

# WHO recommendations on antenatal care for a positive pregnancy experience





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# Contents

Acknowledgements	v
Acronyms and abbreviations	vii
Executive summary	ix
1. Introduction	1
2. Methods	4
3. Evidence and recommendations	13
A. Nutritional interventions	14
B. Maternal and fetal assessment	40
C. Preventive measures	63
D. Interventions for common physiological symptoms	74
E. Health systems interventions to improve the utilization and quality of ANC	85
4. Implementation of the ANC guideline and recommendations: introducing the 2016 WHO ANC model	105
5. Research implications	118
6. Dissemination, applicability and updating of the guideline and recommendations	120
References	123
Annex 1: External experts and WHO staff involved in the preparation of this guideline	137
Annex 2: Other WHO guidelines with recommendations relevant to routine ANC	141
Annex 3: Summary of declarations of interest from the Guideline Development Group (GDG) members and how they were managed	143
Annex 4: Implementation considerations for ANC guideline recommendations	145

## **Web annexes: *WHO recommendations on antenatal care for a positive pregnancy experience\****

- Web annex 1: Priority questions and outcomes for the antenatal care (ANC) interventions identified for this guideline
- Web annex 2: Changes from the approved scope of this guideline
- Web annex 3: Guideline Development Group (GDG) judgements related to the recommendations

## **Web supplement: *WHO recommendations on antenatal care for a positive pregnancy experience: evidence base\****

The standardized criteria used in grading the evidence and the GRADE tables have been published in this separate Web supplement. These evidence tables are referred to within this document by number, prefixed with "EB" (for evidence base), for ease of reference.

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\* available at: [www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/anc-positive-pregnancy-experience/en/](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/)

**« To achieve the Every Woman Every Child vision and the Global Strategy for Women's, Children's and Adolescents' Health, we need innovative, evidence-based approaches to antenatal care. I welcome these guidelines, which aim to put women at the centre of care, enhancing their experience of pregnancy and ensuring that babies have the best possible start in life. »**

Ban Ki-moon, United Nations Secretary-General

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# Acronyms and abbreviations

ANC	antenatal care
ASB	asymptomatic bacteriuria
BMI	body mass index
CERQual	Confidence in the Evidence from Reviews of Qualitative Research
CI	confidence interval
CTG	cardiotocography
DECIDE	Developing and Evaluating Communication strategies to support Informed Decisions and Practice based on Evidence
DOI	declaration of interest
EB	evidence base
EGWG	excessive gestational weight gain
ERG	External Review Group
FANC	focused antenatal care
FIGO	International Federation of Gynecology and Obstetrics
GBS	group B streptococcus
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRC	Guidelines Review Committee
GREAT	Guideline-driven, Research priorities, Evidence synthesis, Application of evidence, and Transfer of knowledge
Hb	haemoglobin
HIC	high-income country
HIV	human immunodeficiency virus
HRP	UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction
ICM	International Confederation of Midwives
IPTp	intermittent preventive treatment in pregnancy
IPTp-SP	intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine
IQR	interquartile range
IUGR	intrauterine growth restriction
IVR	Initiative for Vaccine Research
LMIC	low- and middle-income country
MCA	Department of Maternal, Newborn, Child and Adolescent Health (at WHO)
MD	mean difference
MLCC	midwife-led continuity of care
MMN	multiple micronutrient
MUAC	mid-upper arm circumference
NHD	Department of Nutrition for Health and Development (at WHO)
NRS	non-randomized study

OR	odds ratio
PAHO	Pan American Health Organization (WHO Regional Office for the Americas)
PCG	Pregnancy and Childbirth Group (Cochrane Collaboration)
PICO	population (P), intervention (I), comparator (C), outcome (O)
PLA	participatory learning and action
PMNCH	The Partnership for Maternal, Newborn & Child Health
PMR	perinatal mortality rate
PrEP	pre-exposure prophylaxis
PROM	prelabour rupture of membranes
PWG	participatory women's group
RCT	randomized controlled trial
Rh	rhesus
RHR	Department of Reproductive Health and Research (at WHO)
RR	relative risk
RUTI	recurrent urinary tract infections
SFH	symphysis-fundal height
SGA	small for gestational age
SP	sulfadoxine-pyrimethamine
TB	tuberculosis
TBA	traditional birth attendant
Tdap	tetanus/diphtheria/acellular pertussis
TDF	tenofovir disoproxil fumarate
TT	tetanus toxoid
TT-CV	tetanus toxoid-containing vaccine
TWG	Technical Working Group
UN	United Nations
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UNIMMAP	United Nations international multiple micronutrient preparation
US\$	United States (US) dollar
USAID	United States Agency for International Development
UTI	urinary tract infection
WHO	World Health Organization

# Executive summary

## Introduction

In 2016, at the start of the Sustainable Development Goals (SDGs) era, pregnancy-related preventable morbidity and mortality remains unacceptably high. While substantial progress has been made, countries need to consolidate and increase these advances, and to expand their agendas to go beyond survival, with a view to maximizing the health and potential of their populations.

The World Health Organization (WHO) envisions a world where every pregnant woman and newborn receives quality care throughout the pregnancy, childbirth and the postnatal period. Within the continuum of reproductive health care, antenatal care (ANC) provides a platform for important health-care functions, including health promotion, screening and diagnosis, and disease prevention. It has been established that by implementing timely and appropriate evidence-based practices, ANC can save lives. Crucially, ANC also provides the opportunity to communicate with and support women, families and communities at a critical time in the course of a woman's life. The process of developing these recommendations on ANC has highlighted the importance of providing effective communication about physiological, biomedical, behavioural and sociocultural issues, and effective support, including social, cultural, emotional and psychological support, to pregnant women in a respectful way. These communication and support functions of ANC are key, not only to saving lives, but to improving lives, health-care utilization and quality of care. Women's positive experiences during ANC and childbirth can create the foundations for healthy motherhood.

This is a comprehensive WHO guideline on routine ANC for pregnant women and adolescent girls. The aim is for these recommendations to complement existing WHO guidelines on the management of specific pregnancy-related complications. The guidance is intended to reflect and respond to the complex nature of the issues surrounding the practice and delivery of ANC, and to prioritize person-centred health and well-being – not only the prevention of death and morbidity – in accordance with a human rights-based approach.

The scope of this guideline was informed by a systematic review of women's views, which shows that women want a positive pregnancy experience from ANC. A positive pregnancy experience is defined as maintaining physical and sociocultural normality, maintaining a healthy pregnancy for mother and baby (including preventing or treating risks, illness and death), having an effective transition to positive labour and birth, and achieving positive motherhood (including maternal self-esteem, competence and autonomy).

Recognizing that a woman's experience of care is key to transforming ANC and creating thriving families and communities, this guideline addresses the following questions:

- What are the evidence-based practices during ANC that improve outcomes and lead to a positive pregnancy experience?
- How should these practices be delivered?

## Guideline development methods

These ANC recommendations are intended to inform the development of relevant health-care policies and clinical protocols. The guideline was developed using standard operating procedures in accordance with the process described in the *WHO handbook for guideline development*. Briefly, these procedures include:

(i) identification of priority questions and outcomes; (ii) evidence retrieval and synthesis; (iii) assessment of the evidence; (iv) formulation of the recommendations; and (v) planning for implementation, dissemination, impact evaluation and updating of the guideline. The quality of the scientific evidence underpinning the recommendations was graded using the Grading of Recommendations Assessment, Development and

Evaluation (GRADE) and Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) approaches, for quantitative and qualitative evidence, respectively. Up-to-date systematic reviews were used to prepare evidence profiles for priority questions. The DECIDE (Developing and Evaluating Communication Strategies to support Informed Decisions and Practice based on Evidence) framework, an evidence-to-decision tool that includes intervention effects, values, resources, equity, acceptability and feasibility criteria, was used to guide the formulation and approval of recommendations by the Guideline Development Group (GDG) – an international group of experts assembled for the purpose of developing this guideline – at three Technical Consultations between October 2015 and March 2016.

## Recommendations

The WHO Technical Consultations led to the development of 39 recommendations related to five types of interventions: A. Nutritional interventions, B. Maternal and fetal assessment, C. Preventive measures, D. Interventions for common physiological symptoms, and E. Health system interventions to improve utilization and quality of ANC. Interventions were either recommended, not recommended, or recommended under certain conditions based on the GDG's judgements according to the DECIDE criteria, which informed both the direction and context, if any, of the recommendation. To ensure that each recommendation is correctly understood and applied in practice, the context of all context-specific recommendations is clearly stated within each recommendation, and the contributing experts provided additional remarks where needed. Users of the guideline should refer to these remarks, which are presented along with the evidence summaries within the guideline. In addition, ANC-relevant recommendations from current guidance produced by other WHO departments were systematically identified and 10 such recommendations were consolidated into this guideline for the purpose of providing a comprehensive document for end-users. All 49 recommendations on ANC for a positive pregnancy experience are summarized in Table 1.

In accordance with WHO guideline development standards, these recommendations will be reviewed and updated following the identification of new evidence, with major reviews and updates at least every five years. WHO welcomes suggestions regarding additional questions for inclusion in future updates of the guideline.

At the Technical Consultations, the implementation considerations of individual recommendations and of the guideline as a whole were discussed. The GDG, emphasizing the evidence indicating increased fetal deaths and lesser satisfaction of women with the four-visit model (also known as focused or basic ANC), decided to increase the recommended number of contacts between the mother and the health-care providers at time points that may facilitate assessment of well-being and provision of interventions to improve outcomes if problems are identified (see Recommendation E.7 in Table 1). The recommendations in this guideline should be implemented alongside other quality-improvement activities. Derivative products of this guideline will include a practical implementation manual for health-care practitioners, which will incorporate ANC recommendations and established good clinical practices. Table 1 summarizes the list of all interventions evaluated by the GDG and therefore includes interventions that are recommended, only recommended under certain conditions (including research), and interventions that are not recommended.

**Table 1: Summary list of WHO recommendations on antenatal care (ANC) for a positive pregnancy experience**

These recommendations apply to pregnant women and adolescent girls within the context of routine ANC

A. Nutritional interventions		
	Recommendation	Type of recommendation
Dietary interventions	<b>A.1.1:</b> Counselling about healthy eating and keeping physically active during pregnancy is recommended for pregnant women to stay healthy and to prevent excessive weight gain during pregnancy. <sup>a</sup>	Recommended
	<b>A.1.2:</b> In undernourished populations, nutrition education on increasing daily energy and protein intake is recommended for pregnant women to reduce the risk of low-birth-weight neonates.	Context-specific recommendation
	<b>A.1.3:</b> In undernourished populations, balanced energy and protein dietary supplementation is recommended for pregnant women to reduce the risk of stillbirths and small-for-gestational-age neonates.	Context-specific recommendation
	<b>A.1.4:</b> In undernourished populations, high-protein supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended
Iron and folic acid supplements	<b>A.2.1:</b> Daily oral iron and folic acid supplementation with 30 mg to 60 mg of elemental iron <sup>b</sup> and 400 µg (0.4 mg) of folic acid <sup>c</sup> is recommended for pregnant women to prevent maternal anaemia, puerperal sepsis, low birth weight, and preterm birth. <sup>d</sup>	Recommended
	<b>A.2.2:</b> Intermittent oral iron and folic acid supplementation with 120 mg of elemental iron <sup>e</sup> and 2800 µg (2.8 mg) of folic acid once weekly is recommended for pregnant women to improve maternal and neonatal outcomes if daily iron is not acceptable due to side-effects, and in populations with an anaemia prevalence among pregnant women of less than 20%. <sup>f</sup>	Context-specific recommendation
Calcium supplements	<b>A.3:</b> In populations with low dietary calcium intake, daily calcium supplementation (1.5–2.0 g oral elemental calcium) is recommended for pregnant women to reduce the risk of pre-eclampsia. <sup>g</sup>	Context-specific recommendation
Vitamin A supplements	<b>A.4:</b> Vitamin A supplementation is only recommended for pregnant women in areas where vitamin A deficiency is a severe public health problem, <sup>h</sup> to prevent night blindness. <sup>i</sup>	Context-specific recommendation

- A healthy diet contains adequate energy, protein, vitamins and minerals, obtained through the consumption of a variety of foods, including green and orange vegetables, meat, fish, beans, nuts, whole grains and fruit.
- The equivalent of 60 mg of elemental iron is 300 mg of ferrous sulfate heptahydrate, 180 mg of ferrous fumarate or 500 mg of ferrous gluconate.
- Folic acid should be commenced as early as possible (ideally before conception) to prevent neural tube defects.
- This recommendation supersedes the previous recommendation found in the WHO publication *Guideline: daily iron and folic acid supplementation in pregnant women* (2012).
- The equivalent of 120 mg of elemental iron equals 600 mg of ferrous sulfate heptahydrate, 360 mg of ferrous fumarate or 1000 mg of ferrous gluconate.
- This recommendation supersedes the previous recommendation in the WHO publication *Guideline: intermittent iron and folic acid supplementation in non-anaemic pregnant women* (2012).
- This recommendation is consistent with the WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia (2011) and supersedes the previous recommendation found in the WHO publication *Guideline: calcium supplementation in pregnant women* (2013).
- Vitamin A deficiency is a severe public health problem if  $\geq 5\%$  of women in a population have a history of night blindness in their most recent pregnancy in the previous 3–5 years that ended in a live birth, or if  $\geq 20\%$  of pregnant women have a serum retinol level  $< 0.70 \mu\text{mol/L}$ . Determination of vitamin A deficiency as a public health problem involves estimating the prevalence of deficiency in a population by using specific biochemical and clinical indicators of vitamin A status.
- This recommendation supersedes the previous recommendation found in the WHO publication *Guideline: vitamin A supplementation in pregnant women* (2011).

Zinc supplements	<b>A.5:</b> Zinc supplementation for pregnant women is only recommended in the context of rigorous research.	Context-specific recommendation (research)
Multiple micronutrient supplements	<b>A.6:</b> Multiple micronutrient supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended
Vitamin B6 (pyridoxine) supplements	<b>A.7:</b> Vitamin B6 (pyridoxine) supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended
Vitamin E and C supplements	<b>A.8:</b> Vitamin E and C supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended
Vitamin D supplements	<b>A.9:</b> Vitamin D supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes. <sup>j</sup>	Not recommended
Restricting caffeine intake	<b>A.10:</b> For pregnant women with high daily caffeine intake (more than 300 mg per day), <sup>k</sup> lowering daily caffeine intake during pregnancy is recommended to reduce the risk of pregnancy loss and low-birth-weight neonates.	Context-specific recommendation

## B. Maternal and fetal assessment<sup>l</sup>

	Recommendation	Type of recommendation
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### B.1: Maternal assessment

Anaemia	<b>B.1.1:</b> Full blood count testing is the recommended method for diagnosing anaemia in pregnancy. In settings where full blood count testing is not available, on-site haemoglobin testing with a haemoglobinometer is recommended over the use of the haemoglobin colour scale as the method for diagnosing anaemia in pregnancy.	Context-specific recommendation
Asymptomatic bacteriuria (ASB)	<b>B.1.2:</b> Midstream urine culture is the recommended method for diagnosing asymptomatic bacteriuria (ASB) in pregnancy. In settings where urine culture is not available, on-site midstream urine Gram-staining is recommended over the use of dipstick tests as the method for diagnosing ASB in pregnancy.	Context-specific recommendation
Intimate partner violence (IPV)	<b>B.1.3:</b> Clinical enquiry about the possibility of intimate partner violence (IPV) should be strongly considered at antenatal care visits when assessing conditions that may be caused or complicated by IPV in order to improve clinical diagnosis and subsequent care, where there is the capacity to provide a supportive response (including referral where appropriate) and where the WHO minimum requirements are met. <sup>m,n</sup>	Context-specific recommendation

- j. This recommendation supersedes the previous recommendation found in the WHO publication *Guideline: vitamin D supplementation in pregnant women* (2012).
- k. This includes any product, beverage or food containing caffeine (i.e. brewed coffee, tea, cola-type soft drinks, caffeinated energy drinks, chocolate, caffeine tablets).
- l. Evidence on essential ANC activities, such as measuring maternal blood pressure, proteinuria and weight, and checking for fetal heart sounds, was not assessed by the GDG as these activities are considered to be part of good clinical practice.
- m. Minimum requirements are: a protocol/standard operating procedure; training on how to ask about IPV, and on how to provide the minimum response or beyond; private setting; confidentiality ensured; system for referral in place; and time to allow for appropriate disclosure.
- n. This recommendation is consistent with *Responding to intimate partner violence and sexual violence against women: WHO clinical and policy guidelines* (2013).

Recommendations integrated from other WHO guidelines that are relevant to ANC maternal assessment		
Gestational diabetes mellitus (GDM)	<b>B.1.4:</b> Hyperglycaemia first detected at any time during pregnancy should be classified as either gestational diabetes mellitus (GDM) or diabetes mellitus in pregnancy, according to WHO criteria. <sup>o</sup>	Recommended
Tobacco use	<b>B.1.5:</b> Health-care providers should ask all pregnant women about their tobacco use (past and present) and exposure to second-hand smoke as early as possible in the pregnancy and at every antenatal care visit. <sup>p</sup>	Recommended
Substance use	<b>B.1.6:</b> Health-care providers should ask all pregnant women about their use of alcohol and other substances (past and present) as early as possible in the pregnancy and at every antenatal care visit. <sup>q</sup>	Recommended
Human immuno-deficiency virus (HIV) and syphilis	<b>B.1.7:</b> In high-prevalence settings, <sup>r</sup> provider-initiated testing and counselling (PITC) for HIV should be considered a routine component of the package of care for pregnant women in all antenatal care settings. In low-prevalence settings, PITC can be considered for pregnant women in antenatal care settings as a key component of the effort to eliminate mother-to-child transmission of HIV, and to integrate HIV testing with syphilis, viral or other key tests, as relevant to the setting, and to strengthen the underlying maternal and child health systems. <sup>s</sup>	Recommended
Tuberculosis (TB)	<b>B.1.8:</b> In settings where the tuberculosis (TB) prevalence in the general population is 100/100 000 population or higher, systematic screening for active TB should be considered for pregnant women as part of antenatal care. <sup>t</sup>	Context-specific recommendation

## B.2: Fetal assessment

Daily fetal movement counting	<b>B.2.1:</b> Daily fetal movement counting, such as with “count-to-ten” kick charts, is only recommended in the context of rigorous research.	Context-specific recommendation (research)
Symphysis-fundal height (SFH) measurement	<b>B.2.2:</b> Replacing abdominal palpation with symphysis-fundal height (SFH) measurement for the assessment of fetal growth is not recommended to improve perinatal outcomes. A change from what is usually practiced (abdominal palpation or SFH measurement) in a particular setting is not recommended.	Context-specific recommendation
Antenatal cardiotocography	<b>B.2.3:</b> Routine antenatal cardiotocography <sup>u</sup> is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended

- o. This is not a recommendation on routine screening for hyperglycaemia in pregnancy. It has been adapted and integrated from the WHO publication *Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy* (2013), which states that GDM should be diagnosed at any time in pregnancy if one or more of the following criteria are met:
- fasting plasma glucose 5.1–6.9 mmol/L (92–125 mg/dL)
  - 1-hour plasma glucose  $\geq$  10.0 mmol/L (180 mg/dL) following a 75 g oral glucose load
  - 2-hour plasma glucose 8.5–11.0 mmol/L (153–199 mg/dL) following a 75 g oral glucose load.
- Diabetes mellitus in pregnancy should be diagnosed if one or more of the following criteria are met:
- fasting plasma glucose  $\geq$  7.0 mmol/L (126 mg/dL)
  - 2-hour plasma glucose  $\geq$  11.1 mmol/L (200 mg/dL) following a 75 g oral glucose load
  - random plasma glucose  $\geq$  11.1 mmol/L (200 mg/dL) in the presence of diabetes symptoms.
- p. Integrated from *WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy* (2013).
- q. Integrated from the WHO publication *Guidelines for the identification and management of substance use and substance use disorders in pregnancy* (2014).
- r. High-prevalence settings are defined in the 2015 WHO publication *Consolidated guidelines on HIV testing services* as settings with greater than 5% HIV prevalence in the population being tested. Low-prevalence settings are those with less than 5% HIV prevalence in the population being tested. In settings with a generalized or concentrated HIV epidemic, retesting of HIV-negative women should be performed in the third trimester because of the high risk of acquiring HIV infection during pregnancy; please refer to Recommendation B.1.7 for details.
- s. Adapted and integrated from the WHO publication *Consolidated guidelines on HIV testing services* (2015).
- t. Adapted and integrated from the WHO publication *Systematic screening for active tuberculosis: principles and recommendations* (2013).
- u. Cardiotocography is a continuous recording of the fetal heart rate and uterine contractions obtained via an ultrasound transducer placed on the mother's abdomen.

Ultrasound scan	<b>B.2.4:</b> One ultrasound scan before 24 weeks of gestation (early ultrasound) is recommended for pregnant women to estimate gestational age, improve detection of fetal anomalies and multiple pregnancies, reduce induction of labour for post-term pregnancy, and improve a woman's pregnancy experience.	Recommended
Doppler ultrasound of fetal blood vessels	<b>B.2.5:</b> Routine Doppler ultrasound examination is not recommended for pregnant women to improve maternal and perinatal outcomes. <sup>v</sup>	Not recommended

### C. Preventive measures

	Recommendation	Type of recommendation
Antibiotics for asymptomatic bacteriuria (ASB)	<b>C.1:</b> A seven-day antibiotic regimen is recommended for all pregnant women with asymptomatic bacteriuria (ASB) to prevent persistent bacteriuria, preterm birth and low birth weight.	Recommended
Antibiotic prophylaxis to prevent recurrent urinary tract infections	<b>C.2:</b> Antibiotic prophylaxis is only recommended to prevent recurrent urinary tract infections in pregnant women in the context of rigorous research.	Context-specific recommendation (research)
Antenatal anti-D immunoglobulin administration	<b>C.3:</b> Antenatal prophylaxis with anti-D immunoglobulin in non-sensitized Rh-negative pregnant women at 28 and 34 weeks of gestation to prevent RhD alloimmunization is only recommended in the context of rigorous research.	Context-specific recommendation (research)
Preventive anthelmintic treatment	<b>C.4:</b> In endemic areas, <sup>w</sup> preventive anthelmintic treatment is recommended for pregnant women after the first trimester as part of worm infection reduction programmes. <sup>x</sup>	Context-specific recommendation
Tetanus toxoid vaccination	<b>C.5:</b> Tetanus toxoid vaccination is recommended for all pregnant women, depending on previous tetanus vaccination exposure, to prevent neonatal mortality from tetanus. <sup>y</sup>	Recommended
<b>Recommendations integrated from other WHO guidelines that are relevant to ANC</b>		
Malaria prevention: intermittent preventive treatment in pregnancy (IPTp)	<b>C.6:</b> In malaria-endemic areas in Africa, intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP) is recommended for all pregnant women. Dosing should start in the second trimester, and doses should be given at least one month apart, with the objective of ensuring that at least three doses are received. <sup>z</sup>	Context-specific recommendation
Pre-exposure prophylaxis (PrEP) for HIV prevention	<b>C.7:</b> Oral pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate (TDF) should be offered as an additional prevention choice for pregnant women at substantial risk of HIV infection as part of combination prevention approaches. <sup>aa</sup>	Context-specific recommendation

v. Doppler ultrasound technology evaluates umbilical artery (and other fetal arteries) waveforms to assess fetal well-being in the third trimester of pregnancy.

w. Areas with greater than 20% prevalence of infection with any soil-transmitted helminths.

x. Consistent with the WHO publication *Guideline: preventive chemotherapy to control soil-transmitted helminth infections in high-risk groups* (2016, in press).

y. This recommendation is consistent with the WHO guideline on *Maternal immunization against tetanus* (2006). The dosing schedule depends on the previous tetanus vaccination exposure.

z. Integrated from the WHO publication *Guidelines for the treatment of malaria* (2015), which also states: "WHO recommends that, in areas of moderate-to-high malaria transmission of Africa, IPTp-SP be given to all pregnant women at each scheduled ANC visit, starting as early as possible in the second trimester, provided that the doses of SP are given at least 1 month apart. WHO recommends a package of interventions for preventing malaria during pregnancy, which includes promotion and use of insecticide-treated nets, as well as IPTp-SP". To ensure that pregnant women in endemic areas start IPTp-SP as early as possible in the second trimester, policy-makers should ensure health system contact with women at 13 weeks of gestation.

aa. Integrated from the WHO publication *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV* (2015). Substantial risk of HIV infection is defined by an incidence of HIV infection in the absence of PrEP that is sufficiently high (> 3% incidence) to make offering PrEP potentially cost-saving (or cost-effective). Offering PrEP to people at substantial risk of HIV infection maximizes the benefits relative to the risks and costs.



D. Interventions for common physiological symptoms		
	Recommendation	Type of recommendation
Nausea and vomiting	<b>D.1:</b> Ginger, chamomile, vitamin B6 and/or acupuncture are recommended for the relief of nausea in early pregnancy, based on a woman's preferences and available options.	Recommended
Heartburn	<b>D.2:</b> Advice on diet and lifestyle is recommended to prevent and relieve heartburn in pregnancy. Antacid preparations can be offered to women with troublesome symptoms that are not relieved by lifestyle modification.	Recommended
Leg cramps	<b>D.3:</b> Magnesium, calcium or non-pharmacological treatment options can be used for the relief of leg cramps in pregnancy, based on a woman's preferences and available options.	Recommended
Low back and pelvic pain	<b>D.4:</b> Regular exercise throughout pregnancy is recommended to prevent low back and pelvic pain. There are a number of different treatment options that can be used, such as physiotherapy, support belts and acupuncture, based on a woman's preferences and available options.	Recommended
Constipation	<b>D.5:</b> Wheat bran or other fibre supplements can be used to relieve constipation in pregnancy if the condition fails to respond to dietary modification, based on a woman's preferences and available options.	Recommended
Varicose veins and oedema	<b>D.6:</b> Non-pharmacological options, such as compression stockings, leg elevation and water immersion, can be used for the management of varicose veins and oedema in pregnancy, based on a woman's preferences and available options.	Recommended

E. Health systems interventions to improve the utilization and quality of antenatal care		
	Recommendation	Type of recommendation
Woman-held case notes	<b>E.1:</b> It is recommended that each pregnant woman carries her own case notes during pregnancy to improve continuity, quality of care and her pregnancy experience.	Recommended
Midwife-led continuity of care	<b>E.2:</b> Midwife-led continuity-of-care models, in which a known midwife or small group of known midwives supports a woman throughout the antenatal, intrapartum and postnatal continuum, are recommended for pregnant women in settings with well functioning midwifery programmes.	Context-specific recommendation
Group antenatal care	<b>E.3:</b> Group antenatal care provided by qualified health-care professionals may be offered as an alternative to individual antenatal care for pregnant women in the context of rigorous research, depending on a woman's preferences and provided that the infrastructure and resources for delivery of group antenatal care are available.	Context-specific recommendation (research)
Community-based interventions to improve communication and support	<b>E.4.1:</b> The implementation of community mobilization through facilitated participatory learning and action (PLA) cycles with women's groups is recommended to improve maternal and newborn health, particularly in rural settings with low access to health services. <sup>ab</sup> Participatory women's groups represent an opportunity for women to discuss their needs during pregnancy, including barriers to reaching care, and to increase support to pregnant women.	Context-specific recommendation
	<b>E.4.2:</b> Packages of interventions that include household and community mobilization and antenatal home visits are recommended to improve antenatal care utilization and perinatal health outcomes, particularly in rural settings with low access to health services.	Context-specific recommendation

ab. Integrated from WHO recommendations on community mobilization through facilitated participatory learning and action cycles with women's groups for maternal and newborn health (2014).

Task shifting components of antenatal care delivery <sup>ac</sup>	<b>E.5.1:</b> Task shifting the promotion of health-related behaviours for maternal and newborn health <sup>ad</sup> to a broad range of cadres, including lay health workers, auxiliary nurses, nurses, midwives and doctors is recommended.	Recommended
	<b>E.5.2:</b> Task shifting the distribution of recommended nutritional supplements and intermittent preventive treatment in pregnancy (IPTp) for malaria prevention to a broad range of cadres, including auxiliary nurses, nurses, midwives and doctors is recommended.	Recommended
Recruitment and retention of staff in rural and remote areas <sup>ae</sup>	<b>E.6:</b> Policy-makers should consider educational, regulatory, financial, and personal and professional support interventions to recruit and retain qualified health workers in rural and remote areas.	Context-specific recommendation
Antenatal care contact schedules	<b>E.7:</b> Antenatal care models with a minimum of eight contacts are recommended to reduce perinatal mortality and improve women's experience of care.	Recommended

ac. Recommendations adapted and integrated from the WHO guideline on *Optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting* (OptimizeMNH) (2012).

ad. Including promotion of the following: care-seeking behaviour and ANC utilization; birth preparedness and complication readiness; sleeping under insecticide-treated bednets; skilled care for childbirth; companionship in labour and childbirth; nutritional advice; nutritional supplements; other context-specific supplements and interventions; HIV testing during pregnancy; exclusive breastfeeding; postnatal care and family planning; immunization according to national guidelines.

ae. Recommendation adapted and integrated from the WHO publication *Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations* (2010).

# 1. Introduction

## 1.1 Background

International human rights law includes fundamental commitments of states to enable women and adolescent girls to survive pregnancy and childbirth as part of their enjoyment of sexual and reproductive health and rights and living a life of dignity (1). The World Health Organization (WHO) envisions a world where “every pregnant woman and newborn receives quality care throughout the pregnancy, childbirth and the postnatal period” (2). However, approximately 303 000 women and adolescent girls died as a result of pregnancy and childbirth-related complications in 2015 (3). Around 99% of maternal deaths occur in low-resource settings and most can be prevented (4). Similarly, approximately 2.6 million babies were stillborn in 2015, also mainly in low-resource settings (5). Nevertheless, there is evidence that effective interventions exist at reasonable cost for the prevention or treatment of virtually all life-threatening maternal complications (6), and almost two thirds of the global maternal and neonatal disease burden could be alleviated through optimal adaptation and uptake of existing research findings (7). But a human rights-based approach is not just about avoiding death and morbidity – it is about enabling health and well-being while respecting dignity and rights.

Antenatal care (ANC) can be defined as the care provided by skilled health-care professionals to pregnant women and adolescent girls in order to ensure the best health conditions for both mother and baby during pregnancy. The components of ANC include: risk identification; prevention and management of pregnancy-related or concurrent diseases; and health education and health promotion.

ANC reduces maternal and perinatal morbidity and mortality both directly, through detection and treatment of pregnancy-related complications, and indirectly, through the identification of women and girls at increased risk of developing complications during labour and delivery, thus ensuring referral to an appropriate level of care (8). In addition, as indirect causes of maternal morbidity and mortality, such as HIV and malaria infections, contribute to approximately 25% of maternal deaths and

near-misses (9), ANC also provides an important opportunity to prevent and manage concurrent diseases through integrated service delivery (10).

In low- and middle-income countries (LMICs), ANC utilization has increased since the introduction in 2002 of the WHO ANC model, known as focused ANC (FANC) or basic ANC, which is a goal-orientated approach to delivering evidence-based interventions carried out at four critical times during pregnancy (11, 12). However, globally, during the period 2007–2014, only 64% of pregnant women attended the WHO-recommended minimum four contacts for ANC, suggesting that much more work needs to be done to address ANC utilization and quality.

Currently, WHO guidance on routine ANC is fragmented, with related recommendations published across several different WHO guidelines and practical manuals. The 2002 FANC implementation manual, for example (12), does not contain relevant context-specific guidance, which needs to be sought elsewhere. In addition, evidence on the possible harm of the FANC model has recently become available, necessitating a review.

This up-to-date, consolidated guideline for routine ANC has been produced by the WHO Department of Reproductive Health and Research (RHR), in collaboration with the Department of Nutrition for Health and Development (NHD) and the Department of Maternal, Newborn, Child and Adolescent Health (MCA), as part of WHO’s normative work on supporting evidence-informed policies and practices. By reviewing, updating and bringing together ANC-related WHO recommendations regarding “what” should be offered and “how” it should be delivered in the form of this guideline, it is hoped that policy-makers will more easily be able to adapt, adopt and implement these new ANC recommendations, presented in Chapter 3, which have also been configured to form the 2016 WHO ANC model, presented in Chapter 4.

A scoping review was conducted to inform this guideline, and it revealed that what women want and

expect from ANC is to have a “positive pregnancy experience”.

**A positive pregnancy experience is defined as:**

- maintaining physical and sociocultural normality
- maintaining a healthy pregnancy for mother and baby (including preventing and treating risks, illness and death)
- having an effective transition to positive labour and birth, and
- achieving positive motherhood (including maternal self-esteem, competence and autonomy) (13).

The emotional, psychological and social needs of adolescent girls and vulnerable groups (including women with disabilities, women with mental health concerns, women living with HIV, sex workers, displaced and war-affected women, ethnic and racial minorities, among others) can be greater than for other women. Therefore, the aim of this guideline is to provide a clear, evidence-based framework for ANC practices that empowers all pregnant women and adolescent girls to access the type of person-centred care that they want and need, in accordance with a human rights-based approach. This ANC guideline is part of the ongoing work of WHO in developing evidence-based guidelines to improve quality of care for mothers and their babies throughout the antenatal, intrapartum and postnatal continuum.

## 1.2 Target audience

The recommendations in this guideline are intended to inform the development of relevant national- and local-level health policies and clinical protocols. Therefore, the target audience of this guideline includes national and local public health policy-makers, implementers and managers of national and local maternal and child health programmes, concerned nongovernmental and other organizations, professional societies involved in the planning and management of maternal and child health services, health professionals (including obstetricians, midwives, nurses and general medical practitioners) and academic staff involved in training health professionals.

## 1.3 Scope of the guideline

### Population of interest

This guideline is relevant to all pregnant women and adolescent girls receiving ANC in any health-care facility or community-based setting, and to their unborn fetuses and newborns. While the guideline addresses the detection of pregnancy-related complications and the prevention of concurrent diseases at routine ANC visits, it does not address the subsequent treatment of such complications or diseases, where the consequence of detection is referral for additional management or specialist care from a different provider. Thus, the management of women and adolescent girls with high-risk pregnancies is beyond the scope of this ANC guideline, which is aimed at providing guidance on routine ANC. It is therefore complementary to existing WHO guidance on specific pregnancy-related complications.

### Priority questions

The priority questions and outcomes guiding the evidence review and synthesis for the recommendations in this ANC guideline are listed in Web annex 1 according to the following five headings, which reflect the five types of interventions addressed by the recommendations, as presented in Chapter 3 of this document:

#### A. Nutritional interventions

#### B. Maternal and fetal assessment

#### C. Preventive measures

#### D. Interventions for common physiological symptoms

#### E. Health systems interventions to improve the utilization and quality of ANC.

For further information, see section 2.6: Identifying priority questions and outcomes. Changes made to the approved scope of priority questions for the guideline are described in Web annex 2.

## Outcomes of interest

The outcomes of interests included maternal and fetal/neonatal outcomes, as well as test accuracy and health system outcomes (Box 1).

### Box 1: Guideline outcomes of interest

Maternal outcomes	Fetal/neonatal outcomes
Infections	Neonatal infections
Anaemia	Small for gestational age
Pre-eclampsia/eclampsia	Low birth weight
Gestational diabetes mellitus	Preterm birth
Mode of delivery	Congenital anomalies
Excessive weight gain	Macrosomia/large for gestational age
Intimate partner violence	Fetal/neonatal mortality
Side-effects	
Symptomatic relief	
Maternal mortality	
Maternal satisfaction and/or women's rating of usefulness of treatment	
Test accuracy outcomes	Health system outcomes
Sensitivity and specificity	ANC coverage
	Facility-based delivery

## 2. Methods

The guideline was developed in accordance with the methods described in the *WHO handbook for guideline development* (14). In summary, the process included: identification of priority questions and outcomes, retrieval of evidence, assessment and synthesis of the evidence, formulation of recommendations, and planning for the implementation, dissemination, impact evaluation and updating of the guideline.

### 2.1 WHO Steering Group

The WHO Steering Group that guided the entire guideline development process comprised WHO staff members from the Department of Reproductive Health and Research (RHR), the Department of Maternal, Newborn, Child and Adolescent Health (MCA), and the Department of Nutrition for Health and Development (NHD) (see Annex 1 for the list of members). Regional advisors from WHO regions also participated in the guideline development process. The Steering Group drafted the initial scope of the guideline and drafted the key recommendation questions in PICO format (population, intervention, comparator, outcome), identified individuals to be invited to participate as guideline methodologists and as members of the systematic review teams, the Guideline Development Group (GDG) and the External Review Group (ERG), supervised the evidence retrieval and synthesis, organized the Technical Consultations (or GDG meetings), drafted recommendations, and finalized and published the guideline document. Additionally, the Steering Group will oversee dissemination of the guideline.

### 2.2 Guideline Development Group (GDG)

The Steering Group identified and invited 20 external experts and stakeholders from the six WHO regions to form the GDG, ensuring geographic representation, gender balance, and no important conflicts of interest. The GDG was a diverse group of individuals with expertise in research, guideline development methods, and clinical policy and programmes relating to interventions for ANC and service delivery, also including a patient/consumer representative. The curriculum vitae of the members were published on the RHR departmental website prior to the GDG

meetings (which occurred between October 2015 and March 2016). Subgroups were invited to each of the meetings based on their expertise.

Selected members of the GDG provided input into the drafting of the scope of the guideline, the PICO questions and the prioritization of outcomes, which guided the evidence reviews. The GDG as a whole appraised the evidence used to inform the guideline, advised on the interpretation of this evidence, formulated the final recommendations at face-to-face meetings, and reviewed and approved the final guideline document before its submission to the WHO Guidelines Review Committee (GRC) for approval. A list of the members of the GDG can be found in Annex 1.

### 2.3 External Review Group (ERG)

The membership of the ERG was geographically and gender-balanced, and there were no important conflicts of interest that prohibited any member from serving (see Annex 1 for the list of members). There were six members of the ERG, including technical experts and other stakeholders with sufficient interests in the provision of evidence-based ANC. This group peer reviewed the final guideline document to identify any factual errors and comment on the clarity of the language, contextual issues, and implications for implementation. The group ensured that the guideline decision-making processes had considered and incorporated the contextual values and preferences of persons affected by the recommendations, including pregnant women, health-care professionals and policy-makers. It was not within the ERG's remit to change recommendations previously formulated by the GDG.

### 2.4 Technical Working Group (TWG)

The TWG comprised systematic review teams and guideline methodologists. In relation to quantitative evidence on the effectiveness of different interventions, the Cochrane Pregnancy and Childbirth Group (PCG) provided input on the scoping of the guideline and supervised the updating of all relevant systematic reviews following the standard processes

of the Cochrane Collaboration. The WHO Steering Group worked closely with methodologists from the Centro Rosarino de Estudios Perinatales (CREP), in Argentina, to appraise the evidence from systematic reviews using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology (15).

For qualitative data related to women's and health-care professionals' views on ANC, two qualitative meta-synthesis experts from the University of Central Lancashire, in the United Kingdom of Great Britain and Northern Ireland (United Kingdom), systematically reviewed qualitative studies and synthesized the evidence to inform the GDG's decision-making, in collaboration with the Steering Group and methodologists from the Norwegian Public Health Institute.

In addition, methodologists from Queen Mary University of London, in the United Kingdom, conducted test accuracy reviews of diagnostic tests relevant to the provision of ANC to support this guideline. The Steering Group also worked closely with experts from the Norwegian Public Health Institute, who assisted with methodological issues relating to the GRADE, GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) (16), and DECIDE (Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice Based on Evidence) (17) tools (see sections 2.8, 2.10 and 2.11). In addition, the Steering Group consulted two researchers from the London School of Hygiene and Tropical Medicine and the Norwegian Public Health Institute, who reviewed country case studies to investigate implementation issues relating to the WHO focused ANC (FANC) model. Members of the TWG are listed in Annex 1.

## 2.5 External partners and observers

Representatives of the International Federation of Gynecology and Obstetrics (FIGO), the International Confederation of Midwives (ICM), the United Nations Population Fund (UNFPA), the United States Agency for International Development (USAID) and the United Nations Children's Fund (UNICEF) were invited to the final GDG meeting to serve as observers. All these organizations are potential implementers of the proposed guideline with a history of collaboration with the WHO Departments of RHR and MCA in guideline dissemination and implementation.

## 2.6 Identifying priority questions and outcomes

The WHO Department of RHR, in collaboration with methodologists from CREP, conducted a scoping exercise in 2014 to identify and map clinical practice guidelines related to ANC. Eighty-five documents with ANC recommendations were identified – 15 related to routine ANC and 70 to specific situations relevant to ANC (18). Of the 15 related to routine ANC, three were issued by WHO (19–21), while the rest were issued by governmental and nongovernmental organizations (NGOs) in Australia, Canada, Hong Kong, India, Japan, Poland, the United Kingdom and the United States of America (USA). Similarly, of the 70 guidelines related to specific situations relevant to ANC, 91% were from Canada, the United Kingdom and the USA, i.e. high-income countries (HICs), while low- and middle-income countries (LMICs) were poorly represented. An existing, recent, up-to-date guideline relevant to routine ANC that was adaptable to different resource settings was not identified. This scoping exercise also informed the choice of outcomes for the ANC guideline, which was supplemented by outcomes identified by a preliminary search of the Cochrane Database of Systematic Reviews for existing key systematic reviews relevant to the antenatal period.

Based on these initial steps, the WHO Steering Group developed a framework for discussion at a scoping meeting, held in Geneva in April 2014, to identify priority questions about the provision of ANC as well as to inform the scoping for the guideline in terms of approach, focus, questions and outcomes. At this meeting, it was decided that the scope of this guideline should prioritize the applicability of interventions in LMIC settings. Specific genetic tests for detection of inherited conditions were considered beyond the scope of this guideline. In addition, the scoping process highlighted the need to identify women-centred interventions and outcomes for ANC. To this end, a qualitative systematic review was conducted to understand what women want, need and value in pregnancy and ANC (22). The findings of this systematic review suggested that the primary outcome for pregnant women is a “positive pregnancy experience” (as defined in section 1.1), which requires the provision of effective clinical practices (interventions and tests), relevant and timely information, and psychosocial and emotional support by practitioners with good clinical and interpersonal skills, within a well functioning health system. Initially



a list of ANC outcomes was prioritized for the whole ANC period. However, due to important differences between the types of interventions and the range of potential outcomes, these outcomes were further prioritized separately for individual questions. Informed by the qualitative review of women's views, including values and preferences related to ANC, we included assessment of maternal satisfaction with a particular intervention, and maternal rating of the usefulness of a particular intervention.

Throughout the scoping process, the Steering Group consulted and engaged with other WHO departments that have issued guidelines with implications for the antenatal period, incorporating their feedback and technical expertise into the scoping. The process and approach were also presented at a number of meetings and international conferences between April 2014 and March 2015 to elicit further feedback from stakeholders.

This scoping and consultation process led to the identification of priority questions and outcomes related to the effectiveness of clinical, test accuracy, and health systems interventions aimed at achieving a positive pregnancy experience that includes a healthy mother and a healthy baby. These questions and outcomes are listed in Web annex 1.

## 2.7 ANC-related recommendations in other WHO guidelines

To avoid duplication and ensure harmonization of recommendations across WHO departments and publications, we searched all relevant WHO GRC-approved guidelines and identified 21 guidelines containing recommendations relevant to ANC (see Annex 2). These recommendations were mapped to the priority questions for this new guideline and the Steering Group reached out to the WHO departments and technical units that had issued the relevant guidance to engage and collaborate with them throughout the process of developing this new ANC guideline. Recommendations found in other WHO guidelines that related to health promotion and the identification of risk factors (e.g. smoking, HIV) during ANC were considered to be within the scope of the guideline, whereas recommendations on management and treatment of risk factors, complications and concurrent diseases were deemed to be beyond the scope of the guideline; for these,

the guideline user is referred to the relevant separate WHO guidance via a weblink provided along with the "remarks" following each recommendation.

## 2.8 Focus and approach

To capture and examine the complex nature of the issues that are important during the ANC period, within the context of health systems and the continuum of care, the focus of this guideline is the essential core package of ANC that all pregnant women and adolescent girls should receive, with the flexibility to employ a variety of options based on the context of different countries (i.e. in terms of the content of the model, who provides the care, where the care is provided, and how the care is provided to meet women's needs). Therefore, the overarching questions addressed by this guideline focused on the following:

- **What** are the evidence-based practices during the ANC period for improving outcomes related to the following?
  - nutritional interventions (see section 3.A)
  - maternal and fetal assessment (see section 3.B)
  - preventive measures (see section 3.C)
  - interventions for common physiological symptoms (see section 3.D)
- **How** should these evidence-based practices be delivered to improve outcomes?
  - health systems interventions to improve the utilization and quality of ANC (see section 3.E).

The guideline focuses on the core ANC clinical package that all women should receive at routine ANC visits. The management of identified complications or concurrent diseases or risk factors that require additional treatment or specialist care and follow-up is beyond the scope of this guideline.

The DECIDE framework is a tool that has been developed to help decision-makers consider a range of relevant criteria, including benefits, harms, values, resources, equity, acceptability and feasibility (17). To synthesize and examine evidence across the domains of DECIDE (see section 2.11), the preparatory work for the ANC guideline was organized according to five work streams, using both quantitative and qualitative data sources, as summarized in Box 2.



## Box 2: Five work streams for preparation of the ANC guideline

ANC guideline work streams	Methodology	Assessment of evidence
Individual interventions for clinical practices and delivery of ANC	Effectiveness reviews, systematic reviews	GRADE
Antenatal testing	Test accuracy reviews	GRADE
Barriers and facilitators to access to and provision of ANC	Qualitative evidence synthesis	GRADE-CERQual
Large-scale programme review/country case studies of ANC	Mixed-methods review, focusing on contextual and health system factors affecting implementation	Not applicable
Health-system level interventions to improve access to and provision of ANC services	Effectiveness reviews	GRADE

## 2.9 Evidence identification and retrieval

Evidence to support this guideline was derived from a number of sources by the Technical Working Group (TWG) of methodologists and systematic review teams that worked closely with the Steering Group. Evidence on effectiveness was mostly derived from Cochrane reviews of randomized controlled trials (RCTs). The Steering Group, in collaboration with the Cochrane PCG and methodologists from CREP, initially identified all Cochrane systematic reviews and protocols relevant to ANC. The Cochrane PCG Trials Register<sup>1</sup> was searched for new trials and the relevant systematic reviews were updated accordingly. The updating or completion of Cochrane reviews was a collaborative process between authors of the individual reviews, staff of the PCG, and methodologists from CREP.

Assessment of the quality of individual studies included in Cochrane reviews of intervention studies follows specific and explicit methods for assessing the risk of bias using six standard criteria outlined in the *Cochrane handbook for systematic reviews of interventions* (23). Each included study is

assessed and rated by reviewers to be at low, high or unclear risk of bias for sequence generation, allocation concealment, blinding of study personnel and participants, attrition, selective reporting and other sources of bias, such as publication bias. The assessment of these six criteria provides an overall risk of bias that indicates the likely magnitude and direction of the bias and how it is likely to impact the review findings.

The WHO Steering Group and the methodologists in the TWG determined the suitability of each Cochrane systematic review to provide the evidence base for the key PICO questions. For suitable reviews, CREP methodologists retrieved the evidence relevant to ANC guideline outcomes, which was evaluated according to standard operating procedures approved by the Steering Group.

If a low-quality review or no systematic review was identified on a priority question, a new systematic review was commissioned from external experts. This was the case with all DTA reviews, the qualitative reviews on women's and health-care providers' views on ANC, and the review on "factors affecting ANC intervention implementation at country level". In these instances, the external researchers were asked to prepare standard protocols before embarking on the systematic reviews, including clear PICO questions, criteria for identification of studies (including search strategies for different bibliographic databases), methods for assessing risk of bias and the plan for data analysis. The protocols were reviewed and endorsed by the Steering Group and selected

<sup>1</sup> The Cochrane PCG Trials Register is maintained by the PCG's Trial Search Coordinator and contains trials identified from: monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL); weekly searches of MEDLINE; weekly searches of Embase; hand-searches of 30 journals and the proceedings of major conferences; weekly "current awareness" alerts for a further 44 journals; and monthly BioMed Central email alerts (24). For further information, see: <http://pregnancy.cochrane.org/pregnancy-and-childbirth-groups-trials-register>

content experts among the GDG members. WHO information retrieval specialists reviewed the search strategies.

In addition to the Cochrane review evidence, for three questions related to health systems (i.e. those on women-held case notes, group ANC, and interventions to communicate with and support pregnant women), indirect evidence was sought, due to a paucity of direct evidence. This work was commissioned from experts at the Norwegian Public Health Institute who conducted a systematic search for indirect evidence on effects of these interventions covering the preceding five years (i.e. from January 2011 to January 2016), but found no additional evidence.

The DTA reviews on haemoglobin and urine tests were commissioned from methodologists from Queen Mary University of London, in the United Kingdom. For these reviews, Embase, LILACS, MEDLINE (OVID), SCOPUS and Web of Science were searched from inception to January 2015, and grey literature was sought by searching GreyOpen.

Two qualitative reviews were commissioned from experts from the University of Central Lancashire, United Kingdom:

1. To explore the views, attitudes and experiences of pregnant and postnatal women in high-, medium- and low-income countries in relation to factors that might form barriers to, or facilitators of, their use of routine ANC services.
2. To explore the views, attitudes and experiences of health-care providers in high-, medium- and low-income countries in relation to factors that might form barriers to, or facilitators of, their provision of good quality routine ANC services.

Studies published before 2000 were excluded, to ensure that the data reflected the current generation of women who may encounter ANC, and the current generation of ANC providers. This date range was also intended to capture the time period since the 2002 introduction of the WHO FANC or “basic” ANC model, which includes four goal-orientated ANC visits (12).

Finally, two researchers from the London School of Hygiene and Tropical Medicine and the Norwegian Public Health Institute undertook a review of case studies reporting the experiences of countries. The review focused on methods of uptake and

implementation of the WHO FANC model, problems experienced by service users and other stakeholders, and the broader context. Data were collected from published studies, reports and other policy documents (see the Web supplement<sup>2</sup> for the search strategy), and semi-structured interviews with key stakeholders for each country case study, which included Argentina, Kenya, Thailand and the United Republic of Tanzania.

The entire systematic review development process was iterative, with the methodologists in constant communication with the Steering Group to discuss challenges and agree on solutions. The search strategies for evidence identification and retrieval can be found in Web supplement.

## 2.10 Quality assessment and grading of the evidence

The GRADE approach (15) to appraising the quality of quantitative evidence was used for all the critical outcomes identified in the PICO, and a GRADE profile was prepared for each quantitative outcome within each PICO. Accordingly, the quality of evidence for each outcome was rated as “high”, “moderate”, “low”, or “very low” based on a set of criteria. As a baseline, RCTs provided “high-quality” evidence, while non-randomized trials and observational studies provided “low-quality” evidence. This baseline quality rating was then downgraded based on consideration of risk of bias, inconsistency, imprecision, indirectness and publication bias. For observational studies, other considerations, such as magnitude of effect, could lead to upgrading of the rating if there were no limitations that indicated a need for downgrading. Grading of Cochrane review evidence and DTA evidence was performed by CREP and the methodologists from Queen Mary University of London, respectively, in accordance with standard operating procedures approved by the Steering Group.

Studies identified for the qualitative reviews were subjected to a simple quality appraisal system using a validated instrument that rated studies against 11 criteria, and then allocated a score from A to D, with D indicating the presence of significant flaws that are very likely to affect the credibility, transferability, dependability and/or confirmability of the study (25).

2 Available at: [www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/anc-positive-pregnancy-experience/en/](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/)

Studies scoring D were excluded on grounds of poor quality.

The findings of the qualitative reviews were appraised for quality using the GRADE-CERQual tool (16, 26). The GRADE-CERQual tool, which uses a similar approach conceptually to other GRADE tools, provides a transparent method for assessing and assigning the level of confidence that can be placed in evidence from reviews of qualitative research. The qualitative review team used the GRADE-CERQual tool to assess the confidence in qualitative review findings, which were assigned to evidence domains on values, acceptability and feasibility according to four components: methodological limitations of the individual studies, adequacy of data, coherence and relevance to the review question of the individual studies contributing to a review finding.

## 2.11 Formulation of the recommendations

The Steering Group supervised and finalized the preparation of evidence summaries and evidence profiles in collaboration with the guideline methodologists, using the DECIDE framework (17). DECIDE is an evidence-to-decision (EtD) tool that includes explicit and systematic consideration of evidence on interventions in terms of six domains: effects, values, resources, equity, acceptability and feasibility. For each priority question, judgements are made on the impact of the intervention on each of these domains, in order to inform and guide the decision-making process. Using the DECIDE framework, the Steering Group created summary documents for each priority question covering evidence on each of the six domains.

- **Effects:** The evidence on maternal and perinatal outcomes was described. Where benefits clearly outweighed harms, or vice versa, there was a greater likelihood of a clear judgement in favour of or against the option, respectively. Uncertainty about the net benefits or harms and small net benefits often led to a judgement that neither favoured the intervention nor the comparator. The higher the certainty of evidence on benefits across outcomes, the higher the likelihood of a judgement in favour of the intervention.
- **Values:** This relates to the relative importance assigned to the outcomes of the intervention by those affected by them, how such importance varies within and across settings, and whether this

importance is surrounded by any uncertainty. A scoping review of what women want from ANC informed the ANC guideline (13). Evidence showed that women from high-, middle- and low-resource settings generally valued having a “positive pregnancy experience” achieved through three equally important ANC components – effective clinical practices (interventions and tests), relevant and timely information, and psychosocial and emotional support – each provided by practitioners with good clinical and interpersonal skills within a well functioning health system. Reviewers had high confidence in the evidence. Therefore, interventions that facilitated this composite outcome were more likely to lead to a judgement in favour of the intervention.

- **Resources:** The most relevant resources in the context of the implementation of the ANC interventions in this guideline mainly included costs for providing medicines, supplies, equipment and skilled human resources. A judgement in favour or against the intervention was likely where the resource implications were clearly advantageous or disadvantageous. Cost evaluation relied on reported estimates obtained during the evidence retrieval process, a 2013 treatment assumption report (27), the *WHO compendium of innovative health technologies for low-resource settings* (28), as well as experiences and opinions of the GDG members. It was recognized that actual costing of interventions is context-specific and not feasible for a global guideline.
- **Equity:** This section was informed by the 2015 WHO report on inequalities in reproductive, maternal, newborn and child health, which showed that women in LMICs who are poor, least educated, and residing in rural areas have lower ANC coverage and worse pregnancy outcomes than the more advantaged women in LMICs (29). Their neonates also have worse health outcomes. Therefore, judgements were more likely to favour the interventions if they could reduce health differences among different groups of women and their families.
- **Acceptability:** Qualitative evidence from the systematic reviews on women's and providers' views informed judgements for this domain. The lower the acceptability, the lower the likelihood of a judgement in favour of the intervention.

- **Feasibility:** Feasibility is influenced by factors such as the resources available, infrastructure and training. Qualitative evidence from the systematic reviews and country case studies informed judgements for this domain. Where barriers existed, it was less likely that a judgement would be made in favour of the intervention.

Additional evidence of potential harms or unintended consequences was described in the “additional considerations” sub-section of each evidence summary (see text for each recommendation presented in Chapter 3).

Three types of draft recommendation were made, namely:

- Recommended
- Context-specific recommendation:
  - only in the context of rigorous research
  - only with targeted monitoring and evaluation
  - only in other specific contexts
- Not recommended.

In the absence of evidence of benefits, evidence of potential harm led to a recommendation against the option. Where evidence of potential harm was found for interventions that were also found to have evidence of important benefits, depending on the level of certainty and likely impact of the harm, such evidence of potential harm was more likely to lead to a context-specific recommendation for the intervention (where the context is explicitly stated within the recommendation).

These evidence summaries and draft recommendations, including GRADE tables and other related documents, were provided to members of the GDG for comments in advance of the series of three Technical Consultations on the ANC guideline. The certainty of the graded evidence on effectiveness was systematically interpreted in the text according to guidance on reporting review evidence from the Cochrane Effective Practice and Organization of Care (EPoC) Group (30).

The GDG members and other participants were subsequently invited to attend three Technical Consultations (also called GDG meetings) organized at the WHO headquarters in Geneva, Switzerland, the first two in October 2015 and the third in March 2016 (see Annex 1 for a full list of participants) to review the evidence and formulate recommendations

for the ANC guideline. At these meetings, under the leadership of the GDG chair, GDG members reviewed the evidence summaries, the draft recommendations and any comments received through preliminary feedback. The purpose of the meetings was to reach consensus on each judgement and each recommendation, including its direction and context (if any), and to discuss implementation, monitoring and evaluation, and research priorities related to the recommendations.

## 2.12 Decision-making during the GDG meetings

The GDG meetings were guided by a clear protocol. Each of the three meetings was designed to allow participants to discuss each of the recommendations drafted by the Steering Group. Where necessary, each of these recommendations was revised through a process of group discussion. The final adoption of each recommendation was confirmed by consensus (i.e. full agreement among all GDG members). The GDG also determined the context of recommendations at the meetings by the same process of consensus, based on discussions around the balance of evidence on benefits and disadvantages of the interventions across the domains evaluated. If GDG members had been unable to reach a consensus, the disputed recommendation, or any other decision, would have been put to a vote, by a show of hands.

## 2.13 Declaration of interests (DOI) by external contributors

In accordance with the *WHO handbook for guideline development* (14), all GDG members, ERG members and other external collaborators were asked to declare in writing any competing interests (whether academic, financial or other) at the time of the invitation to participate in the ANC guideline development process. The standard WHO form for DOI was completed and signed by each expert and sent electronically to the responsible technical officer. The WHO Steering Group reviewed all the DOI forms before finalizing experts' invitations to participate. All experts were instructed to notify the responsible technical officer of any change in relevant interests during the course of the process, in order to update and review conflicts of interest accordingly. In addition, experts were requested to submit an electronic copy of their curriculum vitae along with

the completed DOI form. The responsible technical officer collated and reviewed signed DOI forms and curriculum vitae, in conjunction with the director of the WHO Department of RHR and, with input from the Steering Group, determined whether a conflict of interest existed. Where any conflict of interest was declared, the Steering Group determined whether it was serious enough to affect the individual's ability to make objective judgements about the evidence or recommendations. To ensure consistency, the Steering Group applied the criteria for assessing the severity of a conflict of interest in the *WHO handbook for guideline development* (14).

All findings from the received DOI statements were managed in accordance with the WHO DOI guidelines on a case-by-case basis. Where a conflict of interest was not considered significant enough to pose any risk to the guideline development process or reduce its credibility, the expert was only required to declare such conflict at the GDG meeting and no further action was taken. Conflicts of interest that warranted action by WHO staff arose where experts had performed primary research or a systematic review related to any guideline recommendations; in such cases, the experts were restricted from participating in discussions and/or formulating any recommendation related to the area of their conflict of interest. At the final GDG meeting, members were required again to state any conflicts of interest openly to the entire group, and were required to submit a signed and updated version of their earlier DOI statements. A summary of the DOI statements and information on how conflicts of interest were managed are included in Annex 3.

## 2.14 Document preparation and peer review

Following these three GDG meetings, members of the Steering Group prepared a draft of the full guideline document with revisions to accurately reflect the deliberations and decisions of the GDG participants. This draft guideline was then sent electronically to the GDG participants for further comments before it was sent to the ERG. The Steering Group carefully evaluated the input of the peer reviewers for inclusion in the guideline document and made revisions to the guideline draft as needed. After the GDG meetings and peer review process, further modifications to the guideline by the Steering Group were limited to corrections of factual errors and improvements in

language to address any lack of clarity. The revised final version was returned electronically to the GDG for final approval.

## 2.15 Presentation of guideline content

A summary of the recommendations is presented in Table 1 within the executive summary at the beginning of this guideline. As evidence was evaluated for several outcomes and six domains (effects, values, resources, equity, acceptability, feasibility) for each recommendation, we have not presented the decisions on quality of evidence in this summary table. Summary tables of the main considerations (including certainty of the evidence on effects) for each recommendation are presented in Web annex 3.

The “Evidence and recommendations” section of the guideline (Chapter 3) summarizes the evidence and other considerations reviewed by the GDG at the Technical Consultations. To improve readability, the “values” domain has been described (and highlighted in a box entitled “Women’s values”) at the beginning of each section for the five types of interventions, instead of for each recommendation, to avoid repetition. The language used to interpret the Cochrane review evidence on effects is consistent with the EPOC approach (30). Evidence assessed as being of very low certainty is not presented in the text, but can be found in the Web supplement.

The Steering Group consolidated recommendations into this guideline from other recent, GRC-approved WHO guidelines relevant to the provision of comprehensive, integrated routine ANC to women in certain contexts or for certain conditions. In most instances, these recommendations are identical to those found in the specific separate guideline. Where we have integrated recommendations, the strength of the recommendation and quality of the evidence as determined by the respective GDGs for those guidelines has been recorded in the remarks section of the recommendation. Such recommendations are indicated by a footnote in the ANC guideline text specifying that the recommendation has been “integrated from” the specific guideline. A few recommendations required adaptation for the purposes of the ANC guideline, and the Steering Group consulted the relevant WHO departments that produced the specific guidance to confirm that adaptations were consistent with original recommendations. Such recommendations

are indicated by a footnote in the ANC guideline text specifying that the recommendation has been “adapted and integrated from” the specific guideline. An example of where this was done is for the recommendation on task shifting, where the recommendations on multiple interventions were adapted to apply to the task shifting of routine ANC interventions only. In all instances, guideline users

are referred to the specific WHO guidance for more details, including implementation considerations, for these recommendations. Implementation of the ANC guideline and recommendations is discussed in Chapter 4, and implementation considerations related to each GDG recommendation can be found in Annex 4.

# 3. Evidence and recommendations

This ANC guideline includes 39 recommendations adopted by the Guideline Development Group (GDG), and 10 recommendations relevant to ANC that have been consolidated into this guideline from other existing WHO guidelines that have been recently approved by the Guidelines Review Committee (GRC). Evidence on the effectiveness of interventions was derived from 47 systematic reviews (41 Cochrane systematic reviews, 2 test accuracy reviews and 4 non-Cochrane reviews of non-randomized studies) and was summarized in GRADE tables. A scoping review of what women want from ANC and what outcomes matter to women informed the values domain. Two qualitative systematic reviews on women's and providers' views and a review of country case studies contributed evidence on the acceptability and feasibility of interventions. Evidence and considerations on equity and resources also informed the GDG recommendations.

This chapter provides the recommendations with the corresponding narrative summaries, grouped according to the type of intervention, namely:

## A. Nutritional interventions

## B. Maternal and fetal assessment

## C. Preventive measures

## D. Interventions for common physiological symptoms

## E. Health systems interventions to improve the utilization and quality of ANC.

The corresponding GRADE tables for recommendations are referred to in this chapter as "evidence base" (EB) tables, numbered according to the specific recommendations they refer to. These tables are presented separately in the Web supplement to this document.<sup>3</sup> Evidence-to-decision tables with GDG judgements related to the evidence and considerations for all domains are presented in Web annex 3 of this guideline. In addition, implementation considerations and research priorities related to these recommendations, based on the GDG discussions during the Technical Consultations, can be found in the next chapters of the guideline (Chapter 4: Implementation of the ANC guideline and recommendations; Chapter 5: Research implications).

<sup>3</sup> Available at: [www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/anc-positive-pregnancy-experience/en/](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/)



# A. Nutritional interventions

## Background

Pregnancy requires a healthy diet that includes an adequate intake of energy, protein, vitamins and minerals to meet maternal and fetal needs. However, for many pregnant women, dietary intake of vegetables, meat, dairy products and fruit is often insufficient to meet these needs, particularly in low- and middle-income countries (LMICs) where multiple nutritional deficiencies often co-exist. In resource-poor countries in sub-Saharan Africa, south-central and south-east Asia, maternal undernutrition is highly prevalent and is recognized as a key determinant of poor perinatal outcomes (31). However, obesity and overweight is also associated with poor pregnancy outcomes and many women in a variety of settings gain excessive weight during pregnancy. While obesity has historically been a condition associated with affluence, there is some evidence to suggest a shift in the burden of overweight and obesity from advantaged to disadvantaged populations (32).

Anaemia is associated with iron, folate and vitamin A deficiencies. It is estimated to affect 38.2% of pregnant women globally, with the highest prevalence in the WHO regions of South-East Asia (48.7%) and Africa (46.3%), medium prevalence in the Eastern Mediterranean Region (38.9%) and the lowest prevalence in the WHO regions of the Western Pacific (24.3%), the Americas (24.9%) and Europe (25.8%) (33).

Major contributory factors to anaemia include parasitic infections such as malaria, hookworm and schistosomiasis, in areas where these infections are endemic. In addition, chronic infections such as tuberculosis (TB) and HIV, and haemoglobinopathies such as sickle-cell disease, contribute to the prevalence of anaemia. It is estimated that 0.8 million pregnant women globally have severe anaemia (defined as a blood haemoglobin concentration < 70 g/L) (33). In pregnancy, severe anaemia is

associated with an increased risk of maternal and infant mortality (34). It is estimated that about half of the anaemia found in pregnant women is amenable to iron supplementation (33); however, this may be quite variable and is likely to be much lower in malaria-endemic areas.

In addition to causing anaemia, iron deficiency adversely affects the use of energy sources by muscles and, thus, physical capacity and work performance, and also adversely affects immune status and morbidity from infections (35). Folate (vitamin B9) deficiency, in addition to anaemia it is also linked to fetal neural tube defects (36). Vitamin A deficiency affects about 19 million pregnant women, mostly in Africa and South-East Asia, causing night blindness (37).

Calcium deficiency is associated with an increased risk of pre-eclampsia (38), and deficiencies of other vitamins and minerals, such as vitamin E, C, B6 and zinc, have also been postulated to play a role in pre-eclampsia. Zinc deficiency is associated with impaired immunity (39). Vitamin C intake enhances iron absorption from the gut; however, zinc, iron and other mineral supplements may compete for absorption, and it is unclear whether such interactions have health consequences (39).

For the ANC guideline, the GDG evaluated the evidence on various vitamin and mineral supplements that might theoretically lead to improved maternal and perinatal outcomes. In addition, as both undernourishment and overnourishment may have negative consequences for pregnant women and their babies, the GDG also evaluated evidence on the effects of various dietary interventions to reduce the impact of these conditions. Caffeine is possibly the most widely used psychoactive substance in the world (40), and the GDG also evaluated evidence on the impact, if any, of caffeine restriction during pregnancy.



## Women's values

A scoping review of what women want from ANC and what outcomes they value informed the ANC guideline (13). Evidence showed that women from high-, medium- and low-resource settings valued having a positive pregnancy experience, the components of which included the provision of effective clinical practices (interventions and tests, including nutritional supplements), relevant and timely information (including dietary and nutritional advice) and psychosocial and emotional support, by knowledgeable, supportive and respectful health-care practitioners, to optimize maternal and newborn health (high confidence in the evidence).

## A.1: Dietary interventions

### A1.1: Counselling on healthy eating and physical activity

**RECOMMENDATION A.1.1: Counselling about healthy eating and keeping physically active during pregnancy is recommended for pregnant women to stay healthy and to prevent excessive weight gain during pregnancy. (Recommended)**

#### Remarks

- A healthy diet contains adequate energy, protein, vitamins and minerals, obtained through the consumption of a variety of foods, including green and orange vegetables, meat, fish, beans, nuts, whole grains and fruit (41).
- Stakeholders may wish to consider culturally appropriate healthy eating and exercise interventions to prevent excessive weight gain in pregnancy, particularly for populations with a high prevalence of overweight and obesity, depending on resources and women's preferences. Interventions should be woman-centred and delivered in a non-judgemental manner, and developed to ensure appropriate weight gain (see further information in points below).
- A healthy lifestyle includes aerobic physical activity and strength-conditioning exercise aimed at maintaining a good level of fitness throughout pregnancy, without trying to reach peak fitness level or train for athletic competition. Women should choose activities with minimal risk of loss of balance and fetal trauma (42).
- Most normal gestational weight gain occurs after 20 weeks of gestation and the definition of "normal" is subject to regional variations, but should take into consideration pre-pregnant body mass index (BMI). According to the Institute of Medicine classification (43), women who are underweight at the start of pregnancy (i.e. BMI < 18.5 kg/m<sup>2</sup>) should aim to gain 12.5–18 kg, women who are normal weight at the start of pregnancy (i.e. BMI 18.5–24.9 kg/m<sup>2</sup>) should aim to gain 11.5–16 kg, overweight women (i.e. BMI 25–29.9 kg/m<sup>2</sup>) should aim to gain 7–11.5 kg, and obese women (i.e. BMI > 30 kg/m<sup>2</sup>) should aim to gain 5–9 kg.
- Most evidence on healthy eating and exercise interventions comes from high-income countries (HICs), and the GDG noted that there are at least 40 ongoing trials in HICs in this field. The GDG noted that research is needed on the effects, feasibility and acceptability of healthy eating and exercise interventions in LMICs.
- Pregnancy may be an optimal time for behaviour change interventions among populations with a high prevalence of overweight and obesity, and the longer-term impact of these interventions on women, children and partners needs investigation.
- The GDG noted that a strong training package is needed for practitioners, including standardized guidance on nutrition. This guidance should be evidence-based, sustainable, reproducible, accessible and adaptable to different cultural settings.

## Summary of evidence and considerations

### Effects of diet and exercise interventions compared with no diet and exercise interventions (EB Table A.1.1)

The evidence on the effects of healthy eating and exercise interventions was derived from a Cochrane review that included 65 randomized controlled trials (RCTs), mostly conducted in HICs (44). Thirty-four trials recruited women from the general population (i.e. women of a wide range of BMIs at baseline), 24 trials recruited overweight and/or obese women and seven recruited women defined as being at high risk of gestational diabetes. In total, 49 RCTs involving 11 444 women contributed data to the review's meta-analyses. Diet interventions were defined as a special selection of food or energy intake to which a participant was restricted, which were most commonly "healthy eating" types of diets. Exercise interventions were defined by reviewers as any activity requiring physical effort, carried out to sustain or improve health or fitness, and these were either prescribed/unsupervised (e.g. 30 minutes of daily walking), supervised (e.g. a weekly supervised group exercise class) or both. These interventions were usually compared with "standard ANC" and aimed to prevent excessive gestational weight gain (EGWG).

Most trials recruited women between 10 and 20 weeks of gestation. There was substantial variation in the number of contacts (i.e. counselling/exercise sessions), type of intervention and method of delivery. Data were grouped according to the type of intervention (i.e. diet only, exercise only, diet and exercise counselling, diet and supervised exercise) and the average effects across trials were estimated using the random effects model. Separate analyses were performed according to type of intervention and the risk of weight-related complications. Most data in the overall analyses were derived from trials of combined diet and exercise interventions.

### Maternal outcomes

High-certainty evidence shows that women receiving diet and/or exercise interventions as part of ANC to prevent EGWG are less likely to experience EGWG (24 trials, 7096 women; relative risk [RR]: 0.80, 95% confidence interval [CI]: 0.73–0.87; absolute effect of 91 fewer women with EGWG per 1000 on average). Subgroup analyses were consistent with these findings.

High-certainty evidence shows that diet and/or exercise interventions have little or no effect on pre-eclampsia risk (15 trials, 5330 women; RR: 0.95, 95% CI: 0.77–1.16). However, moderate-certainty evidence indicates that diet and/or exercise interventions probably prevent hypertension in pregnancy (11 trials, 5162 women; RR: 0.70, 95% CI: 0.51–0.96).

Low-certainty evidence suggests that diet and/or exercise interventions may have little or no effect on caesarean section (28 trials, 7534 women; RR: 0.95, 95% CI: 0.88–1.03); however, low-certainty evidence from the diet and exercise counselling subgroup of trials suggests that reductions in caesarean section rates may be possible with this intervention (9 trials, 3406 women; RR: 0.87, 95% CI: 0.75–1.01). Moderate-certainty evidence indicates that diet and/or exercise interventions probably make little or no difference to induction of labour (8 trials, 3832 women; RR: 1.06, 95% CI: 0.94–1.19).

Low-certainty evidence suggests that diet and/or exercise interventions may reduce the risk of gestational diabetes mellitus (GDM) (19 trials, 7279 women; RR: 0.82, 95% CI: 0.67–1.01).

### Fetal and neonatal outcomes

Moderate-certainty evidence suggests that diet and/or exercise interventions probably prevent neonatal macrosomia (27 trials, 8598 women; RR: 0.93, 95% CI: 0.86–1.02), particularly in overweight and obese women receiving diet and exercise counselling interventions (9 trials, 3252 neonates; RR: 0.85, 95% CI: 0.73–1.00). However, moderate-certainty evidence indicates that diet and exercise interventions probably have little or no effect on neonatal hypoglycaemia (4 trials, 2601 neonates; RR: 0.95, 95% CI: 0.76–1.18) or shoulder dystocia (4 trials, 3253 neonates; RR: 1.02, 95% CI: 0.57–1.83). Low-certainty evidence suggests that neonatal respiratory morbidity may occur less frequently with diet and exercise counselling interventions than controls, particularly among overweight and obese women (2 studies, 2256 women; RR: 0.47, 95% CI: 0.26–0.85).

Low-certainty evidence suggests that diet and/or exercise interventions may have little or no effect on preterm birth (16 trials, 5923 women; RR: 0.91, 95% CI: 0.68–1.22), and the evidence on low-birth-weight neonates is very uncertain. Perinatal mortality was not reported in the review.

### Additional considerations

- High-certainty evidence from the review also shows that low gestational weight gain is more likely to occur with these interventions (11 trials, 4422 women; RR: 1.14, CI: 1.02–1.27); the clinical relevance of this finding is not known.
- The effects, acceptability and feasibility of diet and exercise interventions in LMICs has not been established.

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Cost implications of diet and exercise interventions for health services are highly variable. For example, supervised diet and exercise interventions can have high associated costs, mainly due to staff costs for time spent supervising, while counselling interventions might have relatively low costs. For pregnant women, the interventions might also have resource implications in terms of transport costs, time off work and child-minding costs, particularly if the intervention requires additional antenatal visits.

### Equity

Most of the evidence came from trials conducted in HICs. Recent studies have reported a shift in the burden of overweight and obesity from advantaged to disadvantaged populations (32). Such a trend increases the risk of associated pregnancy complications, as well as cardiometabolic problems, among pregnant women from disadvantaged

populations. These risks might be further exacerbated among women in low-resource community settings, as these settings may not be equipped to deal with complications.

### Acceptability

Qualitative evidence indicates that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). It also suggests that women may be less likely to engage with health services if advice is delivered in a hurried or didactic manner (high confidence in the evidence) (22). Therefore, these types of interventions are more likely to be acceptable if the interventions are delivered in an unhurried and supportive way, which may also facilitate better engagement with ANC services. Qualitative evidence on health-care providers’ views of ANC suggests that they may be keen to offer general health-care advice and specific pregnancy-related information (low confidence in the evidence) but they sometimes feel they do not have the appropriate training and lack the resources and time to deliver the service in the informative, supportive and caring manner that women want (high confidence in the evidence) (45).

### Feasibility

In a number of LMIC settings, providers feel that a lack of resources may limit implementation of recommended interventions (high confidence in the evidence) (45).

## A.1.2: Nutrition education on energy and protein intake

**RECOMMENDATION A.1.2: In undernourished populations, nutrition education on increasing daily energy and protein intake is recommended for pregnant women to reduce the risk of low-birth-weight neonates.** (*Context-specific recommendation*)

### Remarks

- Undernourishment is usually defined by a low BMI (i.e. being underweight). For adults, a 20–39% prevalence of underweight women is considered a high prevalence of underweight and 40% or higher is considered a very high prevalence (46). Mid-upper arm circumference (MUAC) may also be useful to identify protein–energy malnutrition in individual pregnant women and to determine its prevalence in this population (31). However, the optimal cut-off points may need to be determined for individual countries based on context-specific cost–benefit analyses (31).
- Anthropometric characteristics of the general population are changing, and this needs to be taken into account by regularly reassessing the prevalence of undernutrition to ensure that the intervention remains relevant.
- The GDG noted that a strong training package is needed for practitioners, including standardized guidance on nutrition. This guidance should be evidence-based, sustainable, reproducible, accessible and adaptable to different cultural settings.
- Stakeholders might wish to consider alternative delivery platforms (e.g. peer counsellors, media reminders) and task shifting for delivery of this intervention.
- Areas that are highly food insecure or those with little access to a variety of foods may wish to consider additional complementary interventions, such as distribution of balanced protein and energy supplements (see Recommendation A.1.3).

## Summary of evidence and considerations

### Effects of nutritional education to increase energy and protein intake versus no nutritional education intervention (EB Table A.1.2)

Evidence on the effects of nutritional education was derived from a Cochrane review (47). Five trials conducted between 1975 and 2013 in Bangladesh, Greece and the USA, involving 1090 pregnant women, contributed data to this comparison. Nutritional education interventions were delivered one-to-one or in group classes and included education to improve the “quality” of diet, increase energy and protein intake, or improve knowledge of the nutritional value of different foods, including energy, protein, vitamins and iron. The Bangladesh study also involved cookery demonstrations.

### Maternal outcomes

Evidence on gestational weight gain was of very low certainty. There was no other evidence available on maternal outcomes in the review for this comparison.

### Fetal and neonatal outcomes

Low-certainty evidence shows that antenatal dietary education may reduce low-birth-weight neonates (300 women; RR: 0.04, 95% CI: 0.01–0.14), but may

have little or no effect on small-for-gestational-age (SGA) neonates (2 trials, 449 women; RR: 0.46, 95% CI: 0.21–0.98), stillbirths (1 trial, 431 women; RR: 0.37, 95% CI: 0.07–1.90) or neonatal deaths (1 trial, 448 women; RR: 1.28, 95% CI: 0.35–4.72). Evidence on preterm birth was judged to be of very low certainty.

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Resource costs are variable and mainly related to staffing and counselling time.

### Equity

In many LMICs, pregnancy outcomes and ANC coverage are worse among women who are poor, least educated and residing in rural areas (29). Many low-income countries still struggle with widespread poverty and hunger, particularly among rural populations (48). Findings from a study of antenatal food supplementation and micronutrient supplements in rural Bangladesh suggest that food supplementation interventions might be associated with better ANC adherence among women with

less education but not among those with more education (49). Therefore, providing antenatal food supplements could help to address inequalities by improving maternal nutritional status and increasing ANC coverage among disadvantaged women.

### Acceptability

Qualitative evidence indicates that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). It also suggests that women may be less likely to engage with health services if advice is delivered in a hurried or didactic manner (high confidence in the evidence) (22). Therefore, these types of interventions are more likely to be acceptable if the interventions are delivered in an unhurried

and supportive way, which may also facilitate better engagement with ANC services. Qualitative evidence on health-care providers' views of ANC suggests that they may be keen to offer general health-care advice and specific pregnancy-related information (low confidence in the evidence) but they sometimes feel they do not have the appropriate training and lack the resources and time to deliver the service in the informative, supportive and caring manner that women want (high confidence in the evidence) (45).

### Feasibility

In a number of LMIC settings, providers feel that a lack of resources may limit implementation of recommended interventions (high confidence in the evidence) (45).

### A.1.3: Energy and protein dietary supplements

**RECOMMENDATION A.1.3: In undernourished populations, balanced energy and protein dietary supplementation is recommended for pregnant women to reduce the risk of stillbirths and small-for-gestational-age neonates.** (*Context-specific recommendation*)

#### Remarks

- The GDG stressed that this recommendation is for populations or settings with a high prevalence of undernourished pregnant women, and not for individual pregnant women identified as being undernourished.
- Undernourishment is usually defined by a low BMI (i.e. being underweight). For adults, a 20–39% prevalence of underweight women is considered a high prevalence of underweight and 40% or higher is considered a very high prevalence (46). MUAC may also be useful to identify protein-energy malnutrition in individual pregnant women and to determine its prevalence in this population (31). However, the optimal cut-off points may need to be determined for individual countries based on context-specific cost-benefit analyses (31).
- Establishment of a quality assurance process is important to guarantee that balanced energy and protein food supplements are manufactured, packaged and stored in a controlled and uncontaminated environment. The cost and logistical implications associated with balanced energy and protein supplements might be mitigated by local production of supplements, provided that a quality assurance process is established.
- A continual, adequate supply of supplements is required for programme success. This requires a clear understanding and investment in procurement and supply chain management.
- Programmes should be designed and continually improved based on locally generated data and experiences. Examples relevant to this guideline include:
  - Improving delivery, acceptability and utilization of this intervention by pregnant women (i.e. overcoming supply and utilization barriers).
  - Distribution of balanced energy and protein supplements may not be feasible only through the local schedule of ANC visits; additional visits may need to be scheduled. The costs related to these additional visits should be considered. In the absence of antenatal visits, too few visits, or when the first visit comes too late, consideration should be given to alternative platforms for delivery (e.g. community health workers, task shifting in specific settings).
  - Values and preferences related to the types and amounts of balanced energy and protein supplements may vary.
- Monitoring and evaluation should include evaluation of household-level storage facilities, spoilage, wastage, retailing, sharing and other issues related to food distribution.
- Each country will need to understand the context-specific etiology of undernutrition at the national and sub-national levels. For instance, where seasonality is a predictor of food availability, the programme should consider this and adapt to the conditions as needed (e.g. provision of more or less food of different types in different seasons). In addition, a better understanding is needed of whether alternatives to energy and protein supplements – such as cash or vouchers, or improved local and national food production and distribution – can lead to better or equivalent results.
- Anthropometric characteristics of the general population are changing, and this needs to be taken into account to ensure that only those women who are likely to benefit (i.e. only undernourished women) are included.
- The GDG noted that it is not known whether there are risks associated with providing this intervention to women with a high BMI.

## Summary of evidence and considerations

### Effects of balanced energy and protein supplements compared with no supplements or placebo (EB Table A.1.3)

Evidence on the effects of balanced energy and protein supplements compared with no supplementation or placebo was derived from a Cochrane review (47). Twelve trials, involving 6705 women, were included in this comparison. Most data were derived from trials conducted in LMICs, including Burkina Faso, Colombia, Gambia, Ghana, India, Indonesia, South Africa and Taiwan, China. The balanced energy and protein supplements used were in various forms, including fortified beverages, biscuits and powders.

### Maternal outcomes

The only maternal outcome reported for this comparison in the review, of those outcomes prioritized for this guideline, was pre-eclampsia. However, the evidence on this outcome, based on two small trials, was assessed as very uncertain.

### Fetal and neonatal outcomes

Moderate-certainty evidence shows that balanced energy and protein supplementation probably reduces SGA neonates (7 trials, 4408 women; RR: 0.79, 95% CI: 0.69–0.90) and stillbirths (5 trials, 3408 women; RR: 0.60, 95% CI: 0.39–0.94), but probably has no effect on preterm birth (5 trials, 3384 women; RR: 0.96, 95% CI: 0.80–1.16). Low-certainty evidence suggests that it may have little or no effect on neonatal deaths (5 trials, 3381 women; RR: 0.68, 95% CI: 0.43–1.07). Low birth weight was not reported for this comparison in the review.

### Additional considerations

- In the review, mean birth weight (in grams) was reported and the findings favoured the balanced energy and protein supplementation group (11 trials, 5385 neonates; mean difference [MD]: 40.96, 95% CI: 4.66–77.26). This evidence was graded as moderate-quality evidence in the review (47).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

The cost of balanced energy and protein supplements is relatively high. There may also be cost implications with respect to transport, storage and training.

### Equity

In many LMICs, pregnancy outcomes and ANC coverage are worse among women who are poor, least educated and residing in rural areas (29). Many low-income countries still struggle with widespread poverty and hunger, particularly among rural populations (48). Findings from a study of antenatal food supplementation and micronutrient supplements in rural Bangladesh suggest that food supplementation interventions might be associated with better ANC adherence among women with less education but not among those with more education (49). Therefore, providing antenatal food supplements could help to address inequalities by improving maternal nutritional status and increasing ANC coverage among disadvantaged women.

### Acceptability

Qualitative evidence indicates that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). It also suggests that women may be less likely to engage with health services if advice is delivered in a hurried or didactic manner (high confidence in the evidence) (22). Therefore, these types of interventions are more likely to be acceptable if the interventions are delivered in an unhurried and supportive way, which may also facilitate better engagement with ANC services. Qualitative evidence on health-care providers’ views of ANC suggests that they may be keen to offer general health-care advice and specific pregnancy-related information (low confidence in the evidence) but they sometimes feel they do not have the appropriate training and lack the resources and time to deliver the service in the informative, supportive and caring manner that women want (high confidence in the evidence) (45).

### Feasibility

Providing balanced protein and energy supplements may be associated with logistical issues, as supplements are bulky and will require adequate transport and storage facilities to ensure continual supplies. Qualitative evidence from LMIC settings indicates that providers feel that a lack of resources may limit implementation of recommended interventions (high confidence in the evidence) (45).



## A.1.4: High-protein supplements

**RECOMMENDATION A.1.4: In undernourished populations, high-protein supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes. (Not recommended)**

### Remarks

- The GDG noted that there is insufficient evidence on the benefits, if any, of high-protein supplementation.
- Further research on the effects of high-protein supplements in undernourished populations is not considered a research priority.

## Summary of evidence and considerations

### Effects of high-protein supplementation compared with controls (EB Table A.1.4)

Evidence on the effects of high-protein supplementation was derived from the same Cochrane review as for Recommendations A.1.2 and A.1.3 (47). The review included one trial of high-protein supplementation compared with a micronutrient supplement conducted in the 1970s, involving 1051 low-income, black women in the USA.

### Maternal outcomes

None of the outcomes prioritized for this guideline were reported for this comparison in the review.

### Fetal and neonatal outcomes

High-certainty evidence shows that high-protein supplementation increases SGA neonates (1 trial, 505 neonates; RR: 1.58, 95% CI: 1.03–2.41). Moderate-certainty evidence indicates that high-protein supplementation probably has little or no effect on preterm birth (1 study, 505 women; RR: 1.14, 95% CI: 0.83–1.56). Low-certainty evidence suggests that high-protein supplementation may have little or no effect on stillbirths (1 trial, 529 babies; RR: 0.81, 95% CI: 0.31–2.15; certainty of evidence downgraded due to imprecision) and neonatal deaths (1 trial, 529 neonates; RR: 2.78, 95% CI: 0.75–10.36).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

The cost of high-protein supplements is relatively high. There may also be cost implications with respect to transport, storage and training.

### Equity

In many LMICs, pregnancy outcomes and ANC coverage are worse among women who are poor, least educated and residing in rural areas (29). Many low-income countries still struggle with widespread poverty and hunger, particularly among rural populations (48). Therefore, providing antenatal food supplements could help to address inequalities by improving maternal nutritional status and increasing ANC coverage among disadvantaged women.

### Acceptability

Qualitative evidence indicates that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). It also suggests that women may be less likely to engage with health services if advice is delivered in a hurried or didactic manner (high confidence in the evidence) (22). Qualitative evidence on health-care providers’ views of ANC suggests that they may be keen to offer general health-care advice and specific pregnancy-related information (low confidence in the evidence) but they sometimes feel they do not have the appropriate training and lack the resources and time to deliver the service in the informative, supportive and caring manner that women want (high confidence in the evidence) (45).

### Feasibility

Providing high-protein supplements may be associated with logistical issues, as supplements are bulky and will require adequate transport and storage facilities to ensure continual supplies. Qualitative evidence from LMIC settings indicates that providers feel that a lack of resources may limit implementation of recommended interventions (high confidence in the evidence) (45).



## A.2: Iron and folic acid supplements

### A.2.1: Daily iron and folic acid supplements

**RECOMMENDATION A.2.1: Daily oral iron and folic acid supplementation with 30 mg to 60 mg of elemental iron<sup>a</sup> and 400 µg (0.4 mg) folic acid<sup>b</sup> is recommended for pregnant women to prevent maternal anaemia, puerperal sepsis, low birth weight, and preterm birth.<sup>c</sup>**  
(Recommended)

#### Remarks

- This recommendation supersedes the 2012 WHO *Guideline: daily iron and folic acid supplementation in pregnant women* (36) and should be considered alongside Recommendation A.2.2 on intermittent iron.
- In settings where anaemia in pregnant women is a severe public health problem (i.e. where at least 40% of pregnant women have a blood haemoglobin [Hb] concentration < 110 g/L), a daily dose of 60 mg of elemental iron is preferred over a lower dose.
- In the first and third trimesters, the Hb threshold for diagnosing anaemia is 110 g/L; in the second trimester, the threshold is 105 g/L (50).
- If a woman is diagnosed with anaemia during pregnancy, her daily elemental iron should be increased to 120 mg until her Hb concentration rises to normal (Hb 110 g/L or higher) (34, 51). Thereafter, she can resume the standard daily antenatal iron dose to prevent recurrence of anaemia.
- Effective communication with pregnant women about diet and healthy eating – including providing information about food sources of vitamins and minerals, and dietary diversity – is an integral part of preventing anaemia and providing quality ANC.
- Effective communication strategies are vital for improving the acceptability of, and adherence to, supplementation schemes.
- Stakeholders may need to consider ways of reminding pregnant women to take their supplements and of assisting them to manage associated side-effects.
- In areas with endemic infections that may cause anaemia through blood loss, increased red cell destruction or decreased red cell production, such as malaria and hookworm, measures to prevent, diagnose and treat these infections should be implemented.
- Oral supplements are available as capsules or tablets (including soluble tablets, and dissolvable and modified-release tablets) (52). Establishment of a quality assurance process is important to guarantee that supplements are manufactured, packaged and stored in a controlled and uncontaminated environment (53).
- A better understanding of the etiology of anaemia (e.g. malaria endemicity, haemoglobinopathies) and the prevalence of risk factors is needed at the country level, to inform context-specific adaptations of this recommendation.
- Standardized definitions of side-effects are needed to facilitate monitoring and evaluation.
- Development and improvement of integrated surveillance systems are needed to link the assessment of anaemia and iron status at the country level to national and global surveillance systems.
- To reach the most vulnerable populations and ensure a timely and continuous supply of supplements, stakeholders may wish to consider task shifting the provision of iron supplementation in community settings with poor access to health-care professionals (see Recommendation E.6.1, in section E: Health systems interventions to improve the utilization and quality of ANC).

a The equivalent of 60 mg of elemental iron is 300 mg of ferrous sulfate heptahydrate, 180 mg of ferrous fumarate or 500 mg of ferrous gluconate.

b Folic acid should be commenced as early as possible (ideally before conception) to prevent neural tube defects.

c This recommendation supersedes the previous WHO recommendation found in the 2012 *Guideline: daily iron and folic acid supplementation in pregnant women* (36).

## Summary of evidence and considerations

### Effects of any daily iron and folic acid supplements compared with no daily iron and folic acid supplements (EB Table A.2.1)

The evidence on the effects of daily iron and/or folic acid was derived from a Cochrane review of 61 trials conducted in low-, middle- and high-income countries (54). Twenty-three trials were conducted in countries with some malaria risk, of which two reported malaria outcomes. Overall, 44 trials involving 43 274 women contributed data to the review's meta-analyses. The trials compared daily oral iron supplementation, with or without folic acid or other vitamin and mineral supplements, with various control groups (folic acid only, placebo, no intervention, other vitamin and mineral supplements without iron or folic acid). Most of the evidence was derived from studies comparing iron supplementation with no iron supplementation. In most trials, women began taking supplements before 20 weeks of gestation and continued taking supplements until delivery. The most commonly used dose of elemental iron was 60 mg daily (range: 30–240 mg) and that of folic acid was 400 µg daily.

### Maternal outcomes

Anaemia was reported in many different ways and at different time points during pregnancy and the puerperium. Low-certainty evidence shows that daily iron supplementation may reduce the risk of anaemia at term (defined as blood Hb concentration < 110 g/L at 37 weeks of gestation or later) (14 trials, 2199 women; RR: 0.30, 95% CI: 0.19–0.46) and severe postpartum anaemia (defined as Hb < 80 g/L) (8 trials, 1339 women; RR: 0.04, 95% CI: 0.01–0.28).

Low-certainty evidence also shows that daily iron supplementation may increase maternal Hb concentrations at or near term (34 weeks of gestation or more) (19 trials, 3704 women; MD: 8.88 g/L higher, 95% CI: 6.96–10.8 g/L) and may increase the proportion of women with a high maternal Hb at or near term (Hb > 130 g/L at 34 weeks of gestation or later) (8 trials, 2156 women; RR: 3.07, 95% CI: 1.18–8.02).

Regarding maternal morbidity, moderate-certainty evidence shows that daily iron supplementation probably reduces the risk of maternal puerperal infections (4 trials, 4374 women; RR: 0.68, 95% CI: 0.5–0.92). Low-certainty evidence shows that daily

iron supplementation may have little or no effect on pre-eclampsia (4 trials, 1704 women; RR: 1.63, 95% CI: 0.87–3.07) and antepartum haemorrhage (2 trials, 1157 women; RR: 1.48, 95% CI: 0.51–4.31), and moderate-certainty evidence shows that it probably has little or no effect on postpartum haemorrhage (4 trials, 1488 women; RR: 0.93, 95% CI: 0.59–1.49). Evidence on other morbidity outcomes, including placental abruption and blood transfusions, is of very low certainty.

Low-certainty evidence shows that daily iron supplementation may have little or no effect on maternal mortality (2 trials, 12 560 women; RR: 0.33, 95% CI: 0.01–8.19). Women's satisfaction was evaluated in one small trial (49 women), which found little difference between daily iron and control groups.

**Side-effects:** Moderate-certainty evidence indicates that daily iron supplementation probably has little or no effect on the risk of experiencing any side-effect (11 trials, 2425 women; RR: 1.29, 95% CI: 0.83–2.02), and that it may have little or no effect on constipation (4 trials, 1495 women; RR: 0.95, 95% CI: 0.62–1.43), heartburn (3 trials, 1323 women; RR: 1.19, 95% CI: 0.86–1.66) and vomiting (4 trials, 1392 women; RR: 0.88, 95% CI: 0.59–1.30). Evidence that daily iron has little or no effect on nausea is of low certainty (4 trials, 1377 women; RR: 1.21, 95% CI: 0.72–2.03). High-certainty evidence shows that diarrhoea is less common with daily iron supplements (3 trials, 1088 women; RR: 0.55, 95% CI: 0.32–0.93).

### Fetal and neonatal outcomes

Low-certainty evidence shows that daily iron may reduce the risk of low-birth-weight neonates (< 2500 g) (11 trials, 17 613 neonates; RR: 0.84, 95% CI: 0.69–1.03). High-certainty evidence shows that it does not reduce the risk of preterm birth before 37 weeks of gestation (13 trials, 19 286 women; RR: 0.93, 95% CI: 0.84–1.03), but it does reduce the risk of very preterm birth (i.e. less than 34 weeks of gestation) (5 trials, 3749 women; RR: 0.51, 95% CI: 0.29–0.91).

Low-certainty evidence suggests that daily iron may have little or no effect on congenital anomalies (4 trials, 14 636 neonates; RR: 0.88, 95% CI: 0.58–1.33). Moderate-certainty evidence indicates that daily iron probably has little or no effect on neonatal deaths (4 trials, 16 603 neonates; RR: 0.91, 95% CI: 0.71–1.18). Neonatal infections and SGA were not reviewed as outcomes.

### Additional considerations

- Evidence from subgroups tended to be consistent with the overall findings for the main outcomes. More details can be found in the Web supplement (EB Table A.2.1).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Daily iron and folic acid supplements are relatively low cost, at less than 1 United States dollar (US\$ 1) per pregnant woman (27).

### Equity

Iron deficiency and parasitic infections are more common in LMICs and disadvantaged populations. Poor, rural and least-educated populations also experience the highest maternal, infant and child mortality (29). Increasing coverage of effective nutritional interventions to prevent anaemia, particularly among disadvantaged populations,

might help to address maternal and newborn health inequalities.

### Acceptability

Qualitative evidence suggests that the availability of iron supplements may actively encourage women to engage with ANC providers (low confidence in the evidence) (22). However, where there are additional costs associated with supplementation or where the supplements may be unavailable (because of resource constraints) women are less likely to engage with ANC services (high confidence in the evidence). Lower doses of iron may be associated with fewer side-effects and therefore may be more acceptable to women than higher doses.

### Feasibility

Qualitative evidence about the views of health-care providers suggests that resource constraints, both in terms of the availability of the supplements and the lack of suitably trained staff to deliver them, may limit implementation (high confidence in the evidence) (45).

## A.2.2: Intermittent iron and folic acid supplements

**RECOMMENDATION A.2.2: Intermittent oral iron and folic acid supplementation with 120 mg of elemental iron<sup>a</sup> and 2800 µg (2.8 mg) of folic acid once weekly is recommended for pregnant women to improve maternal and neonatal outcomes if daily iron is not acceptable due to side-effects, and in populations with an anaemia prevalence among pregnant women of less than 20%. (Context-specific recommendation)**

### Remarks

- This recommendation supersedes the previous WHO recommendation in the 2012 Guideline: intermittent iron and folic acid supplementation in non-anaemic pregnant women (55) and should be considered alongside Recommendation A.1.1.
- In general, anaemia prevalence of less than 20% is classified as a mild public health problem (33).
- Before commencing intermittent iron supplementation, accurate measurement of maternal blood Hb concentrations is needed to confirm the absence of anaemia. Therefore, this recommendation may require a strong health system to facilitate accurate Hb measurement and to monitor anaemia status throughout pregnancy.
- If a woman is diagnosed with anaemia (Hb < 110 g/L) during ANC, she should be given 120 mg of elemental iron and 400 µg (0.4 mg) of folic acid daily until her Hb concentration rises to normal (Hb 110 g/L or higher) (34, 51). Thereafter, she can continue with the standard daily antenatal iron and folic acid dose (or the intermittent regimen if daily iron is not acceptable due to side-effects) to prevent recurrence of anaemia.
- Stakeholders may need to consider ways of reminding pregnant women to take their supplements on an intermittent basis and of assisting them to manage associated side-effects.

a The equivalent of 120 mg of elemental iron is 600 mg of ferrous sulfate heptahydrate, 360 mg of ferrous fumarate or 1000 mg of ferrous gluconate.

## Summary of evidence and considerations

### Effects of intermittent iron and folic acid supplements compared with daily iron and folic acid supplements (EB Table A.2.2)

The evidence on the effects of intermittent iron and folic acid was derived from a Cochrane review that included 27 trials from 15 countries; however, only 21 trials (involving 5490 women) contributed data to the review's meta-analyses (56). All trials were conducted in LMICs with some degree of malaria risk (Argentina, Bangladesh, China, Guatemala, India, Indonesia, the Islamic Republic of Iran, Malawi, Malaysia, Mexico, Pakistan, Republic of Korea, Sri Lanka, Thailand and Viet Nam); however, only one trial specifically reported that it was conducted in a malaria-endemic area.

Most of the intermittent iron regimens involved women taking weekly supplements, most commonly 120 mg elemental iron per week (range: 80–200 mg weekly), which was compared with daily regimens, most commonly 60 mg elemental iron daily (range: 40–120 mg daily). Where folic acid was also provided in the trials, it was administered weekly in the intermittent supplement groups (range: 400–3500 µg weekly) compared with the usual standard daily dose for control groups.

### Maternal outcomes

Anaemia was reported in different ways across trials. Low-certainty evidence suggests there may be little or no difference between intermittent and daily iron supplementation in the effect on anaemia at term (4 trials, 676 women; RR: 1.22, 95% CI: 0.84–1.80). Moderate-certainty evidence shows that anaemia at or near term (defined as a Hb of < 110 g/L at 34 weeks of gestation or later) probably occurs more frequently with intermittent than daily iron supplementation (8 trials, 1385 women; RR: 1.66, 95% CI: 1.09–2.53), and that intermittent iron supplementation is probably less likely to be associated with a Hb concentration of more than 130 g/L than daily iron (15 trials, 2616 women; RR: 0.53, 95% CI: 0.38–0.74). No events of severe anaemia occurred in either group in six trials reporting this outcome (1240 women). The evidence on mean Hb concentrations at or near term and severe postpartum anaemia is of very low certainty.

Limited evidence on maternal morbidity from one small trial (110 women) was assessed as

very uncertain. Maternal infections and maternal satisfaction were not evaluated in the review.

**Side-effects:** Moderate-certainty evidence shows that intermittent iron supplementation is probably less commonly associated with nausea than daily iron supplementation (7 trials, 1034 women; RR: 0.60, 95% CI: 0.37–0.97). However, the evidence on other specific side-effects (constipation, diarrhoea, heartburn or vomiting) or any side-effect is of very low certainty.

### Fetal and neonatal outcomes

Low-certainty evidence suggests that intermittent iron supplementation may have a similar effect to daily iron supplementation on low birth weight (< 2500 g) (8 trials, 1898 neonates; RR: 0.82, 95% CI: 0.50–1.22). However, the evidence on preterm birth and very preterm birth was assessed as very uncertain. Evidence on the relative effects of intermittent versus daily iron supplementation on neonatal mortality is also very uncertain. Neonatal infections and SGA outcomes were not included in the review.

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Intermittent iron and folic acid supplementation might cost a little less than daily iron and folic acid supplementation due to the lower total weekly dose of iron.

### Equity

Intermittent iron and folic acid supplementation may have less impact on health inequalities than daily iron and folic acid supplementation, as anaemia is more common in disadvantaged populations.

### Acceptability

Qualitative evidence suggests that the availability of iron supplements may actively encourage women to engage with ANC providers (low confidence in the evidence) (22). However, where there are additional costs associated with supplementation or where the supplements may be unavailable (because of resource constraints) women are less likely to engage with ANC services (high confidence in the evidence). Women may find intermittent iron supplementation more acceptable than daily iron supplementation,

particularly if they experience side-effects with daily iron supplements.

### Feasibility

Intermittent iron may be more feasible in some low-resource settings if it costs less than daily iron.

## A.3: Calcium supplements

**RECOMMENDATION A.3: In populations with low dietary calcium intake, daily calcium supplementation (1.5–2.0 g oral elemental calcium) is recommended for pregnant women to reduce the risk of pre-eclampsia.** (*Context-specific recommendation*)

### Remarks

- This recommendation is consistent with the 2011 *WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia* (57) (strong recommendation, moderate-quality evidence) and supersedes the WHO recommendation found in the 2013 *Guideline: calcium supplementation in pregnant women* (38).
- Dietary counselling of pregnant women should promote adequate calcium intake through locally available, calcium-rich foods.
- Dividing the dose of calcium may improve acceptability. The suggested scheme for calcium supplementation is 1.5–2 g daily, with the total dose divided into three doses, preferably taken at mealtimes.
- Negative interactions between iron and calcium supplements may occur. Therefore, the two nutrients should preferably be administered several hours apart rather than concomitantly (38).
- As there is no clear evidence on the timing of initiation of calcium supplementation, stakeholders may wish to commence supplementation at the first ANC visit, given the possibility of compliance issues.
- To reach the most vulnerable populations and ensure a timely and continuous supply of supplements, stakeholders may wish to consider task shifting the provision of calcium supplementation in community settings with poor access to health-care professionals (see Recommendation E.6.1, in section E: Health systems interventions to improve the utilization and quality of ANC).
- The implementation and impact of this recommendation should be monitored at the health service, regional and country levels, based on clearly defined criteria and indicators associated with locally agreed targets. Successes and failures should be evaluated to inform integration of this recommendation into the ANC package.
- Further WHO guidance on prevention and treatment of pre-eclampsia and eclampsia is available in the 2011 WHO recommendations (57), available at: [http://apps.who.int/iris/bitstream/10665/44703/1/9789241548335\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44703/1/9789241548335_eng.pdf)

## Summary of evidence and considerations

### Effects of calcium supplements compared with no calcium supplements (for outcomes other than hypertension/pre-eclampsia) (EB Table A.3)

Evidence on the effects of calcium supplements on outcomes other than hypertension/pre-eclampsia was derived from a Cochrane systematic review (58). The review included data from 23 trials involving 18 587 pregnant women. The aim of the review was to determine the effect of calcium on maternal and perinatal outcomes other than hypertension. There is a separate Cochrane review on the latter (59), which has been referenced to support existing WHO

recommendations on calcium supplementation to prevent pre-eclampsia in populations with low dietary calcium intake (38, 57).

In 14 trials, daily calcium doses ranged from 1000 mg to 2000 mg, and in the remainder it was less than 1000 mg. Eleven trials started calcium supplementation at or after 20 weeks of gestation, five trials started before 20 weeks, and the rest did not specify when supplementation was initiated. The primary outcome of 16 of the trials was pregnancy-induced hypertension. For outcomes other than hypertension, few trials contributed to each outcome; this is the evidence presented in this section.

### Maternal outcomes

High-certainty evidence shows that calcium supplementation does not have important effects on maternal anaemia (1 trial, 1098 women; RR: 1.04, 95% CI: 0.90–1.22) or caesarean section rates (9 trials, 7440 women; RR: 0.99, 95% CI: 0.89–1.10). Moderate-certainty evidence indicates that calcium supplementation probably has little or no effect on maternal mortality (2 trials, 8974 women; RR: 0.29, 95% CI: 0.06–1.38) and probably makes little or no difference to the risk of urinary tract infections (3 trials, 1743 women; RR: 0.95, 95% CI: 0.69–1.30). Low-certainty evidence suggests that calcium supplementation may make little or no difference to maternal weight gain (3 trials; MD: –29.46 g per week, 95% CI: –119.80 to 60.89 g per week). Maternal satisfaction was not reported in any of the trials included in the Cochrane review.

**Side-effects:** Calcium supplementation makes little or no difference to the risk of “any side-effect”, a composite outcome including headache, vomiting, backache, swelling, vaginal and urinary complaints, dyspepsia and abdominal pain (1 trial, 8312 women; RR: 1.02, 95% CI: 0.93–1.12), and probably makes little or no difference to the risk of urinary stones (3 trials, 13 419 women; RR: 1.11, 95% CI: 0.48–2.54), renal colic (1 trial, 8312 women; RR: 1.67, 95% CI: 0.40–6.99) and impaired renal function (1 trial, 4589 women; RR: 0.91, 95% CI: 0.51–1.64), all assessed as moderate-certainty evidence. Low-certainty evidence suggests that it may have little or no effect on the risk of gallstones (1 trial, 518 women; RR: 1.35, 95% CI: 0.48–3.85).

### Fetal and neonatal outcomes

Calcium supplementation probably has little or no effect on low-birth-weight babies (< 2500 g), as indicated by evidence that was of moderate certainty due to inconsistency (6 trials, 14 162 women; RR: 0.93, 95% CI: 0.81–1.07). Low-certainty evidence suggests that it may have little or no effect on preterm birth before 37 weeks of gestation (13 trials, 16 139 women; RR: 0.86, 95% CI: 0.70–1.05). However, when trials are stratified by dose (< 1000 mg vs ≥ 1000 mg), moderate-certainty evidence shows that high-dose calcium supplementation probably reduces preterm birth (12 trials, 15 479 women; RR: 0.81, 95% CI: 0.66–0.99).

Low-certainty evidence suggests that calcium supplementation may make little or no difference to perinatal mortality (8 trials, 15 785 women; RR: 0.87, 95% CI: 0.72–1.06), and moderate-certainty evidence shows that it probably has little or no effect

on stillbirths or fetal deaths (6 trials, 15 269 women; RR: 0.91, 95% CI: 0.72–1.14).

### Additional considerations

- In the *WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia* (2011), the recommendation on calcium states: “In areas where dietary calcium intake is low, calcium supplementation during pregnancy (at doses of 1.5–2.0 g elemental calcium/day) is recommended for the prevention of pre-eclampsia in all women, but especially in those at high risk of developing pre-eclampsia (strong recommendation)” (57). This recommendation is based on moderate-quality evidence showing a 64% risk reduction (CI: 35–80%) in pre-eclampsia among women or populations with low baseline dietary calcium intake (57).
- In considering the evidence from the review of “non-hypertensive” effects, the GDG agreed that the effect of calcium on preterm birth is probably not distinct from the effect on preventing pre-eclampsia, as preterm birth is frequently a consequence of pre-eclampsia.

### Values

Please see “Women’s values” in section 3.A:

Background (p. 15).

### Resources

The GDG noted that the cost of calcium (3 × 1 tablet 600 mg per day for 6 months = US\$ 11.50) (27) is relatively high compared with supplements such as iron and folic acid. The weight of the supplement may also have cost and logistical implications with respect to storage and transport.

### Equity

In many LMICs, women who are poor, least educated and residing in rural areas have worse pregnancy outcomes than do more advantaged women (29). Preterm birth is the most common cause of neonatal mortality, with the majority of deaths occurring in LMICs. Therefore, effective nutritional interventions in disadvantaged populations aimed at reducing preterm birth could help to address health inequalities.

### Acceptability

Qualitative evidence indicates that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). However,



calcium carbonate tablets might be unpalatable to many women, as they can be large and have a powdery texture (59). In addition, this intervention usually involves taking three tablets a day, which significantly increasing the number of tablets a woman is required to take on a daily basis (i.e. in addition to iron and folic acid). This could have implications for both acceptability and compliance, which needs to be assessed in a programmatic context.

### Feasibility

In addition to the cost, providing calcium supplements may be associated with logistical issues (e.g. supplements are bulky and require adequate transport and storage to maintain stock in facilities) and other challenges (e.g. forecasting). Qualitative evidence on health-care providers' views suggests that resource constraints may limit implementation (high confidence in the evidence) (45).

## A.4: Vitamin A supplements

**RECOMMENDATION A.4: Vitamin A supplementation is only recommended for pregnant women in areas where vitamin A deficiency is a severe public health problem, to prevent night blindness.** (*Context-specific recommendation*)

### Remarks

- This recommendation supersedes the previous WHO recommendation found in the 2011 *Guideline: vitamin A supplementation in pregnant women* (60).
- Vitamin A is not recommended to improve maternal and perinatal outcomes.
- Vitamin A deficiency is a severe public health problem if 5% or more of women in a population have a history of night blindness in their most recent pregnancy in the previous 3–5 years that ended in a live birth, or if 20% or more of pregnant women have a serum retinol level below 0.70 µmol/L (61). Determination of vitamin A deficiency as a public health problem involves estimating the prevalence of deficiency in a population by using specific biochemical and clinical indicators of vitamin A status.
- Pregnant women should be encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet, and to refer to WHO guidance on healthy eating (41).
- In areas where supplementation is indicated for vitamin A deficiency, it can be given daily or weekly. Existing WHO guidance suggests a dose of up to 10 000 IU vitamin A per day, or a weekly dose of up to 25 000 IU (60).
- A single dose of a vitamin A supplement greater than 25 000 IU is not recommended as its safety is uncertain. Furthermore, a single dose of a vitamin A supplement greater than 25 000 IU might be teratogenic if consumed between day 15 and day 60 from conception (60).
- There is no demonstrated benefit from taking vitamin A supplements in populations where habitual daily vitamin A intakes exceed 8000 IU or 2400 µg, and the potential risk of adverse events increases with higher intakes (above 10 000 IU) if supplements are routinely taken by people in these populations (62).

## Summary of evidence and considerations

### Effects of vitamin A supplements compared with no vitamin A supplements (EB Table A.4)

The evidence was derived from a Cochrane systematic review of 19 trials of vitamin A (with or without other supplements) compared with no vitamin A (or placebo, or other supplements) involving over 310 000 women (63). All but one trial (conducted in the United Kingdom) were conducted in LMICs, including Bangladesh, China, Ghana, India, Indonesia, Malawi, Nepal, South Africa and the United Republic of Tanzania. Most trials were

conducted in vitamin A deficient populations, with one study including only women living with HIV. Trials varied considerably in design, including in the dose and timing of the intervention. Ten trials contributed data to the comparison of vitamin A alone versus placebo or no treatment.

### Maternal outcomes

Moderate-certainty evidence shows that vitamin A supplementation in vitamin A deficient populations during pregnancy probably reduces maternal anaemia (3 trials, 15 649 women; RR: 0.64, 95% CI: 0.43–0.94), but that it probably has little or no effect on

maternal mortality (4 trials, 101 574 women; RR: 0.88, 95% CI: 0.65–1.20). Low-certainty evidence on a composite outcome for maternal infection (including fever for more than one week at one week postnatally, puerperal fever greater than 38°C, subclinical mastitis and/or bacterial vaginosis) suggests that vitamin A supplementation may reduce maternal infection (5 trials, 17 313 women; average RR: 0.45, 95% CI: 0.2–0.99). Side-effects and other maternal ANC guideline outcomes were not reported in the trials.

### Fetal and neonatal outcomes

High-certainty evidence shows that vitamin A supplementation makes little or no difference to perinatal mortality (76 176 women; RR: 1.01, 95% CI: 0.95–1.07), neonatal mortality (3 trials, 89 556 neonates; RR: 0.97, 95% CI: 0.90–1.05) or stillbirths (2 trials, 122 850 neonates; RR: 1.04, 95% CI: 0.98–1.10). Moderate-certainty evidence indicates that vitamin A supplementation probably has little or no effect on low birth weight (< 2500 g) (4 trials, 14 599 neonates; RR: 0.102, 95% CI: 0.89–1.16), and low-certainty evidence suggests that it may have little or no effect on preterm birth (5 trials, 40 137 women; RR: 0.98, 95% CI: 0.94–1.01). Neonatal infections and congenital anomalies were not reported in the trials.

### Additional considerations

- Moderate-certainty evidence shows that vitamin A supplementation reduces night blindness in pregnant women living in areas with a high prevalence of this condition (2 trials, approximately 100 000 women; RR: 0.79, 95% CI: 0.64–0.98).
- Miscarriage and teratogenicity have been associated with high vitamin A intake within 60 days of conception; however, a WHO expert group consultation in 1998 concluded that daily doses of

up to 3000 µg per day after day 60 are probably safe, especially in areas where vitamin A deficiency is common (62).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Vitamin A supplements are relatively inexpensive at approximately US\$ 0.30 per woman per month (10 000 IU per day or 25 000 IU per week) (27).

Vitamin A can be given as a daily or weekly supplement.

### Equity

Effective nutritional interventions in disadvantaged populations could help to address health inequalities by improving nutritional status and promoting good maternal health.

### Acceptability

Qualitative evidence suggests that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22).

### Feasibility

Qualitative evidence shows that where there are additional costs associated with supplements (high confidence in the evidence) or where the recommended intervention is unavailable because of resource constraints (low confidence in the evidence), women may be less likely to engage with ANC (45).



## A.5: Zinc supplements

**RECOMMENDATION A.5: Zinc supplementation for pregnant women is only recommended in the context of rigorous research.** (*Context-specific recommendation – research*)

### Remarks

- Many of the included studies were at risk of bias, which influenced the certainty of the review evidence on the effects of zinc supplementation.
- The low-certainty evidence that zinc supplementation may reduce preterm birth warrants further investigation, as do the other outcomes for which the evidence is very uncertain (e.g. perinatal mortality, neonatal sepsis), particularly in zinc-deficient populations with no food fortification strategy in place. Further research should aim to clarify to what extent zinc supplementation competes with iron and/or calcium antenatal supplements for absorption. The GDG considered that food fortification may be a more cost-effective strategy and that more evidence is needed on the cost-effectiveness of food fortification strategies.

### Summary of evidence and considerations

#### Effects of zinc supplements compared with no zinc supplements (EB Table A.5)

The evidence was derived from a Cochrane review that included 21 trials involving more than 17 000 women (64). Most studies were conducted in LMICs, including Bangladesh, Chile, China, Egypt, Ghana, Indonesia, the Islamic Republic of Iran, Nepal, Pakistan, Peru and South Africa. Six trials were conducted in Denmark, the United Kingdom and the USA. Daily zinc supplementation was compared with no intervention or placebo. There was a wide variation among trials in terms of trial size (range: 56–4926 women), zinc dosage (range: 5–90 mg per day), nutritional and zinc status at trial entry, initiation and duration of supplementation (starting before conception in one trial, first or second trimester in the majority, or after 26 weeks of gestation in two trials, until delivery), and compliance with treatment.

#### Maternal outcomes

Moderate-certainty evidence indicates that zinc supplementation probably makes little or no difference to the risk of any maternal infections (3 trials, 1185 women; RR: 1.06; 95% CI: 0.74–1.53). The evidence on caesarean section, pre-eclampsia and side-effects (maternal taste and smell dysfunction) is of very low certainty, and the review did not include anaemia, maternal mortality or maternal satisfaction as review outcomes.

#### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that zinc supplementation probably makes little or no difference to the risk of having SGA (8 trials, 4252

newborns; RR: 1.02; 95% CI: 0.94–1.11) or low-birth-weight neonates (14 trials, 5643 neonates; RR: 0.93, 95% CI: 0.78–1.12). However, low-certainty evidence suggests that zinc supplementation may reduce preterm birth (16 trials, 7637 women; RR: 0.86, 95% CI: 0.76–0.97), particularly in women with presumed low zinc intake or poor nutrition (14 trials, 7099 women; RR: 0.87, 95% CI: 0.77–0.98).

Low-certainty evidence suggests that zinc supplementation may have little or no effect on congenital anomalies (6 trials, 1240 newborns; RR: 0.67, 95% CI: 0.33–1.34) and macrosomia (defined in the review as “high birth weight”; 5 trials, 2837 neonates; RR: 1.00, 95% CI: 0.84–1.18). Evidence on perinatal mortality and neonatal sepsis is of very low certainty.

#### Additional considerations

- The trials were clinically heterogeneous, therefore it is unclear what dose and timing of zinc supplementation, if any, might lead to a possible reduction in preterm birth.
- There is little or no evidence on side-effects of zinc supplementation. In addition, it is unclear to what extent zinc might compete with iron and/or calcium for absorption. Maternal anaemia was not evaluated in the review.

#### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

#### Resources

Zinc costs approximately US\$ 1.30 for 100 tablets of 20 mg (i.e. less than US\$ 3.00 for a 6-month supply based on a daily dose of 20 mg) (27).

### Equity

Effective interventions to improve maternal nutrition in disadvantaged populations could help to address health inequalities. A WHO report shows that inequalities in neonatal, infant and child mortality, as well as stunting prevalence, can be demonstrated according to economic status, education and place of residence in LMICs. The prevalence of stunting may be a good indicator of zinc deficiency in LMICs (39).

### Acceptability

Qualitative evidence suggests that women in a variety of settings tend to view ANC as a source

of knowledge and information and they generally appreciate any professional advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22).

### Feasibility

It may be more feasible to fortify food with zinc rather than to provide zinc as a single supplement, particularly in settings with a high prevalence of stunting in children.

## A.6: Multiple micronutrient (MMN) supplements

**RECOMMENDATION A.6: Multiple micronutrient supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.** (*Not recommended*)

### Remarks

- There is some evidence of additional benefit of MMN supplements containing 13–15 different micronutrients (including iron and folic acid) over iron and folic acid supplements alone, but there is also some evidence of risk, and some important gaps in the evidence. Although the GDG agreed that overall there was insufficient evidence to warrant a recommendation, the group agreed that policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMN supplements on maternal health to outweigh the disadvantages, and may choose to give MMN supplements that include iron and folic acid.
- More research is needed to determine which micronutrients improve maternal and perinatal outcomes, and how these can be optimally combined into a single supplement.

### Summary of evidence and considerations

#### Effects of MMN supplements (with 13–15 different MMNs) compared with iron and folic acid supplements (EB Table A.6)

The evidence was derived from a Cochrane review that included 17 trials involving 137 791 women (65); however, only 14 trials contributed data to this comparison. These 14 trials were all conducted in LMICs: Bangladesh (2), Burkina Faso (1), China (2), Guinea-Bissau (1), Indonesia (2), Mexico (1), Nepal (2), Niger (1), Pakistan (1) and Zimbabwe (1). The trials compared supplements containing 13–15 micronutrients (including iron and folic acid) with iron and folic acid supplements only, except for one trial in which the control arm comprised iron only. Nine trials evaluated supplements with 15 micronutrients, including vitamin A, B1, B2, B6, B12, C, D and E, copper, folic acid, iodine, iron, niacin, selenium and zinc, with exactly the same dosages as the UN international MMN preparation (UNIMMAP

(66). Evidence from these UNIMMAP trials was synthesized together with trials of 13 and 14 MMN supplements, and in separate subgroup analyses using the random effects method. Subgroup analyses were performed according to the dose of iron (60 mg or 30 mg) used in the control arm. Analyses can be found in the Web supplement (EB Table A.6).

#### Maternal outcomes

High-certainty evidence shows that MMN supplementation has a similar effect to iron and folic acid supplements only (standard care) on maternal anaemia (5 trials; RR: 0.98, 95% CI: 0.85–1.13). Compared to iron and folic acid only, moderate-certainty evidence indicates that MMN supplements probably make little or no difference to caesarean section rates (4 trials; RR: 1.03, 95% CI: 0.75–1.43) and low-certainty evidence suggests that they may have little or no effect on maternal mortality (3 trials; RR: 0.97, 95% CI: 0.63–1.48). There was no evidence relating to maternal satisfaction or side-effects.

### Fetal and neonatal outcomes

High-certainty evidence shows that MMN supplementation reduces the risk of having a low-birth-weight neonate compared with iron and folic acid supplements only (14 trials; RR: 0.88, 95% CI: 0.85–0.91), but moderate-certainty evidence indicates that it probably makes little or no difference to the risk of having an SGA neonate (13 trials; RR: 0.98, 95% CI: 0.96–1.00). High-certainty evidence shows that MMN supplements make little or no difference to preterm birth rates (14 trials; RR: 0.95, 95% CI: 0.88–1.03). Moderate-certainty evidence shows that MMN supplements probably make little or no difference to perinatal mortality (11 trials; RR: 1.00, 95% CI: 0.85–1.19), neonatal mortality (11 trials; RR: 0.99, 95% CI: 0.90–1.08) or stillbirths (14 trials; RR: 0.97, 95% CI: 0.86–1.09). The evidence on congenital anomalies is of low certainty and inconclusive (1 trial, 1200 women; RR: 0.99, 95% CI: 0.14–7.00).

High-certainty evidence from analyses restricted to trials of UNIMMAP only are consistent with the overall findings, with the exception that it shows that UNIMMAP reduces the risk of having an SGA neonate compared with iron and folic acid supplements only (8 trials; RR: 0.85, 95% CI: 0.77–0.94).

Subgroup analyses according to the iron dose in the control group are generally consistent with the overall findings. However, for the subgroup of studies that compared MMN supplements to 60 mg iron and 400 µg folic acid, a harmful effect of MMNs on neonatal mortality cannot be excluded (6 trials; RR: 1.22, 95% CI: 0.95–1.57).

### Additional considerations

- A separate review of the effects of MMN supplementation during pregnancy on child health benefits pooled data from nine of the trials included in the Cochrane review and found no evidence of beneficial effects on child mortality, growth or cognitive function (67).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

UNIMMAP supplements cost about US\$ 3 per woman per pregnancy, whereas iron and folic acid supplementation costs less than US\$ 1 (27).

### Equity

Effective interventions to improve maternal nutrition in disadvantaged populations could help to address maternal and neonatal health inequalities by improving maternal health and preventing illness related to nutritional deficiencies. However, the cost difference between MMNs and iron and folic acid supplementation may have an impact on affordability for disadvantaged populations, especially those in remote and rural areas, because they are often expected to pay for visits and supplements in addition to bearing greater transport costs due to the greater distance to travel to ANC services (68).

### Acceptability

Qualitative evidence suggests that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). However, it has been noted that the lack of appropriate training on MMN supplementation has been reported by health-care providers as a major gap (68).

### Feasibility

From the demand side, MMN supplementation should be as feasible as iron and folic acid supplementation if supplements are free and available, and it will face the same challenges in terms of compliance. However, on the supply side, there may be several barriers to overcome, such as changes in regulatory norms and policies (e.g. tariffs, labelling, imports, government oversight, etc.), ensuring sustainable MMN production (local or imported), product availability and quality. Great variability in feasibility across countries and within them would be expected (68).

## A.7: Vitamin B6 (pyridoxine) supplements

**RECOMMENDATION A.7: Vitamin B6 (pyridoxine) supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.** *(Not recommended)*

### Remarks

- Pregnant women should be encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet, and to refer to guidelines on healthy eating (41).
- The GDG agreed that there is insufficient evidence on the benefits and harms, if any, of routine vitamin B6 supplementation in pregnancy. However, research on the effects of routine vitamin B6 supplementation for pregnant women on maternal and perinatal outcomes is not considered a research priority.

### Summary of evidence and considerations

#### Effects of vitamin B6 supplements compared with no vitamin B6 supplements (EB Table A.7)

The evidence was derived from a Cochrane review that included four trials involving approximately 1646 pregnant women (69). Studies were conducted in HICs between 1960 and 1984. Vitamin B6 (pyridoxine) given intramuscularly as a single dose (100 mg) or orally as capsules or lozenges (2.6 mg to 20 mg per day) was compared with placebo or no treatment. Only two out of four studies contributed data to this comparison.

#### Maternal outcomes

Low-certainty evidence suggests that oral pyridoxine supplements may have little or no effect on pre-eclampsia (2 trials, 1197 women; RR: 1.71, 95% CI: 0.85–3.45). No other maternal outcomes relevant to the ANC guideline were reported in the review.

#### Fetal and neonatal outcomes

Trials contributed no data on low birth weight, preterm birth or other ANC guideline outcomes. Mean birth weight was evaluated in one small trial but the evidence is very uncertain. There was no evidence on congenital anomalies.

#### Additional considerations

- Moderate-certainty evidence shows that vitamin B6 probably provides some relief for nausea during pregnancy (see evidence summary for Recommendation D.1, in section D: Interventions for common physiological symptoms).
- Vitamin B6 deficiency alone is uncommon; it mostly occurs in combination with deficiencies of other B vitamins (70).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

As a single supplement, vitamin B6 (pyridoxine hydrochloride tablets) can cost about US\$ 2.50 for 90 × 10 mg tablets (71).

### Equity

Effective interventions to improve maternal nutrition in disadvantaged populations could help to address health inequalities.

### Acceptability

Qualitative evidence suggests that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any professional advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22).

### Feasibility

Qualitative evidence shows that where there are additional costs associated with supplements (high confidence in the evidence) or where the recommended intervention is unavailable because of resource constraints (low confidence in the evidence), women may be less likely to engage with ANC services (45).

## A.8: Vitamin E and C supplements

**RECOMMENDATION A.8: Vitamin E and C supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.** (*Not recommended*)

### Remarks

- The GDG noted that vitamin E and C combined supplements were evaluated mainly in the context of preventing pre-eclampsia. Vitamin C is important for improving the bioavailability of oral iron, but this was not considered within the context of the Cochrane reviews. In addition, low-certainty evidence on vitamin C alone suggests that it may prevent prelabour rupture of membranes (PROM). Therefore, the GDG agreed that future research should consider vitamin C supplements separately from vitamin E and C supplements.
- Pregnant women should be encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet, and to refer to guidelines on healthy eating (41). It is relatively easy to consume sufficient quantities of vitamin C from food sources.

### Summary of evidence and considerations

#### Effects of vitamin E and C supplements compared with no vitamin E and C supplements (EB Table A.8)

The evidence was derived from two Cochrane systematic reviews that included 17 trials conducted in low-, middle- and high-income countries contributed data (72, 73). The trials assessed vitamin E plus vitamin C combined supplements compared with placebo or no vitamin E and C supplements. The most commonly used dose of vitamin E was 400 IU daily (15 trials) and vitamin C was 1000 mg daily (13 trials). The primary outcome of 14 trials was pre-eclampsia and nine of the trials recruited women at “high” or “increased” risk of pre-eclampsia. Most of the trials commenced supplementation in the second trimester.

#### Maternal outcomes

Moderate-certainty evidence shows that vitamin E and C combined supplements probably have little or no effect on the risk of developing pre-eclampsia (14 studies, 20 878 women; RR: 0.91 95% CI: 0.79–1.06) and eclampsia (8 trials, 19 471 women; RR: 1.67, 95% CI: 0.82–3.41). Moderate-certainty evidence also shows that vitamin E and C supplements probably have little or no effect on maternal mortality (7 trials, 17 120 women; RR: 0.60, 95% CI: 0.14–2.51) and caesarean section (6 trials, 15 297 women; RR: 1.02, 95% CI: 0.97–1.07).

**Side-effects:** High-certainty evidence shows that vitamin E and C supplementation is associated with an increased risk of abdominal pain during pregnancy (1 trial, 1877 women; RR: 1.66, 95% CI: 1.16–2.37; absolute effect of 32 more per 1000 women).

#### Fetal and neonatal outcomes

High-certainty evidence indicates that vitamin E and C supplementation does not have an important effect on SGA (11 trials, 20 202 women; RR: 0.98, 95% CI: 0.91–1.06). Moderate-certainty evidence shows that vitamin E and C supplements probably have little or no effect on preterm birth (11 trials, 20 565 neonates; RR: 0.98, 95% CI: 0.88–1.09), neonatal infections (5 trials, 13 324 neonates; RR: 1.10, 95% CI: 0.73–1.67) and congenital anomalies (4 trials, 5511 neonates; RR: 1.16, 95% CI: 0.83–1.63).

#### Additional considerations

- The high-certainty evidence on abdominal pain is derived from a large, well designed trial in which abdominal pain occurred in 7.9% of women in the vitamin E and C supplement group and 4.8% of women in the placebo group.
- Despite the certainty of these effects of vitamin E and C supplementation, the biological explanations for these adverse effects are not established.
- Moderate-certainty evidence indicates that vitamin E and C supplements probably reduce the risk of placental abruption (7 trials, 14 922 women; RR: 0.64, 95% CI: 0.44–0.93; absolute effect of 3 fewer abruptions per 1000) but make little or no difference to the risk of antepartum haemorrhage from any cause (2 trials, 12 256 women; RR: 1.25, 95% CI: 0.85–1.82).
- High-certainty evidence shows vitamin E and C supplementation increases PROM at term (37 weeks of gestation or more) (2 trials, 2504 women; RR: 1.77, 95% CI: 1.37–2.28; absolute effect of 52 more cases of PROM per 1000).
- The trial contributing the most data on PROM was stopped early, based on their PROM data, when

only a quarter of the planned sample (10 000 women) had been accrued.

- Low- to moderate-certainty evidence on vitamin C only suggests that vitamin C alone (in doses ranging from 100 mg to 1000 mg) may reduce preterm PROM (5 studies, 1282 women; RR: 0.66, 95% CI: 0.48–0.91) and term PROM (1 study, 170 women; RR: 0.55, 95% CI: 0.32–0.94).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Vitamin E (tocopherol) 400 IU daily can cost about US\$ 8 for a month’s supply. Costs of vitamin C vary widely; chewable vitamin C tablets (1000 mg) can cost about US\$ 3 for a month’s supply (74).

### Equity

Effective interventions to reduce pre-eclampsia could help to address health inequalities because

mortality from pre-eclampsia mainly occurs among disadvantaged populations.

### Acceptability

Qualitative evidence suggests that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any professional advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22).

### Feasibility

Qualitative evidence shows that where there are additional costs associated with supplements (high confidence in the evidence) or where the recommended intervention is unavailable because of resource constraints (low confidence in the evidence), women may be less likely to engage with ANC services (45).

## A.9: Vitamin D supplements

**RECOMMENDATION A.9: Vitamin D supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.** *(Not recommended)*

### Remarks

- This recommendation supersedes the previous WHO recommendation found in the 2012 Guideline: vitamin D supplementation in pregnant women (75).
- Pregnant women should be advised that sunlight is the most important source of vitamin D. The amount of time needed in the sun is not known and depends on many variables, such as the amount of skin exposed, the time of day, latitude and season, skin pigmentation (darker skin pigments synthesize less vitamin D than lighter pigments) and sunscreen use (75).
- Pregnant women should be encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet, and to refer to guidelines on healthy eating (47).
- For pregnant women with documented vitamin D deficiency, vitamin D supplements may be given at the current recommended nutrient intake (RNI) of 200 IU (5 µg) per day.
- According to the Cochrane review, there are 23 ongoing or unpublished studies on vitamin D supplementation in pregnancy (76). Evidence from these trials should help to clarify the current uncertainties regarding vitamin D effects, particularly the effect on preterm birth, and any other associated benefits or harms of vitamin D when combined with other vitamins and minerals, particularly calcium.

### Summary of evidence and considerations

The evidence was derived from a Cochrane systematic review that included 15 trials assessing 2833 women (76). Nine trials were conducted in LMICs (Bangladesh, Brazil, China, India and the

Islamic Republic of Iran) and six were conducted in HICs (France, New Zealand, Russia and the United Kingdom). Sample sizes ranged from 40 to 400 women. Nine trials compared the effects of vitamin D alone versus placebo or no supplementation, and six trials compared the effects of vitamin D plus calcium



versus placebo or no supplementation. The dose and regimen of vitamin D varied widely among the trials.

#### a) Effects of vitamin D supplements alone versus placebo or no supplement (EB Table A.9)

Nine trials contributed data to this comparison. Six trials evaluated daily vitamin D with daily doses ranging from 400 IU to 2000 IU. Two trials evaluated a single dose of 200 000 IU given at about 28 weeks of gestation, one trial evaluated a weekly dose of 35 000 IU during the third trimester, and one trial administered 1–4 vitamin D doses (60 000–480 000 IU in total) depending on the participants' baseline serum 25-hydroxy-vitamin D levels.

##### Maternal outcomes

The evidence on pre-eclampsia, GDM, maternal mortality, caesarean section and side-effects is very uncertain (i.e. all findings were assessed as very low-certainty evidence).

##### Fetal and neonatal outcomes

Low-certainty evidence suggests that vitamin D supplementation may reduce low-birth-weight neonates (3 trials, 493 women; RR: 0.40, 95% CI: 0.24–0.67) and preterm birth (< 37 weeks of gestation) (3 trials, 477 women; RR: 0.36, 95% CI: 0.14–0.93), but may have little or no effect on neonatal deaths (2 trials, 282 women, RR: 0.27; 95% CI: 0.04–1.67) and stillbirths (3 trials, 540 women; RR: 0.35, 95% CI: 0.06–1.99).

#### b) Effects of vitamin D plus calcium supplements versus placebo or no supplement (EB Table A.9)

Six trials contributed data to this comparison. Vitamin D doses ranged from 200 IU to 1250 IU daily and calcium doses ranged from 375 mg to 1250 mg daily.

##### Maternal outcomes

Moderate-certainty evidence shows that vitamin D plus calcium probably reduces pre-eclampsia (3 trials, 798 women; RR: 0.51; 95% CI: 0.32–0.80), but low-certainty evidence suggest that it may have little or no effect on GDM (1 trial, 54 women, 1 event; RR: 0.43, 95% CI: 0.05–3.45).

##### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that vitamin D plus calcium probably increases preterm birth

(< 37 weeks of gestation) (3 trials, 798 women; RR: 1.57, 95% CI: 1.02–2.43). Low-certainty evidence suggests that vitamin D plus calcium has little or no effect on neonatal mortality (1 trial, 660 women; RR: 0.20, 95% CI: 0.01–4.14).

##### Additional considerations

- Due to the limited evidence currently available to directly assess the benefits and harms of the use of vitamin D supplementation alone in pregnancy for improving maternal and infant health outcomes, the use of this intervention during pregnancy as part of routine ANC is not recommended (75).
- The moderate-certainty evidence showing that adding vitamin D to calcium supplementation probably increases preterm birth is of concern and this potential harm needs further investigation.

##### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

##### Resources

Vitamin D supplements can cost from US\$ 2 per month, depending on the dose prescribed (74).

##### Equity

Effective interventions to improve maternal nutrition in disadvantaged populations could help to address health inequalities.

##### Acceptability

Qualitative evidence suggests that women in a variety of settings tend to view ANC as a source of knowledge and information and that they generally appreciate any professional advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22).

##### Feasibility

Qualitative evidence shows that where there are additional costs associated with supplements (high confidence in the evidence) or where the recommended intervention is unavailable because of resource constraints (low confidence in the evidence), women may be less likely to engage with ANC services (45).

## A.10: Restricting caffeine intake

**RECOMMENDATION A.10: For pregnant women with high daily caffeine intake (more than 300 mg per day),<sup>a</sup> lowering daily caffeine intake during pregnancy is recommended to reduce the risk of pregnancy loss and low-birth-weight neonates. (Context-specific recommendation)**

### Remarks

- Pregnant women should be informed that a high daily caffeine intake (> 300 mg per day) is probably associated with a higher risk of pregnancy loss and low birth weight.
- Caffeine is a stimulant found in tea, coffee, soft-drinks, chocolate, kola nuts and some over-the-counter medicines. Coffee is probably the most common source of high caffeine intake. A cup of instant coffee can contain about 60 mg of caffeine; however, some commercially brewed coffee brands contain more than 150 mg of caffeine per serving.
- Caffeine-containing teas (black tea and green tea) and soft drinks (colas and iced tea) usually contain less than 50 mg per 250 mL serving.

a This includes any product, beverage or food containing caffeine (i.e. brewed coffee, tea, cola-type soft drinks, caffeinated energy drinks, chocolate, caffeine tablets).

### Summary of evidence and considerations

#### a) Effects of decaffeinated coffee versus caffeinated coffee (RCT evidence) (EB Table A.10a)

Some evidence on the effects of caffeine intake was derived from a Cochrane review that included two RCTs (40). Only one of the trials, conducted in Denmark, contributed evidence. In this trial, 1207 pregnant women drinking more than three cups of coffee a day were randomized to receive instant decaffeinated coffee (intervention group) versus instant caffeinated coffee (control group) in order to assess the effect of caffeine reduction during pregnancy. In this trial, a cup of caffeinated coffee was estimated to contain 65 mg caffeine. Other sources of caffeine, such as cola, tea and chocolate were not restricted. Mean daily caffeine intake in the decaffeinated coffee group was 117 mg per day (interquartile range [IQR]: 56–228 mg) compared with 317 mg per day (IQR: 229–461 mg) in the caffeinated coffee group.

#### Maternal outcomes

None of the maternal outcomes addressed in the ANC guideline were reported in the review.

#### Fetal and neonatal outcomes

Low-certainty evidence from one trial shows that restricting caffeine intake (replacing caffeinated coffee with decaffeinated coffee) may have little or no effect on SGA (1150 neonates; RR: 0.97, 95% CI: 0.57–1.64), mean birth weight (1197 neonates; MD: 20.00, 95% CI: –48.68 to 88.68) and preterm birth (1153 neonates; RR: 0.81, 95% CI: 0.48–1.37).

No data were available on congenital anomalies or perinatal mortality.

#### b) Effects of high caffeine intake versus moderate, low or no caffeine intake (non-randomized study evidence) (EB Table A.10b)

The GDG considered the evidence from RCTs to be insufficient to make a recommendation on caffeine restriction and additional evidence from reviews of non-randomized studies (NRSs) was thus evaluated. Two NRS reviews asked the question, “Is there an association between maternal caffeine intake and the risk of low birth weight?” (77, 78), and two reviews asked the question “Is there an association between maternal caffeine intake and the risk of pregnancy loss?” (79, 80). In these reviews, low caffeine intake was defined as less than 150 mg caffeine per day, and high caffeine intake was defined as more than 300 mg or more than 350 mg per day. All four reviews adjusted data for smoking and other variables, and performed dose-response meta-analyses.

#### Fetal and neonatal outcomes: low birth weight

Moderate-certainty evidence from one review shows that high caffeine intake (more than 300 mg) is probably associated with a greater risk of low birth weight than low or no caffeine intake (12 studies; odds ratio [OR]: 1.38, 95% CI: 1.10–1.73) (78). Very low- to moderate-certainty evidence from the other review was stratified according to dose and shows that very low caffeine intake may be associated with fewer low-birth-weight neonates than low (5 studies; RR: 1.13, 95% CI: 1.06–1.21), moderate (7 studies; RR: 1.38, 95% CI: 1.18–1.62) or high caffeine intake (8 studies; RR: 1.60, 95% CI: 1.24–2.08) (77).



### Fetal and neonatal outcomes: stillbirths

The reviews reported “pregnancy loss”, a composite outcome comprising stillbirths and miscarriages. Moderate-certainty evidence from one review (80) shows that any caffeine intake probably increases pregnancy loss compared with controls (no exposure) (18 studies; OR: 1.32, 95% CI: 1.24–1.40). However, pregnancy loss is probably more common among pregnant women with moderate caffeine intake (18 studies; OR: 1.28, 95% CI: 1.16–1.42) and high caffeine intake (17 studies, OR: 1.60, 1.46–1.76), but not more common with low caffeine intake (13 studies; OR: 1.04, 95% CI: 0.94–1.15) compared with controls. This NRS evidence was upgraded to “moderate-certainty” due to the presence of a dose-response relationship. A dose-response relationship was also observed in the other review but the evidence was less certain (79).

### Values

Please see “Women’s values” in section 3.A: Background (p. 15).

### Resources

Communicating with pregnant women about the probable risks of high caffeine intake during pregnancy is a relatively low-cost intervention.

### Equity

Interventions to restrict coffee intake during pregnancy are unlikely to impact health inequalities as coffee consumption tends to be associated with affluence. However, it is unclear whether the consumption of caffeine through other sources might be a problem for pregnant women in disadvantaged populations.

### Acceptability

Qualitative evidence indicates that women in a variety of settings generally appreciate any advice (including dietary or nutritional) that may lead to a healthy baby and a positive pregnancy experience (high confidence in the evidence) (22). Evidence on health-care providers’ views on ANC suggests that they may be keen to offer general health-care advice and specific pregnancy-related information (low confidence in the evidence) but they sometimes feel they do not have the appropriate training and lack the resources and time to deliver the service in the informative, supportive and caring manner that women want (high confidence in the evidence) (45).

### Feasibility

A lack of suitably trained staff to deliver health promotion interventions may limit implementation (high confidence in the evidence) (45).

## B. Maternal and fetal assessment

### B.1: Maternal assessment

#### Background

Hypertensive disorders of pregnancy are important causes of maternal and perinatal morbidity and mortality, with approximately a quarter of maternal deaths and near misses estimated to be due to pre-eclampsia and eclampsia (9). Antenatal screening for pre-eclampsia is an essential part of good ANC. It is routinely performed by measuring maternal blood pressure and checking for proteinuria at each ANC contact and, upon detection of pre-eclampsia, specific management is required to prevent eclampsia and other poor maternal and perinatal outcomes (57). The GDG did not evaluate evidence or make a recommendation on this procedure, therefore, which it considers to be an essential component of Good Clinical Practice in ANC.

As part of the ANC guideline development, specifically in relation to maternal assessment, the GDG considered evidence and other relevant information on interventions to detect the following conditions in pregnancy:

- **Anaemia:** Defined as a blood haemoglobin (Hb) concentration below 110 g/L, anaemia is the world's second leading cause of disability, and one of the most serious global public health problems, with the global prevalence of anaemia among pregnant women at about 38% (33). Clinical assessment (inspection of the conjunctiva for pallor) is a common method of detecting anaemia but has been shown to be quite inaccurate. In HICs, performing a full blood count, which quantifies the blood Hb level, is part of routine ANC (81). However, this and other available tests may be expensive, complex or impractical for use in rural or LMIC settings. A low-cost and reliable method of detecting anaemia is therefore needed for places with no or limited access to laboratory facilities. WHO developed the haemoglobin colour scale, a low-cost method that is performed by placing a drop of undiluted blood on specially made chromatography paper and matching it against a range of colours representing

different Hb values in 20 g/L increments (82). With haemoglobinometer tests, undiluted blood is placed directly into a microcuvette, which is inserted into the haemoglobinometer (or photometer) to produce a reading (82).

- **Asymptomatic bacteriuria (ASB):** ASB is a common urinary tract condition that is associated with an increased risk of urinary tract infections (cystitis and pyelonephritis) in pregnant women. *Escherichia coli* is associated with up to 80% of isolates; other pathogens include *Klebsiella* species, *Proteus mirabilis* and group B streptococcus (GBS) (83). Methods for diagnosing ASB include midstream urine culture (the gold standard), Gram stain and urine dipstick tests. A urine culture can take up to seven days to get a result, with the threshold for diagnosis usually defined as the presence of  $10^5$  colony-forming units (cfu)/mL of a single organism (84). The Gram stain test uses colour stains (crystal violet and safrinin O) to exaggerate and distinguish between Gram-positive (purple) and Gram-negative (red) organisms on a prepared glass slide. Urine dipsticks test for nitrites, which are not found in normal urine, and leucocytes, which are identified by a reaction with leucocyte esterase, to identify the presence of bacteria and pus in the urine, respectively. ASB is associated with an increased risk of preterm birth; once detected it is, therefore, usually actively managed with antibiotics (see also Recommendation C.1, in section C: Preventive measures).
- **Intimate partner violence (IPV):** IPV, defined as any behaviour within an intimate relationship that causes physical, psychological or sexual harm to those in the relationship, is now recognized as a global public health issue. Worldwide, almost one third of all women who have been in a relationship have experienced physical and/or sexual violence by their intimate partner (85). Emotional abuse (being humiliated, insulted, intimidated and subjected to controlling behaviours such as not being permitted to see friends or family) also adversely impacts the health of individuals (85).

IPV is associated with chronic problems in women, including poor reproductive health (e.g. a history of STIs including HIV, unintended pregnancy, abortion and/or miscarriage), depression, substance use and other mental health problems (85). During pregnancy, IPV is a potentially preventable risk factor for various adverse outcomes, including maternal and fetal death. Clinical enquiry about IPV aims to identify women who have experienced or are experiencing IPV, in order to offer interventions leading to improved outcomes. Some governments and professional organizations recommend screening all women for IPV rather than asking only women with symptoms (86).

### Women's values

A scoping review of what women want from ANC and what outcomes they value informed the ANC guideline (13). Evidence showed that women from high-, medium- and low-resource settings valued having a positive pregnancy experience. Within the context of maternal and fetal assessment, women valued the opportunity to receive screening and tests to optimize their health and that of their baby as long as individual procedures were explained to them clearly and administered by knowledgeable, supportive and respectful health-care practitioners (high confidence in the evidence).

In addition to GDG recommendations on the above, recommendations on diagnosing gestational diabetes mellitus (GDM) and screening for tobacco smoking, alcohol and substance abuse, TB and HIV

infection have been integrated into this chapter from the respective existing WHO guidance on these conditions.

## B.1.1: Anaemia

**RECOMMENDATION B.1.1: Full blood count testing is the recommended method for diagnosing anaemia during pregnancy. In settings where full blood count testing is not available, on-site haemoglobin testing with a haemoglobinometer is recommended over the use of the haemoglobin colour scale as the method for diagnosing anaemia in pregnancy.**  
(Context-specific recommendation)

### Remarks

- The GDG agreed that the high recurrent costs of Hb testing with haemoglobinometers might reduce the feasibility of this method in some low-resource settings, in which case the WHO haemoglobin colour scale method may be used.
- Other low-technology on-site methods for detecting anaemia need development and/or investigation.

## Summary of evidence and considerations

### Test accuracy of on-site Hb testing with haemoglobinometer and haemoglobin colour scale (HCS) methods to detect anaemia (EB Table B.1.1)

The evidence was derived from a test accuracy review conducted to support the ANC guideline (81). Only one study (671 women) contributed data (87). The study, conducted in Malawi, assessed the test accuracy of on-site Hb testing with a haemoglobinometer (HemoCue®) and the HCS method in comparison to a full blood count test performed by an electronic counter (Coulter counter), the reference standard.

Moderate-certainty evidence shows that the sensitivity and specificity of the haemoglobinometer test in detecting anaemia (Hb < 110 g/L) are approximately 0.85 (95% CI: 0.79–0.90) and 0.80 (95% CI: 0.76–0.83), respectively, while the sensitivity and specificity of the HCS method are lower at approximately 0.75 (95% CI: 0.71–0.80) and 0.47 (95% CI: 0.41–0.53), respectively.

For severe anaemia (defined in the study as Hb < 60 g/L), moderate-certainty evidence shows that the sensitivity and specificity of the haemoglobinometer test are approximately 0.83 (95% CI: 0.44–0.97) and 0.99 (95% CI: 0.98–1.00), respectively, while for the HCS method they are approximately 0.50 (95% CI: 0.15–0.85) and 0.98 (95% CI: 0.97–0.99), respectively.

### Additional considerations

- In absolute numbers, the data mean that in settings with an anaemia prevalence of 38%, the haemoglobinometer test will probably miss about 57 anaemic women (95% CI: 38–80) out of every 1000 women tested, whereas the HCS method will probably miss about 95 anaemic women (95% CI: 76–110) out of every 1000 women tested. For populations with a severe anaemia prevalence of 5%, the haemoglobinometer test will probably miss about nine women with severe anaemia (95% CI: 2–27) out of every 1000 women tested, whereas the HCS method will probably miss about 25 women with severe anaemia (95% CI: 3–43) out of every 1000 women tested.
- The main limitation of the evidence is the low number of women identified with severe anaemia, which affects the precision of the estimates. However, the evidence suggests that the haemoglobinometer test is probably more accurate than the HCS method. As there are no direct comparisons in test accuracy studies and, as confidence intervals for sensitivity and specificity of the two methods overlap, there is some uncertainty about the relative accuracy of these tests.
- The review also evaluated the test accuracy of clinical assessment (4 studies, 1853 women), giving a sensitivity for clinical assessment of 0.64 (95% CI: 22–94) and a specificity of 0.63 (95% CI: 23–91) for detecting anaemia (Hb < 110 g/L). Thus, the HCS method might be more sensitive but less specific than clinical assessment.
- In settings where iron supplementation is routinely used by pregnant women, the consequence of missing women with severe anaemia is more serious than that of missing women with mild or moderate anaemia, as women with severe anaemia usually require additional treatment. Therefore, the accuracy of on-site Hb tests to detect severe anaemia in pregnancy is probably more important than the ability to detect Hb below 110 g/L.
- A study of various Hb testing methods in Malawi found the haemoglobinometer method to be the most user-friendly method (82).

### Values

Please see “Women’s values” in section 3.B.1: Maternal assessment: Background (p. 41).

### Resources

Any health-care provider can perform both the haemoglobinometer and HCS methods after minimal training. The haemoglobinometer and HCS methods have been estimated to cost approximately US\$ 0.75 and US\$ 0.12 per test, respectively (82). Both methods require needles for finger pricks, cotton balls, gloves and Sterets® skin cleansing swabs; however, the higher costs associated with haemoglobinometer tests are mainly due to supplies (cuvettes and controls), equipment costs and maintenance.

### Equity

The highest prevalence of maternal anaemia occurs in Africa and South-East Asia, where parasitic infections are major contributory factors (33). Anaemia increases perinatal risks for mothers and newborns and contributes to preventable mortality. Accurate, low-cost, simple-to-use tests to detect anaemia might help to address health inequalities by improving the detection and subsequent management of women with anaemia, particularly severe anaemia, in low-resource settings.

### Acceptability

Qualitative evidence from a variety of settings indicates that women generally appreciate clinical tests that support their well-being during pregnancy (moderate confidence in the evidence) (22). However, evidence from LMICs indicates that where there are likely to be additional costs associated with tests, or where the recommended interventions are unavailable because of resource constraints, women may be less likely to engage with ANC services (high confidence in the evidence).

### Feasibility

Qualitative evidence from providers in various LMICs indicates that a lack of resources, both in terms of the availability of the diagnostic equipment and potential treatments, as well as the lack of suitably trained staff to deliver the service, may limit implementation of recommended interventions (high confidence in the evidence) (45).

## B.1.2: Asymptomatic bacteriuria (ASB)

**RECOMMENDATION B.1.2: Midstream urine culture is the recommended method for diagnosing asymptomatic bacteriuria (ASB) in pregnancy. In settings where urine culture is not available, on-site midstream urine Gram-staining is recommended over the use of dipstick tests as the method for diagnosing ASB in pregnancy. (Context-specific recommendation)**

### Remarks

- This recommendation should be considered alongside Recommendation C.1 on ASB treatment (see section C: Preventive measures).
- The GDG agreed that the higher resource costs associated with Gram stain testing might reduce the feasibility of this method in low-resource settings, in which case, dipstick tests may be used.
- The GDG agreed that ASB is a priority research topic, given its association with preterm birth and the uncertainty around urine testing and treatment in settings with different levels of ASB prevalence. Specifically, studies are needed that compare on-site testing and treatment versus testing plus confirmation of test with treatment on confirmatory culture, to explore health and other relevant outcomes, including acceptability, feasibility and antimicrobial resistance. In addition, better on-site tests need to be developed to improve accuracy and feasibility of testing and to reduce overtreatment of ASB. Research is also needed to determine the prevalence of ASB at which targeted testing and treatment rather than universal testing and treatment might be effective.

## Summary of evidence and considerations

### Test accuracy of on-site urine Gram staining and dipsticks to detect ASB (EB Table B.1.2)

The evidence was derived from a test accuracy review of on-site urine tests conducted to support the ANC guideline (88). Four studies (1904 pregnant women) contributed data on urine Gram staining and eight studies (5690 pregnant women) contributed data on urine dipsticks. Most of the studies were conducted in LMICs. The average prevalence of ASB in the studies was 8%. A Gram stain was positive if one or more bacteria were detected per oil-immersed field, and a dipstick test was positive if it detected either nitrites or leucocytes. The reference standard used was urine culture with a threshold of  $10^5$  cfu/mL.

However, the certainty of the evidence on the accuracy of both Gram stain tests and dipstick tests is very low, with pooled sensitivity and specificity of the Gram stain test estimated at 0.86 (95% CI: 0.80–0.91) and 0.97 (95% CI: 0.93–0.99), respectively, and pooled sensitivity and specificity for urine dipsticks estimated at 0.73 (95% CI: 0.59–0.83) and 0.89 (95% CI: 0.79–0.94), respectively. A positive nitrite test alone on dipsticks was found to be less sensitive but more specific than when urine leucocytes were also considered.

### Additional considerations

- A high level of accuracy in detecting ASB is important to avoid treating women unnecessarily, particularly in view of increasing antimicrobial resistance. Based on the uncertain evidence above, and assuming a prevalence of ASB of 9%, there would be 18 and 118 false-positive tests per 1000 women tested with Gram stain and dipstick tests, respectively. This suggests that, in settings where pregnant women are treated for ASB, dipstick diagnosis of ASB might lead to many women receiving unnecessary treatment.
- Dipstick tests are multi-test strips that, in addition to testing for nitrites and leucocytes, may also include detection of urine protein and glucose. However, the accuracy of dipsticks to detect conditions associated with proteinuria (pre-eclampsia) and glycosuria (diabetes mellitus) is considered to be low.

### Values

Please see “Women’s values” in section 3.B.1: Maternal assessment: Background (p. 41).

### Resources

Dipsticks are relatively low cost compared with the Gram stain test, as the latter requires trained staff and laboratory equipment and supplies (microscope, glass slides, reagents, Bunsen burner or slide warmer). Gram stain tests take longer to perform and

to produce results than urine dipstick tests (10–30 minutes vs 60 seconds).

### Equity

Preterm birth is the leading cause of neonatal death worldwide, with most deaths occurring in LMICs. Timely diagnosis and treatment of risk factors associated with preterm birth might therefore help to address health inequalities.

### Acceptability

Qualitative evidence from a range of settings suggests that women view ANC as a source of knowledge, information and clinical expertise and that they generally appreciate the tests and advice they are offered (high confidence in the evidence) (22). However, engagement with ANC services may be limited if tests and procedures are not explained properly or when women feel their beliefs and traditions are being overlooked or ignored by health-care professionals. In addition, if the Gram stain test is associated with long waiting times at ANC

or having to return for test results, this may be less acceptable to women, as it might have additional cost and convenience implications for them (high confidence in the evidence). Health professionals are likely to prefer the dipstick test as it is associated with less effort (no need to label samples for laboratory assessment, perform tests or schedule follow-up visits to provide the results) and might provide additional information pertaining to other conditions (pre-eclampsia and diabetes mellitus) (high confidence in the evidence).

### Feasibility

Qualitative evidence indicates that, in some LMIC settings, the lack of diagnostic equipment at ANC facilities discourages women from attending, and that providers often do not have the diagnostic equipment, supplies or skills to perform tests (high confidence in the evidence) (45). Therefore, urine dipstick tests, which are cheaper and easy to perform, might be more feasible in low-resource settings.

### B.1.3: Intimate partner violence (IPV)

**RECOMMENDATION B.1.3: Clinical enquiry about the possibility of intimate partner violence (IPV) should be strongly considered at antenatal care visits when assessing conditions that may be caused or complicated by IPV in order to improve clinical diagnosis and subsequent care, where there is the capacity to provide a supportive response (including referral where appropriate) and where the WHO minimum requirements are met.<sup>a</sup> (Context-specific recommendation)**

#### Remarks

- This recommendation is consistent with the 2013 publication *Responding to intimate partner violence and sexual violence against women: WHO clinical and policy guidelines* (86). The evidence on clinical enquiry was indirect (strong recommendation) and the evidence on universal screening was judged as being of low to moderate quality (conditional recommendation).
- “Universal screening” or “routine enquiry” (i.e. asking all women at all health-care encounters) about IPV is not recommended. However, the WHO guidelines identify ANC as a setting where routine enquiry could be implemented if providers are well trained on a first-line response and minimum requirements are met (86).
- Examples of conditions during pregnancy that may be caused or complicated by IPV include (86):
  - traumatic injury, particularly if repeated and with vague or implausible explanations;
  - intrusive partner or husband present at consultations;
  - adverse reproductive outcomes, including multiple unintended pregnancies and/or terminations, delay in seeking ANC, adverse birth outcomes, repeated STIs;
  - unexplained or repeated genitourinary symptoms;
  - symptoms of depression and anxiety;
  - alcohol and other substance use;
  - self-harm, suicidality, symptoms of depression and anxiety.
- The GDG agreed that, despite a paucity of evidence, it was important to make a recommendation due to the high prevalence and importance of IPV. ANC provides an opportunity to enquire about IPV among women for whom barriers to accessing health care may exist, and also allows for the possibility for follow-up during ANC with appropriate supportive interventions, such as counselling and empowerment interventions. However, the evidence on benefits and potential harms of clinical enquiry and subsequent interventions is lacking or uncertain.
- A minimum condition for health-care providers to ask women about violence is that it must be safe to do so (i.e. the partner is not present) and that identification of IPV is followed by an appropriate response. In addition, providers must be trained to ask questions in the correct way and to respond appropriately to women who disclose violence (86).
- Research on IPV is needed to answer the following questions:
  - Which are the most effective strategies for identifying, preventing and managing IPV in pregnancy?
  - Does asking routinely about violence impact on ANC attendance?
  - Can interventions targeted at partners of pregnant women prevent IPV?
- Detailed guidance on responding to IPV and sexual violence against women can be found in the 2013 WHO clinical and policy guidelines (86), available at: <http://www.who.int/reproductivehealth/publications/violence/9789241548595/en/>

<sup>a</sup> Minimum requirements are: a protocol/standard operating procedure; training on how to ask about IPV, and on how to provide the minimum response or beyond; private setting; confidentiality ensured; system for referral in place; and time to allow for appropriate disclosure.



## Summary of evidence and considerations

### Effects of universal screening to detect IPV compared with no screening (usual care) (EB Table B.1.3)

The evidence on screening for IPV was derived from a Cochrane review that included two trials conducted in urban ANC settings in HICs (Canada and the USA), involving 663 pregnant women (89). In one trial, 410 women were randomized before 26 weeks of gestation to a computer-based abuse assessment screening tool, with and without a provider cue sheet (giving the results of the assessment to the provider), prior to ANC consultation with a health-care provider. In the other trial (a cluster-RCT), providers administered a face-to-face screening tool that screened for 15 risk factors, including IPV, to women between 12 and 30 weeks of gestation in the intervention clusters, while women in the control clusters received usual ANC.

Low-certainty evidence from the review suggests that abuse assessment screening may identify more pregnant women with IPV than those identified through usual ANC (2 trials, 663 women; OR: 4.28, 95% CI: 1.77–10.36).

### Additional considerations

- The review also pooled data on IPV screening versus no IPV screening from other health-care settings (involving pregnant and non-pregnant women), and the pooled effect estimate favoured screening to detect IPV (7 trials, 4393 women; OR: 2.35, 95% CI: 1.53–3.59).
- Another Cochrane review evaluated interventions to prevent or reduce IPV (90). Uncertain evidence from one study suggests that pregnant women who receive IPV interventions (e.g. multiple counselling sessions) to prevent or reduce IPV may report fewer episodes of partner violence during pregnancy and the postpartum period (306 women; RR: 0.62, 95% CI: 0.43–0.88), but evidence on this and other outcomes is largely inconclusive.
- Most of the review evidence comes from HICs where the prevalence of women experiencing IPV in the previous 12 months ranged from 3% to 6%. However, in many settings, particularly those where economic and sociocultural factors foster a culture more permissive of violence against women, the lifetime prevalence is higher than 30%. Notably, the prevalence among young women (under 20 years old) approaches 30%,

suggesting that violence commonly starts early in women's relationships (85).

- Severe IPV in pregnancy (such as being beaten up, choked or burnt on purpose, being threatened with or having a weapon used against her, and sexual violence) (85) is more common among women who are in relationships that have also been severely abusive outside of pregnancy.
- WHO's clinical handbook on *Health care for women subjected to intimate partner violence or sexual violence* (2014) provides practical guidance on how to respond (91).

### Values

Please see "Women's values" in section 3.B.1: Maternal assessment: Background (p. 41).

### Resources

Clinical enquiry about IPV can be conducted face-to-face or by providing women with a written or computer-based questionnaire. Although the costs of implementing these methods can vary, they might be relatively low. Subsequent management and IPV support linked to the screening intervention, however, requires sophisticated training and can therefore have significant cost implications. The GDG considered that training and resources in low-resource settings might be best targeted towards first response to IPV rather than IPV screening.

### Equity

IPV is highly prevalent in many LMICs and among disadvantaged populations (92, 93). Effective interventions to enquire about IPV in disadvantaged populations might help to identify those at risk of IPV-related adverse outcomes, and facilitate the provision of appropriate supportive interventions leading to improved equity. However, more evidence is needed.

### Acceptability

Qualitative evidence from a range of settings on women's views of ANC suggests that pregnant women would like to be seen by a kind and supportive health-care provider who has the time to discuss issues of this nature in a private setting (high confidence in the evidence) (22). However, evidence from LMICs suggests that women may be unlikely to respond favourably to cursory exchanges of information with providers who they sometimes perceive to be hurried, uncaring and occasionally abusive (high confidence in the evidence). In addition, some women may not appreciate enquiries of this nature, particularly those living in male-dominated,



patriarchal societies, where women's financial dependence on their husbands may influence their willingness to discuss IPV, especially if the health professional is male (22).

From the providers' perspective, qualitative evidence mainly from HICs suggests that providers often find it difficult to enquire about IPV for the following reasons: they do not feel they have enough knowledge, training or time to discuss IPV in a sensitive manner; the presence of the partner acts as a barrier; they may have experienced IPV themselves; and they lack knowledge and guidance about the availability of additional support services (counselling, social work, etc.) (high confidence in the evidence). Providers highlight the midwife-led continuity of care (MLCC) model as a way of achieving a positive,

trusting and empathetic relationship with pregnant women (moderate confidence in the evidence) (see Recommendation E.2, in section E: Health systems interventions to improve the utilization and quality of ANC).

### Feasibility

Following IPV clinical enquiry, complex, multifaceted, culturally specific interventions are required to manage IPV, which could be challenging in many low-resource settings. However, emerging evidence from HICs shows that medium-duration empowerment counselling and advocacy/support, including a safety component, offered by trained health-care providers could be beneficial, and the feasibility of such interventions in LMIC settings needs investigation (86).

## B.1.4: Gestational diabetes mellitus (GDM)

**RECOMMENDATION B1.4: Hyperglycaemia first detected at any time during pregnancy should be classified as either gestational diabetes mellitus (GDM) or diabetes mellitus in pregnancy, according to WHO criteria.<sup>a</sup> (Recommended)**

### Remarks

- This recommendation has been integrated from the 2013 WHO publication *Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy* (the strength of the recommendation and the quality of the evidence were not stated) (94).
- WHO currently does not have a recommendation on whether or how to screen for GDM, and screening strategies for GDM are considered a priority area for research, particularly in LMICs.
- Diabetes mellitus in pregnancy differs from GDM in that the hyperglycaemia is more severe and does not resolve after pregnancy as it does with GDM.
- A systematic review of cohort studies shows that women with hyperglycaemia (diabetes mellitus and GDM) detected during pregnancy are at greater risk of adverse pregnancy outcomes, including macrosomia, pre-eclampsia/hypertensive disorders in pregnancy, and shoulder dystocia. Treatment of GDM, which usually involves a stepped approach of lifestyle changes (nutritional counselling and exercise) followed by oral blood-glucose-lowering agents or insulin if necessary, is effective in reducing these poor outcomes (94).
- There are many uncertainties about the cost-effectiveness of different screening strategies, the prevalence of GDM and diabetes mellitus according to the 2013 criteria in diverse populations, and the impact of earlier diagnosis on pregnancy outcomes (see Chapter 5: Research implications) (94).
- The usual window for diagnosing GDM is between 24 and 28 weeks of gestation. Risk factor screening is used in some settings as a strategy to determine the need for a 2-hour 75 g oral glucose tolerance test (OGTT). These include a BMI of greater than 30 kg/m<sup>2</sup>, previous GDM, previous macrosomia, family history of diabetes mellitus, and ethnicity with a high prevalence of diabetes mellitus (95). In addition, glycosuria on dipstick testing (2+ or above on one occasion, or 1+ on two or more occasions) may indicate undiagnosed GDM and, if this is observed, performing an OGTT could be considered (95).
- The management approach for women classified with diabetes mellitus in pregnancy (i.e. severe hyperglycaemia first detected in pregnancy) usually differs from the approach for women with GDM, particularly when diagnosed early in pregnancy; however, the principles of management are similar and both require referral and increased monitoring.
- Further information and considerations related to this recommendation can be found in the 2013 WHO guideline (94), available at: [http://www.who.int/diabetes/publications/Hyperglycaemia\\_In\\_Pregnancy/en/](http://www.who.int/diabetes/publications/Hyperglycaemia_In_Pregnancy/en/)

a This is not a recommendation on routine screening for hyperglycaemia in pregnancy. It has been adapted and integrated from the 2013 WHO publication (94), which states that GDM should be diagnosed at any time in pregnancy if one or more of the following criteria are met:

- fasting plasma glucose 5.1–6.9 mmol/L (92–125 mg/dL)
- 1-hour plasma glucose  $\geq$  10.0 mmol/L (180 mg/dL) following a 75 g oral glucose load
- 2-hour plasma glucose 8.5–11.0 mmol/L (153–199 mg/dL) following a 75 g oral glucose load

Diabetes mellitus in pregnancy should be diagnosed if one or more of the following criteria are met:

- fasting plasma glucose  $\geq$  7.0 mmol/L (126 mg/dL)
- 2-hour plasma glucose  $\geq$  11.1 mmol/L (200 mg/dL) following a 75 g oral glucose load
- random plasma glucose  $\geq$  11.1 mmol/L (200 mg/dL) in the presence of diabetes symptoms..

## B.1.5: Tobacco use

**RECOMMENDATION B.1.5: Health-care providers should ask all pregnant women about their tobacco use (past and present) and exposure to second-hand smoke as early as possible in pregnancy and at every antenatal care visit. (Recommended)**

### Remarks

- This strong recommendation based on low-quality evidence has been integrated from the 2013 *WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy* (96). Related recommendations from this guideline include the following:
  - Health-care providers should routinely offer advice and psychosocial interventions for tobacco cessation to all pregnant women who are either current tobacco users or recent tobacco quitters (strong recommendation based on moderate quality evidence).
  - All health-care facilities should be smoke-free to protect the health of all staff, patients and visitors, including pregnant women (strong recommendation based on low-quality evidence).
  - Health-care providers should provide pregnant women, their partners and other household members with advice and information about the risks of second-hand smoke (SHS) exposure from all forms of smoked tobacco, as well as strategies to reduce SHS in the home (strong recommendation based on low-quality evidence).
  - Health-care providers should, wherever possible, engage directly with partners and other household members to inform them of all the risks of SHS exposure to pregnant women from all forms of tobacco, and to promote reduction of exposure and offer smoking cessation support (strong recommendation based on low-quality evidence).
- Further guidance on strategies to prevent and manage tobacco use and SHS exposure can be found in the 2013 WHO recommendations (96), available at: <http://www.who.int/tobacco/publications/pregnancy/guidelinstobaccosmokeexposure/en/>

## B.1.6: Substance use

**RECOMMENDATION B.1.6: Health-care providers should ask all pregnant women about their use of alcohol and other substances (past and present) as early as possible in the pregnancy and at every antenatal care visit. (Recommended)**

### Remarks

- This strong recommendation based on low-quality evidence has been integrated from the 2014 *WHO Guidelines for the identification and management of substance use and substance use disorders in pregnancy* (97). The overarching principles of this guideline aimed to prioritize prevention, ensure access to prevention and treatment services, respect women's autonomy, provide comprehensive care, and safeguard against discrimination and stigmatization.
- The GDG responsible for the recommendation noted that asking women at every ANC visit is important as some women are more likely to report sensitive information only after a trusting relationship has been established.
- Pregnant women should be advised of the potential health risks to themselves and to their babies posed by alcohol and drug use.
- Validated screening instruments for alcohol and other substance use and substance use disorders are available (refer to Annex 3 of the 2014 guidelines [97]).
- Health-care providers should be prepared to intervene or refer all pregnant women who are identified as using alcohol and/or drugs (past and present).
- For women identified as being dependent on alcohol or drugs, further recommendations from the guideline include the following:
  - Health-care providers should at the earliest opportunity advise pregnant women dependent on alcohol or drugs to cease their alcohol or drug use and offer, or refer them to, detoxification services under medical supervision, where necessary and applicable (strong recommendation based on very low-quality evidence).
  - Health-care providers should offer a brief intervention to all pregnant women using alcohol or drugs (strong recommendation based on low-quality evidence).
- It was decided that despite the low-quality evidence on effects of brief psychosocial interventions, the benefit (potential reduction of alcohol and substance use) outweighed any potential harms, which were considered to be minimal.
- A brief intervention is a structured therapy of short duration (typically 5–30 minutes) offered with the aim of assisting an individual to cease or reduce use of a psychoactive substance.
- Further guidance on interventions and strategies to identify and manage substance use and substance use disorders in pregnancy can be found in the 2014 WHO guidelines (97), available at: [http://www.who.int/substance\\_abuse/publications/pregnancy\\_guidelines/en/](http://www.who.int/substance_abuse/publications/pregnancy_guidelines/en/)

## B.1.7: Human immunodeficiency virus (HIV) and syphilis

**RECOMMENDATION B.1.7:** In high-prevalence settings,<sup>a</sup> provider-initiated testing and counselling (PITC) for HIV should be considered a routine component of the package of care for pregnancy women in all antenatal care settings. In low-prevalence settings, PITC can be considered for pregnant women in antenatal care settings as a key component of the effort to eliminate mother-to-child transmission of HIV, and to integrate HIV testing with syphilis, viral or other key tests, as relevant to the setting, and to strengthen the underlying maternal and child health systems. (*Recommended*)

### Remarks

- This recommendation has been integrated from the 2015 WHO *Consolidated guidelines on HIV testing services* (98) (the strength of the recommendation and the quality of the evidence were not stated).
- PITC denotes an HIV testing service that is routinely offered in a health-care facility and includes providing pre-test information and obtaining consent, with the option for individuals to decline testing. PITC has proved highly acceptable and has increased the uptake of HIV testing in LMICs (98).
- The availability of HIV testing at ANC services is responsible for the high level of knowledge of HIV status among women in many countries, which has allowed women and infants to benefit from ART.
- WHO recommends that ART should be initiated in all pregnant women diagnosed with HIV at any CD4 count and continued lifelong (99). This recommendation is based on evidence that shows that providing ART to all pregnant and breastfeeding women living with HIV improves individual health outcomes, prevents mother-to-child transmission of HIV, and prevents horizontal transmission of HIV from the mother to an uninfected sexual partner.
- Other recommendations relevant to ANC services from the *Consolidated guidelines on HIV testing services* include the following (98):
  - On disclosure: Initiatives should be put in place to enforce privacy protection and institute policy, laws and norms that prevent discrimination and promote tolerance and acceptance of people living with HIV. This can help create environments where disclosure of HIV status is easier (strong recommendation, low-quality evidence).
  - On retesting: In settings with a generalized HIV epidemic:<sup>b</sup> Retest all HIV-negative pregnant women in the third trimester, during labour or postpartum because of the high risk of acquiring HIV infection during pregnancy (strength of recommendation and quality of evidence not stated).
  - On retesting: In settings with a concentrated HIV epidemic:<sup>c</sup> Retest HIV-negative pregnant women who are in a serodiscordant couple or from a key population group<sup>d</sup> (strength of recommendation and quality of evidence not stated).
  - On retesting before ART initiation: National programmes should retest all people newly and previously diagnosed with HIV before they enrol in care and initiate ART (strength of recommendation and quality of evidence not stated).
  - On testing strategies: In settings with greater than 5% HIV prevalence in the population being tested, a diagnosis of HIV-positive should be issued to people with two sequential reactive tests. In settings with less than 5% HIV prevalence in the population being tested, a diagnosis of HIV-positive should be issued to people with three sequential reactive tests (strength of recommendation and quality of evidence not stated).
  - On task shifting: Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (strong recommendation, moderate-quality evidence).
- Further guidance on HIV testing can be found in the 2015 WHO guidelines (98), available at: <http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/>
- In addition, the 2015 *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV* (99) is available at: <http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/>
- To prevent mother-to-child transmission of syphilis, all pregnant women should be screened for syphilis at the first ANC visit in the first trimester and again in the third trimester of pregnancy. For further guidance

on screening, please refer to the 2006 WHO publication *Prevention of mother-to-child transmission of syphilis (100)*, available at: [http://www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/prevention\\_mtct\\_syphilis.pdf](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/prevention_mtct_syphilis.pdf)

- The latest (2016) WHO guidelines on the treatment of chlamydia, gonorrhoea and syphilis, and on the prevention of sexual transmission of Zika virus (101–104), are available at: <http://www.who.int/reproductivehealth/publications/rtis/clinical/en/>

- a High-prevalence settings are defined in the 2015 WHO publication *Consolidated guidelines on HIV testing services* as settings with greater than 5% HIV prevalence in the population being tested. Low-prevalence settings are settings with less than 5% HIV prevalence in the population being tested (98).
- b A generalized HIV epidemic is when HIV is firmly established in the general population. Numerical proxy: HIV prevalence is consistently over 1% in pregnant women attending antenatal clinics (98).
- c A concentrated HIV epidemic is when HIV has spread rapidly in a defined subpopulation (or key population, see next footnote) but is not well established in the general population (98).
- d Key populations are defined in the 2015 WHO guidelines as the following groups: men who have sex with men, people in prison or other closed settings, people who inject drugs, sex workers and transgender people (98).

## B.1.8: Tuberculosis (TB)

**RECOMMENDATION B.1.8: In settings where the tuberculosis (TB) prevalence in the general population is 100/100 000 population or higher, systematic screening for active TB should be considered for pregnant women as part of antenatal care.** (*Context-specific recommendation*)

### Remarks

- This recommendation has been adapted and integrated from the 2013 WHO publication *Systematic screening for active tuberculosis: principles and recommendations*, where it was considered a conditional recommendation based on very low-quality evidence (105).
- Systematic screening is defined as the systematic identification of people with suspected active TB in a predetermined target group, using tests, examinations or other procedures that can be applied rapidly. Options for initial screening include screening for symptoms (either for cough lasting longer than two weeks, or any symptoms compatible with TB, including a cough of any duration, haemoptysis, weight loss, fever or night sweats) or screening with chest radiography. The use of chest radiography in pregnant women poses no significant risk but the national guidelines for the use of radiography during pregnancy should be followed (105).
- Before screening is initiated, high-quality TB diagnosis, treatment, care, management and support should be in place, and there should be the capacity to scale these up further to match the anticipated rise in case detection that may occur as a result of screening.
- The panel responsible for making this recommendation noted that it may not be possible to implement it in resource-constrained settings.
- Other recommendations relevant to ANC services from the same publication include the following (105):
  - Household contacts and other close contacts should be systematically screened for TB (strong recommendation, very low-quality evidence).
  - People living with HIV should be systematically screened for active TB at each visit to a health-care facility (strong recommendation, very low-quality evidence).
  - Systematic screening for active TB may be considered also for other subpopulations that have very poor access to health care, such as people living in urban slums, homeless people, people living in remote areas with poor access to health care, and other vulnerable or marginalized groups including some indigenous populations, migrants and refugees (conditional recommendation, very low-quality evidence).
- TB increases the risk of preterm birth, perinatal death and other pregnancy complications. Initiating TB treatment early is associated with better maternal and infant outcomes than late initiation (105).
- To better understand the local burden of TB in pregnancy, health systems may benefit from capturing pregnancy status in registers that track TB screening and treatment.
- Further information and considerations related to this recommendation can be found in the 2013 WHO recommendations (105), available at: <http://www.who.int/tb/tbscreening/en/>

## B.2: Fetal assessment

### Background

Assessment of fetal growth and well-being is an important part of ANC. The GDG considered evidence and other relevant information on the following interventions to assess fetal growth and well-being in healthy pregnant women not at risk of adverse perinatal outcomes:

■ **Daily fetal movement counting:** Maternal perception of reduced fetal movements is associated with poor perinatal outcomes, including fetal death (106). Daily fetal movement counting, such as the Cardiff “count-to-ten” method using kick charts, is a way of screening for fetal well-being, by which a woman counts daily fetal movements to assess the condition of her baby. The aim of this is to try to reduce perinatal mortality by alerting health workers when the baby might be compromised (107). Daily fetal movement counting may be used routinely in all pregnant women or only in women who are considered to be at increased risk of adverse perinatal outcomes. Early detection of fetal compromise could lead to timely clinical interventions to reduce poor perinatal outcomes but might lead to maternal anxiety or unnecessary clinical interventions. It is also possible that the period between decreased fetal movements and fetal death might be too short to allow effective action to be taken (108).

■ **Symphysis-fundal height (SFH) measurement:** SFH measurement is a commonly-practiced method of fetal growth assessment that uses a tape measure to measure the SFH, in order to detect intrauterine growth restriction (IUGR). It also has the potential to detect multiple pregnancy, macrosomia, polyhydramnios and oligohydramnios. For fetuses growing normally, from 24 weeks of gestation, the SFH measurement in centimetres should correspond to the number of weeks of gestation, with an allowance of a 2-cm difference either way (109). Other methods of fetal growth assessment include abdominal palpation of fundal height in relation to anatomical landmarks such as the umbilicus and xiphisternum, abdominal girth measurement, and serial ultrasound measurement of the fetal parameters (109). Accurate low-cost methods for detecting abnormal growth are desirable because ultrasound, the most

accurate screening tool, is resource-intensive and not widely available in LMICs.

■ **Routine antenatal cardiotocography (CTG):**

CTG is a continuous recording of the fetal heart rate and uterine contractions obtained via an ultrasound transducer placed on the mother’s abdomen. CTG is widely used in pregnancy as a method of assessing fetal well-being, predominantly in pregnancies with increased risk of complications and during labour.

■ **Fetal ultrasound examination:** Diagnostic ultrasound examination is employed in a variety of specific circumstances during pregnancy, such as where there are concerns about fetal growth and after clinical complications. However, because adverse outcomes may also occur in pregnancies without clear risk factors, assumptions have been made that antenatal ultrasound examination in all pregnancies will prove beneficial by enabling earlier detection of problems that may not be apparent (110) – such as multiple pregnancies, IUGR, congenital anomalies, malpresentation and placenta praevia – and by allowing accurate gestational age estimation, leading to timely and appropriate management of pregnancy complications.

■ **Fetal Doppler ultrasound examination:** Doppler ultrasound technology evaluates umbilical artery (and other fetal arteries) waveforms to assess fetal well-being in the third trimester of pregnancy. It is widely used in high-risk pregnancies to identify fetal compromise and thus reduce perinatal mortality (111, 112). Therefore, it might also be useful when performed as an antenatal intervention to detect fetal compromise and predict complications, particularly IUGR and pre-eclampsia, in apparently healthy pregnancies. Doppler ultrasound is useful for distinguishing between fetuses that are growth-restricted (IUGR) and those that are constitutionally small (SGA) (113). It can be performed as part of a fetal ultrasound examination or separately. The examination quantifies blood flow through the umbilical artery as either a pulsatility index or a resistive index (114). A high resistance to blood flow often indicates an increased risk of IUGR and pre-eclampsia and indicates the need for further investigation.



## Women's values

A scoping review of what women want from ANC and what outcomes they value informed the ANC guideline (13). Evidence showed that women from high-, medium- and low-resource settings valued having a positive pregnancy experience. Within the context of maternal and fetal assessment, women valued the opportunity to receive screening and tests to optimize their health and that of their baby as long as individual procedures were explained to them clearly and administered by knowledgeable, supportive and respectful health-care practitioners (high confidence in the evidence).

### B.2.1: Daily fetal movement counting

**RECOMMENDATION B.2.1: Daily fetal movement counting, such as with “count-to-ten” kick charts, is only recommended in the context of rigorous research.** (*Context-specific recommendation – research*)

#### Remarks

- Fetal movement counting is when a pregnant woman counts and records her baby's movements in order to monitor the baby's health. Various methods have been described, with further monitoring variously indicated depending on the method used, for example, if fewer than six distinct movements are felt within 2 hours (115) or fewer than 10 distinct movements are felt within 12 hours (the Cardiff “count to ten” method) (106).
- While daily fetal movement counting is not recommended, healthy pregnant women should be made aware of the importance of fetal movements in the third trimester and of reporting reduced fetal movements.
- Clinical enquiry by ANC providers at each ANC visit about maternal perception of fetal movements is recommended as part of good clinical practice. Women who perceive poor or reduced fetal movements require further monitoring (e.g. with daily fetal movement counting) and investigation, if indicated.
- The GDG agreed that more research is needed on the effects of daily fetal movement counting in the third trimester of pregnancy, particularly in LMIC settings with a high prevalence of unexplained stillbirths.

### Summary of evidence and considerations

#### Effects of daily maternal fetal movement counting compared with standard ANC (EB Table B.2.1)

The evidence on the effects of daily fetal movement counting was derived from a Cochrane review (107). Two RCTs from HICs contributed data for this comparison. One was a large, multicentre, cluster RCT (68 654 women) conducted in Belgium, Ireland, Sweden, the United Kingdom and the USA, which compared a “count-to-ten” fetal movement counting kick chart with standard ANC in women with uncomplicated pregnancies recruited between 28 and 32 weeks of gestation. Women in the standard ANC group were asked about fetal movements at each ANC visit. The other trial was a multicentre RCT conducted in Norway involving 1123 women that

compared a modified “count-to-ten” fetal movement counting protocol with standard care.

#### Maternal outcomes

Low-certainty evidence suggests that daily fetal movement counting may make little or no difference to caesarean section (1 trial, 1076 women; RR: 0.93, 95% CI: 0.60–1.44) or assisted vaginal delivery rates (1 trial, 1076 women; RR: 1.04, 95% CI: 0.65–1.66).

With regard to maternal satisfaction, low-certainty evidence suggests that daily fetal movement counting may reduce mean anxiety scores (1 trial, 1013 women; standardized MD: –0.22, 95% CI: –0.35 to –0.10).

#### Fetal and neonatal outcomes

Low-certainty evidence suggests that there may be little or no difference to preterm birth (1 trial, 1076



neonates; RR: 0.81, 95% CI: 0.46–1.46) and low birth weight (1 trial, 1076 neonates; RR: 0.98, 95% CI: 0.66–1.44) with daily fetal movement counting.

There were no perinatal deaths in the Norwegian trial (1076 women). Low-certainty evidence from the large cluster RCT, which reported the weighted mean difference in stillbirth rates between intervention and control clusters, suggests that fetal movement counting may make little or no difference to stillbirth rates (weighted MD: 0.23, 95% CI: –0.61 to 1.07).

### Additional considerations

- These trials were conducted in HICs with low stillbirth rates, therefore the findings on effects may not apply equally to settings with high stillbirth rates.
- In the cluster RCT, despite fetal movement counting, most fetuses detected as being compromised by reduced fetal movements had died by the time the mothers received medical attention.
- There was a trend towards increased CTG and antenatal hospital admissions in the intervention clusters of the cluster RCT. Antenatal hospital admissions were also more frequent in the intervention arm of the Norwegian RCT (107).
- Findings from an additional RCT that was unpublished at the time of the Cochrane review support the Cochrane evidence that daily fetal movement counting may reduce maternal anxiety (115).

### Values

Please see “Women’s values” in section 3.B.2: Fetal assessment: Background (p. 54).

### Resources

Fetal movement counting is a low-cost intervention on its own, but it could be resource-intensive if it leads to unnecessary additional interventions or hospital admissions.

### Equity

LMICs bear the global burden of perinatal morbidity and mortality, and women who are poor, least educated and residing in rural areas of LMICs have lower ANC coverage and worse pregnancy outcomes than more advantaged women (29). Therefore, simple, effective, low-cost antenatal interventions to assess fetal well-being could help to address health inequalities by improving detection of complications in low-resource settings.

### Acceptability

Qualitative evidence shows that women generally appreciate the knowledge and information they can acquire from health-care providers during ANC visits, provided this is explained properly and delivered in a consistent, caring and culturally sensitive manner (high confidence in the evidence) (22). It also shows that health professionals want to give appropriate information and advice to women but sometimes they don’t feel suitably trained to do so (high confidence in the evidence) (45).

### Feasibility

From the perspective of women who live far from ANC clinics and who may not have the resources or time to attend ANC regularly, and the perspective of ANC providers with limited resources, this intervention may offer a practical and cost-effective approach to monitoring fetal well-being if it’s shown to be effective (high confidence in the evidence) (22, 45).

## B.2.2: Symphysis-fundal height (SFH) measurement

**RECOMMENDATION B.2.2: Replacing abdominal palpation with symphysis-fundal height (SFH) measurement for the assessment of fetal growth is not recommended to improve perinatal outcomes. A change from what is usually practiced (abdominal palpation or SFH measurement) in a particular setting is not recommended. (Context-specific recommendation)**

### Remarks

- SFH measurement is routinely practiced in many ANC settings. Due to a lack of clear evidence of accuracy or superiority of either SFH measurement or clinical palpation to assess fetal growth, the GDG does not recommend a change of practice.
- The GDG agreed that there is a lack of evidence on SFH, rather than a lack of effectiveness, particularly in LMIC settings.
- Apart from false reassurance, which might occur with both SFH measurement and clinical palpation, there is no evidence of harm with SFH measurement.
- Research is needed to determine the role of SFH measurement in detecting abnormal fetal growth and other risk factors for perinatal morbidity (e.g. multiple pregnancy, polyhydramnios) in settings where antenatal ultrasound is not available.

## Summary of evidence and considerations

### Effects of SFH measurement versus abdominal palpation (EB Table B.2.2)

The evidence on the effects of SFH measurement was derived from a Cochrane review that included only one trial conducted in Denmark involving 1639 pregnant women enrolled at about 14 weeks of gestation (109). SFH measurement or abdominal palpation were performed from 28 weeks of gestation. Most women had at least three assessments, with measurements plotted on a chart.

### Maternal outcomes

Low-certainty evidence suggests that there may be little or no difference in the effect of SFH measurement versus clinical palpation on caesarean section (1639 women; RR: 0.72, 95% CI: 0.31–1.67) and induction of labour (1639 women; RR: 0.84, 95% CI: 0.45–1.58).

### Fetal and neonatal outcomes

Moderate-certainty evidence shows that SFH measurement versus clinical palpation probably makes little or no difference to the antenatal detection of SGA neonates (1639 women; RR: 1.32, 95% CI: 0.92–1.90) and low-certainty evidence suggests that it may make little or no difference to perinatal mortality (1639 women; RR: 1.25, 95% CI: 0.38–4.07). No other ANC guideline outcomes were reported in the review.

### Additional considerations

- The GDG also considered evidence from a test accuracy review regarding the accuracy of SFH

in predicting SGA at birth (birthweight < 10th centile), where SGA was a proxy outcome for IUGR (116). The DTA review included seven studies conducted in HICs, which used different measurement thresholds to detect SGA. SFH measurement had a sensitivity ranging from 0.27 to 0.76, suggesting that it fails to identify up to 73% of pregnancies affected by SGA at birth. However, there was generally a high degree of specificity (0.79–0.92), suggesting that a normal SFH measurement may be a reasonable indicator of a healthy baby. In practice, this could mean that few healthy pregnancies are referred for ultrasound examination; however, most true SGA cases may be missed. Comparable test accuracy evidence on abdominal palpation is not available.

### Values

Please see “Women’s values” in section 3.B.2: Fetal assessment: Background (p. 54).

### Resources

Both abdominal palpation and SFH measurement are low-cost interventions with the main cost being staff training. SFH requires tape measures to be available.

### Equity

LMICs bear the global burden of perinatal morbidity and mortality, and women who are poor, least educated and residing in rural areas of LMICs have lower ANC coverage and worse pregnancy outcomes than more advantaged women (29). Therefore, simple, effective, low-cost, routine antenatal

interventions to assess fetal well-being could help to address health inequalities by improving detection of complications in low-resource settings.

### Acceptability

SFH and clinical palpation are non-invasive approaches for fetal assessment, which are widely used and not known to be associated with acceptability issues.

However, in some settings women experience a sense of shame during physical examinations, and this needs to be addressed with sensitivity by health-care providers (low confidence in the evidence) (22).

### Feasibility

Both methods are considered equally feasible, provided tape measures are available.

## B.2.3: Antenatal cardiotocography (CTG)

**RECOMMENDATION B.2.3: Routine antenatal cardiotocography is not recommended for pregnant women to improve maternal and perinatal outcomes.** (*Not recommended*)

### Remarks

- CTG is the continuous recording of the fetal heart rate and uterine contractions obtained via an ultrasound transducer placed on the mother's abdomen.
- There is currently no evidence on effects or other considerations that supports the use of antenatal (prelabour) CTG as part of routine ANC.
- A lack of evidence of benefits associated with CTG in high-risk pregnancies suggests that the evaluation of antenatal CTG in healthy pregnant women is not a research priority.

## Summary of evidence and considerations

### Effects of routine antenatal CTG versus no routine antenatal CTG (EB Table B.2.3)

A Cochrane review of routine antenatal CTG for fetal assessment identified no eligible studies of routine CTG and all six included studies involved women with high-risk pregnancies (117).

### Additional considerations

- Low-certainty evidence on antenatal CTG in high-risk pregnancies suggests that this intervention may have little or no effect on perinatal mortality and caesarean section (117).

### Values

Please see "Women's values" in section 3.B.2: Fetal assessment: Background (p. 54).

### Resources

CTG machines are costly (starting from about US\$ 450)<sup>4</sup>, require maintenance and supplies of ultrasound gel, and require staff training in their use and interpretation.

## Equity

Simple, effective, low-cost, antenatal interventions to assess fetal well-being could help to address health inequalities by improving detection of complications in low-resource settings, which bear the burden of perinatal mortality.

### Acceptability

Qualitative evidence from a variety of settings indicates that women generally appreciate the use of technology to monitor pregnancy (high confidence in the evidence), and a lack of modern equipment at ANC facilities in LMICs may discourage women from attending (moderate confidence in the evidence) (22). However, in some LMICs, women hold the belief that pregnancy is a healthy condition and may be resistant to CTG use unless they have experienced a previous pregnancy complication (high confidence in the evidence). Acceptability may be further compromised if the reasons for using CTG are not properly explained (high confidence in the evidence).

### Feasibility

Health-care providers in LMIC settings feel that a lack of modern equipment and training limits the implementation of this type of intervention (high confidence in the evidence) (45).

4 Crude estimate based on Internet search.

## B.2.4: Ultrasound scan

**RECOMMENDATION B.2.4: One ultrasound scan before 24 weeks of gestation (early ultrasound) is recommended for pregnant women to estimate gestational age, improve detection of fetal anomalies and multiple pregnancies, reduce induction of labour for post-term pregnancy, and improve a woman's pregnancy experience. (Recommended)**

### Remarks

- The benefits of an early ultrasound scan are not improved upon and cannot be replicated with a late ultrasound scan where there has not been an early ultrasound scan. Therefore, an ultrasound scan after 24 weeks of gestation (late ultrasound) is not recommended for pregnant women who have had an early ultrasound scan. However, stakeholders should consider offering a late ultrasound scan to pregnant women who have not had an early ultrasound scan, for the purposes of identifying the number of fetuses, presentation and placental location.
- The GDG noted that the effects of introducing antenatal ultrasound on population health outcomes and health systems in rural, low-resource settings are unproven. However, the introduction of ultrasound to detect pregnancy complications and confirm fetal viability to the woman and her family in these settings could plausibly increase ANC service utilization and reduce morbidity and mortality, when accompanied by appropriate gestational age estimation, diagnosis, referral and management.
- The ongoing multicountry trial that is under way should contribute further evidence on health effects, health care utilization and implementation-related information on ultrasound in rural, low-resource settings (118).
- The GDG acknowledged that the use of early pregnancy ultrasound has not been shown to reduce perinatal mortality. The GDG put emphasis on other benefits of ultrasound (mentioned in points above) and the increased accuracy of gestational age assessment, which would assist management in case of suspected preterm birth and reduce labour induction for post-term pregnancies.
- The GDG acknowledges that implementing and scaling up this recommendation in low-resource settings will be associated with a variety of challenges that may include political (budgeting for fees and tariffs), logistical (equipment maintenance, supplies, technical support), infrastructural (ensuring a reliable power supply and secure storage) and resources.
- The GDG noted that antenatal ultrasound is an intervention that can potentially be task shifted from trained sonographers and doctors to trained nurses, midwives and clinical officers, provided that ongoing training, staff retention, quality improvement activities and supervision are ensured.
- Stakeholders might be able to offset/reduce the cost of antenatal ultrasound if the ultrasound equipment is also used for other indications (e.g. obstetric emergencies) or by other medical departments.
- The implementation and impact of this recommendation on health outcomes, facility utilization and equity should be monitored at the health service, regional and country levels, based on clearly defined criteria and indicators associated with locally agreed targets.<sup>a</sup>
- For further guidance, please refer to the WHO *Manual of diagnostic ultrasound* (119), available at: [http://www.who.int/medical\\_devices/publications/manual\\_ultrasound\\_pack1-2/en/](http://www.who.int/medical_devices/publications/manual_ultrasound_pack1-2/en/)

<sup>a</sup> Two members of the GDG (Lisa Noguchi and Charlotte Warren) indicated that they would prefer to recommend this intervention in specific contexts with capacity to conduct close monitoring and evaluation to ensure a basic standard of implementation (including adequate capacity to diagnose and manage complications) and monitor for potential adverse effects on delivery of other critical maternal and newborn health interventions.

### Summary of evidence and considerations

#### a) Effects of an ultrasound scan before 24 weeks of gestation (early ultrasound scan) versus selective ultrasound scan (EB Table B.2.4a)

The evidence on early ultrasound was derived from a Cochrane review that included 11 RCTs conducted in Australia, Norway, South Africa, Sweden, the United Kingdom and the USA, involving 37 505

women (120). The intervention in all trials involved an ultrasound scan before 24 weeks of gestation, with women in the control arm undergoing selective scans if indicated (or, in one study, concealed scans, the results of which were not shared with clinicians unless requested). The scans usually included assessment of gestational age (biparietal diameter with or without head circumference and femur length), fetal anatomy, number of fetuses and

location of the placenta. Scans were performed in most trials between 10 and 20 weeks of gestation, with three trials evaluating scans before 14 weeks, and three trials evaluating an intervention comprising both early (at 18–20 weeks) and late scans (at 31–33 weeks).

### Maternal outcomes

Moderate-certainty evidence suggests that an early ultrasound scan probably has little or no effect on caesarean section rates (5 trials, 22 193 women; RR: 1.05; 95% CI: 0.98–1.12). However, low-certainty evidence suggests that early ultrasound may lead to a reduction in induction of labour for post-term pregnancy (8 trials, 25 516 women; RR: 0.59, 95% CI: 0.42–0.83).

Regarding maternal satisfaction, low-certainty evidence suggests that fewer women may report feeling worried about their pregnancy after an early ultrasound scan (1 trial, 635 women; RR: 0.80, 95% CI: 0.65–0.99).

### Fetal and neonatal outcomes

Low-certainty evidence suggests that early ultrasound scans may increase the detection of congenital anomalies (2 trials, 17 158 women; RR: 3.46, 95% CI: 1.67–7.14). However, detection rates were low for both groups (16% vs 4%, respectively) with 346/387 neonates with abnormalities (89%) being undetected by 24 weeks of gestation.

Low-certainty evidence suggests that early ultrasound may make little or no difference to perinatal mortality (10 trials, 35 737 births; RR: 0.89, 95% CI: 0.70–1.12) and low birth weight (4 trials, 15 868 neonates; RR: 1.04, 95% CI: 0.82–1.33). Moderate-certainty evidence also shows that it probably has little or no effect on SGA (3 trials, 17 105 neonates; RR: 1.05, 95% CI: 0.81–1.35).

#### b) Effects of an ultrasound scan after 24 weeks of gestation (late ultrasound scan) versus no late ultrasound scan (EB Table B.2.4b)

This evidence on late ultrasound was derived from a Cochrane review that included 13 RCTs conducted in HICs (121). Most women in these trials underwent early ultrasound scan and were randomized to receive an additional third trimester scan or to selective or concealed ultrasound scan. The purpose of the late scan in these trials, which was usually performed between 30 and 36 weeks of gestation, variably included assessment of fetal anatomy, estimated

weight, amniotic fluid volume and/or placental maturity.

### Maternal outcomes

Moderate-certainty evidence suggests that a late ultrasound scan probably has little or no effect on caesarean section (6 trials, 22 663 women; RR: 1.03, 95% CI: 0.92–1.15), instrumental delivery (5 trials, 12 310 women; RR: 1.05, 95% CI: 0.95–1.16) and induction of labour (6 trials, 22 663 women; RR: 0.93, 95% CI: 0.81–1.07). Maternal satisfaction was not assessed in this review.

### Fetal and neonatal outcomes

Moderate-certainty evidence suggests that a late ultrasound scan probably has little or no effect on perinatal mortality (8 trials, 30 675 births; RR: 1.01, 95% CI: 0.67–1.54) and preterm birth (2 trials, 17 151 neonates; RR: 0.96, 95% CI: 0.85–1.08). Low-certainty evidence suggests that it may have little or no effect on SGA (4 trials, 20 293 neonates; RR: 0.98, 95% CI: 0.74–1.28) and low birth weight (3 trials, 4510 neonates; RR: 0.92, 95% CI: 0.71–1.18).

### Additional considerations

- The evidence on ultrasound is derived mainly from HICs, where early ultrasound is a standard component of ANC to establish an accurate gestational age and identify pregnancy complications. The impact of ultrasound screening in low-resource settings is currently unknown but the low rates of maternal and perinatal mortality experienced in HICs indirectly suggests that ultrasound is an important component of quality ANC services.
- Evidence from the Cochrane review on early ultrasound suggests that multiple pregnancies may be less likely to be missed/undetected by 24–26 weeks of gestation with early ultrasound (120). Of 295 multiple pregnancies occurring in seven trials (approximately 24 000 trial participants), 1% (2/153) were undetected by 24–26 weeks of gestation with early ultrasound screening compared with 39% (56/142) in the control group (RR: 0.07, 95% CI: 0.03–0.17; graded by review authors as low-quality evidence).
- The Cochrane review also evaluated several safety outcomes in offspring and found no evidence of differences in school performance, vision and hearing, disabilities or dyslexia.
- An ongoing multicountry cluster RCT of antenatal ultrasound in the Democratic Republic of the Congo, Guatemala, Kenya, Pakistan and Zambia

should contribute data on health outcomes and health care utilization, as well as implementation-related information on ultrasound in rural, low-resource settings (118). The trial intervention involves a two-week obstetric ultrasound training course for health workers (e.g. midwives, nurses, clinical officers) to perform ultrasound scans at 18–22 weeks and 32–36 weeks of gestation in each participant enrolled.

- Accurate gestational age dating is critical for the appropriate delivery of time-sensitive interventions in pregnancy, as well as management of pregnancy complications, particularly pre-eclampsia and preterm birth, which are major causes of maternal and perinatal morbidity and mortality in LMICs, and early ultrasound is useful for this purpose.

### Values

Please see “Women’s values” in section 3.B.2: Fetal assessment: Background (p. 54).

### Resources

The cost of ultrasound equipment, especially portable compact units, has decreased (122), and they are currently available at less than US\$ 10 000 (28). Thus, given the cost of equipment, maintenance, supplies (ultrasound gel), replacement batteries, initial and ongoing staff training and supervision, and staffing costs (allowing 15–45 minutes per scan), routine ultrasound scans may have considerable resource implications for LMIC settings.

### Equity

Effective interventions to increase uptake and quality of ANC services, and improve the experience of care, are needed in LMICs to prevent maternal and perinatal mortality and improve equity. However, if women are expected to pay for ultrasound scans, or if scans are not available to women living in rural areas due to feasibility issues, this intervention could perpetuate inequalities. In addition, ultrasound sexing of the fetus in some low-income countries has a negative impact on gender equity and needs to be monitored.

### Acceptability

Qualitative evidence shows that women generally appreciate the knowledge and information they can acquire from health-care providers and that they are willing to be screened and tested for a variety of conditions, provided the information and procedures are explained properly and delivered in a caring and culturally sensitive manner (high confidence in the evidence) (22). Evidence also shows that, in some LMICs, the lack of modern technology (like ultrasound equipment) at ANC facilities discourages some women from attending (high confidence in the evidence) (22). This suggests that the offer of ultrasound might attract women to use ANC facilities, which may also lead to earlier ANC attendance. Specific studies not included in the main qualitative review indicate that women value the opportunity to see their baby via ultrasound and find the test reassuring (123). However, there is some evidence that women do not understand that ultrasound is a diagnostic tool, and that adverse findings during scans might increase anxiety and distress (124).

Qualitative evidence from health-care providers shows that they generally want to provide screening and testing procedures, but sometimes don’t feel suitably trained to do so (high confidence in the evidence) (45). This suggests that they might welcome ultrasound scans to assist with accurate gestational age estimation and to identify potential risk factors, such as multiple pregnancies, if appropriately trained and supported.

### Feasibility

Feasibility challenges of antenatal ultrasound scans in LMICs includes equipment procurement and staff training, ensuring a power supply (via a power point or rechargeable batteries) and secure storage, regular equipment maintenance, maintaining adequate and continual supplies of ultrasound gel, and ongoing technical support and supervision.



## B.2.5: Doppler ultrasound of fetal blood vessels

**RECOMMENDATION B.2.5: Routine Doppler ultrasound examination is not recommended for pregnant women to improve maternal and perinatal outcomes.** (*Not recommended*)

### Remarks

- The GDG noted that the evidence base for the use of Doppler ultrasound of fetal blood vessels in high-risk pregnancy is already established.
- The GDG agreed that the value of a single Doppler ultrasound examination of fetal blood vessels for all pregnant women in the third trimester needs rigorous evaluation, particularly in LMIC settings. Future trials should be designed to evaluate the effect of a single Doppler ultrasound on preventable perinatal deaths.

### Summary of evidence and considerations

#### Effects of Doppler ultrasound examination of fetal blood vessels compared with no Doppler ultrasound examination (EB Table B.2.5)

The evidence on Doppler ultrasound examination was derived from a Cochrane review that included five trials involving 14 624 women in HICs (Australia, France and the United Kingdom) (114). One study evaluated a single Doppler examination at 28–34 weeks of gestation, three studies evaluated multiple Doppler examinations from as early as 18 weeks, and one study evaluated women undergoing single or multiple examinations from 26 to 36 weeks of gestation. Data were evaluated together and separately for single and multiple examinations. Women in the control arms received standard ANC with no (or concealed) Doppler examination.

#### Maternal outcomes

The available moderate-certainty evidence suggests that antenatal Doppler ultrasound probably makes little or no difference to caesarean section rates (2 trials, 6373 women; RR: 0.98, 95% CI: 0.85–1.13) and assisted vaginal birth (2 trials, 6884 women; RR: 1.04, 95% CI: 0.96–1.12). No other maternal outcomes that were prioritized for the ANC guideline were reported in the trials.

#### Fetal and neonatal outcomes

Low-certainty evidence suggests that Doppler ultrasound may have little or no effect on perinatal mortality (4 trials, 11 183 women; RR: 0.80, 95% CI: 0.35–1.83). Moderate-certainty evidence indicates that the intervention probably has little or no effect on preterm birth (4 trials, 12 162 women; RR: 1.02, 95% CI: 0.87–1.18).

### Additional considerations

- Subgroup analyses according to the number of Doppler ultrasound examinations (single or multiple) are largely consistent with the overall findings. However, low-certainty evidence from the single examination subgroup suggests that a single Doppler ultrasound examination might reduce perinatal mortality (1 trial, 3890 women; RR: 0.36, 95% CI: 0.13–0.99).

### Values

Please see “Women’s values” in section 3.B.2: Fetal assessment: Background (p. 54).

### Resources

The cost of ultrasound equipment, especially portable compact units, has decreased (122), and they are currently available at less than US\$ 10 000 (28). Thus, given the cost of equipment, maintenance, supplies (ultrasound gel), replacement batteries, initial and ongoing staff training and supervision, and staffing costs, routine Doppler ultrasound scans may have considerable resource implications for LMIC settings.

### Equity

RCT evidence on maternal and perinatal effects of Doppler ultrasound examination is currently derived from HICs and high-quality research is needed on this intervention in LMICs to determine whether, by improving detection of pregnancy complications, it can reduce perinatal mortality and improve health equity.

### Acceptability

Qualitative evidence shows that women generally appreciate the knowledge and information they can acquire from health-care providers and that they



are willing to be screened and tested for a variety of conditions, provided the information and procedures are explained properly and delivered in a caring and culturally sensitive manner (high confidence in the evidence) (22). Evidence also shows that, in some LMICs, the lack of modern technology (like ultrasound equipment) at ANC facilities discourages some women from attending (high confidence in the evidence) (22).

Qualitative evidence from health-care providers shows that they generally want to provide screening and testing procedures, but sometimes don't feel suitably trained to do so (high confidence in the

evidence) (45). This suggests that they might welcome Doppler ultrasound scans to identify potential risk factors, if appropriately trained and supported.

### Feasibility

Feasibility challenges of Doppler ultrasound scans in LMICs include equipment procurement and staff training, ensuring a power supply (via a power point or rechargeable batteries) and secure storage, regular equipment maintenance, maintaining adequate and continual supplies of ultrasound gel, and ongoing technical support and supervision.

# C. Preventive measures

## Background

The GDG considered the evidence and other relevant information to inform recommendations on antenatal interventions to prevent the following conditions.

■ **Asymptomatic bacteriuria (ASB):** Defined as true bacteriuria in the absence of specific symptoms of acute urinary tract infection, ASB is common in pregnancy, with rates as high as 74% reported in some LMICs (125). *Escherichia coli* is associated with up to 80% of isolates (83). Other pathogens include *Klebsiella* species, *Proteus mirabilis* and group B streptococcus (GBS). While ASB in non-pregnant women is generally benign, in pregnant women obstruction to the flow of urine by the growing fetus and womb leads to stasis in the urinary tract and increases the likelihood of acute pyelonephritis. If untreated, up to 45% of pregnant women with ASB may develop this complication (126), which is associated with an increased risk of preterm birth.

■ **Recurrent urinary tract infections:** A recurrent urinary tract infection (RUTI) is a symptomatic infection of the urinary tract (bladder and kidneys) that follows the resolution of a previous urinary tract infection (UTI), generally after treatment. Definitions of RUTI vary and include two UTIs within the previous six months, or a history of one or more UTIs before or during pregnancy (127). RUTIs are common in women who are pregnant and have been associated with adverse pregnancy outcomes including preterm birth and small-for-gestational-age newborns (127). Pyelonephritis (infection of the kidneys) is estimated to occur in 2% of pregnancies, with a recurrence rate of up to 23% within the same pregnancy or soon after the birth (128). Little is known about the best way to prevent RUTI in pregnancy.

■ **Rhesus D alloimmunization:** Rhesus (Rh) negative mothers can develop Rh antibodies if they have an Rh-positive newborn, causing haemolytic disease of the newborn (HDN) in subsequent pregnancies. Administering anti-D immunoglobulin to Rh-negative women within 72 hours of giving birth to an Rh-positive baby is an effective way of

preventing RhD alloimmunization and HDN (129). However, Rhesus alloimmunization occurring in the third trimester due to occult transplacental haemorrhages will not be prevented by postpartum anti-D.

■ **Soil-transmitted helminthiasis:** Over 50% of pregnant women in LMICs suffer from anaemia, and helminthiasis is a major contributory cause in endemic areas (33). Soil-transmitted helminths are parasitic infections caused mainly by roundworms (*Ascaris lumbricoides*), hookworms (*Necator americanus* and *Ancylostoma duodenale*), and whipworms (*Trichuris trichiura*). These worms (particularly hookworms) feed on blood and cause further bleeding by releasing anticoagulant compounds, thereby causing iron-deficiency anaemia (130). They may also reduce the absorption of iron and other nutrients by causing anorexia, vomiting and diarrhoea (131).

■ **Neonatal tetanus:** Tetanus is an acute disease caused by an exotoxin produced by *Clostridium tetani*. Neonatal infection usually occurs through the exposure of the unhealed umbilical cord stump to tetanus spores, which are universally present in soil, and newborns need to have received maternal antibodies via the placenta to be protected at birth. Neonatal disease usually presents within the first two weeks of life and involves generalized rigidity and painful muscle spasms, which in the absence of medical treatment leads to death in most cases (132). Global vaccination programmes have reduced the global burden of neonatal tetanus deaths and continue to do so; estimates show a reduction from an estimated 146 000 in 2000 to 58 000 (CI: 20 000–276 000) in 2010 (133). However, because tetanus spores are ubiquitous in the environment, eradication is not biologically feasible and high immunization coverage remains essential (134).

In addition to GDG recommendations on the above, this section of the guideline includes two recommendations on disease prevention in pregnancy that have been integrated from WHO guidelines on malaria and HIV prevention that are relevant to routine ANC.

## Women's values

A scoping review of what women want from ANC and what outcomes they value informed the ANC guideline (13). Evidence showed that women from high-, medium- and low-resource settings valued having a positive pregnancy experience. This included the tailored (rather than routine) use of biomedical tests and effective preventive interventions to optimize pregnancy and newborn health, and the ability of health-care practitioners to explain and deliver these procedures in a knowledgeable, supportive and respectful manner (high confidence in the evidence).

## C.1: Antibiotics for asymptomatic bacteriuria (ASB)

**RECOMMENDATION C.1: A seven-day antibiotic regimen is recommended for all pregnant women with asymptomatic bacteriuria (ASB) to prevent persistent bacteriuria, preterm birth and low birth weight. (Recommended)**

### Remarks

- This recommendation should be considered alongside the recommendation on ASB diagnosis (Recommendation B.1.2).
- Stakeholders may wish to consider context-specific ASB screening and treatment based on ASB and preterm birth prevalence, as it may not be appropriate in settings with low prevalence.
- Evidence on preterm birth is of low certainty and large multicentre trials are needed to confirm whether screening and antibiotic treatment reduces preterm birth and perinatal mortality in LMICs. Such trials should also aim to evaluate the effects of group B streptococcus (GBS) screening and treatment.
- Studies have shown that GBS bacteriuria is a sign of heavy GBS colonization, which may not be eradicated by antibiotic treatment. GBS bacteriuria is a risk factor for having an infant with early onset GBS disease. WHO recommends that pregnant women with GBS colonization receive intrapartum antibiotic administration to prevent early neonatal GBS infection (see *WHO recommendations for prevention and treatment of maternal peripartum infections* [135]).
- Preterm birth indicators should be monitored with this intervention, as should changes in antimicrobial resistance.

## Summary of evidence and considerations

### Effects of antibiotics for ASB versus no antibiotics or placebo (EB Table C.1)

The evidence on the effects of antibiotics for ASB was derived from a Cochrane review that included 14 trials involving approximately 2000 women (83). Most trials were conducted in HICs between 1960 and 1987. Types of antibiotics included sulfonamides, ampicillin, nitrofurantoin and some antibiotics that are no longer recommended for use in pregnancy, such as tetracycline. Treatment duration between trials varied widely from a single dose, to continuous treatment throughout pregnancy. Bacteriuria was usually defined as at least one clean-catch, midstream or catheterized urine specimen with more than 100 000 bacteria/mL on culture, but other definitions were also used.

### Maternal outcomes

The only maternal ANC guideline outcomes reported were infection outcomes. Low-certainty evidence suggests that antibiotics may reduce persistent bacteriuria (4 trials, 596 women; RR: 0.30, 95% CI: 0.18–0.53); however, the evidence on the effect on pyelonephritis is very uncertain.

### Fetal and neonatal outcomes

Low-certainty evidence suggests that antibiotics for ASB may reduce low-birth-weight neonates (8 trials, 1437 neonates; RR: 0.64, 95% CI: 0.45–0.93) and preterm birth (2 trials, 142 women; RR: 0.27, 95% CI: 0.11–0.62). No other ANC guideline outcomes were reported.

### Additional considerations

- The GDG also evaluated evidence on treatment duration (single dose versus short-course

[4–7 days]] from a related Cochrane review that included 13 trials involving 1622 women (136). Ten trials compared different durations of treatment with the same antibiotic, and the remaining three compared different durations of treatment with different drugs. A wide variety of antibiotics was used. The resulting pooled evidence on bacterial persistence (7 trials), recurrent ASB (8 trials) and pyelonephritis (2 trials) was judged as very uncertain. However, on sensitivity analysis including high-quality trials of amoxicillin and nitrofurantoin only, the high-certainty evidence indicates that bacterial persistence is reduced with a short course rather than a single dose (2 trials, 803 women; RR: 1.72, 95% CI: 1.27–2.33). High-certainty evidence from one large trial shows that a seven-day course of nitrofurantoin is more effective than a one-day treatment to reduce low birth weight (714 neonates; RR: 1.65, 95% CI: 1.06–2.57). Low-certainty evidence suggests that single-dose treatments may be associated with fewer side-effects (7 trials, 1460 women; RR: 0.70, 95% CI: 0.56–0.88). See Web supplement (EB Table C.1).

- The GDG also evaluated evidence on the test accuracy of urine Gram staining and dipstick testing (see Recommendation B.1.2 in section 3.B).

### Values

See “Women’s values” at the beginning of section 3.C: Background (p. 64).

### Resources

Antibiotic costs vary. Amoxicillin and trimethoprim are much cheaper (potentially around US\$ 1–2 for a week’s supply) than nitrofurantoin, which can cost about US\$ 7–10 for a week’s supply of tablets (137).

Repeated urine testing to check for clearance of ASB has cost implications for laboratory and human resources, as well as for the affected women. The emergence of antimicrobial resistance is of concern and may limit the choice of antimicrobials (125).

### Equity

Preterm birth is the leading cause of neonatal death worldwide, with most deaths occurring in LMICs; therefore, preventing preterm birth among disadvantaged populations might help to address inequalities.

### Acceptability

In LMICs, some women hold the belief that pregnancy is a healthy condition and may not accept the use of antibiotics in this context (particularly if they have no symptoms) unless they have experienced a previous pregnancy complication (high confidence in the evidence) (22). Others view ANC as a source of knowledge, information and medical safety, and generally appreciate the interventions and advice they are offered (high confidence in the evidence). However, engagement may be limited if this type of intervention is not explained properly. In addition, where there are likely to be additional costs associated with treatment, women are less likely to engage (high confidence in the evidence).

### Feasibility

A lack of resources in LMICs, both in terms of the availability of the medicines and testing, and the lack of suitably trained staff to provide relevant information and perform tests, may limit implementation (high confidence in the evidence) (45).

## C.2: Antibiotic prophylaxis to prevent recurrent urinary tract infections (RUTI)

**RECOMMENDATION C.2: Antibiotic prophylaxis is only recommended to prevent recurrent urinary tract infections in pregnant women in the context of rigorous research.**  
(Context-specific recommendation – research)

### Remarks

- Further research is needed to determine the best strategies for preventing RUTI in pregnancy, including the effects of antibiotic prophylaxis on pregnancy-related outcomes and changes in antimicrobial resistance.

## Summary of evidence and considerations

### Effects of prophylactic antibiotics to prevent RUTI compared with no antibiotics (EB Table C.2)

The evidence on the effects of prophylactic antibiotics to prevent RUTI was derived from a Cochrane review in which only one trial in the USA involving 200 pregnant women contributed data (127). Women admitted to hospital with pyelonephritis were randomized, after the acute phase, to prophylactic antibiotics (nitrofurantoin 50 mg three times daily) for the remainder of the pregnancy plus close surveillance (regular clinic visits and urine culture, with antibiotics on positive culture), or to close surveillance only.

#### Maternal outcomes

Evidence from this single study on the risk of recurrent pyelonephritis and RUTI with prophylactic antibiotics is very uncertain. No other maternal ANC guideline outcomes were reported in the study.

#### Fetal and neonatal outcomes

Evidence on the risk of low birth weight and preterm birth with prophylactic antibiotics is very uncertain. No other fetal and neonatal ANC guideline outcomes were reported in the study.

#### Additional considerations

- Antibiotic prophylaxis to prevent RUTI may lead to increased antimicrobial resistance and there is a lack of evidence on this potential consequence.

#### Values

See “Women’s values” at the beginning of section 3.C: Background (p. 64).

#### Resources

Antibiotic costs vary. Trimethoprim is cheaper than nitrofurantoin, which can cost about US\$ 5 for 28 × 100 mg tablets (137).

#### Equity

Impact not known.

#### Acceptability

In LMICs, some women hold the belief that pregnancy is a healthy condition and may not accept the use of antibiotics in this context (particularly if they have no symptoms) unless they have experienced a previous pregnancy complication (high confidence in the evidence) (22). Others view ANC as a source of knowledge, information and medical safety and generally appreciate the interventions and advice they are offered (high confidence in the evidence). However, engagement may be limited if this type of intervention is not explained properly. In addition, where there are likely to be additional costs associated with treatment, women are less likely to engage (high confidence in the evidence).

#### Feasibility

A lack of resources in LMICs, both in terms of the availability of the medicines and testing, and the lack of suitably trained staff to provide relevant information and perform tests, may limit implementation (high confidence in the evidence) (45).

## C.3: Antenatal anti-D immunoglobulin prophylaxis

**RECOMMENDATION C.3: Antenatal prophylaxis with anti-D immunoglobulin in non-sensitized Rh-negative pregnant women at 28 and 34 weeks of gestation to prevent RhD alloimmunization is recommended only in the context of rigorous research.** (*Context-specific recommendation – research*)

#### Remarks

- This context-specific recommendation relates to anti-D prophylaxis during pregnancy and not the practice of giving anti-D after childbirth, for which there is high-certainty evidence of its effect of reducing RhD alloimmunization in subsequent pregnancies (129). Anti-D should still be given postnatally when indicated.
- Determining the prevalence of RhD alloimmunization and associated poor outcomes among women in LMIC settings, as well as developing strategies to manage this condition, is considered a research priority

## Summary of evidence and considerations

### Effects of antenatal anti-D immunoglobulin prophylaxis in non-sensitized Rh-negative pregnant women compared with no intervention (EB Table C.3)

The evidence on the effects of antenatal anti-D prophylaxis was derived from a Cochrane review that included two RCTs involving over 4500 Rh-negative pregnant women (138). Most participants were primigravidas. Both trials compared antenatal anti-D prophylaxis with no antenatal anti-D prophylaxis. One trial used a dose of 500 IU, the other used 250 IU, given at 28 and 34 weeks of gestation. Data were available for 3902 pregnancies, and more than half the participants gave birth to Rh-positive newborns (2297). All women with Rh-positive newborns received postpartum anti-D immunoglobulin as per usual management. The primary outcome was the presence of Rh-antibodies in maternal blood (a proxy for neonatal morbidity). No maternal ANC guideline outcomes (including maternal satisfaction and side-effects) and few perinatal guideline outcomes were reported in these trials.

### Fetal and neonatal outcomes

Evidence on the effect of antenatal anti-D on RhD alloimmunization during pregnancy, suggesting little or no difference in effect, is very uncertain. In addition, the evidence on the effect on postpartum RhD alloimmunization and alloimmunization up to 12 months postpartum among women giving birth to Rh-positive newborns ( $n = 2297$  and  $2048$ , respectively) is very uncertain, partly because events were rare. Evidence on the effect of antenatal anti-D on neonatal morbidity (jaundice) from one trial (1882 neonates) is also very uncertain, partly because events were rare. No other ANC guideline outcomes were reported in the review.

### Additional considerations

- Low-certainty evidence from the Cochrane review suggests that Rh-negative women who receive antenatal anti-D are less likely to register a positive Kleihauer test (which detects fetal cells in maternal blood) during pregnancy (1 trial, 1884 women; RR: 0.60, 95% CI: 0.41–0.88) and at the birth of a Rh-positive neonate (1 trial, 1189 women; RR: 0.60, 95% CI: 0.46–0.79).
- In the Cochrane review, the rate of RhD alloimmunization during pregnancy, the postpartum period and up to 12 months later among women in the control group was 0.6%, 1.1% and 1.5%, respectively.

- Rates of RhD alloimmunization in subsequent pregnancies were not reported in the trials.
- There is no evidence on optimal dose of antenatal anti-D prophylaxis and various regimens are used. There are two ongoing studies listed in the Cochrane review, which may help to clarify issues around effects and dosage once completed.
- Only 60% of Rh-negative primigravidas will have an Rh-positive newborn, therefore 40% of Rh-negative women will receive anti-D unnecessarily with antenatal anti-D prophylaxis (138).

### Values

See “Women’s values” at the beginning of section 3.C: Background (p. 64).

### Resources

A single dose of anti-D can cost around US\$ 50 (500 IU) to US\$ 87 (1500 IU) (139), depending on the brand and local taxes; therefore, the cost of antenatal prophylaxis for two 500 IU doses could be as much as US\$ 100 per woman. Additional costs will include screening for blood typing in settings where Rh blood tests are not currently performed.

### Equity

The contribution of RhD alloimmunization to perinatal morbidity and mortality in various LMIC settings is uncertain and it is not known whether antenatal anti-D for non-sensitized Rh-negative women will impact on equity.

### Acceptability

Anti-D immunoglobulin is derived from human plasma and is administered by injection, which may not be acceptable to all women. Qualitative evidence indicates that engagement may be limited if tests and procedures are not explained properly to women, or when women feel their beliefs, traditions and social support mechanisms are overlooked or ignored by health-care professionals (high confidence in the evidence) (22).

### Feasibility

In a number of LMIC settings providers feel that a lack of resources, both in terms of the availability of the medicines and the lack of suitably trained staff to provide relevant information, may limit implementation of recommended interventions (high confidence in the evidence) (45). Anti-D needs refrigeration at 2–8°C, which may not be feasible in some LMIC settings.

## C.4: Preventive anthelmintic treatment

**RECOMMENDATION C.4: In endemic areas,<sup>a</sup> preventive anthelmintic treatment is recommended for pregnant women after the first trimester as part of worm infection reduction programmes. (Context-specific recommendation)**

### Remarks

- This recommendation is consistent with the WHO *Guideline: preventive chemotherapy to control soil-transmitted helminth infections in high-risk groups* (140), which states that:  
 “Preventive chemotherapy (deworming), using single-dose albendazole (400 mg) or mebendazole (500 mg) is recommended as a public health intervention for pregnant women, after the first trimester, living in areas where both: (1) the baseline prevalence of hookworm and/or *T. trichiura* infection is 20% or more and (2) where anaemia is a severe public health problem, with prevalence of 40% or higher among pregnant women, in order to reduce the burden of hookworm and *T. trichiura* infection (conditional recommendation, moderate quality of evidence).”
- Endemic areas are areas where the prevalence of hookworm and/or whipworm infection is 20% or more. Anaemia is considered a severe public health problem when the prevalence among pregnant women is 40% or higher.
- Infected pregnant women in non-endemic areas should receive anthelmintic treatment in the second or third trimester on a case-by-case basis (140). A single dose of albendazole (400 mg) or mebendazole (500 mg) should be used (140, 141).
- The safety of these drugs in pregnancy has not been unequivocally established; however, the benefits are considered to outweigh the disadvantages (141, 142).
- WHO recommends a treatment strategy comprising two treatments per year in high-risk settings with a prevalence of  $\geq 50\%$  for soil-transmitted helminthiasis, and once per year in areas with a 20–50% prevalence (140).
- For further guidance on soil-transmitted helminth infections, refer to the WHO *Guideline: preventive chemotherapy to control soil-transmitted helminth infections in high-risk groups* (currently in press) (140).

a Greater than 20% prevalence of infection with any soil-transmitted helminths.

### Summary of evidence and considerations

#### Effects of prophylactic anthelmintic treatment against soil-transmitted helminths administered in the second trimester of pregnancy compared with no intervention or placebo (EB Table C.4)

The following evidence on the effects of prophylactic anthelmintic treatment was derived from a Cochrane review that included four trials conducted in Peru, Sierra Leone and Uganda, involving 4265 pregnant women (142). In two trials (Peru and Sierra Leone), the anthelmintic medication (albendazole or mebendazole) was administered as a single dose in the second trimester, with or without daily iron and folic acid supplements, irrespective of the presence of proven helminthiasis. The frequency of anaemia ( $Hb < 110$  g/L) in these two trials was 56% and 47%, respectively, and the frequency of intestinal worms ranged from 20% to 64.2% for roundworm, 46.4% to 65.6% for hookworm, and 74.4% to 82% for whipworm. One small Ugandan trial administered a

single dose of albendazole (400 mg) or placebo to women in the second trimester, irrespective of the proven presence of helminthiasis; baseline prevalence was 15%, 38% and 6% for ascariasis, hookworm and trichuriasis, respectively. The other Ugandan RCT contributed data on albendazole plus ivermectin versus ivermectin only, administered as single doses to pregnant women in the second trimester; all women were infected with an intestinal helminth at trial entry.

#### Maternal outcomes

Low-certainty evidence suggests that a single dose of albendazole or mebendazole in the second trimester of pregnancy may have little or no effect on maternal anaemia (defined as  $Hb < 11$  g/dL) (4 trials, 3266 women; RR: 0.94; 95% CI: 0.81–1.10).

#### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that a single dose of albendazole or mebendazole in the second



trimester of pregnancy probably has little or no effect on preterm birth (2 trials, 1318 women; RR: 0.88, 95% CI: 0.43–1.78) or perinatal mortality (2 trials, 3385 women; RR: 1.09, 95% CI: 0.71–1.67). No other ANC guideline outcomes were reported in the review.

### Additional considerations

- None of the trials in the Cochrane review evaluated effects of more than one dose of anthelmintics. Findings from large non-randomized studies (NRSs) suggest that prophylactic anthelmintic treatment may have beneficial effects for mothers and newborns living in endemic areas (143–145):
  - One NRS, including approximately 5000 pregnant women in Nepal with a 74% prevalence of hookworm infection, reported a 41% reduction in six-month infant mortality among women receiving two doses of albendazole (one each in the second and third trimesters) compared with no treatment (95% CI: 18–57%) (143). This study also showed reductions in severe maternal anaemia with albendazole.
  - A study from Sri Lanka involving approximately 7000 women compared mebendazole with no treatment and found fewer stillbirths and perinatal deaths among women receiving mebendazole (1.9% vs 3.3%; OR: 0.55, 95% CI: 0.40–0.77), and little difference in the occurrence of congenital anomalies (1.8% vs 1.5%, for intervention and controls, respectively; OR: 1.24, 95% CI: 0.80–1.91), even among the 407 women who had taken mebendazole in the first trimester against medical advice (145).
- The WHO manual on *Preventive chemotherapy in human helminthiasis* stresses that every opportunity should be taken to reach at-risk populations through existing channels (141).
- Cross-referencing other WHO guidelines, the upcoming 2016 WHO *Guideline: preventive chemotherapy to control soil-transmitted helminth infections in high-risk groups* recommends that a single dose of albendazole or mebendazole should be offered to pregnant women in the second and third trimesters of pregnancy where the prevalence of any soil-transmitted helminth infection (roundworm, hookworm and whipworm) exceeds 20% (140).

- Preventive helminthic treatment helps to lessen the burden of other infections, e.g. HIV, malaria and TB, and contributes to a sustained reduction of transmission (142).

### Values

See “Women’s values” at the beginning of section 3.C: Background (p. 64).

### Resources

Preventive chemotherapy against helminthic infections is a cost-effective intervention. The market price of a single tablet of generic albendazole (400 mg) or mebendazole (500 mg) is about US\$ 0.02–0.03 (141).

### Equity

Helminthic infections are widely prevalent in poverty-stricken regions and control of this disease aims to alleviate suffering, reduce poverty and support equity (141).

### Acceptability

Affected women are often asymptomatic and may not perceive the need for treatment. Therefore, the prevalence of soil-based helminthiasis in a particular setting is likely to influence women’s and providers’ preferences. Studies of anthelmintic programmes among non-pregnant cohorts, e.g. schoolchildren, in endemic areas have shown high levels of acceptability (146). For women receiving preventive treatment in endemic areas, worms are often visible in the stools the day after treatment, and this may reinforce the value of the intervention. However, where there are likely to be additional costs associated with treatment (high confidence in the evidence) or where the intervention is unavailable because of resource constraints (low confidence in the evidence) women may be less likely to engage with services (45).

### Feasibility

In a number of LMIC settings providers feel that a lack of resources, both in terms of the availability of the medicines and the lack of suitably trained staff to provide relevant information, may limit implementation of recommended interventions (high confidence in the evidence) (45).

## C.5: Tetanus toxoid vaccination

**RECOMMENDATION C.5: Tetanus toxoid vaccination is recommended for all pregnant women, depending on previous tetanus vaccination exposure, to prevent neonatal mortality from tetanus. (Recommended)**

### Remarks

- This recommendation is consistent with recommendations from the 2006 WHO guideline on *Maternal immunization against tetanus* (134). The GDG endorses the 2006 guideline approach, which recommends the following.
  - If a pregnant woman has not previously been vaccinated, or if her immunization status is unknown, she should receive two doses of a tetanus toxoid-containing vaccine (TT-CV) one month apart with the second dose given at least two weeks before delivery. Two doses protect against tetanus infection for 1–3 years in most people. A third dose is recommended six months after the second dose, which should extend protection to at least five years.
  - Two further doses for women who are first vaccinated against tetanus during pregnancy should be given after the third dose, in the two subsequent years or during two subsequent pregnancies.
  - If a woman has had 1–4 doses of a TT-CV in the past, she should receive one dose of a TT-CV during each subsequent pregnancy to a total of five doses (five doses protects throughout the childbearing years).
- Tetanus vaccination and clean delivery practices are major components of the strategy to eradicate maternal and neonatal tetanus globally (147).
- Effective surveillance is critical for identifying areas or populations at high risk of neonatal tetanus and for monitoring the impact of interventions.
- A monitoring system should include an immunization register, personal vaccination cards and maternal health records, which should be held by the woman.
- For effective implementation, ANC health-care providers need to be trained in tetanus vaccination and the vaccine, equipment and supplies (refrigerator, needles and syringes) need to be readily available at ANC services.
- Policy-makers in low prevalence/high-income settings may choose not to include tetanus vaccination among ANC interventions if effective tetanus immunization programmes and good post-exposure prophylaxis exist outside of pregnancy.
- ANC contacts should be used to verify the vaccination status of pregnant women, and administer any vaccines that are recommended in the national immunization schedule. ANC contacts are also opportunities to explain the importance of infant vaccination and communicate the infant/child vaccination schedule to pregnant women.
- Further information can be found in the WHO guidance (134), available at: [http://www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/immunization\\_tetanus.pdf](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/immunization_tetanus.pdf); and in WHO's vaccine position papers, available at: <http://www.who.int/immunization/documents/positionpapers/en>

### Summary of evidence and considerations

#### Effects of antenatal tetanus toxoid (TT) vaccination compared with no, other or placebo vaccination (EB Table C.5)

The evidence on the effects of TT vaccination was derived from a Cochrane review that assessed the effect of tetanus vaccination in women of reproductive age or pregnant women to prevent neonatal tetanus (148). Two RCTs contributed data: one was conducted in Colombia between 1961 and

1965 and compared a tetanus vaccine (aluminium phosphate adsorbed tetanus toxoid [10LF]; 3 doses) with an influenza vaccine (1618 women, 1182 neonates); the other was conducted in the USA and compared a combined vaccine (tetanus/diphtheria/acellular pertussis [Tdap]; 1 dose) with saline placebo in 48 pregnant women between 30 and 32 weeks of gestation. Due to the relative paucity of RCT data, additional evidence on effects is also considered in the “Additional considerations” section.

### Maternal outcomes

Low-certainty evidence suggests that local side-effects, such as pain, were more common with the Tdap vaccination than placebo (48 women; RR: 3.94, 95% CI: 1.41-11.01). There is no evidence on other maternal outcomes.

### Fetal and neonatal outcomes

Low-certainty evidence from the Colombian trial suggests that there may be fewer neonatal tetanus cases among neonates whose mothers receive TT vaccination than among those who do not (1182 neonates; RR: 0.20, 95% CI: 0.10-0.40). Moderate-certainty evidence suggests that two or more doses of TT probably reduce neonatal mortality from any cause (1 trial, 688 neonates; RR: 0.31, 95% CI: 0.17-0.55). Further low-certainty evidence suggests that neonatal mortality from tetanus may be reduced among neonates whose mothers receive at least two TT doses (1 trial, 688 neonates; RR: 0.02, 95% CI: 0.00-0.30), but not among neonates whose mothers receive only one dose (1 trial, 494 neonates; RR: 0.57, 95% CI: 0.26-1.24). Congenital anomalies and other ANC guideline outcomes were not reported in the trials.

### Additional considerations

- A systematic review that pooled data from the Colombian trial with that of a large cohort study of antenatal TT vaccination from India found moderate-certainty evidence to support a large effect (94% reduction) on neonatal tetanus deaths in favour of TT vaccination with at least two doses in pregnant women and women of childbearing age (2 trials, 2146 neonates; RR: 0.06, 95% CI: 0.02-0.20) (149).
- TT vaccination has been widely used over 40 years, leading to a substantial decrease in neonatal tetanus and an increase in neonatal survival, with no sign of possible harm to pregnant women or their fetuses (150). The WHO strategy for eliminating maternal and neonatal tetanus includes immunization of pregnant women, supplementary immunization activities in selected high-risk areas, promotion of clean deliveries and clean cord practices, and reliable neonatal tetanus surveillance (134).

### Values

See “Women’s values” at the beginning of section 3.C: Background (p. 64).

### Resources

The cost of three doses of TT vaccine has been estimated at around US\$ 3 per woman (151), although lower costs in vaccination programmes have been reported (152). The need for cold-chain equipment and staff training may add to costs.

### Equity

Most deaths from neonatal tetanus occur in countries with low coverage of facility-based births, ANC and tetanus vaccination (149). In addition, in LMICs, ANC coverage and infant mortality is often unequal between the most- and least-educated, urban and rural, and richest and poorest populations (29). Therefore, increasing tetanus immunity in LMICs and among disadvantaged populations could help to address inequalities.

### Acceptability

Qualitative evidence indicates that most women view ANC as a source of knowledge, information and medical safety, and generally appreciate the interventions and advice they are offered. However, engagement may be limited if vaccinations are not explained properly or when women feel their beliefs, traditions and social support mechanisms are overlooked or ignored by health-care professionals (high confidence in the evidence) (22). Lack of engagement may be compounded if services are delivered in a hurried, inflexible, didactic manner (high confidence in the evidence).

### Feasibility

Antenatal services provide a convenient opportunity for vaccinating pregnant women, particularly in settings without effective childhood immunization programmes. Qualitative evidence indicates that if there are additional costs associated with vaccination (including transport costs and loss of earnings), uptake may be limited (high confidence in the evidence) (22). In addition, ANC providers in many LMIC settings feel that a lack of resources, both in terms of the availability of vaccines and the lack of suitably trained staff, may limit implementation (high confidence in the evidence) (45).

## C.6: Intermittent preventive treatment of malaria in pregnancy (IPTp)

**RECOMMENDATION C.6:** In malaria-endemic areas in Africa, intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP) is recommended for all pregnant women. Dosing should start in the second trimester, and doses should be given at least one month apart, with the objective of ensuring that at least three doses are received. (*Context-specific recommendation*)

### Remarks

- This recommendation has been integrated from the WHO *Guidelines for the treatment of malaria* (2015), where it is considered to be a strong recommendation based on high-quality evidence (153).
- Malaria infection during pregnancy is a major public health problem, with substantial risks for the mother, her fetus and the newborn. WHO recommends a package of interventions for preventing and controlling malaria during pregnancy, which includes promotion and use of insecticide-treated nets, appropriate case management with prompt, effective treatment, and, in areas with moderate to high transmission of *Plasmodium falciparum*, administration of IPTp-SP (153).
- The high-quality evidence supporting this recommendation was derived from a systematic review of seven RCTs conducted in malaria-endemic countries, which shows that three or more doses of sulfadoxine-pyrimethamine (SP) is associated with reduced maternal parasitaemia, fewer low-birth-weight infants and increased mean birth weight compared with two doses only (154).
- The malaria GDG noted that most evidence was derived from women in their first and second pregnancies; however, the limited evidence on IPTp-SP from women in their third and subsequent pregnancies was consistent with benefit (153).
- To ensure that pregnant women in endemic areas start IPTp-SP as early as possible in the second trimester, policy-makers should ensure health system contact with women at 13 weeks of gestation. Policy-makers could also consider supplying women with their first SP dose at the first ANC visit with instructions about the date (corresponding to 13 weeks of gestation) on which the medicine should be taken.
- SP acts by interfering with folic acid synthesis in the malaria parasite, thereby inhibiting its life-cycle. There is some evidence that high doses of supplemented folic acid (i.e. 5 mg daily or more) may interfere with the efficacy of SP in pregnancy (155). Countries should ensure that they procure and distribute folic acid supplements for antenatal use at the recommended antenatal dosage (i.e. 0.4 mg daily).
- The malaria GDG noted that there is insufficient evidence on the safety, efficacy and pharmacokinetics of most antimalarial agents in pregnancy, particularly during the first trimester (153).
- Detailed evidence and guidance related to the recommendation can be found in the 2015 guidelines (153), available at: <http://www.who.int/malaria/publications/atoz/9789241549127/en/>

## C.7: Pre-exposure prophylaxis for HIV prevention

**RECOMMENDATION C.7: Oral pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate (TDF) should be offered as an additional prevention choice for pregnant women at substantial risk of HIV infection as part of combination prevention approaches.**

*(Context-specific recommendation)*

### Remarks

- This recommendation has been integrated from the *WHO guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV* (2015), where it is considered to be a strong recommendation based on high-quality evidence (99). The evidence and further guidance related to the recommendation can be found in this guideline.
- “Substantial risk” is provisionally defined as HIV incidence greater than 3 per 100 person-years in the absence of PrEP, but individual risk varies within this group depending on individual behaviour and the characteristics of sexual partners. Local epidemiological evidence concerning risk factors and HIV incidence should be used to inform implementation.
- Thresholds for offering PrEP may vary depending on a variety of considerations, including resources, feasibility and demand.
- The level of protection is strongly correlated with adherence.
- Detailed evidence and guidance related to this recommendation can be found in the 2015 guideline (99), available at: <http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/>

## D. Interventions for common physiological symptoms

### Background

Women's bodies undergo substantial changes during pregnancy, which are brought about by both hormonal and mechanical effects. These changes lead to a variety of common symptoms – including nausea and vomiting, low back and pelvic pain, heartburn, varicose veins, constipation and leg cramps – that in some women cause severe discomfort and negatively affects their pregnancy experience. In general, symptoms associated with mechanical effects, e.g. pelvic pain, heartburn and varicose veins, often worsen as pregnancy progresses.

Symptoms of nausea and vomiting are experienced by approximately 70% of pregnant women and usually occur in the first trimester of pregnancy (156); however, approximately 20% of women may experience nausea and vomiting beyond 20 weeks of gestation (157). Low back and pelvic pain is estimated to occur in half of pregnant women, 8% of whom experience severe disability (158). Symptoms of heartburn occur in two thirds of pregnant women, and may be worse after eating and lying down (159). Varicose veins usually occur in the legs, but can also occur in the vulva and rectum, and may be associated

with pain, night cramps, aching and heaviness, and worsen with long periods of standing (160).

Constipation can be very troublesome and may be complicated by haemorrhoids (161). Leg cramps often occur at night and can be very painful, affecting sleep and daily activities (162). Suggested approaches to manage common physiological symptoms include a variety of non-pharmacological and pharmacological options and the GDG considered the evidence and other relevant information on these approaches.

#### Women's values:

A scoping review of what women want from ANC and what outcomes they value informed the ANC guideline (13). Evidence showed that women from high-, medium- and low-resource settings valued having a positive pregnancy experience. This included woman-centred advice and treatment for common physiological symptoms (high confidence in the evidence). In many LMICs, this also included support and respect for women's use of alternative or traditional approaches to the diagnosis and treatment of common pregnancy-related symptoms (moderate confidence in the evidence).

### D.1: Interventions for nausea and vomiting

**RECOMMENDATION D.1: Ginger, chamomile, vitamin B6 and/or acupuncture are recommended for the relief of nausea in early pregnancy, based on a woman's preferences and available options. (Recommended)**

#### Remarks

- In the absence of stronger evidence, the GDG agreed that these non-pharmacological options are unlikely to have harmful effects on mother and baby.
- Women should be informed that symptoms of nausea and vomiting usually resolve in the second half of pregnancy.
- Pharmacological treatments for nausea and vomiting, such as doxylamine and metoclopramide, should be reserved for those pregnant women experiencing distressing symptoms that are not relieved by non-pharmacological options, under the supervision of a medical doctor.

## Summary of evidence and considerations

### Effects of interventions for nausea and vomiting compared with other, no or placebo interventions (EB Table D.1)

The evidence on the effects of various interventions for nausea and vomiting in pregnancy was derived from a Cochrane systematic review (157). The review included 41 trials involving 5449 women in whom a wide variety of pharmacological and non-pharmacological interventions were evaluated. Trials were conducted in a variety of HICs and LMICs, and most included pregnant women at less than 16 weeks of gestation with mild to moderate nausea and vomiting. Alternative therapies and non-pharmacological agents evaluated included acupuncture, acupressure, vitamin B6, ginger, chamomile, mint oil and lemon oil. Pharmacological agents included antihistamines, phenothiazines, dopamine-receptor antagonists and serotonin 5-HT3 receptor antagonists. Due to heterogeneity among the types of interventions and reporting of outcomes, reviewers were seldom able to pool data. The primary outcome of all interventions was maternal relief from symptoms (usually measured using the Rhodes Index), and perinatal outcomes relevant to this guideline were rarely reported.

### Non-pharmacological agents versus placebo or no treatment

Ten trials evaluated non-pharmacological interventions including ginger (prepared as syrup, capsules or powder within biscuits) (7 trials from the Islamic Republic of Iran, Pakistan, Thailand and the USA involving 578 participants), lemon oil (one Iranian study, 100 participants), mint oil (one Iranian study, 60 participants), chamomile (one Iranian study, 105 participants), and vitamin B6 interventions (two studies in Thailand and the USA; 416 participants) compared with no treatment or placebo.

**Ginger:** Low-certainty evidence from several small individual studies suggests that ginger may relieve symptoms of nausea and vomiting. A study from Pakistan found that ginger reduced nausea symptom scores (68 women; MD: 1.38 lower on day 3, 95% CI: 0.03–2.73 lower), and vomiting symptom scores (64 women; MD: 1.14 lower, 95% CI: 0.37–1.91 lower), and an Iranian study showed improvements in nausea and vomiting symptom scores on day 7 in women taking ginger supplements compared with placebo (95 women; MD: 4.19 lower, 95% CI: 1.73–6.65

lower). Data from the studies in Thailand and the USA showed a similar direction of effect on nausea symptoms in favour of ginger.

**Lemon oil:** Low-certainty evidence from one small Iranian study suggests that lemon oil may make little or no difference to nausea and vomiting symptom scores (100 women; MD: 0.46 lower on day 3, 95% CI: 1.27 lower to 0.35 higher), or to maternal satisfaction (the number of women satisfied with treatment) (1 trial, 100 women; RR: 1.47, 95% CI: 0.91–2.37).

**Mint oil:** The evidence on mint oil's ability to relieve symptoms of nausea and vomiting is of very low certainty.

**Chamomile:** Low-certainty evidence from one small study suggests that chamomile may reduce nausea and vomiting symptoms scores (70 women; MD: 5.74 lower, 95% CI: 3.17–8.31 lower).

**Vitamin B6 (pyridoxine):** Moderate-certainty evidence from two trials (one used 25 mg oral vitamin B6 8-hourly for 3 days, the other used 10 mg oral vitamin B6 8-hourly for 5 days) shows that vitamin B6 probably reduces nausea symptoms scores (388 women, trials measured the change in nausea scores from baseline to day 3; MD: 0.92 higher score change, 95% 0.4–1.44 higher), but low-certainty evidence suggests that it may have little or no effect on vomiting (2 trials, 392 women; RR: 0.76, 95% CI: 0.35–1.66).

### Acupuncture and acupressure versus placebo or no treatment

Five studies (601 participants) evaluated P6 (inner forearm) acupressure versus placebo, one Thai study (91 participants) evaluated auricular acupressure (round magnetic balls used as ear pellets) versus no treatment, one study in the USA (230 participants) evaluated P6 acustimulation therapy (nerve stimulation at the P6 acupuncture point) versus placebo, and a four-arm Australian study (593 women) evaluated traditional Chinese acupuncture or P6 acupuncture versus P6 placebo acupuncture or no intervention.

Low-certainty evidence suggests that P6 acupressure may reduce nausea symptom scores (100 women; MD: 1.7 lower, 95% CI: 0.99–2.41 lower) and reduce the number of vomiting episodes (MD: 0.9 lower, 95% CI: 0.74–1.06 lower). Low-certainty evidence



suggests that auricular acupressure may also reduce nausea symptom scores (91 women; MD: 3.6 lower, 95% CI: 0.58–6.62 lower), as may traditional Chinese acupuncture (296 women; MD: 0.7 lower, 95% CI: 0.04–1.36 lower). Low-certainty evidence suggests that P6 acupuncture may make little or no difference to mean nausea scores compared with P6 placebo acupuncture (296 women; MD: 0.3 lower, 95% CI: 1.0 lower to 0.4 higher).

### Pharmacological agents versus placebo

One study evaluated an antihistamine (doxylamine) and another evaluated a dopamine-receptor antagonist (metoclopramide). Certain other drugs evaluated in the review (hydroxyzine, thiethylperazine and fluphenazine) are from old studies and these drugs are no longer used in pregnant women due to safety concerns.

Moderate-certainty evidence suggests that doxylamine plus vitamin B6 probably reduces nausea and vomiting symptom scores compared with placebo (1 study, 256 women; MD: 0.9 lower on day 15, 95% CI: 0.25–1.55 lower). Low-certainty evidence from this study suggests that there may be little or no difference in headache (256 women; RR: 0.81, 95% CI: 0.45–1.48) or drowsiness (256 women; RR: 1.21, 95% CI: 0.64–2.27) between doxylamine plus vitamin B6 and placebo.

Low-certainty evidence on metoclopramide (10 mg) suggests that this agent may reduce nausea symptom scores (1 trial, 68 women; MD: 2.94 lower on day 3, 95% CI: 1.33–4.55 lower). There was no side-effect data on metoclopramide in the review.

No studies compared ondansetron (a 5HT<sub>3</sub> receptor antagonist) with placebo. Two small studies compared ondansetron with metoclopramide and doxylamine, respectively, but evidence on relative effects was uncertain.

### Additional considerations

- Low-certainty evidence from single studies comparing different non-pharmacological interventions with each other – namely acupuncture plus vitamin B6 versus P6 acupuncture plus placebo (66 participants), traditional acupuncture and P6 acupuncture (296 participants), ginger versus chamomile (70 participants), P6 acupuncture versus ginger (98 participants), and ginger versus vitamin B6

(123 participants) – suggests there may be little or no difference in effects on relief of nausea symptoms.

- Low-certainty evidence suggests that there may be little or no difference between ginger and metoclopramide on nausea symptom scores (1 trial, 68 women; MD: 1.56 higher, 95% CI: 0.22 lower to 3.34 higher) or vomiting symptom scores (68 women; MD: 0.33 higher, 95% CI: 0.69 lower to 1.35 higher) on day 3 after the intervention.
- Side-effects and safety of pharmacological agents were poorly reported in the included studies. However, drowsiness is a common side-effect of various antihistamines used to treat nausea and vomiting.
- Metoclopramide is generally not recommended in the first trimester of pregnancy, but is widely used (163). A study of over 81 700 singleton births in Israel reported that they found no statistically significant differences in the risk of major congenital malformations, low birth weight, preterm birth or perinatal death between neonates exposed (3458 neonates) and not exposed to metoclopramide in the first trimester of gestation.

### Values

See “Women’s values” at the beginning of section 3.D: Background (p. 74).

### Resources

Costs associated with non-pharmacological remedies vary. Acupuncture requires professional training and skills and is probably associated with higher costs. Vitamin B6 (pyridoxine hydrochloride tablets) could cost about US\$ 2.50 for 90 × 10 mg tablets (74).

### Equity

The impact on equity is not known.

### Acceptability

Qualitative evidence from a range of LMICs suggests that women may be more likely to turn to traditional healers, herbal remedies or traditional birth attendants (TBAs) to treat these symptoms (moderate confidence in the evidence) (22). In addition, evidence from a diverse range of settings indicates that while women generally appreciate the interventions and information provided during antenatal visits, they are less likely to engage with services if their beliefs, traditions and socioeconomic circumstances are ignored or overlooked by health-care providers and/or policy-makers (high confidence

in the evidence). This may be particularly pertinent for acupuncture or acupressure, which may be culturally alien and/or poorly understood in certain contexts.

### Feasibility

A lack of suitably trained staff may limit feasibility of certain interventions (high confidence in the evidence) (45).

## D.2: Interventions for heartburn

**RECOMMENDATION D.2: Advice on diet and lifestyle is recommended to prevent and relieve heartburn in pregnancy. Antacid preparations can be offered to women with troublesome symptoms that are not relieved by lifestyle modification.** (*Recommended*)

### Remarks

- Lifestyle advice to prevent and relieve symptoms of heartburn includes avoidance of large, fatty meals and alcohol, cessation of smoking, and raising the head of the bed to sleep.
- The GDG agreed that antacids, such as magnesium carbonate and aluminium hydroxide preparations, are probably unlikely to cause harm in recommended dosages.
- There is no evidence that preparations containing more than one antacid are better than simpler preparations.
- Antacids may impair absorption of other drugs (164), and therefore should not be taken within two hours of iron and folic acid supplements.

## Summary of evidence and considerations

### Effects of interventions for heartburn compared with other, no or placebo interventions (EB Table D.2)

The evidence on the effects of various interventions for heartburn in pregnancy comes from a Cochrane review that included nine trials involving 725 pregnant women with heartburn; however, only four trials (358 women) contributed data (159). One of these, from the 1960s, evaluated intramuscular prostigmine, which is no longer used, therefore these data were not considered for the guideline. The three remaining studies conducted in Brazil, Italy and the USA evaluated a magnesium hydroxide–aluminium hydroxide–simeticone complex versus placebo (156 women), sucralfate (aluminium hydroxide and sulfated sucrose) versus advice on diet and lifestyle changes (66 women), and acupuncture versus no treatment (36 women). Evidence on symptom relief was generally assessed to be of low to very low certainty and no perinatal outcomes relevant to this guideline were reported. Evidence on side-effects for all comparisons was assessed as being of very low certainty.

### Pharmacological interventions versus placebo

Low-certainty evidence suggests that complete relief from heartburn may occur more frequently with magnesium hydroxide–aluminium hydroxide–

simeticone liquid and tablets than placebo (156 women; RR: 2.04, 95% CI: 1.44–2.89).

### Pharmacological interventions versus advice on diet and lifestyle changes

Low-certainty evidence suggests that complete relief from heartburn may occur more frequently with sucralfate than with advice on diet and lifestyle changes (65 women; RR: 2.41, 95% CI: 1.42–4.07).

### Acupuncture versus no treatment

Data on relief of heartburn was not available in the review for this comparison. Low-certainty evidence suggests that weekly acupuncture in pregnant women with heartburn may improve the ability to sleep (36 women; RR: 2.80, 95% CI: 1.14–6.86) and eat (36 women; RR: 2.40, 95% CI: 1.11–5.18), a proxy outcome for maternal satisfaction.

### Additional considerations

- Heartburn during pregnancy is a common problem that can be self-treated with over-the-counter products containing antacids such as magnesium carbonate, aluminium hydroxide or calcium carbonate.
- The Cochrane review found no evidence on prescription drugs for heartburn, such as omeprazole and ranitidine, which are not known to be harmful in pregnancy (159).

### Values

See “Women’s values” at the beginning of section 3.D: Background (p. 74).

### Resources

Costs of antacids vary widely, but generic products can be relatively low cost. Acupuncture requires professional training and skills and is likely to be associated with higher costs.

### Equity

The prevalence of health-seeking behaviour and treatment for heartburn in pregnancy may be unequal among advantaged and disadvantaged women. However, it is not known whether interventions to relieve heartburn might impact inequalities.

### Acceptability

Qualitative evidence from a range of LMICs suggests that women may be more likely to turn to traditional healers, herbal remedies or TBAs to treat these symptoms (moderate confidence in the evidence)

(22). In addition, evidence from a diverse range of settings indicates that while women generally appreciate the interventions and information provided during antenatal visits, they are less likely to engage with services if their beliefs, traditions and socioeconomic circumstances are ignored or overlooked by health-care providers and/or policy-makers (high confidence in the evidence). This may be particularly pertinent for an intervention like acupuncture, which may be culturally alien and/or poorly understood in certain contexts. Indirect evidence also indicates that women welcome the pregnancy-related advice and guidance given by health-care professionals during antenatal visits, so may respond to lifestyle suggestions favourably (moderate confidence in the evidence).

### Feasibility

Qualitative evidence suggests that a lack of resources may limit the offer of treatment for this condition (high confidence in the evidence) (45).

## D.3: Interventions for leg cramps

**RECOMMENDATION D.3: Magnesium, calcium or non-pharmacological treatment options can be used for the relief of leg cramps in pregnancy, based on a woman’s preferences and available options. (Recommended)**

### Remarks

- The review found no evidence on the effect of non-pharmacological therapies, such as muscle stretching, relaxation, heat therapy, dorsiflexion of the foot and massage.
- The evidence on magnesium and calcium is generally of low certainty. However, the GDG agreed that they are unlikely to be harmful in the dose schedules evaluated in included studies.
- Further research into the etiology and prevalence of leg cramps in pregnancy, and the role (if any) of magnesium and calcium in symptom relief, is needed.

### Summary of evidence and considerations

#### Effects of interventions for leg cramps compared with other, no or placebo interventions (EB Table D.3)

The evidence on the effects of various interventions for leg cramps in pregnancy is derived from a Cochrane review that included six small trials involving 390 pregnant women with leg cramps (162). Three studies from Norway (42 women), Sweden (69 women) and Thailand (86 women) contributed data on oral magnesium compared with placebo. One study from Sweden (43 women) compared oral calcium with no treatment; a study conducted in the

Islamic Republic of Iran (42 women) compared oral vitamins B6 and B1 with no treatment; and another conducted in Sweden compared oral calcium with vitamin C (30 women). Symptom relief, measured in different ways, was the primary outcome in these studies, and other maternal and perinatal outcomes relevant to this guideline were not reported.

#### Oral magnesium versus placebo

In three small studies, women in the intervention group were given 300–360 mg magnesium per day in two or three divided doses. Studies measured persistence or occurrence of leg cramps in different ways, so results could not be pooled. Moderate-

certainty evidence from the Thai study suggests that women receiving magnesium are more likely to experience a 50% reduction in the number of leg cramps (1 trial, 86 women; RR: 1.42, 95% CI: 1.09–1.86). The same direction of effect was found in the Swedish study, which reported the outcome “no leg cramps” after treatment, but the evidence was of low certainty (1 trial, 69 women; RR: 5.66, 95% CI: 1.35–23.68). Low-certainty evidence suggests that oral magnesium has little or no effect on the occurrence of potential side-effects, including nausea, diarrhoea, flatulence and bloating. Evidence from the third study was judged to be very uncertain.

#### **Oral calcium versus no treatment**

Calcium, 1 g twice daily for two weeks, was compared with no treatment in one small study. Low-certainty evidence suggests that women receiving calcium treatment are more likely to experience no leg cramps after treatment (43 women; RR: 8.59, 95% CI: 1.19–62.07).

#### **Oral calcium versus vitamin C**

Low-certainty evidence suggests that there may be little or no difference between calcium and vitamin C in the effect (if any) on complete symptom relief from leg cramps (RR: 1.33, 95% CI: 0.53–3.38).

#### **Oral vitamin B1 and B6 versus no treatment**

One study evaluated this comparison, with 21 women receiving vitamin B1 (100 mg) plus B6 (40 mg) once daily for two weeks and 21 women receiving no treatment; however, the low-certainty findings are contradictory and difficult to interpret.

#### **Additional considerations**

- The review found no evidence on non-pharmacological therapies, such as muscle stretching, massage, relaxation, heat therapy and dorsiflexion of the foot.

#### **Values**

See “Women’s values” at the beginning of section 3.D: Background (p. 74).

#### **Resources**

Magnesium and calcium supplements are relatively low-cost interventions, particularly when administered for limited periods of two to four weeks.

#### **Equity**

The potential etiology of leg cramps being related to a nutritional deficiency (magnesium) suggests that the prevalence of leg cramps might be higher in disadvantaged populations. In theory, therefore, nutritional interventions may have equity implications, but evidence is needed.

#### **Acceptability**

Qualitative evidence from a diverse range of settings suggests that women generally appreciate the pregnancy-related advice given by health-care professionals during ANC, so may respond to supplement suggestions favourably (moderate confidence in the evidence) (22). Evidence from some LMICs suggests that women hold the belief that pregnancy is a healthy condition and may turn to traditional healers and/or herbal remedies to treat these kinds of associated symptoms (high confidence in the evidence).

#### **Feasibility**

Qualitative evidence suggests that a lack of resources may limit the offer of treatment for this condition (high confidence in the evidence) (45). In addition, where there are additional costs for pregnant women associated with treatment, women are less likely to use it.

## D.4: Interventions for low back and pelvic pain

**RECOMMENDATION D.4: Regular exercise throughout pregnancy is recommended to prevent low back and pelvic pain. There are a number of different treatment options that can be used, such as physiotherapy, support belts and acupuncture, based on a woman's preferences and available options. (Recommended)**

### Remarks

- Exercise to prevent low back and pelvic pain in pregnancy can take place on land or in water. While exercise may also be helpful to relieve low back pain, it could exacerbate pelvic pain associated with symphysis pubis dysfunction and is not recommended for this condition.
- Regular exercise is a key component of lifestyle interventions, which are recommended for pregnant women as part of ANC to prevent excessive weight gain in pregnancy (see Recommendation A.9).
- Pregnant women with low back and/or pelvic pain should be informed that symptoms usually improve in the months after birth.
- Women should be informed that it is unclear whether there are side-effects to alternative treatment options due to a paucity of data.
- Standardized reporting of outcomes is needed for future research on treatment for low back and/or pelvic pain in pregnancy.

### Summary of evidence and considerations

#### Effects of interventions for low back and pelvic pain compared with other, no or placebo interventions (EB Table D.4)

The evidence on the effects of various interventions for low back and pelvic pain in pregnancy was derived from a Cochrane review that included 34 trials involving 5121 women (165). The definitions and terminology of low back and pelvic pain varied such that in 15 trials the interventions were aimed at reducing low back pain, in six trials interventions were for pelvic pain, and in 13 trials the interventions were for low back and pelvic pain. Most trials evaluated treatment; however, six trials evaluated prevention. Few trials contributed data to analyses and several individual study findings were described only in narrative. Main outcomes were relief of symptoms and functional disability, and perinatal outcomes relevant to this guideline were not reported.

Comparisons included:

1. any exercise (plus standard care) versus standard care
2. acupuncture (plus standard care) versus sham acupuncture (plus standard care)
3. acupuncture (plus standard care) versus individualized physiotherapy (plus standard care)
4. osteopathic manipulation (plus standard care) versus standard care
5. one type of support belt versus another type
6. multimodal interventions versus standard care.

#### Any exercise (plus standard care) versus standard care

Seven trials (645 women) contributed data to this comparison for low back pain. Trials were conducted in Brazil, the Islamic Republic of Iran, Norway, South Africa and Thailand. Exercise interventions varied from individually supervised exercise to group exercise, including yoga and aqua-aerobics, and some included education via CDs and booklets. Interventions ran for 8-12 weeks and the presence or intensity of pain was assessed in most trials using visual analogue scales. However, the evidence on symptom relief from a meta-analysis of these seven studies is very uncertain. Low-certainty evidence suggests that functional disability scores are better with exercise interventions for low back pain (2 trials, 146 women; standardized MD: 0.56 lower, 95% CI: 0.23-0.89 lower). Evidence on pain intensity (symptom scores) for low back pain was assessed as very uncertain.

Low-certainty evidence suggests that an 8- to 12-week exercise programme may reduce low back and pelvic pain compared with standard care (4 trials, 1176 women; RR: 0.66, 95% CI: 0.45-0.97) and moderate-certainty evidence shows that healthy pregnant women taking part in an exercise programme are probably less likely to take sick leave related to low back and pelvic pain (2 trials, 1062 women; RR: 0.76; 95% CI: 0.62-0.94).

### **Acupuncture (plus standard care) versus sham acupuncture (plus standard care)**

Four small studies conducted in Sweden and the USA evaluated the effects of acupuncture plus standard care versus sham acupuncture plus standard care. However, little data were extracted from these studies and data could not be pooled. Low-certainty evidence from one study suggests that acupuncture may relieve low back and pelvic pain (72 women; RR: 4.16, 95% CI: 1.77–9.78). Evidence from other studies was variously reported and very uncertain.

### **Acupuncture (plus standard care) versus individualized physiotherapy (plus standard care)**

One small study conducted in Sweden involving 46 women with low back and pelvic pain evaluated this comparison. Women's satisfaction with treatment was the main outcome, but the evidence was assessed as very uncertain.

### **Osteopathic manipulation therapy (OMT) (plus standard care) versus no osteopathic manipulation (standard care)**

Three studies evaluated OMT; however, data could not be pooled and the evidence from individual studies is inconsistent. The largest study involving 400 women compared OMT plus standard care with placebo ultrasound plus standard care, or standard care only. Limited data from this study suggests that OMT may relieve low back pain symptoms more than standard care, and may lead to lower functional disability scores, but may not be better than placebo ultrasound for these outcomes.

### **One type of support belt versus another type**

One small study conducted in Australia compared two types of support belts in women with low back pain, the BellyBra® and Tubigrip® (N = 94) and the evidence from this study was assessed as very low-certainty evidence.

### **Multimodal interventions versus standard care**

One study in the USA reported the effect of a multimodal intervention that included weekly manual therapy by a chiropractic specialist, combined with daily exercise at home, and education versus standard care (rest, exercise, heat pads and analgesics) on low back and pelvic pain. Moderate-certainty evidence suggests that the multimodal intervention is probably associated with better pain scores (1 study, 169 women; MD: 2.70 lower, 95% CI: 1.86–3.54 lower) and better functional disability scores (MD: 1.40 lower; 95% CI: 0.71–2.09 lower) compared with standard care.

### **Additional considerations**

- It is not clear whether the evidence on exercise interventions applies equally to low back pain and pelvic pain, or equally to prevention and treatment, as data from studies of prevention and treatment were pooled. Evidence from two studies on the effect of exercise plus education suggests that such interventions may have little or no effect on preventing pelvic pain (RR: 0.97; 95% CI: 0.77–1.23).
- Very low-certainty evidence on a number of other interventions, such as transcutaneous electrical nerve stimulation (TENS), progressive muscle relaxation with music, craniosacral therapy, and acetaminophen (paracetamol) – which were evaluated in single small trials with apparent relief of symptoms relative to standard care – was also presented in the review.
- Standard care of low back and pelvic pain symptoms usually comprises rest, hot or cold compresses, and paracetamol analgesia.
- There is a paucity of evidence on potential side-effects of alternative therapies, e.g. chiropractic and osteopathic manipulation, and further high-quality research is needed to establish whether these therapies are beneficial for low back and/or pelvic pain and safe during pregnancy.
- Exercise in pregnancy has been shown to have other benefits for pregnant women, including reducing excessive gestational weight gain (see Recommendation A.9).

### **Values**

See “Women's values” at the beginning of section 3.D: Background (p. 74).

### **Resources**

Exercise can be administered in a group setting and individually at home; therefore, the cost of exercise interventions varies. Support belts are available commercially from under US\$ 10 per item.<sup>5</sup> Physiotherapy and acupuncture require specialist training and are therefore likely to be more resource intensive.

### **Equity**

Improving access to low back and pelvic pain interventions may reduce inequalities by reducing functional disability and sick leave related to low back and pelvic pain among disadvantaged women.

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<sup>5</sup> Based on Internet search.



### Acceptability

Qualitative evidence from a diverse range of settings, indicates that while women generally appreciate the interventions and information provided during antenatal visits, they are less likely to engage with services if their beliefs, traditions and socioeconomic circumstances are ignored or overlooked by health-care providers and/or policy-makers (high confidence in the evidence) (22). This may be particularly pertinent for an intervention like acupuncture, which

may be culturally alien and/or poorly understood in certain contexts. In addition, where there are likely to be additional costs associated with treatment or where the treatment may be unavailable (because of resource constraints), women are less likely to engage with health services (high confidence in the evidence).

### Feasibility

A lack of resources may limit the offer of treatment for this condition (high confidence in the evidence) (45).

## D.5: Interventions for constipation

**RECOMMENDATION D.5: Wheat bran or other fibre supplements can be used to relieve constipation in pregnancy if the condition fails to respond to dietary modification, based on a woman's preferences and available options. (Recommended)**

### Remarks

- Dietary advice to reduce constipation during pregnancy should include promoting adequate intake of water and dietary fibre (found in vegetables, nuts, fruit and whole grains).
- For women with troublesome constipation that is not relieved by dietary modification or fibre supplementation, stakeholders may wish to consider intermittent use of poorly absorbed laxatives.

## Summary of evidence and considerations

### Effects of interventions for constipation compared with other, no or placebo interventions (EB Table D.5)

The evidence on the effects of various interventions for constipation in pregnancy was derived from a Cochrane review to which only two small RCTs involving 180 women contributed data (161). Both studies were conducted in the United Kingdom among pregnant women with constipation. One compared fibre supplementation with no intervention (40 women), the other compared stimulant laxatives with bulk-forming laxatives (140 women). No perinatal outcomes relevant to this guideline were reported.

### Fibre supplementation versus no intervention

Evidence from the small study evaluating fibre supplementation versus no intervention on constipation relief (reported as mean frequency of stools) was assessed as being very uncertain.

### Stimulant laxatives versus bulk-forming laxatives

Two stimulant laxatives were used in this 1970s study, senna and Normax®. The latter (containing dantron) is potentially carcinogenic and now only used in terminally ill people; however, data on stimulant

laxatives were not available separately for senna. Evidence on relative symptom relief, side-effects (abdominal discomfort, diarrhoea), and maternal satisfaction for stimulant laxatives versus bulk-forming laxatives (sterculia with or without frangula) was assessed as being very uncertain.

### Additional considerations

- Various bulk-forming (wheat bran or oat bran fibre supplements, sterculia, methylcellulose, ispaghula husk), osmotic (lactulose) and stimulant laxatives (senna) are available as over-the-counter medications for constipation and are not known to be harmful in pregnancy (166).
- The absorption of vitamins and mineral supplements could potentially be compromised by laxatives.

### Values

See "Women's values" at the beginning of section 3.D: Background (p. 74).

### Resources

Costs will vary according to the intervention and region. Cereal fibre supplements can be relatively low-cost at around US\$ 1.5 per 375 g bag of wheat bran.<sup>6</sup>

6 Based on Internet search.



### Equity

It is not known whether interventions to relieve constipation might impact inequalities.

### Acceptability

Qualitative evidence from a range of LMICs suggests that women may be more likely to turn to traditional healers, herbal remedies or TBAs to treat these symptoms (moderate confidence in the evidence) (22). Evidence from a diverse range of settings indicates that while women generally appreciate

the interventions and information provided during antenatal visits, they are less likely to engage with services if their beliefs, traditions and socioeconomic circumstances are ignored or overlooked by health-care providers and/or policy-makers (high confidence in the evidence).

### Feasibility

Other qualitative evidence suggests that a lack of resources may limit the offer of treatment for constipation (high confidence in the evidence) (45).

## D.6: Interventions for varicose veins and oedema

**RECOMMENDATION D.6: Non-pharmacological options, such as compression stockings, leg elevation and water immersion, can be used for the management of varicose veins and oedema in pregnancy based on a woman's preferences and available options. (Recommended)**

### Remarks

- Women should be informed that symptoms associated with varicose veins may worsen as pregnancy progresses but that most women will experience some improvement within a few months of giving birth.
- Rest, leg elevation and water immersion are low-cost interventions that are unlikely to be harmful.

## Summary of evidence and considerations

### Effects of interventions for varicose veins and oedema compared with other, no or placebo interventions (EB Table D.6)

The evidence on the effects of various interventions for varicose veins in pregnancy was derived from a Cochrane review that included seven small trials involving 326 women with varicose veins and/or oedema, and various types of interventions, including rutoside (a phlebotonic drug) versus placebo (two trials), foot massage by a professional masseur for five days versus no intervention (1 trial, 80 women), intermittent external pneumatic compression with a pump versus rest (1 trial, 35 women), standing in water at a temperature between 29°C and 33°C for 20 minutes (water immersion) versus leg elevation (1 trial, 32 women) and reflexology versus rest (1 trial, 55 women) (160). Another trial comparing compression stockings with rest in the left lateral position did not contribute any data. Fetal and neonatal outcomes relevant to the ANC guideline were not reported in these studies.

### Pharmacological interventions versus placebo or no intervention

Only one small trial conducted in 1975 (69 women) contributed data. Low-certainty evidence from this

trial suggests that rutoside may reduce symptoms (nocturnal cramps, paraesthesia, tiredness) associated with varicose veins compared with placebo (69 women; RR: 1.89, 95% CI: 1.11–3.22). However, no side-effect data were reported.

### Non-pharmacological interventions versus placebo or no intervention

Low-certainty evidence suggests that *reflexology* may reduce oedema symptoms compared with rest only (55 women; RR: 9.09, 95% CI: 1.41–58.54) and that water immersion may reduce oedema symptoms (leg volume) compared with leg elevation (32 women; RR: 0.43, 95% CI: 0.22–0.83). Low-certainty evidence suggests that there may be little or no difference in oedema symptoms (measured as lower leg circumference in centimetres) between foot massage and no intervention (80 women; MD in cm: 0.11 less, 95% CI: 1.02 less to 0.80 more) and between intermittent pneumatic compression and rest (measured as mean leg volume, unit of analysis unclear) (35 women; MD: 258.8 lower, 95% CI: 566.91 lower to 49.31 higher). Only one study (reflexology versus rest) evaluated women's satisfaction, but the evidence is of very low certainty.

### Additional considerations

- Compression stockings combined with leg elevation is the most common non-surgical management for varicose veins and oedema; however, the Cochrane review found no evidence on this practice in pregnancy (160). Compression stockings are also widely used to prevent morbidity in non-pregnant people with varicose veins and the evidence for this practice in a related Cochrane review of compression stockings was generally very uncertain (167).

### Values

See “Women’s values” at the beginning of section 3.D: Background (p. 74).

### Resources

Postural interventions are low-cost interventions. The cost of compression stockings varies but they can cost more than US\$ 15 per pair. Reflexology and professional massage require specialist training, and are, therefore, likely to be more costly.

### Equity

It is not known whether interventions to relieve varicose veins and oedema might impact inequalities.

### Acceptability

Qualitative evidence from a range of LMICs suggests that women may be more likely to turn to traditional healers, herbal remedies or TBAs to treat these symptoms (moderate confidence in the evidence) (22). In addition, evidence from a diverse range of settings indicates that while women generally appreciate the interventions and information provided during antenatal visits, they are less likely to engage with services if their beliefs, traditions and socioeconomic circumstances are ignored or overlooked by health-care providers and/or policy-makers (high confidence in the evidence). This may be particularly pertinent for an intervention like reflexology, which may be culturally alien and/or poorly understood in certain contexts. Qualitative evidence shows that, where there are likely to be additional costs associated with treatment or where the treatment may be unavailable (because of resource constraints), women are less likely to engage with health services (high confidence in the evidence).

### Feasibility

The evidence also suggests that a lack of resources may limit the offer of treatment for varicose veins and oedema (high confidence in the evidence) (45).

# E. Health systems interventions to improve the utilization and quality of ANC

## Background

There is a multitude of interventions that can be employed to improve the utilization and quality of ANC depending on the context and setting. For the purposes of this guideline, the GDG considered the following interventions:

1. Women-held case notes (home-based records)
2. Midwife-led continuity of care models
3. Group ANC
4. Community-based interventions to improve communication and support
5. Task shifting
6. Recruitment and retention of staff
7. ANC contact schedules.

How to deliver the type and quality of ANC that women want is a vast and complex field of research. Interventions designed to increase staff competency, to improve staff well-being, and other interventions (e.g. financial incentives) to increase access and use of ANC are broad topics that were considered beyond the scope of this guideline.

■ **Women-held case notes:** In many countries, women are given their own case notes (or home-based records) to carry during pregnancy. Case notes may be held in paper (e.g. card, journal, handbook) or electronic formats (e.g. memory stick), and women are expected to take them along to all health visits. If women then move, or are referred from one facility to another, and in the case of complications where immediate access to medical records is not always possible, the practice of women-held case notes may improve the availability of women's medical records (168). Women-held case notes might also be an effective tool to improve health awareness and client-provider communication (169). Inadequate infrastructure and resources often hamper efficient record-keeping, therefore, case notes may be less likely to get lost when held personally. In addition, the practice may facilitate more accurate

estimation of gestational age, which is integral to evidence-based decision-making, due to improved continuity of fetal growth records (170).

■ **Midwife-led continuity of care (MLCC) models:**

Midwives are the primary providers of care in many ANC settings (171). In MLCC models, a known and trusted midwife (caseload midwifery), or small group of known midwives (team midwifery), supports a woman throughout the antenatal, intrapartum and postnatal period, to facilitate a healthy pregnancy and childbirth, and healthy parenting practices (172). The MLCC model includes: continuity of care; monitoring the physical, psychological, spiritual and social well-being of the woman and family throughout the childbearing cycle; providing the woman with individualized education, counselling and ANC; attendance during labour, birth and the immediate postpartum period by a known midwife; ongoing support during the postnatal period; minimizing unnecessary technological interventions; and identifying, referring and coordinating care for women who require obstetric or other specialist attention (173). Thus, the MLCC model exists within a multidisciplinary network in which consultation and referral to other care providers occurs when necessary. The MLCC model is usually aimed at providing care to healthy women with uncomplicated pregnancies.

■ **Group ANC:** ANC conventionally takes the form of a one-on-one consultation between a pregnant woman and her health-care provider. However, group ANC integrates the usual individual pregnancy health assessment with tailored group educational activities and peer support, with the aim of motivating behaviour change among pregnant women, improving pregnancy outcomes, and increasing women's satisfaction (174). The intervention typically involves self-assessment activities (e.g. blood pressure measurement), group education with facilitated discussion, and

time to socialize. Group ANC needs to be delivered in a space large enough to accommodate a group of women, with a private area for examinations.

■ **Community-based interventions to improve communication and support:**

The scoping review conducted for the ANC guideline identified communication and support for women as integral components of positive pregnancy experiences. The term “communicate” refers to the act of sharing information, education and communication with women about timely and relevant physiological, biomedical, behavioural and sociocultural issues; “support” refers to social, cultural, emotional and psychological support (13). Having access to appropriate communication and support is a key element of a quality ANC service. A human-rights-based approach recognizes that women are entitled to participate in decisions that affect their sexual and reproductive health (1). In addition, pregnant women have a right to access quality health-care services and, particularly in low-resource settings, may need to be empowered to do so. Interventions that increase the dialogue around awareness of a women’s rights, barriers and facilitators to utilizing ANC services and keeping healthy during pregnancy and beyond (including dialogue around newborn care and postnatal family planning), and providing women and their partners with support in addressing challenges they may face, may lead to improved ANC uptake and quality of care.

- **ANC contact schedules:** In 2002, the WHO recommended a focused or goal-orientated approach to ANC to improve quality of care and

increase ANC coverage, particularly in LMICs (12). The focused ANC (FANC) model, also known as the basic ANC model, includes four ANC visits occurring between 8 and 12 weeks of gestation, between 24 and 26 weeks, at 32 weeks, and between 36 and 38 weeks. Guidance on each visit includes specific evidence-based interventions for healthy pregnant women (called “goal-oriented”), with appropriate referral of high-risk women and those who develop pregnancy complications. The number of visits in this model is considerably fewer than in ANC models used in HICs.

The GDG considered the available evidence and other relevant information on these interventions to determine whether they should be recommended for ANC (Recommendations E1 to E5). The GDG also considered existing recommendations from other WHO guidelines on task shifting and recruitment and retention of staff in rural areas (Recommendations E5 and E6).

### Women’s values

A scoping review of what women want from ANC and what outcomes they value informed the ANC guideline (13). Evidence showed that women from high-, medium- and low-resource settings valued having a positive pregnancy experience. Within a health systems context, this included the adoption of flexible appointment systems and continuity of provider care where women were given privacy and time to build authentic and supportive relationships with maternity-care providers (high confidence in the evidence).

## E.1: Women-held case notes

**RECOMMENDATION E.1: It is recommended that each pregnant woman carries her own case notes during pregnancy to improve continuity, quality of care and her pregnancy experience.**  
(Recommended)

### Remarks

- The GDG noted that women-held case notes are widely used and are often the only medical records available in various LMIC settings.
- The GDG agreed that the benefits of women-held case notes outweigh the disadvantages. However, careful consideration should be given as to what personal information it is necessary to include in the case notes, to avoid stigma and discrimination in certain settings. In addition, health-system planners should ensure that admission to hospitals or other health-care facilities do not depend on women presenting their case notes.
- Health-system planners should consider which form the women-held case notes should take (electronic or paper-based), whether whole sets of case notes will be held by women or only specific parts of them, and how copies will be kept by health-care facilities.
- For paper-based systems, health-system planners also need to ensure that case notes are durable and transportable. Health systems that give women access to their case notes through electronic systems need to ensure that all pregnant women have access to the appropriate technology and that attention is paid to data security.
- Health-system planners should ensure that the contents of the case notes are accessible to all pregnant women through the use of appropriate, local languages and appropriate reading levels.

## Summary of evidence and considerations

### Effects of women-held case notes compared with other practices (EB Table E.1)

The evidence on the effects of women-held case notes was mostly derived from a Cochrane review that included four small trials involving 1176 women (168). Trials were conducted in Australia, Mongolia and the United Kingdom (2 trials). In three trials, women in the intervention groups were given their complete antenatal records (paper) to carry during pregnancy. In the remaining trial, a cluster randomized controlled trial (RCT) involving 501 women in Mongolia, women in the intervention group carried a maternal and child health handbook that included antenatal, postnatal and child health records. Antenatal records were facility-held in the control groups. Data on ANC coverage for the Mongolian trial were derived separately from another Cochrane review (175).

### Maternal outcomes

With regard to maternal satisfaction, moderate-certainty evidence indicates that women who carry their own case notes are probably more likely to feel in control of their pregnancy experience than women whose records are facility-held (2 trials, 450 women; RR: 1.56, 95% CI: 1.18–2.06). Low-certainty evidence suggests that women-held case notes may have

little or no effect on women's satisfaction with ANC (2 trials, 698 women; RR: 1.09, 95% CI: 0.92–1.29). Evidence on caesarean section was very uncertain and other guideline outcomes were not reported in the review.

### Fetal and neonatal outcomes

Low-certainty evidence suggests that women-held case notes may have little or no effect on perinatal mortality (2 trials, 713 women; RR: 0.77, 95% CI: 0.17–3.48). No other fetal and neonatal outcomes were reported in the review.

### Coverage outcomes

Low-certainty evidence suggests that women-held case notes may have little or no effect on ANC coverage of four or more visits (1 trial, 501 women; RR: 1.25, 95% CI: 0.31–5.00).

### Additional considerations

- Other evidence from the review suggests that there may be little or no difference in the risk of case notes being lost or left at home for a visit (2 trials, 347 women; RR: 0.38, 95% CI: 0.04–3.84).
- A WHO multicentre cohort study of home-based maternal records (HBMR), involving 590 862 women in Egypt, India, Pakistan, Philippines,

Senegal, Sri Lanka, Yemen and Zambia, was conducted between 1984 and 1988 (176). The study reported that “The introduction of the HBMR increased the diagnosis and referral of at-risk pregnant women and newborn infants, improved family planning and health education, increased tetanus toxoid immunization, and provided a means of collecting health information in the community. The HBMR was liked by mothers, community health workers and other health-care personnel because, by using it, the mothers became more involved in looking after their own health and that of their babies.”

### Values

See “Women’s values” at the beginning of section 3.E: Background (p. 86).

### Resources

Resource implications differ depending on whether electronic or paper-based systems are used. Electronic systems require more resources. Paper-based systems require the production of durable, transportable journals, as well as systems for keeping copies. The need to adapt and/or translate journals may add to costs.

### Equity

The GDG considered that women-held case notes could be subject to abuse and used to discriminate against women who do not have them, or if the information contained in the notes is associated with stigma (e.g. HIV-positive status). Less-educated women with lower health literacy may be less able to read and understand their own case notes, which might perpetuate inequalities.

### Acceptability

Qualitative evidence suggests that women from a variety of settings are likely to favour carrying their case notes because of the increased opportunity to acquire pregnancy and health-related information and the associated sense of empowerment this brings (high confidence in the evidence) (22). There may be potential for abuse of the system in some LMIC settings, for example, by limiting access to hospitals for women who do not have case notes, particularly where maternity services are under-resourced (moderate confidence in the evidence). Further evidence from a mixed-methods review supports RCT evidence that women feel more satisfied when they carry, or have access to, their own case notes (177). These review findings were not subject to GRADE-CERQual assessments of confidence, and were derived primarily from high-income settings (36 out of 37 studies). Findings also suggest that providers are generally happy for women to carry their own case notes, but feel the implementation of the approach may generate additional administrative responsibilities. Providers also raised concerns about data security, sensitivity of the shared information, and the potential for data to be lost because of fragmented systems.

### Feasibility

There may be prohibitive additional costs associated with using an electronic system (USB memory sticks, software packages, etc.) in some LMIC settings (high confidence in the evidence), although paper-based records may require little in the way of extra cost or resources (45).

## E.2: Midwife-led continuity of care (MLCC)

**RECOMMENDATION E.2: Midwife-led continuity-of-care models, in which a known midwife or small group of known midwives supports a woman throughout the antenatal, intrapartum and postnatal continuum, are recommended for pregnant women in settings with well functioning midwifery programmes. (Context-specific recommendation)**

### Remarks

- MLCC models are models of care in which a known and trusted midwife (caseload midwifery), or small group of known midwives (team midwifery), supports a woman throughout the antenatal, intrapartum and postnatal period, to facilitate a healthy pregnancy and childbirth, and healthy parenting practices.
- MLCC models are complex interventions and it is unclear whether the pathway of influence producing these positive effects is the continuity of care, the midwifery philosophy of care or both. The midwifery philosophy inherent in MLCC models may or may not be enacted in standard midwife practice in other models of care.
- Policy-makers in settings without well functioning midwife programmes should consider implementing this model only after successfully scaling up of the number and quality of practising midwives. In addition, stakeholders may wish to consider ways of providing continuous care through other care providers, because women value continuity of care.
- The panel noted that with this model of care it is important to monitor resource use, and provider burnout and workload, to determine whether caseload or team care models are more sustainable in individual settings.
- MLCC requires that well trained midwives are available in sufficient numbers for each woman to see one or only a small group of midwives throughout pregnancy and during childbirth. This model may therefore require a shift in resources to ensure that the health system has access to a sufficient number of midwives with reasonable caseloads.
- The introduction of MLCC may lead to a shift in the roles and responsibilities of midwives as well as other health-care professionals who have previously been responsible for antenatal and postnatal care. Where this is the case, implementation is likely to be more effective if all relevant stakeholders are consulted and human resources departments are involved. In some settings, government-level consultation with professional organizations could also aid implementation processes.
- The need for additional one-off or continuing training and education should be assessed, and should be provided where necessary.

## Summary of evidence and considerations

### Effects of MLCC models compared with other models of care (EB Table E.2)

The evidence on the effects of MLCC models of care was derived from a Cochrane review that included 15 trials involving 17 674 women, in which pregnant women were randomized to receive ANC either by MLCC models or by other models of care (172). All the studies included were conducted in public health systems in HICs (Australia, Canada, Ireland and the United Kingdom) and 14 out of 15 contributed data. Eight trials compared an MLCC model with a shared care model, three trials compared MLCC with medical-led care, and three compared MLCC with “standard care” (mixed-care options, including midwife-led non-continuous care, medical-led, and shared care). Some MLCC models included routine

visits to an obstetrician and/or family doctor. Eight trials included women with “low-risk” pregnancies only; six also included women with “high-risk” pregnancies. Four trials evaluated one-to-one (caseload) MLCC and 10 trials evaluated team MLCC. Caseload sizes for one-to-one models ranged from 32 to 45 pregnant women per midwife per year. Levels of continuity of care were measured (as the proportion of births attended to by a known carer), and were in the ranges of 63–98% for MLCC and 0–21% for other models. A random effects model was used in all meta-analyses.

### Maternal outcomes

Moderate-certainty evidence shows that MLCC compared with other models of care probably slightly increases the chance of a vaginal birth (12 trials, 16 687 participants; RR: 1.05, 95% CI: 1.03–1.07).



MLCC may reduce caesarean sections (14 trials, 17 674 participants; RR: 0.92, 95% CI: 0.84–1.00), however, this evidence is of low certainty and includes the possibility of no effect. Low-certainty evidence suggests that MLCC models may be associated with lower rates of instrumental vaginal delivery than other models (13 trials, 17 501 participants; RR: 0.90, 95% CI: 0.83–0.97).

**Maternal satisfaction:** The Cochrane review tabulated data on women's satisfaction pertaining to various aspects of antenatal, intrapartum and postnatal care. A meta-analysis on satisfaction with ANC only was performed for the purposes of this guideline (see EB Table E.2), the findings of which suggest that MLCC models may increase the proportion of women reporting high levels of satisfaction with the ANC compared with other models (4 trials, 5419 women; RR: 1.31, 95% CI: 1.11–1.54; *low-certainty evidence*).

### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that MLCC probably reduces the risk of preterm birth (8 trials, 13 338 participants; RR: 0.76, 95% CI: 0.64–0.91) and probably reduces perinatal mortality (defined in the review as fetal loss after 24 weeks of gestation and neonatal death) (13 trials, 17 561 women; RR: 0.84, 95% CI: 0.71–0.99). However, low-certainty evidence suggests that it may have little or no effect on low birth weight (7 trials, 11 458 women; RR: 0.96, 95% CI: 0.82–1.13). Evidence on other ANC guideline outcomes was not available in the review.

### Additional considerations

- Although the mechanism for the probable reduction in preterm birth and perinatal death is unclear, the GDG considered the consistency of the results and the absence of harm to be important.

### Values

See “Women's values” at the beginning of section 3.E: Background (p. 86).

### Resources

In settings with well functioning midwife programmes, a shift in resources may be necessary to ensure

that the health system has sufficient midwives with reasonable caseloads. There may also be training costs associated with changing to an MLCC model. However, one study in the Cochrane review found that ANC provider costs were 20–25% lower with the MLCC model than other midwife-led care due to differences in staff costs (178).

### Equity

Equitable coverage and improvements in the quality of midwifery practice are major challenges in many LMICs (171). MLCC models in any setting have the potential to help to address health inequalities, for example, by providing a more supportive setting for disadvantaged women to disclose information that may facilitate the identification of risk factors for poor outcomes, such as intimate partner violence.

### Acceptability

Qualitative evidence synthesized from a wide variety of settings and contexts indicates that women welcome the opportunity to build supportive, caring relationships with a midwife or a small number of midwives during the maternity phase (high confidence in the evidence) and appreciate a consistent, unhurried, woman-centred approach during ANC visits (high confidence in the evidence) (22). Evidence from providers, mainly in HICs, indicates that they view MLCC as a way of achieving the authentic, supportive relationships that women desire (moderate confidence in the evidence). There is very little evidence on MLCC models from LMICs. However, indirect evidence from providers in these locations suggests that they would welcome the opportunity to use an MLCC model but feel they do not have the resources to do so (low confidence in the evidence).

### Feasibility

Qualitative evidence from high-, medium- and low-resource settings highlights concerns among providers about potential staffing issues, e.g. for the delivery of caseload or one-to-one approaches (high confidence in the evidence) (45).

## E.3: Group antenatal care

**RECOMMENDATION E.3: Group antenatal care provided by qualified health-care professionals may be offered as an alternative to individual antenatal care for pregnant women in the context of rigorous research, depending on a woman's preferences and provided that the infrastructure and resources for delivery of group antenatal care are available.** (*Context-specific recommendation – research*)

### Remarks

- With the group ANC model, the first visit for all pregnant women is an individual visit. Then at subsequent visits, the usual individual pregnancy health assessment, held in a private examination area, is integrated into a group ANC session, with facilitated educational activities and peer support.
- Health-care facilities need to be seeing sufficient numbers of pregnant women, as allocation to groups is ideally performed according to gestational age.
- Health-care providers need to have appropriate facilities to deal with group sessions, including access to large, well ventilated rooms or sheltered spaces with adequate seating. A private space should be available for examinations, and opportunities should be given for private conversations.
- Group ANC may take longer than individual ANC, and this may pose practical problems for some women in terms of work and childcare. Health-care providers should be able to offer a variety of time slots for group sessions (morning, afternoon, evening) and should consider making individual care available as well.
- The GDG noted that group ANC may have acceptability and feasibility issues in settings where perceived differences keep people apart, e.g. women from different castes in India may not wish to be in a group together.
- Group ANC studies are under way in Nepal, Uganda and five other low-income countries, and the GDG was informed by a GDG member that some of these studies are due to report soon. Core outcomes of studies of group ANC should include maternal and perinatal health outcomes, coverage, and women's and providers' experiences.

## Summary of evidence and considerations

### Effects of group ANC compared with individual ANC (EB Table E.3)

The evidence on the effects of group ANC was derived from a Cochrane review that included four trials involving 2350 women (174). Two trials from the USA used a group ANC model known as CenteringPregnancy®, in which group ANC was conducted in circles of 8–12 women of similar gestational age, meeting for 8–10 sessions during pregnancy, with each session lasting 90–120 minutes. Sessions included self-assessment activities (blood pressure measurement), facilitated educational discussions and time to socialize, with individual examinations performed in a private/screened-off area. One trial conducted in Sweden used a group model similar to the USA model but mainly assessed provider outcomes and contributed little data to the review. The fourth trial, conducted in the Islamic Republic of Iran, was a cluster-RCT in which group ANC was described as being similar to the CenteringPregnancy® approach.

### Maternal outcomes

Moderate-certainty evidence indicates that group ANC probably does not have an important effect on vaginal birth rates compared with individual ANC (1 trial, 322 women; RR: 0.96, 95% CI: 0.80–1.15). But low-certainty evidence suggests that it may lead to higher women's satisfaction scores (1 trial, 993 women; MD: 4.9, 95% CI: 3.10–6.70).

### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that group ANC probably has little or no effect on low birth weight (3 trials, 1935 neonates; RR: 0.92, 95% CI: 0.68–1.23) and low-certainty evidence suggests that it may have little or no effect on perinatal mortality (3 trials, 1943 neonates; RR: 0.63, 95% CI: 0.32–1.25). However, low-certainty evidence also suggests that group ANC may reduce preterm birth (3 trials, 1888 women; RR: 0.75, 95% CI: 0.57–1.00); this evidence includes the possibility of no effect. Evidence on the risk of having an SGA neonate is of a very low certainty.

### Additional considerations

- There is little evidence on the effects of group ANC from LMICs. However, a feasibility study conducted in Ghana suggests that group ANC might improve women's pregnancy experiences, and providers' experiences, and potentially improve health outcomes in low-income settings, due to improved health literacy and better engagement of pregnant women with ANC (179).
- It is plausible that group ANC may have an impact on other outcomes outside the scope of the ANC guideline, such as breastfeeding initiation and postnatal contraception, by improving communication and social support related to these healthy behaviours; but the evidence on these potential effects is limited (180).

### Values

See "Women's values" at the beginning of section 3.E: Background (p. 86).

### Resources

It has been suggested that group ANC may be associated with lower health-care provider costs due to increased staff productivity and efficiency; e.g. health-care providers do not need to repeat advice to each woman individually, and they may be less likely to feel overwhelmed by long queues of women waiting to be seen (181, 182). However, training and supervising health-care providers to conduct group-based counselling and participatory discussions is also associated with cost. Group ANC visits take longer than individual visits, therefore, from a user perspective, there may be additional costs associated with the time each pregnant woman needs to take off work. However, in many settings, long waiting times are the norm, so group ANC with a scheduled appointment could represent a reduced visit time.

### Equity

Less-educated women are more likely to have poor maternal health literacy than more-educated women (179). Therefore, interventions such as group ANC that aim to improve women's ability to access, understand and use educational materials could have a positive impact on reducing health inequalities by improving maternal health literacy among disadvantaged women. In addition, social support is often lacking for disadvantaged women and group ANC may help to reduce inequalities by facilitating the development of peer support networks. However, in certain settings, where group ANC sessions take longer than standard ANC visits, there may be greater cost implications

for disadvantaged women. In addition, in settings with poor transport systems or variable weather, the appointment system with group ANC may not be suitable and may have a negative impact on equity for women living in remote areas. Furthermore, some disadvantaged women might find it harder to disclose personal information in a group setting and might prefer a more private approach to ANC.

### Acceptability

Qualitative evidence from several HICs suggests that women enjoy the group format and use the opportunity to build socially supportive relationships with other pregnant women and health-care professionals (high confidence in the evidence) (22). The flexibility of the format allows women to exchange valuable information with each other and discuss pregnancy-related concerns in a relaxed and informal manner (high confidence in the evidence). Most women appreciate the additional time inherent in the group approach (high confidence in the evidence), although some women do not attend group sessions because of the additional time commitments (moderate confidence in the evidence). Some women have reservations about the lack of privacy during the group sessions, particularly during physical examinations (low confidence in the evidence) and the desire to have partners/husbands included varies (moderate confidence in the evidence). Evidence from providers in HICs suggests they find group sessions to be enjoyable and satisfying and a more efficient use of their time (moderate confidence in the evidence) (45). Providers also identified the group approach as a way of providing continuity of care (moderate confidence in the evidence).

### Feasibility

Qualitative evidence from high-resource settings suggests that health-care professionals view the facilitative components of group ANC as a skill requiring additional investment in terms of training and provider commitment (moderate confidence in the evidence) (45). Some providers also feel that clinics need to be better equipped to deliver group sessions, i.e. clinics need to have large enough rooms with adequate seating (moderate confidence in the evidence). The feasibility of group ANC in low-resource settings needs further research; however, pilot studies in Ghana, Malawi and the United Republic of Tanzania suggest that group ANC is feasible in these settings (181). It has been suggested that group ANC may be a feasible way of improving

ANC quality in settings where relatively few providers attend to relatively large numbers of women in a limited time and, as such, effective communication

can be challenging (182). Others have suggested that the group approach may be a sustainable way of providing continuity of care (181).

## E.4: Community-based interventions to improve communication and support

### E.4.1: Facilitated participatory learning and action (PLA) cycles with women's groups

**RECOMMENDATION E.4.1: The implementation of community mobilization through facilitated participatory learning and action (PLA) cycles with women's groups is recommended to improve maternal and newborn health, particularly in rural settings with low access to health services. Participatory women's groups represent an opportunity for women to discuss their needs during pregnancy, including barriers to reaching care, and to increase support to pregnant women.**  
(Context-specific recommendation)

#### Remarks

- Part of this recommendation was integrated from *WHO recommendations on community mobilization through facilitated participatory learning and action cycles with women's groups for maternal and newborn health* (2014) (183).
- The pathways of influence of this multifaceted, context-specific intervention on maternal and newborn outcomes are difficult to assess. Women meeting to identify their needs and seek solutions plays an important role; mechanisms related to additional activities that are organized based on the solutions identified at the meetings may also play a role.
- Detailed information and guidance related to the recommendation, including important implementation considerations, can be found in the 2014 WHO recommendations on PLA cycles (183), available at: [http://www.who.int/maternal\\_child\\_adolescent/documents/community-mobilization-maternal-newborn/en/](http://www.who.int/maternal_child_adolescent/documents/community-mobilization-maternal-newborn/en/)

### Summary of evidence and considerations

#### Effects of community mobilization through facilitated PLA cycles and women's groups versus standard care (EB Table E.4.1)

The evidence on the effects of community mobilization interventions was synthesized for this guideline from data derived from a Cochrane review of health system and community-level interventions for improving ANC coverage and health outcomes (175). Seven cluster-RCTs conducted between 1999 and 2011, involving approximately 116 805 women, contributed data to this comparison. Trials were conducted in Bangladesh (2), India (2), Malawi (2) and Nepal (1), and six out of seven were conducted in low-resource, rural settings (184-190). The intervention consisted of involving women (pregnant and non-pregnant) in PLA cycles facilitated by trained facilitators, with the aim of identifying, prioritizing and addressing problems women face around pregnancy, childbirth and after birth, and empowering women to seek care and choose healthy pregnancy and newborn care behaviours (191).

Meetings were usually held on a monthly basis and specific activities were prioritized according to the local context and conditions. Coverage of women's group meetings ranged from one group per 309 to one group per 1414 people in the population among included trials, with the proportion of pregnant women attending groups ranging from 2% to 51%. Five out of seven trials were conducted against a backdrop of context-specific health system strengthening in both intervention and control arms; these included training of TBAs and provision of basic equipment to TBAs and/or primary care facilities in four trials. Random effects models were used and sensitivity analyses were performed by including only those trials in which pregnant women comprised more than 30% of the women's groups.

#### Maternal outcomes

Low-certainty evidence suggests that participatory women's groups (PWGs) may reduce maternal mortality (7 trials; RR: 0.78, 95% CI: 0.60-1.03). This interpretation is confirmed by the sensitivity analysis that included only those trials in which the women's

groups included more than 30% pregnant women (4 trials; RR: 0.67, 95% CI: 0.47–0.95).

### Fetal and neonatal outcomes

Low-certainty evidence suggests that PWGs may reduce perinatal mortality (6 trials; RR: 0.91, 95% CI: 0.82–1.01). This interpretation is confirmed by the sensitivity analysis that included only those trials in which pregnant women comprised more than 30% of the women's groups (4 trials; RR: 0.85, 95% CI: 0.77–0.94).

### Coverage outcomes

Low-certainty evidence suggests that PWGs may have little or no effect on ANC coverage of at least four visits (3 trials; RR: 1.05, 95% CI: 0.78–1.41), facility-based delivery (5 trials; RR: 1.04, 95% CI: 0.89–1.22) and ANC coverage of at least one visit (6 trials; RR: 1.43, 95% CI: 0.81–2.51). However, evidence from the sensitivity analysis, which included only those trials in which pregnant women comprised more than 30% of the women's groups, suggests that PWGs may increase ANC coverage of at least one visit (3 trials; RR: 1.77, 95% CI: 1.21–2.58).

### Additional considerations

Findings are consistent with a 2013 review of PWGs (191), which provided low-quality evidence that women's groups reduced maternal mortality (OR: 0.63, 95% CI: 0.32–0.94) and moderate-quality evidence that women's groups reduced neonatal mortality (OR: 0.77, 95% CI: 0.65–0.90). The latter review formed the evidence base for the 2014 WHO recommendation on PWGs (183).

- The existing WHO recommendation on PWGs is as follows:

"The implementation of community mobilization through facilitated participatory learning and action cycles with women's groups is recommended to improve maternal and newborn health, particularly in rural settings with low access to health services (strong recommendation; moderate-quality evidence on neonatal mortality, low-quality evidence for maternal mortality and care-seeking outcomes)" (183).

The GDG that developed this recommendation advised that any intervention designed to increase access to health services should be implemented in tandem with strategies to improve the quality of the health services. It also highlighted the need for more research to understand the effects of community mobilization on care-seeking outcomes in different contexts, and recommended the need for close monitoring and evaluation to ensure high quality implementation adapted to the local context.

### Values

See "Women's values" at the beginning of section 3.E: Background (p. 86).

### Resources, Equity, Acceptability and Feasibility

See the "Summary of evidence and considerations" for Recommendation E.4.2.

## E.4.2: Community mobilization and antenatal home visits

**RECOMMENDATION E.4.2: Packages of interventions that include household and community mobilization and antenatal home visits are recommended to improve antenatal care utilization and perinatal health outcomes, particularly in rural settings with low access to health services.**  
(Context-specific recommendation)

### Remarks

- The GDG agreed that the extent to which these packages improve communication and support for pregnant women is not clear.
- As a stand-alone intervention, the evidence does not support the use of antenatal home visits by lay health workers during pregnancy to improve ANC utilization health outcomes. While the quality and effectiveness of communication during home visits, and the extent to which they increase support for women, is not clear, antenatal home visits may be helpful in ensuring continuity of care across the antenatal, intrapartum and postnatal periods and in promoting other healthy behaviour.
- Stakeholders need to be clear that antenatal home visits by lay health workers do not replace ANC visits.
- Stakeholders should implement health system strengthening interventions alongside these community-based interventions.
- Health-care providers need initial and ongoing training in communication with women and their partners. For women's groups and community mobilization, providers also need training on group facilitation, in the convening of public meetings and in other methods of communication.
- Information for women and community members should be provided in languages and formats accessible to them and programme planners need to ensure that health-care providers/facilitators have reliable supplies of appropriate information materials.
- Programme planners should be aware of the potential for additional costs associated with home visits and community mobilization initiatives, including the potential need for extra staff and travel expenses.
- When considering the use of antenatal home visits, women's groups, partner involvement or community mobilization, programme planners need to ensure that these can be implemented in a way that respects and facilitates women's needs for privacy as well as their choices and their autonomy in decision-making. By offering pregnant women a range of opportunities for contact, communication and support, their individual preferences and circumstances should also be addressed.
- Further research is needed on the acceptability and feasibility of mixed-gender communication, the optimal methods for community mobilization, the best model for integration with health systems, continuity elements of home visits, and the mechanisms of effect of these interventions.

## Summary of evidence and considerations

### Effects of communication and support provided to women through community mobilization and home visits during pregnancy versus standard care (EB Table E.4.2)

The evidence on the effects of community mobilization and antenatal home visits was synthesized from data derived from a Cochrane review of health system and community-level interventions for improving ANC coverage and health outcomes (175). Four large cluster-RCTs conducted in rural Bangladesh, India and Pakistan contributed data on packages of interventions involving community mobilization and antenatal home visits versus no intervention (192–195). Health system

strengthening occurred in both the intervention and control groups in two of the trials. The focus of these packages was generally to promote maternal health education, ANC attendance and other care-seeking behaviour, tetanus toxoid vaccinations and iron and folic acid supplements, and birth and newborn-care preparedness. Household visits were performed by trained lay health workers and consisted of at least two visits during pregnancy. In two trials, these visits were targeted to occur at 12–16 weeks of gestation and 32–34 weeks; in one trial, these visits both occurred in the third trimester; and in the fourth trial the timing of the visits was not specified. Multilevel community mobilization strategies included advocacy work with community stakeholders (community leaders, teachers, and



other respected members), TBAs, husbands or partners, and households (husbands or partners, women, and other family members). Two intervention packages included group education sessions for women focusing on key knowledge and behaviour around pregnancy and early neonatal care, including promotion of ANC and other health education. One intervention package included husband education via booklets and audio cassettes. Training of TBAs to recognize common obstetric and newborn emergencies was a component of three intervention packages. In one trial, telecommunication systems with transport linkages were also set up as part of the intervention package. In another trial, community health committees were encouraged to establish an emergency transport fund and use local vehicles, in addition to advocacy work, household visits and women's meetings.

### Maternal outcomes

Moderate-certainty evidence indicates that intervention packages with community mobilization and antenatal home visits probably have little or no effect on maternal mortality (2 trials; RR: 0.76, 95% CI: 0.44–1.31).

### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that intervention packages with community mobilization and antenatal home visits probably reduce perinatal mortality (3 trials; RR: 0.65, 95% CI: 0.48–0.88).

### Coverage outcomes

High-certainty evidence shows that intervention packages with community mobilization and antenatal home visits improve ANC coverage of at least one visit (4 trials; RR: 1.76, 95% CI: 1.43–2.16). However, moderate-certainty evidence indicates that they probably have little or no effect on ANC coverage of at least four visits (1 trial; RR: 1.51, 95% CI: 0.50–4.59) or facility-based birth (3 trials; RR: 1.46, 95% CI: 0.87–2.46).

### Additional considerations

- The GDG also considered evidence on antenatal home visits as a stand-alone intervention, but did not make a separate recommendation on this intervention due to the lack of evidence of benefits related to the ANC guideline outcomes. In brief, evidence of moderate- to high-certainty suggests that stand-alone antenatal home visits have little or no effect on ANC visit coverage of at least four visits (4 trials; RR: 1.09, 95% CI:

0.99–1.22), facility-based birth (4 trials; RR: 1.08, 95% CI: 0.87–1.35), perinatal mortality (4 trials; RR: 0.91, 95% CI: 0.79–1.05) and preterm birth (1 trial; RR: 0.88, 95% CI: 0.54–1.44) (see Web supplement).

- The 2013 *WHO recommendations on postnatal care of the mother and newborn* include the following recommendation:

“Home visits in the first week after birth are recommended for care of the mother and newborn (strong recommendation based on high-quality evidence for newborns and low-quality evidence for mothers).” This recommendation is accompanied by the remark “Depending on the existing health system in different settings, these home visits can be made by midwives, other skilled providers or well trained and supervised CHWs [community health workers]” (196).

- The 2011 WHO guidelines on *Preventing early pregnancy and poor reproductive outcomes among adolescents in developing countries* strongly recommend the following in relation to the outcome “Increase use of skilled antenatal, childbirth and postnatal care among adolescents”:
  - “Provide information to all pregnant adolescents and other stakeholders about the importance of utilizing skilled antenatal care.”
  - “Provide information to all pregnant adolescents and other stakeholders about the importance of utilizing skilled childbirth care.”
  - “Promote birth and emergency preparedness in antenatal care strategies for pregnant adolescents (in household, community and health facility settings)” (197).
- Several WHO recommendations included in the 2015 WHO recommendations on health promotion interventions for maternal and newborn health are relevant to community-based interventions to improve communication and support for women during pregnancy (198) – these are presented in Box 3.

### Values

See “Women’s values” at the beginning of section 3.E: Background (p. 86).

### Resources

A systematic review of the cost-effectiveness of strategies to improve the utilization and provision of maternal and newborn health care in low- and lower-middle-income countries reported that there was reasonably strong evidence for the



### **Box 3: Relevant recommendations from the 2015 WHO recommendations on health promotion interventions for maternal and newborn health**

**Recommendation 1:** Birth preparedness and complication readiness interventions are recommended to increase the use of skilled care at birth and to increase the timely use of facility care for obstetric and newborn complications. (Strong recommendation, very low-quality evidence.)

**Recommendation 2:** Interventions to promote the involvement of men during pregnancy, childbirth and after birth are recommended to facilitate and support improved self-care of women, improved home care practices for women and newborns, and improved use of skilled care during pregnancy, childbirth and the postnatal period for women and newborns. (Strong recommendation, very low-quality evidence.) These interventions are recommended provided that they are implemented in a way that respects, promotes and facilitates women's choices and their autonomy in decision-making, and supports women in taking care of themselves and their newborns. In order to ensure this, rigorous monitoring and evaluation of implementation is recommended.

**Recommendation 3** on interventions to promote awareness of human, sexual and reproductive rights and the right to access quality skilled care: Because of the paucity of evidence available, additional research is recommended. The GDG supports, as a matter of principle, the importance for MNH programmes to inform women about their right to health and to access quality skilled care, and to continue to empower them to access such care.

**Recommendation 6** on partnership with traditional birth attendants (TBAs): Where TBAs remain the main providers of care at birth, dialogue with TBAs, women, families, communities and service providers is recommended in order to define and agree on alternative roles for TBAs, recognizing the important role they can play in supporting the health of women and newborns. (Strong recommendation, very low-quality evidence.)

**Recommendation 7:** Ongoing dialogue with communities is recommended as an essential component in defining the characteristics of culturally appropriate, quality maternity care services that address the needs of women and newborns and incorporate their cultural preferences. Mechanisms that ensure women's voices are meaningfully included in these dialogues are also recommended. (Strong recommendation, very low-quality evidence.)

**Recommendation 11:** Community participation in quality-improvement processes for maternity care services is recommended to improve quality of care from the perspectives of women, communities and health-care providers. Communities should be involved in jointly defining and assessing quality. Mechanisms that ensure women's voices are meaningfully included are also recommended. (Strong recommendation, very low-quality evidence.)

**Recommendation 12:** Community participation in programme planning, implementation and monitoring is recommended to improve use of skilled care during pregnancy, childbirth and the postnatal period for women and newborns, increase the timely use of facility care for obstetric and newborn complications and improve maternal and newborn health. Mechanisms that ensure women's voices are meaningfully included are also recommended. (Strong recommendation, very low-quality evidence.)

Source: WHO, 2015 (198).

cost-effectiveness of the use of PLA cycles (199). Estimated costs per life saved for PLA cycle interventions alone was US\$ 268 and for community mobilization combined with home visits during pregnancy and/or health system strengthening, costs ranged from US\$ 707 to US\$ 1489 per death averted. However, costs of these interventions are difficult to estimate and depend on context. Costing must also take into account the facilitators' time, training and supervision; these elements are considered key to the quality of implementation and the success of the intervention.

#### **Equity**

Interventions such as PLA cycles, community mobilization and home visits during pregnancy are a way of facilitating dialogue and action with, and empowering, disadvantaged populations to engage in efforts to improve health and to strengthen broader community support. The women's groups PLA cycles, in particular, were conducted in marginalized areas where other support mechanisms often do not exist. Interventions to engage male partners/husbands and others in the community to support women to make healthy choices for themselves and their children

may help to address inequalities. However, when engaging men, it is important to consider women's preferences, as including male partners could also have a negative effect for women who would prefer to discuss pregnancy-related and other matters without their partner's involvement.

### Acceptability

Qualitative evidence suggests that women in a variety of settings and contexts readily engage with interventions designed to increase communication and support, provided they are delivered in a caring and respectful manner (high confidence in the evidence) (22). The use of women's groups is likely to fulfil two key requirements of ANC from a woman's perspective – the opportunity to receive and share relevant information and the opportunity to develop supportive relationships with other women and health-care providers (high confidence in the evidence). Evidence from women and providers in LMICs also highlighted the importance of active community engagement in the design and delivery of informational-based services, especially in communities where traditional beliefs may differ from conventional understandings (moderate confidence in the evidence). Qualitative

evidence from providers suggests that there is a willingness to supply pregnancy-related information and offer psychological/emotional support to women provided that resources are available (high confidence in the evidence) and the services are delivered in a coordinated, organized manner with appropriate managerial support (moderate confidence in the evidence) (45).

### Feasibility

Qualitative evidence suggests that, where health-care providers are involved in facilitating women's groups, they may need additional training to help with the facilitative components and this may be a barrier in some resource-poor settings (high confidence in the evidence). Similarly, the extra costs associated with home visits in terms of additional staff and extra resources may limit implementation in some LMICs (high confidence in the evidence) (45). It has been suggested that community-based interventions introduced through existing public sector health workers and local health systems may be more feasible and more likely to succeed than project-based interventions (200).

## E.5: Task shifting components of antenatal care delivery

**RECOMMENDATION E.5.1: Task shifting the promotion of health-related behaviours for maternal and newborn health<sup>a</sup> to a broad range of cadres, including lay health workers, auxiliary nurses, nurses, midwives and doctors is recommended.** (*Recommended*)

**RECOMMENDATION E.5.2: Task shifting the distribution of recommended nutritional supplements and intermittent preventive treatment in pregnancy (IPTp) for malaria prevention to a broad range of cadres, including auxiliary nurses, nurses, midwives and doctors is recommended.** (*Recommended*)

### Remarks

- Recommendations E.5.1 and E.5.2 have been adapted and integrated from *Optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting* (OptimizeMNH) (2012) (201).
- The GDG noted that, while task shifting has an important role to play in allowing flexibility in health-care delivery in low-resource settings, policy-makers need to work towards midwife-led care for all women.
- Lay health workers need to be recognized and integrated into the system, and not be working alone, i.e. task shifting needs to occur within a team approach.
- The mandate of all health workers involved in task shifting programmes needs to be clear.
- In a separate guideline on HIV testing services (98), WHO recommends that lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid tests (see Recommendation B.1.8).
- The GDG noted that it may be feasible to task shift antenatal ultrasound to midwives with the appropriate training, staffing, mentoring and referral systems in place.
- Further research is needed on the mechanism of effect of MLCC and whether continuity of care can be task shifted.
- Further information on this recommendation can be found in the OptimizeMNH guideline (201), available at: [http://www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/978924504843/en/](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/978924504843/en/)

<sup>a</sup> Including promotion of the following: care-seeking behaviour and ANC utilization; birth preparedness and complication readiness; sleeping under insecticide-treated bednets; skilled care for childbirth; companionship in labour and childbirth; nutritional advice; nutritional supplements; HIV testing during pregnancy; exclusive breastfeeding; postnatal care and family planning; immunization according to national guidelines.

## E.6: Recruitment and retention of staff in rural and remote areas

**RECOMMENDATION E.6: Policy-makers should consider educational, regulatory, financial, and personal and professional support interventions to recruit and retain qualified health workers in rural and remote areas.** (*Context-specific recommendation*)

### Remarks

- Recommendation E.6 has been adapted and integrated for the ANC guideline from the 2010 WHO publication *Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations* (202).
- Strong recommendations (abridged) on recruitment and staff retention from the above guideline include the following.
  - Use targeted admission policies to enrol students with a rural background in education programmes for various health disciplines and/or establish a health-care professional school outside of major cities.
  - Revise undergraduate and postgraduate curricula to include rural health topics and clinical rotations in rural areas so as to enhance the competencies of health-care professionals working in rural areas.
  - Improve living conditions for health workers and their families and invest in infrastructure and services (sanitation, electricity, telecommunications, schools, etc.).
  - Provide a good and safe working environment, including appropriate equipment and supplies, supportive supervision and mentoring.
  - Identify and implement appropriate outreach activities to facilitate cooperation between health workers from better-served areas and those in underserved areas, and, where feasible, use tele-health to provide additional support.
  - Develop and support career development programmes and provide senior posts in rural areas so that health workers can move up the career path as a result of experience, education and training, without necessarily leaving rural areas.
  - Support the development of professional networks, rural health-care professional associations, rural health journals, etc., to improve the morale and status of rural providers and reduce feelings of professional isolation.
  - Adopt public recognition measures such as rural health days, awards and titles at local, national and international levels to lift the profile of working in rural areas.
- Conditional educational, regulatory and financial recommendations from this guideline can be found in the WHO global policy recommendations document (202), available at: <http://www.who.int/hrh/retention/guidelines/en/>

## E.7: Antenatal care contact schedules

### **RECOMMENDATION E.7: Antenatal care models with a minimum of eight contacts are recommended to reduce perinatal mortality and improve women's experience of care.**

*(Recommended)*

#### **Remarks**

- The GDG stresses that the four-visit focused ANC (FANC) model does not offer women adequate contact with health-care practitioners and is no longer recommended. With the FANC model, the first ANC visit occurs before 12 weeks of pregnancy, the second around 26 weeks, the third around 32 weeks, and the fourth between 36 and 38 weeks of gestation. Thereafter, women are advised to return to ANC at 41 weeks of gestation or sooner if they experience danger signs. Each ANC visit involves specific goals aimed at improving triage and timely referral of high-risk women and includes educational components (12). However, up-to-date evidence shows that the FANC model, which was developed in the 1990s, is probably associated with more perinatal deaths than models that comprise at least eight ANC visits. Furthermore, evidence suggests that more ANC visits, irrespective of the resource setting, is probably associated with greater maternal satisfaction than less ANC visits.
- The GDG prefers the word “contact” to “visit”, as it implies an active connection between a pregnant woman and a health-care provider that is not implicit with the word “visit”. In terms of the operationalization of this recommendation, “contact” can be adapted to local contexts through community outreach programmes and lay health worker involvement.
- The decision regarding the number of contacts with a health system was also influenced by the following:
  - evidence supporting improving safety during pregnancy through increased frequency of maternal and fetal assessment to detect problems;
  - evidence supporting improving health system communication and support around pregnancy for women and families;
  - evidence from HIC studies indicating no important differences in maternal and perinatal health outcomes between ANC models that included at least eight contacts and ANC models that included more (11–15) contacts (203);
  - evidence indicating that more contact between pregnant women and knowledgeable, supportive and respectful health-care practitioners is more likely to lead to a positive pregnancy experience.
- Implementation considerations related to this recommendation and the mapping of guideline recommendations to ANC contacts are presented in Chapter 4: Implementation of the ANC guideline and recommendations.

## **Summary of evidence and considerations**

### **Effects of the FANC model (with four visits) compared with “standard” ANC (with at least eight ANC visits planned) (EB Table E.7)**

The evidence on the effects of FANC (the four-visit ANC model) was derived from a Cochrane review on “reduced-visit” ANC models versus “standard” care models (with at least eight ANC visits planned) that included seven RCTs (203). Four individual RCTs were conducted in HICs (the United Kingdom and the USA) and three large cluster-RCTs were conducted in LMICs, including one conducted in Argentina, Cuba, Saudi Arabia and Thailand (204), and two conducted in Zimbabwe. The LMIC trials evaluated the FANC model compared with “standard” ANC models that planned for at least eight visits (12). Three cluster-

RCTs involving more than 50 000 women contributed data. The median number of visits achieved in the FANC arms of these trials ranged from four to five visits and the median number of visits achieved in the standard ANC arms ranged from four to eight visits.

### **Maternal outcomes**

High-certainty evidence shows that FANC had little or no effect on caesarean section rates (1 trial, 24 526 women; RR: 1.00, 95% CI: 0.89–1.11), and low-certainty evidence suggests that it may make little or no difference to maternal mortality (3 trials, 51 504 women; RR: 1.13, 95% CI: 0.5–2.57).

With regard to maternal satisfaction, outcomes were reported narratively in the review, as data were sparse. In a survey conducted among a subset of

women participating in the WHO trial, fewer women were satisfied with the frequency of visits in the FANC model than in the standard model (77.4% versus 87.2%) and women in the FANC model were less likely to be satisfied with the spacing between visits compared with the standard model (72.7% versus 81%). This evidence was not formally graded due to insufficient data.

### Fetal and neonatal outcomes

Moderate-certainty evidence indicates that FANC probably increases perinatal mortality compared with “standard” ANC with more visits (3 trials, 51 323 women; RR: 1.15, 95% CI: 1.01–1.32). Based on this RR, the illustrative impact on perinatal mortality rates are shown in Box 4.

Moderate-certainty evidence indicates that FANC probably has little or no effect on preterm birth (3 trials, 47 094 women; RR: 0.99, 95% CI: 0.91–1.08) and low birth weight (3 trials, 46 220 women; RR: 1.04, 95% CI: 0.97–1.12) compared with “standard” ANC. In addition, low-certainty evidence suggests that FANC probably makes little or no difference to SGA (3 trials, 43 094 women; RR: 1.01, 95% CI: 0.88–1.17).

### Additional considerations

- The GDG noted that the review authors explored reasons for the effect on perinatal mortality and the effect persisted in various exploratory analyses.
- In 2012, the WHO undertook a secondary analysis of perinatal mortality data from the WHO FANC trial (205). This secondary analysis, which included 18 365 low-risk and 6160 high-risk women, found an increase in the overall risk of perinatal mortality between 32 and 36 weeks of gestation with FANC compared with “standard” ANC in both low- and high-risk populations.
- It is not clear whether the philosophy of the FANC approach, with regard to improving quality of care at each ANC visit, was implemented effectively in the trials. However, if this element is neglected, a poorly executed FANC model may then simply represent reduced health provider contact, and a reduced opportunity to detect risk factors and complications, and to address women’s concerns.
- The GDG panel considered unpublished findings of a two-year audit of perinatal mortality from the Mpumalanga region of South Africa that has implemented the FANC model (206). The audit from September 2013 to August 2015 comprised data of 149 308 births of neonates weighing more than 1000 g, among which there were 3893 perinatal deaths (giving a PMR of 24.8 per 1000 births). Stillbirth risk was plotted according to gestational age and three peaks in the occurrence of stillbirths were noted, one at around 31 weeks of gestation, another at around 37 weeks, and the third occurring at 40 weeks or more. When these data were compared with stillbirth data from another South Africa province, which uses a model of ANC that includes fortnightly ANC visits from 28 weeks of gestation, the latter showed a gradual rise in the overall stillbirth risk from 28 weeks, with a single (and lower) peak at 40 weeks or more, i.e. no additional peaks at 30 and 37 weeks. These data are consistent with those from the secondary analysis of the WHO trial and suggest that additional visits in the third trimester may prevent stillbirths.
- The GDG also considered the evidence from the Cochrane review on reduced visit ANC models of at least eight visits versus “standard” ANC models with 11–15 visits from four RCTs in HICs (203). Low-certainty evidence suggested that the reduced-visit model (with at least eight visits) may be associated with increased preterm birth

#### Box 4: Illustration of the impact of focused ANC (FANC) on perinatal mortality rates (PMR)

Assumed PMR (“Standard” ANC)	Illustrative PMR <sup>a</sup> (FANC model)	Absolute increase in perinatal deaths
10 deaths per 1000 births	12 deaths per 1000 births (10–13 deaths)	2 deaths per 1000 births (0–3 deaths)
25 deaths per 1000 births	29 deaths per 1000 births (25–33 deaths)	4 deaths per 1000 births (0–8 deaths)
50 deaths per 1000 births	58 deaths per 1000 births (50–66 deaths)	8 deaths per 1000 births (0–16 deaths)

a Based on RR: 1.15, 95% CI: 1.01–1.32.

(3 trials; RR: 1.24, 1.01-1.52), but no other important effects on health outcomes were noted. In general, however, evidence from these individual studies also suggests that the reduced-visit models may be associated with lower women's satisfaction.

- The GDG considered unpublished evidence from four country case studies (Argentina, Kenya, Thailand and the United Republic of Tanzania) where the FANC model has been implemented (207). Provider compliance was noted to be problematic in some settings, as were shortages of equipment, supplies and staff. Integration of services was found to be particularly challenging, especially in settings with a high prevalence of endemic infections (e.g. malaria, TB, sexually transmitted infections, helminthiasis). Guidance on implementation of the FANC model in such settings was found to be inadequate, as was the amount of time allowed within the four-visit model to provide integrated care.
- Findings on provider compliance from these case studies are consistent with published findings from rural Burkina Faso, Uganda and the United Republic of Tanzania (208). Health-care providers in this study were found to variably omit certain practices from the FANC model, including blood pressure measurement and provision of information on danger signs, and to spend less than 15 minutes per ANC visit. Such reports suggest that fitting all the components of the FANC model into four visits is difficult to achieve in some low-resource settings where services are already overstretched. In addition, in low-resource settings, when the target is set at four ANC visits, due to the various barriers to ANC use, far fewer than four visits may actually be achieved.
- Programmatic evidence from Ghana and Kenya indicates similar levels of satisfaction between FANC and standard ANC, with sources of dissatisfaction with both models being long waiting times and costs associated with care (209, 210).
- Emotional and psychosocial needs are variable and the needs of vulnerable groups (including adolescent girls, displaced and war-affected women, women with disabilities, women with mental health concerns, women living with HIV, sex workers, ethnic and racial minorities, among others) can be greater than for other women. Therefore, the number and content of visits should be adaptable to local context and to the individual woman.

## Values

See "Women's values" at the beginning of section 3.E: Background (p. 86).

## Resources

Two trials evaluated cost implications of two models of ANC with reduced visits, one in the United Kingdom and one in two LMICs (Cuba and Thailand). Costs per pregnancy to both women and providers were lower with the reduced visits models in both settings. Time spent accessing care was also significantly shorter with reduced visits models. In the United Kingdom trial, there was an increase in costs related to neonatal intensive care unit stays in the reduced visit model.

## Equity

Preventable maternal and perinatal mortality is highest among disadvantaged populations, which are at greater risk of various health problems, such as nutritional deficiencies and infections, that predispose women to poor pregnancy outcomes. This suggests that, in LMICs, more and better quality contact between pregnant women with health-care providers would help to address health inequalities.

## Acceptability

Evidence from high-, medium- and low-resource settings suggests that women do not like reduced visit schedules and would prefer more contact with antenatal services (moderate confidence in the evidence) (22). Women value the opportunity to build supportive relationships during their pregnancy (high confidence in the evidence) and for some women, especially in LMIC settings, the reduced visit schedule may limit their ability to develop these relationships, both with health-care professionals and with other pregnant women (low confidence in the evidence). In some low-income settings where women rely on husbands or partners to financially support their antenatal visits, the reduced visit schedule limits their ability to procure additional finance (low confidence in the evidence). However, the reduced visit schedule may be appreciated by some women in a range of LMIC settings because of the potential for cost savings, e.g. loss of domestic income from extra clinic attendance and/or associated travel costs (low confidence in the evidence). Indirect evidence also suggests that women are much more likely to engage with antenatal services if care is provided by knowledgeable, kind health-care professionals who have the time and resources to deliver genuine woman-centred care, regardless of the number of



visits (high confidence in the evidence). Specific evidence from providers relating to reduced visit schedules or the adoption of FANC is sparse and, in some LMICs, highlights concerns around the availability of equipment and resources, staff shortages and inadequate training – issues that are pertinent to all models of ANC delivery in low-resource settings.

### Feasibility

Qualitative evidence suggests that some providers in LMICs feel that the reduced visit schedule is a

more efficient use of staff time and is less likely to deplete limited supplies of equipment and medicine (moderate confidence in the evidence) (45).

Programme reports from Ghana and Kenya stress that inadequate equipment, supplies, infrastructure and training may hamper implementation (209, 210). Providers have also raised concerns about the difficulty of incorporating all of the FANC components into relatively short appointments, especially in LMICs (Burkina Faso, Uganda and the United Republic of Tanzania) where services are already stretched (208, 211).

## 4. Implementation of the ANC guideline and recommendations: introducing the 2016 WHO ANC model

The ultimate goal of this guideline and its recommendations is to improve the quality of ANC and to improve maternal, fetal and newborn outcomes related to ANC. These ANC recommendations need to be deliverable within an appropriate model of care that can be adapted to different countries, local contexts and the individual woman. With the contributions of the members of the Guideline Development Group (GDG), WHO reviewed existing models of delivering ANC with full consideration of the range of interventions recommended within this guideline (Chapter 3). Recommendation E.7 states that “Antenatal care models with a minimum of eight contacts are recommended to reduce perinatal mortality and improve women’s experience of care”; taking this as a foundation, the GDG reviewed how ANC should be delivered in terms of both the timing and content of each of the ANC contacts, and arrived at a new model – the 2016 WHO ANC model – which replaces the previous four-visit focused ANC (FANC) model. For the purpose of developing this new ANC model, the ANC guideline recommendations were mapped to the eight contacts based on the evidence supporting each recommendation and the optimal timing of delivery of the recommended interventions to achieve maximal impact.

The 2016 WHO ANC model recommends a minimum of eight ANC contacts, with the first contact scheduled to take place in the first trimester (up to 12 weeks of gestation), two contacts scheduled in the second trimester (at 20 and 26 weeks of gestation) and five contacts scheduled in the third trimester (at 30, 34, 36, 38 and 40 weeks). Within this model, the word “contact” has been used instead of “visit”, as it implies an active connection between a pregnant woman and a health-care provider that is not implicit with the word “visit”. It should be noted that the list of interventions to be delivered at each contact and details about where they are delivered and by whom (see Table 2) are not meant to be prescriptive but, rather, adaptable to the individual woman and the

local context, to allow flexibility in the delivery of the recommended interventions. Different to the FANC model, an additional contact is now recommended at 20 weeks of gestation, and an additional three contacts are recommended in the third trimester (defined as the period from 28 weeks of gestation up to delivery), since this represents the period of greatest antenatal risk for mother and baby (see Box 5). At these third-trimester contacts, ANC providers should aim to reduce preventable morbidity and mortality through systematic monitoring of maternal and fetal well-being, particularly in relation to hypertensive disorders and other complications that may be asymptomatic but detectable during this critical period.

### Box 5: Comparing ANC schedules

WHO FANC model	2016 WHO ANC model
<i>First trimester</i>	
Visit 1: 8–12 weeks	Contact 1: up to 12 weeks
<i>Second trimester</i>	
Visit 2: 24–26 weeks	Contact 2: 20 weeks Contact 3: 26 weeks
<i>Third trimester</i>	
Visit 3: 32 weeks	Contact 4: 30 weeks Contact 5: 34 weeks Contact 6: 36 weeks Contact 7: 38 weeks Contact 8: 40 weeks
Visit 4: 36–38 weeks	
Return for delivery at 41 weeks if not given birth.	

If the quality of ANC is poor and women’s experience of it is negative, the evidence shows that women will not attend ANC, irrespective of the number of recommended contacts in the ANC model. Thus, the overarching aim of the 2016 WHO ANC model is to provide pregnant women with respectful,

individualized, person-centred care at every contact, with implementation of effective clinical practices (interventions and tests), and provision of relevant and timely information, and psychosocial and emotional support, by practitioners with good clinical and interpersonal skills within a well functioning health system. Effective implementation of ANC requires a health systems approach and strengthening focusing on continuity of care, integrated service delivery, availability of supplies and commodities and empowered health-care providers.

There are many different ways for health system planners to optimize ANC delivery by employing a range of strategies that can improve the utilization and quality of ANC. The health system recommendations in this guideline have focused mainly on those strategies that address continuity of care, and improve communication with, and support for, women (Recommendations E.1–E.4). The recommendations on task shifting and recruitment of staff (Recommendations E.5.1, E.5.2 and E.6) are also important, as provider experience and attitudes have an impact on the capacity of health systems to deliver quality ANC; barriers to provider recruitment and job satisfaction will need to be addressed to successfully implement this guideline. Such barriers have been shown to be significant in LMICs, and can prevent the provision of quality midwifery care (212). In addition to improving the quality of care, these health system recommendations are intended to encourage health system planners to operationalize the recommended eight ANC contacts in ways that are feasible in the local context.

Table 2 shows the WHO ANC guideline recommendations mapped to the eight recommended contacts, thus presenting a summary framework for the 2016 WHO ANC model in support of a positive pregnancy experience. This table does not include good clinical practices, such as measuring blood pressure, proteinuria and weight, checking for fetal heart sounds, which would be included as part of an implementation manual aimed at practitioners. Practices that are not recommended have been included in the table for informational purposes and highlighted in grey. Context-specific recommendations for which rigorous research is required before they can be considered for implementation have not been mapped to the schedule of contacts.

Any intervention that is missed at an ANC contact, for any reason, should in principle be included at the next contact. Effective communication should be facilitated at all ANC contacts, to cover: presence of any symptoms; promotion of healthy pregnancies and newborns through lifestyle choices; individualized advice and support; timely information on tests, supplements and treatments; birth-preparedness and complication-readiness planning; postnatal family planning options; and the timing and purpose of ANC contacts. Topics for individualized advice and support can include healthy eating, physical activity, nutrition, tobacco, substance use, caffeine intake, physiological symptoms, malaria and HIV prevention, and blood test results and retests. Communication should occur in a respectful, individualized and person-centred way. An effective referral system and emergency transport are also essential components of this ANC model.

Within the 2016 WHO ANC model, there are two opportunities to arrange a single early ultrasound scan (i.e. before 24 weeks of gestation): either at the first contact (up to 12 weeks of gestation) or at the second contact (20 weeks). The GDG suggests this pragmatic approach in order to increase the proportion of pregnancies with accurate gestational age assessments, especially in settings where ANC utilization is historically low; lack of accurate gestational age assessment can compromise the diagnosis and/or management of complications (such as preterm birth and pre-eclampsia). It is important to highlight that the frequency and exact timing of some of these ANC practices and interventions – especially related to malaria, tuberculosis and HIV – may need to be adapted, based on the local context, population and health system. Please refer to Box 6 at the end of this chapter for considerations related to the adoption, scale-up and implementation of the 2016 WHO ANC model.

The GDG agreed that implementation of the 2016 WHO ANC model should not wait for a large multicentre trial to be conducted to determine the optimal number of contacts, or the impact of the additional recommended interventions, such as ultrasound, on pregnancy outcomes, resources, equity and the other domains; rather, following implementation of the model, it should be subject to ongoing monitoring and evaluation. It should be remembered that the four-visit model has

significantly increased stillbirth risk compared to standard models with eight or more contacts. Understandably, policy-makers and health-care providers might feel that an increase in the number of ANC contacts with an emphasis on quality of care will increase the burden on already overstretched health systems. However, the GDG agreed that there is likely to be little impact on lives saved or improved without substantial investment in improving the quality of ANC services provided in LMICs. International human rights law requires that States use “maximum available resources” to realize economic, social and cultural rights, which includes women’s rights to

sexual and reproductive health (1). Ensuring that women’s rights to sexual and reproductive health are supported requires meeting standards with regard to the availability, accessibility, acceptability and quality of health-care facilities, supplies and services (1). Specifically, in addition to other health system strengthening initiatives, investment is urgently needed to address the shortage and training of midwives and other health-care providers able to offer ANC. Such investment should be considered a top priority as quality health care around pregnancy and childbirth has far-reaching benefits for individuals, families, communities and countries.

**Table 2: The 2016 WHO ANC model for a positive pregnancy experience: recommendations mapped to eight scheduled ANC contacts**

**Overarching aim:** To provide pregnant women with respectful, individualized, person-centred care at every contact, with implementation of effective clinical practices (interventions and tests), and provision of relevant and timely information, and psychosocial and emotional support, by practitioners with good clinical and interpersonal skills within a well functioning health system.

**Notes:**

- These recommendations apply to pregnant women and adolescent girls within the context of routine ANC.
- This table does not include good clinical practices, such as measuring blood pressure, proteinuria and weight, and checking for fetal heart sounds, which would be included as part of an implementation manual aimed at practitioners.
- Remarks detailed in the shaded box with each recommendation should be taken into account when planning the implementation of these recommendations.

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1	2	3	4	5	6	7	8
			(12 weeks)	(20 weeks)	(26 weeks)	(30 weeks)	(34 weeks)	(36 weeks)	(38 weeks)	(40 weeks)
A. Nutritional interventions										
Dietary interventions	A.1.1: Counselling about healthy eating and keeping physically active during pregnancy is recommended for pregnant women to stay healthy and to prevent excessive weight gain during pregnancy. <sup>a</sup>	Recommended	X	X	X	X	X	X	X	X
	A.1.2: In undernourished populations, nutrition education on increasing daily energy and protein intake is recommended for pregnant women to reduce the risk of low-birth-weight neonates.	Context-specific recommendation	X	X	X	X	X	X	X	X
	A.1.3: In undernourished populations, balanced energy and protein dietary supplementation is recommended for pregnant women to reduce the risk of stillbirths and small-for-gestational-age neonates.	Context-specific recommendation	X	X	X	X	X	X	X	X
	A.1.4: In undernourished populations, high-protein supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended								
Iron and folic acid supplements	A.2.1: Daily oral iron and folic acid supplementation with 30 mg to 60 mg of elemental iron <sup>b</sup> and 400 µg (0.4 mg) of folic acid <sup>c</sup> is recommended for pregnant women to prevent maternal anaemia, puerperal sepsis, low birth weight, and preterm birth. <sup>d</sup>	Recommended	X	X	X	X	X	X	X	X

a. A healthy diet contains adequate energy, protein, vitamins and minerals, obtained through the consumption of a variety of foods, including green and orange vegetables, meat, fish, beans, nuts, whole grains and fruit.

b. The equivalent of 60 mg of elemental iron is 300 mg of ferrous sulfate heptahydrate, 180 mg of ferrous fumarate or 500 mg of ferrous gluconate.

c. Folic acid should be commenced as early as possible (ideally before conception) to prevent neural tube defects.

d. This recommendation supersedes the previous recommendation found in the 2012 WHO publication *Guideline: daily iron and folic acid supplementation in pregnant women* (36).

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Iron and folic acid supplements</b>	<b>A.2.2:</b> Intermittent oral iron and folic acid supplementation with 120 mg of elemental iron <sup>e</sup> and 2800 µg (2.8 mg) of folic acid once weekly is recommended for pregnant women to improve maternal and neonatal outcomes if daily iron is not acceptable due to side-effects, and in populations with an anaemia prevalence among pregnant women of less than 20%. <sup>f</sup>	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Calcium supplements</b>	<b>A.3:</b> In populations with low dietary calcium intake, daily calcium supplementation (1.5–2.0 g oral elemental calcium) is recommended for pregnant women to reduce the risk of pre-eclampsia. <sup>g</sup>	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Vitamin A supplements</b>	<b>A.4:</b> Vitamin A supplementation is only recommended for pregnant women in areas where vitamin A deficiency is a severe public health problem, <sup>h</sup> to prevent night blindness. <sup>i</sup>	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Zinc supplements</b>	<b>A.5:</b> Zinc supplementation for pregnant women is only recommended in the context of rigorous research.	Context-specific recommendation (research)								
<b>Multiple micronutrient supplements</b>	<b>A.6:</b> Multiple micronutrient supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended								
<b>Vitamin B6 (pyridoxine) supplements</b>	<b>A.7:</b> Vitamin B6 (pyridoxine) supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended								

e. The equivalent of 120 mg of elemental iron equals 600 mg of ferrous sulfate heptahydrate, 360 mg of ferrous fumarate or 1000 mg of ferrous gluconate.

f. This recommendation supersedes the previous recommendation in the 2012 WHO publication *Guideline: intermittent iron and folic acid supplementation in non-anaemic pregnant women* (55).

g. This recommendation is consistent with the 2011 WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia (57) and supersedes the previous recommendation found in the 2013 WHO publication *Guideline: calcium supplementation in pregnant women* (38).

h. Vitamin A deficiency is a severe public health problem if ≥ 5% of women in a population have a history of night blindness in their most recent pregnancy in the previous 3–5 years that ended in a live birth, or if ≥ 20% of pregnant women have a serum retinol level < 0.70 µmol/L. Determination of vitamin A deficiency as a public health problem involves estimating the prevalence of deficiency in a population by using specific biochemical and clinical indicators of vitamin A status.

i. This recommendation supersedes the previous recommendation found in the 2011 WHO publication *Guideline: vitamin A supplementation in pregnant women* (60).

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Vitamin E and C supplements</b>	<b>A.8:</b> Vitamin E and C supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended								
<b>Vitamin D supplements</b>	<b>A.9:</b> Vitamin D supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes. <sup>j</sup>	Not recommended								
<b>Restricting caffeine intake</b>	<b>A.10.1:</b> For pregnant women with high daily caffeine intake (more than 300 mg per day), <sup>k</sup> lowering daily caffeine intake during pregnancy is recommended to reduce the risk of pregnancy loss and low-birth-weight neonates.	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>B. Maternal and fetal assessment<sup>l</sup></b>										
<b>Anaemia</b>	<b>B.1.1:</b> Full blood count testing is the recommended method for diagnosing anaemia in pregnancy. In settings where full blood count testing is not available, on-site haemoglobin testing with a haemoglobinometer is recommended over the use of the haemoglobin colour scale as the method for diagnosing anaemia in pregnancy.	Context-specific recommendation	X		X			X		
<b>Asymptomatic bacteriuria (ASB)</b>	<b>B.1.2:</b> Midstream urine culture is the recommended method for diagnosing asymptomatic bacteriuria (ASB) in pregnancy. In settings where urine culture is not available, on-site midstream urine Gram-staining is recommended over the use of dipstick tests as the method for diagnosing ASB in pregnancy.	Context-specific recommendation	X		X		X			

j. This recommendation supersedes the previous recommendation found in the 2012 WHO publication *Guideline: vitamin D supplementation in pregnant women (75)*.

k. This includes any product, beverage or food containing caffeine (i.e. brewed coffee, tea, cola-type soft drinks, caffeinated energy drinks, chocolate, caffeine tablets).

l. Evidence on essential ANC activities, such as measuring maternal blood pressure, proteinuria and weight, and checking for fetal heart sounds, was not assessed by the GDG as these activities are considered to be part of good clinical practice.



Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Intimate partner violence (IPV)</b>	<b>B.1.3:</b> Clinical enquiry about the possibility of intimate partner violence (IPV) should be strongly considered at antenatal care visits when assessing conditions that may be caused or complicated by IPV in order to improve clinical diagnosis and subsequent care, where there is the capacity to provide a supportive response (including referral where appropriate) and where the WHO minimum requirements are met. <sup>m,n</sup>	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Gestational diabetes mellitus (GDM)</b>	<b>B.1.4:</b> Hyperglycaemia first detected at any time during pregnancy should be classified as either, gestational diabetes mellitus (GDM) or diabetes mellitus in pregnancy, according to WHO 2013 criteria. <sup>o</sup>	Recommended	X	X	X	X	X	X	X	X
<b>Tobacco use</b>	<b>B.1.5:</b> Health-care providers should ask all pregnant women about their tobacco use (past and present) and exposure to second-hand smoke as early as possible in the pregnancy and at every antenatal care visit. <sup>p</sup>	Recommended	X	X	X	X	X	X	X	X
<b>Substance use</b>	<b>B.1.6:</b> Health-care providers should ask all pregnant women about their use of alcohol and other substances (past and present) as early as possible in the pregnancy and at every antenatal care visit. <sup>q</sup>	Recommended	X	X	X	X	X	X	X	X

m. Minimum requirements are: a protocol/standard operating procedure; training on how to ask about IPV, and on how to provide the minimum response or beyond; private setting; confidentiality ensured; system for referral in place; and time to allow for appropriate disclosure.

n. This recommendation is consistent with the 2013 publication *Responding to intimate partner violence and sexual violence against women: WHO clinical and policy guidelines* (86).

o. This is not a recommendation on routine screening for hyperglycaemia in pregnancy. It has been adapted and integrated from the 2013 WHO publication *Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy* (94), which states that GDM should be diagnosed at any time in pregnancy if one or more of the following criteria are met:

- fasting plasma glucose  $\geq 5.1$ – $6.9$  mmol/L (92–125 mg/dL)
  - 1-hour plasma glucose  $\geq 10.0$  mmol/L (180 mg/dL) following a 75 g oral glucose load
  - 2-hour plasma glucose  $\geq 8.5$ – $11.0$  mmol/L (153–199 mg/dL) following a 75 g oral glucose load.
- Diabetes mellitus in pregnancy should be diagnosed if one or more of the following criteria are met:
- fasting plasma glucose  $\geq 7.0$  mmol/L (126 mg/dL)
  - 2-hour plasma glucose  $\geq 11.1$  mmol/L (200 mg/dL) following a 75 g oral glucose load
  - random plasma glucose  $\geq 11.1$  mmol/L (200 mg/dL) in the presence of diabetes symptoms.

p. Integrated from the 2013 publication *WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy* (96).

q. Integrated from the 2014 WHO publication *Guidelines for the identification and management of substance use and substance use disorders in pregnancy* (97).

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Human immunodeficiency virus (HIV) and syphilis</b>	<b>B.1.7:</b> In high prevalence settings, <sup>r</sup> provider-initiated testing and counselling (PITC) for HIV should be considered a routine component of the package of care for pregnant women in all antenatal care settings. In low-prevalence settings, PITC can be considered for pregnant women in antenatal care as a key component of the effort to eliminate mother-to-child transmission of HIV, and to integrate HIV testing with syphilis, viral or other key tests, as relevant to the setting, and to strengthen the underlying maternal and child health systems. <sup>s</sup>	Recommended	X							
<b>Tuberculosis (TB)</b>	<b>B.1.8:</b> In settings where the tuberculosis (TB) prevalence in the general population is 100/100 000 population or higher, systematic screening for active TB should be considered for pregnant women as part of antenatal care. <sup>t</sup>	Context-specific recommendation	X							
<b>Daily fetal movement counting</b>	<b>B.2.1:</b> Daily fetal movement counting, such as with “count-to-ten” kick charts, is only recommended in the context of rigorous research.	Context-specific recommendation (research)								
<b>Symphysis-fundal height (SFH) measurement</b>	<b>B.2.2:</b> Replacing abdominal palpation with symphysis-fundal height (SFH) measurement for the assessment of fetal growth is not recommended to improve perinatal outcomes. A change from what is usually practiced (abdominal palpation or SFH measurement) in a particular setting is not recommended.	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Antenatal cardiotocography</b>	<b>B.2.3:</b> Routine antenatal cardiotocography <sup>u</sup> is not recommended for pregnant women to improve maternal and perinatal outcomes.	Not recommended								

r. High-prevalence settings are defined in the 2015 WHO publication *Consolidated guidelines on HIV testing services as settings with greater than 5% HIV prevalence in the population being tested* (98). Low-prevalence settings are those with less than 5% HIV prevalence in the population being tested. In settings with a generalized or concentrated HIV epidemic, retesting of HIV-negative women should be performed in the third trimester because of the high risk of acquiring HIV infection during pregnancy; please refer to Recommendation B.1.7 for details.

s. Adapted and integrated from the 2015 WHO publication *Consolidated guidelines on HIV testing services* (98).

t. Adapted and integrated from the 2013 WHO publication *Systematic screening for active tuberculosis: principles and recommendations* (105).

u. Cardiotocography (CTG) is a continuous recording of the fetal heart rate and uterine contractions obtained via an ultrasound transducer placed on the mother's abdomen.

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Ultrasound scan</b>	<b>B.2.4:</b> One ultrasound scan before 24 weeks of gestation (early ultrasound) is recommended for pregnant women to estimate gestational age, improve detection of fetal anomalies and multiple pregnancies, reduce induction of labour for post-term pregnancy, and improve a woman's pregnancy experience.	Recommended	X	X						
<b>Doppler ultrasound of fetal blood vessels</b>	<b>B.2.5:</b> Routine Doppler ultrasound examination is not recommended for pregnant women to improve maternal and perinatal outcomes. <sup>v</sup>	Not recommended								
<b>C. Preventive measures</b>										
<b>Antibiotics for asymptomatic bacteriuria (ASB)</b>	<b>C.1:</b> A seven-day antibiotic regimen is recommended for all pregnant women with asymptomatic bacteriuria (ASB) to prevent persistent bacteriuria, preterm birth and low birth weight.	Recommended	X		X			X		
<b>Antibiotic prophylaxis to prevent recurrent urinary tract infections</b>	<b>C.2:</b> Antibiotic prophylaxis is only recommended to prevent recurrent urinary tract infections in pregnant women in the context of rigorous research.	Context-specific recommendation (research)								
<b>Antenatal anti-D immunoglobulin administration</b>	<b>C.3:</b> Antenatal prophylaxis with anti-D immunoglobulin in non-sensitized Rh-negative pregnant women at 28 and 34 weeks of gestation to prevent RhD alloimmunization is only recommended in the context of rigorous research.	Context-specific recommendation (research)								
<b>Preventive anthelmintic treatment</b>	<b>C.4:</b> In endemic areas <sup>w</sup> , preventive anthelmintic treatment is recommended for pregnant women after the first trimester as part of worm infection reduction programmes. <sup>x</sup>	Context-specific recommendation		X						

v. Doppler ultrasound technology evaluates umbilical artery (and other fetal arteries) waveforms to assess fetal well-being in the third trimester of pregnancy.

w. Areas with greater than 20% prevalence of infection with any soil-transmitted helminths.

x. Consistent with the 2016 WHO publication *Guideline: preventive chemotherapy to control soil-transmitted helminth infections in high-risk groups* (140).

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Tetanus toxoid vaccination</b> <sup>y</sup>	<b>C.5:</b> Tetanus toxoid vaccination is recommended for all pregnant women, depending on previous tetanus vaccination exposure, to prevent neonatal mortality from tetanus. <sup>y</sup>	Recommended	X							
<b>Malaria prevention: Intermittent preventive treatment in pregnancy (IPTp)</b>	<b>C.6:</b> In malaria-endemic areas in Africa, intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP) is recommended for all pregnant women. Dosing should start in the second trimester, and doses should be given at least one month apart, with the objective of ensuring that at least three doses are received. <sup>z</sup>	Context-specific recommendation	X (13 weeks)	X	X	X		X		X
<b>Pre-exposure prophylaxis for HIV prevention</b>	<b>C.7:</b> Oral pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate (TDF) should be offered as an additional prevention choice for pregnant women at substantial risk of HIV infection as part of combination prevention approaches. <sup>aa</sup>	Context-specific recommendation	X							

#### D. Interventions for common physiological symptoms

<b>Nausea and vomiting</b>	<b>D.1:</b> Ginger, chamomile, vitamin B6 and/or acupuncture are recommended for the relief of nausea in early pregnancy, based on a woman's preferences and available options.	Recommended	X	X	X					
<b>Heartburn</b>	<b>D.2:</b> Advice on diet and lifestyle is recommended to prevent and relieve heartburn in pregnancy. Antacid preparations can be used to women with troublesome symptoms that are not relieved by lifestyle modification.	Recommended	X	X	X	X	X	X	X	X

y. This recommendation is consistent with the 2006 WHO guideline on *Maternal immunization against tetanus* (134). The dosing schedule depends on the previous tetanus vaccination exposure; please refer to Recommendation C.5 for details.

z. Integrated from the 2015 WHO publication *Guidelines for the treatment of malaria*, which also states: "WHO recommends that, in areas of moderate-to-high malaria transmission of Africa, IPTp-SP be given to all pregnant women at each scheduled antenatal care visit, starting as early as possible in the second trimester, provided that the doses of SP are given at least 1 month apart. WHO recommends a package of interventions for preventing malaria during pregnancy, which includes promotion and use of insecticide-treated nets, as well as IPTp-SP" (153). To ensure that pregnant women in endemic areas start IPTp-SP as early as possible in the second trimester, policy-makers should ensure health system contact with women at 13 weeks of gestation.

aa. Integrated from the 2015 WHO publication *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV* (99). Substantial risk of HIV infection is defined by an incidence of HIV infection in the absence of PrEP that is sufficiently high (> 3% incidence) to make offering PrEP potentially cost-saving (or cost-effective). Offering PrEP to people at substantial risk of HIV infection maximizes the benefits relative to the risks and costs.

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Leg cramps</b>	<b>D.3:</b> Magnesium, calcium or non-pharmacological treatment options can be used for the relief of leg cramps in pregnancy, based on a woman's preferences and available options.	Recommended	X	X	X	X	X	X	X	X
<b>Low back and pelvic pain</b>	<b>D.4:</b> Regular exercise throughout pregnancy is recommended to prevent low back and pelvic pain. There are a number of different treatment options that can be used, such as physiotherapy, support belts and acupuncture, based on a woman's preferences and available options.	Recommended	X	X	X	X	X	X	X	X
<b>Constipation</b>	<b>D.5:</b> Wheat bran or other fibre supplements can be used to relieve constipation in pregnancy if the condition fails to respond to dietary modification, based on a woman's preferences and available options.	Recommended	X	X	X	X	X	X	X	X
<b>Varicose veins and oedema</b>	<b>D.6:</b> Non-pharmacological options, such as compression stockings, leg elevation and water immersion, can be used for the management of varicose veins and oedema in pregnancy, based on a woman's preferences and available options.	Recommended	X	X	X	X	X	X	X	X
<b>E: Health systems interventions to improve utilization and quality of antenatal care</b>										
<b>Woman-held case notes</b>	<b>E.1:</b> It is recommended that each pregnant woman carries her own case notes during pregnancy to improve continuity, quality of care and her pregnancy experience.	Recommended	X	X	X	X	X	X	X	X
<b>Midwife-led continuity of care</b>	<b>E.2:</b> Midwife-led continuity of care models, in which a known midwife or small group of known midwives supports a woman throughout the antenatal, intrapartum and postnatal continuum, are recommended for pregnant women in settings with well functioning midwifery programmes.	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Group antenatal care</b>	<b>E.3:</b> Group antenatal care provided by qualified health-care professionals may be offered as an alternative to individual antenatal care for pregnant women in the context of rigorous research, depending on a woman's preferences and provided that the infrastructure and resources for delivery of group antenatal care are available.	Context-specific recommendation (research)								

Type of intervention	Recommendation	Type of recommendation	Eight scheduled ANC contacts (weeks of gestation)							
			1 (12 weeks)	2 (20 weeks)	3 (26 weeks)	4 (30 weeks)	5 (34 weeks)	6 (36 weeks)	7 (38 weeks)	8 (40 weeks)
<b>Community-based interventions to improve communication and support</b>	<b>E.4.1:</b> The implementation of community mobilization through facilitated participatory learning and action (PLA) cycles with women's groups is recommended to improve maternal and newborn health, particularly in rural settings with low access to health services. <sup>ab</sup> Participatory women's groups represent an opportunity for women to discuss their needs during pregnancy, including barriers to reaching care, and to increase support to pregnant women.	Context-specific recommendation	X	X	X	X	X	X	X	X
	<b>E.4.2:</b> Packages of interventions that include household and community mobilization and antenatal home visits are recommended to improve antenatal care utilization and perinatal health outcomes, particularly in rural settings with low access to health services.	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Task shifting components of antenatal care delivery<sup>ac</sup></b>	<b>E.5.1:</b> Task shifting the promotion of health-related behaviours for maternal and newborn health <sup>ad</sup> to a broad range of cadres, including lay health workers, auxiliary nurses, nurses, midwives and doctors is recommended.	Recommended	X	X	X	X	X	X	X	X
	<b>E.5.2:</b> Task shifting the distribution of recommended nutritional supplements and intermittent preventive treatment in pregnancy (IPTp) for malaria prevention to a broad range of cadres, including auxiliary nurses, nurses, midwives and doctors is recommended.	Recommended	X	X	X	X	X	X	X	X
<b>Recruitment and retention of staff in rural and remote areas<sup>ae</sup></b>	<b>E.6:</b> Policy-makers should consider educational, regulatory, financial, and personal and professional support interventions to recruit and retain qualified health workers in rural and remote areas.	Context-specific recommendation	X	X	X	X	X	X	X	X
<b>Antenatal care contact schedules</b>	<b>E.7:</b> Antenatal care models with a minimum of eight contacts are recommended to reduce perinatal mortality and improve women's experience of care.	Recommended	X	X	X	X	X	X	X	X

ab. Integrated from the 2014 publication *WHO recommendations on community mobilization through facilitated participatory learning and action cycles with women's groups for maternal and newborn health* (183).

ac. Including promotion of the following: care-seeking behaviour and ANC utilization; birth preparedness and complication readiness; sleeping under insecticide-treated bednets; skilled care for childbirth; companionship in labour and childbirth; nutritional advice; nutritional supplements; other context-specific supplements and interventions; HIV testing during pregnancy; exclusive breastfeeding; postnatal care and family planning; immunization according to national guidelines.

ad. Recommendations adapted and integrated from the 2012 WHO guideline on *Optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting* (OptimizeMNH) (201).

ae. Adapted and integrated from the 2010 WHO publication *Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations* (202).



## **Box 6: Considerations for the adoption, scale-up and implementation of the 2016 WHO ANC model**

### **Health policy considerations for adoption and scale-up of the model**

- There needs to be a firm government commitment to scale up implementation of ANC services to achieve national coverage at health-care facilities; national support must be secured for the whole package rather than for specific components, to avoid fragmentation of services.
- In low-income countries, donors may play a significant role in scaling up the implementation of the model. Sponsoring mechanisms that support domestically driven processes to scale up the whole model are more likely to be helpful than mechanisms that support only a part of the package.
- To set the policy agenda, to secure broad anchoring and to ensure progress in policy formulation and decision-making, stakeholders should be targeted among both elected and bureaucratic officials. In addition, representatives of training facilities and the relevant medical specialties should be included in participatory processes at all stages, including prior to an actual policy decision, to secure broad support for scaling-up.
- To facilitate negotiations and planning, information on the expected impact of the model on users, providers (e.g. workload, training requirements) and costs should be assessed and disseminated.
- The model must be adapted to local contexts and service-delivery settings.

### **Health system or organizational-level considerations for implementation of the model**

- Introduction of the model should involve pre-service training institutions and professional bodies, so that training curricula for ANC can be updated as quickly and smoothly as possible.
- Long-term planning is needed for resource generation and budget allocation to strengthen and sustain high-quality ANC services.
- In-service training and supervisory models will need to be developed according to health-care providers' professional requirements, considering the content, duration and procedures for the selection of providers for training. These models can also be explicitly designed to address staff turnover, particularly in low-resource settings.
- Standardized tools will need to be developed for supervision, ensuring that supervisors are able to support and enable health-care providers to deliver integrated, comprehensive ANC services.
- A strategy for task shifting may need to be developed to optimize the use of human resources.
- Tools or "job aids" for ANC implementation (e.g. ANC cards) will need to be simplified and updated with all key information in accordance with the model.
- Strategies will need to be devised to improve supply chain management according to local requirements, such as developing protocols for the procedures of obtaining and maintaining the stock of supplies, encouraging providers to collect and monitor data on the stock levels and strengthening the provider-level coordination and follow-up of medicines and health-care supplies required for implementation of the ANC model.

### **User-level considerations for implementation of the model**

- Community-sensitizing activities should be undertaken to disseminate information about the importance of each component of ANC, and pregnant women's right to attend ANC for their health and the health of their unborn baby. This information should provide details about the timing and content of the recommended ANC contacts, and about the expected user fees.
- It may be possible to reduce waiting times by reorganizing ANC services and/or client flow.

For specific implementation considerations related to the individual recommendations, see Annex 4.



## 5. Research implications

During the guideline development process, the Guideline Development Group (GDG) identified important knowledge gaps that need to be addressed through primary research. The certainty of evidence was rated as “low” or “very low” for a number of interventions evaluated. According to GRADE methodology (15), this implies that further research on interventions with “low” or “very low” certainty evidence for important outcomes is likely to have an impact on future certainty and subsequent

recommendations related to these interventions. The GDG identified knowledge gaps based on this concept and prioritized related research questions according to whether further research would be likely to promote equity, be feasible to implement, and contribute to improvements in the pregnancy experience of women. In Box 7, priority research questions are grouped according to the grouping of the recommendations in this ANC guideline (i.e. types of interventions) and are listed in a similar order to the recommendations.

### Box 7: Priority research questions, by type of intervention

#### A. Nutritional interventions

- What are the effects, feasibility, acceptability and equity implications of healthy eating and exercise interventions in LMICs?
- Can an intervention package with standardized guidance on nutrition be developed that is evidence-based, sustainable, reproducible, accessible and adaptable to different cultural settings?
- Research is needed at country level to better understand the context-specific etiology of under-nutrition. Do alternatives to energy and protein supplements, such as cash or vouchers for pregnant women, or improved local and national food production and distribution, lead to improved maternal and perinatal outcomes?
- What is the most effective, acceptable and feasible regimen of recommended supplements (iron, calcium and folic acid)? Could micronutrients be combined into a single, or slow-release, formulation? To what extent do iron and calcium (or zinc) supplements compete for absorption?
- What is the most cost-effective iron compound and formulation (coated versus not) in terms of benefits and side-effects?
- Can a rapid, portable, less invasive, and field-friendly test for iron deficiency anaemia be developed?
- Are there haemoconcentration risks associated with haemoglobin concentrations of more than 130 g/L in pregnancy?
- What are the biological mechanisms underlying the relationships among calcium supplementation, pre-eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count) and preterm birth?
- What is the minimal dose and optimal commencement schedule for calcium supplementation to achieve a positive effect on pre-eclampsia and preterm birth?
- What is the effect of zinc supplementation on maternal outcomes (e.g. infections) and perinatal outcomes (e.g. preterm birth, SGA, neonatal infections, perinatal morbidity)? What is the optimal dose of zinc supplementation in pregnancy, particularly in zinc-deficient populations with no food fortification strategy in place?
- Does vitamin C reduce PROM and improve maternal and perinatal outcomes?
- Does vitamin D increase the risk of preterm birth when it's combined with calcium?

#### B. Maternal and fetal assessment

- Can better and more cost-effective on-site tests to diagnose anaemia be developed?
- What are the effects of on-site urine testing (dipsticks or Gram stain) with antibiotic treatment for ASB versus urine testing plus culture confirmation of urine test, followed by ASB treatment if indicated, on pregnancy and other relevant outcomes, including equity, acceptability, feasibility and antimicrobial resistance?
- Can better on-site tests to diagnose ASB be developed to improve accuracy and feasibility of ASB testing and reduce overtreatment of ASB? What is the threshold prevalence of ASB at which targeted testing and treatment rather than universal testing and treatment might be a more effective strategy?
- Which strategies to enquire about and manage IPV are the most effective? Do interventions to enquire about IPV have an impact on ANC attendance? Can interventions focusing on partners prevent IPV? Does enquiry about IPV (with appropriate referral) have an impact on maternal and perinatal outcomes?

- What is the prevalence of GDM and diabetes mellitus in pregnancy, according to the new criteria, in various populations and ethnic groups? What are the best screening strategies for GDM and what are the prevalence thresholds at which these are cost-effective?
- What is the effect of daily fetal movement counting, such as the use of “count-to-ten” kick charts, in the third trimester of pregnancy on perinatal outcomes in LMICs?
- What are the effects and accuracy of SFH measurement to detect abnormal fetal growth and other risk factors for perinatal morbidity (e.g. multiple pregnancy, polyhydramnios) in settings without routine ultrasound?
- Can a single routine Doppler ultrasound examination of fetal blood vessels for all pregnant women in the third trimester accurately detect or predict pregnancy complications, particularly IUGR and pre-eclampsia, and lead to improved pregnancy outcomes?

### C. Preventive measures

- What are the effects of prophylactic antibiotics to prevent RUTI in pregnancy, compared to monitoring with use of antibiotics only when indicated, on maternal infections, perinatal morbidity and antimicrobial drug resistance?
- What is the prevalence of Rh alloimmunization and associated poor outcomes among pregnant women in LMIC settings? Can cost-effective strategies be developed to manage this condition in LMICS and improve equity?

### D. Interventions for common physiological symptoms

- What is the prevalence of common physiological symptoms among pregnant women in low-resource settings, and can the offer of treatment of these symptoms reduce health inequality, improve ANC coverage and improve women's pregnancy experiences?
- What is the etiology of leg cramps in pregnancy, and does treatment with magnesium and/or calcium relieve symptoms?

### E. Health systems interventions to improve utilization and quality of ANC

- What should be included in women-held case notes, and how can discrepancies across different records be reduced to improve quality of care?
- What is the pathway of influence of midwife-led continuity of care (MLCC)? Is it specifically the continuity, the provider-client relationship or the midwifery philosophy that leads to better health outcomes and maternal satisfaction? Can this effect be replicated with other cadres of health-care providers, e.g. auxiliary nurse midwives, nurses, family doctors, etc.? How can ANC in LMICs be structured to incorporate the active ingredients of MLCC, particularly in settings where the number of midwives is very limited?
- What are the effects, feasibility and resource implications of MLCC in LMICs? Which models are most feasible (i.e. caseload or team models)? Can a continuity model for group ANC be developed for settings where other MLCC models are not feasible?
- Can a group ANC model be developed for LMICs, to provide guidance on the optimal group size, frequency and content of group ANC contacts?
- Is group ANC acceptable (data should include the views of women who decline to participate), feasible and cost-effective in LMIC settings?
- Are mixed models (group and individual ANC) feasible and acceptable, and are there benefits to mixed models?
- What are the effects of group ANC on maternal and perinatal health outcomes, coverage outcomes (ANC contacts and facility-based births), and women's and providers' experiences?
- Should women with complicated pregnancies also be offered group ANC, for the communication and social support aspects, in addition to receiving specialist care?
- How acceptable and feasible are mixed-gender community mobilization groups? What are the optimal methods for community-based interventions to improve communication and support for pregnant women and adolescent girls; to improve integration of community-based mobilization efforts with health systems; and to ensure continuity of care with home visits? What are the mechanisms of effect of these interventions?
- Can the 2016 WHO ANC model with a minimum of eight contacts impact the quality of ANC in LMICs, and what is the effect on health, values, acceptability, resources, feasibility and equity parameters?

ANC: antenatal care; ASB: asymptomatic bacteriuria; GDM: gestational diabetes mellitus; IPV: intimate partner violence; LMICs: low- and middle-income countries; MLCC: midwife-led continuity of care; PROM: prelabour rupture of membranes; RUTI: recurrent urinary tract infections; SFH: symphysis-fundal height; SGA: small for gestational age

## 6. Dissemination, applicability and updating of the guideline and recommendations

### 6.1 Dissemination

This guideline will be available online for download and also as a printed publication. Online versions will be available via the websites of the WHO Departments of Reproductive Health and Research (RHR), Nutrition for Health and Development (NHD) and Maternal, Newborn, Child and Adolescent Health (MCA), and through the WHO Reproductive Health Library (RHL).<sup>7</sup> Print versions will be distributed to WHO regional and country offices, ministries of health, WHO collaborating centres, NGO partners and professional associations, using the same distribution list that was developed for the implementation of focused ANC (FANC). The guideline will be accompanied by an independent critical appraisal based on the AGREE instrument (Appraisal of Guidelines for Research & Evaluation) (213). Technical meetings will be held within the WHO Departments of RHR, NHD and MCA to share the recommendations and derivative products, which will include a practical manual for implementation of the new 2016 WHO ANC model, with the teams responsible for policy and programme implementation.

Two sets of evidence briefs will be developed: one set for policy-makers and programme managers and the other set for health-care professionals. These evidence briefs, which will highlight the recommendations and implementation-related contextual issues, will be developed and disseminated in collaboration USAID, FIGO and ICM. The briefs will be organized in alignment with the different sections of the guideline, for example focusing on nutrition, maternal and fetal assessment or preventive measures to allow for derivative products to be tailored and disseminated accordingly to partners.

The executive summary and recommendations from this publication will be translated into the six UN languages for dissemination through the WHO

regional offices and during meetings organized by, or attended by, staff of the WHO Departments of RHR, MCA and NHD.

In addition to online and print versions of this guideline, an interactive web-based version is planned, which will be developed by a professional infographics group. This will facilitate the dissemination and uptake of the guideline recommendations by making them available online in a user-friendly format, and will allow a platform for cross-referenced recommendations to be updated on an ongoing basis to ensure that the recommendations are up to date. Furthermore, this would allow for products to be organized by different topics (e.g. nutrition) and allow for focused activities and products to be developed. English, French, Portuguese and Spanish (the latter in collaboration with the WHO Regional Office for the Americas/Pan American Health Organization [PAHO]) web-based versions are planned and have been budgeted for.

The guideline will also be launched on the WHO Department of RHR official website as part of the monthly "HRP News". This site currently has over 3000 subscribers including clinicians, programme managers, policy-makers and health service users from all around the world. In addition, a number of articles presenting the recommendations and key implementation considerations will be published, in compliance with WHO's open access and copyright policies. Relevant WHO clusters, departments and partnerships, such as HIV/AIDS, Tuberculosis and Malaria, the Initiative for Vaccine Research (IVR) and the Partnership for Maternal, Newborn & Child Health (PMNCH) will also be part of this dissemination process.

In an effort to increase dissemination of WHO guidelines on sexual and reproductive health and rights, a search function with the ability to search the database of WHO guidelines and recommendations has been created and recently launched by

<sup>7</sup> RHL is available at: <http://apps.who.int/rhl/en/>

the Department of RHR.<sup>8</sup> The ANC guideline recommendations will be made available via this new search function.

The Maternal and Perinatal Health and Preventing Unsafe Abortion team of the WHO Department of RHR, in collaboration with the Departments of NHD and MCA and other partners, will support national and subnational working groups to adapt and implement the guideline. This process will include the development or revision of existing national guidelines or protocols in line with the WHO guideline. The GREAT Network (Guideline-driven, Research priorities, Evidence synthesis, Application of evidence, and Transfer of knowledge) will be used to bring together relevant stakeholders to identify and assess the priorities, barriers and facilitators to guideline implementation, and to support the efforts of stakeholders to develop adaptations and guideline implementation strategies tailored to the local context (214). This includes technical support for local guideline implementers in the development of training manuals, flow charts and quality indicators, as well as participation in stakeholder meetings.

## 6.2 Applicability issues

### Anticipated impact of the guideline on the organization of ANC

Effective implementation of the recommendations in this guideline will likely require reorganization of care and redistribution of health-care resources, particularly in low- and middle-income countries (LMICs). The potential barriers to implementation include the following:

- lack of human resources with the necessary expertise and skills to implement, supervise and support recommended practices, including client counselling;
- lack of infrastructure to support interventions, e.g. lack of power to support ultrasound equipment;
- lack of physical space to conduct individual or group-based counselling;
- lack of community understanding of the new model of care, particularly around the contact schedule and potentially longer wait times;
- lack of physical resources, e.g. equipment, test kits, supplies, medicines and nutritional supplements;

- lack of effective referral mechanisms and care pathways for women identified as needing additional care;
- lack of understanding of the value of newly recommended interventions among health-care providers and system managers.
- lack of health information management systems (HMISs) designed to document and monitor recommended practices (e.g. client cards, registers, etc.).

Given the potential barriers noted above, a phased approach to adoption, adaptation and implementation of the guideline recommendations may be prudent. Various strategies for addressing these barriers and facilitating implementation have been suggested in the list of considerations at the end of Chapter 4.

### Monitoring and evaluating the impact of the guideline

The implementation and impact of these recommendations will be monitored at the health-service, regional and country levels, based on clearly defined criteria and indicators that are associated with locally agreed targets. In collaboration with the monitoring and evaluation teams of the WHO Departments of RHR and MCA, data on country- and regional-level implementation of the recommendations will be collected and evaluated in the short to medium term to evaluate their impact on national policies of individual WHO Member States. Interrupted time series, clinical audits or criterion-based audits could be used to obtain the relevant data on the interventions contained in this guideline.

## 6.3 Updating the guideline

In accordance with the concept of WHO's GREAT Network, which employs a systematic and continuous process of identifying and bridging evidence gaps following guideline implementation (214), the proposed guideline will be updated five years after publication unless significant new evidence emerges that necessitates earlier revision. The WHO Steering Group will continue to follow the research developments in the area of ANC, particularly for those questions for which no evidence was found and those that are supported by low-quality evidence, where new recommendations or a change in the published recommendation may be warranted,

<sup>8</sup> This can be accessed at: [search.optimizemnh.org](http://search.optimizemnh.org)

respectively. Any concern about the validity of any recommendation will be promptly communicated via the interactive website for the guideline,<sup>9</sup> and plans will be made to update the recommendation, as needed.

Two years after publication and dissemination of the guideline, an online survey will be conducted through WHO regional and country offices and through selected respondents of other user groups (e.g. professional societies, NGOs) to gauge the status and extent of in-country utilization and adaptation, and whether any recommendations in the guideline have been implemented or influenced policy decisions. This survey will also help in gathering feedback relevant to future modifications. Requests for additional guidance may also be received from WHO Member States. Stakeholders can address suggestions for additional questions for inclusion in the updated version of the guideline to the WHO Department of RHR by email (reproductivehealth@who.int).

As the guideline nears the end of the proposed five-year validity period, the responsible technical officer (or another designated WHO staff person), in conjunction with the WHO Steering Group, will assess the currency of the recommendations and the need for new guidance on the topic. This will be achieved by performing a scoping exercise among technical experts, health professionals, researchers and service users to identify controversial or priority areas where further evidence-based guidance may be needed.

All technical products developed during the process of developing this guideline – including full reports of systematic reviews, corresponding search strategies and dates of searches, Cochrane Review Manager (RevMan)<sup>10</sup> files customized for priority outcomes, and the basis for quality rating of outcomes within the GRADE process – will be archived in the departmental shared folder for future reference and use. Where there are concerns about the validity of a particular recommendation based on new evidence, the systematic review addressing the primary question will be updated. To update the review, the search strategy used for the initial review will be applied, possibly by the same systematic review team or another team if the initial review team is no longer available.

Any new questions identified following the scoping exercise at the end of five years will undergo a similar process of evidence retrieval, synthesis and grading in accordance with the WHO standards for guideline development.

The guideline development process exposed several knowledge gaps related to antenatal screening of GDM, syphilis and haemoglobinopathies. WHO aims to develop further guidance around these topics so that the appropriate recommendations can be included in updated ANC guidance. In addition, future updates will aim to include more recommendations on how to improve ANC utilization, quality and delivery, which will be informed by new WHO guidance on improving the quality of care throughout the antenatal, intrapartum and postnatal continuum.

<sup>9</sup> Available at: [www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/anc-positive-pregnancy-experience/en/](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/)

<sup>10</sup> For further information, see: <http://www.cochrane.org/revman>

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## Annex 2: Other WHO guidelines with recommendations relevant to routine ANC

WHO guideline title	Year of publication	WHO department responsible	Approach
<b>1.</b> Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations	2010	Various WHO departments and regional representatives.	Recommendation relevant to ANC was adapted for, and integrated into, the ANC guideline.
<b>2.</b> Guideline: vitamin A supplementation in pregnant women	2011	Department of Nutrition for Health and Development (NHD) Department of Reproductive Health and Research (RHR) Department of Maternal, Newborn, Child and Adolescent Health (MCA)	New recommendation in the ANC guideline supersedes the recommendation in this 2011 guideline.
<b>3.</b> WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia	2011	RHR, MCA	Cross-checked for consistency
<b>4.</b> Preventing early pregnancy and poor reproductive outcomes	2011	MCA, RHR, Department of Child and Adolescent Health (CAH), Making Pregnancy Safer	Referenced
<b>5.</b> WHO recommendations: optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting (OptimizeMNH)	2012	RHR	Recommendation relevant to ANC was adapted for, and integrated into, the ANC guideline.
<b>6.</b> Guideline: vitamin D supplementation in pregnant women	2012	NHD, RHR, MCA	New recommendation in the ANC guideline supersedes the recommendation in this 2012 guideline.
<b>7.</b> Guideline: intermittent iron and folic acid supplementation in non-anaemic pregnant women	2012	NHD, RHR, MCA	New recommendation in the ANC guideline supersedes the recommendation in this 2012 guideline.
<b>8.</b> Guideline: daily iron and folic acid supplementation in pregnant women	2012	NHD, RHR, MCA	New recommendation in the ANC guideline supersedes the recommendation in this 2012 guideline.
<b>9.</b> Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy	2013	Chronic Diseases Prevention and Management, RHR	Recommendation relevant to ANC was integrated into the ANC guideline.
<b>10.</b> Responding to intimate partner violence and sexual violence against women	2013	RHR	Cross-checked for consistency
<b>11.</b> Guideline: calcium supplementation in pregnant women	2013	NHD	New recommendation in the ANC guideline supersedes the recommendation in this 2013 guideline.

WHO guideline title	Year of publication	WHO department responsible	Approach
<b>12.</b> Systematic screening for active tuberculosis: principles and recommendations	2013	Strategic and Technical Advisory Group for Tuberculosis	Recommendation relevant to ANC was integrated into the ANC guideline.
<b>13.</b> WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy	2013	Department of Prevention of Noncommunicable Diseases	Recommendations relevant to ANC were integrated into the ANC guideline.
<b>14.</b> Guidelines for the identification of substance use and substance use disorders in pregnancy	2014	Department of Mental Health and Substance Abuse	Recommendation relevant to ANC was integrated into the ANC guideline.
<b>15.</b> WHO recommendations on community mobilization through facilitated participatory learning and action cycles with women's groups for maternal and newborn health	2014	MCA	Referenced
<b>16.</b> Guidelines for the treatment of malaria	2015	Global Malaria Programme	Recommendation relevant to ANC was integrated into the ANC guideline.
<b>17.</b> Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV	2015	Department of HIV	Recommendation relevant to ANC was integrated into the ANC guideline.
<b>18.</b> Consolidated guidelines on HIV testing services	2015	Department of HIV	Recommendation relevant to ANC was integrated into the ANC guideline.
<b>19.</b> WHO recommendations for prevention and treatment of maternal peripartum infections	2015	RHR	Referenced
<b>20.</b> WHO recommendations on health promotion interventions for maternal and newborn health	2015	MCA	Referenced and cross-checked for consistency
<b>21.</b> Guideline: preventive chemotherapy to control soil-transmitted helminths in high-risk groups	2016	WHO Evidence and Programme Guidance Unit, NHD, Preventive Chemotherapy and Transmission Control, Department of Control of Neglected Tropical Diseases	Referenced and cross-checked for consistency

## Annex 3: Summary of declarations of interest from the Guideline Development Group (GDG) members and how they were managed

Name	Expertise	Disclosure of interest	Conflict of interest and management
<b>Dr Ariful Alam</b>	Nutrition, health systems	None declared	Not applicable
<b>Dr Françoise Cluzeau</b>	Evidence synthesis and guideline development using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach	None declared	Not applicable
<b>Dr Luz Maria De-Regil</b>	Nutrition, epidemiology, systematic reviews, programme implementation	Full staff employee of the Micronutrient Initiative and part of the working group that advised on the International Federation of Gynecology and Obstetrics (FIGO) recommendations on nutrition.	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation.
<b>Dr Atf Ghérissi</b>	Systematic reviews, qualitative evidence, maternal and perinatal health, community health	None declared	Not applicable
<b>Mrs Gill Gyte</b>	Patient representative, pregnancy and childbirth	Voluntary work for the Cochrane Pregnancy and Childbirth Group, which is funded by United Kingdom Department of Health.	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation.
<b>Dr Rintaro Mori</b>	Perinatology, neonatology, systematic reviews, evidence synthesis and guideline development using GRADE	None declared	Not applicable
<b>Prof. Jim Neilson</b>	General obstetrics, perinatology, gynaecology, systematic reviews, evidence synthesis and guideline development using GRADE	None declared	Not applicable
<b>Dr Lynnette Neufeld</b>	Micronutrients, programmes, epidemiology	Previous employer received funding from the Canadian Government to design and implement iron/folic acid and other programmes related to nutrition during pregnancy; designed demonstration projects with local partners and academic institutions to integrate nutrition actions into antenatal care (ANC).	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation.
<b>Prof. Nafissa Osman</b>	Obstetrics and gynaecology, implementation research	None declared	Not applicable
<b>Prof. Bob Pattinson</b>	Obstetrics and gynaecology, delivery of care, evidence synthesis	None declared	Not applicable

<b>Dr Erika Ota</b>	Nutrition, evidence synthesis, guideline development	None declared	Not applicable
<b>Dr Kathleen Rasmussen</b>	Maternal and child nutrition	None declared	Not applicable
<b>Dr Niveen Abu Rmeileh</b>	Community and public health, statistical epidemiology	None declared	Not applicable
<b>Prof. H.P.S. Sachdev</b>	Paediatrics, nutrition, systematic reviews	None declared	Not applicable
<b>Ms Rusidah Selamat</b>	Maternal and infant nutrition, community-based programmes, implementation research	None declared	Not applicable
<b>Dr Lisa Noguchi</b>	Midwifery, delivery of care, implementation science	Technical advisor to Bill & Melinda Gates Foundation-funded study on group ANC for increasing facility delivery; travel costs supplied by the Maternal and Child Survival Program.	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation.
<b>Dr Tomas Pantoja</b>	Obstetrics and gynaecology, health systems	None declared	Not applicable
<b>Dr Charlotte Warren</b>	Maternal and perinatal health, systematic reviews, implementation research	None declared	Not applicable
<b>Prof. Charles Wisonge</b>	Health systems, systematic reviews, delivery of care	None declared	Not applicable

## Annex 4: Implementation considerations for ANC guideline recommendations

Implementation considerations for ANC guideline recommendations				
	Need to know	Need to do	Need to have	Consider
<b>A. Nutritional interventions</b>				
<b>A.1.1.</b> Nutritional counselling on a healthy diet and physical activity	<ul style="list-style-type: none"> <li>Healthy diet and exercise in local context</li> <li>Prevalence of overweight</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Counselling skills</li> <li>Time and space for counselling</li> </ul>	<ul style="list-style-type: none"> <li>Gender issues and cultural expectations of women</li> <li>Local food security</li> </ul>
<b>A.1.2.</b> Nutritional education on increasing daily energy and protein intake	<ul style="list-style-type: none"> <li>If your setting has an undernourished population</li> <li>How to do counselling</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Time to counsel</li> <li>Counselling skills</li> </ul>	<ul style="list-style-type: none"> <li>Capacity-building for ANC providers on nutrition counselling</li> <li>Task shifting</li> <li>Group-based counselling</li> </ul>
<b>A.1.3.</b> Balanced energy and protein supplementation in undernourished populations	<ul style="list-style-type: none"> <li>What balanced energy and protein supplementation means</li> <li>What is available locally that provides this</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Time to counsel</li> <li>Counselling skills</li> </ul>	<ul style="list-style-type: none"> <li>Capacity-building for ANC providers on nutrition counselling</li> <li>Task shifting</li> <li>Group-based counselling</li> </ul>
<b>A.1.4.</b> High protein supplementation in undernourished populations	<ul style="list-style-type: none"> <li>If this is in use</li> </ul>	<ul style="list-style-type: none"> <li>If in use, advise against high protein supplementation during pregnancy</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>
<b>A.2.</b> Iron and folic acid supplements	<ul style="list-style-type: none"> <li>That iron and folic acid is still recommended</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> <li>Dispensing</li> </ul>	<ul style="list-style-type: none"> <li>Time to counsel</li> <li>Counselling skills</li> <li>Commodities management</li> </ul>	<ul style="list-style-type: none"> <li>Timing of iron vs calcium dosing</li> <li>Community-based dispensing</li> <li>Task shifting</li> <li>Group-based counselling</li> </ul>
<b>A.3.</b> Calcium supplements	<ul style="list-style-type: none"> <li>If dietary calcium is low in the local population</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> <li>Dispensing</li> </ul>	<ul style="list-style-type: none"> <li>Time to counsel</li> <li>Counselling skills</li> <li>Commodities management</li> </ul>	<ul style="list-style-type: none"> <li>Timing of iron vs calcium dosing</li> <li>Community-based dispensing</li> <li>Task shifting</li> <li>Group-based counselling</li> </ul>
<b>A.4.</b> Vitamin A supplements	<ul style="list-style-type: none"> <li>If night blindness is endemic</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> <li>Dispensing</li> </ul>	<ul style="list-style-type: none"> <li>Time to counsel</li> <li>Counselling skills</li> <li>Commodities management</li> </ul>	<ul style="list-style-type: none"> <li>Referencing existing guideline</li> <li>Community-based dispensing</li> <li>Task shifting</li> <li>Group-based counselling</li> </ul>



## Implementation considerations for ANC guideline recommendations

	Need to know	Need to do	Need to have	Consider
<b>A.10.<sup>a</sup></b> Restricting caffeine intake	<ul style="list-style-type: none"> <li>Whether local women typically have caffeine in their diet</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Counselling skills</li> <li>Time and space for counselling</li> </ul>	<ul style="list-style-type: none"> <li>Gender issues and cultural norms for and expectations of women</li> <li>Task shifting</li> </ul>
<b>B. Maternal and fetal assessment</b>				
<b>B.1. Maternal assessment</b>				
<b>B.1.1.</b> Diagnosing anaemia	<ul style="list-style-type: none"> <li>What method is in place to diagnose anaemia</li> <li>What method is feasible to start with</li> <li>How to interpret and manage</li> </ul>	<ul style="list-style-type: none"> <li>Collect specimens</li> <li>Follow kit instructions</li> <li>Maintain infection control standards</li> </ul>	<ul style="list-style-type: none"> <li>Capacity to conduct</li> <li>Kits</li> <li>Quality assurance/quality control (QA/QC) for any lab testing</li> <li>Commodities for treatment</li> </ul>	<ul style="list-style-type: none"> <li>Switching to full blood count or haemoglobinometer method, if feasible</li> </ul>
<b>B.1.2.</b> Diagnosing asymptomatic bacteriuria (ASB)	<ul style="list-style-type: none"> <li>What method is in to diagnose ASB</li> <li>What method is feasible to start</li> <li>How to interpret and manage</li> </ul>	<ul style="list-style-type: none"> <li>Collect specimens</li> <li>Follow kit instructions</li> <li>Maintain infection control standards</li> </ul>	<ul style="list-style-type: none"> <li>Capacity to conduct</li> <li>Kits</li> <li>QA/QC for any lab testing</li> <li>Commodities for treatment</li> </ul>	<ul style="list-style-type: none"> <li>What levels of care are feasible for each type of test, with urine culture and sensitivity (C&amp;S) being gold standard but dipstick sufficient in facilities without capacity</li> </ul>
<b>B.1.3.</b> Enquiry about intimate partner violence (IPV)	<ul style="list-style-type: none"> <li>Local resources available to address IPV if identified during ANC</li> <li>How to enquire if WHO minimum requirements are in place<sup>b</sup></li> <li>Country-level guidelines and policies</li> </ul>	<ul style="list-style-type: none"> <li>Ask about IPV</li> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Well trained providers on first-line response</li> <li>Resources and referral mechanisms in place</li> <li>Time to counsel</li> <li>Sufficient confidential counselling space</li> <li>Counselling skills</li> </ul>	<ul style="list-style-type: none"> <li>Forming linkages to supportive and social services if not already in place</li> </ul>
<b>B.1.4.</b> Diagnosing gestational diabetes mellitus (GDM)	<ul style="list-style-type: none"> <li>National guidance/standard of care</li> <li>Guidelines for management of abnormal results</li> <li>Information on local context</li> </ul>	<ul style="list-style-type: none"> <li>Counselling and testing</li> </ul>	<ul style="list-style-type: none"> <li>Mechanisms and systems for testing and receiving results</li> <li>Time and space to counsel</li> <li>Counselling skills</li> <li>Commodity management for oral glucose solution and testing supplies</li> <li>QA/QC</li> <li>Clinical algorithm</li> </ul>	<ul style="list-style-type: none"> <li>Reference existing guideline</li> <li>Feasibility and acceptability of screening strategies</li> </ul>

a. Recommendations A.5-A.9 are not included because interventions that are not recommended are excluded from the implementation considerations table.

b. Minimum requirements are: a protocol/standard operating procedure; training on how to ask about IPV, and on how to provide the minimum response or beyond; a private setting; confidentiality ensured; system for referral in place; and time to allow for appropriate disclosure.

Implementation considerations for ANC guideline recommendations				
	Need to know	Need to do	Need to have	Consider
<b>B.1.5.</b> Screening for tobacco use	<ul style="list-style-type: none"> <li>How to screen/enquire</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Counselling skills</li> <li>Time to counsel</li> </ul>	<ul style="list-style-type: none"> <li>Gender issues and cultural norms for and expectations of women</li> <li>Task shifting</li> </ul>
<b>B.1.6.</b> Screening for alcohol and substance abuse	<ul style="list-style-type: none"> <li>Information on local context</li> <li>Local norms and behaviours around these risks</li> <li>Refer to the specific WHO guideline<sup>c</sup></li> </ul>	<ul style="list-style-type: none"> <li>Counselling and testing</li> </ul>	<ul style="list-style-type: none"> <li>Time and space to counsel</li> <li>Counselling skills</li> </ul>	<ul style="list-style-type: none"> <li>Referencing existing guideline</li> <li>Cultural context and local norms, impact of gender</li> <li>Impact of routine questioning in specific settings</li> <li>Task shifting</li> <li>Group-based counselling</li> </ul>
<b>B.1.7.</b> HIV testing	<ul style="list-style-type: none"> <li>Retest women in high prevalence settings or in key high-risk groups</li> </ul>	<ul style="list-style-type: none"> <li>Counselling and testing</li> </ul>	<ul style="list-style-type: none"> <li>Commodities for testing</li> <li>Time to counsel</li> <li>Counselling skills</li> <li>Linkage to treatment</li> </ul>	<ul style="list-style-type: none"> <li>Task shifting</li> </ul>
<b>B.1.8.</b> Tuberculosis (TB) screening	<ul style="list-style-type: none"> <li>Population prevalence of TB</li> </ul>	<ul style="list-style-type: none"> <li>Refer to the specific WHO guidance<sup>d</sup></li> </ul>		<ul style="list-style-type: none"> <li>Consider having TB clinics track pregnancy as a column in the register, to allow for better estimation of the local burden of TB in pregnancy.</li> </ul>
<b>B.2. Fetal assessment</b>				
<b>B.2.1.</b> Routine daily fetal movement (FM) counting	<ul style="list-style-type: none"> <li>If routine daily FM counting is being advised</li> </ul>	<ul style="list-style-type: none"> <li>If ANC providers are advising daily FM counting in routine ANC counselling, instruct them to omit it, due to lack of evidence.</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>
<b>B.2.2.</b> Symphysis-fundal height (SFH) measurement	<ul style="list-style-type: none"> <li>What methods are being used for fetal growth and gestational age (GA) assessment</li> </ul>	<ul style="list-style-type: none"> <li>Continue to include GA assessment and fetal growth assessment (by SFH or clinical palpation) in ANC contacts and documentation</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>No proven benefit to switching to fundal height measurement in settings where not currently in place.</li> </ul>

c. WHO guidelines for the identification and management of substance use and substance use disorders in pregnancy. Geneva: World Health Organization; 2014 ([http://apps.who.int/iris/bitstream/10665/107130/1/9789241548731\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/107130/1/9789241548731_eng.pdf), accessed 28 September 2016).

d. Systematic screening for active tuberculosis: principles and recommendations Geneva: World Health Organization; 2013 ([http://apps.who.int/iris/bitstream/10665/84971/1/9789241548601\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/84971/1/9789241548601_eng.pdf), accessed 28 September 2016).

### Implementation considerations for ANC guideline recommendations

	Need to know	Need to do	Need to have	Consider
<b>B.2.3.</b> Routine antenatal cardiotocography (CTG)	<ul style="list-style-type: none"> <li>If routine antenatal CTG is being conducted</li> </ul>	<ul style="list-style-type: none"> <li>If being conducted, instruct providers to omit this from practice, due to lack of evidence.</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>
<b>B.2.4.</b> Routine ultrasound scans	<ul style="list-style-type: none"> <li>Health system level               <ul style="list-style-type: none"> <li>Number and capacity of ultrasound providers to act as providers and trainers/mentors</li> <li>Number of functional machines available and geographic distribution</li> <li>Regulations around ultrasound use</li> <li>Cadres – who can perform?</li> <li>Available pre-service education and other certification</li> </ul> </li> <li>Provider level               <ul style="list-style-type: none"> <li>Training to do anatomy scan or on referral</li> <li>How to interpret results and do counselling</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Health system level               <ul style="list-style-type: none"> <li>Determine appropriate settings and timeline for introduction of ultrasound</li> <li>Obtain machines</li> <li>Capacity-building plan</li> </ul> </li> <li>Provider level               <ul style="list-style-type: none"> <li>Conduct or refer</li> <li>Document results</li> <li>Provide guidance on how to estimate GA and delivery date (EDD), depending on certainty of last menstrual period (LMP) and estimated GA at time of ultrasound, e.g. WHO's Manual of diagnostic ultrasound<sup>e</sup> and the American Institute of Ultrasound in Medicine (AIUM) guidelines<sup>f</sup></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Health system level               <ul style="list-style-type: none"> <li>Transportation for women if services are not sufficiently decentralized</li> <li>Cadres with skills to provide quality services</li> </ul> </li> <li>Facility level               <ul style="list-style-type: none"> <li>Machines</li> <li>Mechanism to review results and get reports</li> </ul> </li> <li>Service contracts for machines               <ul style="list-style-type: none"> <li>Surge protection</li> <li>Power supply</li> </ul> </li> <li>Counselling skills               <ul style="list-style-type: none"> <li>Security and environmental protection for costly machine</li> <li>Space for machine</li> <li>Ultrasound gel supply</li> <li>Staff and supplies to keep equipment clean</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Cost – of purchase, maintenance, training, impact of shifting resources to ultrasound from other key costs</li> <li>Local availability/feasibility of service contracts to support machine maintenance, especially in areas not previously prioritized for ultrasound market development</li> <li>Power supply – availability and stability</li> <li>Protection from power surges, which can permanently damage machines</li> <li>Extreme fragility of ultrasound transducers (one drop on a concrete floor may necessitate purchase of a new transducer, costing thousands of dollars)</li> <li>Relative benefits compared to other interventions</li> <li>Burden to mother</li> <li>Burden to providers and facility</li> <li>Creative, alternative models of service delivery that do not burden women with travel and related costs</li> <li>Feasibility studies in settings without widely available ultrasonography</li> <li>Studies on quality of ultrasound</li> </ul>
<b>B.2.5.</b> Routine Doppler ultrasound	<ul style="list-style-type: none"> <li>If routine Doppler ultrasound is being conducted</li> </ul>	<ul style="list-style-type: none"> <li>If being conducted, instruct providers to omit or consider in the context of research</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>Research context</li> </ul>

e. Manual of diagnostic ultrasound, second edition. Geneva: World Health Organization; 2013 ([http://www.who.int/medical\\_devices/publications/manual\\_ultrasound\\_pack1-2/en/](http://www.who.int/medical_devices/publications/manual_ultrasound_pack1-2/en/), accessed 21 October 2016).

f. AIUM practice parameter for the performance of obstetric ultrasound examinations. Laurel (MD): American Institute of Ultrasound in Medicine (AIUM); 2013 (<http://www.aium.org/resources/guidelines/obstetric.pdf>, accessed 21 October 2016).

Implementation considerations for ANC guideline recommendations				
	Need to know	Need to do	Need to have	Consider
<b>C. Preventive measures</b>				
<b>C.1.</b> Antibiotics for ASB	<ul style="list-style-type: none"> <li>What ASB is and how to diagnose it</li> </ul>	<ul style="list-style-type: none"> <li>Prescribing</li> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Commodity management</li> <li>Counselling skills</li> <li>Time and space for counselling</li> </ul>	<ul style="list-style-type: none"> <li>Capacity-building for providers in contexts where this is an unfamiliar concept and practice – value of treatment, risk of non-treatment, antibiotic stewardship/avoidance of resistance</li> </ul>
<b>C.2.</b> Antibiotic prophylaxis to prevent recurrent urinary tract infections	<ul style="list-style-type: none"> <li>Whether currently being performed</li> </ul>	<ul style="list-style-type: none"> <li>Instruct to omit, if necessary</li> </ul>		<ul style="list-style-type: none"> <li>Research context</li> </ul>
<b>C.3.</b> Antenatal anti-D immunoglobulin administration	<ul style="list-style-type: none"> <li>What is practised in the context</li> </ul>	<ul style="list-style-type: none"> <li>Context-specific</li> </ul>	<ul style="list-style-type: none"> <li>Availability of blood-typing</li> </ul>	<ul style="list-style-type: none"> <li>Research context</li> <li>Recognize that this practice is routine in many high-resource settings; however, more evidence may be needed</li> </ul>
<b>C.4.</b> Preventive anthelmintic treatment	<ul style="list-style-type: none"> <li>Local endemicity of helminth infections</li> <li>Local status of worm infestation-reduction programmes</li> </ul>	<ul style="list-style-type: none"> <li>Provide or omit, depending on context</li> </ul>	<ul style="list-style-type: none"> <li>Commodities management</li> </ul>	<ul style="list-style-type: none"> <li>Task shifting</li> <li>Community-based distribution</li> </ul>
<b>C.5.</b> Tetanus toxoid vaccination	<ul style="list-style-type: none"> <li>That this practice is still recommended</li> <li>Local prevalence of neonatal tetanus</li> </ul>	<ul style="list-style-type: none"> <li>Provide vaccine according to established guidance</li> </ul>	<ul style="list-style-type: none"> <li>Commodities management</li> </ul>	<ul style="list-style-type: none"> <li>Consider quality improvement (QI) activities if gaps in coverage</li> <li>NOTE: Refer to dosing schedule in WHO 2006 guideline on maternal immunization against tetanus<sup>g</sup></li> </ul>
<b>C.6.</b> Intermittent preventive treatment in pregnancy	<ul style="list-style-type: none"> <li>See detailed implementation guidance in the specific WHO guideline on malaria<sup>h</sup></li> </ul>			<ul style="list-style-type: none"> <li>Emerging evidence on task shifting to community-based distribution</li> <li>Ways of ensuring that women receive the first dose at 13 weeks of gestation</li> </ul>

g. Maternal immunization against tetanus: integrated management of pregnancy and childbirth (IMPAC). Standards for maternal and neonatal care 1.1. Geneva: Department of Making Pregnancy Safer, World Health Organization; 2006 ([http://www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/immunization\\_tetanus.pdf](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/immunization_tetanus.pdf), accessed 28 September 2016).

h. Guidelines for the treatment of malaria, third edition. Geneva: World Health Organization; 2015 (<http://www.who.int/malaria/publications/atoz/9789241549127/en/>, accessed 10 October 2016).

### Implementation considerations for ANC guideline recommendations

	Need to know	Need to do	Need to have	Consider
<b>C.7.</b> Pre-exposure prophylaxis (PrEP) for HIV prevention	<ul style="list-style-type: none"> <li>Health system level: status of national PrEP guidelines and whether they include pregnant women, who to consider at substantial risk of HIV infection, sociocultural barriers to antiretroviral (ARV) use by HIV-uninfected pregnant women, availability of providers to counsel and train, availability of ARVs, cost to patients, capacity of laboratory to conduct recommended baseline and follow-up renal function tests</li> <li>Provider level: how to initiate and follow up, how to recognize renal toxicity, when to discontinue PrEP</li> </ul>	<ul style="list-style-type: none"> <li>Health system: capacity-building plan</li> <li>Provider level: prescribe and/or dispense; counselling about the risks, benefits and alternatives to continuing to use PrEP during pregnancy and breastfeeding</li> </ul>	<ul style="list-style-type: none"> <li>Commodities management</li> <li>Time and space for counselling, confidential dispensing</li> </ul>	<ul style="list-style-type: none"> <li>Best mechanisms for the setting (ANC vs other)</li> <li>Stigma associated with ARV use</li> <li>Potential social harms to pregnant women, including IPV</li> <li>Pending evidence from the National Institute of Child Health and Human Development (NICHD) study on safety and feasibility of PrEP in pregnancy</li> <li>Additional research recommended by WHO and others</li> <li>Cost and frequency of stock-outs – distribution of drug for treatment vs PrEP</li> </ul>
<b>D. Interventions for common physiological symptoms</b>				
<b>D.1-6</b>	<ul style="list-style-type: none"> <li>Cultural norms around treatment, harmful vs non-harmful practices</li> </ul>	<ul style="list-style-type: none"> <li>Counselling</li> </ul>	<ul style="list-style-type: none"> <li>Time to counsel</li> <li>Counselling skills</li> </ul>	<ul style="list-style-type: none"> <li>Building ANC providers' capacity for counselling and listening, woman-centered care, etc.</li> </ul>
<b>E. Health system interventions to improve utilization and quality of antenatal care</b>				
<b>E.1.</b> Woman-held case notes	<ul style="list-style-type: none"> <li>What is currently being used</li> </ul>	<ul style="list-style-type: none"> <li>Ensure case notes are available in the appropriate language and at the appropriate education level for setting</li> <li>Adapt the case notes according to context</li> <li>Ensure durable product</li> </ul>	<ul style="list-style-type: none"> <li>Commodities management</li> <li>Resources for production</li> <li>Method for retaining a facility copy</li> </ul>	<ul style="list-style-type: none"> <li>What format is appropriate</li> <li>Whether it is necessary to exclude certain personal information to avoid stigmatization</li> </ul>

### Implementation considerations for ANC guideline recommendations

	Need to know	Need to do	Need to have	Consider
<b>E.2.</b> Midwife-led continuity of care (MLCC)	<ul style="list-style-type: none"> <li>What model of care is currently being used</li> <li>Whether there are sufficient numbers of trained midwives</li> <li>Whether resources are available or can be shifted to facilitate this model</li> </ul>	<ul style="list-style-type: none"> <li>Consult all relevant stakeholders, including human resource departments and professional bodies</li> <li>Assess the need for additional training in MLCC</li> <li>Ensure that there is a well-functioning referral system in place</li> <li>Monitor midwife workload and burnout</li> </ul>	<ul style="list-style-type: none"> <li>A well functioning midwifery programme</li> </ul>	<ul style="list-style-type: none"> <li>Strategies to scale up the quality and number of practising midwives</li> <li>Ways of providing continuity of care through other care providers, e.g. lay health workers</li> <li>Whether a caseload or team MLCC model is more appropriate</li> </ul>
<b>E.3.</b> Group ANC	<ul style="list-style-type: none"> <li>Cultural norms and women's preferences regarding group ANC</li> </ul>	<ul style="list-style-type: none"> <li>Consider evaluating in research context</li> </ul>	<ul style="list-style-type: none"> <li>Appropriate facilities to deal with group sessions, including access to large, well ventilated rooms, or sheltered spaces and adequate seating, and a private area for individual examination</li> <li>Providers trained in group facilitation and communication</li> </ul>	<ul style="list-style-type: none"> <li>Research context</li> </ul>
<b>E.4.</b> Community-based interventions to improve communication and support	<ul style="list-style-type: none"> <li>Community demographics and cultural norms</li> <li>Who are the key stakeholders in the community</li> </ul>	<ul style="list-style-type: none"> <li>Train facilitators in group facilitation, convening public meetings, and communication techniques</li> <li>Ensure sufficient facilitators and resources to support them</li> <li>Train community volunteers/lay health workers to identify pregnant women in the community and encourage their attendance</li> <li>Ensure that the individual woman's preferences are respected, e.g. with regard to partner involvement</li> </ul>	<ul style="list-style-type: none"> <li>Group spaces to hold meetings</li> <li>Culturally and educationally appropriate educational material, e.g. videos, flip charts, pictorial booklets and/or cards</li> <li>Ongoing supervision and monitoring of facilitators</li> <li>Resources, e.g. additional staff, transport and budget for material, for community mobilization initiatives</li> </ul>	<ul style="list-style-type: none"> <li>Appropriate format and language of communication</li> <li>Whether meetings should include men and women together or separately</li> <li>Offering women a range of opportunities for communication and support, so that their individual preferences and circumstances can be catered for</li> <li>Implementing health system strengthening interventions, such as staff training, and improving equipment, transport, supplies, etc.</li> </ul>

### Implementation considerations for ANC guideline recommendations

	Need to know	Need to do	Need to have	Consider
<b>E.5.</b> Task shifting components of ANC delivery	<ul style="list-style-type: none"> <li>Task shifting allows flexibility in certain contexts, but policy-makers need to work towards MLCC for all women</li> </ul>	<ul style="list-style-type: none"> <li>Give health workers involved in task shifting a clear mandate</li> <li>Ensure that lay health workers are integrated into the health system and given appropriate supervision</li> </ul>	<ul style="list-style-type: none"> <li>Ongoing supervision and monitoring</li> <li>Commodities management</li> </ul>	<ul style="list-style-type: none"> <li>Refer to specific WHO guideline on task shifting<sup>j</sup></li> </ul>
<b>E.6.</b> Recruitment and retention of staff in rural and remote areas	<ul style="list-style-type: none"> <li>Refer to specific WHO guideline on recruitment and retention<sup>i</sup></li> </ul>			<ul style="list-style-type: none"> <li>Many pregnant women prefer receiving care from women health workers</li> <li>Personal safety can impact a woman health worker's decision to apply for, and remain in, rural positions</li> <li>Rotation of health workers from urban to rural areas and vice versa</li> <li>Agreeing the terms and period of rural deployment upfront</li> </ul>
<b>E.7.</b> ANC contact schedules	<ul style="list-style-type: none"> <li>Timing and content of ANC contacts</li> <li>How to adapt to local settings, e.g. which context-specific recommendations apply?, what can be task shifted?</li> </ul>	<ul style="list-style-type: none"> <li>Secure national support for increased number of ANC contacts</li> <li>Conduct community sensitizing activities</li> <li>Involve pre-service training institutions and professional bodies</li> <li>Assess context-specific implications for resources, including staff, infrastructure, equipment, etc.</li> </ul>	<ul style="list-style-type: none"> <li>Long-term planning and resource generation</li> <li>Provider training and supervision for newly introduced interventions</li> <li>Updated "job aids" (e.g. ANC case notes) that reflect changes</li> <li>Updated ANC training curricula and clinical manuals</li> <li>Ongoing supervision and monitoring</li> </ul>	<ul style="list-style-type: none"> <li>Reorganizing services to reduce waiting times</li> <li>Other considerations can be found in Chapter 4 of the ANC guideline (Implementation of the ANC guideline and recommendations)</li> </ul>

i. WHO recommendations: optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting. Geneva: World Health Organization; 2012 ([www.optimizemnh.org](http://www.optimizemnh.org), accessed 10 October 2016).

j. Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations. Geneva: World Health Organization; 2010 (<http://www.who.int/hrh/retention/guidelines/en/>, accessed 10 October 2016).





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