



SCIENTIFIC **ADVICE**

Antenatal screening for HIV,
hepatitis B, syphilis and
rubella susceptibility
in the EU/EEA – addressing
the vulnerable populations

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This report was commissioned by the European Centre for Disease Prevention and Control (ECDC) and coordinated by Otilia Mårdh and Tarik Derrough, with additional input from Andrew Amato-Gauci and Helena de Carvahlo-Gomes.

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Abbreviations

ANS	Antenatal screening
CRS	Congenital rubella syndrome
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
MMR	Measles, mumps, rubella vaccine
MTCT	Mother-to-child transmission
PICO (T)	Population, intervention, comparison, outcome, time
PWID	People who inject drugs
STI	Sexually transmitted infection
TESSy	The European Surveillance System
WHO	World Health Organization

Glossary

Antenatal screening	Testing of a pregnant woman to detect conditions that may threaten the health of the foetus or child.
Antenatal screening programme	National or regional programme for diagnostic testing of pregnant women to detect certain conditions; programmes clearly state their aims and objectives, include data collection, evaluate results and regularly audit the entire programme.
Effectiveness of antenatal screening	The ability of antenatal screening to reduce or prevent infections during pregnancy that could potentially lead to mother-to-child transmission. In the case of rubella, susceptible mothers are identified.
Effectiveness of antenatal screening as prevention	As above, but extended to the factors influencing the implementation of measures to prevent the infection of the child by vertical (i.e. mother-to-child) transmission at any stage of pregnancy or during infancy and/or breastfeeding.
Operational effectiveness	Provides information on how well the intended programmatic measures (e.g. screening and interventions) are implemented in terms of coverage, specificity, quality and necessary follow-up with regard to the targeted population.
Infant	A child of less than 12 months of age.
Migrant	In this document, the term 'migrant' is used in its widest sense to embrace a number of population groups mentioned in the literature.
Mother-to-child transmission	Transmission of an infectious agent from the mother to the child before birth, during labour and delivery, or during infancy (the first year of life). Also referred to as vertical transmission.
Mandatory screening	Systematic testing at the population level, without the real possibility of declining the test, or a test that is taken as a condition to gain access to care, benefits, services, or any form of application of individual rights (i.e. travel, schooling, day care, employment, etc.). Declining the screening test may lead to sanctions or restrictions of individual civil rights.
Newborn	A child less than one month of age.
Neonatal	Of, relating to, or affecting the newborn and the infant during the first month after birth.
Diagnostic testing	A test in order to identify a health condition of the individual, administered with the explicit intention of clinically managing the condition.
Opt-in testing	Individuals seeking care are informed that testing is recommended. The individual is required to give explicit consent before the test is performed.
Opt-out testing	Testing is performed as part of routine care. Pre-test information is made available, and consent is assumed unless the individual explicitly declines testing.
Rubella susceptibility	Lack of protective antibodies for rubella virus. Protective antibodies can result from natural infection or vaccination.
Universal screening	Testing systematically offered to the entire relevant population (mandatory or voluntary); covers opt-in and opt-out testing.
Prenatal	Before birth; during or relating to pregnancy (synonym for antenatal).
Recommendation	Suggestion or proposal by an authoritative body.

Screening	The systematic application of tests, examinations, or other procedures (in the context of this report, testing for HIV, hepatitis B, syphilis infection or susceptibility for rubella infection), with the intention of identifying previously unrecognised health conditions at the population level. The relevant population is dependent on the condition to be identified and the intended interventions and must be defined.
Selective screening	Testing systematically offered to the relevant subpopulation (mandatory or voluntary), covers both opt-in and opt-out testing.
Universal screening	The entire relevant population are systematically offered testing (mandatory or voluntary), covers both opt-in and opt-out testing.
Voluntary screening	Testing systematically offered to the entire relevant population whereby refusal does not lead to immediate negative consequences, restrictions of civil rights or sanctions for the individual belonging to that population.
Vulnerable populations	For the purpose of this guidance, subpopulation groups that are at increased risk of contracting HIV, HBV, syphilis or rubella during pregnancy or are already infected, and are hard to reach through antenatal screening programmes.

Executive summary

Purpose and scope

This document aims to support the strengthening of antenatal screening (ANS) programmes for HIV, hepatitis B (HBV), syphilis and rubella susceptibility in the general population and in groups identified as vulnerable to mother-to-child-transmission (MTCT) in the EU/EEA. Vulnerable groups specifically targeted by this guidance include: 1) migrant women and women from ethnic minority groups; 2) women engaging in high-risk behaviour or with a partner at high risk for HIV, HBV and syphilis infections; and 3) women belonging to minority groups refusing vaccinations. The target audience of this document includes policymakers and national antenatal screening programme coordinators in the EU/EEA Member States.

Guidance development

As an initial step, a 2013 ECDC survey of Member States collected information on antenatal screening practices, pointed out challenges to the effective implementation of screening programmes, and identified population groups still vulnerable to MTCT.

Literature reviews were performed to retrieve scientific evidence for the development of guidance recommendations on: 1) key elements that define the effectiveness and cost-effectiveness of antenatal screening programmes for HIV, hepatitis B, syphilis and rubella susceptibility, and 2) antenatal screening approaches which are effective to prevent MTCT of HIV, hepatitis B, syphilis and rubella in the vulnerable groups. The search covered the period from January 1990 to January 2014 for the cost-effectiveness review, from January 2000 to March 2014 for the effectiveness review, and from January 2000 to April 2015 for the vulnerable groups review.

In addition, a multi-disciplinary expert panel was convened by ECDC; an expert meeting was organised on 17–18 September 2015 in Sweden to review the draft guidance conclusions.

Conclusions

The conclusions were formulated after due consideration was given to the survey findings, the available evidence-base and the opinions of the ECDC expert panel.

General considerations for the effective implementation of national antenatal screening programmes include the following options:

- National antenatal screening programmes for these infections should be implemented as part of the general antenatal care.
- Testing (with additional provision of information to the persons tested) should take place during the first trimester of pregnancy.
- The testing offer should be repeated during the third trimester for pregnant women at increased risk of infection and/or for those who refused testing.
- Testing should be offered at delivery to women who had not previously been tested
- A universal (voluntary, general population, opt-out) approach should be considered for the antenatal screening for HIV and syphilis.
- National (or regional) antenatal screening data should be collected, analysed and assessed.
- National screening programme should be evaluated regularly.
- Nationally relevant groups vulnerable to MTCT should be identified and specifically targeted.

For improving antenatal screening uptake among vulnerable groups, the following options should be considered:

- Appropriate assistance to remove communication obstacles (by taking into account language, literacy levels, or individual or cultural specifics).
- Improved access to antenatal care through outreach services and informal networks.
- Increasing the level of awareness in policymakers, healthcare providers and the general public with regard to the importance of ANS.

Possible implications for public health practice and research

This guidance conclusions should be considered in the context of the national social, economic and epidemiological situation. Further scientific evidence is needed to inform policymakers about adjusting antenatal screening programmes in order to effectively target all groups that are still vulnerable to MTCT. Also needed is further scientific advice on how to identify nationally relevant hard-to-reach/vulnerable groups and how to reach them.

1 Introduction

1.1 Objectives and target audience

This guidance aims to support policymakers and national programme coordinators in the Member States in their efforts to strengthen antenatal screening (ANS) programmes for HIV, hepatitis B (HBV), syphilis and rubella susceptibility in the general population and in groups identified as still vulnerable to mother-to-child-transmission (MTCT) in the EU/EEA. These groups, identified through a survey conducted by ECDC in 2013 [1], are:

- migrant women and women from ethnic minority groups;
- women who engage in high-risk behaviours or have a partner at high risk for HIV, HBV and syphilis infection; and
- women belonging to minority groups refusing vaccinations.

This document presents the results from an evidence search and the outcome of an expert consultation on key elements that a) define the effectiveness and cost-effectiveness of national antenatal screening programmes and b) describe antenatal screening approaches that are effective for preventing MTCT in vulnerable groups.

1.2 Questions addressed

The guidance aims to answer two main questions:

- What elements of an antenatal screening programme for infections influence its (cost)-effectiveness and what are the specific issues when screening for HIV, HBV, syphilis and rubella susceptibility?
- What specific approaches can be used to reach vulnerable populations and increase the uptake of antenatal screening in order to:
 - decrease the rate of MTCT or reduce the number of MTCT for HIV, HBV and syphilis; and
 - increase the number of pregnant women tested for rubella antibodies during pregnancy?

Assessing the criteria for initiating or discontinuing antenatal screening programmes was not included in the objectives of this guidance.

2 Background

Mother-to-child transmission (MTCT) of HIV, HBV, syphilis and even of rubella is still a cause of significant child mortality and morbidity, despite the existence of effective interventions that can prevent transmission from the mother to the child during pregnancy, delivery or early childhood. MTCT of these infections still occurs in the EU/EEA, as indicated by surveillance data reported to ECDC by the Member States.

Antenatal screening for infections (testing the pregnant women for the evidence of an infection or in the case of rubella for the lack of protective immunity, followed by appropriate interventions such as preventive treatment or vaccinations) aims at preventing MTCT and infection manifestations in the child.

2.1 Epidemiological and policy context in the EU/EEA

More than five million live births are recorded in the European Union annually. Almost as many pregnant women are subject to antenatal screenings for infections.

Cases of vertical transmission of HIV, syphilis, HBV and rubella are reported in the EU/EEA with some variation across countries. Differences in case reporting practice, differences in antenatal screening policies and in vaccination recommendations, and the background prevalence of these infections in women of reproductive age may explain these variations.

HIV. The number of HIV infections associated with MTCT reported by the EU/EEA Member States in 2014 was 236. In 2012 and 2013, 243 and 258 HIV cases were reported, respectively [2]. Calculating an annual, national or EU/EEA incidence rate – important information for antenatal screening programmes – is difficult because reported numbers include people born outside the reporting country. In addition, information on the year of birth of the cases is often not available and therefore not captured in ECDC's TESSy surveillance database. Antenatal HIV screening is widely implemented in the EU/EEA (24/26 countries), with testing coverage for testing at any time during pregnancy at above 95% in most (12/18) reporting countries. Testing is repeated later in pregnancy in 10 out of 26 countries, either as a general recommendation (5/10 countries) or among high-risk groups (5/10 countries) [1].

Syphilis. The number of congenital syphilis cases reported by the EU/EEA Member States was 64 in 2013, 92 in 2012, and 92 in 2011. The corresponding EU/EEA rate per 100 000 live births was 2.0 cases in 2013 and 2.3 cases in both 2012 and 2011 [3]. Zero cases of congenital syphilis were reported by 12/21 countries in 2013, by 13/24 in 2012 and 12/24 in 2011. It is likely that the EU/EEA figures underestimate the MTCT of syphilis. This results from the fact that not all countries report this condition to TESSy; the applied case definitions are limited to infections diagnosed in newborns or infants and do not include other pregnancy outcomes, such as stillbirth/foetal loss, neonatal death, preterm/low birth weight, which further distorts the reported figures. All EU/EEA countries (26/26) participating in the ECDC 2013 survey implement antenatal screening for syphilis. Most (22/24) countries test pregnant women during the first trimester of pregnancy. Seven countries reported repeat testing during the third trimester of pregnancy as a general recommendation and another three countries offer repeat testing for women in risk groups. The reported coverage of antenatal screening of syphilis was high: 14/18 countries reported a coverage of $\geq 95\%$, while three reported a coverage of $\geq 90\%$ [1].

Hepatitis B. MTCT was the most commonly (43.5%) reported route of transmission for hepatitis B cases diagnosed in the EU/EEA in 2013 which were reported as 'chronic' infections; the route of transmission, however, was reported for only 21.3% of cases [4]. The identification of MTCT cases in EU/EEA residents was complicated by the low number of complete datasets submitted to TESSy. Antenatal screening for hepatitis B is implemented in 23/26 countries; in the majority of reporting countries (8/13), screening coverage was $\geq 95\%$ [1].

Rubella. In 2013, 38 847 rubella cases were reported from 27 EU/EEA countries. Most (99%) cases were associated with the large rubella outbreak in Poland, where two cases of congenital rubella were reported in 2013 [5]. In Romania, 22 cases of congenital rubella syndrome were notified following the 2011–2012 outbreak (September 2011 to December 2012), during which 119 rubella cases were reported among pregnant women [6].

Most cases of MTCT related to HIV, HBV, syphilis and rubella that were reported in recent years were associated with population groups still at risk: pregnant women from ethnic minorities and migrants from high-prevalence areas outside the EU, women presenting (or being reached late) for antenatal care, people who inject drugs, and mobile populations like intra-EU-migrants. Common challenges to effective ANS reported by EU/EEA countries were deficiencies in data reporting/collection at the national level, insufficient capacity to reach groups at risk, and a general lack of resources for these activities.

3 Guidance development

After a survey in 2013 identified remaining challenges for effective implementation of antenatal screening programmes and the need for strengthening screening among the vulnerable populations in the EU/EEA, this guidance was developed through systematic reviews of scientific literature, combined with a consultation of a multidisciplinary group of experts.

3.1 Member States survey

An ECDC survey entitled 'Effectiveness of antenatal screening programmes for the prevention of mother-to-child transmission of HIV, hepatitis B, syphilis and rubella in the EU/EEA' was organised in 2013 with the aim of mapping policies and describing practices for the antenatal screening for infections in the EU/EEA countries. The survey included five sets of questions: one general questionnaire inquiring about ANS strategies, implementation and financing, data collection and ANS programme evaluation; and four disease-specific questionnaires collecting data about testing practice, antenatal care and MTCT subsequent interventions recommendations and their coverage. The population groups still vulnerable to mother-to-child transmission (MTCT) together with the main challenges for effective implementation of ANS programmes were reported by survey respondents based on a country self-assessment. The full description of the methods and the survey results are published in a technical report [1].

3.2 Literature reviews

Two literature reviews were performed for the development of the guidance: on the effectiveness and cost-effectiveness of antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility, and on antenatal screening approaches that are effective to prevent MTCT of HIV, hepatitis B, syphilis and rubella in vulnerable groups.

3.2.1 Literature review on effectiveness and cost-effectiveness of antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility¹

For the literature search on the topic of effectiveness of ANS, the research question was: Are national programmes for universal antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility effective, and which factors influence their effectiveness?

The literature review on the topic of effectiveness was based on the following PICO elements:

- P (population): pregnant women belonging to vulnerable groups and their unborn children
- I (intervention): national programmes for the universal screening for syphilis, HIV, hepatitis B and for rubella susceptibility offered to all pregnant women; and therapeutic intervention for those with positive test results (rubella susceptibility, vaccination to prevent MTCT in future pregnancies)
- C (comparison): no screening or screening for high-risk groups only
- O (outcome): avoided infections in children.

The search covered the period from 1 January 2000 to 13 March 2014 and the following databases were searched: Ovid MEDLINE, Ovid MEDLINE (R) Daily Update, Ovid MEDLINE (R) In-Process & Other Non-Indexed Citations, NLM PubMed (e-pubs ahead of print), Centre for Reviews and Dissemination, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials.

The search retrieved 261 titles for HIV, 140 for hepatitis B, 160 for syphilis and 72 for rubella susceptibility, of which 19 studies for HIV, 6 for hepatitis B, 5 for syphilis and 7 for rubella susceptibility were included in the analysis. However, these studies were in general descriptive, did not include a comparison group and were assessed as of low quality evidence.

For the literature search on the topic of cost-effectiveness the research question was: Are national programmes for universal antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility cost-effective?

¹ European Centre for Disease Prevention and Control. Effectiveness and cost-effectiveness of antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility. Stockholm: ECDC; 2017.

The literature review on cost-effectiveness was based on the following PICO (T) elements:

- P (population): Pregnant women and their unborn children
- I (intervention): National programmes for universal screening offered to all pregnant women for syphilis, HIV, hepatitis B and for rubella susceptibility; and therapeutic intervention for those with test-positive results (in rubella susceptibility, vaccination to prevent MTCT in future pregnancies)
- C (comparator, reference intervention): No screening or screening for high-risk groups only
- O (outcome): Avoided infections in children and cost per infection avoided
- T (time factor): From maternal screening sample to confirmation of the child's infection status.

The literature search covered the period from 1 January 1990 to 15 January 2014; the searched databases were the same as for the literature search on the topic of effectiveness. The search identified 348 citations, nine of which were accepted as relevant: three were on HIV, three on hepatitis B, two on syphilis and one on rubella. The nine studies were of high quality, fulfilling all or more than seven of the ten Drummond [7] criteria.

3.2.2 Literature review on antenatal screening approaches that are effective to prevent MTCT of HIV, hepatitis B, syphilis and rubella in vulnerable groups²

The research question was formulated as: How is antenatal screening of vulnerable groups performed; how can screening attendance be increased; and what are the results with regard to health gains?

The PICO element on which the literature search was based were formulated as follows:

- P (population): pregnant women belonging to vulnerable groups and their unborn children
- I (intervention): any screening or other intervention offered to pregnant women for HIV, hepatitis B, syphilis and for rubella susceptibility; interventions aimed at the prevention of MTCT for those with positive test results or susceptibility in the case of rubella
- C (comparator): no specific interventions or untargeted screening only
- O (outcome): increased participation rates; positive pregnancies identified or number of MTCT averted.

On 2 March 2015, the literature search was performed in the following databases: Ovid MEDLINE, Ovid MEDLINE Daily Update, Ovid MEDLINE In-Process & Other Non-Indexed Citations, NLM PubMed (e-pubs ahead of print), the Centre for Reviews and Dissemination, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials. On 1 April 2015, Embase was searched for relevant literature through Embase.com. All studies published between 1 January 2000 and 2 March/1 April 2015 were included.

Of the 504 articles retrieved, 54 were retained. There were no studies on vulnerable groups that compared screening with non-screening options. The risk of bias in cohort studies was evaluated using the checklists provided by the Critical Appraisal Skills Programme.

An in-depth description of the methods and findings can be consulted in the technical reports^{2,3}.

3.3. Expert consultation

An expert meeting in Sweden was scheduled for 17–18 September 2015 in order to discuss a draft guidance which contained the conclusions of the two literature reviews. ECDC invited experts from the following fields: policymaking at the EU and country levels, national programme coordination for ANS, ANS and antenatal care practice for pregnant women in risk groups (migrant women, women engaging in high-risk behaviours, women from ethnic minority groups, and women from population groups refusing vaccinations), evidence-based medicine methods, guidance development for the screening of migrants, clinical care of pregnant women and their newborns positive for infections. Eleven experts accepted ECDC's invitation (Appendix 1) and were sent the draft guidance manuscript for consultation/review before the meeting.

During the meeting, experts from Finland, Romania, Sweden and the United Kingdom presented models and experiences from their countries on ANS for infections (Appendix 2). Finland presented a decision tree designed to support decisions on national screening (Appendix 2).

The draft guidance conclusions were discussed in detail. Items were ranked according to their relevance on a five-point Likert scale using the *TurningPoint* interactive polling software (Appendices 3 and 4). After the meeting, the authors edited the text and finalised the key points of the guidance.

² European Centre for Disease Prevention and Control. Antenatal screening approaches effective in preventing mother-child transmission of HIV, hepatitis B, syphilis and rubella in vulnerable populations. Stockholm: ECDC; 2017.

³ European Centre for Disease Prevention and Control. Effectiveness and cost-effectiveness of antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility. Stockholm: ECDC; 2017.

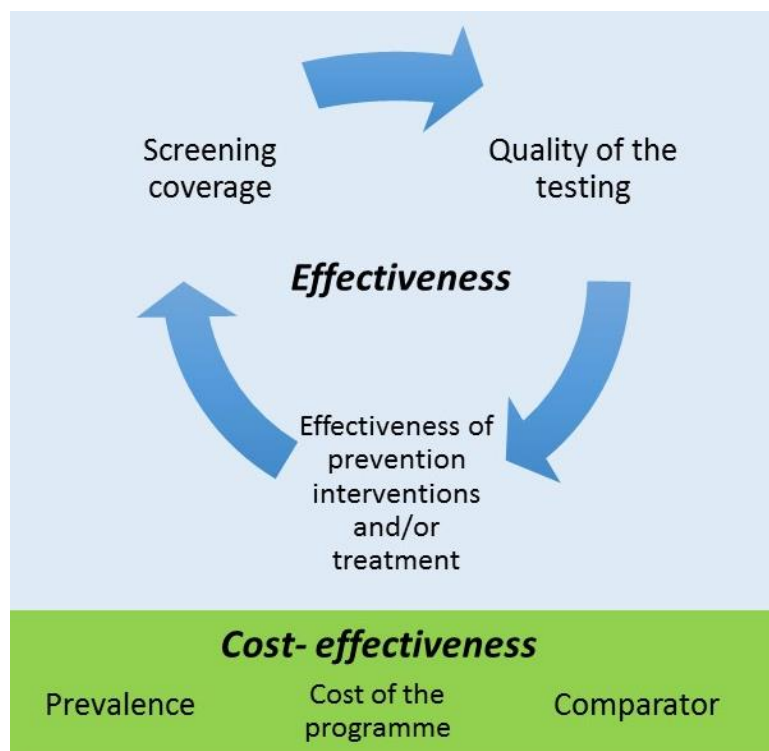
The evidence review did not identify any comparative, high-quality evidence studies on factors influencing the effectiveness of antenatal screening for infections (HIV, syphilis, HBV and rubella) from Europe or other high-income countries. Hence, the guidance conclusions were drawn from a limited number of publications and are mostly based on the recommendations or opinions of the authors of these publications, which in turn are supported by data on the current practice of antenatal screening collected through the ECDC survey [1]. Draft guidance conclusions were reviewed by the expert panel.

4 Conclusions

4.1 Key features of a (cost)-effective antenatal screening programme

The effectiveness of antenatal screening for each of the target infections depends primarily on the coverage of the screening programme, the quality of testing, and the effectiveness of treatment or preventive measures. In addition to these factors, cost-effectiveness is influenced by the prevalence of these infections among pregnant women, the cost of the screening programme, and the cost of the screening practice used as a comparator (Figure 1). A full description of the evidence search is provided in a technical report⁴.

Figure 1. Factors affecting the (cost)-effectiveness of antenatal screening for HIV, HBV, syphilis, and rubella susceptibility



4.1.1 Effectiveness

Effectiveness of antenatal screening, defined as the successful prevention of MTCT and its adverse effects, critically depends on:

- the proportion of pregnant women that are screened
- the proportion of infected pregnant women to whom an effective intervention is administered and, if the prevention of vertical transmission fails,
- the proportion of infected children to whom adequate follow-up and treatment/other support is available.

Another important factor that influences effectiveness is the availability of long-term, adequate treatment for chronically infected (with HIV or hepatitis B) pregnant women whose infection was identified through screening.

For a screening programme to be effective it needs to reach women in groups at high risk of MTCT, especially those women who are at risk of being missed by the national programme/standard testing offer. The organisational details of the system, its quality features and its acceptance among the target group are assumed to be major determinants of a programme's success.

⁴European Centre for Disease Prevention and Control. Effectiveness and cost-effectiveness of antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility. Stockholm: ECDC; 2017.

Screening coverage

The coverage of a screening programme and the compliance with a universal screening policy can be enhanced by increasing the level of public awareness through information; enhancing awareness among healthcare providers; facilitating access to testing, treatment and follow-up; and by allocating adequate resources [9].

Universal screening is considered simpler to manage and more acceptable than a programme only focused on risk groups; universal screening is also able to detect women who do not fall into a known risk profile [10-15].

Specific interventions targeted at vulnerable populations to increase screening coverage include targeted screening and targeted pre-conception care. The prerequisite of targeted interventions is defining the target group and capturing all vulnerable women in it. However, being defined/assigned to a vulnerable group may cause fear of stigma.

In total, the available evidence for targeted intervention is of low quality and suggests universal screening instead of targeted screening.

As established by WHO, in order to achieve and validate the elimination of mother-to-child transmission of HIV and syphilis, countries should reach and document the target levels of $\geq 95\%$ for antenatal testing coverage and antenatal care (defined as at least one visit) [16]. In the EU/EEA, the percentage of women tested at least once during pregnancy was estimated as 95% or higher in 12/18 countries for HIV and in 14/18 countries for syphilis [1].

While global efforts for the elimination of MTCT of hepatitis B and congenital rubella syndrome do not clearly specify targets for antenatal screening testing, data on testing coverage exist for a fraction of EU/EEA countries. Screening coverage is reported or estimated to be over 95% in 8/13 of the countries for hepatitis B and between 60 and 95% in six countries reporting data for rubella susceptibility testing coverage [1].

Quality of testing

The quality of testing depends on the screening tests used, and their sensitivity and specificity. In addition to the technical performance of the tests, the quality of testing also includes timing of sampling in regard to the course of infection during pregnancy, operator errors and process errors. Quality of testing is a complex issue, and all aspects should be considered carefully. Quality of testing was not within the scope of this guidance and as such was not included in the literature searches.

Effectiveness of prevention of mother-to-child transmission methods

The methods of prevention of MTCT apart from the antenatal testing were not within the scope of this guidance and were not included in the literature searches. The expert panel was strongly supportive for effective MTCT prevention interventions to be administered to pregnant women with test-positive results or susceptibility in the case of rubella.

The 2004 *Dublin Declaration on Partnership to fight HIV/AIDS in Europe and Central Asia* aims to ensure that all HIV-positive women and expectant mothers have access to high-quality maternal and reproductive healthcare services in order to prevent mother-to-child transmission [16]. The coverage of antiretroviral therapy in HIV-positive pregnant women was reported or estimated to be between 95 and 100% in 17/23 EU/EEA countries [1]. Virtual elimination of HIV mother-to-child transmission in the EU/EEA, with the number of reported cases less than 1% of all new HIV diagnoses yearly, was highlighted in the latest progress monitoring report [86].

WHO has set the target of coverage of hepatitis B birth-dose vaccination and of other prevention approaches to 90% worldwide by 2030 [18]; for the European Region, WHO wants to reach 90% coverage by 2020 [19]. EU/EEA countries offer the first dose at birth either as a general recommendation to all newborns (7/31) or targeted to newborns from mothers from groups at risk or mothers with HBV infection (24/31) [87]. Data on coverage were not collected by ECDC survey.

WHO target for treatment of syphilis-seropositive pregnant women is $\geq 95\%$ [16]. The proportion of women positive for syphilis treated during pregnancy was estimated to be between 80–100% in EU/EEA countries responding to the survey [1].

WHO recommends that a very high coverage level ($\geq 95\%$) should be achieved and sustained, with at least one dose of rubella vaccine given in the course of high-quality routine immunisation services. The elimination of endemic rubella will also lead to the elimination of CRS (by 2015) [22]. Two doses of MMR vaccine for all children are recommended in all EU/EEA countries [23].

The view of the expert panel was that the vaccination of identified risk groups should be considered – either before planning a pregnancy or in the post-partum period – if there is no documented evidence of the rubella status, in accordance with the national recommendations. The expert panel opined that all countries should consider having guidelines on the management of unknown rash illnesses in pregnancy. Several countries have addressed this issue in guidance documents for rubella susceptibility screening (the Czech Republic, Germany, Greece, Luxembourg and Malta) or in a separate guidance (Denmark, France, the Netherlands, Romania, Sweden and the UK).

Surveillance and monitoring

The quality of the national surveillance system is of pivotal importance when it comes to assessing the effectiveness of an antenatal screening programme. Without a surveillance system that provides timely and accurate data on cases of MTCT and its outcomes, an ANS programme operates in the dark, without any possibility of comprehensively assessing whether screening and prevention measures have any effect.

4.1.2 Cost-effectiveness

The cost-effectiveness of an antenatal screening programme depends on the effectiveness and costs of the screening programmes to which it is compared. It also depends heavily on the prevalence of infections among pregnant women; in countries with a relatively high prevalence of infection, the cost per case averted is of course lower than in countries with low prevalence.

Programme costs depend mainly of the cost of administering and analysing the screening/confirmatory tests, the type of healthcare personnel and their time, cost of medication and other necessary treatment, and patient compliance. Screening is usually only provided once (in the early stages of pregnancy). A second screening late during the pregnancy is highly unlikely to be cost-effective, especially in countries with relatively low incidence of HIV, HBV and syphilis [10].

Cost-effectiveness analyses of antenatal screening programmes often cover the time period from the screening until the establishment of the infant's infection status, but they can also include the cost of treating congenital infections over a longer period or even the lifetime of the child. Inclusion of later treatment costs changes cost-effectiveness dramatically, especially if the disease causes severe problems in the development of the infected child. Lifetime healthcare costs or the costs of care for a disabled child vary widely between health and social care systems.

When a new screening programme is initiated, the investment costs of establishing the programme also include the costs for planning and delivering information to the general public and the healthcare personnel, in addition to the costs for setting up systems for testing, treatment, and monitoring. If an antenatal infection screening programme has already been established, adding coverage for a new disease probably results in lower incremental costs because tests can be combined and administered together. During the planning stage, planners should be aware that the overall costs of an ANS programme also include the costs for monitoring the effectiveness of ANS; the costs of regular audits should also be calculated into the cost estimates. Overall costs should be proportionate to the outcomes.

Estimating the cost and effectiveness of antenatal screening programmes needs to be done individually for each country. The availability and reliability of essential data determines the quality of national cost estimates. There are risks involved in transferring effectiveness and especially cost information from one country to another; such practice is not recommended unless the countries have a very similar health systems and cost levels as well as similar valuations and priorities.

For both effectiveness and cost-effectiveness, all data are naturally linked to the epidemiological situation and the organisation of antenatal screening practices in each country. It is therefore not possible to suggest a generic approach that would suit all EU/EEA countries; instead, programme planners should refer to the main factors that affect the costs and effectiveness of screening programmes as presented in this document.

4.2 Options for the effective implementation of national ANS programmes

The key factors influencing effective antenatal screening programmes are presented below as an overview in Box 1. Each **option for intervention** is then – point by point – addressed individually in an explanatory section.

Specific practices to increase the uptake of antenatal screening for risk groups are presented in Box 2. The conclusions of this guidance mostly concern policies or actions that have no direct basis in research literature. The evidence base used for informing this guidance was of low quality, if available at all, thus the conclusions were formulated based on a general understanding of European healthcare systems and of the four infections of concern, validated through expert consultation.

Box 1. Suggested options for the effective implementation of national antenatal screening programmes

- National antenatal screening programmes for these infections should be implemented in conjunction with general antenatal care
- Testing (with additional provision of information to the tested person) should take place during the first trimester of pregnancy
- Testing offers should be repeated during the third trimester for pregnant women at increased risk of infection and/or for those who refused testing earlier
- Testing should be offered at delivery to women who had not previously been tested
- A universal (voluntary, general population, opt-out) approach should be implemented for the antenatal screening for HIV and syphilis
- National (or regional) antenatal screening data should be collected, analysed and assessed
- National screening programmes should be evaluated regularly
- Nationally relevant groups vulnerable to MTCT should be identified and targeted.

• National antenatal screening programmes for infections should be implemented

Evidence review: No direct or strong evidence from the literature review on the effectiveness of nationally guided antenatal screening programmes for infectious diseases.

Expert opinion: **strongly supportive**. National recommendations for antenatal screening, including professional guidelines, should be in place. The recommendations should be infection specific. A screening programme should include objectives, measurable outcomes, and plans for evaluation. In addition, the choice of the implementation methods (e.g. the used tests and their sensitivity) should be clearly stated.

EU/EEA practice: Almost all EU/EEA countries (25/26) have produced national guidance documents, recommendations, or a strategy on the antenatal screening for infectious diseases, with the number of infections actually covered differing from country to country. National antenatal screening programmes for syphilis are widely implemented (26/26) in EU/EEA countries. A majority of EU/EEA countries implement national programmes for HIV (24/26) and hepatitis B (23/26). Rubella susceptibility screening is implemented in 14/26 EU/EEA countries but was discontinued in several countries (Denmark, Finland, Hungary and Slovenia) because of high vaccination coverage and low disease prevalence [1]. In April 2016, it was also discontinued in England [24].

Conclusion: According to expert opinion and EU/EEA practices, national antenatal screening programmes for infections should be implemented. The decision which infections should be covered has to be taken at the national level, based on epidemiological situation and/or vaccination policy in the country.

• Antenatal screening for infections should be implemented in conjunction with general antenatal care

Evidence review: No specific literature search was carried out on this subtopic.

Expert opinion: **strongly supportive**. The screening programmes should attempt to reach the entire target population. Further access to general antenatal care should be ensured to all women.

EU/EEA practice: According to a survey, screening of infectious diseases is integrated into antenatal HIV care in 21/25 countries. Integrated screening for HBV is offered in 22/25 countries, integrated screening for syphilis is practiced in 23/26 countries, and integrated screening for rubella susceptibility is available in 12/23 countries [1].

Conclusion: According to expert opinion and good practice, antenatal screening for infections should be implemented in conjunction with general antenatal care if this approach is considered to be more efficient, better coordinated, and more cost-effective.

• Testing (with provision of information to the tested person) should take place during the first trimester of pregnancy

Evidence review: Timeliness of HIV testing should be ensured in order to enable prophylactic therapy or treatment during the pregnancy [25]. A systematic review on early antenatal care of syphilis found that women who sought care in the first two trimesters were more likely to have a healthy infant, compared to women screened and treated during the third trimester [26]. According to US guidelines, universal screening during the second trimester can help to stop the MTCT of hepatitis B [27]. If mothers who are at high risk of transmitting HBV are screened

and diagnosed in time, maternal HBV DNA concentrations could be decreased through antiviral drugs, ideally to levels undetectable at delivery; this offers great potential for controlling the epidemic, particularly in conjunction with universal early vaccination [28].

Expert opinion: **strongly supportive**. Testing should always occur during the first trimester of pregnancy; it should be offered together with information on the reasons for, and benefits of, testing.

EU/EEA practice: ANS is recommended during the first trimester of pregnancy in 21/23 countries for HIV in 14/20 countries for HBV, in 22/24 countries for syphilis, and in 10/11 countries for rubella susceptibility. Whether pregnant women were informed on the significance and benefits of antenatal screening was not addressed by the survey [1].

Conclusion: According to evidence from the literature review, HIV, hepatitis B and syphilis testing should take place during the first two trimesters of pregnancy. Current EU/EEA practice supports testing for HIV and syphilis during the first trimester of pregnancy; the expert panel agreed that testing for all infections mentioned above should occur during the first trimester.

● Testing offers should be repeated during the third trimester for pregnant women at increased risk of infection and/or for those who refused testing earlier

Evidence review: Women who engage in risk behaviour are at higher risk of being infected; screening only once during the early stages of pregnancy is considered insufficient and should be complemented by a second offer for testing [29-31]. A US cost-effectiveness analysis found that universal third-trimester syphilis rescreening would require a large number of women to be screened at a high combined cost to the healthcare system to prevent a very low number of adverse outcomes from maternal syphilis; the US study did not consider this as cost-effective [32].

Expert opinion: **strongly supportive**. Women who refused testing in early pregnancy should be offered testing again (with information on purpose and significance) so that they can benefit from screening.

EU/EEA practice: Repeat testing for HIV is recommended for all women during the third trimester in 5/23 countries and to women belonging to nationally defined risk groups in other 5/23 countries. Repeat testing for syphilis is recommended for all women in 8/24 countries and to women belonging to risk groups in other 3/24. One country reported repeat testing for HBV recommended for the third trimester [1].

Conclusion: According to evidence from literature, expert opinion and EU/EEA practices, testing offers should be repeated during the third trimester for those that have not been tested earlier and for country-defined risk groups.

● Testing should be offered at delivery to women who had not previously been tested

Evidence review: In order to prevent transmission during delivery or after birth, the test should be performed at the time of delivery (does not apply to rubella susceptibility) if the woman had not already received adequate antenatal care or taken screening tests [33,34].

Expert opinion: **strongly supportive**. Women presenting late for screening are considered an important risk group for MTCT.

EU/EEA practice: A number of countries recommend that women who did not get tested earlier in pregnancy should be tested at delivery; in an ECDC survey, 9/23 countries recommended this for HIV, 6/20 for HBV, and 6/24 for syphilis [1].

Conclusion: According to evidence from literature, expert opinion and EU/EEA practices, testing for HIV, hepatitis B and syphilis should be offered at delivery if not already conducted earlier.

● A universal (voluntary, general population, opt-out) approach should be implemented for antenatal screening for HIV and syphilis

Evidence review: The universal opt-out approach (where information on testing is made available and consent is assumed unless the individual explicitly declines testing) is effective in improving testing uptake [10,35-38]. Universal screening for hepatitis B was recommended in several studies [11,12,39], because targeted screening might not identify women in risk groups [12,40] and because universal screening reduces possible stigma associated with testing for women from countries with a higher prevalence of HBV [12].

Expert opinion: **strongly supportive**. A universal antenatal screening approach was recommended; testing should be offered and made available for all pregnant women. Attention should be given to ensuring human rights

and to equity. Screenings should avoid stigmatisation and discrimination while ensuring the confidentiality of testing results.

EU/EEA practice: A universal opt-out strategy is the most common strategy in Europe and implemented in 15/23 countries (HIV) and in 16/26 countries (syphilis) [1].

Conclusion: According to evidence and expert opinion, a universal opt-out strategy should be implemented for the antenatal screening of HIV and syphilis; it should be considered for hepatitis B, depending on the national vaccination strategy.

● National (or regional) antenatal screening data should be collected, analysed and assessed

Evidence review: No direct evidence was found through the literature search.

Expert opinion: **strongly supportive**. An analysis of screening data may identify emerging patterns. It is important to differentiate between the number of tested women and the number of conducted tests; linking clinical register entries (e.g. the number of screened women and laboratory testing results) may support the analysis.

EU/EEA practice: Data on antenatal screening are collected, stored and analysed at the national level in 11 countries for HIV, in eight for HBV, in eight for syphilis and in only three countries for rubella susceptibility [1].

Conclusion: According to current EU/EEA practices, screening data are not widely collected, analysed and assessed. This has been identified in the survey [1] as a barrier to the effective implementation of ANS programmes. According to expert opinion and international guidelines, all screening data should be collected, analysed and assessed. Information on the number of new versus pre-existing infections, the number of screened women, the number of performed screening tests, and the number of women with positive results (susceptible in the case of rubella) will facilitate estimating testing coverage and positivity rate. A WHO guidance document on the validation of elimination goals for MTCT of HIV and syphilis specifies a set of process indicators [16].

● National screening programmes should be evaluated regularly

Evidence review: No direct evidence found from the literature search. In the UK, a monitoring policy for the Antenatal Infection Screening Surveillance programme [41] provides local healthcare providers with comparative data and indicators of their relative success. Local audits of health settings that offer antenatal care can improve antenatal screening practice. An audit in the Irish National Maternity Hospital showed that there is an urgent need for a centralised national programme to ensure adequate follow-up and management of all infants born to women with HBV in Ireland [42].

Expert opinion: **supportive**. As a minimum requirement, an evaluation should be conducted after each programme modification, provided that there are data and information to allow for comparison. Peer-to-peer comparisons between clinics or regions are recommended for auditing programme implementation.

EU/EEA practice: Monitoring or evaluating the effectiveness of ANS programmes for HIV were reported by Denmark [43], Finland [44], France [45], Ireland, the Netherlands [10,46], Romania [47], Slovakia and the UK. For HBV, monitoring and evaluation schemes are maintained by Denmark [43], Finland [44], France [48], Italy [49], the Netherlands [10,46], Slovakia and the UK. Monitoring and evaluation for syphilis programme effectiveness is conducted by Denmark, Finland [44], Italy, the Netherlands [10], Slovakia and the UK. Monitoring or evaluating rubella susceptibility with regard to programme effectiveness was reported from Ireland, Slovakia and the UK [1].

Conclusion: There is no common practice in EU/EEA countries with regard to the systematic evaluation of national screening programmes. Expert opinion and the outcomes of audits indicate the need for such evaluations.

● Nationally relevant groups vulnerable to MTCT should be identified and targeted

Evidence review: No direct evidence was found through the literature search.

Expert opinion: **strongly supportive**. It was noted that migrants, mobile populations and ethnic minority groups differ between countries. It is important to note that ethnic group and minority are not synonymous, nor should it be assumed that (minority) ethnic groups are necessarily vulnerable.

EU/EEA practice: There is no comprehensive information currently available, except for the ANS survey, which reflects the assessment of the respondents.

Conclusion: Expert opinion is that EU/EEA countries should define which minorities or ethnic groups are vulnerable to MTCT in order to appropriately direct prevention measures. The prevalence of infections in subpopulation groups may differ from the prevalence in the general population due to behavioural, cultural and socio-economic risk

factors. Recently arrived migrants or asylum seekers may also face a higher risk of infection on their way to, or in, the destination country.

4.3 Antenatal screening among vulnerable groups – factors influencing effectiveness

This section summarises barriers and challenges to antenatal screening among pregnant women in risk groups as identified through the literature review⁵. It also presents the opinions of the expert panel and the authors.

4.3.1 HIV

Migrant women

Migrant women of childbearing age represent a considerable and growing proportion of newly diagnosed HIV cases [50]. Several studies cite foreign nationality as a major factor for not receiving an HIV diagnosis prior to pregnancy [51,52]. In Spain between 1992 and 2010, 70% of HIV-infected foreign-born women were diagnosed during pregnancy, while 81% of HIV-infected Spanish-born women were diagnosed before pregnancy [53]. In Italy, HIV-infected Italian-born women received their HIV diagnosis predominantly before pregnancy (81%); only 61% of HIV-infected migrant women were diagnosed prior to pregnancy [54]. Sub-Saharan African immigrants in Scotland were found to be disproportionately affected by HIV; they also used sexual health services ineffectively [55].

There are several barriers to timely access to antenatal care services: migrants are not always fully aware of their healthcare entitlements, have a general level of mistrust towards the system [50], and have a number of concerns and fears such as fear of stigma, fear of criminal conviction, fear of legal and immigration problems, fear of violence, and fear of death and disease [50,56,57].

Services provided to undocumented migrants differ across the EU/EEA countries, according to the consulted experts. Preventive and health promotion services are usually not provided to recent migrants, and undocumented migrants are not likely to seek care or screening.

Several approaches should be considered to improve antenatal screening among migrant women. Language and cultural differences should be addressed/acknowledged when providing health interventions to migrant women [13,31,57-59]. Migrant women have been found to be frequently unaware of their HIV status [54]. There is a need for culturally sensitive health promotion targeted at African women to increase their knowledge of STI and HIV, and to address the cultural behaviour that inhibits their use of sexual health services [55,56].

The *Canadian guidelines on sexually transmitted infections* recommend that immigrants and refugees should be screened for sexually transmitted infections, including HIV and syphilis [60].

In 2015, ECDC published an Expert Opinion on the public health needs of irregular migrants, refugees or asylum seekers across the EU's southern and south-eastern borders⁶ [61].

Women engaging in high-risk behaviours

There is only very limited evidence on the effectiveness of antenatal screening of women who engage in high-risk behaviours.

HIV-positive women in Romania infected through injecting drugs use were reported to have a high vertical transmission rate (15.6%) and to be co-infected with HCV. Often, HIV was not discovered until delivery [62]. However, with rapid identification and appropriate management, this group is not at an increased risk of MTCT compared with people who do not inject drugs [63]. The offer of HIV testing in addiction services in Ukraine is reported to have enabled more women who inject drugs to become aware of their HIV-positive status before pregnancy than, for example, people who do not inject drugs [64]. The proportion of people who inject drugs diagnosed before conception increased from 31% in 2000–2001 to 60% in 2008–2009. However, among women with unknown HIV status at conception, injecting drug users were more likely to be diagnosed late. [64].

Women with multiple sex partners and/or those whose partners were not integrated into prevention strategies for MTCT, were reported as at risk to seroconvert during pregnancy or breastfeeding in a study from France. Improved counselling in pregnant women and repeat testing in late pregnancy was recommended [30].

The ECDC expert panel was of the opinion that partner tracing as part of the screening programme for women who engage in high-risk behaviours (e.g. multiple sex partners) would be difficult to implement.

⁵European Centre for Disease Prevention and Control. Antenatal screening approaches effective in preventing mother-child transmission of HIV, hepatitis B, syphilis and rubella in vulnerable populations. Stockholm: ECDC; 2017.

⁶European Centre for Disease Prevention and Control. Expert Opinion on the public health needs of irregular migrants, refugees or asylum seekers across the EU's southern and south-eastern borders. Stockholm: ECDC; 2015. Available from: <http://ecdc.europa.eu/en/publications/Publications/Expert-opinion-irregular-migrants-public-health-needs-Sept-2015.pdf>

The ECDC expert panel emphasised the importance of offering testing for other sexually transmitted infections to pregnant women who were diagnosed with HIV.

Other groups – groups refusing HIV testing

The available scientific evidence on the screening of groups that refuse HIV testing was very limited. However, it was shown that testing was rarely refused when offered [35,36]. Expert opinion was that refusals should be recorded so that testing could be offered again later in pregnancy.

According to two European studies, the main reasons for declining HIV testing were previous testing, parity, not perceiving the need for testing, and religious affiliation [65,66]. Two-thirds of the women that declined HIV testing in a UK study accepted all other antenatal screening tests [65]. In a study from the USA, the following reasons for declining HIV testing were given: fear of being stigmatised as sexually promiscuous or as someone who injects drugs, denial about the possibility of being infected, fatalism, and fear of rejection leading to loss of emotional and financial support [67].

Even though HIV-related stigma decreased over the years, HIV-positive pregnant women still face prejudices and discrimination. Antenatal healthcare providers need to increase their awareness of the infection and its pregnancy outcomes and at the same time alleviate the fears of HIV-positive pregnant women.

4.3.2 Hepatitis B

Migrant women

HBsAg prevalence among migrants in European countries was reported to range from 1.0% to 15.4% and, on average, was found to be six times higher than in the general population. The review also found evidence that HBsAg screening in migrants born in endemic countries is cost-effective [11].

Several interventions were retrieved by the evidence review, for example vaccination of all immigrants against hepatitis B [13,68] and offering all newborns from immigrant mothers the first dose of HBV vaccine at birth, regardless of maternal HBsAg status [69]. The opinion of the ECDC expert panel was to vaccinate newborns if the mother is positive or the mother's status is unknown, in line with the recommendations outlined in the national guidelines.

Women engaging in high-risk behaviours

HBV prevalence in people who inject drugs in European countries was found to be, on average, nine times higher than in the general population [11]. Injecting drug use was identified as a risk factor for hepatitis B infection and a criterion for selective antenatal screening [70]. In Norway, injecting drug users constitute the largest risk group for hepatitis B [13]. A study from the United Kingdom found that HBV prevalence was nearly twice as high in women who refuse HIV testing compared with those who accept testing [71].

The scientific evidence that supports the screening of women who inject drugs is scarce or of low quality and points to similar challenges as the ones encountered in reaching other groups at risk (e.g. migrant women, women refusing vaccinations or testing): low reachability, low compliance, and hence inadequate antenatal care.

4.3.3 Syphilis

Migrant women

Several studies from Europe point to the fact that the number of syphilis cases among foreign-born people is high [14,31,72,73]. A UK study found that selective antenatal screening by country of birth or by ethnic group would detect most syphilis cases but might be administratively difficult, politically sensitive, difficult to implement and likely to result in poor uptake of tests [14]. Encountered challenges include lack of knowledge of healthcare services [73], difficult physical access to antenatal care, language barriers, and poor knowledge of the importance of maternal health [31].

Women engaging in high-risk behaviours

In a European cohort study that investigated the prevalence of sexually transmitted diseases (STIs) among 1050 HIV-positive pregnant women, 25% were diagnosed with one or more STI during their pregnancy, syphilis being the most common bacterial STI (2% prevalence) [74]. The authors recommended antenatal screening for STIs during pregnancy for HIV-positive women and supported counselling and follow-up for treatment and prevention.

A US study recommended on-site testing and same-day treatment for syphilis for women who engage in risk behaviours to minimise missed opportunities among women who infrequently access healthcare [75]. The ECDC expert panel suggested that rapid tests should be used only for outreach testing but not in antenatal screening, as the decision for treatment is usually based on a confirmatory test.

In countries with low syphilis incidence, universal screening might not be cost-effective and selective screening should be considered as an alternative. Selective screening, however, could fail to identify emerging risk groups [14].

4.3.4 Rubella susceptibility

Migrant women

An increase in rubella-susceptible women has been reported from several European countries, partly due to increased immigration. Pregnant women born outside Europe are more likely to be seronegative than ethnic Europeans. Intensified targeted screening and postpartum vaccination for migrants have been recommended in several studies [69,76,77]. Other studies recommend offering vaccination to migrants during their first visit to a European healthcare facility [76-79].

Other groups – groups refusing vaccination

Even though the vaccination coverage for rubella is high in Europe and vertical transmission of rubella is rare, groups refusing vaccination continue to be a challenge. There are several studies on groups refusing vaccination for religious reasons from the Netherlands [10,80]. There is also an increasing number of people who refuse vaccinations for their children because of ideological or other reasons [81,82].

As rubella infection is becoming increasingly rare in many European countries, the possible consequences of the illness will become less known and less visible among the general public, among healthcare personnel and among decision makers.

4.4 Antenatal screening among vulnerable groups – approaches for increasing the uptake

Most of the approaches for providing more antenatal screenings early in pregnancy apply to all women and are not specific to certain risk factors or vulnerable groups. Many of the approaches suggested in the literature for increasing antenatal screening uptake in risk groups are already included in the recommendations for national programmes. Only three additional practices concerning risk groups were suggested (Box 2).

Box 2. Specific practices to improve the uptake of antenatal screening among risk groups

- Offer appropriate assistance to lower communication barriers (by taking into account language, literacy levels, or individual or cultural specifics)
- Facilitate access to antenatal care through outreach services and informal networks
- Increase the level of awareness in policymakers, healthcare providers and the general public with regard to the importance of ANS

• Offer appropriate assistance to lower communication hurdles

Literature review: A US study observed that immigrants had an increased risk of receiving substandard care due to cultural, linguistic, financial, legal, systematic and other barriers that may complicate the screening and care for infectious diseases [58]. A UK study found the following main barriers to the early initiation of ANC of socially disadvantaged and vulnerable women: the complexity of the UK healthcare system, lack of knowledge regarding the purpose and importance of ANC, preference for local services, women's perception that healthcare professionals do not or will not treat them respectfully and sensitively, failure to provide professional interpreters when needed, and concerns that cultural preferences (i.e. being seen by female healthcare staff) may not be respected. Asylum seekers and refugees also experienced barriers related to the lack of a fixed address and financial issues [83]. Several other studies suggested the need for culturally appropriate approaches in the immigrants primary language [31,55,57,59].

Expert opinion: **strongly supportive.** Communication barriers include language problems, hearing and visual impairments, lack of understanding, and illiteracy. External assistance to facilitate communication and arrangements to prevent disclosure of infection status to family members would be an asset. Cultural sensitivities (including faith-based barriers) should be taken into account to reduce misunderstanding, confusion and prejudice. Smartphones and social media could be used to reach different vulnerable groups.

Conclusion: According to the evidence from the literature and expert opinion, communication barriers should be lowered by offering appropriate assistance based on the needs of the target group in order to facilitate access to antenatal care.

● Facilitate access to antenatal care through outreach services and informal networks

Evidence review: In a UK study, several measures were implemented to target disadvantaged and vulnerable groups of women: improved access to local services, proactive case finding followed by assistance entering/navigating the healthcare system, bilingual outreach/community-based workers or clinics catering to the needs of the female target group, and training and education of staff to improve cultural sensitivity. The study concluded that the evidence that 'existing interventions targeting disadvantaged and vulnerable groups of women' were effective in increasing early initiation of antenatal care in other populations was weak [83]. Another study stated that community-based interventions needed further research [84]. An Italian study on syphilis during pregnancy recommended the dissemination of user-friendly, translated information materials in aggregation sites, the use of cultural mediators in health facilities, and increased efforts on the part of healthcare services to facilitate access to antenatal care for migrants [31].

Expert opinion: **strongly supportive**. Outreach might be necessary to facilitate access to antenatal care for women belonging to vulnerable groups.

Conclusion: Evidence from the literature supporting the effectiveness of outreach services was weak but suggested that this topic was worth exploring. According to the expert panel, different outreach services and informal networks should be used to facilitate access to antenatal care for all risk groups.

● Increase the level of awareness in policymakers, healthcare providers and the general public with regard to the importance of ANS

Evidence review: In order to control a rubella outbreak in Spain among women born in Latin America, interventions included a health education campaign on congenital rubella and a training programme for health professionals on case management [78]. A US study found that promotional campaigns in the community helped to improve testing uptake in Hispanic/Latino communities, especially if combined with improved knowledge on the HIV epidemiologic profile [85]. A study from Scotland found that women of African origin had gaps in their knowledge of STIs and lacked information on sexual healthcare services. Health promotional activities were suggested [55].

Expert opinion: **strongly supportive**. Increasing awareness among decision makers, target groups and health service providers with regard to the benefits of antenatal screening among vulnerable groups is bound to increase the uptake of testing and of antenatal care.

Conclusion: There was little evidence that raising awareness among policymakers towards the difficulties of screening vulnerable groups for infections is beneficial; there is, however, evidence that increased awareness among healthcare providers and the general public towards the benefits of ANS has a positive effect. The expert panel supports increased advocacy and awareness at all levels, including policymakers, healthcare providers and pregnant mothers.

4.5 Limitations and knowledge gaps

Several limitations apply to the way vulnerable groups were identified in the ANS survey. The identification of vulnerable groups was largely based on the opinions and judgements of the respondents' and less on country-wide quantitative assessments [1]. An accurate estimate of MTCT rates for HIV and hepatitis B in native-born citizens of reporting countries could not be conducted because of incomplete TESSy data.

The literature review on approaches addressing vulnerable groups focused on antenatal screening and did not include the entire process of antenatal care. It is likely that the search failed to identify a number of publications on women who engage in high-risk behaviours, on women who refuse vaccinations and testing, or disadvantaged and vulnerable groups of women in general. Moreover, behavioural studies on effective antenatal care may have been missed. Little information was found concerning risk behaviours of pregnant mothers or their partners, and even less on groups refusing vaccinations or testing.

During the development of this guidance expert opinions proved to be essential because the searched literature did not provide a strong scientific foundation for recommendations. The expert meeting held at the end of the process was therefore of great value. The participating experts came from various disciplines and areas of expertise, but a larger panel would have provided an even broader knowledge base. A certain level of bias is present in any expert group, as individual experts tend to be biased and limited to their own experiences; consequently, the strength of the evidence provided in this guidance document does not possess the same quality as that of a well-designed comparative study.

5 Possible implications for public health practice and research

Policymakers in EU/EEA Member States are advised to consider the conclusions of this document in the context of their own national social, economic and epidemiological profiles.

During the preparation of this guidance, a number of gaps in the evidence base were revealed. These gaps make it difficult to provide decision makers with high-quality evidence to support improved antenatal screening and targeted help for those groups that are most vulnerable to MTCT.

Despite these and other limitations, several research topics that could add value to the implementation of antenatal screening were identified:

- Scientific advice on how to reach hard-to-reach/vulnerable groups in general (groups may differ in each country)
- Development of criteria/tools for defining and identifying relevant risk groups at the national level
- Development of indicators for measuring effectiveness of ANS programmes (and specific interventions) among hard-to-reach/vulnerable groups
- Scientific advice on how to increase the uptake of antenatal care and screening services; identify reasons why women decline antenatal HIV testing; develop interventions that increase testing uptake
- Studies on how to decrease late presentation
- Defining criteria for the discontinuation of (ANS) screening for infections.

The validity of this guidance depends on changes in the epidemiology of HIV, HBV, syphilis and rubella in Europe. In addition, changes in antenatal screening and vaccination practice (HBV and rubella) can effect the validity of this guidance. As more evidence becomes available, an update of this document may become necessary.

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Appendix 1. Expert group

Participants in the expert panel meeting on ECDC Guidance for antenatal screening for HIV, syphilis, hepatitis B and rubella susceptibility – addressing the vulnerable groups; 17–18 September 2015, Uppsala, Sweden

Attending experts			
Name	Country	Affiliation	Area of expertise
Darina O'Flanagan	Ireland	Health Protection Surveillance Centre	Guidance target audience – policymaker, national level
Marianne Forsgren	Sweden	INFPREG	Guidance target audience – ANS national programme coordinator
Vasileia Konte	Greece	Hellenic Centre for Disease Control and Prevention	ANS policies and practice for migrant women
Anneli Uusküla	Estonia	University of Tartu	ANS policies and practice for people who inject drugs
Mariana Mardaescu	Romania	Matei Bals Institute	Member State – high-level MTCT HIV (Romanian MTCT database)
Tonka Varleva	Bulgaria	MoH	Member State – high-level MTCT syphilis
Ilze Kreicberga	Latvia	Riga Maternity hospital	Member State – high-level MTCT HBV
Lisa Vicente	Portugal	MoH	Member State – antenatal care, OBGYN, national coordination
Pat Tookey	United Kingdom	University College London, UK	Member State – effectiveness analysis syphilis, HIV, rubella
Kevin Pottie	Canada	Centre for Global Health Institute for Population Health, University of Ottawa	EBM expert, migrant screening guidance development
Ruxandra Draghicesoiu	Romania	Matei Bals Institute	Member State – high-level MTCT HIV, neonatal care
Areas not covered because invited experts did not attend			
Guidance target audience – policymaker, EU level			
ANS policies and practice for anthroposophic communities, other groups refusing vaccines, or medical interventions			
ANS policies and practice – reaching ethnic minorities			
Member State – high level of CRS			
Clinical practice – antenatal care guidance and evidence-based methodology			
Project team THL Helsinki, Finland			
Carita Savolainen-Kopra	Project team lead, PhD, adjunct professor, chief specialist, head of viral infections unit		
Mia Kontio	Project team member, MSc, researcher		
Marjukka Mäkelä	Project team member, MD, PhD, Professor, specialist in evidence-based medicine		
Paula Tanhuanpää	Technical project manager, MSc, senior expert, development manager		
ECDC staff			
Andrew Amato	Gianfranco Spiteri		
Otilia Mårdh	Erika Duffell		
Tarik Derrough	Lara Tavoschi		
Niklas Danielson	Egle Obcarskaite		
Helena de Carvalho Gomes	Ann-Christin Lugg		
Anastasia Pharris			

Appendix 2. Summary of presentations, expert meeting

United Kingdom: Infectious Diseases in Pregnancy Screening (IDPS) programme

The UK National Screening Committee formulated evidence-based recommendations for the use of the four UK governments. Currently, antenatal screening is performed for HIV, hepatitis B and syphilis. Regular reviews, updating of standards, service specifications and key performance indicators are managed by the Infectious Diseases in Pregnancy Screening (IDPS) programme. The outcomes of the screening programme are monitored through three projects: National Study of HIV in Pregnancy and Childhood (NSHPC), Surveillance of Antenatal Syphilis Screening (SASS) study, and hepatitis B in pregnancy audit.

Source: <https://www.gov.uk/topic/population-screening-programmes/infectious-diseases-in-pregnancy>

Romania: MTCT database – identifying the risk factors

The national registry for HIV-infected pregnant women and perinatally exposed children serves as an operational tool for collecting data on mother-child pairs and for providing a national overview of mother-to-child transmission events. Since 2013, the registry has been used to store data on demographics for the mother and the child; HIV infection history, risk factors and therapy for the mother; medical history, type of birth, immunological and virological investigations for the child. It also stores information about the father and the child's siblings. In addition to providing descriptive statistics and trends, the registry allows for the identification of groups of pregnant women at high risk for MTCT and identifies determinants for vertical transmission. The data are used to choose prevention methods and adjust patient care procedures.

Source: http://www.cnlas.ro/images/doc/24112015_2_eng.pdf

Sweden: INFPREG – a website providing information on infections during pregnancy to healthcare providers and the public

INFPREG is an interactive, internet-based platform that was introduced in 1999 and offers multidisciplinary information on 31 different infectious diseases, the use of antibiotics, vaccinations during pregnancy, screening programmes, and official regulations. Two versions are available: one for medical personnel and one for the general public. Information on the platform is frequently updated and can be printed out as a flyer (and handed out directly to the pregnant woman and her partner). An evaluation of the system showed that the information provided by INFPREG was readily accepted and implemented.

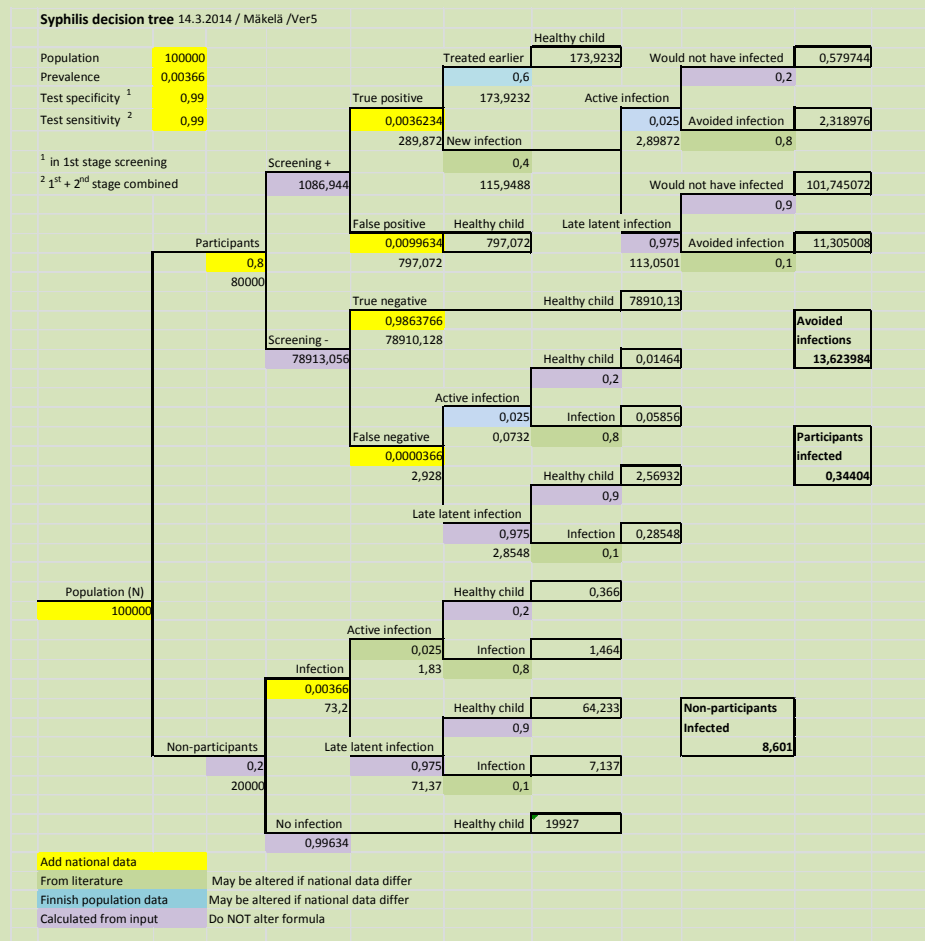
INFPREG (<http://www.medscinet.se/infpreg/mobile>) is optimised for smartphones.

Source: www.infpreg.se

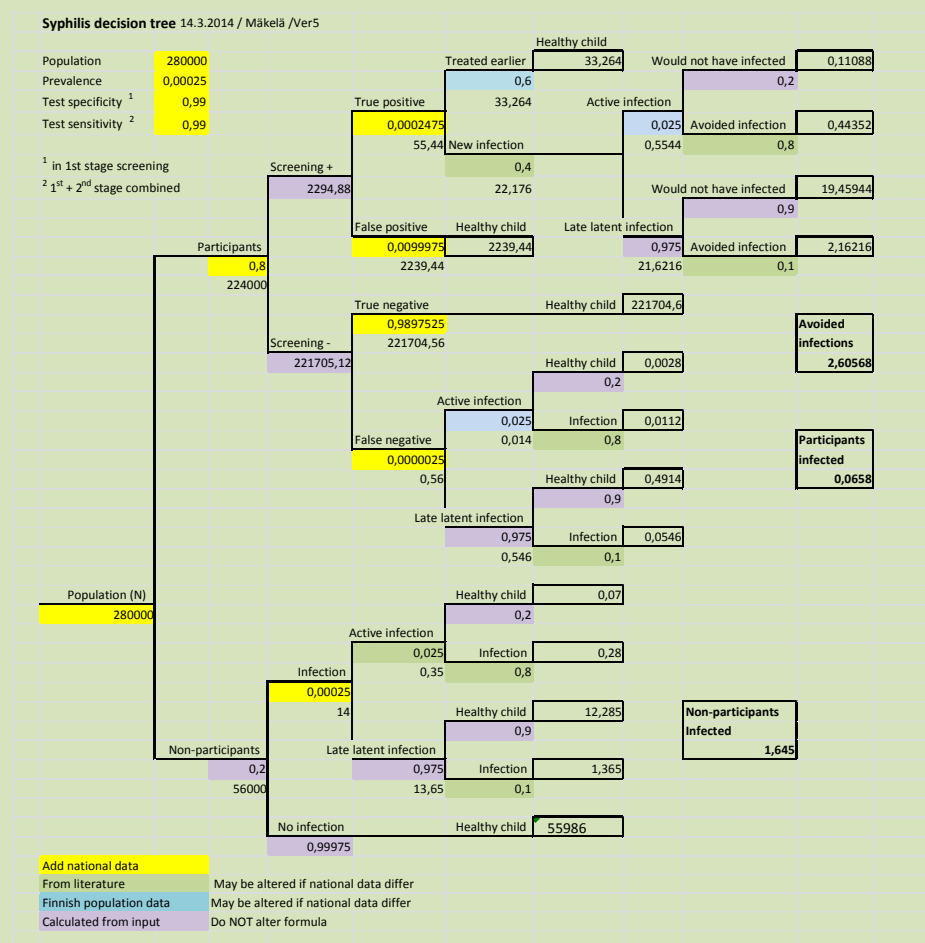
Finland: Functional Excel model – decision tree for screening programme effects

A decision-tree model in Microsoft Excel to support national screening decisions was developed by THL, the Finnish public health agency in Helsinki [1]. The Excel file lets the user calculate the effects of implementing screening programmes. Two examples are shown below (screenshots 1 and 2). Data for the model are taken from the literature (green fields) or from the Finnish screening registers (blue). The yellow data fields (top left) can be adjusted according to national data. The spreadsheet calculate the number of avoided infections based on a number of parameters such as the number of pregnant women, the prevalence of syphilis among a population (number of women who tested positive in the first screening round), and the characteristics (sensitivity and specificity) of the screening tests.

Screenshot 1: Basic model



Screenshot 2: Basic model, adjusted for larger population and lower prevalence



Note: The blue boxes ('treated earlier') represent the proportion of screening-detected infections that were treated earlier; 'active infection' gives the proportion of new infections that are active (i.e. not latent). The Excel file can be requested from the author (Marjukka Mäkelä, National Institute for Health and Welfare, Finland).

Source: Surcel HM, Haula T, Mäkelä M, Aho I, Hiltunen-Back E, Salo E, et al. Alkuraskauden infektiöseulonta Suomessa. [Screening of infectious diseases during early pregnancy in Finland]. [Finnish]. THL Raportti 7/2014. Tampere: Juvenes Print, Suomen Yliopistopaino Oy; 2014.

Appendix 3. Expert vote on recommendations for national programmes

Recommendations		Expert panel opinion (5-1)
1	National antenatal screening programme for infectious diseases should be implemented	Av=4.4; Mo=5; Md=4.5 strongly supportive
2	ANS for infections should be implemented in association with general antenatal care	Av=4.4; Mo=5; md=4.5 strongly supportive
3	Testing (with information) should occur during the first trimester of pregnancy	Av=4.2; Mo=4; Md=4 strongly supportive
4	Testing should be repeated during the third trimester in pregnant women at increased risk of infection and/or for those who refused testing earlier	Av=4.3; Mo=5; Md=4.5 strongly supportive
5	Testing should be offered at delivery if not done earlier	Av=4.9; Mo=5; Md=5 strongly supportive
6	Universal (voluntary, general population, opt-out) approach should be implemented for ANS for HIV and syphilis	Av=4.5; Mo=4; Md=4.5 strongly supportive
7	National (or regional) antenatal screening data should be collected, analysed and assessed	Av=4.6; Mo=5; Md=5 strongly supportive
8	Implementation of the national screening programme should be evaluated regularly	Av=3.9; Mo=4; Md=4 supportive
9	Nationally relevant groups vulnerable to MTCT should be identified	Av=4.3; Mo=5; Md=4.5 strongly supportive

The voting scale: 1 = not important; 2 = of little importance; 3 = important; 4 = very important; 5 = extremely important.

Average scores were categorised as:

Av < 2.0 Not supportive

Av = 2.0–3.9 Supportive

Av > 4 Strongly supportive

Appendix 4. Expert vote on recommendations for vulnerable groups

Recommendation		Expert panel opinion (5-1)
1	Communication hurdles should be lowered by offering appropriate assistance	Av=4.2; Mo=4; Md=4 strongly supportive
2	Cultural sensitivity should be taken into account to reduce misunderstanding, confusion and prejudice (includes faith-based barriers)	Av=4.3; Mo=4; Md=4 strongly supportive
3	Outreach services and informal networks should be used to facilitate access to antenatal care	Av=4.1; Mo=4; Md=4 strongly supportive
4	Awareness of policymakers, healthcare providers and the general public should be increased.	Av=4.4; Mo=5; Md=5 strongly supportive

The voting scale: 1 = not important; 2 = of little importance; 3 = important; 4 = very important; 5 = extremely important.

Average scores were categorised as:

Av < 2.0 Not supportive

Av = 2.0–3.9 Supportive

Av > 4 Strongly supportive

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