxiety of seeking care), overdiagnosis during more visits, or, conversely, if under the new model with a reduced number of visits, genuine cases of pre-eclampsia are overlooked.

The finding of lower rates of eclampsia in Zimbabwe is encouraging (Majoko et al., 2007); however, the interval between 32 and 38 weeks might result in early cases being missed. In commenting on the trial in rural Zimbabwe, Gülmezoglu and Hofmeyr (2007) suggested that the persistent failure of reduced-visit trials to detect the onset of pre-eclampsia in time to prevent serious complications might indicate that other strategies are needed. Health promotion could be useful in this respect (MacGillivray et al., 2004).

2.5.6 Public good attributed to the work of HRP

Like Thailand, Ghana adopted the WHO focused antenatal care package in order to improve access to and the quality and continuity of antenatal care services to pregnant women (see Nyarko et al., 2006). The measures include exemption from fees for antenatal care, as such fees have been identified as a barrier to accessing services. The acceptance of the model in Ghana is probably related to its promotion by USAID and indicates that the model is assuming a life of its own, beyond the active involvement of HRP. Use of the model in the Federated States of Micronesia is an example of successful diffusion of the technique by distance learning.

2.6 Cost-effectiveness

2.6.1 Cost savings to beneficiaries and contribution to poverty reduction

The cost-effectiveness of the new antenatal care programme was evaluated by comparing it with existing, standard antenatal services (Mugford et al., 1998). The comparison included health-care costs incurred up to six weeks postpartum (antenatal care, inpatient care before, during and after delivery, and neonatal intensive care) and the

Table 2. Changes in infant mortality rates and maternal mortality ratio, Corrientes, Argentina, 2002 and 2006

Geographical area	Year	Outcome				
		Infant mortality	Early neonatal mortality	Late neonatal mortality	Postnatal mortality	Maternal mortality
Province	2002	23.7	13.4	3.5	6.8	110
	2006	17.1	9.9	2.9	4.4	75
Region	2002	25.9	16.1	4.2	5.7	
	2006	19.3	11.2	3.7	4.4	
Capital	2002	26.4	16.9	4.4	5.1	
	2006	18.1	10.4	3.5	4.2	
Argentina	2002	16.8				77
	2006	12.6				39

Sources: Pan American Health Organization (2002, 2007) and personal communication

cost of attending for antenatal care (e.g. transport, consultation and prescription costs, opportunity cost of time, lost income to women and persons accompanying them to the clinic). Costing studies were conducted prospectively during the trial in Cuba and Thailand, retrospectively in Argentina and by cost transfer and modelling in Saudi Arabia.

The time that women spent in accessing antenatal care and their out-of-pocket costs were significantly lower with the new model than in the standard clinics. Although there was little difference in the package of services provided to the two groups of women, except in Argentina where there was a difference in iron and folate supplementation (Villar et al., 2001a), the cost per pregnancy to the health sector was lower in the model facilities, mainly because of the reduced number of visits.

While 75% of women in the model clinics qualified for the basic four-visit programme, the 25% who required more care made a median of two additional visits. While no direct contribution to poverty reduction would be expected, personal and health-sector savings might be redistributed to other activities, such as nutrition or skilled care at delivery. As improved maternal heath is one of the MDGs, in countries where maternal mortality is high and effective maternal health service coverage is low, a more cost-effective model of maternal health service delivery will allow better coverage within a fixed budget.

The new model had three elements: screening, interventions to prevent or treat known conditions and health promotion. Relative success was found in achieving the first two goals, but the findings were paradoxical with regard to the third. While more women in the intervention arm were satisfied with the information provided, the contact time in the health promotion component of the new model, which was intended to increase from < 10 minutes to around 30 min, did not increase (Langer et al., 2002). This suggests that either the time taken to communicate the messages was significantly less than the initially estimated 15 minutes or this component was not delivered as intended. Villar et al. (2001a) suggested that the health promotion

component was the least likely to be adhered to in the new model.

When women and providers were questioned about receipt and delivery of health information, there were major divergences. Women in the intervention and control arms recognized 3.4 and 2.9 of six messages, respectively, while health-care providers said they were communicating 5.6 and 5.2 of the messages (Villar et al., 2001a). Thus, health-care providers were either delivering the messages ineffectively or not at all. As the results indicated that this component of care might have been unrealistic, it may have been abandoned by the providers.

During the trial, the median waiting time to see a doctor or midwife was shorter (30 min) for patients in the new model than those in the standard model (45 min); however, Langer et al. (2002) reported no difference in the median time spent with a health-care provider (15 min). In Thailand in 2007, the average contact time at first visit was about 1 hour, and that at subsequent visits was 20–25 min. Individual health promotion was found not to be feasible and was replaced by a mix of group sessions and individual counselling for persons with health or social problems. This increased the efficiency of the new approach while remaining true to the spirit of the model.

2.6.2 Global benefits of the new approach to antenatal care

A study was conducted of the potential global savings that would accrue if the new, efficacious, cost-effective approach to antenatal care were widely adopted. The basic approach and results are presented here, while the data sources and methods are given in Annex 4. The global costs of implementing the four-visit WHO model were compared with the global costs of implementing the standard antenatal care model. The costs were estimated by multiplying the global number of pregnancies by the cost per pregnancy in the four-visit model and in the standard model. Three types of costs were examined: medical costs, marginal medical costs and opportunity costs to the pregnant women. Medical costs are those incurred by the health system and out-of-pocket payments made by clients. As health systems are often rigid, not all medical costs can be assessed as suitable for cost-cutting. For example, medical personnel are frequently covered by strict civil service laws that do not allow re-posting or termination, and some health system expenditures are tied directly to individual patient care. The marginal costs include those for drugs and medical supplies, which can be reduced immediately when health practices are changed. Opportunity costs are those borne by women in obtaining services, such as the cost of transport and the value of their time spent obtaining services, including travel time, waiting time and time spent while services are rendered. Like marginal costs, reduced opportunity costs represent savings that can be immediately realized with a change in service delivery model. In a completely flexible health system, staff and facilities could be re-allocated immediately as priorities or approaches changed. Staff shown to be redundant or inappropriately skilled could be terminated or retrained and compensated according to their new rather than their old function.

Table 3 summarizes the per pregnancy costs extracted from the costing studies and from references in Annex 2. In all cases, the four-visit model was less expensive per pregnancy than the standard model. For example, in Thailand, if the health system were completely flexible, US$ 24 (reduction from US$ 127 to US$ 103) could be saved per pregnancy with the four-visit model.

As the health system is not completely flexible, marginal medical costs, a modest US$ 3.60 per pregnancy, are probably more representative of possible savings in the short run. The savings to clients were significant, however, at US$ 9.30. Out-of-pocket costs declined by US$ 4.00 per pregnancy, and opportunity costs were more than halved.

As the four-visit model was implemented in the field, adjustments were made, such as adding a further antenatal visit. Table 4 shows estimates for provider costs and marginal costs adjusted by adding the unit cost of a single antenatal visit, as calculated in the costing reports. Even with the additional visit, the cost was lower in all countries except Argentina, where, by this calculation, the marginal costs would exceed the standard antenatal care regime (US$ 132 vs US$ 128). A certainty, not calculated here, is that women's opportunity costs would increase due to travel expenses, waiting time and travel time associated with the additional visit.

The cost of the four-visit regime with an extra, fifth visit is probably overestimated, as the method of calculation did not correspond to the careful costing in the analyses. First, the marginal cost per antenatal visit should decrease with the extra visit (e.g. the cost of the two antenatal vaccines would be spread over five visits instead of four). The overall marginal costs per pregnancy might not fall, but the marginal cost per antenatal visit would be less than that calculated here. Secondly, the extra visit might avert a proportion of complications that would have resulted in expensive inpatient

Table 3. Average costs (2006 US$ value) per pregnancy with the four-visit and the standard model of antenatal care

Country	Average medical costs		Marginal medical costs		Average out-of-pocket costs		Average opportunity costs of time for woman	
	Four-visit	Standard	Four-visit	Standard	Four-visit	Standard	Four-visit	Standard
Argentina	1073.0	1118.9	122.0	128.1	0.0	0.0	10.4	13.9
Cuba	425.3	474.9	124.5	136.5	88.5	123.0	8.1	12.7
Saudi Arabia	3048.6	3778.0	762.1	944.5				
Thailand	102.7	126.9	24.2	27.8	7.4	11.4	9.2	18.5

Table 4. Average costs (2006 US$ value) per pregnancy and effect on cost of adding a further antenatal visit to the four-visit regime

Country	Four-visit regime with an additional antenatal visit		Four-visit regime		Standard antenatal care regime	
	Provider costs	Marginal costs	Provider costs	Marginal costs	Provider costs	Marginal costs
Argentina	1107.8	131.6	1073.0	122.0	1118.9	128.1
Cuba	440.1	130.1	425.3	124.5	474.9	136.5
Saudi Arabia	3536.3	884.1	3048.6	762.1	3778.0	944.5
Thailand	109.6	26.0	102.7	24.2	126.9	27.8

care, again reducing provider costs. In sum, we believe that an added visit would not negate the cost-effectiveness of the new approach.

Table 5 shows the potential global savings accrued by implementing the four-visit antenatal care regime as in the clinical trial. Different health systems have different cost profiles for delivery of services, and, in general, poorer countries can provide services more cheaply than wealthier countries; salaries are lower, facilities are less expensive to build, and pharmaceutical companies often sell medicines more cheaply in developing countries than in developed countries. The results of one of the four costing studies (in Argentina, Cuba, Saudi Arabia and Thailand) were assigned to each of 181 countries on the basis of per capita income and whether they had a socialized health system. Socialist and former socialist countries were assigned the costs associated with Cuba, and the other countries were assigned by per capita gross national income as evaluated by the World Bank in 2005. The results of the study in Thailand were assigned to countries with a gross national income per capita less than US$ 3000, those for Argentina were assigned to countries with an income between US$ 3000 and US$ 11 000, and those for Saudi Arabia were assigned to countries with an income above US$ 11 000.

In general, countries where maternal mortality is high have a less developed health infrastructure and poorer delivery of health services. The results in Table 5 are therefore disaggregated by level of maternal mortality in a given country, as follows:

- high: more than 500 maternal deaths per 100 000 live births;
- medium: 50–500 maternal deaths per 100 000 live births;
- low: 20–50 maternal deaths per 100 000 live births; and
- very low: fewer than 20 maternal deaths per 100 000 live births.

The costs in Table 5 are expenditures that would be incurred if all pregnant women followed the four-visit or the standard antenatal care regime. Globally, annual savings in medical costs could be more than US$ 16 billion. More than half of those savings would accrue to countries where maternal mortality is already very low. As most women

Table 5. Expected annual global benefits from implementing the new WHO approach to antenatal care

Country	Total medical costs[a] (billion 2006 US$ value)			Marginal costs (billion 2006 US$ value)			Opportunity costs, excluding high-income countries[b] (million 2006 US$ value)		
	Four-visit	Standard	Potential savings	Four-visit	Standard	Potential savings	Four-visit	Standard	Potential savings
All[c]	140.3	156.7	16.4	23.1	26.5	3.5			
High	4.1	5.2	1.0	0.9	1.0	0.1	336.4	674.2	337.8
Medium	67.6	72.0	4.4	8.7	9.5	0.8	674.8	957.4	282.6
Low	23.4	24.6	1.2	2.9	3.0	0.2			
Very low	40.3	49.9	9.6	10.1	12.4	2.4			

[a] Sum of provider costs and out-of-pocket costs.

[b] Calculated for countries with gross national income per capita less than US$ 11 000, from the World Bank in 2005.

[c] Does not correspond to the sum of categories, as estimates of maternal mortality were not available for several countries.

in such settings receive good antenatal care, there would be opportunities for saving money in the longer run. In the short run, entrenched practices and inertia due to inflexibility of staffing patterns and fear of litigation (fewer visits might be perceived as less care and blamed for poor outcomes) might mean that only a fraction of those savings are realized.

The data must be interpreted differently for countries with high and medium mortality rates. In these countries, the four-visit model would not replace standard antenatal care but would displace substandard or inexistent care. The costs in the table are better interpreted as the amount of money that should be spent rather than estimates of what is spent in countries with lower mortality rates. Not only marginal costs (drugs and medical supplies) but also wages and infrastructure, included in total medical costs, could be economized with implementation of the four-visit model. Flexibility of staffing and infrastructure are more likely to exist in countries with medium or high mortality rates than in those with lower rates. Exceptions exist, however, and degrees of flexibility vary. For example, India's rigid civil service rules and the endemic problem of health professionals not showing up at their posts create a very inflexible environment. In countries with insufficient numbers of health professionals, there is more flexibility.

In countries with higher maternal mortality rates, the difference in total medical costs is closer to the potential savings from using the four-visit model than in countries with low or very low rates. For example, the reduced personnel costs associated with the four-visit model could potentially be mobilized without eliminating or reassigning staff, in cases where staff are insufficient. The potential short-run savings to health systems in countries with medium and high mortality rates could approach US$ 5.4 billion (i.e. US$ 4.4 billion plus US$ 1.0 billion). For countries with low rates, the difference in marginal costs probably more closely represents money that could be saved in the short run. Table 5 shows that the differences in marginal costs in countries with low and very low mortality rate are considerable, at more than US$ 2.6 billion.

The final set of columns represents the opportunity costs to women for accessing antenatal care services. As in the costing study in Saudi Arabia the opportunity cost of time was not estimated, these costs were not estimated for countries with a per capita annual income greater than US$ 11 000. The opportunity costs of time are considerably less than the medical costs. The significant decrease in the number of visits also reduces a large proportion of the opportunity costs. In countries with high mortality rates, the reduction in opportunity costs exceeds the savings in marginal costs (US$ 337 million versus US$ 0.1 billion).

In summary, the four-visit model is less expensive than the standard model both for the health system and for women seeking care. All necessary expenditures would not be reduced immediately owing to rigidity in health systems. Globally, by reductions in marginal costs, US$ 3.5 billion dollars could be saved in the short run by switching to the four-visit model. As health systems are less expensive in poor countries, the saving in marginal costs would be only US$ 0.9 billion in countries with high and medium mortality rates. For the reasons discussed above, however, US$ 5.4 billion might be saved in total medical costs in countries with high and medium rates if they adopted this model instead of standard antenatal care.

3. Discussion

3.1 Research ethics

Use of personal information on women in the control arm without permission was considered acceptable, as the outcome data were to be used in the same way as they would be by clinical departments or health authorities in analysing information on risk outcome. This is not exactly the case, as the data were integrated into an international database, outside the health facility. While this practice is consistent with that in other randomized trials (Zelen, 1979), its use should be reviewed. If both groups are not equally informed, the potential for reporting bias due to a possible Hawthorne effect exists.

In North–South research relationships, limited access to technical support or resources (e.g. literature) and issues of co-authorship, particularly lead authorship in cases in which English is a second language for research partners, require attention to ensure that partners can produce articles that survive peer review. The solutions identified by Jentsch and Hussein (2007) include shared guidance of the article content among researchers for whom English is a second language so they can qualify as first author; and building the capacity of partners to become lead authors. The publications from the trial show that collaborators in all countries had the opportunity to be lead authors. Other HRP programmes, such as financing subscriptions of developing countries to the Health InterNetwork Access to Research Initiative (HINARI) web site (http://www.who.int/hinari), improve the access of researchers to published material at little or no cost.

3.2 Trial findings

3.2.1 Contact time

The failure of the trial to document a difference in the time spent with health-care providers suggests that some aspects of the new model, particularly the health promotion component, were not implemented as planned. A simulation by von Both et al. (2006) in the United Republic of Tanzania indicated that the contact time at first visits in the new model would increase from 15 minutes to 46 minutes and that at repeat visits from 9 to 36 minutes. This estimate is based on the time required for the health promotion component, which changed from 1.30 to 15 minutes for a first visit and from none to 15 minutes for repeat visits. In the Tanzanian trial, HIV screening and counselling were added. In Thailand in 2007, the average contact time at a first visit was about 1 hour and that at subsequent visits was 20–25 min. In Thailand, individual health promotion was replaced by a mix of group sessions and individual counselling.

3.2.2 Cost-effectiveness

Majoko et al. (2007) estimated that the new model would be as or more expensive in rural Zimbabwe, as more women underwent haemoglobin measurement. In countries with few resources, the time gained by fewer visits might be consumed by the significant increase in contact time. In places characterized by late initiation of antenatal care, it might not be feasible to reduce the number of visits, and greater emphasis should be placed on improving quality.

Obstetricians and gynaecologists were available at all the antenatal clinics in the trial; however, this would not be the case in most of the developing world. Thus, the model of Thailand, where midwives provide basic care, supported by physicians for referrals, is a more realistic one for developing countries, as reflected in the significantly lower costs in that country than in countries where antenatal care is provided by an obstetrician (Argentina) or a general practitioner (Cuba, Saudi Arabia). Care by midwives is feasible,

acceptable and cost-effective for low-risk women, an important finding for countries with few resources (Khan-Neelofur et al., 1998).

3.3 Contribution to reducing infant and maternal mortality

While it is unlikely that the observed decrease in perinatal mortality, low birth weight and maternal mortality in countries where implementation of the new model has been scaled up could be attributed to this factor alone, environmental factors that facilitate implementation of these and other interventions, including better quality antenatal care, could contribute to the observed improvements. The ability to reduce risk factors, such as infection in pregnancy, known to contribute to preterm birth and infant deaths, and the relation noted by Stanton et al. (2007) between increased attendance for antenatal care and use of a skilled birth attendant, could result in improved pregnancy outcomes in the long term.

3.4 Barriers to and facilitators of global implementation: the experts' view

3.4.1 Barriers

Global attention to reducing maternal mortality has shifted the focus from antenatal care to labour and delivery. With renewed interest in maternal and neonatal outcomes, antenatal care might regain priority, given its benefits to the newborn. Another policy concern is whether efforts to change or improve antenatal services will divert attention and interest away from improvement of delivery services. Policy-makers and health system managers must be convinced in an understandable way that it is not harmful to make fewer antenatal care visits.

Implementation of the new model might be delayed due to resistance of health-care providers to change and anxiety that complications might be missed with fewer visits, especially as the trial showed an excess likelihood of missing early cases of pre-eclampsia. Where antenatal care is provided by private practitioners, they may be reluctant to reduce the number of visits for fear of losing income and clients, and concern about litigation. Practitioners often fear 'doing nothing' or 'not doing enough': they will intervene if it is safe, as the relative benefits of 'inaction' (watching and waiting) are not clear; this attitude has resulted in rising rates of caesarean section. Involvement of private practitioners in research might encourage them to adopt positive results.

In the public sector, lack of information, limited funding to train personnel, high staff turnover and inadequate manpower, equipment and supplies to support scaling-up are important concerns. In many settings, reaching the minimum of four high-quality antenatal care visits will require upgrading of facilities to provide the range of services suggested, and programme managers must commit themselves to providing a consistent supply of the necessary tools (e.g. syphilis test kits, iron and folate supplements, tetanus vaccine, urine dipsticks).

At the community level, women have preconceived ideas of the care they should receive. Efforts to reduce the number of visits in countries where maternal mortality is high might appear to be a contradiction, on the assumption that more antenatal care visits would contribute to fewer deaths. Where antenatal care is not well organized, with late bookings and attendance by need rather than planned, asking women to plan for four visits might be seen as an unfeasible and unnecessary change. Community education is needed to change these attitudes.

3.4.2 Facilitators

System change often requires a motivated champion (as in Thailand) to bring the issue to the attention of decision-makers. International commitment to achieving the MDGs while providing more cost-effective care could find favour with policy-makers.

The new pattern of care should be recommended as the standard by national societies of obstetrics and gynaecology. If governments provide the policy environment by endorsing and approving evidence-based practice, they must support practitioners, private or public, in litigation. Medical councils and practitioner associations should agree to speak with one voice. Health insurers should be convinced to cover the new evidence-based approach instead of the standard model of care for low-risk women.

The principle of targeted activities during specific visits, linked to a well-designed, patient-held antenatal record on which activities are recorded, should be implementable globally. Fewer visits in early pregnancy should be the goal, coupled with strategies to encourage an early first visit. Because of the high incidence of pre-eclampsia, more visits might be advisable in later pregnancy. Not only health benefits but system benefits should be emphasized, including fewer high-quality visits and more midwives with more time to spend with women.

Women and their families must be satisfied that their care is the best that can be provided. After years of conditioning that "antenatal care is good", their expectations should be backed by provision of information. Satisfaction and internalization of the information that "four visits is best" will take time to achieve.

The women's lobby should be engaged. If women lobby for less antenatal care (or caesarean section), providers feel safer. If the benefits of antenatal care rebound to both the mother and the infant, both the the maternal lobby and the neonatal health lobby should be used to advocate for better antenatal care.

3.4.3 Advocacy by HRP

WHO and RHR have a critical role in helping to promote a climate conducive to adoption of evidence-based practices within countries, just as researchers and commissioning agencies have a duty to influence practice and policy without infringing on the role of others. WHO can help identify local champions to influence local governments to catalyse, but not necessarily effect, change. Awareness should be raised before research starts, not after the findings are produced, in order to instill a sense of ownership. RHR has a responsibility to disseminate evidence-based findings, both from its own research and that of other high-quality teams, for example, through *The WHO Reproductive Health Library*. Other activities include supporting the organization of continuing education.

To promote the model, its use should be monitored by the routine health information systems and through other international monitoring studies such as Demographic and Health Surveys (DHS) and the UNICEF multiple indicator cluster surveys (MICS). At country level, advocacy should be moved from central government to districts; otherwise, the pace of implementation of activities will remain slow or nil.

3.5 Role of HRP: maternal and perinatal health

3.5.1 Capacity-building

Training a team of health-care providers to design, implement, analyse and report on research is critical for developing countries so that they can use evidence to influence public policy and practice. Once they are trained, other opportunities, in the form of grants, fellowships, technology transfer and training, will become available. Drawing principal investigators from the academic community has a multiplier effect, as they can share their skills and experience with their students.

3.5.2 Information dissemination

While principal investigators have shared their experience and findings locally, they should take advantage of HRP-sponsored regional meetings or their attendance at professional meetings to share their experiences more widely, thus distributing these resources more widely to promote effective strategies.

3.5.3 Maternal and perinatal health team

The maternal and perinatal health team at HRP consists of four persons (Mario Merialdi, coordinator; Ana Pilar Betran, medical officer; Mariana Widmer, technical officer; Margrit Kaufmann, administrative assistant). Their unrelenting attention to the setting up and promotion of this intervention while working on new areas is highly commendable. Their continued effectiveness in promoting the scaling-up of this and other new strategies globally will depend on their ability to make a good product and to use the resources of other WHO teams and other international stakeholders working on Safe Motherhood (e.g. USAID and the Department for International Development of the United Kingdom) to market their products. Use of the WHO model by USAID is a positive endorsement of its quality, which is facilitated by the open access provided by HRP to information and technical material.

4. Conclusions and recommendations

4.1 Conclusions

4.1.1 Strengths

The MDG5 monitoring framework has accepted the WHO recommendation to include a new indicator of antenatal care use, which is a measure of the proportion of the world's women who attend for one and four antenatal visits. The results obtained by HRP have therefore contributed to setting the global standard for antenatal care. The improvements in key indicators due to the new model are shown in Annex 5.

The four-visit model is less expensive than the standard antenatal care model. Globally, US$ 3.5 billion could be saved in the short run (US$ 16.4 billion in the long run) by switching to the four-visit model, with savings of US$ 0.9 billion in the short run (US$ 5.4 billion in the long run) in countries with medium maternal mortality ratios (50–500/100 000) and those with high ratios (> 500/100 000). The four-visit model is also cheaper for women seeking care. In countries with medium and high maternal mortality ratios, reduced travel expenses, travel time and waiting time would result in savings of more than US$ 0.6 billion, potentially contributing to poverty reduction.

The external validity of the model will depend on a country's ability to adapt the basic concepts to local circumstances, on the basis of the evidence (Villar, 2003). Countries should see the model as a blueprint on which to build. HRP has begun to adapt it to the African setting, adding components on HIV and violence prevention and updating the recommendations on syphilis and anaemia management.

While the trial and scaling-up were conducted in developing countries providing conventional antenatal care, its performance in Africa, where attendance for antenatal care has been low, validates the robustness of the approach for a range of settings.

Obstetricians and gynaecologists were available in all the antenatal clinics in the trial. As this is not the case in most of the developing world, the model of Thailand, where midwives provide basic care, supported by physicians for referrals, is more realistic for developing countries. For low-risk women, midwife care is feasible, acceptable and cost-effective, an important finding for countries with few resources (Khan-Neelofur et al., 1998).

4.1.2 Weaknesses

Several investigators (e.g. Lumbiganon et al., 2004; Majoko et al., 2007) reported that compliance with new components, such as fundal height measurement, pelvic assessment and gynaecological examinations, examination for anaemia and health promotion (recommendations for emergencies, delivery, lactation and contraception), was low, for various reasons. In addition, the proportion of women who underwent examination for external cephalic version was low in both groups. Research is needed to understand why these elements were not implemented, so that corrective action can be taken.

Limiting factors include inadequate skills, resources and supplies; inadequate referral systems; poor compliance due to distance, hospital fees, irregular transport, poor roads and lack of drugs; negative staff attitudes; and a lack of conviction about risk status by women, who view pregnancy as a natural, normal life event (Carroli et al., 2001a).

While quality has been improved by raising clinical standards, little attention has been paid to the social factors necessary for acceptance of these standards by both mothers and health teams. The behaviour change required might have been

underestimated. For example, care givers should explain to women why certain interventions that they have come to expect (e.g. routine weighing) will no longer be provided (Mathole et al., 2005).

Overattention to medical evidence at the expense of psychosocial and health communication must be addressed. Some elements might have been too ambitious and therefore neglected, but continuing operations research can be used to investigate and correct those elements. Advocacy is needed to ensure wider acceptance and integration of evidence into practice in both the developed and developing world.

4.1.3 Opportunities

The WHO antenatal care model should not be limited to reducing the number of visits but should focus the attention of health-care providers on delivering a range of essential, high-quality services known to improve maternal and perinatal outcomes.

The new approach must be integrated into the curricula of nursing, midwifery and medical schools, with opportunities for re-educating staff and trainees. Advocacy to integrate questions on the new approach into professional registration, specialty board examinations and continuing education programmes could accelerate knowledge about the new strategy, as assessment drives learning. The e-learning tools being designed by HRP in collaboration with Boston University and the Massachusetts Institute of Technology could be promoted to facilitate knowledge dissemination.

4.1.4 Threats

In a commentary in *The WHO Reproductive Health Library* (RHL), Matthews Mathai (Mathai 2002) suggested that apprehension about potential loss of earnings by health-care providers might delay implementation. One possible solution would be to market antenatal care as a package, instead of asking women to pay per visit.

In Kenya, where USAID promoted the approach, the new model increased the quality of care, especially in the detection of disease and counselling on family planning postpartum. Clients reported satisfaction with most aspects of the new model (see Birungi, Onyango-Ouma, 2006). Among the challenges were high staff turnover, which limited the impact of the approach. Focused visits resulted in longer waiting times for delivery of the improved range of services because of limited human resources.

In Khon Kaen, Thailand, limited experience in pelvic assessment indicated the need for special training. Staff required assurance that pelvic examinations during the first trimester would not increase the risk for early fetal loss. As the belief that this was so was strong, the assessment was postponed to the 20-week visit. Managers must remain vigilant concerning such issues, so that they can address problems in a timely way.

4.2 Recommendations

4.2.1 New research

High-quality antenatal care for high-risk mothers

The focus of the new antenatal care model is low-risk women; however, it is high-risk women who are at increased risk for complications, maternal and perinatal death. While Thailand has strategies to manage high-risk patients, based on a simplified version of the WHO Integrated Management of Pregnancy and Childbirth manual (WHO, 2003), an abridged version of this manual, restricted to the outpatient components of antenatal care, would

assist other developing countries in improving the quality of care for high-risk antenatal women.

Women's views

Women in both developed (Clement et al., 1996) and developing countries (Nigander et al., 2003) value health-care providers who listen to their concerns, provide an opportunity to ask questions, discuss their problems and show them respect. If the schedule of fewer visits is to be acceptable to women, the visits must qualitatively address both physical health and psychosocial concerns. Research is needed on the psychosocial needs satisfied by antenatal contact, especially for young or first mothers, including women who might be depressed.

Enabling policy change

More research is needed to identify facilitating factors and to reduce barriers to the acceptance of proven, evidence-based methods by policy-makers and their translation into routine practice.

Impact on the health system

An evaluation is needed of how the new approach alters relationships within the health system. Referral hospitals might need more doctors to attend women newly classified as at high risk. If use of antenatal care and skilled delivery is low, the potential increase in demand for both, due to improved quality of care, will require appropriate management. While savings will be realized in systems in which the commonly used standard antenatal care model is currently used, costs may increase in countries with limited resources and currently inadequate levels of care, where the need is greatest.

4.2.2 Advocacy and dissemination

The network of WHO departments (e.g. Making Pregnancy Safer), collaborating centres and institutions should be used to promote the new antenatal care model, especially where use of antenatal care and skilled birth attendants is low. HRP is also encouraged to exploit the network of nongovernmental organizations and development partners. The latter must, however, be encouraged to support the whole package and not individual components, which would continue the highly inefficient vertical approach to care.

Dissemination of these findings to countries (e.g. the Commonwealth of Independent States) challenged by high health-care costs but which use the commonly used standard model is of particular importance.

4.3 Summary

The WHO antenatal care trial demonstrates that cost-effective interventions can be systematically designed on the basis of sound clinical evidence, field-tested and implemented on a wide scale. After three years, Thai women and health-care providers remain satisfied with the new approach. Fewer visits mean shorter waiting times and less cost to access care; but, more importantly, health-care providers have more time to spend with women, especially those who have health problems. Significant cost savings are possible due to the reduced workload and better quality care, without compromising outcome. A political environment receptive to evidence-based approaches will make the transition from research to practice easier. Leadership is critical, as an active change agent will be more effective in bringing new evidence into policy and practice.

Implementing this model should not be seen simply as an intensive effort to reduce the number of antenatal visits but as an attempt to move towards a wider conception of quality antenatal care and

to improve the system (avoiding long queues of women waiting for hours to see a harrassed midwife for two minutes). Providing orderly antenatal clinics in which women can develop positive relationships with health-care providers who have the time and energy to give individual care designed for their specific needs will promote the model as something bigger than 'reducing the number of visits'.

The HRP team has effectively demonstrated its capacity to marshall an international team of researchers and investigators, who scrupulously documented the research process and its findings. The small maternal and perinatal health team has continued to promote the findings through operations research in Thailand, in order to design training and education which could be disseminated more widely. This represents effective use of limited international resources for the greatest public good. The experts have demonstrated that the model now has a life of its own. Global ownership is the ultimate goal.

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Annex 1. Persons interviewed during site visit to Thailand, 25–30 November 2007, and other experts contacted

Persons interviewed in Thailand

26 November

Dr Mongkol Na Songkhla, Minister of Public Health

Dr Narongsakdi Aungkasuvapala, Director General, Department of Health, Ministry of Public Health

Dr Renu Srisamit, Deputy Executive Secretary, National Health Security Office

Dr Somsak Patarakulvanich, Director, Health Promotion Bureau, Department of Health, Ministry of Public Health

Dr Somchai Peerapakorn, National Professional Officer, Maternal and Perinatal Health, World Health Organization, Thailand

27 November

Professor Suwachai Intaraprasert, President, Royal Thai College of Obstetricians and Gynaecologists

Professor Somboon Kunathikom, Executive Secretary, Royal Thai College of Obstetricians and Gynaecologists

Dr Kamron Chaisiri, Health Inspector, Ministry of Public Health

28 November

Dr Weerachai Wanasarnmeta, Director, Phol Hospital, Khon Kaen

Dr Wuthisak Kruawan, Chairman, Maternal and Child Health Board, Phol Hospital, Khon Kaen

29 November

Dr Vithya Jarupoonphol, Medical Director, Khon Kaen Regional Hospital, Khon Kaen

Dr Sirijit Wasanawatana, Director, Medical Education Centre, Khon Kaen Hospital, Khon Kaen

Dr Thitiporn Siriwachirachai, Head, Department of Obstetrics and Gynaecology, Khon Kaen Hospital, Khon Kaen

Dr Nopphadol Pathipat, Chief Provincial Medical Officer, Khon Kaen

30 November

Dr Narong Winiyakul, Director, Health Promotion Centre, Region 6, Khon Kaen

International experts contacted electronically and who responded

Dr Deanna Ashley, Retired Director of Health Promotion, Ministry of Health and Environment, Kingston, Jamaica

Dr Vincent de Brouwere,[a] Institute for Tropical Medicine, Brussels, Belgium

Dr. G. Justus Hofmeyr, Professor of Obstetrics and Gynaecology, University of Witwatersrand, East London, South Africa

Dr Julia Hussein, Public Health Obstetrician, University of Aberdeen, Aberdeen, Scotland

Dr Marge Koblinsky, Director, Public Health Sciences Division, International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh

[a] Dr de Brouwere shared the questionnaire and received answers from a medical doctor, regional health programme team, Benin; the Director of Family Health, central level (including 'Making Pregnancy Safer') in Burkina Faso; a medical doctor, central level health programme team, Côte d'Ivoire; a regional health director in Mauritania; a medical doctor, central level health programme team, Morocco; and the director of family health at central level (including 'Making Pregnancy Safer') in Senegal.

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Annex 3. Modifications made to WHO antenatal care model, Thailand, 2007

The antenatal care model was modified to ensure that the risk criteria would be consistent with the guidelines with which the staff were already familiar and to address psychosocial and logistical concerns.

- 'Large baby' was redefined as weighing > 4000 g instead of > 4500 g.
- For high-risk adolescent pregnancy, age was changed to < 17 years from < 16 years; for 'elderly mother', age was changed to > 35 years from > 40 years.
- Severe anaemia, thyroid disease (iodine deficiency) and systemic lupus erythematosus listed as important medical conditions during pregnancy.
- As on-site testing and feedback of results the same day are not feasible, tests other than for syphilis are performed at the first visit and include screening for HIV and thalassaemia (prevalence, > 30% of the population); women can telephone the health facility for their results the following week, but, if the results are positive for HIV, syphilis or thalassaemia, the women are contacted by the health facility for treatment, testing of their partner, and counselling.
- In view of concern about the long gap between the first visit and 26 weeks and the low prevalence of women who know the exact date of their last menstruation, a second visit was added for early attenders at 20 weeks to follow up earlier screening and to provide an opportunity for ultrasound examination, including accurate assessment of gestational age.
- Screening for sexually transmitted infections and anaemia is repeated at the fourth visit, around 32 weeks, with another visit one week later for results and health education.
- At the fifth visit, around 38 weeks, women are given an appointment to return at the end of the 40th week if they have not yet delivered.
- Within one week of delivery, women are contacted by telephone to ensure that the mother and infant are recovering well (in lieu of a visit on day 7). Those with problems are invited to attend their health-care facility for a check-up. The standard postpartum visit is scheduled for four weeks after delivery instead of six weeks.
- Women are screened not only for health problems but also for socioeconomic risk factors that can adversely affect pregnancy outcome.

Annex 4. Data sources and methods for estimating the cost-effectiveness of the new model of antenatal care

Calculation of number of pregnancies

Good estimates of numbers of pregnancies do not exist. Here, the number of pregnancies was estimated as the number of births in a given country multiplied by 1.095 to correct for late fetal loss and perinatal mortality. The number of births was calculated by multiplying country-level age-specific fertility rates by the number of women in an age cohort.

Limitations of the analysis

The projections are meant to display orders of magnitude of potential global cost savings. The costing methods in different countries were not identical, as this component of the project was underfunded. The Thai and Cuban studies were conducted prospectively during the trial, while a retrospective method was used in Argentina. In Saudi Arabia, a cost transfer and modelling approach based on unit costs from Argentina, Cuba and Thailand was used. Although the methods were not strictly comparable, the reviewers considered that they could be combined into a single analysis for deriving orders of magnitude.

Sources of costing information

The marginal and average medical costs for Argentina, Cuba, Thailand (Hutton et al., personal communication) and Saudi Arabia (Smith et al., 2001) are as reported. The marginal costs in Saudi Arabia were not reported but were estimated to represent 25% of average medical costs. The out-of-pocket and opportunity costs of women's time in Cuba and Thailand are given by Villar et al. (2001), while the opportunity costs in Argentina (Borghi et al., 2000) and the out-of-pocket costs in Saudi Arabia (Smith et al., 2001) were taken from country reports. In Saudi Arabia, the opportunity costs of women obtaining antenatal services were not analysed, and the Argentinian health system is organized in such a way that out-of-pocket payments are not necessary.

Purchasing power parity versus constant 1998 United States dollar value

The results of most of the costing studies were reported in 1998 US dollar value, which were converted to 2006 US dollar value. Some authors also presented values for 'purchasing power parity'. These were not used, as the exchange rates in Argentina, Cuba, Saudi Arabia and Thailand would not apply to all the countries for which these countries were proxies.

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Annex 5. Reproductive health indicators in countries in the WHO antenatal care trial and in corresponding regions, before and after introduction of the WHO antenatal care model

Indicator	Year	Argentina	Cuba	Saudi Arabia	Thailand
Population (million)	1994	34.2	11.0	17.5	58.2
	2005	38.7	11.3	24.5	64.2
Total fertility rate	1990–1994	2.7	1.8	6.2	2.1
	2000–2005	2.4	1.6	4.1	1.9
Prevalence of use of modern contraceptive methods (%)	-	-	72 (2000)	29 (2005)	70 (1997)
Antenatal care coverage (≥ four visits) (%)	-	95 (2001)	100 (2001)	73 (1996)	86 (2001)
Births attended by skilled birth attendant (%)	-	99 (2004)	100 (2004)	93 (2002)	99 (2002)
Maternal mortality[a]	1980–1992	140	39	41	50
	2000	84 (54–110)	33 (16–66)	23 (12–46)	44 (22–88)
Low birth weight (%)	1990	6	9	7	13
	2000	7	6	11	9
Infant mortality[b]	1994	24	9	31	27
Perinatal mortality[c]	2000	14	14	21	20
Gross domestic product per capita in constant 2000 US$ value	1993	7169	Not available	9402	1771
Gross domestic product per capita in constant 2000 US$ [d]	2003	6932	Not available	9261	2241
% subregional population		10.3	29.0	11.4	11.5
Subregional estimates[e]		South America	Caribbean	Western Asia	South-East Asia
Population (million)	2005	375	39	214	556
Total fertility rate	2000–2005	2.5	2.5	3.4	2.5
Prevalence of use of modern contraceptive methods (%)		66 (1997)	57 (2000)	28 (1996)	51 (2002)
Antenatal care coverage (≥ four visits) (%)		Not available	Not available	Not available	Not available
Births attended by skilled birth attendant (%)	2000	86.8%	73.7%	73.4%	69.1%
Maternal mortality [a]	2000	Not available	Not available	190	210
Low birth weight (%)	2000	9.6	13.7	15.4	11.6
Perinatal mortality [c]	2000	14	14	21	20

Source: http://www.who.int/reproductive_indicators/RHRIndicators2006.xls. accessed 21 September 2007.

[a] Per 100 000 live births; uncertainty estimate for 2000 country value is given in brackets.
[b] Per 1000 live births.
[c] Per 1000 total births.
[d] *Source*: The World Bank. *World Development Indicators Online* (accessed 10 April 2008).
[e] Reproductive health estimates not available for 1994.