Integrated Management of Pregnancy and Childbirth

Standards for Maternal and Neonatal Care

Department of
Making Pregnancy Safer

World Health
Organization

2007

Introduction

What are the Standards for Maternal and Neonatal Care?

The *Standards for Maternal and Neonatal Care* consists of a set of user-friendly leaflets that present World Health Organization (WHO) key recommendations on the delivery of maternal and neonatal care in health facilities, starting from the first level of care. Facilities at higher levels of care should also have these standards in place as a minimum (essential) care for all mothers and babies; in addition, they should have standards for the care of women and newborns in need of obstetric and special care. The *Standards for Maternal and Neonatal Care* are part of the WHO Integrated Management of Pregnancy and Childbirth Care (IMPAC) Package, which provides guidance for assisting countries to improve the health and survival of women and their newborn babies during pregnancy, childbirth and the postnatal period.

Why implement the Standards for Maternal and Neonatal Care?

Studies clearly indicate that countries with high maternal, perinatal and neonatal mortality have inadequate and poor quality health services and this can be associated with reduced utilization of health care services. As such, increased emphasis is being placed on the need for standards of care, as well as mechanisms which address the barriers to provision and use of quality care. Evidence also suggests that explicit, evidence-based guidelines improve the process and outcomes of health care when appropriately implemented. Experience from countries indicates that the characteristics of the guidelines, the process used in their development and a clear implementation strategy supported by effective monitoring and supervision influence the impact of practice guidelines.

What is the purpose of the Standards for Maternal and Neonatal Care?

The purpose of the *Standards for Maternal and Neonatal Care* is to assist programme managers and health care providers to:

- develop evidence-based national and sub-national standards on maternal and neonatal health care;
- introduce standards setting and a quality improvement process at facility level as a means to improve access and quality of maternal and neonatal health services;
- provide effective maternal and neonatal health services;
- use existing resources to achieve the optimal health care outcomes; and
- improve individuals', families' and community's satisfaction and utilization of maternal and neonatal health services.

How are the Standards for Maternal and Neonatal Care structured?

Overall the *Standards for Maternal and Neonatal Care* include the most relevant topics that need to be addressed for ensuring quality maternal and neonatal health services. They are grouped in six sections: five sections focus on clinical standards, where as the sixth encompasses health service delivery standards that are crucial to ensure the provision of quality maternal and neonatal care.

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The Standards for Maternal and Neonatal Care currently comprise the following sections:

- General standards of care for healthy pregnancy and childbirth
- Standards for safe care in childbirth and the immediate postpartum period
- Standards for postnatal care
- Standards of care for managing major complications in pregnancy, childbirth and after birth
- Standards of care for managing major complications in the newborn
- Health service delivery standards

How is each of the Standards for Maternal and Neonatal Care structured?

While presented in a package, each standard is structured to be self-standing, complete with all the elements needed for implementation. This format is meant to facilitate country use by encouraging a stepwise implementation of the standards according to country needs and availability of resources. In addition, such a format should allow for more effective updating. The section on efficacy and effectiveness of the proposed recommendations in each of the standards will be periodically updated as new evidence is gathered.

The key elements common to all standards are:

- the *title*, which identifies the standard;
- the *standard statement*, which is based on the best available evidence, feasibility and cost effectiveness;
- the *aim,* which indicates the public health intent and goal of implementing the standard;
- a section titled *requirements*, which indicates a checklist form the conditions that need to be in place to implement the standard;
- a section called *applying the standard,* which briefly explains what the health provider (for the first five sections) or the health manager (for the section on health service delivery standards) must do to implement the standard;
- a section focusing on *audit*, with suggested input, process and outcome indicators to be used to monitor the correct implementation and impact of the standard;
- a narrative part called *rationale*, which comprises two sections, namely the *burden of suffering* of the condition that the standard addresses, and the *efficacy and effectiveness* section which describes the importance of the recommendations and the evidence in support of the standard;
- a *table of evidence,* which summarizes the most important results of the available evidence;
- a list of *references* used to develop the standard; and
- a list of *links and additional readings,* which will assist the users in implementing the standards.

How were the Standards for Maternal and Neonatal Care developed?

In order to appropriately reflect the diversity of expert opinion and disciplinary perspectives, a systematic, participatory process was used in the development of these standards, in accordance with WHO Guidelines for Guidelines (http://whqlibdoc.who.int/hq/2003/EIP_GPE_EQC_2003_1.pdf). Draft standards were developed by WHO technical staff in the *Making Pregnancy Safer (MPS) Department* and the *Department of Reproductive Health and Research*. These drafts were then shared with other relevant departments for ensuring technical accuracy and consistency with other WHO programmes, and with WHO Regional Offices and MPS country focal persons, to gather input on their applicability in different contexts. Additional inputs have been requested from external experts and institutions throughout the entire development process.

The standards which are included in this guideline are only limited to those for which there is extensive experience or scientific evidence to support the recommendation. Three guiding principles were used in the selection of the topics:

1. public health relevance, as major causes of maternal, fetal or neonatal mortality and/or morbidity;
2. feasibility of implementation at first level facilities in settings with limited resources, both from the health service delivery and community perspective;
3. cost implications, such as cost-effectiveness (where information was available).

To develop the standards, a systematic process and methodology for gathering and summarizing the evidence was developed. The search for evidence followed a sequential process, beginning with higher level evidence, and including observational studies whenever hard evidence (randomized controlled trials or systematic reviews) were not available. For the Clinical Standards the following sources were used: Medline, Embase, and Cinhal (Silverplatter platform), the Cochrane Library, Medline and the WHO Reproductive Health Library, WHO publications based on technical working groups and expert reviews, and a number of articles and websites based on reference lists review and WHO guidelines. For the Health Service Delivery Standards the search included: PubMed, Sciencedirect, EconLit, Interscience, Popline, IDEA, and ECONbase, as well as the databases of relevant organizations, departments, and institutions, such as the World Health Organization, World Bank, Save the children and others as identified by the standards development sub-group.

A table summarizing the evidence complements each standard by presenting the analysis of the studies retrieved, their quality, the population considered in the studies including the specific baseline risk and an estimate of the efficacy of the intervention for major outcomes (benefits and harms). The level of evidence presented in the clinical standards is based on the SIGN methodology which uses a scale from 1 to 4 as shown in the table below.

Levels of evidence

1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 -	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2 -	Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Given the nature of the Health Service Delivery Standards, the studies mostly fell in categories 3 and 4. Therefore, the decision was made by the technical consultation team to use an alternative system scale for this group of standards. The scale is rated from 1 to 5 (1 = not very relevant and 5 = very relevant evidence as it relates to the standard). Each standard is completed by a list of references used in its development and a list of links and additional readings which can be used to facilitate the implementation and auditing process.

These standards were developed under the overall guidance of a Steering Group which has overseen the work of a Development Advisory Group, organized in three sub-groups on maternal, neonatal and health service delivery issues respectively. The development process included extensive consultations with relevant WHO departments (including Child and Adolescent Health and Development; Stop TB; Roll Back Malaria; HIV/AIDS, Nutrition

for Health and Development; Immunization, Vaccines and Biologicals; Essential Drugs and Medicines Policy; Essential Health Technologies; Health Systems Policy and Operations; and Human Resources for Health), WHO Regional Offices, professional organizations (International Confederation of Midwives and International Federation of Gynaecology and Obstetrics), the UNFPA, and experts and individuals from developing as well as developed countries.

For which audience are the Standards for Maternal and Neonatal Care intended?

The Standards for Maternal and Neonatal Care should be of interest to:

- policy-makers;
- programme managers and health planners at national, district and facility levels,
- maternal and neonatal health professionals;
- NGOs, including private sector health organizations, involved or interested in the provision of maternal and neonatal health services; and
- community organizations interested in improving maternal and neonatal health care practices.

Given the differences between countries in relation to the categories of health workers providing maternal and neonatal care, and rather than measure on a specific health care cadre, this document focuses more on the skills and services required to ensure that maternal and neonatal ill health conditions are possibly prevented and properly identified and managed. For the majority of cases and particularly in relation to routine maternal and neonatal care, the health care provider with these skills will better correspond to the skilled attendant*. However, it must be considered that a proportion of women and babies might require specialized care and consequently knowledge and skills of health care providers that are beyond those of the skilled attendant and that are not covered by this document.

How can the Standards for Maternal and Neonatal Care be utilized?

The *Standards for Maternal and Neonatal Care* are intended to be generic standards, which can be adapted and implemented according to the needs, financial and health systems capacities in different countries. They can be used individually or as a package. They are cross-referenced with each other for ease of use.

The standards can be used at the national and sub-national level to establish or to update current norms in line with the latest available evidence. Ideally, most of these standards should be in place to ensure quality maternal and neonatal health services. However, country users may wish to implement them in a stepwise manner (incrementally), for example, beginning with implementation only a few at one time, and then gradually scaling up to implement additional standards.

The standards can serve to further develop guidelines as well as design training curricula for the skilled attendants and other health care providers of maternal and neonatal care. They can also be used in the adaptation process of the *Pregnancy Childbirth Postpartum and Newborn Care practice guide,* the *Manual for Complications in Pregnancy and Childbirth,* the *Manual for Newborn Problems,* and other relevant WHO guidelines.

* The term "skilled attendant" in the document refers exclusively to people with midwifery skills (for example midwives, doctors and nurses) who have been trained to proficiency in skills necessary to manage normal births and diagnose, manage or refer obstetric and neonatal complications. Skilled attendants may practice in hospitals, clinics, health units, homes, or in any other service setting. Skilled attendants must be registered and/or legally licensed to practise. *(Making Pregnancy Safer: the critical role of the skilled attendant. A joint statement by WHO, ICM and FIGO. Geneva 2004)*

At the facility level, the *Standards for Maternal and Neonatal Care* can represent a useful tool for facilitating a systematic approach to evaluate and improve the care provided by maternal and neonatal health services. They can be the vehicle for introducing clinical audits which are the systematic review of the quality of care based on standards of care agreed upon by all the relevant health providers, or focus on a broader quality improvement process within the health facility.

It is envisaged that the process of setting standards, using standards to audit clinical practice and implementing agreed changes will contribute to improving provider's performance and clinical practice. It is intended that the *Standards for Maternal and Neonatal Care* will assist to enhance both health providers' and managers' awareness of quality of care and of their role to ensure best practices in communities with maternal and neonatal health services.

The WHO Making Pregnancy Safer Department intends to assist countries in adapting and implementing the *Standards for Maternal and Neonatal Care* as one of the key MPS strategies to influence policy decisions and improve health service provision towards the reduction of maternal and neonatal mortality and morbidity, thus contributing to the achievement of MDG4 and MDG5.

The *Standards for Maternal and Neonatal Care* will be updated as scientific evidence and experience in their use accumulates and will be modified to support the implementation of better maternal and neonatal services in countries.

Development Process

1. Introduction

In accordance with WHO's mandate and comparative advantage, the Department of Making Pregnancy Safer (MPS) has developed generic standards for maternal and neonatal care, with the purpose of providing countries and the international community with a tool for establishing evidence-based national standards of care. Where appropriate, MPS will assist countries and partners to develop and implement their own standards based on this generic tool. This work is one of the strategies to improve health service provision for women and newborn babies and complements other Integrated Management of Pregnancy and Childbirth (IMPAC) clinical and managerial tools.

2. Process

2.1 Overall process

In order to appropriately reflect the diversity of expert opinion and disciplinary perspectives, a systematic consultative process was used in the development of these standards. A *Steering Committee* and a *Standards Development Advisory Group* were established, whose composition and functions are described in Section 3. Drafts standards were developed internally by the technical staff in MPS in consultation with additional experts from the Department of Reproductive Health and Research (RHR) and experts external to WHO. These drafts were then shared with other relevant departments, including Child and Adolescent Health and Development (CAH); Stop TB; Global Malaria Programme (GMP); HIV/AIDS; Nutrition for Health and Development (NHD); Immunization, Vaccines and Biologicals (IVB); Technical Cooperation for Essential Drugs and Traditional Medicine (HTP/TCM); Essential Health Technologies; Health Policy, Development and Services (HDS); and Human Resources for Health (HRH) for ensuring technical accuracy and consistency with other WHO programmes. Starting from their early development stage the drafts were also shared with WHO Regional offices and Making Pregnancy Safer country focal points, to gather input on their applicability in different contexts. Additional inputs have been requested from external experts and institutions throughout the entire development process.

The Clinical Standards were reviewed in a technical consultation in Geneva,14-16 October 2002, where as the Health Service Delivery Standards were reviewed in a technical consultation in Geneva, 26-28 October 2004.

2.2 Methodology

In the selection of the list of topics for the standards, the following principles have been used:

- public health relevance as a major cause of maternal, fetal or neonatal mortality and/or morbidity;
- feasibility of implementation at first level facilities in settings with limited resources, both from the health service delivery and community perspective;
- cost implications, such as cost-effectiveness (where information was available).

After having agreed on the standards' framework and having defined the list of standards based on established guiding principles, the following process was applied for the development of each standard:

- Refinement of the questions to be addressed in each standard.
- Undertaking of a systematic review, critically appraise, synthesize and grade the evidence. All evidence, including that on safety, to be clearly laid out in an evidence table. Meta-analysis to be done when the data permitted.
- Development of model standard recommendations, including criteria for the implementation of the standard and suggested indicators for audit, and description of the application in different scenarios.
- Peer review held by widely circulating the standard to experts, professional organizations, regional offices and target audiences in countries.
- Dissemination plans made, including plans for contextualisation and evaluation, within an agreed standard setting framework.
- Completion of documentation of the standard development process.
- Submission to the Steering Group for reviewed approval of draft version, a well as to the Director of the Department for final approval.

2.3 Source of evidence

To develop the standards, a systematic process and methodology for gathering and summarizing the evidence was developed. The search for evidence followed a sequential process, beginning from higher level evidence (systematic review, randomized controlled trials) and included observational studies whenever randomized controlled trials or systematic reviews were not available.

The basic search strategy was developed using the National Library of Medicine medical Subject Headings (MeSH) key word nomenclature developed for each of the databases used. The initial search was performed in The Cochrane Library using the identified term both as a MeSH and as a free term. Clinical evidence was always consulted as a second step to update the Cochrane search results. When insufficient evidence was found, a further step was designed to search in MEDLINE (and then to duplicate the search in EMBASE and CINHAL). Selection was limited to human subjects. No time limits were applied. Three different specific search filters, as developed by Scottish Intercollegiate Guidelines Network (SIGN), were used to progressively identify Systematic review and Metanalysis, Randomized Controlled Trial and all other studies. The filters are more sensitive and less specific than the ones developed and used by the Cochrane Collaboration. For the purpose of our search higher sensitivity was preferred; and a second phase based on hand selection of all the studies retrieved was successively performed.

Finally, a free search was performed in Tripdatabase to identify any further important article. When the same authors or group of authors published more than one article on the same topic and with the same conclusion, the most recent one was reported. Relevant studies not selected through the filters but known by the standards development group or identified among the references of other studies were also included

In summary, for the Clinical Standards, the following sources were used: Medline, Embase, and Cinhal (Silverplatter platform), The Cochrane Library, and the WHO Reproductive Health Library, WHO publications based on technical working groups and expert reviews, and a number of articles and websites based on the review of references lists and WHO guidelines. In addition, for the Health Service Delivery Standards the search included: PubMed, Sciencedirect, EconLit, Interscience, Popline, IDEA, and ECONbase, as well as the databases of relevant organizations, departments, and institutions, such as the World Health Organization, the World Bank, Save the Children and others as identified by the standards development sub-group.

2.4 Presenting the evidence

The evidence in support of the standards is presented in three ways: a narrative section named *efficacy and effectiveness*, which describes the importance of the recommendations and the evidence in support of the specific standard; a list of references; and a table of evidence, which summarized the most relevant articles, their quality, the population considered in the studies, including the population specific baseline risk and an estimate of the efficacy of the intervention for major outcomes (benefits and harms).

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked for the Standard	Results		Comments
Prendville 2003 Most recent substantive amendment March 2000 **Systematic review 1++**	6477 women. 5 studies, 3 in UK 1 in Ireland, 1 in United Arab Emirates. In three studies only low risk women. All maternity hospitals. Baseline risk=11-14%	To assess the effects of active* versus expectant** management of the III stage of labour.	Moderate PPH Severe PPH Blood transfusion	**Active vs. Expectant**		Two out of five studies included **are not clear about the three components** included in "active management"
				All women NNT 12 (10-14) 4 studies 6284 women 3616 women NNT 57 (41-89) 4 studies 6284 women NNT 65 (47-106) 5 studies 4 studies	**Low risk women** 11 (9-14) 3 studies 3616 women 88 (51-306) 3 studies women 3616 women 74 (49-147) 4 studies 3809 women	

*Active management of the third stage of labour, which is here defined as the package of interventions comprising:

(i) administration of a prophylactic oxytocic with or immediately after delivery of the baby and usually;

(ii) early cord clamping and cutting (only in two studies); and

(iii) controlled cord traction to deliver the placenta.

**Expectant management of the third stage of labour which is here defined as a 'hands off' policy, where signs of separation are awaited and the placenta allowed to deliver spontaneously or with the aid of gravity or nipple stimulation. The components of active management described above are not routinely employed.

To facilitate the interpretation of the evidence, the identified articles relevant for the standard contents were tabulated as follows:

- In the first column, we indicated the author and publication year, the *Study type and level of evidence*. Level of evidence assignment is based on SIGN methodology. In case of a systematic review from The Cochrane Library, we report the year of most recent substantive amendment.
- In the second column, we described the *Study population and setting*. We decided to have this specific column to give as much information as possible on population and setting of the considered studies (if possible, the baseline risk of the condition under study in the given population is reported), to allow comparison and proper decision making since the standard will be used in different settings and with different health priorities (external validity of the studies retrieved and reproducibility).
- The third column reports *Objectives and Intervention* as described in the study.
- In the fourth column, *Outcomes relevant for the standard* are selected. In some cases, (especially when reporting the results of a systematic review), the reported outcomes are not the whole set of outcomes under study; and as a consequence the population for the specific outcome can differ from the one presented in the systematic review. Number of studies and specific population for the outcome selected are therefore reported in the next column, under *Results*.

- The fifth column reports *Results* for each of the selected outcomes. We decided to present the results, whenever possible and adequate, as Number Needed to Treat (NNT) and/or Number Needed to Harm (NNH), with 95% CI, since this will enable policy-makers to choose whether to introduce the intervention in their programmes and make recommendations as part of the localization process of the standard.
- *Comments* on the importance and relevant aspects of each study with respect to the standard revised are finally presented in the last column.

The level of evidence presented in the clinical standards is based on the SIGN methodology which uses a scale from 1 to 4 as shown in the table below.

	Levels of evidence
1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 -	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2 -	Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Given the nature of the Health Service Delivery Standards, the studies related to health service delivery issues mostly fell in categories 3 and 4. Therefore, the decision was made by the technical consultation in October 2004 to use an alternative system scale for this group of standards. The scale is rated from 1 to 5 (1 = not very relevant and 5 = very relevant evidence as it relates to standard). Each standard is completed by a list of references used in its development and a list of links and additional readings which can be used to facilitate the implementation and auditing process.

3. Organizational structure, roles and responsibilities

The development of the Standards for Maternal and Neonatal Care (SMNC) was guided by an overall *Steering Committee*, composed mainly by WHO staff, who gave direction to and had responsibility for the entire process from development to implementation. A technical *Standards Development Advisory Group*, composed by WHO staff and external experts from different fields, was also established with the responsibility of developing the standards and provide advice on technical issues. This group was organized in three main subgroups, focusing on maternal, neonatal and health service delivery issues respectively. While the main responsibility of each subgroup was to develop the standards related to their area of expertise, members of the other subgroups were also acting as advisory body for the review of the standards developed by the other subgroups. Whenever necessary, the Standards Development Advisory Group was complemented by *Technical Resource Persons* who were identified within WHO or externally to provide technical inputs on specific issues, and the formulation of *Task Forces* to undertake systematic reviews of the evidence or conduct consultation with experts if evidence was lacking.

Finally, managerial and administrative support was provided by WHO secretariat.

3.1 SMNC Steering Committee

The Steering Committee was an in-house group composed of WHO technical experts with the general function of overseeing each step of the development process of the standards.

3.1.1 Functions

The Steering Committee was charged with the following functions:

- Define the general parameters of the SMNC.
- Draft broad guidelines for the Standards Development Advisory Group (SDAG), subgroups and appropriate task forces.
- Select the chair and members of the SDAG and task forces.
- Orient the SDAG to the specific TOR and the process of development of the SMNC.
- Regularly monitor the development of the SMNC.
- Ensure all processes are in place to comply with the *WHO guidelines for guidelines* (http://whqlibdoc.who.int/hq/2003/EIP_GPE_EQC_2003_1.pdf
- Ensure a rigorous external review of each of the standards.
- Review the final draft of the standards for approval by the Assistant Director-General of the Family and Community Health Cluster in WHO.

3.1.2 Composition

- Chair: Paul Van Look, Director Reproductive Health and Research Department (RHR)
- Coordinator: Ornella Lincetto, Medical Officer, Making Pregnancy Safer Department (MPS)
- Members: 6 persons from within the MPS team who together had the following skills and expertise:
  a) Expertise in guidelines development and evidence-based methodologies
  b) Familiarity with implementation of programmes in developing countries in the area related to the SMNC
  c) Knowledge of the subject /topic/content of the guideline, such as midwifery services and training (Della Sherratt), Obstetric Care (Luc de Bernis and Rita Kabra), Neonatal Care (Ornella Lincetto), Health Service Delivery (Helga Fogstad), and Health Promotion (Annie Portela).
- At least 1 member from outside the MPS team who has expertise in developing evidence based guidelines (Nicola Magrini, Director of CeVEAS – Centre for evaluation of effectiveness of health care)

3.2 Standards Development Advisory Group (SDAG)

The Standards Development Advisory Group was a large multidisciplinary group, organized in three subgroups according to three main areas of work: maternal (coordinated by Della Sherratt), neonatal (coordinated by Ornella Lincetto) and health delivery system (coordinated by Helga Fogstad), with the responsibility of developing the SMNC, in-line with guidance from the Steering Committee.

3.2.1 Functions

- Define the specific issues to be addressed by each of the standards.
- Provide technical advice on topics/areas on which additional expertise is required.
- Undertake a systematic search for evidence.
- Review the evidence available.
- Develop recommendations linked to the strength of the evidence.
- Draft and review the standards.
- Discuss and incorporate, where relevant, comments of external reviewers.
- Draft the final version of standards.

- Make recommendations on standards setting process and dissemination strategy.
- Document the process of guideline development.

3.2.2 Composition

- Coordinators: Della Sherratt, Ornella Lincetto and Helga Fogstad

  Criteria for selection of the coordinators:

  - Be credible and command respect in the field/subject area.
  - Have experience in guideline development.
  - Expert in the field of Maternal and Neonatal or Health System for MNH.
- 8-12 members representing multidisciplinary background, including:
  - Professionals (experts in maternal or neonatal health and health systems);
  - Methodologists; and
  - Stakeholders.
- At least 1 member from each of the Regional Offices (MPS regional coordinators):
  - MPS Coordinator AFRO, Seipati Mothebesoane-Anoh;
  - MPS Coordinator AMRO, Vicky Camacho;
  - MPS Coordinator EMRO, Ramez Mahaini;
  - MPS Coordinator EURO, Alberta Bacci;
  - MPS Coordinator SEARO, Ardi Kaptiningsih; and
  - MPS Coordinator WPRO, Ruyan Pang/Khine Sabai Latt.
- At least 1 member from each of the Regional Offices as it relates to MNH health system issues:
  - Head of Reproductive and Child Services, Ministry of Health, Tanzania, representing AFRO, Catherine Sanga;
  - Head of Women's Health Program Ministry of Health, Chile, representing AMRO, Rene Castro;
  - Health Care Delivery Regional Adviser, representing EMRO, Ahmed Abdel Latif;
  - Health Systems Expert, Switzerland, representing EURO, Gelmius Siupsinskas;
  - Nursing and Midwifery Regional Adviser, representing SEARO, Duangvadee Sungkhobol; and
  - Health Systems, Maternal and Child Medical Research Centre, Mongolia, representing WPRO, Dashzeveg Natsuvd.
- All external technical advisers were asked to sign a declaration of interest form (attached as Annex 1).

3.3 SMNC Technical Resource Persons

There were additional resource persons either within WHO or externally, who were identified by the Steering Committee and/or SDAG to provide technical input on specific issues.

3.3.1 Functions

- Provide input on specific technical issues as requested by the SDAG or Steering Committee.
- Partake in technical discussions with SDAG and Steering Committee.
- Review specific parts of the draft document and provide comments as requested by the Steering Committee or SDAG.

3.3.2 Composition

- Dependent on the specific needs as identified by the Steering Committee or SDAG.
- All external technical experts involved in the guideline development process were requested to sign a declaration of interest form (attached as Annex 1).

3.4 Taskforces

Taskforces were established by the SDAG as needed to undertake systematic reviews of the evidence or conduct consultations with experts when evidence was lacking.

3.4.1 Functions

- Undertake systematic reviews if and when appropriate.
- Review and synthesize the evidence for possible standards as agreed by SDAG.
- Draft recommendations on evidence using the agreed process.
- Revise draft standard based on feedback and recommendations from the SDAG.
  All external technical advisers involved in the guideline development process were requested to sign a declaration of interest form (attached as Annex 1).

3.5. Secretariat

The managerial and administrative support to the Steering Committee and the SDAG were provided by WHO staff of the Department of Making Pregnancy Safer (MPS).

3.5.1 Functions

- Assisting in the planning of activities and monitoring progress according to plans.
- Providing relevant background information and materials to the SDAG and the Steering Committee.
- Organizing the necessary reviews of drafts provided by the SDAG.
- Assisting in organizing necessary meetings and workshops in Geneva.
- Liaising with the RHR documents committee.

3.5.2 Composition

- Coordinators of the SDAG: Ornella Lincetto, Della Sherratt, Helga Fogstad
- WHO administrative support: Catherine Legros, Shamilah Akrams, Nini Zotomayor

Annex A: DECLARATION OF INTERESTS FOR WHO EXPERTS

World Health Organization

Title of meeting or work to be performed, including description of subject-matter, substance (compounds and organisms), technology or process to be considered:_____

_____

Public health considerations have a primary importance in all WHO technical work. Measures need to be taken to ensure that the best possible assessment of scientific evidence is achieved in an independent atmosphere free of either direct or indirect pressures. Thus, to assure the technical integrity and impartiality of WHO's work, it is necessary to avoid situations in which financial or other interests might affect the outcome of that work.

Each expert is therefore asked to declare any interests that could constitute a real, potential or apparent conflict of interest, with respect to his/her involvement in the meeting or work, between (1) commercial entities and the participant personally, and (2) commercial entities and the administrative unit with which the participant has an employment relationship. "Commercial entity" refers to any company, association (e.g., trade association), organization or any other entity of any nature whatsoever, with commercial interests.

In addition, as a result of WHO's strong stance against tobacco use, it is considered relevant for the Organization to know whether experts working with it have, or have had, any relationship with any part of what may be called "the tobacco industry". Nevertheless, declaration of such an interest would not necessarily be considered a reason to disqualify an expert.

What is a conflict of interest?

Conflict of interest means that the expert or his/her partner ("partner" includes a spouse or other person with whom s/he has a similar close personal relationship), or the administrative unit with which the expert has an employment relationship, has a financial or other interest that could unduly influence the expert's position with respect to the subject-matter being considered. An apparent conflict of interest exists when an interest would not necessarily influence the expert but could result in the expert's objectivity being questioned by others. A potential conflict of interest exists with an interest which any reasonable person could be uncertain whether or not should be reported.

Different *types of financial or other interests*, whether personal or with the administrative unit with which the expert has an employment relationship, can be envisaged and the following list, which is not exhaustive, is provided for your guidance. For example, the following types of situations should be declared:

1. a current proprietary interest in a substance, technology or process (e.g. ownership of a patent), to be considered in - or otherwise related to the subject-matter - of the meeting or work;
2. a current financial interest, e.g. shares or bonds, in a commercial entity with an interest in the subject-matter of the meeting or work (except share holdings through general mutual funds or similar arrangements where the expert has no control over the selection of shares);
3. an employment, consultancy, directorship, or other position during the past 4 years, whether or not paid, in any commercial entity which has an interest in the subject-matter of the meeting/ work, or an ongoing negotiation concerning prospective employment or other association with such commercial entity;
4. performance of any paid work or research during the past 4 years commissioned by a commercial entity with interests in the subject-matter of the meetings or work;
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With respect to the above, an interest in a competing substance, technology or process, or an interest in or association with, work for or support by a commercial entity having a direct competitive interest must similarly be disclosed.

How to complete this Declaration: Please complete this Declaration and submit it to the Secretariat. Any financial or other interests that could constitute a real, potential or apparent conflict of interest should be declared (1) with respect to yourself or partner, as well as (2) with respect to the administrative unit with which you have an employment relationship. Only the name of the commercial entity and the nature of the interest is required to be disclosed, no amounts need to be specified (though they may be, if you consider this information to be relevant to assessing the interest). With respect to items 1 and 2 in the list above, the interest should only be declared if it is current. With respect to items 3, 4 and 5, any interest during the past 4 years should be declared. If the interest is no longer current, please state the year when it ceased. With respect to item 5, the interest ceases when a financed post or fellowship is no longer occupied, or when support for an activity ceases.

Assessment and outcome: The information submitted by you will be used to assess whether the declared interests constitute an appreciable real, potential or apparent conflict of interest. Such conflict of interest will, depending on the situation, result in (i) you being asked not to take part in the portion of the discussion or work affecting that interest, (ii) being asked not to take part in the meeting or work altogether, or (iii) if deemed by WHO to be appropriate to the particular circumstances, and with your agreement, you taking part in the meeting or work and your interest being publicly disclosed.

Information disclosed on this Form may be made available to persons outside of WHO only when the objectivity of the meeting or work has been questioned such that the Director-General considers disclosure to be in the best interests of the Organization, and then only after consultation with you.

Declaration: Have you or your partner any financial or other interest in the subject-matter of the meeting or work in which you will be involved, which may be considered as constituting a real, potential or apparent conflict of interest?
Yes: No: If yes, please give details in the box below.

Do you have, or have you had during the past 4 years, an employment or other professional relationship with any entity directly involved in the production, manufacture, distribution or sale of tobacco or any tobacco products, or directly representing the interests of any such entity?
Yes: No: If yes, please give details in the box below.

Type of interest, e.g. patent, shares, employment, association, payment (including details on any compound, work, etc.)	Name of commercial entity	Belongs to you, partner or unit?	Current interest? (or year ceased)

Is there anything else that could affect your objectivity or independence in the meeting or work, or the perception by others of your objectivity and independence?

_____

_____

I hereby declare that the disclosed information is correct and that no other situation of real, potential or apparent conflict of interest is known to me. I undertake to inform you of any change in these circumstances, including if an issue arises during the course of the meeting or work itself.

_____ _____

Signature Date

_____ _____

Name Institution

Maternal immunization against tetanus

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

The standard

All women giving birth and their newborn babies should be protected against tetanus.

Aim

To prevent maternal and neonatal tetanus (MNT).

Requirements

- ☐ A national policy and national strategies to achieve high vaccination coverage with tetanus toxoid (TT or Td) among pregnant women are available and are correctly implemented.
- ☐ In countries with areas at high risk for MNT, strategies and plans to implement a "high-risk approach", including vaccination of women of childbearing age, are in place.
- ☐ All pregnant women attend antenatal clinic or can be reached by health staff in the community.
- ☐ Antenatal care (ANC) providers have been trained in tetanus immunization.
- ☐ The vaccine, equipment and supplies (refrigerator, syringes, needles, etc.) needed to conduct tetanus immunization are readily available in the health facilities, particularly at ANC services.
- ☐ An effective tetanus vaccination monitoring system is in place, including immunization register, personal vaccination cards and maternal health records.
- ☐ All pregnant women are issued a personal immunization card, which should be available for reference at each ANC visit and at any other contact with the health system throughout life.
- ☐ Health education activities to increase community awareness of the importance of tetanus immunization are carried out.
- ☐ Maternal and neonatal tetanus are included in the national surveillance system.

Applying the standard

Health providers of maternal and neonatal health care, in particular, must:

- Follow universal standards for prevention of infection in all circumstances.
- If the woman has a tetanus-prone wound, including a woman who underwent an unsafe abortion, protect her against future tetanus risks by immunizing her immediately if she is considered not protected (see table 1). In addition, offer prophylaxis with tetanus immunoglobulins if the wound is large and possibly infected with soil or instruments contaminated with animal excreta.

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- Before administering the vaccine, shake the vial with TT so that the sediment at the bottom mixes completely with the liquid. If it is suspected that the vaccine has been frozen and thawed, check for damage using the shake test. Previously frozen vaccine should not be administered.
- In the ANC service, check the immunization status of the pregnant woman (either by history or by card), regardless of whether there is an intention to continue the pregnancy. Administer tetanus toxoid if the woman qualifies for it:
  - if the woman has not previously been vaccinated, or if her immunization status is unknown, give two doses of TT/Td one month apart before delivery, and further doses as per table 1;
  - if the woman has had 1–4 doses of tetanus toxoid in the past, give one dose of TT/Td before delivery (a total of five doses protects throughout the childbearing years);

Table 1 Tetanus toxoid immunization schedule for women of childbearing age and pregnant women without previous exposure to TT, Td or DTP[a]

Dose of TT or Td (according to card or history)	When to give	Expected duration of protection
1	At first contact or as early as possible in pregnancy	None
2	At least 4 weeks after TT1	1-3 years
3	At least 6 months after TT2 or during subsequent pregnancy	At least 5 years
4	At least one year after TT3 or during subsequent pregnancy	At least 10 years
5	At least one year after TT4 or during subsequent pregnancy	For all childbearing age years and possibly longer

[a] Source: *Core information for the development of immunization policy. 2002 update*. Geneva. World Health Organization, 2002 (document WHO/V&B/02.28), page 130.

  - if the woman can show written proof of vaccination in infancy, childhood or adolescence with tetanus-containing vaccine (e.g. DTP, DT, Td, TT) administer doses as indicated in the table 2.

Table 2 Guidelines for tetanus toxoid immunization of women who were immunized during infancy, childhood or adolescence[b]

Age at last vaccination	Previous immunizations (based on written records)	Recommended Immunizations	
		At present contact/pregnancy	Later (at intervals of at least one year)
Infancy	3 DTP	2 doses of TT/Td (min.4 weeks interval between doses)	1 dose of TT/Td
Childhood	4 DTP	1 dose of TT/Td	1 dose of TT/Td
School age	3 DTP + 1 DT/Td	1 dose of TT/Td	1 dose of TT/Td
School age	4 DTP + 1 DT/Td	1 dose of TT/Td	None
Adolescence	4 DTP + 1 DT at 4-6 yrs + 1 TT/Td at 14-16 yrs	None	None

[b] Adapted from: Galazka AM. *The immunological basis for immunization series. Module 3: tetanus.* Geneva, World Health Organization, 1993 (WHO/EPI/GEN/93.13), page 17.

- For the woman to be protected during pregnancy, the last dose of tetanus toxoid must be given at least two weeks prior delivery.
- Record the doses given on a standard tetanus toxoid immunization register and on a personal immunization card or maternal health record. The personal immunization card should be kept with the woman.

- If a case of neonatal tetanus is identified, give the mother one dose of tetanus toxoid as soon as possible and treat the baby according to national guidelines. A second dose should be given (at least) four weeks after the first, and a third dose should be given (at least) six months after the second. A search should be made for other non-immunized women living in the same area, and vaccination provided accordingly.
- Record all cases of NT and report to the district authority. All NT cases from low-risk areas should be investigated.
- Record and report all cases of tetanus occurring in other age groups separately. Where possible, cases of maternal tetanus should be highlighted, for example through reporting.

Audit

Input indicators

- A national policy and strategies and plans related to MNT are available in health facilities.
- ANC care providers are acquainted with the vaccination schedule and know how to check whether tetanus toxoid vaccine has been damaged.
- Tetanus vaccines (TT and/or Td) are available in health facilities offering maternal care.
- Community-based health education activities are carried out in order to increase ANC and TT immunization coverage.
- Outreach activities are carried out in order to increase ANC and TT immunization coverage.

Process and output indicators

- The proportion of ANC services providing tetanus immunization services.
- The proportion of pregnant women immunized with at least two doses of tetanus toxoid (TT2+) or the proportion of neonates "protected at birth" (PAB).
- Monthly reports on NT cases are completed and delivered on time.

Outcome indicators

- Incidence of neonatal tetanus (the target is less than 1 case per 1000 live births at district level).
- Incidence of maternal tetanus.

Rationale

Burden of suffering

Worldwide, tetanus kills an estimated 180 000 neonates *(1)* (about 5% of all neonatal deaths (2002 data)) and up to 30 000 women *(2)* (about 5% of all maternal deaths) each year. If the mother is not immunized with the correct number of doses of tetanus toxoid vaccine, neither she nor her newborn infant is protected against tetanus at delivery.

Tetanus is caused by a toxin produced during the anaerobic growth of *Clostridium tetani*. Infection is acquired through environmental exposure of any broken skin or dead tissue —such as a wound or when the umbilical cord is cut—to the spores of the bacteria. These spores are universally present in the soil. Poverty, poor hygiene and limited access to health services increase the risk of MNT. WHO estimates that only 5% of NT cases are reported, even from countries with well-developed surveillance systems. Since 1989, when the World Health Assembly called for the elimination of NT, 110 out of 161 developing countries are thought to have achieved elimination (as of the end of 2004). UNICEF, WHO and UNFPA agreed in 1999 to set the year 2005 as the target date for worldwide elimination. Elimination is defined as the reduction of NT cases to less than 1 per 1000 live births in every district of every country. This definition is also being used as a proxy for the elimination of maternal tetanus.

Efficacy and effectiveness

The purpose of giving the vaccine to women of childbearing age and to pregnant women is to protect them from tetanus and to protect their newborn infants against NT *(3,4)*. Tetanus vaccination produces protective antibody levels in more than 80% of recipients after two doses *(1–3)*. Two doses protect for 1–3 years, although some studies indicate even longer protection *(3)*. Tetanus vaccine is safe to give during pregnancy *(4,5)*.

Because tetanus spores are ubiquitous in the environment, eradication is not biologically feasible. High immunization coverage of pregnant women, clean delivery and the identification and implementation of corrective action in high-risk areas are the three primary strategies for eliminating MNT (see also standard 2.4.2 "Care of the umbilical cord"). Antenatal services provide a convenient opportunity for vaccinating pregnant women *(6,7)*. Where ANC coverage is inadequate, mass immunization of women of childbearing age could be an alternative though more costly option *(3,5)*. About US$ 1.20 is needed to protect a woman with three doses of TT/Td using the high-risk approach. Reminding patients, tracking and outreach activities are effective in increasing immunization coverage *(8)*.

Services dealing with patients with a tetanus-prone wound, including women who underwent an unsafe abortion, should also immunize the patient if she is considered not protected to ensure that she is no longer at risk in the future. In addition, prophylaxis with tetanus immunoglobulins may be required if the wound is large and possibly infected with soil or instruments contaminated with animal excreta *(9)*.

Effective surveillance is crucial to monitoring progress, and is possible even where resources are scarce *(9)*. However, obtaining complete and reliable data has proven to be difficult, as shown by the low efficacy of reporting. In circumstances where abortion is illegal or socially unacceptable, post-abortion tetanus cases are neglected and underreporting can be even more common.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes considered for the Standard	Results	
3. Koenig et al. 1998 **Observational study nested in a randomized controlled trial** **2+**	41 571 non-pregnant adult women Bangladesh (Matlab cholera trial 1974) Baseline NT* mortality rate: 14.4/1000 live births	To assess vaccine efficacy to reduce mortality from NT 1 or 2 injections of tetanus toxoid vs control given to pregnant women	Vaccine efficacy rate Neonatal mortality on days 4–14 (suspected NT) – 3 years post-immunization – 10 years post-immunization NT mortality – 10 years post-immunization	*1 dose vs. control* 91 (33-99) NS [a] NS	*2 doses vs. control* 56 (17-76) 48 (3-73) 74 (23-91)
8. Szilagyi et al. 2003 Most recent substantive amendment August 2002 **Systematic review** **1++**	41 studies; more than 50 000 patients (children and adults over 20 years of age) Community setting Australia, Canada, Denmark, New Zealand, USA Baseline immunization rate: – minimum 3% – maximum 95%	To identify effective intervention to improve immunization rate Utilization of patient reminder/recall systems	Increased immunization rate – minimum – maximum	*Patient reminders vs. control* NNT [b] 24 (17-35) NNT 34 (30-41)	

* Neonatal tetanus [a] Non-significant [b] Number needed to treat

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9. D. Heymann. *Control of communicable diseases manual*, 18th Edition, WHO and APHA 2004, p.531.
10. John TJ et al. Disease surveillance at district level: a model for developing countries. *Lancet*, 1998, 352:58–61.

Links and additional sources

I. *Field manual for neonatal tetanus elimination*. Geneva, World Health Organization, 1999 (document WHO/V&B/99.14) (http://www.who.int/vaccines-documents/DocsPDF/www9563.pdf, accessed 7 December 2004).

II. *Maternal and neonatal tetanus elimination by 2005. Strategies for achieving and maintaining elimination*. Geneva, UNICEF, WHO, UNFPA, 2000 (document WHO/V&B/02.09) (http://www.who.int/vaccines-documents/DocsPDF02/www692.pdf, accessed 7 December 2004).

III. *WHO-recommended standards for surveillance of selected vaccine-preventable diseases*. Geneva, World Health Organization, 2003 (document WHO/V&B/03.01) (http://www.who.int/vaccines-documents/DocsPDF06/843.pdf, accessed 8 March, 2006).

IV. *Immunization in practice. A practical resource guide for health workers. 2004 update. Module 3: The cold chain. Module 8: Building community support for immunization*. Geneva, World Health Organization, 2004 (http://www.who.int/vaccines-documents/DoxTrng/h4iip.htm, accessed 7 December 2004).

V. Galazka AM. *The immunological basis for immunization series. Module 3: tetanus*. Geneva, World Health Organization, 1993 (document WHO/EPI/GEN/93.13) (http://www.who.int/vaccines-documents/DocsPDF-IBI-e/mod3_e.pdf, accessed 7 December 2004).

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Prevention and management of sexually transmitted and reproductive tract infections

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

Standards for Maternal and Neonatal Care

1.2

The standard

All women seen during pregnancy, childbirth and the postnatal period should be given appropriate information on the prevention and recognition of sexually transmitted infections (STIs) and reproductive tract infections (RTIs). They should be assessed for STIs/RTIs and, when required, provided with prompt and effective treatment for themselves and, in the case of STIs, their partners.

Aim

To reduce maternal and perinatal morbidity and mortality and infertility caused by STIs/RTIs.

Requirements

- ☐ A national policy and locally adapted guidelines on the prevention and management of STIs/RTIs are available and are correctly implemented.
- ☐ Maternal and neonatal health care providers are available and are competent to inform women on the prevention of STIs/RTIs and to diagnose and treat these infections.
- ☐ All essential equipment, supplies and drugs for the diagnosis and management of, and counselling on, STIs are available at all levels of care.
- ☐ STI health care services are accessible and affordable to pregnant women and their partners.
- ☐ A mechanism for recording tests for, and treatment of, STIs is available.
- ☐ Health education activities are carried out to increase community awareness on the prevention and management of STIs/RTIs.

Applying the standard

Providers of maternal and neonatal health care, in particular skilled attendants, must:

- Ask the pregnant woman at each antenatal care (ANC) visit, near delivery and in the postpartum visit and in a sensitive and culturally acceptable manner, if she has any complaint which may suggest a STI/RTI.
- If the woman has a complaint suggesting a STI/RTI (such as abnormal vaginal discharge, ulcer, lower abdominal pain, etc.) assess her for signs and symptoms of reproductive tract infection, including vaginal examination.
- Perform an on-site syphilis test in all pregnant women, preferably at the first ANC visit, and at delivery or in the postpartum period (see also standard 1.3 “Prevention of mother-to-child transmission of syphilis”) if not done earlier.

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- Immediately treat or arrange treatment for the woman, her partner(s) and the infant according to the results of STI/RTI case-finding, the on-site syphilis test and examination of the baby, and refer if treatment is not available at that level of care.
- Discuss with the woman the importance of treatment for herself, her partner(s) and the baby, explain the consequences of not treating the infection, and discuss the necessity of condom use during treatment.
- Provide information on the primary prevention of STIs, condom use, signs and symptoms of STIs and the consequences for the woman and the infant of leaving infections untreated, including advice on HIV prevention and on voluntary counselling and testing for HIV infection.
- Provide follow-up and refer the woman, her baby or partner(s) in case of complications or treatment failure.
- Record the diagnosis and treatment provided in the health facility's logbook and in the client's card.

Audit

Input indicators

- National policies and strategies and guidelines on STI/RTI prevention and treatment in pregnancy are available in health facilities.

Process and output indicators

- The proportion of primary-level facilities offering appropriate STI diagnosis and treatment at primary-care level.
- The number of STI cases identified and properly treated (records in antenatal, maternity and postnatal clinics and monthly reports).
- The proportion of neonates treated for complications due to STIs.

Outcome indicators

- Prevalence of syphilis in pregnancy.
- Incidence of gonorrhoea and chlamydial infections in pregnancy.
- Perinatal mortality due to syphilis.
- Neonatal morbidity and sequelae due to STIs (ophthalmia).
- HIV transmission.
- Women's and families' awareness of the nature of STIs, how to avoid them, when to suspect them, where to go for treatment and the need to treat sexual partners.

Rationale

Burden of suffering

WHO estimates that worldwide about 340 million new cases of curable STIs occur annually, a large proportion of them among women in the reproductive age *(1)*. In addition, many millions of cases of incurable viral STIs, including an estimated 5 million HIV infections, occur annually. Most infections before conception and during pregnancy go ignored by many women, because the symptoms are mild or access to health care and drugs is limited *(1)*.

Surveys in family planning and antenatal clinics in developing countries indicate that the prevalences of syphilis, gonorrhoea and chlamydial infections range between 6% and 40% *(2)*. In many countries, STIs are among the top five conditions for which both men and women seek care, representing a considerable drain on health services. Although infection rates are similar in both men and women, the burden of serious consequences of STIs falls mostly on women and their infants. Failure to diagnose and

treat STIs at an early stage may result in serious complications and sequelae, including infertility, fetal wastage, neonatal and infant infections, as well as ectopic pregnancy, anogenital cancer and premature death *(3)*. In addition, the presence of STIs increases the risk of transmission of HIV *(1,3)*.

Efficacy and effectiveness

Effective management of STIs is key to their control, as it prevents the development of complications and sequelae, reduces the spread of these diseases in the community and offers a unique opportunity for targeted education on HIV prevention. Therefore, appropriate treatment of STI patients at their first encounter with the health services, and in particular interventions to detect and treat STIs in pregnancy, are believed to be among the most cost-effective uses of public health resources *(4)*. In developing countries, the prevalence and incidence of STIs are high and their complications are very frequent, especially in African countries *(5–8)*. Therefore, the need for providing screening and treatment at the first visit, which for a woman is often an ANC visit, is such that health providers should have skills in counselling and in identifying and managing STIs at all levels of care.

WHO suggests a number of strategies to prevent and manage STIs in health facilities in low-income countries during pregnancy and in the postpartum period. These include: case-finding; syndromic management and presumptive treatment of combined diseases; on-site RPR tests on all pregnant women; treatment of partner(s) and of the newborn baby; and individual counselling and other forms of health education. The effectiveness of some of these strategies has been reported through systematic reviews *(5,6,9–11)*.

Case-finding means identifying those at risk by (a) asking the woman if her partner(s) has/have urethral discharge or other symptoms of STI, (b) looking for signs of infection at the antenatal clinic, during labour and delivery and during postnatal visits, and (c) managing accordingly.

Syndromic management and presumptive treatment of combined diseases, such as gonorrhoea and chlamydia, or syphilis and chancroid, must be adapted to the epidemiological context and treatment policy of the country in question *(5,6)*. The strategy is motivated by the fact that different infections may coexist or even reinforce one another *(12,13)*, laboratory diagnosis is difficult, expensive and often not accurate *(12-17)*, while treatment is relatively cheap and easy *(5)*. Selected syndromic case definition includes genital ulcer, urethral discharge, vaginal discharge and lower abdominal pain. Syndromic management for genital ulcers in both sexes and urethral discharge in men has proved valid and feasible *(5)*. However, evidence from studies conducted in pregnant women is still limited. Vaginal discharge and abdominal pain algorithms have shown some limitations, particularly if applied to the management of cervical (gonococcal and chlamydial) infections. Contemporary direct examination of vaginal discharge specimen under the microscope may improve sensitivity and specificity, even though they remain far from optimal *(6)*. In addition, the equipment and skills to use microscopy are not always available at the primary health care level.

An on-site RPR test on all pregnant women has the advantages of being cheap, simple and rapid despite the relatively low specificity that is even more reduced in HIV-positive patients *(13)*. Among the different available rapid STI diagnostic tests, on-site RPR and voluntary counselling and testing for HIV infection are the only recommended in primary level facilities (for syphilis see also standard 1.3 "Prevention of mother-to-child transmission of syphilis").

In the case of an STI, the partner(s) should be treated whenever possible *(9)*. Different partner notification strategies have been used *(18)*. It should always be borne in mind that disclosing the woman's condition to her partner(s) can have a disruptive effect and can expose the woman to risk. WHO recommends preventive treatment of asymptomatic newborn babies if the mother tests positive for syphilis and as part of routine newborn care to prevent ophthalmia neonatorum (see also standard 2.5.2 "Eye care").

Recent reviews indicate that a number of antibiotics effect a "microbiological cure" of gonorrhoea and chlamydia infections and are safe for use in pregnancy *(19–21)*. However, the extent to which such a "microbiological cure" corresponds to the prevention of neonatal or postnatal infection in the mother has not been established *(19,20)*. Ceftriaxone and erythromycin are the recommended treatments for gonorrhoea and

chlamydial infection, respectively *(4,19,20)*. Amoxicillin is cheaper and better tolerated than erythromycin, and may represent an acceptable alternative to erythromycin in the treatment of chlamydial infections in pregnancy *(19)*. For gonorrhoea, the success of therapy with penicillins depends on the proportion of penicillinase-producing Neisseria gonorrhoea (PPNG), which in developing countries might be as high as 30%; it is commonly accepted that whenever PPNG prevalence exceeds 3% it is more cost-effective to treat empirically with an antibiotic active against PPNG strains than to screen and treat non-PPNG strains with ampicillin *(4)*. Individual counselling and other forms of health education aim to increase community awareness of STI transmission and the consequences for the infant if the pregnant woman is infected. Some health education strategies have undergone systematic review, mainly including studies conducted in western countries *(10,11)*. While it is clear that health education increases sexual knowledge, promotes behavioural change and shows clinical impact, the benefits are seen only when counselling includes the development of negotiation skills and the creation of a supportive environment *(11)*. Setting-specific counselling is of the utmost importance and requires specific training of health care providers.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked to the Standard	Results	Comments
5. Sangani, Rutherford & Wilson 2004 Most recent substantive amendment February 2004 **Systematic review** **1++**	Five randomized controlled trials; more than 58 000 general adult population and people with STIs Peru, South Africa, Uganda, United Republic of Tanzania Baseline risk HIV incidence 1.8% STI prevalence – minimum 1.2% – maximum 54% Safe sexual behaviour – minimum 11% – maximum 62%	To determine the impact of population-based STIs interventions on the frequency of HIV and STIs infection and quality of STI management (that is % of patient correctly examined, diagnosed, treated, compliant, cured, given partner notification card, condoms and counseling)		*Any intervention vs control*	*Syndromic management vs control*
			HIV incidence	NS [a] 2 studies, 17 925 patients	NNT [b] 146 (99-462) 1 study, 8549 patients
			STIs prevalence	min. NNT 490 (397-595) max. NNT 11 (9-13) 8 studies, 49 657 patients	NNT 52 (37-103) 1 study, 8772 patients
			Quality of treatment	——	min. NNT 146 (107-210) max. NNT 2 (1-2) 8 studies, 1786 patients
			Safer sexual behaviour	min. NNT 61 (41-114) max. NNT 11 (7-20) 4 studies, 24 762 patients	NS 1 study, 967 patients These are results
3. Sloan 2000 **Systematic review of validation studies** **2++**	32 studies conducted in antenatal, family planning, mother and child health clinics (moderate prevalence <20%- of combined gonorrhoea and chlamydia) and in STD clinics or among female sex workers (high prevalence >20% - of combined gonorrhoea and chlamydia)	To assess the ability of simple tools using a combination of risk factors, algorithms, clinical flow charts, risk scoring and simple laboratory screening tests (including WHO algorithm) to identify gonorrhoea and chlamydial infection in women in developing countries		*Sensitivity* / *False positive*	In a hypothetical group of 1000 women with moderate prevalence of infection, using the screening tools analysed, we will correctly treat 35 of 100 infected and incorrectly treat 225 of 900 uninfected
			Individual risk factors		
			– moderate prevalence	12-69% / 76-92%	
			– high prevalence	45-90% / 59-70%	
			Symptoms and signs		
			– moderate prevalence	29-45% / 77-92%	
			– high prevalence	20-58% / 59-71%	
			Simple laboratory screening tests		
			– moderate prevalence	31-52% / 89-90%	
			– high prevalence	42-48% / 35-42%	
			Algorithms and risk scoring		
			– moderate prevalence	28-54% / 82-90%	
			– high prevalence	47-78% / 54-67%	

[a] Non-significant [b] Number needed to treat

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked to the Standard	Results		Comments
10. Wald & Link 2002 **Systematic review of cohort and case-control studies** **2++**	31 studies (9 cohort or nested case-control and 22 case-control); 15 studies included women, 7 included men who have sex with men (MSM) and 14 included heterosexual men 20 studies performed in poor countries and 11 in rich countries	To determine the contribution of herpes simplex type 2 (HSV2) infection to the risk of HIV acquisition Diagnosis of HSV2: type-specific serology (no history of genital herpes)	Risk of HSV2-infected people becoming HIV-infected – longitudinal studies – case-control/cross-sectional studies Risk of HIV-infected people becoming HSV2-infected – longitudinal studies Population attributable risk [a] of HIV due to HSV2 infection HSV2 prevalence 22% (general population, USA) HSV2 prevalence 50% (Afro-American or MSM, USA) HSV2 prevalence >80% (commercial sex workers)	Relative risk 2.1 (1.4–3.2) Odds ratio 3.9 (3.1–5.1) Relative risk 4.7 (3.3–6.7) 19% 35% 47%		Success of mass treatment of bacterial STIs as a strategy for HIV prevention may be significantly limited by the high prevalence of HSV2 infection
16. Brocklehurst & Rooney 2004 Most recent substantive amendment June 1998 **Systematic review** **1++**	11 randomized controlled trials involving 1449 pregnant women with genital Chlamydia trachomatis infection Setting not specified Baseline risk of microbiological cure failure – minimum 6.6% – maximum 27.6%	To assess the effects of different antibiotics in the treatment of genital infection with Chlamydia trachomatis during pregnancy with respect to neonatal and maternal morbidity Treatment given to the woman and to the partner		*Amoxicillin vs erythromycin*	*Azithromycin vs erythromycin*	None of the studies included results on neonatal death, ophthalmia neonatorum, neonatal pneumonitis, maternal postpartum endometritis, clinical cure
			Microbiological cure	NS [b] 3 studies, 390 women	min. NNT [c] 25 (19–61) max. NNT 7 (5–18) 4 studies, 290 women	
			Side-effects sufficient to stop treatment avoided	NNT 11(10–13) 4 studies, 503 women	NNT 6 (6–11) 3 studies, 160 women	

[a] Population attributable risk: percentage of sexually transmitted HIV infections that can be attributed to HSV2 infection (calculated from longitudinal studies)

[b] Non-significant

[c] Number needed to treat

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Standards
for Maternal and Neonatal Care

Prevention of mother-to-child transmission of syphilis

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

Standards for Maternal and Neonatal Care

1.3

The standard

All pregnant women should be screened for syphilis at the first antenatal visit within the first trimester and again in late pregnancy. At delivery, women who for some reason do not have test results should be tested/retested. Women testing positive should be treated and informed of the importance of being tested for HIV infection. Their partners should also be treated and plans should be made to treat their infants at birth.

Aim

To reduce maternal morbidity, fetal loss and neonatal mortality and morbidity due to syphilis.

Requirements

- ☐ A national policy and locally adapted guidelines on syphilis prevention, management and care in pregnant women are available and are correctly implemented.
- ☐ All women have access to care during pregnancy, childbirth and the postpartum period.
- ☐ Health care providers are competent in syphilis prevention, screening during pregnancy, treatment of seropositive pregnant women and their partners, prophylaxis and treatment in the newborn, counselling on STI prevention, and how to prevent re-infection during pregnancy by promoting condom use.
- ☐ One on-site screening method is available in antenatal care (ANC) clinics and maternity wards.
- ☐ Supplies for testing are available at both ANC and laboratory level.
- ☐ Laboratory centres and facilities to ensure quality laboratory testing are available.
- ☐ Penicillin is available in the ANC clinic, maternity ward and postnatal clinic.
- ☐ A functioning referral system ensures that pregnant women who are allergic to penicillin can be referred for treatment to a higher level of care.
- ☐ An effective syphilis monitoring and information system is available for pregnant women.
- ☐ Health education activities are carried out to raise the awareness of individuals, families and communities of the importance of attending ANC clinics early in pregnancy for syphilis prevention and treatment.

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Applying the standard

Providers of maternal and neonatal health care, in particular skilled attendants, must:

- Screen all pregnant women for syphilis with on-site RPR or other available rapid test at the first antenatal visit. Screening should be done preferably before 16 weeks of gestation to prevent congenital infection, and again in the third trimester.
- Review syphilis test results at subsequent visits and at time of delivery. If the woman was not tested during pregnancy, syphilis screening should be offered after delivery.
- Treat all seroreactive women with benzathine benzylpenicillin at the recommended dosage of at least 2.4 million units intramuscularly as a single dose, after having excluded allergy to penicillin. In the case of allergy to penicillin, the attendant should desensitize and treat with penicillin if trained to do so, or refer the patient to a higher level of care.
- Advise women who test positive that their partner(s) must also be treated with the same regimen, as well as the baby as soon as possible after birth.
- Advise women who test negative how to remain negative by promoting condom use during pregnancy.
- Test for syphilis all women with a history of adverse pregnancy outcome (abortion, stillbirth, syphilitic infant, etc.) and treat accordingly.
- Treat women with clinical disease or a history of exposure to a person with infectious syphilis.
- Screen all women with syphilis for other STIs and HIV infection, and provide counselling and treatment accordingly.
- Offer voluntary counselling and testing of HIV to all women who screen positive for syphilis.
- Make plans for treating the baby at birth.
- Record testing results and treatment in the facility's logbook and in the woman's card.

Audit

Input indicators

- A national policy and locally adapted guidelines on syphilis prevention, management and care in pregnant women are available and are correctly implemented.
- The proportion of health facilities providing ANC that have a screening test for syphilis available.
- The availability of a screening test for syphilis in primary level health facilities.
- The availability of penicillin at the primary care level (including ANC and childbirth care).
- Health providers know when and how to perform the RPR test or VDRL (Venereal Disease Research Laboratory) test or the test which is available in the facility.
- Health providers know when and how to treat or refer women and their infants with syphilis.

Process and output indicators

- Coverage of RPR testing (or other used test) in pregnant women in ANC.
- Coverage of correct treatment in the ANC clinic.
- Coverage of partners tested and treated accordingly.
- Coverage of asymptomatic babies born to a positive mother who received prophylactic treatment.

Outcome indicators

- Incidence of congenital syphilis.
- Perinatal and neonatal mortality and morbidity due to congenital syphilis.
- Stillbirth rate.

Rationale

Burden of suffering

Syphilis is a chronic, often latent infection with some clinically recognizable stages. Where the disease is prevalent most cases may be asymptomatic. Although estimates vary, at least 50% of women with acute syphilis suffer adverse pregnancy outcomes. The adverse pregnancy outcomes are estimated to be distributed as follow: 50% are stillbirths or spontaneous abortion, and 50% perinatal death, serious neonatal infection or low birth weight. Mortality in infected infants can be higher than 10% *(1)*.

The more recent the maternal infection, the more likely the infant will be affected *(2)*. Transmission occurs more commonly in the last two trimesters, but the spirochete can cross the placenta at any time during pregnancy *(2)*. Clinical similarity with other congenital diseases and the limitations of diagnostic tests make it difficult to arrive at an early diagnosis in the newborn *(1)*.

Efficacy and effectiveness

Syphilis control in pregnant women through universal antenatal screening and treatment of positive cases has been established as a feasible and cost-effective intervention *(3,4)*, especially owing to the high direct and indirect cost of complications of syphilis in pregnancy *(5)* and the availability of cheap and effective therapy *(6–8)*. Nevertheless, in low-income countries a number of technical, logistical and structural constraints make case detection and treatment through antenatal screening difficult *(4,9)*, resulting in avoidable perinatal mortality *(10,11)*.

Non-treponemal tests such as RPR and VDRL are helpful indicators of infection and are cheaper and easier to perform than treponemal tests. Their sensitivity increases from primary to secondary syphilis, while their specificity is generally high in the absence of an underlying chronic condition *(7)*; they are therefore useful for follow-up after treatment *(6–8,12)*. Titres in affected persons usually rise with infection and decrease after treatment (7). The on-site RPR test is quick and simple to use, and allows treatment to be given immediately if indicated; this "fast protocol" has proven cost-effective in settings where syphilis prevalence is higher than 0.15% *(13)*. Nevertheless, these tests may give false-negative results in the affected mother or her baby *(7,14)*. RPR and VDRL can also give false-positive results owing to tissue damage from other causes, such as viral infections, vaccinations, intravenal drug abuse and chronic disease *(7)*. Ideally, non-treponemal tests should be confirmed by a treponemal test. Treponemal tests such as the Treponema pallidum haemagglutination assay (TPHA) have higher sensitivity and specificity but do not correlate with disease activity, are difficult and costly to conduct, and are thus not recommended for primary health care facilities *(7,15,16)*. Therefore, the lack of resources and higher prevalence of syphilis in less developed countries justify the treatment of all people testing seropositive with RPR *(12)*.

New treponemal-based tests for syphilis make on-site testing feasible. Simple and effective screening tests for syphilis are now available, which can even be used at the lowest levels of health service delivery. A simple strip of paper, impregnated with treponemal antigen, is used to test blood obtained by finger prick. Results are available in just a few minutes. These point-of-care diagnostic tests are accurate, affordable and simple to perform. Unlike earlier diagnostic tests, they do not require access to a laboratory or a refrigerator. In short, the new tests offer a practical alternative to older techniques. These tests have the potential to change the whole approach to syphilis testing even in isolated clinics. Because the results can be available immediately, women can be tested and receive treatment at the same visit. The new tests cost a mere US$ 0.93-1.44 per woman screened *(16)*. Although this is more costly than the previous standard tests, the new tests are in fact more cost-effective, since more women can be tested and treated in a timely manner and hence more cases of congenital syphilis prevented. It is estimated that the new rapid treponemal based tests cost only US$ 7 for each case of congenital syphilis averted *(17)*.

Adequate penicillin treatment usually ends infectivity within 24–48 hours. A Cochrane review *(18)* indicates that, while there is no doubt that penicillin is effective in treating syphilis in pregnancy and in preventing congenital syphilis, uncertainty remains about the optimal treatment regimen (dose, duration and preparation) *(18)*. Benzylpenicillin, administered parenterally in a single dose, is the preferred drug for treating pregnant women and prevent mother-to-child transmission of syphilis *(6–8,18)*.

Single dose, however, won't treat latent syphilis in pregnant women. Based on the available evidence, pregnant women with a history of penicillin allergy should be desensitized before treatment with benzylpenicillin *(8)*.

International guidelines recommend that every woman who tests seropositive for syphilis be also tested for HIV infection *(8)*. Although there is no conclusive evidence, it is possible that HIV coinfection alters the predictive value of diagnostic tests *(7,8,15)*. HIV coinfection could increase the possibility of early development of neurosyphilis and could increase the possibility of treatment failure; some guidelines therefore suggest modifying currently recommended dose regimens in the case of HIV coinfection *(6–8)* (see also standard 1.2 "Prevention and management of sexually transmitted and reproductive tract infections").

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes considered for the Standard	Results	Comments
10. Rotchford et al. 2000 **Observational study 2+**	158 pregnant women with syphilis ANC clinical setting; South Africa *Baseline risk* – Syphilis prevalence among pregnant women 9% (8–10%) – Perinatal death in offspring of inadequately treated pregnant women with syphilis 20%	To study the impact on perinatal mortality of inadequate treatment for maternal syphilis despite adequate screening *Definition* – Complete syphilis treatment: three doses of penicillin at weekly intervals (2.4 mega-units of benzathine benzylpenicillin intramuscularly) – Adequate syphilis treatment: two or more doses of penicillin – Inadequate syphilis treatment: one or no doses of penicillin	Inadequate syphilis treatment Partner notification Partner treatment Perinatal death	30% 77% 26% Adequate vs inadequate treatment NNT [a] 5 (3–13)	Despite effective screening, many pregnant women with syphilis remain inadequately treated, resulting in avoidable perinatal mortality
18. Walker 2004 Most recent substantive amendment March 2001 **Systematic review 1++**	26 studies met the criteria for detailed scrutiny; none of the studies included in the review	To identify the most effective antibiotic regimen for syphilis in pregnant women, with and without concomitant HIV infection		While there is no doubt that penicillin is effective in the treatment of syphilis in pregnancy and in the prevention of congenital syphilis, uncertainty remains about optimum treatment regimens	

[a] Number needed to treat

Study (Type & Level of evidence)	Title & author/ organization	Contents of the recommendations	Comments
8. CDC 2002 **Guideline 4**	Sexually transmitted diseases treatment guidelines Centres for Disease Control and Prevention United States	All patient who have syphilis should be tested for HIV infection. Coinfection with HIV can increase the risk of neurologic complication and the risk of treatment failure with currently recommended regimens. All women should be screened serologically for syphilis at the first prenatal visit. In setting of high syphilis prevalence, serologic testing should be performed twice during the third trimester. **Parenteral Penicillin G is the only therapy with documented efficacy for syphilis during pregnancy.** Based on available evidence, pregnant women who have a history of penicillin allergy should be desensitized and treated with penicillin	Parenteral benzylpenicillin has been used effectively for syphilis treatment and prevention for more than 50 years; nevertheless, no comparative trials have been adequately conducted to guide the selection of an optimal regimen (dose, duration and preparation)

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Prevention of congenital rubella syndrome (CRS)

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

The standard

In countries where rubella vaccine is included in the national immunization programme, women should be immunized against rubella before they become pregnant. In all countries, pregnant women with suspected rubella or exposure to rubella should be followed up and reported. In all countries, infants with suspected congenital rubella syndrome (CRS) should be assessed and reported.

Aim

To prevent congenital rubella syndrome (CRS).

Requirements

- ☐ In countries where rubella vaccine is included in the national immunization programme, a policy to provide vaccine for women of childbearing age is available; a national policy, national immunization programme and locally adapted guidelines on rubella immunization are available and are correctly implemented to ensure sustained high coverage.
- ☐ The vaccine, equipment and supplies (cold chain, auto-disable syringes, needles, etc.) needed to conduct rubella immunization are readily available in the health facilities.
- ☐ Health personnel have the knowledge and skills to determine when and how to vaccinate against rubella (including injection safety and safe waste disposal), and to advise pregnant women on prevention of rubella.
- ☐ A system is in place to monitor coverage with rubella vaccine in women of childbearing age.
- ☐ Surveillance is conducted for rubella in all age groups and for congenital rubella syndrome in children <12 months of age using appropriate case definitions. Investigation of cases of rubella in pregnancy and rubella exposure during pregnancy is given priority.
- ☐ Health education activities are carried out to increase community awareness on the importance of preventing rubella and congenital rubella syndrome.

NOTE: Recommendations in this standard are restricted to those relevant to management of women in the pre-pregnancy, antenatal and postpartum periods, and the neonate. Extensive recommendations on rubella and congenital rubella syndrome are available from the WHO Department of Immunization, Vaccines and Biologicals.

Department of Making Pregnancy Safer World Health Organization 2006

Applying the standard

Prior to pregnancy and in the postpartum period

In countries where rubella vaccine has been introduced into the national immunization schedule, health providers of maternal and child services must:

- Vaccinate children aged 12 months or older and/or schoolgirls and/or women of childbearing age against rubella, according to national policy and guidelines.

During pregnancy

In all countries, health providers of maternal and neonatal services, and skilled attendants in particular, must:

- Ensure that rubella vaccine is not offered to pregnant women and that women are advised to avoid pregnancy for one month after rubella vaccination.
- Inform pregnant women of the importance of avoiding contact with individuals with rubella.
- Report and investigate suspected rubella in pregnancy, exposure of a pregnant woman to rubella, and infants with suspected CRS.
- Be able to counsel women with confirmed rubella infection during pregnancy on the risk of fetal abnormalities and relevant laws and regulations with respect to termination of the pregancy, if they so wish.
- Report and investigate cases of suspected congenital rubella syndrome in newborns and infants promptly, as required by the national communicable disease surveillance system.

Audit

Input indicators

- National guidelines for immunization of women against rubella are available in the health facilities and are known to the health care staff.
- Rubella vaccine is available and is correctly stored.
- Health providers correctly offer and administer rubella vaccine to women as recommended by the national policy (either in mass campaigns, to adolescents in or out of school, in the workplace, at family planning clinics, in the premarital period, or postpartum).
- A system is in place to monitor rubella vaccine coverage in women.
- There is a functioning surveillance system for rubella in all age groups, with priority for investigation of suspected rubella or exposure to rubella in pregnant women, and for congenital rubella syndrome in children <12 months of age.
- Health providers advise pregnant women on rubella prevention.

Process and output indicators

- The number and proportion of women of childbearing age vaccinated against rubella by district and by month.
- The proportion of women of childbearing age who are seropositive for rubella.

Outcome indicators

- Number of cases of rubella in all age groups.
- Number of cases of rubella in pregnant women.
- Number of cases of congenital rubella syndrome in infants <12 months of age.
- Perinatal mortality due to congenital rubella.

Rationale

Burden of suffering

Rubella infection occurs worldwide. It is a mild, self-limiting infection in children and adults but its effects on the fetus can be devastating *(1)*. Fetuses infected with rubella early in pregnancy are at greatest risk of intrauterine death, spontaneous abortion and congenital malformations of major organ systems *(1)*. Typically, congenital rubella syndrome (CRS) is characterized by congenital heart disease, cataracts and deafness, but infants with CRS may also present with single or combined defects including microcephaly, microphthalmia, congenital glaucoma, meningoencephalitis, mental retardation, purpura, hepatosplenomegaly and bone disease *(1,2)*. Severe and moderate cases are recognized at birth, but mild cases with only slight cardiac involvement or deafness may not be detected until later in infancy or in childhood. CRS also has late-onset manifestations, including autism, diabetes mellitus, and thyroiditis *(3)*. A large prospective study in England and Wales that followed infants for a mean period of 26 months, found that the risk of rubella birth defects was 90% when the mother was infected in the first 11 weeks of pregnancy; 33% in weeks 11-12; 11% in weeks 13-14; and 24% in weeks 15-16 *(4)*. A study in Sweden found that the risk was 2% when the mother was infected during weeks 17-20 of pregnancy, with deafness as the sole defect *(5)*.

In 1996, WHO sponsored a global epidemiology review to assess the evidence for the occurrence of CRS in developing countries *(6)*. More than 50 developing countries were found to have conducted studies on the burden of CRS, and 14 of these provided incidence rates for number of CRS cases per 1000 live births. In the outbreak setting, the incidence of CRS was 0.6-2.2 per 1000 live births. These rates are similar to those reported in industrialized countries before vaccination was introduced. These data exclude abortion and are underestimates of congenital malformations, since only anomalies that were manifest at birth or during the first months of life were included. Altogether 43 developing countries had conducted rubella serosurveys in healthy women of childbearing age with a sample size of at least 100 women. In 12 countries ≥25% of women of childbearing age were susceptible and in 20 countries 10-24% were susceptible; high susceptibility rates indicate that there are many women at risk for delivery of an infant with CRS. Based on serosurvey data, a model was developed which predicted there were some 110,000 new cases of CRS in infants in developing countries (excluding those in the European Region) in 1996 *(7)*.

Guidelines on surveillance for rubella in persons of all ages, during pregnancy, and for CRS in infants were published by WHO *(8,9)*. Since 2000, all countries have been requested to report the annual number of cases of rubella and CRS on the WHO-UNICEF Joint Reporting Form, and these data are maintained by the WHO Department of Immunization, Vaccines and Biologicals in Geneva. In recent years, there has been enormous improvement in the global understanding of rubella epidemiology, thanks to the nearly 700 laboratories (reference, regional, national, and subnational) participating in the WHO Global Measles/Rubella Laboratory Network. WHO regions with rubella elimination targets (the Americas and Europe) have standards for reporting cases of rubella and CRS weekly or monthly. In the Region of the Americas, countries report cases of rubella and CRS weekly, with publication of these data (http://www.paho.org/english/AD/FCH/IM/Measles.htm). In the European Region, 47 of 52 countries have established rubella surveillance and these data are reported monthly (http://www.euro.who.int/vaccine).

By 2003, some 131 countries/territories (60%) out of a total of 215 countries/territories have added rubella vaccine to their national immunization system. Two WHO regions - the Americas and Europe - have established regional targets for elimination of rubella and CRS by the year 2010 *(10-14)*.

Efficacy and effectiveness

There is no specific therapy for maternal or congenital rubella infection. The value of immunoglobulin given after exposure early in pregnancy has not been established. The primary means of preventing CRS is by rubella immunization. Rubella vaccine is highly effective: a single dose of the most commonly used RA27/3 rubella vaccine strain leads to seroconversion in at least 95% of vaccinees and is thought to afford lifelong protection *(3)*. All studies that have examined cost-effectiveness of rubella vaccination have found a positive cost-benefit ratio *(15)*.
A WHO position paper on rubella vaccines

provides extensive guidance for countries *(3)*. WHO recommends that all countries should assess their rubella situation and, if appropriate, make plans for the introduction of rubella vaccine.

The primary purpose of rubella vaccination is to prevent CRS. Two approaches are recommended: *(a)* prevention of CRS only, through immunization of women of childbearing age; or *(b)* elimination of rubella as well as CRS, through immunization of young children as well as women of childbearing age *(3)*. The decision to include rubella vaccine is made at the national level and the choice of approach should be based on the level of rubella susceptibility in women of childbearing age; the burden of disease due to CRS; the strength of the basic immunization programme as indicated by routine measles vaccine coverage (which should be >80% for several years before implementing childhood rubella vaccination); infrastructure and resources for child and adult immunization programmes; assurance of injection safety; and other disease priorities.A policy of rubella vaccination of women of childbearing age only is essentially free of risks of altering rubella transmission dynamics, whereas inadequately implemented childhood vaccination runs the risk of increasing the number of cases of CRS *(16,17)*. Therefore, childhood rubella vaccine introduction is not recommended unless the national programme will be able to sustain high levels of coverage (above 80%) on a long-term basis.

Rubella vaccine should be avoided in pregnancy because of the theoretical but never demonstrated teratogenic risk *(3)*. No case of CRS has been reported in more than 1000 susceptible pregnant women who inadvertently received rubella vaccine in early pregnancy; thus, inadvertent rubella vaccination during pregnancy is not an indication for abortion *(18)*. If pregnancy is being planned, then an interval of one month should be observed after rubella vaccination.

Generally, the adverse events following vaccination with RA27/3 rubella vaccine are mild *(3)*. Common adverse events include pain, redness and induration at the site of injection. Joint symptoms are common in adolescent and adult women who receive rubella vaccine; they include arthralgia (25%) and arthritis (10%) that usually last a few days to 2 weeks. These transient reactions seem to occur in seronegative individuals only, for whom the vaccine is important. Although concerns have been raised that rubella vaccination of adult women might occasionally lead to chronic arthritis, large epidemiological studies have not supported a role for rubella vaccine in chronic joint disease *(3)*.

Persons with a history of anaphylactic reaction to neomycin should not receive rubella vaccine. Rubella vaccine should not be given to immunodeficient individuals, although it is recommended for asymptomatic HIV-positive people *(3)*. Persons with active tuberculosis should not receive rubella vaccine until treatment is established. Breastfeeding is not a contraindication to postpartum rubella vaccination. Although vaccine virus has been detected in breast milk and transmission can occur, no illness has been reported in infants *(19,20)*.

Routine antenatal rubella IgG antibody screening is not recommended for all countries, as this is expensive. Rather, laboratory resources should be directed to diagnosis of rubella in pregnant women who have suspected rubella or have been exposed to rubella. A blood specimen needs to be obtained as soon as possible after suspected rubella infection and this should be sent for rubella IgM antibody testing. Where further clarification is needed, rubella IgG antibody tests may be helpful if these are available. Research is ongoing to determine how best to use rubella avidity tests as an additional diagnostic method for pregnant women.

Neonates with CRS shed rubella virus during the first months of life, and care should be taken that these infants are not in contact with pregnant women.

*CRS congenital rubella syndrome

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked to the Standard	Results	Comments
16. Panagiotopoulos et al. 1999 **Observational study** **3**	Children, adolescents and women of childbearing age Greece	To describe the events leading to the epidemic of CRS in Greece after a major rubella epidemic	1977: MMR vaccination optional 1989: MMR vaccination (one dose) compulsory for children 1 year old 1991: MMR vaccination (two doses) compulsory (at 15 months and 11–12 years) Average coverage with MMR in the 1990s: 50–60% Proportion of pregnant women susceptible to rubella during the 1980s: 12% (1980) → 36% (1990) Rubella epidemic: 1993 (Feb.–June); 64% of cases were 15 years old or over CRS epidemic: 1993 (Sept.–Dec.); 25 cases serologically confirmed with 7 deaths Rubella and CRS surveillance were passive, with likely high rates of underreporting	With low vaccination coverage, the immunization of children aged 1 year against rubella without any immunization of women in the postpartum period or in the childbearing age carries the risk of increasing the occurrence of CRS	
18. Vynnycky, Guy Cutts 2003 **Modelling study**	Dynamic transmission model		Assumes that MMR vaccination is restricted to young children	Model indicates that in countries with a medium to high force of rubella infection, levels of MMR * vaccine coverage <80% would lead, in the long-term, to an increase in CRS	Highlights the risks of private sector MMR vaccination. Concludes that systematic rubella vaccination should be conducted among adult women
15. Hinman, Irons & Kandola 2002 **Systematic review of economic studies** **1+**	Different populations (children, women of childbearing age, infants) in different parts of the world 12 studies in developed countries; 10 studies in developing countries	To investigate whether the incorporation of rubella vaccination into immunization programmes in developing countries is economically justified	Annual cost of treating a CRS case Lifetime cost of treating a CRS case Benefit-to-cost ratio	Average US$ 2000–14 000 Average US$ 50 000–64 000 Always positive, ranging from 2 to 40 depending on the strategy adopted	Only results from developing countries reported here
7. Cutts & Vynnycky. 1999 Modelling based on serological data	Rubella serosurvey data from developing countries abstracted for preparation of a simple catalytic model to estimate CRS incidence	To model the incidence of CRS in developing countries of different WHO regions (excluding Europe) in 1996	Estimated mean number of new cases of CRS in infants born in 1996 in developing countries, by WHO region	Africa 22,471 Americas 15,994 E. Mediterranean 12,080 SE Asia 46,621 W Pacific 12,634	Mean global total of 110,000 CRS cases in developing countries indicates CRS is an under-recognized health problem in many developing countries

* Measles, mumps and rubella

Study (Type & Level of evidence)	Population & Setting	Objective & intervention	Outcomes linked to the Standard	Results	Comments
6. Cutts, Robertson, Diaz-Ortega & Samuel 1997 **Systematic review of disease burden studies from developing countries** **1+** **Systematic review of serosurveys on rubella immunity of women of childbearing age in developing countries** **1+**	CRS surveillance studies with incidence data: 14 studies from 12 developing countries Rubella (serum IgG) susceptibility in 45 developing countries, each of which had at least one serosurvey of healthy women with a sample size >100	To assess the incidence of CRS among infants in developing countries To assess the potential risk of CRS	Annual incidence of CRS per 1000 live births Rubella susceptibility in women of childbearing age	Range from 0.6 - 2.2 CRS cases /1000 live births in the outbreak setting >25% susceptible in 12 countries; 10-24% susceptible in 20 countries; <10% susceptible in 13 countries	Incidence comparable to that reported by industrialised countries in the pre-vaccination era Review limited to developing countries, since all industrialized countries had already adopted rubella vaccine

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Standards for Maternal and Neonatal Care

Prevention of neural tube defects

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

The standard

All women, from the moment they begin trying to conceive until 12 weeks of gestation, should take a folic acid supplement. Women who have had a fetus diagnosed as affected by a neural tube defect (NTD) or have given birth to a baby with NTD should receive information on the risk of recurrence, be advised on the protective effect of periconceptional[1] folate supplementation and be offered high-dose supplementation.

Aim

To prevent NTDs and other congenital malformations in the fetus.

Requirements

- ☐ A national policy and locally adapted guidelines on folic acid supplementation are available and are correctly implemented.
- ☐ Health providers are competent in the following areas: the risk of folic acid deficiency; the benefits of folic acid supplementation before conception and during early pregnancy; correct supplement dosages; and the importance of advising pregnant women to take folic acid before conception and during the first trimester of pregnancy.
- ☐ Folic acid is available and affordable to women.
- ☐ A method to record the preventive treatment provided is in place.
- ☐ Health education activities are conducted to raise the awareness of women and of the community on the importance of taking folic acid supplements in the periconceptional period.

Applying the standard

Health providers in antenatal and family planning clinics must:

- Advise women trying to conceive to take a dose of 400 µg folic acid daily, starting two months before the planned pregnancy.
- Advise women who have not been supplementing their diet and who suspect themselves to be pregnant to begin taking 400 µg folic acid daily and to continue until they are 12 weeks pregnant.
- Counsel pregnant women who have previously had a baby with NTD or who have diabetes or who are under anticonvulsant treatment about the increased risk of a future baby being affected, and advise them to take 5 mg folic acid daily and increase their food intake of folate.
- Record the treatment given in the maternal card.
- Record cases of NTD, in accordance with local guidelines, in the logbook and in the woman's record.

[1] Before pregnancy and in the first three months of pregnancy.

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Audit

Input indicators

- Policy and local guidelines on folic acid supplementation are available in clinics.
- Training on folic acid supplementation and NTDs is provided to health staff of antenatal and family planning clinics.
- Information on the benefits of increasing folic acid intake is available and displayed in antenatal and family planning clinics.

Process and output indicators

- The proportion of ANC cards reporting whether or not a woman has taken folic acid prior to conception and/or during the first 12 weeks of pregnancy.
- The proportion of women reporting taking folic acid supplements during the periconceptional period.

Outcome indicators

- Incidence of neural tube defects in the newborn.

Rationale

Burden of suffering

NTDs represent one of the most common congenital malformations in neonates worldwide *(1)*. They constitute a heterogeneous group of disorders that occur during the first weeks of gestation, involving specific elements of the neural tube and its derivatives *(1,2)*. The incidence of NTDs in the general population varies from 1 per 1000 pregnancies in the USA to 12 per 1000 in parts of Ireland and Wales and among Indian Sikhs and certain ethnic groups in Egypt *(1,2)*.

The exact cause of NTDs is not known; over 95% occur in couples with a negative family history *(1,2)*. Nevertheless, the risk of recurrence is 1 in 33 couples with one affected pregnancy and 1 in 10 for those with two affected pregnancies *(1)*. Sisters of women with an affected child have a 1 in 100 risk and sisters of a man with an affected child have a 1 in 300 risk *(1)*. Folic acid and zinc deficiencies have been proposed as possible causes. Known factors associated with higher risk include maternal diabetes, alcohol abuse by the mother, aminopterin ingestion and antenatal X-irradiation *(1)*. Suspected contributing factors are anticonvulsant therapy, maternal hyperthermia, antenatal exposure to rubella and hallucinogen ingestion *(2)*.

Efficacy and effectiveness

Folic acid supplementation before conception and during the first trimester of pregnancy is one of the few public health interventions effective in reducing the risk of NTDs *(2–5)*. Controlled randomized clinical studies showed that folic acid supplementation during the perinatal period reduced the risk of recurrence in women who had previously borne a child with NTDs *(3)*. The evidence indicates that periconceptional folate supplementation reduces the incidence of NTDs in the general population *(2,4,5)*. The reduction is similar for first and recurrent cases of defects. Owing to the heterogeneous etiology of NTDs, however, the risk cannot be eliminated by this intervention.

Among other factors possibly associated with NTDs is a genetic mutation involving the methylenetetrahydrofolate reductase gene (the C677T allelic variant) *(6)*, but it is not clear if the occurrence of NTDs among the offspring of women with such a mutation is reduced by a higher intake of folate *(7)*. It is also unclear whether there is a link between vitamin B_{12} deficiency and NTDs *(8)*, but any future supplementation scheme could also include this vitamin *(4,9)*. Folate supplementation could be especially important in women undergoing folate-depleting treatment, such as with antiepileptic drugs *(2,10)*, aminopterin, methotrexate, sulfamethoxazole or pyrimethamine, but further research is needed to reach a firm conclusion.

Randomized trials, supported by many observational studies, indicate that periconceptional use of folic acid in multivitamin supplements reduces the overall risk of birth defects, even after excluding NTDs *(11)*. This overall reduction seems to be due to a reduced risk of cardiovascular anomalies (reduction of 34-58% in different studies), orofacial defects (reduction of

30%), limb deficiencies (reduction of 46-81%), urinary defects (reduction 40-83%), and onphalocele and imperforate anus.

Folate supplementation has been associated with a small increase in multiple gestation, but a recent systematic review does not support this finding *(3)*. No harmful effects of folate supplementation have been demonstrated, either in the short or the long term *(2,12)*. However, if an increase in multiple gestation is confirmed, it might be necessary to reconsider the benefits of folate supplementation. The effectiveness of the intervention, both in developed and in less developed countries, depends on informing women of childbearing age and on the ability to plan a pregnancy *(13)*. Possible alternatives or complements to giving folate supplements as pills could be information on changing the diet *(7,14)* and food fortification *(5)*, although these interventions alone are less effective in increasing plasma folate levels owing to lower bioavailability *(5,7,14)*. If food fortification is employed, it is recommended that a higher level of folate (350 µg/100 g food) be used *(15)*. In the North American setting, high-dosage fortification is considered to have a high benefit-to-cost ratio *(15)*. It is still unclear as to whether NTDs can be prevented by increasing the consumption of foods rich in folates. There is also uncertainty as to the benefits and risks for the whole population from fortification of basic foods with folate; this is linked mainly to the possibility of masking pernicious anaemia in elderly patients who receive folate supplementation *(4)*.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked to the standard	Results	Comments
2. Lumley et al. 2004 Most recent substantive amendment April 2001 **Systematic review** **1++**	4 trials, 6425 women Australia, Canada, France, Hungary, Ireland, Israel, United Kingdom, countries of the former USSR Baseline risk of NTD – minimum 0.2% – maximum 7.8%	To assess the effects of periconceptional increased consumption of folate or multivitamins on the prevalence of NTD The dose of folate in the trials ranged from 0.36 to 4 mg/day	NTD incidence – minimum – maximum Miscarriage Stillbirth Multiple gestation	Folate + vitamin supplement vs control NNT [a] 694 (575–1190) NNT 18 (15–30) 4 studies, 6424 women NS [b] 3 studies, 7600 women NS 3 studies, 7600 women NS 3 studies, 6241 women	Two trials comparing folate alone vs vitamins alone showed that reduction in NTD is due to folate and not to vitamins
8. Ray & Blom 2003 **Systematic review of case control studies** **2++**	17 case-control studies were included, mean sample size 33 cases and 93 controls.	To investigate the association between low maternal B12 and increased risk of fetal NTD	NTD	Low level vs high level of serum vitamin B12 Odds ratio 0.9–13.3 (0.4–65.5)	There seems to be a moderate association between low maternal vitamin B12 status and the risk of fetal NTDs; no final conclusions can be drawn

[a] Number needed to treat [b] Non-significant

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II. *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice*. Geneva, World Health Organization, 2003 (http://whqlibdoc.who.int/publications/2003/924159084X.pdf, accessed 7 December 2004).

This document is part of the Standards for Maternal and Neonatal Care developed by the Department of Making Pregnancy Safer, World Health Organization.

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Standards for Maternal and Neonatal Care Steering Committee
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This standard was developed by Ornella Lincetto with valuable inputs from members of the above steering committee and WHO Regional Offices and reviewed at a Technical Consultation in Geneva, 14-16 October 2002. Members of the Center for evaluation of effectiveness of health care-CeVEAS (Simona di Mario, Vittorio Basevi, Gianfranco Gori, Daniela Spettoli, Dante Baronciani and Nicola Magrini) developed the table of evidence and provided additional insightful review of the evidence section. We thank Bruno de Benoist for reviewing final draft, Frank Teckston for the editing and Duke Gyamerah for the layout.

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Provision of effective antenatal care

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

The standard

All pregnant women should have at least four antenatal care (ANC) assessments by or under the supervision of a skilled attendant. These should, as a minimum, include all the interventions outlined in the new WHO antenatal care model and be spaced at regular intervals throughout pregnancy, commencing as early as possible in the first trimester.

Aim

To prevent, alleviate or treat/manage health problems/diseases (including those directly related to pregnancy) that are known to have an unfavourable outcome on pregnancy, and to provide women and their families/partners with appropriate information and advice for a healthy pregnancy, childbirth and postnatal recovery, including care of the newborn, promotion of early exclusive breastfeeding and assistance with deciding on future pregnancies in order to improve pregnancy outcomes.

Requirements

- ☐ A national policy and locally adapted guidelines are in place that protect the rights of all women, regardless of their socioeconomic status or place of residence, to access good quality ANC services.
- ☐ National evidence-based guidelines exist detailing the essential minimum components of ANC, in line with the country epidemiological profile and country priorities and based on WHO guidelines and recommendations.
- ☐ The health system ensures that sufficient skilled attendants are recruited and deployed to be able to provide all women with good quality ANC.
- ☐ Services and care are organized to ensure that ANC is available and acceptable to all the women in the service area, regardless of social, religious or ethnic background.
- ☐ The health system ensures that all necessary equipment and drugs to provide essential ANC are in place and are in good working order.
- ☐ Each pregnant woman receives an individual record card on which details of ANC are given, including all action taken, advice and treatment given, the results of all tests and examinations and proposed plans for the actual birth; ideally, this record is held by the woman.
- ☐ All skilled attendants are linked to, and have the capacity to refer any pregnant woman to, a facility capable of managing obstetrical and neonatal complications.
- ☐ National or locally-adapted evidence-based protocols and/or guidelines for the management of pregnancy-related complications are available and are widely distributed to all skilled attendants and other health care providers offering ANC.

- ☐ National and local health education activities and programmes are in place to promote the need for all women to access ANC, and for all pregnant women, their partners and families to make a birth and emergency preparedness plan.

Applying the standard

Skilled attendants, and other health care providers offering antenatal care services, must:

- Organize ANC services, including scheduling clinic attendance where appropriate, to ensure that all pregnant women in the locality can access the services.
- Work with community leaders and other influential parties to ensure that the community understands the benefits of ANC and especially the need for early ANC.
- Apply accurately all components of the national antenatal care model identified for the period of gestation in question, or as outlined by WHO *(1,2)*, and record these on the home-based ANC record card.
- Provide appropriate health education to all pregnant women and their partners and families, including healthy lifestyles, healthy diet, smoking cessation where required, preparation for parenthood, relaxation therapy and/or other activities as required, such as exercises to prepare the woman for the process of birth.
- Ensure that ANC is conducted in a suitable environment that affords privacy.
- Provide information and counselling to both partners on postpartum family planning methods.
- Ensure that, at some point in the pregnancy, all women have the opportunity to discuss their pregnancy and personal concerns confidentially, with or without the presence of the partner.
- Refer all pregnant women requiring specialized medical care/treatment and all women with signs of complications of pregnancy.
- Refer women with social and/or psychological problems or concerns to an appropriate advice/service agency.
- Record findings on the maternal card.

Audit

Input indicators

- A national ANC policy and locally adapted guidelines are in place.
- The availability of skilled ANC attendants.

Process and output indicators

- The proportion of pregnant women having at least one ANC visit.
- The proportion of pregnant women having four or more ANC visits.
- The proportion of pregnant women able to access ANC within a specified distance or time span.
- The proportion of pregnant women immunized against tetanus.
- The proportion of pregnant women screened for syphilis.
- The proportion of pregnant women with a written birth plan by 37 weeks of pregnancy.

Outcome indicators

- Proportion of pregnant women satisfied with the ANC services they receive, increased from the baseline value.
- Proportion of pregnant women with a major complication of pregnancy directly referred by the skilled attendant, increased from the baseline value.
- Proportion of pregnant women referred who are assessed by the referral facility as having received appropriate first-line management as identified by WHO *(2)*, increased from the baseline value.

Rationale

Burden of suffering

Many maternal and perinatal deaths occur in women who have received no ANC. Nevertheless, true progress has been made globally in terms of increasing access and use. A recent study on antenatal care estimated that worldwide only 70% of women ever receive any ANC, whereas in industrialized countries more than 95% of pregnant women receive ANC *(3)*.

Efficacy and effectiveness

Epidemiological studies have demonstrated the benefits of ANC in reducing maternal and perinatal complications, although the exact components and timing of such ANC has been difficult to demonstrate *(4)*. This uncertainty leads to the adoption of antenatal practices that are not comparable and are largely inconsistent between and within countries *(5,6)*. There is evidence to show that certain components of care appear to be more critical than others, whilst some long-held traditional components have little scientific basis *(4,7)*. Also, there is growing agreement that ANC should be limited to a small number of specific tests carried out at certain critical times in the pregnancy *(4,8,9)*. The optimum number of ANC visits for countries with limited resources is still the subject of considerable debate, the problem being linked not only with effectiveness but also with costs and other barriers to ANC access *(5)*. Nevertheless, a recent systematic review *(7)* showed that essential interventions required by healthy women with no underlying medical problems can be provided over four visits at specified intervals. The results of the review also revealed that women in developed countries receiving ANC through this four-visit model were less satisfied and felt their expectations were not met, although they did not perceive that the care they received was of lower quality *(4,8)*. The results of this review prompted WHO to define a

Box 1. The essential elements of care in pregnancy

The essential elements of care in pregnancy are as follows.

- Pregnancy surveillance of the woman and her unborn child.
- Preventive measures, including immunization (especially with tetanus toxoid) and screening for underlying conditions and diseases such as anaemia, malaria, sexually transmitted infections (of which syphilis is particularly important owing to its negative impact on maternal and neonatal health and the links to a high incidence of stillbirth and low birth weight), HIV infection, and underlying mental health problems and/or symptoms of stress or domestic violence.
- Recognition and management of pregnancy-related complications.
- Recognition and treatment of underlying or concurrent illness or disease.
- Advice and support to the woman and her family in developing a birth and emergency preparedness plan.
- Health education and promotion for the woman and her family:
  - to increase awareness of maternal and neonatal health needs and self-care during pregnancy and the postnatal period, including the need for social support during and after pregnancy;
  - to increase health in the home, including healthy lifestyles, healthy diet, health and safety/injury prevention, and support and care in the home (including adherence to advice on prophylactic treatments such as iron supplementation, and use of insecticide-treated bednets);
  - to support care-seeking behaviour, including recognition of danger signs for the woman and the newborn;
  - to promote postpartum family planning/birth spacing; and
  - to prepare emotionally and physically the pregnant woman and her partner and, where required, supporters for birth.

new model of ANC *(1)*, the essential elements of which are outlined in Box 1.

Evidence suggests that, given the need for early identification of underlying problems to ensure efficacious treatment, the first ANC visit should be as early as possible in pregnancy, preferably in the first trimester *(4)*. At this visit, there should be a general assessment of the woman's health, with appropriate remedial action or treatment of underlying medical conditions, if required, to try to ensure that the woman is as healthy as possible during pregnancy and for birth *(4)*. It is also suggested that, given the lack of sensitivity in predicting problems, especially those that occur during or around birth, all pregnant women should be encouraged to make a birth and emergency preparedness plan (see *Standard 1.9 Birth and emergency preparedness in antenatal care* for further details). An antenatal assessment at around 37 weeks or near the expected date of confinement/birth is also advisable, to ensure that appropriate action is taken to prevent problems. Such appropriate action should include advice on avoiding postmaturity and the identification of malpresentations, especially breech presentation, in which case an attempt should be made at external cephalic version *(9)*.

Thus, there is general consensus that all women with an uncomplicated pregnancy should have a minimum of four visits, as outlined by WHO *(1,2)*.

Evidence also indicates that good record-keeping is essential to facilitate appropriate decision-making and interventions. These records should be available at all times. The best mechanism to ensure that essential information is always available is for the record to stay with the woman. Ensuring the woman can hold her own records is also a way to encourage women to feel involved in their care. A number of studies have shown the benefits of hand-held or home-based antenatal care records *(10,11)*. Women who hold their own records are more likely to keep follow-up appointments, to ask questions about their health and to feel in control of their pregnancy *(11)*. Therefore, home-based or hand-held records are recommended. Countries may design their own antenatal care records, but should ensure that all the essential information is readily available to the caregiver. A prototype form is included in the new WHO model of ANC *(1)*.

Finally, family and community membership has been shown to be a major determinant in access to antenatal care services *(12)*. Lone or unsupported pregnant women, especially adolescents, therefore need services that are specifically targeted to their needs; service providers should do all they can to seek out such women and take the services to them, if they are unable or unwilling to attend a clinic.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked to the Standard	Results	Comments
7. Villar et al. 2004 Most recent substantive amendment, August 2001 **Systematic review** **1++**	10 trials, 7 conducted in developed countries (individual randomization trials) and 3 in developing countries (cluster randomization trials) Over 60 000 pregnant women attending ANC clinics and considered to be at low risk of developing complications during pregnancy and labour	To assess the effects of ANC programmes for low-risk women Intervention: ANC programme with reduced frequency and timing of visits compared with standard frequency and timing of visits; ANC programme based on midwife support versus programme including obstetric/ gynaecological personnel	Neonatal and maternal outcomes Satisfaction with care received	*Fewer vs standard number of visits* No difference in any of the negative maternal and perinatal outcomes reviewed Trials from developed countries: women can be less satisfied with the reduced number of visits and feel that their expectations of care are not fulfilled ANC by a midwife/ general practitioner vs obstetric/ gynaecological personnel Improved perception of care by women No difference in clinical effectiveness	
13. Bricker & Neilson 2003 Most recent substantive amendment, October 1999 **Systematic review** **1++**	7 trials recruiting 25 036 women in late pregnancy (after 24 weeks' gestation) Australia, New Zealand, Norway, United Kingdom, USA *Baseline risk* Post-term delivery rate – minimum 0.4% – maximum 4.6%	To assess the effects of routine late pregnancy ultrasound (after 24 weeks' gestation), in women with either unselected or low-risk pregnancies, on obstetric practice and pregnancy outcome Intervention: routine ultrasound versus no or selected or concealed ultrasound after 24 weeks of gestation	Caesarean section Instrumental delivery Post-term delivery (>42 weeks) Apgar score <7 at 5 minutes Perinatal mortality	*Routine vs no or selective ultrasound* NS [a] 3 studies, 3886 women NS 4 studies, 19 037 women min. NNT [b] 809 (597–1320) max. NNT 72 (53–119) 2 studies, 1751 neonates* NS 3 studies, 3891 neonates NS 6 studies, 22 278 neonates	*Significant data only from one large study

[a] Non-significant [b] Number needed to treat. (95% confidence interval)

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Malaria prevention and treatment

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

The standard

In malarious areas, all pregnant women should sleep under an insecticide-treated bednet (ITN). In addition, in areas of stable transmission of falciparum malaria, all pregnant women should be given intermittent preventive treatment (IPT). Pregnant women suspected of having malaria should be assessed and treated in accordance with national protocols. In the postnatal period, both the mother and the baby should sleep under an insecticide-treated bednet.

Aim

To reduce the incidence of negative outcomes in women and their babies due to malaria during pregnancy.

Requirements

- ☐ A national policy and guidelines on prevention, diagnosis and treatment of malaria in pregnancy are available and are correctly implemented.
- ☐ Health providers have been trained and are competent in: malaria-related risks during pregnancy; administration of IPT; advising on the use of ITNs; and diagnosis and treatment of malaria during pregnancy, delivery and the postpartum period.
- ☐ Women have access to maternity care, particularly in the antenatal period.
- ☐ Antimalarials for IPT and treatment of symptomatic malaria and ITNs are available and affordable.
- ☐ Health education activities to increase community awareness of malaria prevention and treatment are carried out.

Applying the standard

Providers of maternal and neonatal health care must:

- In areas of stable falciparum malaria transmission give all pregnant women at least two doses of IPT after quickening (2nd and 3rd trimester) and advise them to seek care in case of fever. Doses should be given at an interval at least one month. To ensure that women receive at least two doses, IPT should be carried out during routine visits to the antenatal clinic. WHO currently recommends a schedule of four antenatal clinic visits, three of them after quickening.
- In malaria-endemic areas, encourage all pregnant women to sleep under an ITN from as early in pregnancy as possible and to continue using an ITN during the postpartum period, together with their babies. They should also be encouraged to seek care if the baby shows danger signs such as fever or difficult breathing.
- Assess any pregnant woman with anaemia and/or fever who has been exposed to malaria and treat her for malaria according to country guidelines.

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- Give advice on preventive measures to all pregnant women living in or travelling to malarious areas.
- Record the treatment provided in the woman's antenatal care card.

Audit

Input indicators

- A national policy and standards and locally adapted guidelines on malaria in pregnancy are available in health facilities.
- Antimalarial drugs and ITNs are available in antenatal clinics and/or accessible through the commercial market.

Process and output indicators

- Proportion of pregnant women receiving IPT.
- Proportion of pregnant women using ITN.
- Appropriate case management of malaria illness.

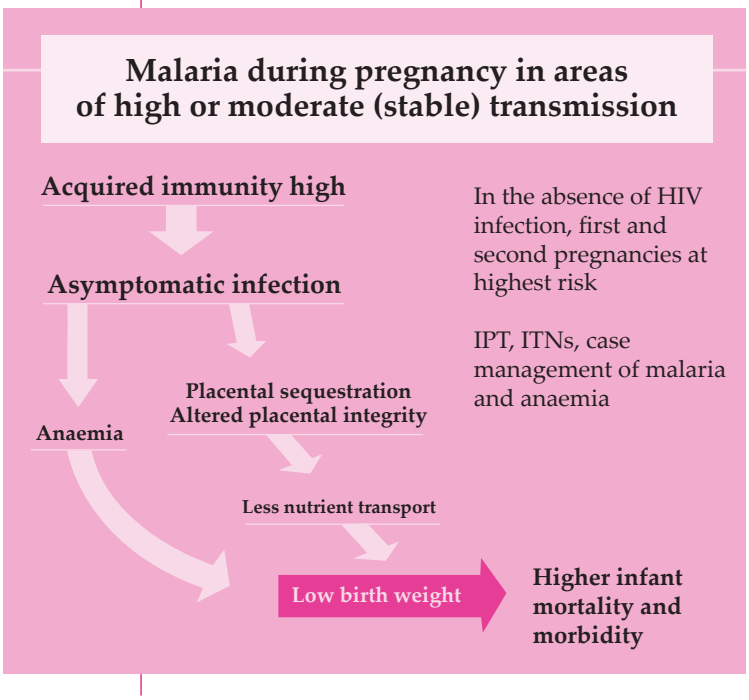
Outcome indicators

- Incidence of complications (anaemia, severe malaria, abortion, preterm delivery) in the mother.
- Perinatal/neonatal mortality and morbidity (stillbirth, premature birth, low birth weight, anaemia, congenital malaria).
- Awareness of women and their families of the risk of malaria for themselves and their babies.

Rationale

Burden of suffering

The deleterious effects of malaria infection during pregnancy on maternal, fetal and infant health are caused chiefly by *Plasmodium falciparum*. In Africa, at least 25 million pregnancies are threatened by malaria each year, resulting in an estimated 2–15% of maternal anaemia. Maternal malaria infection accounts for almost 30% of all the causes of low birth weight that can be prevented during pregnancy. Maternal malaria infection is estimated to account for 3–8% of all infant deaths *(1)*. In areas of high and moderate (stable) malaria transmission, adult women acquire immunity, and most malaria infections in pregnant women are asymptomatic. Nevertheless, these asymptomatic infections contribute to the development of severe anaemia in the mother, resulting in an increased risk of maternal mortality and morbidity. The health of the fetus and infant is affected by maternal infection during the second half of pregnancy. Malarial infection of the placenta and maternal anaemia due to malaria contribute to low birth weight and preterm birth, which lead to higher infant mortality and morbidity and impaired development of the child. Stable transmission predominates in Africa south of the Sahara, and consequently this region bears the greatest burden of malaria infections during pregnancy. In these areas of high or moderate (stable) malaria transmission, the ill-health effects are particularly apparent in the first and second pregnancies exposed to malaria *(2)*.



In areas of epidemic and low (unstable) malaria transmission, adult women have no significant level of immunity and will develop clinical illness if they have parasitaemia. Pregnant women with no immunity are at risk of dying from severe malarial disease and/or experiencing spontaneous abortion, premature delivery, low birth weight or stillbirth. All pregnant women are at similar risk for malarial infection, irrespective of parity. Abortion is common in the first trimester, and prematurity is common in the third trimester. Other consequences during pregnancy commonly associated with *P. falciparum* infection include hypoglycaemia, hyperpyrexia, severe haemolytic anaemia and pulmonary oedema *(2)*.

HIV infection diminishes a pregnant woman's ability to control *P. falciparum* infections. The prevalence and intensity of malaria infection during pregnancy is higher in women who are HIV-infected. Women with HIV infection are more likely to have symptomatic disease and to be at increased risk of malaria-associated adverse birth outcomes. Multigravidae with HIV infection are similar to primigravidae without HIV infection in terms of their susceptibility to and negative consequences of malaria infection.

The effects of the other three parasites that cause malaria in humans (*P. vivax*, *P. malariae* and *P. ovale*) are less clear. There is a need for studies to better define the impact of *P. vivax* infection on the health of pregnant women and neonates.

Efficacy and effectiveness

IPT seems to be a feasible and effective strategy for reducing the risk of severe anaemia *(2,3)*, placental and peripheral parasitaemia *(2–5)*, low birth weight *(4–6)* and perinatal death *(3)* in primigravidae and secundigravidae living in malaria-endemic areas, and it is more efficient than selective case management of clinical malaria *(5)*. Currently, the most effective drug for IPT is sulfadoxine-pyrimethamine, because of its safety for use during pregnancy, efficacy in reproductive-age women and feasibility for use in programmes as it can be delivered as a single-dose treatment under observation by the health worker *(1,2,5,7)*. Nevertheless, a study in Malawi showed that, even if IPT is adopted as national policy, obtaining a wide coverage of pregnant women and assuring effective implementation is not easily achievable *(8)*. Cost–effectiveness studies of IPT are based on the assumption that ANC coverage is relatively high and will further increase. Consequently, ANC represents the best entry point for reaching pregnant women with this intervention *(7,9,10)*.

Studies in Kenya and Malawi have demonstrated that more doses of IPT may be beneficial in HIV-infected pregnant women. In such women, three doses after quickening may be needed to derive benefits similar to those obtained in uninfected women with two doses over the entire pregnancy *(5)*. No adverse effects are apparent, in either mothers or their infants, of IPT given in the second and third trimesters of pregnancy *(2,5)*.

The use of an ITN by a pregnant woman benefits the woman and her family. Studies on adults and children indicate that ITNs reduce the risk of malarial infection and overall mortality *(11,12)*. In highly malarious western Kenya, studies indicate that women protected by ITNs every night in their first four pregnancies delivered approximately 25% fewer babies who were either small for gestational age or born prematurely than women who were not protected by ITNs *(13)*. In endemic areas, priority should be given to developing antenatal clinic-based programmes that provide both IPT and ITNs, along with other essential preventive interventions. ITNs reduce human–vector contact by physically excluding mosquitoes and either killing or repelling them, thereby driving them from the vicinity of sleepers. Because of their documented effect in several studies on reducing malaria-related illness and death, ITNs are being promoted for use through both public and private sector outlets in African countries.

ITNs are still recommended for areas with unstable malaria transmission, whereas IPT cannot be recommended for these areas because of lack of evidence. Studies should be carried out in areas of low/unstable malaria transmission and where the parasite is *P. vivax*.

One randomized controlled trial specifically assessed the willingness of people to pay for ITNs in an Indian rural area *(14)*. Some 20% of the population was unwilling to pay any amount of money for ITNs. Of those willing to pay, almost 30% preferred to do so on an instalment basis and to pay no more than €1–2 per net.

Operational problems relate, among others, to the difficulty to implement IPT in areas of low ANC coverage *(7)*.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked for the Standard	Results	
3. Garner & Gülmezoglu 2003 Most recent substantive amendment, July 2002 **Systematic review** **1++**	14 trials, 8768 women (in some studies only primigravidae included) 13 trials in African countries, 1 in Thailand *Baseline risk* Severe antenatal anaemia – minimum 4% – maximum 24% Perinatal death – minimum 11/1000 – maximum 178/1000 Low birth weight – minimum 9% – maximum 34%	To assess drug effectiveness in preventing clinical malaria and its consequences among pregnant women living in malarious areas Interventions: antimalarial drug regimens described as "prophylaxis" (typically chloroquine given weekly) or as "presumptive treatment" (typically SP [a] given intermittently)		**Malaria prophylaxis vs control**	
				1st and 2nd pregnancies only	*All women*
			Maternal mortality	NS[b] 2 studies, 772 women	NS 1study, 1049 women
			Severe antenatal anaemia (haemoglobin <8g/l)	min. NNT [c] 63 (48–108) max. NNT 11 (8–19) 4 studies, 2809 women	—
			Antenatal parasite prevalence	NNT 5 (5–7) 6 studies, 2495 women	NNT 10 (7–33) 2 studies, 328 women
			Perinatal death	min. NNT 337 (193–9090) max. NNT 21 (12–562) 3 studies, 1986 neonates	NS 4 studies, 2890 neonates
			Low birth weight	min. NNT 25 (20–37) max. NNT 6 (5–10) 6 studies, 1947 neonates	NS 2 studies, 1438
11. Lengeler 2004 Most recent substantive amendment, January 2004 **Systematic review** **1++**	14 cluster and 8 individual randomized controlled trials, more than 150 000 people Africa, South America, Middle Asia and South-East Asia	To assess the effects of ITNs or curtains in preventing malaria Bednets were treated with synthetic pyrethroid insecticide at different concentrations	Child mortality from all causes	*ITNs vs all controls* Relative risk 0.83 (*0.76–0.89*) 5 studies, 149 221 children	
			Lives potentially saved in children 1–59 months	5.5/1000 children protected/year	
			Severe malaria (area of stable malaria)	45% protective efficacy	
			Average haemoglobin level in children	Increased by 1.7% packed cell volume	

[a] Sulfadoxine-pyrimethamine

[b] Non-significant

[c] Number needed to treat. (95% confidence interval)

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Iron and folate supplementation

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

The standard

All pregnant women in areas of high prevalence of malnutrition should routinely receive iron and folate supplements, together with appropriate dietary advice, to prevent anaemia. Where the prevalence of anaemia in pregnant women is high (40% or more), supplementation should continue for three months in the postpartum period.

Aim

To prevent and treat iron deficiency anaemia in women during pregnancy and in the postpartum period in order to improve maternal and perinatal health.

Requirements

- ☐ A national policy and locally adapted guidelines on iron and folate supplementation are in place and are correctly implemented.
- ☐ Health care providers of maternal and neonatal care are competent in: the importance of iron supplementation during pregnancy and the postpartum period; the correct dosage and duration of supplementation for the prevention and treatment of anaemia; anaemia detection in pregnant women; and when to refer women for further diagnosis and treatment.
- ☐ Iron and folate supplements are available at all levels of care.
- ☐ There is a functioning referral system that ensures timely referral of pregnant women for monitoring and treatment, especially in the case of severe anaemia.
- ☐ A mechanism is in place for recording cases and care of anaemia.
- ☐ Health education activities are carried out to increase awareness among women and in the community of the importance of iron and folate supplementation in pregnancy.

Applying the standard

Health providers, in particular skilled attendants, attending women during antenatal and postpartum visits must:

- Give all pregnant women a standard dose of 60 mg iron + 400 µg folic acid daily for 6 months or, if 6 months of treatment cannot be achieved during the pregnancy, either continue supplementation during the postpartum period or increase the dosage to 120 mg iron during pregnancy.
- Where the prevalence of anaemia in pregnancy is over 40%, advise the woman to continue the prophylaxis for three months in the postpartum period.
- Give iron supplementation even if folic acid is not available.
- Examine or screen all women for anaemia during antenatal and postpartum visits.

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- Treat anaemia with doses of 120 mg iron daily for three months.
- Follow up in two weeks to check clinical progress, test results and compliance and again four weeks later all women with severe anaemia that have been treated with iron and folate.
- Refer women with severe anaemia to a higher level of care if they are in the last month of pregnancy, have signs of respiratory distress or cardiac abnormalities such as oedema, or when the conditions do not improve or worsen after one week of iron/folate therapy.
- Provide advice on the consumption of iron-rich foods and vitamin C.
- Record test results and the treatment provided in the woman's card.

Audit

Input indicators

- National standards and locally adapted guidelines for the control of iron deficiency anaemia are available in health facilities.
- Iron/folate supplements are available and are properly managed.
- Staff are available in antenatal care (ANC) and postpartum care (PPC) to prescribe, provide and administer iron/folate supplements.

Process and output indicators

- The proportion of women routinely receiving iron/folate supplements during ANC or PPC.
- The proportion of women receiving dietary advice during ANC and PPC.
- The proportion of women with severe anaemia referred.

Outcome indicators

- Maternal mortality associated with severe anaemia.
- Maternal complications associated with severe anaemia.
- Perinatal mortality associated with severe anaemia in pregnancy.
- Incidence of low birth weight associated with anaemia in pregnancy.

Rationale

Burden of suffering

Iron-deficiency anaemia is the most common micronutrient deficiency in the world, affecting more than two billion people globally *(1)*. It contributes to low birth weight, lowered resistance to infection, poor cognitive development and reduced work capacity *(1)*. Pregnant and postpartum women and children aged 6–24 months are usually the most affected groups *(1,2)*. It is highly prevalent in less developed countries, where, in addition to poor nutrition, parasitic and bacterial infections can contribute to depletion of iron reserves *(1–4)*.

Anaemia in pregnancy is defined as haemoglobin <11g/dl or haematocrit <33% *(1)*. It aggravates the effects of maternal blood loss and infections at childbirth, and is associated with increased maternal and perinatal mortality and morbidity *(3,4)*. Where anaemia is prevalent, iron deficiency is usually the most common cause *(1)*.

A substantial reduction in iron deficiency anaemia by the year 2000 was among the most important nutritional goals adopted by the first World Summit for Children (1990), reiterated by the International Conference on Nutrition (1992) *(1)*.

Efficacy and effectiveness

Anaemia prophylaxis

Where the prevalence of anaemia in pregnant women is <40%, a dose of 60 mg iron and 400 µg folic acid daily for 6 months is considered to meet the physiological requirements for iron in pregnancy. If the duration of supplementation is shorter, a higher dose (120 mg) is recommended. However, the majority of the systematic reviews on this

topic refer to a dose of around 100 mg iron and 350–500 μg folic acid daily for 16 weeks or more during pregnancy *(5–7)*. In areas with a higher prevalence of anaemia, it is recommended that supplementation continue for three months postpartum.

Based on the possible association between maternal anaemia and negative perinatal outcome *(8)*, it is assumed that effective iron-supplementing programmes where anaemia is prevalent may reduce the incidence of low birth weight and perinatal mortality, as well as maternal mortality and obstetrical complications associated to severe anaemia. According to currently available reviews, however, while there is clear evidence of a positive effect of routine iron supplementation during pregnancy in preventing low haemoglobin at delivery or at six weeks postpartum *(5,6)*, there is no evidence of any effect, beneficial or harmful, on clinical outcomes for the mother and the baby *(5,6)*. The lack of a positive effect might be due to the small sample size in the studies that tried to assess those clinical aspects. The results of the largest trial included in one review suggest that routine iron supplementation may reduce the need for postpartum blood transfusions *(5)*. This result must be interpreted with caution since, as noted by the authors of the review, the trial was not blind in respect of treatment allocation and therapeutic decisions could thus have been biased. Nevertheless, if confirmed, this result could have implications in HIV-prevalent areas.

Anaemia treatment

There is consensus on the need for higher dosages in treating women with anaemia *(9)*. There is evidence that a combined treatment with iron and vitamin A could have a greater impact in anaemia treatment during the second trimester of pregnancy *(9)*. Severe anaemia is not frequent, but may cause a large proportion of severe morbidity and mortality related to iron deficiency. Prompt detection and timely treatment or referral of women with severe anaemia are therefore important at the primary care level. With proper training, and using a multiple-site assessment (inferior conjunctiva, palm and nail bed) *(10)*, health workers can assess extreme pallor or very low haemoglobin levels with reasonable sensitivity and high specificity *(10–12)*. Further improvement of the sensitivity and specificity of the clinical assessment could be achieved by adding a few anamnestic symptoms to the pallor assessment and using a simple colorimetric scale *(12)*.

Since the effectiveness of oral iron supplementation is hindered by many factors, including supply problems and poor adherence to regimens owing to the frequency of side-effects *(5,13,14)*, a variety of other interventions have been proposed to prevent and correct iron-deficiency anaemia, including food fortification, healthy dietary education and antiparasitic treatment. The effectiveness of these interventions is still unclear. Dietary improvements *(15)* and fortification of water *(16)* and foods *(17)* are not supported by strong evidence of effectiveness, while control of parasitic (helminth and plasmodium) infections seems to enhance iron prophylaxis and the efficacy of therapy *(14,18)*. More research is needed in communities where iron-deficiency anaemia is prevalent to establish the most appropriate strategies.

There is promising evidence from studies whereby iron cooking pots are introduced at community level. Cooking in iron pots has led to a significant increase in haemoglobin concentrations, especially among adults *(19)*, but there are problems of acceptability (pots are heavy and when not properly dried will become rusty) *(20)*.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & intervention	Outcomes linked to the Standard	Results	Comments
5. Mahomed 2004 Most recent substantive amendment, August 1997 **Systematic review** **1++**	20 trials; pregnant women prior to 28 weeks' gestation and with normal haemoglobin levels (>10 g/dl) (number of enrolled women not specified) Europe, North America, Australia, Gambia, India, Myanmar, Niger Baseline risk Low pre-delivery haemoglobin level – minimum 9% – maximum 56% Low post-delivery haemoglobin level – minimum 9.7%	To assess the effects of iron supplementation on haematological and biochemical parameters and on pregnancy outcomes Intervention: 100 mg elemental iron orally compared with placebo or no treatment In one study: iron given routinely vs iron given selectively to women with haemoglobin <10 g/dl	Low pre-delivery haemoglobin (<10 g/dl) Low haemoglobin 6 weeks postpartum Caesarean section Mother: blood transfusion needed Stillbirth/neonatal death Side-effects from treatment avoided	*Iron vs no iron* min. NNT [a] 13 (12–14) max. NNT 2 (2–3) 12 studies, 1802 women min. NNT 15 (13–19) max. NNT 7 (6–10) 2 studies, 1482 women *Selective vs routine iron* NNH [b] 42 (20–369) NNH 75 (31–1011) NNT 200 (150–13 459) NNT 11 (9–13) 1 study, 2694 women	Comment from the authors: increase in caesarean sections and blood transfusions in the selective iron supplementation group possibly due to fear of midwife and doctors (not blind to treatment)
6. Mahomed 2004 Most recent substantive amendment, August 1997 **Systematic review** **1++**	8 trials involving 5449 pregnant women prior to 28 weeks' gestation and with normal haemoglobin levels (>10g/dl) including adolescent women Myanmar, Nigeria, United Kingdom, Baseline risk Low pre-delivery haemoglobin level – minimum 14% – maximum 56% Low post-delivery haemoglobin level – minimum 10% – maximum 20% Caesarean section – minimum 9% – maximum 11%	To assess the effects of routine iron and folate supplementation on haematological and biochemical parameters and on pregnancy outcomes Intervention: 100 mg elemental iron plus 350 µg folic acid taken daily by mouth compared with placebo or no treatment	Low pre-delivery haemoglobin (<10 g/dl) Low haemoglobin 6 weeks postpartum Caesarean section Low birth weight Stillbirth/neonatal death	*Iron & folic acid vs placebo* min. NNT 9 (9–10) max. NNT 3 (2–3) 6 studies, 1099 women min. NNT 11 (11–12) max. NNT 5 (5–6) 2 studies, 2896 women min. NNT 14 (12–69) max. NNT 11 (9–55) 2 studies, 104 women NS [c] 1 study, 48 women NS 1 study, 48 women	Results of relevant clinical outcomes are based on a very small single study (low birth weight, stillbirth, preterm delivery)

[a] Number needed to treat. (95% confidence interval)
[b] Number needed to harm. (95% confidence interval)
[c] Non-significant

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Study (Type & level of evidence)	Population & setting	Objective & intervention	Outcomes linked to the standard	Results	Comments
13. Sloan, Jordan & Winikoff 2002 **Systematic review** **1++**	23 randomized controlled trials, 15 of which conducted in developing countries; the majority set in antenatal clinics; only 2 set in rural areas; around 1000 pregnant women Average baseline haemoglobin level <11 g/dl	To review the efficacy of iron supplementation on haemoglobin level in pregnant women Here results refer only to developing country studies Supplementation dosages vary from <60 mg/day to >120 mg/day, the majority being >90 mg/day	Haemoglobin increase by daily dose of iron supplement Haemoglobin increase by additional effect of folate Haemoglobin increase by iron and antimalarials Haemoglobin increase by iron and vitamin A Adherence to supplementation	60 mg: + 0.41 (±0.027) g/dl 61–90 mg: + 0.86 (±0.018) g/dl 91–120 mg: + 1.87 (±0.027) g/dl >120 mg: + 1.78 (±0.042) g/dl No additional effect of folate compared to iron alone (6 studies) Only one small study: iron + antimalarial is not more effective than antimalarial alone In one study there is additive effect The majority of the studies reported it as a problem Only two studies quantify this aspect: 42% adherence that increases (61%) with slow-release gastric delivery system; low adherence is due to side-effects and these are dose-dependent	The authors question the opportunity of recommending large-scale, public health oral iron supplementation programmes as a means of reducing global maternal anaemia and call for further studies to determine the effectiveness of other approaches (prevention of hookworm infection, food fortification, prenatal prophylactic treatment of falciparum malaria)
10. Stoltzfus et al. 1999 Validation study	945 pregnant women and 720 women at 3 months postpartum from rural area Nepal	To study the association between clinical pallor as detected by health workers opportunely trained and haemoglobin concentration (sensitivity and specificity) Clinical pallor assessed in three sites: inferior conjunctiva, palm and nail bed Two days of training	Haemoglobin 10 g/dl – sensitivity – specificity Haemoglobin 9 g/dl – sensitivity – specificity Haemoglobin 8 g/dl – sensitivity – specificity Haemoglobin 7 g/dl – sensitivity – specificity	Pregnancy / 3 months postpartum 18.2% / 35.7% 94.1% / 94.3% 28% / 51.5% 93.4% / 92.2% 45.8% / 62.7% 92.3% / 89.8% 67.5% / 81.0% 91.5% / 88.1%	Multiple site assessment is highly recommended (increase in sensitivity with just slight decrease of specificity)

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Birth and emergency preparedness in antenatal care

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH **(IMPAC)**

Standards for Maternal and Neonatal Care

1.9

The standard

All pregnant women should have a written plan for birth and for dealing with unexpected adverse events, such as complications or emergencies, that may occur during pregnancy, childbirth or the immediate postnatal period, and should discuss and review this plan with a skilled attendant at each antenatal assessment and at least one month prior to the expected date of birth.

Aim

To assist women and their partners and families to be adequately prepared for childbirth by making plans on how to respond if complications or unexpected adverse events occur to the woman and/or the baby at any time during pregnancy, childbirth or the early postnatal period.

Requirements

- ☐ National and local policies support all pregnant women having access to maternal and neonatal health care, including referral care regardless of their socioeconomic situation or place of residence.
- ☐ The health care system ensures that all health care providers who come into contact with pregnant women and their families have the capacities, including interpersonal communication and intercultural skills, to support the woman in preparing a birth and emergency plan.
- ☐ The health care system ensures that all pregnant women are able to discuss and review their written birth and emergency plan with a skilled attendant, ideally at each antenatal assessment but at least one month prior to the expected date of birth.
- ☐ A national or locally adapted card or home-based record exists to facilitate the development and recording of the birth and emergency plan.
- ☐ National and local health education activities are undertaken to promote the need for all women to access maternal and neonatal health care, and for all pregnant women to make a birth and emergency plan during pregnancy.
- ☐ National and local activities are in place to facilitate community action to participate in, or where necessary mobilize, local efforts to ensure the timely transfer of women and babies with pregnancy- and birth-related complications, especially emergencies, to a facility that has the capacity to manage such complications or emergencies.

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Applying the standard

Health providers, especially community workers and skilled attendants who come into contact with pregnant women, their families and supporters, must:

- Provide information to pregnant women, their families and the broader community on the signs of labour and when to seek care if danger signs appear during pregnancy, birth and (for both the woman and her baby) the postnatal period.
- Support women and their families in developing and reviewing the birth and emergency preparedness plan, including helping them to identify a safe place for the birth (taking account of personal and local circumstances) and deciding on the other elements of the plan such as child care and transport.
- Support women, when needed, in discussing the plan with their partners and families.
- Discuss with traditional healers, traditional birth attendants (where they exist), other lay health workers and community leaders the need to promote the development of birth and emergency plans during pregnancy, and possible community or group action to support women and their babies in accessing appropriate care when needed.
- Disseminate information in the community on danger signs during pregnancy, birth and the postnatal period.
- Regularly discuss with women and community leaders possible community action and/or plans to mobilize local assets and participate in local efforts for the emergency transfer of women and newborn infants with pregnancy- or birth-related complications.
- Identify women and families who have a problem accessing appropriate pregnancy, birth or postnatal care and take action to help them ensure access or, where this is not possible, report such cases to the local authorities responsible for the provision of maternal and neonatal care.

Audit

Input indicators

- The proportion of pregnant women receiving antenatal care.
- The proportion of pregnant women with a birth and emergency plan.
- The proportion of communities where leaders, traditional birth attendants, etc. are promoting birth and emergency plans for pregnant women.

Process and output indicators

- The proportion of pregnant women and of community members with knowledge of danger signs.
- A nationally or locally adapted card exists and is used for developing a birth and emergency plan.
- Supporting educational materials for developing a birth and emergency plan are available and are in use.

Outcome indicators

- The proportion of births at which a skilled attendant is present.
- The proportion of births at which a birth companion, designated by the woman, is present.
- The proportion of women who recently gave birth whose delivery took place where planned.
- Transport is available to referral facilities.

Rationale

Burden of suffering

Childbirth is a normal physiological process for the majority of women and a process that, like all other life events, is looked upon with a mixture of anticipation and happy expectation. Studies in developed countries have shown a positive impact on pregnancy and birth outcomes when the woman feels in control of the process of pregnancy and birth; making a birth plan has been shown to facilitate this feeling of self-control and autonomy.

Historical evidence shows that no country has managed to bring its maternal mortality ratio below 100 per 100 000 live births without ensuring that all women are attended by an appropriately skilled health professional during labour, birth and the period immediately afterwards *(1)*. Many of the complications that result in maternal deaths and many that contribute to perinatal deaths are unpredictable, and their onset can be both sudden and severe. Delay in responding to the onset of labour and such complications has been shown to be one of the major barriers to reducing mortality and morbidity surrounding childbirth *(2)*. Information on how to stay healthy during pregnancy and the need to obtain the services of a skilled birth attendant, on recognizing signs of the onset of labour, and on recognizing danger signs for pregnancy-related complications and what to do if they arise would significantly increase the capacities of women, their partners and their families to remain healthy, to take appropriate steps to ensure a safe birth and to seek timely skilled care in emergencies. Interventions to reduce the other barriers to seeking care, such as transport costs, perceptions of poor quality of care and cultural differences, must also be addressed.

Efficacy and effectiveness

Two types of interventions for developing birth plans were identified, each emphasizing a different aspect of care. Interventions that were conducted in higher-resource countries focused mainly on the woman's psychological and physical comfort (birth plan), while those in lower-resource countries tended to focus on measures to ensure a safe birth with the appropriate attendant and to prepare for emergencies (birth and emergency preparedness). Birth and emergency preparedness (also known as birth preparedness and complication readiness *(3,4)*) is considered by WHO and other agencies to be a useful and practical intervention with several advantages *(5)*. In particular, it can contribute to increased use of services by assisting women and their families to plan for the necessary support, clothing and equipment for the birth, etc., and by making women and their partners/families aware of the potential for unexpected events *(6)*.

A birth plan/emergency preparedness plan includes identification of the following elements *(6–8)*: the desired place of birth; the preferred birth attendant; the location of the closest appropriate care facility; funds for birth-related and emergency expenses; a birth companion; support in looking after the home and children while the woman is away; transport to a health facility for the birth; transport in the case of an obstetric emergency; and identification of compatible blood donors in case of emergency.

Birth preparedness is not easy to achieve. Many people in developing countries live on less than US $1 a day, which is hardly sufficient for them to feed and clothe themselves let alone put aside money for the possibility of an obstetric emergency. In rural areas, the situation is even more complex: even if transportation (and the money to pay for it) is available in the case of an obstetric emergency, distance and lack of maintained roads may still cause delays sufficient to put the life of the woman in danger *(9)*.

Although little empirical evidence exists as yet to show a direct correlation between birth preparedness and reducing maternal and/or perinatal mortality and morbidity, limited and small-scale studies suggest that there is considerable benefit to be gained from this intervention *(9–12)*. Given the difficulties in predicting pregnancy-related complications, providing information, education and advice to the woman, her family and the community on seeking necessary care is seen as an important part of antenatal care *(5)*.

Studies show that, while no clear relationship has been found between improved knowledge and increased health-seeking behaviour, the adoption of new practices associated with planning (such as setting aside money for the birth, transport arrangements and the use of birth planning cards) at family and community levels is encouraging *(9)*.

The presence of a person of the woman's own choice to provide social support during childbirth has also been shown to have a positive effect *(13,14)*. Thus, an important part of preparing for birth is seeking contact with and obtaining the services of a skilled birth attendant. Developing a birth plan can assist the woman to decide where she wishes to give birth and which attendant she feels most comfortable with.

Birth plans have been used by many women in a number of developed countries for more than a decade, with different and sometimes conflicting results *(15–17)*. There is also evidence that such planning for birth can be used in other settings, including low-resource settings *(18)* but few studies have examined the effectiveness of these interventions and existing studies are flawed owing to study and sample design *(19)*. Nevertheless, in an unpublished WHO review *(9)*, eight projects had encouraging results in using a birth plan/emergency preparedness plan as an essential component of their safe motherhood activities.

The current consensus of those working in safe motherhood is that, if people are aware of the importance of having care from a skilled birth attendant, know where to go in an emergency, and plan accordingly for costs and other practical matters, it is more likely they will get the support they need in these circumstances. Taking advantage of antenatal care to support the woman in preparing for birth, using health education philosophy, holds much potential for improvements in maternal and neonatal health *(4)*.

The lack of evidence demonstrating a negative impact of birth plans/emergency preparedness plans, the right of women and families to self-determination, and recognition of the capacities of women and families to contribute significantly to maternal and neonatal health has led WHO to recommend this intervention as a fundamental component of all antenatal care programmes. Consequently, birth plans/emergency preparedness plans are included in the new WHO antenatal care model *(5)* and the integrated management of pregnancy and childbirth (IMPAC) *(6)*. A handbook on counselling and communicating information on pregnancy, childbirth, postpartum and newborn care, including a session on how best to support the woman and her family to develop such a plan, is in preparation.

The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the *Introduction to the Standards for Maternal and Neonatal Care* and the *Process to develop the Standards for Maternal and Neonatal Care* on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

Study (Type & Level of evidence)	Population & Setting	Objective & Intervention	Outcomes linked to the Standard	Results
11. CARE 2000 **Observational studies 2–**	219 women, 128 who had given birth in the previous year and had been introduced to birth planning and 91 who had not been introduced to birth planning Bangladesh	To evaluate an approach to facilitate birth planning Birth planning by families promoted through interpersonal communication and a pictorial birth planning card	Savings/generation of small emergency fund at family level Organization of emergency transport Preparation for emergency blood transfusion Knowledge of appropriate hospital	Intervention (N = 128) vs control (N = 91) 95% vs 25% 35% vs 0% 5% vs 0% 40% vs 7%
12. The Communication Initiative 2004 **Observational studies 2–**	Data collection involving more than 1700 interviews with randomly selected individuals to produce a representative sample Indonesia	Use of radio, television, print materials, special events and training programmes to reach Indonesian families and communities with the concept of being alert (siaga) to emergencies during childbirth	Women aware of "bleeding" as an indicative danger sign during pregnancy Women reported using a skilled provider for childbirth	Exposed vs non-exposed 40.7% vs 16.4% 67.0% vs 44.2%

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