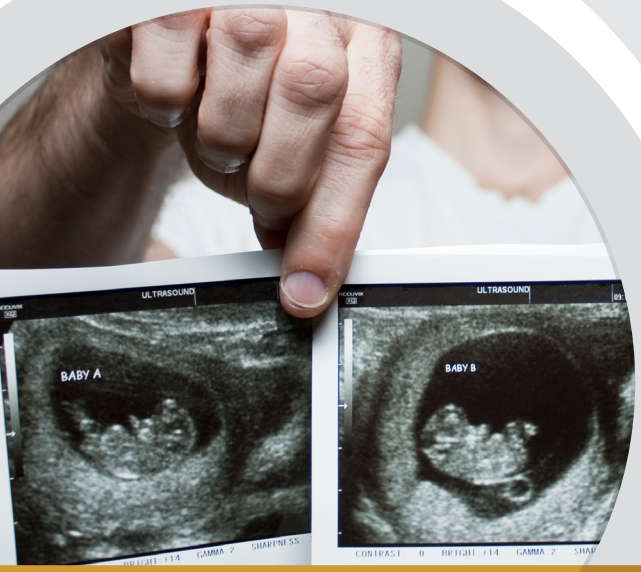

TECHNICAL REPORT

Antenatal screening approaches effective in preventing mother-child-transmission of HIV, hepatitis B, syphilis and rubella in vulnerable populations

Literature review

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Literature review

This report was commissioned by the European Centre for Disease Prevention and Control (ECDC) and coordinated by Otilia Mårdh, Tarik Derrough and Andrew Amato-Gauci.

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Abbreviations

AIDS	Acquired immunodeficiency syndrome
ANS	Antenatal screening
CASP	Critical Appraisal Skills Programme
CRS	Congenital rubella syndrome
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EU	European Union
EEA	European Economic Area
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
IDU	Intravenous drug use (user)
LYG	Life years gained
LYS	Life years saved
MMR	Measles, mumps, rubella vaccine
MTCT	Mother-to-child transmission
PMTCT	Prevention of mother-to-child transmission
PICO	Population, intervention, comparator, outcome
PICO (T)	Patient, intervention, comparative, outcome, time
PWID	People who inject drugs
QALY	Quality adjusted life year
RNA	Ribonucleic acid
STI	Sexually transmitted infection

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 entire relevant population (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

Background

As part of a project to map antenatal screening practices on HIV, hepatitis B, syphilis and rubella susceptibility, a survey was conducted to identify self-observed challenges in the EU/EEA Member States. This survey found that reaching groups who are vulnerable to mother-to-child transmission (MTCT) of HIV, hepatitis B, syphilis and rubella susceptibility was considered a major obstacle to the successful prevention of mother-to-child transmission (PMTCT). In order to collect evidence on types of antenatal screening intervention that are effective for population groups vulnerable to MTCT, a review of the existing published literature was performed. The purpose of the review was to provide an evidence-base for a guidance on strengthening antenatal screening programmes for infections in the EU/EEA countries.

Methods

The research question (PICO) was formulated to include: 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, and PMTCT intervention 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. Where available, secondary outcomes were also included, such as averted infections in children, life years gained (LYG), life years saved (LYS), and any other relevant outcomes that had been reliably measured. The searches were made during March and April 2015 in the following databases: Ovid MEDLINE (R); Ovid MEDLINE (R) Daily Update; Ovid MEDLINE (R) In-Process & Other Non-Indexed Citations; NLM PubMed (e-publications ahead of print); Centre for Reviews and Dissemination; Cochrane Database of Systematic Reviews; Cochrane Central Register of Controlled Trials and Embase through Embase.com. The literature was screened by two independent researchers and selected based on a set of agreed inclusion criteria. The articles were evaluated for quality using the CASP methodology [1].

Results

The literature review identified studies reporting challenges in reaching vulnerable populations for antenatal care, rather than interventions to address these hurdles. The observed challenges included linguistic, cultural and racial disparities, lack of knowledge and understanding of the purpose and importance of screening and uncertainty on how to reach antenatal screening services. These challenges were observed among migrants and mobile populations and those with high-risk behaviour. Refusing testing was considered to be a challenge in the case of HIV and refusal to vaccination in the case of rubella.

Conclusions

The literature review showed a gap in the published comparative research on increasing uptake and effectiveness of antenatal screening among groups identified as vulnerable to MTCT. Reversing the challenges described in the studies retrieved can serve as a basis for strengthening current national and/or targeted antenatal screening programmes.

Practices that increase uptake of antenatal screening among risk groups are:

- Eliminating communication/linguistic hurdles
- Giving due consideration to cultural sensitivity
- Reducing fear of stigma, criminal convictions and immigration restrictions
- Increasing awareness of the risk of infections for the mother and the newborn and the benefit of antenatal screening.

There is a need to identify country- or region-specific vulnerable groups as they may differ across countries.

1. Background

In 2011, ECDC began a project aiming to evaluate the effectiveness of antenatal screening programmes of HIV, hepatitis B, syphilis and rubella susceptibility in the EU/EEA.

The project began with a survey of the EU/EEA Member States to obtain information on the current practice of antenatal screening for infectious diseases in order to describe country-specific approaches and identify both areas in need of improvement and models of good practice [2]. This was followed by a literature review of the existing published literature on the effectiveness and cost-effectiveness of antenatal screening.

In the 2013 survey of the EU Member States, certain groups were identified as being vulnerable to MTCT, thereby challenging successful implementation of antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility.

This systematic literature review aimed to retrieve information on antenatal screening (ANS) practices effective for preventing MTCT of HIV, syphilis, hepatitis B and rubella among the vulnerable populations in EU/EEA countries.

For the purpose of this review, and based on findings from the ANS survey 2013, the vulnerable groups are defined as follows:

- Migrants and mobile populations
- Those exhibiting specific risk behaviour (drug use by pregnant women or their partners, bisexual partners)
- Other minority groups including those refusing vaccinations.

2. Review methods

2.1 Search strategy

The literature search was planned by information specialists and content experts, both with expertise in evidence-based methods. The search was based on the research question (PICO) as agreed with ECDC, and the approaches were tested until a suitable set of keywords/search terms/concepts was found. Searches were limited to relevant high-income countries (Europe, North America, Australia and New Zealand) and were done at the title and abstract level from 1 January 2000 onwards in Ovid MEDLINE (R), Ovid MEDLINE (R) Daily Update, Ovid MEDLINE (R) In-Process & Other Non-Indexed Citations, NLM PubMed (epubs ahead of print), Centre for Reviews and Dissemination, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (searches made on 2 March 2015) and Embase through Embase.com (1 April 2015). The search strategy presented here (Appendix 1) was adapted to different databases and their search functionalities.

Searches (Appendix 1) were done separately for each of the four diseases, except for the Embase search. The results were combined to exclude duplicates. The references of included articles were checked for relevant new articles (i.e. ancestry search).

The main research questions were: How is antenatal screening of vulnerable groups (i.e. migrants and mobile populations, those exercising risk behaviour (drug use by pregnant woman or her partner, bisexual partners), or those belonging to other minority groups including those refusing vaccinations) performed? How can attendance for screening be increased? What are the results in health gains (averted infections in children, life years gained (LYG), life years saved (LYS), and any other relevant outcomes)? The PICO was 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 and PMTCT intervention for those with test-positive results or susceptibility in the case of rubella.
- C (comparator, reference intervention): no specific interventions or untargeted screening only.
- O (outcome): increased participation rates and positive pregnancies identified or number of MTCT averted. Secondary outcomes if available: averted infections in children, life years gained (LYG), life years saved (LYS), and any other relevant outcomes that have been reliably measured.

2.2 Study selection criteria and procedure

At least two members of the project team independently selected articles in two screening rounds. Discrepancies were collectively discussed. At the first screening (title and abstract screening) any paper that either one found possibly useful was included. The exclusion criteria for the search results at the first screening were:

- Non-vulnerable groups (as identified through the ECDC survey)
- Country not Europe, USA, Canada, Australia or New Zealand
- Publication or abstract not in English (a list of titles/references retrieved in languages other than English is provided as an appendix to this report).

The second screening was based on full-text papers. Two project members independently evaluated the papers and inclusion criteria were:

- Correct PICO
- Population large enough for PICO presented (case reports or case series were not accepted)
- Publication type suitable for the PICO presented.

Due to lack of comparative studies targeting the PICO question directly, we accepted both studies with a broader population scope than the specified vulnerable groups, as long as data on these groups could be extracted, and studies without a comparison group or with outcomes other than originally planned. The search and selection process is shown in PRISMA flow diagrams and additional comments are given in the tables (Section 3.5 onwards).

For each disease, we then selected studies with the strongest designs. Case studies and retrospective case series were only accepted if stronger designs (cohort, case-control) were not available. The articles were evaluated for quality using the Cochrane risk of bias tool for randomised trials [3] and CASP methodology for other types of study design [1]. The results are presented in table format showing study quality and a description of relevant study results. The absence of comparative studies prevented construction of evidence tables. For the same reason, the risk of bias was assessed as high for all the results.

One researcher extracted and transferred the most relevant and best-quality information into a narrative text describing each study. Another researcher checked the text against the publications. Large differences in the

variability/heterogeneity of the studies prevented quantitative synthesis or the grading of evidence strength for each specific review question. In the synthesis of the available information relevant literature identified in the literature search for ANS effectiveness and cost-effectiveness was included, as was literature identified by ECDC from other sources. Grey literature from national repositories was not included.

3. Review results

3.1 Results of search findings

In total, 264 articles were identified in the Medline searches in March 2015 and 240 in the Embase search in April 2015 (Figures 1 and 2). From the Medline searches 46 articles were included (25 HIV, 11 hepatitis B, three syphilis and seven rubella) and from the Embase search a further eight articles were included.

Figure 1. Medline search PRISMA diagram

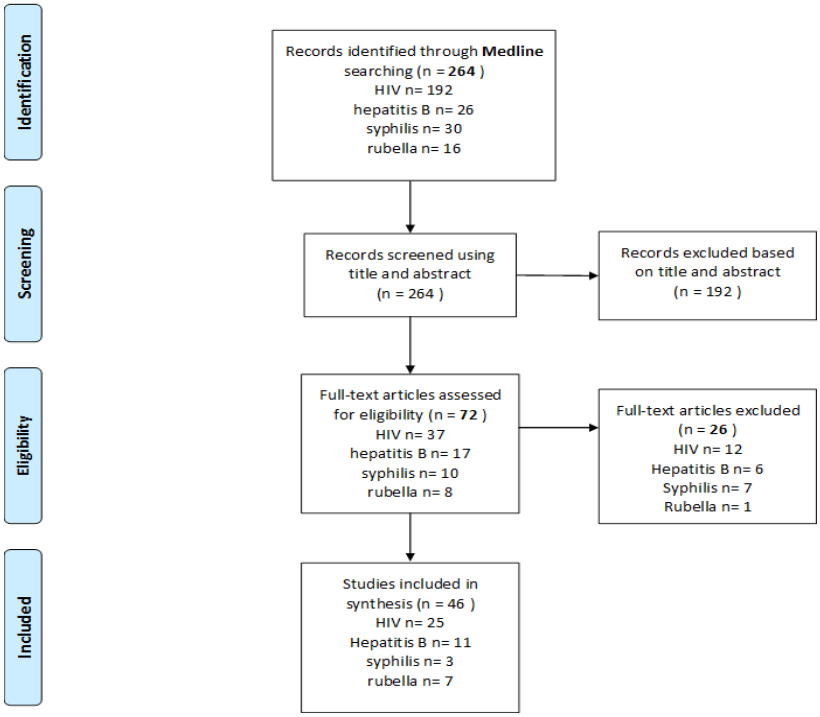
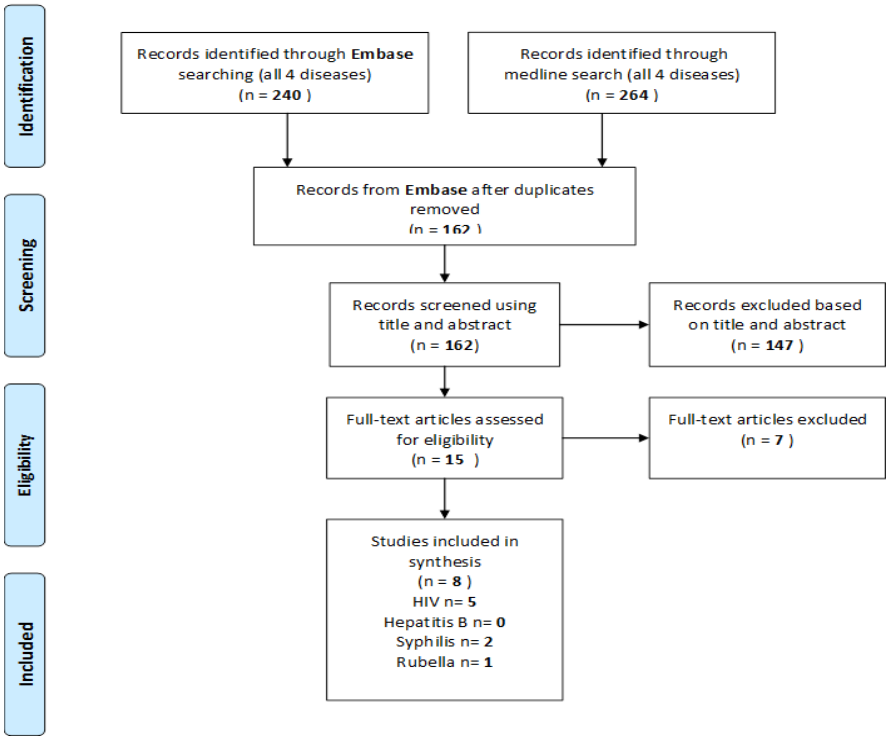


Figure 2. Embase search PRISMA diagram



3.2. Migrant women and ethnic groups

Based on the literature search results it was decided to include 'women belonging to ethnic groups' under the same category as migrant women since these two groups may overlap and were often discussed together in the literature. Mobile populations, originally to be discussed together with migrant populations, were omitted as the literature did not specifically concentrate on this group.

The prevalence of HIV, hepatitis B, syphilis and seronegativity for rubella antibodies is often higher in migrant populations than in general populations and migrant women face considerable challenges in accessing healthcare services.

3.2.1 HIV

No controlled studies on antenatal screening for HIV among migrant women or ethnic groups were found, however, 21 descriptive studies were included and some excerpts from these appear below.

A European review described the situation for women living with HIV [4]. Most women who are diagnosed with HIV in Europe are of childbearing age. Migrants represent a considerable and growing proportion of HIV cases and they may face significant barriers to accessing healthcare services. They are not fully aware of their healthcare entitlements and may not trust the system. The paper published by Fakoya et al. 2008 discussed the barriers to HIV testing for sub-Saharan migrants in western Europe, with particular emphasis on the experience in the UK and the Netherlands [5]. Several factors including stigma, criminal convictions and poverty can be barriers to testing. Fear of death and disease may override the benefits of testing, especially for those with no access to HIV care. The complex regulations of access to services have led to confusion and prejudice. Immigration policies that include HIV-related restrictions may also create fear about testing. Due to culturally inappropriate and inadequately targeted health promotion, Africans often rely on informal networks. Lack of political will, restrictive immigration policies and the absence of African representation in decision-making processes were identified as the major factors preventing Africans from testing.

In France, the proportion of mothers from sub-Saharan Africa increased from 12% in 1984–1986 to 64% in 2003–2004 in a perinatal cohort of HIV-positive pregnancies [6]. Access to HIV testing of women from sub-Saharan African countries was subject to longer delays than for French-born mothers. Moreover, among women who discovered their HIV status during the pregnancy, screening was done later in African women. However, once HIV diagnosis was made, PMTCT initiation was similar in French and sub-Saharan African mothers.

In Italy, Madeddu et al. reported an increase in the proportion of new HIV diagnoses in pregnant women in Sardinia from 8.6% in 1997–2000 to 20.6% in 2001–2004. The proportion of pregnant foreign women diagnosed also increased from 0% to 57% during the respective periods [7]. Maternal-foetal wellbeing and pregnancy outcomes were studied among immigrant mothers attending a clinic in Udine during the period 2001–2008. The largest group of migrant women originated from eastern Europe, followed by sub-Saharan Africa and Arab countries. African women were more frequently HIV positive and showed a greater tendency towards poor pregnancy outcomes requiring longer hospitalisation [8]. Foreign nationality was one out of the four factors found to be related to the occurrence of a first HIV positive test during pregnancy [9]. HIV diagnosis before pregnancy was more frequent in Italians (91%) than migrants (61%) [10]. In addition, an association between non-Italian nationality and detectable HIV RNA at delivery was demonstrated. Specific public health interventions should target migrant women who are frequently unaware of their HIV status at the time of pregnancy.

A study from Scotland [11] found sub-Saharan African immigrants disproportionately affected by HIV and that they are not accessing sexual health facilities effectively. In brief, they found that a) African women in Scotland do not have access to correct, up-to-date information on sexually transmitted diseases (STIs) and this may affect the uptake of sexual health services, meaning that there is a need for health promotion interventions tailored to the needs of African women in Scotland; b) African women's knowledge of STI and HIV needs updating; c) there is a need for African women to build up their skills/confidence in order to address the cultural behaviour that inhibits their use of sexual health services; d) there is a need for HIV prevention programmes to be set up within the African community in Scotland, partnering with sexual health service providers; e) there is a need for more research on African women's sexual health issues in order to identify the most effective ways to promote positive health. Nevertheless, another UK study found that ethnic origin is not a risk factor for refusing HIV testing [12].

In Spain, in a study in southern Madrid during the period 1992–2010, the majority of HIV-positive, foreign-born women were diagnosed during pregnancy (70%), while those who were Spanish-born were mostly diagnosed before pregnancy (81%) [13]. The overall MTCT rate during the study period was 1.3%.

A US CDC study characterised the trends in diagnoses among children with perinatal HIV infection by race/ethnicity for the period 2004–2007 [14]. The average annual rate of diagnoses of perinatal HIV infection was highest, 12.3/100 000, among blacks, 2.1/100 000 among Hispanics, and 0.5/100 000 among whites. Although disparity narrowed between 2004 and 2007, it was recommended that HIV-infected pregnant women, particularly black and Hispanic, should receive more timely prenatal care and initiation of comprehensive interventions to further reduce

perinatal HIV transmission and racial/ethnic disparities. Lawrence et al. described the trends in HIV testing during pregnancy among the insured population from 1997 to 2006. Testing prevalence increased from 78% to 91% during the study period. Non-Hispanic white women were least likely to be tested [15]. Variation in prenatal HIV testing within-group and between group was investigated among low-income pregnant and recently postpartum women [16]. The majority of the women in this study were counselled about the HIV test (88 %) and tested (70%) during pregnancy. Predictors of prenatal testing uptake differed by race. Receiving prenatal care in a community health centre or hospital outpatient clinic increased the probability of testing for Hispanics. Being a recent victim of intimate partner violence was associated with less frequent testing for blacks. Positive beliefs about HIV screening were associated with testing for blacks, Hispanics and whites. Another study, analysing data from the 2000 National Health Interview Survey in the US indicated that two thirds of Hispanics had never been tested for HIV (excluding blood donations) and 88% had no intention of being tested in the near future. Pregnant women were nearly three times more likely to have been tested for HIV than non-pregnant women [17]. The most common reason for not having undergone HIV testing was not considering oneself to be at risk. In a study from North Carolina, between 2002 and 2005, 30% of young women with newly diagnosed HIV were pregnant at the time of HIV diagnosis [18]. Pregnant women were more likely to be Hispanic, but did not report typical risk factors, such as drug use and high-risk sexual behaviour. This finding supports universal HIV testing during prenatal care. A study on the health of immigrant women found that many cultural and psychosocial barriers to HIV testing and education may exist, among them fear of legal and immigration ramifications, fear of violence, abandonment, or reprisals and cultural and social stigma [19]. These issues must be approached with great sensitivity and understanding, preferably in the migrant's primary language and with peer educators.

A study (conducted 2010-2011) on HIV testing beliefs at a health centre in a predominantly Hispanic community suggests that Hispanics are either unaware of or disagree with the latest CDC recommendations for routine HIV testing. Self-reported spoken English language was associated with knowledge of HIV testing recommendations [20].

In USA, between 1996 and 2000, missed opportunities for perinatal HIV prevention contributed to more than half of the cases of HIV-infected infants. Illicit drug use was strongly associated with lack of prenatal care, and lack of HIV testing before delivery with perinatal HIV transmission [21]. Another study in USA assessed the effect of a change in testing policy on HIV testing rates and found that a policy of routine HIV testing incorporated into the package of antenatal tests, with patient notification and active refusal may be more effective than voluntary counselling and testing [22].

In Canada, race was indicative of whether or not an HIV test would be accepted [23]. Asian women were significantly less likely and Hispanic women significantly more likely to be tested. Women who were fluent in English were also more likely to be tested. Another Canadian study, characterising trends in live births, adverse neonatal outcomes and socio-demographic characteristics of pregnant women, concluded that further research was required to identify factors causing disparities that can be targeted by prenatal risk reduction initiatives [24].

In New Zealand, women of reproductive age from different socio-demographic and ethnic backgrounds were interviewed [25]. All women favoured routine antenatal HIV screening. Most women also favoured general consent for all antenatal screening and would agree to be HIV tested if the test was offered and recommended. Women wanted also to know about treatment to reduce the risk of MTCT.

3.2.2 Hepatitis B

No controlled studies were found on antenatal screening of migrant women or ethnic groups for hepatitis B, however, a total of eight descriptive studies were included and excerpts of these appear below.

Hahne et al. 2013 reviewed the hepatitis B prevalence for 34 European countries and the cost-effectiveness of screening for chronic HBV infection [26]. The HBsAg prevalence in migrants ranged from 1.0–15.4% and was on average six times higher than that in the general population. The estimated anti-HCV-Ab prevalence was twice as high among migrants. It was shown that although screening of migrants in outpatient settings was the most cost-effective approach it reached the lowest number of participants. HBsAg screening of pregnant women and migrants was found to be cost-effective for reducing the burden of disease due to viral hepatitis. It was recommended that European countries that had selective or no antenatal HBsAg screening programmes, including Bulgaria, Lithuania, Luxembourg, Romania, and Norway, should consider implementing universal antenatal screening. The four publications examining HbsAg screening of migrants born in endemic countries (HbsAg prevalence ≥ 2%) suggest that this was cost-effective. HBsAg screening of pregnant women and migrants was also considered very likely to be cost-effective.

In Norway, hepatitis B screening is offered to defined risk groups, including immigrants from countries with a high incidence of hepatitis B [27]. Hepatitis B infection is more prevalent in pregnant Pakistani immigrants than in the native population of Norway. Their recommendation is that for the immigrant population HBV vaccine should be given to all newborns regardless of maternal HBsAg status. Another study observed that there is little data regarding the uptake of testing and vaccination among at-risk populations and recommended evaluation of

surveillance systems for hepatitis B as well as the effectiveness of screening and vaccinating immigrant populations [28]. The authors concluded that universal screening of pregnant women should be introduced.

United Kingdom has adopted a selective immunisation strategy targeting high risk groups which, since April 2000, includes universal antenatal HBV screening and immunisation of infants born to HBV- positive women [29]. Their study showed that half of the cases were diagnosed in foreign-born children, often from countries that were late adopters of universal HBV immunisation. Contrary to a previous hypothesis, they observed that over half of the cases remained under the local care of general practitioners and/or paediatricians instead of being referred to a specialist centre after diagnosis. The ethnic distribution of the cases suggested an imported HBV burden from sub-Saharan Africa, eastern Europe and countries only recently identified as high-risk (e.g. Afghanistan).

In Denmark, the guidelines recommend HBsAg screening if pregnant women or their partners are from intermediate- to high-endemicity areas [30]. According to a study conducted in one hospital a significant number of women at risk were not identified using this selective approach. Among these pregnant women the overall prevalence of HBsAg carriage is about four times higher (0.4%) than the expected prevalence in Denmark. While most of the women with positive markers belonged to an identifiable risk group, 19 women (14%, 95% CI 9_/21%) had markers indicating former or present hepatitis B infection but did not belong to a risk group. Furthermore, they pointed out that universal screening would tend to reduce the stigmatisation of women from areas with a higher prevalence of HBV.

Since selective screening of high-risk pregnant women for HBsAg has failed to identify a significant proportion of HBV-infected mothers, prenatal HBsAg testing of all pregnant women has been recommended in Greece since 1998 [31]. In a study from 2003, 3.2% of women had no documented prenatal or perinatal HBsAg screening and they were more likely to be chronically-infected with HBV (4.2% versus 2.3%, p = 0.10). Risk factors for not being screened included delivering in a public hospital and maternal illiteracy. Immigrant women represented almost 20% of the child-bearing population between 2007 and 2009 [32]. Higher HBV disease burden and low vaccination-induced protection were characteristic in pregnant women who had not undergone HBsAg prenatal testing. The lack of adherence to maternal HBV screening was found to be associated with increased HBsAg seroprevalence among women of Roma origin (5.3%) and immigrants from Asia (4.3%) or eastern Europe (3.4%), indicating that these populations should be targeted by the public authorities for information campaigns as well as screening and immunisation programmes. One striking finding of the study was the extremely low vaccination-induced protection rates observed among multi-ethnic women who had not undergone HBV maternal screening.

In Italy, HBV transmission is progressively declining, even in the immigrant population [33]. Nevertheless, particular attention should still be given to pregnant women of foreign origin, who were twice as likely not to undergo prenatal screening.

An observation from USA found that an increased risk of receiving sub-standard care due to cultural, linguistic, financial, legal, systematic and other barriers may complicate the screening and provision of care for infectious disease among immigrants [34]. Being black, aged under 20 years and using street drugs are factors associated with inadequate prenatal care [35]. Those at risk may therefore miss being screened for HBV. Because many Asian and African immigrants do not engage in the behaviour commonly associated with HBV infection (drug use, for example) physicians do not see an obvious reason for ordering an HBV panel.

3.2.3 Syphilis

No controlled studies were found on antenatal screening of migrant women or ethnic groups for syphilis, however, a total of three descriptive studies were identified mentioning immigrants as the greatest concern in terms of syphilis management.

A UK study [36] found three groups with high prevalence for syphilis: pregnant women in the Thames region, non-white ethnic groups and women born outside the UK. Selective antenatal screening by country of birth or ethnic group could detect at least 70% of syphilis cases but a targeted strategy could be difficult in terms of administration, politically sensitive, hard to implement and would be likely to result in a poor uptake. Targeted screening could also miss new risk groups.

In Italy, congenital syphilis was strictly related to immigration from eastern Europe with the highest risk among young women who did not receive adequate prenatal care because they were unaware of free healthcare services [37]. A multidisciplinary team with experience in the management of syphilis should review antenatal screening results to ensure the best possible evaluation of the mother during pregnancy and the treatment and follow-up of the infant.

In Tuscany, Italy, the Romanian population has grown to be the largest foreign ethnic group but there is also a constant immigration flow from other regions with a higher prevalence of syphilis, such as African and Latin American countries. Screening for syphilis in pregnancy is free in Italy but the difficulty in accessing antenatal care was greater among foreign-born women. The reasons were found to be difficulty in physically accessing facilities (absence of transport), problems leaving the work place and getting to healthcare services, language barriers and

poor knowledge of the importance of maternal health. Activities should be implemented aiming to facilitate access to antenatal care by migrant pregnant women (such as diffusion of informal, translated informative material at social centres, use of cultural mediators at health facilities and reorientation of healthcare services) [38].

3.2.4 Rubella susceptibility

No controlled studies were found on antenatal screening of rubella susceptibility in migrant women or ethnic groups, however a total of nine descriptive studies were included and excerpts from some of these appear below.

One paper describes the situation in Norway for Pakistani immigrants in 2011 [27]. A total of 8% of the Pakistani immigrants were rubella seronegative, compared to 2–5% of ethnic Norwegians. The recommendation was that the rubella antenatal screening programme to be intensified in Norway and that there should be more focus on rubella vaccination postpartum for the immigrant population.

In UK, it was observed that during 2005–2009 there had been a significant increase in those with rubella antibody levels <10 IU/ml [39]. Mothers born abroad especially in sub-Saharan Africa and southern Asia were more likely to be seronegative than UK-born mothers [40]. They recommended supplementary vaccination activities targeted at newly arrived migrants and their families at their first point of contact with UK healthcare services. Byrne et al. 2012 also noted that the majority of congenital rubella syndrome (CRS) cases in recent years were acquired abroad or following infection in immigrant women. In the absence of immunity boosting as a result of natural infection for the many women already considered protected during a pregnancy, antibody levels may decline below the current threshold in future pregnancies. Unless action is taken this will lead to a substantial increase in demand for post-partum measles, mumps, and rubella (MMR) vaccine immunisation. This could also potentially cause increased anxiety among antenatal women labelled as susceptible, particularly those who have children attending nurseries or schools where rash-illness is common or those who work in occupations where exposure to a rash is likely [41]. The study recommended collection of more specific ethnicity data along with country of birth to obtain better information for targeted immunisation strategies.

Ireland observed that the increased rate of rubella seronegativity in the general population in 2009 was associated with an increase in migration [42]. They concluded that focusing on this easily identifiable group of non-EU immigrants (Africa, South-East Asia and the Americas) for screening and vaccination prior to pregnancy would be cost-effective. It may also be more cost-efficient to vaccinate women from countries without rubella programmes without first undertaking serological testing.

In Spain in 2004, the adult immigrant population, especially that originating from Latin America, was considered to constitute a susceptible group [43]. The interventions proposed were a vaccination programme targeting immigrants; rubella serology testing at the first visit to healthcare services; a health education campaign to prevent congenital rubella, and a health professional training programme case management. Another Spanish study from 2015 also found the postpartum immunisation strategy an opportunity to protect women of childbearing age and to increase vaccination coverage against rubella and other vaccine-preventable diseases [44].

In the Netherlands following a study in 2010 [45] a recommendation was made for immigrant women originating from a non-Western country to be screened for rubella antibodies. However, this recommendation was not supported by an economic evaluation and rubella screening was not included in the antenatal screening programme, and thus it is not standard practice in routine midwifery.

Canada has recommended that immigrant women of childbearing age originating from the developing world should be offered MMR vaccination at their first encounter with the healthcare system, since they account for a large number of CRS cases and waiting for results of serological screening may result in a missed opportunity to vaccinate them [46].

3.3 Women with high-risk behaviour

No controlled studies were found on antenatal screening for any of the relevant infections in women with high-risk behaviour.

3.3.1 HIV

A total of four descriptive studies addressing women with high risk behaviour were included and excerpts from these appear below.

Previously in western Europe and currently in much of eastern Europe, a large proportion of infants vertically infected with HIV were/are born to women actively using illicit drugs in pregnancy or having had a history of intravenous drug use (IDU) [47]. Moreover, there was relatively little intervention to prevent MTCT among IDUs. With prompt identification of HIV status and appropriate management, this group is not at greater risk of MTCT than non-IDUs.

In Ukraine, a cohort study between 2000 and 2010 compared the clinical status and MTCT rates between HIV-infected IDUs and non-IDUs [48]. The proportion of IDUs diagnosed with HIV before their pregnancy increased

from 31% in 2000 and 2001 to 60% in 2008 and 2009. More IDUs knew their HIV-positive status before pregnancy than non-IDUs, probably reflecting HIV testing within addiction services. However, among women with unknown HIV status at conception, IDUs were more likely to be diagnosed late. IDU was associated with an MTCT risk that was twice as high and IDUs contributed around one third of all vertical transmissions.

In France, most of the native French children newly diagnosed with HIV infection between 2006 and 2012 were born to mothers who tested negative in early pregnancy [49]. All the women who seroconverted during pregnancy or breast-feeding reported multiple sexual partners during pregnancy and/or their male partner not having participated in PMTCT strategies. Improving HIV counselling in pregnant women, extending HIV counselling and testing of male partners and ensuring repeated HIV testing during pregnancy could reduce MTCT from recently infected mothers.

A US study looked at the gender differences related to HIV testing among drug users [50]. Women were more motivated to accept testing due to concerns related to family and significant others in their life, particularly during pregnancy. Men were more often motivated to test when they perceived personal benefits.

3.3.2 Hepatitis B

A total of four descriptive studies addressing women with high-risk behaviour were included and excerpts of these are set out below.

Hahne et al, 2013 note that the existing HBV screening programmes in Europe stem from an era when treatment options for chronic viral hepatitis were limited. Hence they are mainly aimed at primary prevention, targeting blood donors, pregnant women, and behavioural high-risk groups [26]. Estimates of antenatal HBsAg prevalence were found for 11 countries, ranging from 0.1% to 4.4%. The antenatal HBsAg prevalence was on average three times higher than for the general population prevalence in six of the seven countries with both estimates available. The HBsAg prevalence in people who inject drugs (PWID) was on average nine times higher than that in the general population.

In Denmark the guidelines recommend HBsAg screening if pregnant women or their partners are or have been intravenous drug users, have high-risk sexual behaviour or are exposed through occupational risk [30]. As mentioned earlier, in the case of migrant women, a significant number of women at risk were not identified using this selective approach.

In Norway, IDUs remain the largest risk group for acute hepatitis B [51] and therefore screening is recommended.

In USA street drug use has been associated with inadequate prenatal care [35].

3.3.3 Syphilis

Two descriptive studies addressing women with high-risk behaviour were included and excerpts of these studies appear below.

In USA on-site testing and same-day treatment for syphilis may minimise missed opportunities among women who infrequently access healthcare [35].

A European study on prevalence of sexually transmitted infections in HIV-1-infected pregnant women found that 25% were diagnosed with one or more STIs during their pregnancy [52]. HIV-infected women should receive adequate screening for STIs during the antenatal period, as well as appropriate counselling and follow-up for treatment and prevention.

3.3.4 Rubella susceptibility

No relevant publications were identified.

3.4 Groups refusing testing or vaccinations

No controlled studies were found on antenatal screening for any of the relevant infections in groups refusing vaccinations or testing.

3.4.1 HIV

A total of three descriptive studies were included on the subject of women refusing testing and excerpts of these appear below.

In the UK, high rates of acceptance of HIV testing were found. However, a significant minority of women (15%) declined the offer of an HIV test [53]. Two-thirds of those who declined HIV testing accepted every other antenatal screening tests. The greatest/highest risk factors for refusing an HIV test were parity and previous testing. Another significant risk factor was religious affiliation. Further research is needed to identify the precise reasons for women refusing antenatal HIV tests and to determine what can be done to increase uptake.

In Spain, the main reasons for not having had an HIV test were not having been offered the test, not perceiving the need for testing and/or having been tested previously [54]. The coverage of HIV testing was significantly higher in public than private hospitals. Nearly three-quarters of the women in the study reported having received little or very little information about HIV testing or none at all. Most women who reported HIV testing during pregnancy were tested during the first trimester (90%). Women with lower levels of education are less likely to report having being tested. Prenatal HIV testing is often not documented in medical records and women are unaware of having been tested.

In the US, 5% of all women, and 15% of women who had not previously been HIV tested, indicated that they would refuse HIV testing [55]. The reasons for not wanting HIV testing were grouped around four themes: fear of being stigmatised as sexually promiscuous or as IDU; denial of the possibility of being infected, fatalism, or rejection leading to loss of emotional and financial support. Many women have concerns about HIV testing but despite these concerns, most women agreed that they would be tested if their physician recommended it. Physicians and policy makers need to be aware of women's concerns and fears when implementing HIV testing policies.

3.4.2 Hepatitis B

In UK, in 2004, HBV prevalence was nearly twice as high in women who refused HIV testing as in those who accepted testing [56].

3.4.3 Syphilis

No publications were identified.

3.4.4 Rubella susceptibility

The only country where the groups refusing vaccinations have been specifically targeted by antenatal screening effectiveness analysis is the Netherlands. In low vaccination coverage regions of the Netherlands people often reject participation in the national immunisation programme for religious reasons, as described in a 2010 study [45]. Screening of pregnant women for rubella antibodies in order to offer postpartum vaccination to seronegative women is cost-effective if targeting unvaccinated women in low vaccination coverage regions of the Netherlands. The programme would be cost-effective (EUR 1 100/QALY gained) when assuming a 20% acceptability of vaccination in women belonging to Orthodox protestant risk groups. The acceptance among women – particularly in the Orthodox protestant risk groups – would have to be further investigated before implementation.

3.5 Summary of findings and quality of evidence

The summaries of findings in different vulnerable groups are presented by infection (Tables 1, 4, 7 and 10). Furthermore, challenges identified and authors' recommendations are displayed. Excluded articles are shown in Tables 2, 5, 8 and 11. The evaluation of the quality of evidence is presented in Tables 3, 6, 9, 12 and 13.

The identified articles with a relevant PICO were first screened for studies with experimental designs. There were no studies comparing screening programmes with a no screening option in vulnerable groups. Cohort studies on representative populations and systematic reviews were assessed for risk of bias using the Critical Appraisal Skills Programme (CASP) checklists [1] and economic evaluations using the Drummond checklist [57]. Retrospective studies were not evaluated due to inherent bias.

CASP validity criteria for cohort studies:

- Did the study address a clearly focused issue?
- Was the cohort recruited in an acceptable way?
- Was the exposure accurately measured to minimise bias?
- Was the outcome accurately measured to minimise bias?
- Have the authors identified all important confounding factors?
- Have they taken account of the confounding factors in the design and/or analysis?
- Was the follow-up of subjects complete enough?
- Was the follow-up of subjects long enough?

3.5.1 Studies on population groups vulnerable to MTCT of HIV

Table 1. Studies on population groups vulnerable to MTCT of HIV

Reference	Study design	Study question	Country, target group definition	Findings	Screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Migrants and mobile populations including ethnic groups							
Antoniu 2014 [24]	Retrospective cohort	Trends in live births and adverse neonatal outcomes	Canada; Women diagnosed with HIV in Ontario 2002-2010	No significant secular trends in the rates of live births			Community based interventions, further research needed
Arya 2013 [20]	Survey	Patient beliefs on who should be tested for HIV	USA; a predominantly Hispanic community	71% thought pregnant women should be tested for HIV,		Unawareness or disagreement with the recommendations for routine HIV testing	HIV testing should also be promoted in the community
Holgado-Juan 2013 (in Spanish) [13]	Retrospective case series	Clinical and epidemiological differences between foreign-born and Spanish women	Spain; HIV infected women in southern Madrid	Spanish women were diagnosed before pregnancy, foreign-born women were diagnosed during pregnancy	Universal screening		Health campaigns especially in primary care; combination of HIV serology with cervical cancer screening
Miralles 2013 [4]	Non-systematic review	Situation of women living with HIV	Europe; HIV infected women	41% of HIV as a result of MTCT in migrants from sub-Saharan Africa; migrant women likely to present late for therapy; most women diagnosed with HIV are of childbearing age		Migrant population represents growing proportion of HIV infections and AIDS cases; may face barriers to accessing healthcare services	Care most effective when individualised
Izzo 2011 [10]	Case series	Variables associated with detectable HIV RNA at delivery	Italy; all pregnant women attending one clinic, 1999-2008	Migrants a vulnerable population due to being unaware of their HIV status	Universal opt-in	In ¼ of women who delivered, HIV RNA was not measured in the 30 before delivery	Start of highly active antiretroviral therapy (HAART) as soon as possible in pregnant women; public health interventions targeting migrant women.
CDC 2010 [14]	Report	Racial and ethnic disparities	USA; children with diagnoses of perinatal HIV infection (34 states)	Perinatal HIV diagnoses 23 times higher among black and four times higher among Hispanic children than white children			Effective primary HIV prevention programs available for women
Salvador 2010 (in Italian) [8]	Retrospective cohort	Comparison of indices for maternal well-being between immigrant and native pregnant women	Italy; parturients in one clinic 2001-2008	Largest group of immigrants from eastern Europe; worst outcome of pregnancy found in African women, African women found to be HIV-seropositive more frequently than others.		Continuous increase in female immigration and number of births by immigrant mothers	Monitoring, pre-conceptional and during pregnancy needs to be intensified, especially among African women.
Torrone 2010 [58]	Retrospective cohort	Evaluation of testing and referral services	USA; women pregnant at time of HIV diagnosis, one state 2002-2005	30.1% diagnosed while pregnant; did not report typical risk factors such as drug use and high-risk sexual behaviour.			Universal testing during prenatal care; need for testing during routine healthcare visits prior to pregnancy care.
Yakubu 2010 [11]	Survey and group discussions	Sources of sexual health information	Scotland; African women	African women have a mixed knowledge of STIs, effects, symptoms, risk reduction, transmission mode and seeking information		African women have no access to correct up to date information on STIs	Need for health promotion interventions strategy tailored to the needs of African women.
Lawrence 2009 [15]	Retrospective cohort	Description of trends in HIV testing	USA; California Health plan members who had one or more pregnancies.	Women less likely to be tested after first birth or if enrolling in prenatal care in the third trimester.			

Reference	Study design	Study question	Country, target group definition	Findings	Screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Fakoya 2008 [5]	Discussion paper	Barriers to HIV testing for sub-Saharan migrants	Western Europe with emphasis on the UK and the Netherlands.	Stigma, criminal convictions and poverty barriers to testing; awareness of HIV not translated into perceived individual risk.		Legal and political environments that do not maximise the health and productivity of migrant Africans.	Future strategies to increase HIV testing to address fear of diagnosis, highlight the success of treatment and tackle HIV-related stigma.
Jasseron 2008 [6]	Retrospective cohort	Comparison - indicators of access to prevention of MTCT and rate of transmission.	France, cohort of HIV pregnancies; comparison of sub-Saharan African and French mothers.	After diagnosis, MTCT prevention similar for sub-Saharan African and French women delivering in France.	Universal voluntary testing in first trimester.	Immigrant numbers increasing, late start of care among them.	Maintain universal free access to testing and antenatal care.
Southgate 2008 [12]	Retrospective cohort	Women from high-risk groups more likely to decline antenatal HIV screening	UK; women offered testing for HIV using opt-out policy, one hospital.	High uptake of testing for all groups, black African women more likely than white or Asian to undergo screening; ethnic origin is not a risk factor for refusing HIV testing.	Universal testing, opt-out		
Madeddu 2007 [7]	Retrospective cohort	Evaluation of changes in demographic and behavioural characteristics of HIV-infected individuals.	Italy; new HIV infections diagnosed in northern Sardinia 1997-2004	Increase in proportion of new diagnoses in pregnant women 8.6% to 20.6%.		One in five women diagnosed during screening tests related to pregnancy.	Targeted prevention activities aimed at homosexual men, women and migrants, HIV testing routinely offered to pregnant women.
Yudin 2007 [23]	Prospective cohort and chart review	HIV test acceptance using opt-out strategy	Canada: pregnant women in one hospital.	Testing rates higher with opt-out than opt-in; rates influenced by race and fluency in English.	Provinces 50% opt-out, 50% opt-in		Opt –out strategy to be used.
Floridia 2006 [9]	Epidemiology; national observational study	Assess the rate of previously undetected HIV among pregnant women with HIV.	Italy; all HIV pregnant women.	Voluntary HIV testing among sexually active women delayed until pregnancy; factors related to first positive test during pregnancy: foreign nationality, no pre-conceptional counselling, first pregnancy and asymptomatic status.	Universal opt-in	63% with a new diagnosis with a history of previous pregnancy	Targeted intervention measures directed to increase voluntary testing among women of childbearing age
Pearlman 2005 [16]	Case series, pre-screening survey	Factors associated with prenatal testing	USA; pregnant and postpartum women	Predictors of prenatal HIV testing differed by race		Racial bias may be influencing providers approach to testing.	Social marketing campaigns modified and provider training improved.
Lopez-Quintero 2005 [17]	Case series/survey	Barriers to HIV testing	USA; civilian, non-institutionalised adult population.	Pregnant women nearly three times more likely to have been tested than non-pregnant women			Prevention messages culturally appropriate
Peters 2003 [21]	Retrospective cohort	Trends in perinatal HIV prevention methods	USA; infant medical records from 6 sites 1996-2000	56% of mothers of HIV-infected infants had missed opportunities for perinatal HIV prevention.		Illicit drug use, lack of HIV testing before delivery.	Universal testing during pregnancy.
Avery 2001 [19]	Non-systematic review	Infectious diseases in immigrant women's health.		Cultural and psychological barriers to HIV testing and education.		Fear of legal and immigration ramifications.	Issues to be approached with sensitivity and in the immigrants' primary language; counselling before and after testing essential.
Heckert 2001 [25]	Interviews	Acceptability of HIV screening during pregnancy	New Zealand; women of reproductive age in one city	Women were in favour of routine antenatal screening; most favoured general consent for all antenatal screening	Not routine		Acceptable methods to identify HIV infected methods

Reference	Study design	Study question	Country, target group definition	Findings	Screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Stringer 2001 [22]	Prospective study	Assessment of the effect of change in testing policy	USA; all women on initial antenatal visit in eight maternity clinics 1999-2000	Routine testing with active refusal increased testing rates compared to voluntary counselling and testing			Routine testing with opt-out rather than voluntary testing
Women with high-risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)							
Frange 2014 [49]	Case series	Circumstances of HIV diagnosed in children	France; HIV-infected children	Most native children born to mothers testing negative at start of pregnancy	Universal	Children born abroad and diagnosed late	Improve HIV counselling in pregnant women, extend counselling/testing to partners, repeat testing late pregnancy.
Thorne 2012 [48]	Prospective cohort	Comparison of factors in pregnancy between HIV-infected IDUs and non-IDUs.	Ukraine, HIV centres: pregnant HIV-infected women.	IDU associated with MTCT risk which is twice as high, IDUs more likely to be diagnosed late in pregnancy if status unknown before.	Universal	Barriers to service access; geographical, administrative, chaotic, mobile life-style.	Comprehensive care package for IDUs; linkage between these services and reproductive health services.
Thorne 2006 [47]	Prospective cohort	Characteristics of pregnant HIV-infected women with IDU.	European collaborative study; HIV-infected women.	Characteristics of current and ex-IDUs differed; decline in HIV-infected pregnant women; low use of intervention.	Varies		Prompt identification and appropriate management of IDU pregnant women.
Riess 2001 [50]	Interviews	Gender differences in testing for HIV in drug users	USA; Three counties	Women more motivated to test, especially during pregnancy.			Male and female testers should be targeted differently in terms of marketing.
Other minority groups, e.g. those refusing testing or vaccinations							
Conaty 2005 [53]	Audit	Reasons for refusing antenatal HIV screening	UK; pregnant women in three London hospitals	Significant minority declined; parity, refused other tests, Jewish religion and previous HIV testing associated with refusal, not region, origin or age.	Universal testing		Further research needed to identify precise reasons
Perez 2004 [54]	Case series, survey	Coverage of HIV testing	Spain; pregnant women in Catalonia	Good coverage of HIV testing, lower in private hospitals, documentation of testing lacking, no information on testing.			Increase awareness of the advantages of early HIV testing among pregnant women and staff, training staff and improve recording of screening and results
Schrag 2003 [35]	Retrospective cohort, stratified random sample of births	Adherence with recommendations for screening	USA; eight surveillance areas in 1998-1999	Testing rate low for HIV 57.2%, blacks more likely to receive screening tests and Asians less likely, higher rates of screening with opt-out than voluntary.	Universal prenatal screening & counselling for HIV; areas with opt-out laws have more prenatal testing.	Counselling not well documented. Anonymous testing not registered.	Targeting high-risk groups may overlook others.
Parra 2001 [55]	Case series, survey	Factors affecting decision to undergo HIV testing in pregnancy.	USA; pregnant women in four health clinics, predominantly Mexican American community.	15% refused testing; fear of being stigmatised as being sexually promiscuous or IDU, denial of risk, fatalism of life and fear of rejection by sexual partner or loss of a job if tested positive.			Greater emphasis on describing benefits of treatment.

Table 2. Excluded HIV studies

Reference	Study design	Country, target group definition	Comment
Riskin-Mashiah 2014		Israel	Wrong country*, Hebrew
Gennotte 2013	Case series	Belgium; 224 patients by 10 trained GPs	HIV testing with rapid tests
Zhang 2013	Retrospective cohort	USA; pregnant HIV-infected	Antiretroviral treatment, not screening
CDC 2012	Morbidity and Mortality weekly report; summary guidance	USA	Integrated prevention services; not especially pregnant.
Mor 2012		Israel	Wrong country, Hebrew
Thompson 2012	Guidelines, systematic review	International Association of Physicians in AIDS care	Entry into and retention to care, not screening
Birkhead 2010	Retrospective cohort	USA; HIV-exposed births in New York state	No screening
Mur Sierra 2010 (in Spanish)	Retrospective case series	Spain, one hospital 2003–2004	Population newborns
Rosenheck 2010		Tanzania	Wrong country
Blood 2009	Retrospective cohort	USA, HIV-infected refugees	One hospital
Campbell-Stennett 2009	Prospective case series	Jamaica	Wrong country
Moodley 2009	Cross-sectional study	South Africa	Wrong country, incidence of HIV during pregnancy.
Elchalal 2008	Prospective cohort	Israel	Wrong country, deliveries by HIV positive mothers
McDonald 2007	Epidemiology	UK; HIV-positive women, one hospital in south east London.	No screening
Boxall 2004	Retrospective case-control	UK; women infected with hepatitis B, 1 city	No means for increased screening uptake
Bulterys 2004	Prospective cohort	USA	Rapid HIV testing during labor, not screening
DiClemente 2004	Interviews	USA; African-American teens, one hospital	Population not relevant
Caplinskas 2004	Epidemiology, register study	Lithuania; database of Lithuanian AIDS centre	Epidemiological situation of HIV infection in general
Kelly 2004	Survey	USA; 351 women receiving prenatal care.	Attitudes toward being tested for HIV; relevance for Europe?
Rowe 2004	Systematic review	UK; studies published after 1979	Outdated
Herndon 2003	Retrospective cohort	USA	HIV testing homeless women, not pregnant
Tedaldi 2002	Retrospective cohort	USA	Postpartum therapy, not screening
Baldo 2000	Sero-epidemiology	Italy; pregnant women attending antenatal clinic	HIV positivity, not screening
Goldberg 2000	Prospective cohort	UK; Scotland, antenatal patients and women undergoing therapeutic termination of pregnancy	Prevalence, not screening
Machuca 2000	Methodology	Spain;	HTLV antibody screening
Mofenson 2000	Non-systematic review	USA;	Outdated

** Non EU/EEA or other high-income country*

Table 3. Quality of evidence for HIV cohort studies using the CASP criteria [1]

Study author (year)	Study question	Cohort recruitment	Exposure measurement	Outcome measurement	Confounders identified	Confounders considered	Folow-up complete enough	Folow-up long enough
Migrants and mobile populations including ethnic groups								
Yudin 2007 (15)	(●)	●	●	●	●	●	●	●
Floridia 2006 (16)	(●)	●	●	●	●	●	●	●
Stringer 2001 (22)	(●)	●	●	●	●	●	●	●
Women with high risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)								
Thorne 2012 (24)	(●)	●	●	●	●	●	●	●
Thorne 2006 (25)								

Colour code:

● Yes	● Cannot tell	● No

Study question marked (●) denotes studies where the study question is clearly defined but does not fully match the review PICO.
Yudin: Opt-out compared with provincial opt-in strategy; MCTC not measured.
Floridia: No comparison group; MTCT measured in only 25% of pregnancies.
Stringer: Historical comparison group; MCTC not measured
Thorne 2012: Women with IDU compared with those without; no new intervention.

3.5.2 Studies on population groups vulnerable to MTCT of hepatitis B

Table 4. Studies on population groups vulnerable to MTCT of hepatitis B

Reference	Study design	Study question	Country, target group definition	Findings	Current screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Migrants and mobile populations including ethnic groups							
Hahne 2013 [59]	Systematic review	To inform screening policies; prevalence and cost-effectiveness of screening.	Europe: general population, five subgroups and data for PWID and blood donors from two European organisations.	Estimates of HBsAg prevalence in migrants found for five countries. Prevalence 1.0-15.4% (2-6x vs general population); four economic analyses of screening migrants.		Difficult to reach target group; no or selective screening; wide variation in prevalence.	Universal screening; appraisal of the evidence for screening the general population in mid- and highly-endemic countries in Europe.
Bjerke 2011 [27]	Prospective case series	Immune status and factors associated with susceptibility	Norway: Pregnant Pakistani immigrants participating in ultrasound screening.	Hepatitis B infection is more prevalent in pregnant Pakistani immigrants than native population.	Risk group screening, vaccination of newborns with parents from high-HBV-prevalence countries	Uptake of testing and vaccination not studied; difficulty of reaching target group and compliance.	HB vaccine for all newborns regardless of maternal HBsAg status.
Rimseliene 2011 [28]	Retrospective case series	Epidemiological study to assess the validity of current risk groups and recommended preventive measures.	Norway: Infection register study, all cases reported 1992–2009.	Incidence of hepatitis B same range as other Nordic countries.	Risk group screening, vaccination of newborns with parents from high-HBV-prevalence countries.	Increase in newly diagnosed chronic hepatitis B related to increasing number of immigrants, some immigrant groups hard to reach.	Screening and vaccination of immigrants from highly-endemic countries essential; universal vaccination should be considered; formal evaluation of effectiveness of screening and vaccinating immigrant populations and surveillance system.
Ladhani 2014 [29]	Prospective case series	Prevalence of childhood chronic hepatitis B infection (CHB)	UK: All reported CHB cases in children aged <16 years	Data strongly supports antenatal screening; infected children sub-Saharan Africa, eastern Europe, Afghanistan at risk.	Universal screening and selective immunisation	Cases remain under local care instead of referral.	Strengthen current antenatal screening programme; newly diagnosed cases should be referred for specialist follow-up; opportunistic assessment and testing of new immigrant families.
Jensen 2003 [30]	Prospective cohort	Evaluation of efficacy of selective antenatal screening	Denmark: All pregnant women coming for ultrasound scan in one hospital in Copenhagen.	Prevalence of HBsAg carriage four times higher than expected. High motivation for screening; 72% HBsAg women found by selective screening.	Selective screening for immigrants	Not all women identified in selective screening; little knowledge of HBV infection among doctors not treating patients with hepatitis; language problems.	Universal screening
Papaevangelou 2006 [31]	Prospective cohort	Evaluation of adherence to national guidelines.	Greece: all women delivering 17–30.3.2003	91.3% screened; immigrants comprise 20% of child-bearing populations; Roma, Asian, eastern Europeans at risk.	Universal screening	Lack of adherence in public hospitals	Universal vaccination at birth, perinatal testing of all not tested prenatally.

Reference	Study design	Study question	Country, target group definition	Findings	Current screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Karatapanis 2012 [32]	Prospective cohort with historical control group	Seroprevalence study with unclear and multiple aims.	Greece, parturient women without ANS for HBV in one hospital vs. retrospective cohort of ANS participants.	10.6% of women delivering unable to report HBsAg status, 70.4% of women first tested in delivery room were immigrants.	Universal screening	Delivering women who escape prenatal testing more likely to be chronically infected, lack of adherence to maternal prevention measures coupled with low vaccination-induced protection.	Need for better access to routine HBV prenatal screening for immigrant women; presumptive eligibility programmes for immigrant women.
Spada 2011 [33]	Prospective cohort	Evaluation of compliance with the protocol for preventing perinatal hepatitis B.	Italy: All pregnant women coming for delivery in 41 hospitals in 13 regions.	Compliance good, declining spread, also in immigrant populations.	Universal screening	Lack of adherence in public hospitals, in southern Italy and among foreign women.	Focus on foreign pregnant women
Meints 2010 [34]	Retrospective cohort	Description and comparison of infectious diseases.	USA; Immigrant women from multiple global areas.	Asians and Africans more likely to be positive for HBsAg.		Increased risk of receiving substandard care due to cultural, linguistic, financial, legal, systematic and other barriers.	Targeted screening, improvement of testing strategies, more knowledge of disease burden across immigrant groups.
Schrag 2003 [35]	Retrospective cohort, non-systematic review	Adherence with recommendations for screening.	USA; eight surveillance areas in 1998–1999.	Screening rate for HBsAg 96.5%.		Reaching women without prenatal care and administering appropriate interventions to HBsAg-positive women.	Reducing racial disparities in receipt of prenatal testing.
Women with high-risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)							
Hahne 2013 [26]	Systematic review	To inform screening policies; prevalence and cost-effectiveness of screening.	Europe: general population, five sub-groups and data for PWID and blood donors from two European organisations.	HBsAg prevalence in PWID on average nine times higher than in general population.			Universal screening; appraisal of the evidence for screening the general population in mid- and highly endemic countries in Europe.
Jensen 2003 [30]	Prospective cohort	Evaluating efficacy of selective antenatal screening.	Denmark: IDU, sexual behaviour risk, occupational risk.	77% of women at risk according to guidelines were screened.	Selective screening	Misidentification as vulnerable	Universal screening
Rimseliene 2011 [28]	Retrospective case series	Epidemiological study to assess the validity of current risk groups and recommended preventive measures	Norway: Infection register study, all cases reported 1992–2009.	IDUs are the largest risk group for acute hepatitis B; 70% of reported sexually acquired infections from Norway, 29% abroad (48% in Asia, 41% in Europe)	Risk group screening, vaccination of newborns with parents from high-HBV-prevalence countries.	Decreasing number of infections in IDUs, probably due to vaccination, availability of needles and syringes and decreasing number of IDUs.	Universal screening
Schrag 2003 [35]	Retrospective cohort	Adherence with recommendations for screening.	USA; eight surveillance areas in 1998-1999	Street drug use associated with inadequate prenatal care.		Reaching women without prenatal care and administering appropriate interventions to HBsAg-positive women.	

Reference	Study design	Study question	Country, target group definition	Findings	Current screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Other minority groups, e.g. those refusing testing or vaccinations							
Boxall 2004 [60]	Retrospective audit	Are those refusing HIV testing in higher risk of infection	UK; women found to be infected with hepatitis B.	Prevalence of HBV twice as high in women refusing HIV screening than in women accepting.	Universal screening	Significant differences between refusers and acceptors	Integration of HIV screening with other antenatal tests, need to improve screening uptake.

Table 5. Excluded hepatitis B studies

Reference	Study design	Country, target group definition	Comment
Baldo 2000	Prospective cohort	Italy, antenatal clinic attendants in one hospital	Seroprevalence study, no information on screening.
O'Sullivan 2004	Retrospective cohort	Australia, national serological survey, opportunistic sample of all age groups vs. regional ANS database.	Seroprevalence study, no information on non-screened or screening effect
Patton 2014	Non-systematic review	Not specified	No primary data
van Steenbergen 2001	Cohort study	The Netherlands; Amsterdam 1993–1998	Evaluation of screening and neonatal immunisation programme; evaluation of screening and neonatal immunisation programme.
Mur Sierra 2010	Retrospective case series	Spain; pregnant women and their children	One hospital, hepatitis B infection higher in immigrants.
Reekie 2013	Retrospective cohort (register study)	Australia; mothers giving birth	Seroprevalence study, effect of screening not discussed
Loo 2012	Non-systematic review	USA; Minnesota not pregnant especially	No information on antenatal screening
Jeal 2004	Case series	UK, Bristol street-based prostitute health services (not especially for pregnant women).	Sex workers, wrong population.

Table 6. Quality of evidence for hepatitis B cohort studies using the CASP criteria [1]

Study author (year)	Study question	Cohort recruitment	Exposure measurement	Outcome measurement	Confounders identified	Confounders considered	Folow-up complete enough	Folow-up long enough
Migrants and mobile populations including ethnic groups								
Karatapanis 2012	(●)	●	●	●	●	●	●	●
Bjerke 2011	(●)	●	●	●	●	●	●	●
Spada 2011	(●)	●	●	●	●	●	●	●
Papaevangelou 2006	(●)	●	●	●	●	●	●	●
Jensen 2003	(●)	●	●	●	●	●	●	●
Women with high-risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)								
Jensen 2003	(●)	●	●	●	●	●	●	●

Colour code:

● Yes	● Cannot tell	● No

Study question marked (●) denotes studies where the study question is clearly defined but does not fully match the review PICO.
Karatapanis: Prospective cohort of parturient women lacking documented antenatal screening for HBV; control group results reported poorly; MCTC not reported.
Bjerke: Prospective cohort of pregnant immigrants; no comparison group; MCTC not reported.
Spada: Prospective cohort, prenatal screening information by questionnaire at delivery;
Papaevangelou: Prospective cohort, screening information by questionnaire at delivery; MCTC not reported.
Jensen: Prospective cohort
Hahne 2013 is a systematic review on HBV and HCV prevalence and cost-effectiveness of screening (modelling studies). The quality of the publication is confirmed by authors saying that PRISMA methodology has been used, but detailed information on methodology is not available in the publication.
Excluded prospective studies:
Ladhani: Wrong population (children with chronic hepatitis B)

3.5.3 Studies on population groups vulnerable to MTCT of syphilis

Table 7. Studies on population groups vulnerable to MTCT of syphilis

Reference	Study design	Study question	Country, target group definition	Findings	Current screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Migrants and mobile populations including ethnic groups							
Tridapalli 2007 [37]	Prospective cohort	Evaluation of prevalence of syphilis at delivery and neonatal syphilis infection.	Italy, all pregnant women at delivery in one hospital.	Congenital syphilis strictly related to immigration from eastern Europe.	ANS in first trimester.	Young immigrants without adequate prenatal care at highest risk. No HIV+, few IDU.	Repeated screening at 3rd trimester and delivery for immigrants. ANS results to be reviewed in multidisciplinary group.
Connor 2000 [36]	Cost effectiveness analysis.	Identification of possible screening options.	UK	Screening could target pregnant women in Thames region, non-white ethnic groups or those born outside the UK.	Universal screening	Targeted screening would save relatively little money, would not find all, politically and practically difficult.	Universal screening should continue.
Zammarchi 2012 [38]	Case series, epidemiology.	Epidemiological impact of syphilis in pregnancy.	Italy; Tuscany 2000–2010	Syphilis in pregnancy emerging in Tuscany, two different risk patterns for Italian and migrant women.	Universal screening	Italian women more involved in local transmission, difficulty in physically accessing facilities, language barrier, poor knowledge of importance of maternal health.	Additional screening test in the third trimester and educational campaigns, facilitation of access to antenatal care, translation of informative material, use of cultural mediators, reorientation of healthcare services.
Women with high-risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)							
Schrag 2003 [35]	Retrospective cohort, non-systematic review, stratified random sample of births.	Adherence with recommendations for screening	USA, eight surveillance areas in 1998–1999.	Mandatory screening increased participation, positive syphilis test more common among blacks.	ANS for syphilis x 3 for high-risk group.	Risk for not screening: IDU. Failure to test late in pregnancy.	Late antenatal test essential for prevention of neonatal syphilis, reducing racial disparities in receipt of prenatal testing, on-site testing and treatment.
Landes 2007 [52]	Cohort study, epidemiology.	Prevalence of STIs	Ukraine and western European centres; pregnant women with HIV infection.	25% of HIV-infected women diagnosed with one or more STIs during pregnancy.	Universal screening	Risk of co-infection with another STI	HIV-infected women should receive adequate screening for STIs and appropriate counselling and follow-up.

Table 8. Excluded syphilis studies

Reference	Study design	Country, target group definition	Comment
de la Calle 2012	Retrospective case series, epidemiology	Spain	In Spanish, not screening.
Giraudon 2009	Epidemiology	UK; 30 maternity units in London.	Incorrect P; vulnerable groups not described.
Jakopanec 2010	Epidemiology	Norway; whole population.	Incorrect P; mostly men who have sex with men.
Llenas-García 2012	Retrospective case series	Spain; patients in an HIV unit.	Incorrect P; HIV-positive immigrants not pregnant.
Meints 2010	retrospective cohort	USA; one hospital	General article not especially syphilis; included in rubella and hepatitis B.
Psutka 2013	Epidemiology	New Zealand.	Incorrect P; sexual health clinic patients.
Fowler 2008	Epidemiology	USA; blacks and Hispanics.	Not a relevant population for Europe.

Table 9. Quality of evidence for syphilis cohort studies using the CASP criteria [1]

Study author (year)	Study question	Cohort recruitment	Exposure measurement	Outcome measurement	Confounders identified	Confounders considered	Folow-up complete enough	Folow-up long enough
Migrants and mobile populations including ethnic groups								
Tridapalli 2007	(●)	●	●	●	●	●	●	●
Women with high-risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)								
Schrag 2003	(●)	●	●	●	●	●	●	●
Landes 2007	(●)	●	●	●	●	●	●	●

Colour code:

● Yes	● Cannot tell	● No

Study question marked (●) denotes studies where the study question is clearly defined but does not fully match the review PICO.
Tridapalli: Historical comparison group, change of screening test.
Schrag: Register study, no information on MTCT.
Landes: HIV-infected women.

3.5.4 Studies on population groups vulnerable to MTCT of rubella

Table 10. Studies on population groups vulnerable to MTCT of rubella

Reference	Study design	Study question	Country, target group definition	Findings	Current screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
Migrants and mobile populations including ethnic groups							
Bjerke 2011 [27]	Prospective case series	Immune status and factors associated with susceptibility	Norway: pregnant Pakistani immigrants participating in ultrasound screening.	8% of Pakistani immigrants rubella seronegative.	Screening offered to defined risk groups, routine postpartum vaccination.	Uptake of testing and vaccination not studied; difficult to reach target group and compliance problems.	Intensified antenatal screening, postpartum vaccination of negatives.
Matthews 2011 [39]	Serological survey	Antibody status of pregnant women 2005–2009	UK; two hospitals in South Wales.	Significant increase in those with antibody levels <10IU/ml.	Universal screening	No reliable data on post-partum vaccine uptake.	Monitoring of the increase in possible susceptibles with < 10IU/ml.
Hardelid 2009 [40]	Seroprevalence study	Use of dried blood spots linked to maternal characteristics as determinants of rubella seronegativity.	UK; North Thames newly delivered mothers.	Mothers aged under 20 years, women born abroad, from North West London more likely to be seronegative.	Universal screening	Sub-Saharan African and southern Asian mothers seronegative. No reliable data on post-partum vaccine uptake.	Supplementary targeted vaccinations for newly arrived migrant women and their families.
Lemos 2004 [43]	Case study	Outbreak description	Spain; Madrid community in 2003; not especially pregnant women.	19 cases, 14 cases/74%) in women of childbearing age.	Universal screening	Latin American community a new susceptible group.	Vaccination programme for immigrants; women of childbearing age tested for susceptibility at first visit to healthcare services; health education campaign; health professional training.
Vilajeliu 2015 [44]	Seroprevalence study	Assessment of rubella susceptibility, factors associated with susceptible women, adherence to postpartum immunisation.	Spain; women who gave birth in one hospital in Barcelona 2008–2013.	More likely to be susceptible if < 19 years, primiparas or not born in Spain.	Universal screening	Overall susceptibility 5.9% and 7.6% in immigrant women, language barrier may affect adherence to postpartum vaccination.	Increase postpartum vaccination coverage.
Lugner 2010 [45]	Cost-utility analysis	Cost-utility analysis of three scenarios for screening and vaccination programme.	Netherlands	Screening cost-effective if targeted at unvaccinated women in low vaccination coverage regions (LVR).	Immigrant girls (up to 12) and women (up to 18) vaccinated when entering the country.		Ad-hoc screening in pregnant immigrant women and women in LVR to be assessed; all immigrant women of childbearing age should be screened; screening and vaccination to be included in pre-conception advice.
Meints 2010 [34]	Retrospective cohort	Description and comparison of infectious diseases.	USA; Immigrant women from multiple global areas	Rubella immunity ranged from 93%-98%		Increased risk of receiving substandard care due to cultural, linguistic, financial, legal, systematic and other barriers.	Targeted screening, improvement of testing strategies, more knowledge of disease burden across immigrant groups.
Schrag 2003 [35]	Retrospective cohort, non-systematic review, stratified random sample of births.	Adherence with recommendations for screening	USA; eight surveillance areas in 1998-1999	Rubella screening rate 97.3%, post-partum vaccination documented for 65.7% of susceptible women.		Failure to vaccinate post-partum.	Improved postpartum vaccination implementation, reducing racial disparities in receipt of prenatal testing

Reference	Study design	Study question	Country, target group definition	Findings	Current screening policy	Identified challenges for prevention of MTCT	Authors' recommendations
From the effectiveness search							
Byrne 2012 [41]	Seroprevalence study	Factors associated with low rubella antibody levels.	UK; antenatal women tested by NHS Blood and Transplant 2004-2009.	Ethnic minorities at increased risk of rubella susceptibility.	Universal screening	Quality of data collection to monitor rubella susceptibility.	Collection of specific ethnicity data needed for targeted immunisation strategies.
O'Dwyer 2013 [42]	Comprehensive national study	Identification of women who would have benefitted from pre-pregnancy vaccination.	Ireland; all 20 maternal hospitals.	Rubella status known for 96.7% of delivered women; immunity to rubella <95%.	Universal screening	Increased seronegativity associated with increase in immigrants.	Focus on women who are young, nulliparous and born outside the EU; especially from Africa, south-east Asia and the Americas.
Robinson 2006 [46]	Non-systematic review	Rationale and efficacy of immunisation and screening strategies.	Developing and developed countries; rubella immunisation programmes.			Lower compliance with screening if clinician has to order specific tests; barriers to postpartum immunisation; need for reimmunisation of women who serorevert or remain seronegative after vaccination.	Immigrant women of childbearing age should be offered MMR at first encounter with healthcare system.
Women with high-risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)							
Schrag 2003 [35]	Retrospective cohort, non-systematic review, stratified random sample of births	Adherence to recommendations for screening	USA; eight surveillance areas in 1998–1999.	Street drug use associated with inadequate antenatal care.			Improved postpartum vaccination implementation.
From the effectiveness search							
Koumans 2012 [61]	Two population-based surveys.	Description of prenatal screening.	USA	Up to 80% of women or infants with indications failed to receive interventions; 15–49% of susceptible women had documentation of postpartum vaccination.		Inadequate prenatal care; association of rubella susceptibility with white race and illicit drug use.	Improved prenatal screening and administration of indicated interventions.
Other minority groups, e.g. those refusing testing or vaccinations							
Lugner 2011 [45]	Cost-utility analysis	Cost-utility analysis of three scenarios for screening and vaccination programme.	Netherlands	Screening cost-effective if targeted at unvaccinated women in low vaccination coverage regions (LVR).			Ad-hoc screening in pregnant immigrant women and women in LVR to be assessed; acceptance of vaccination should be further investigated among Orthodox protestants.

Table 11. Excluded rubella studies

Reference	Study design	Country, target group definition	Comment
Giraudon 2009	Prevalence study	UK; 30 maternity units in London	Incorrect P; vulnerable groups not described.

Table 12. Quality of evidence for rubella cohort studies using the CASP criteria [1]

Study Author (year)	Study question	Cohort recruitment	Exposure measurement	Outcome measurement	Confounders identified	Confounders considered	Folow-up complete enough	Folow-up long enough
Migrants and mobile populations including ethnic groups								
O'Dwyer 2013	(●)	●	●	●	●	●	●	●
Bjerke 2011	(●)	●	●	●	●	●	●	●
Lugner 2010	n/a							
Women with high risk behaviour: IDU, sex workers, women with partners at increased risk (IDU, bisexuals)								
Koumans 2012	(●)	●	●	●	●	●	●	●
Lugner 2010	n/a							

Colour code:

● Yes	● Cannot tell	● No

Study question marked (●) denotes studies where the study question is clearly defined but does not fully match the review PICO.
O'Dwyer: Retrospective cohort; MCTC not reported.
Bjerke: No comparison group; MCTC not reported.
Koumans: Retrospective cohort; MCTC not reported.
Lugner 2010 is a modelling study (cost-utility analysis based on data from a rubella epidemic in unvaccinated persons) and has been evaluated using Drummond criteria (Table 13).

Table 13. Economic assessment - screening of rubella susceptibility during pregnancy using Drummond checklist [57]

Publication (country)	Comparator	Type of analysis, perspective, time horizon, cohort, prevalence, test assumptions	Findings
Rubella			
Lugner et al. 2010 (Netherlands)	Screening based on vaccination status	• CUA (cost utility analysis) • Healthcare • Lifetime • 16 years screening • 2004–2005 outbreak rubella inf. 32 CRS 11	• The annual expected costs of screening all non-vaccinated pregnant women LVR (1) EUR 17 900, screening all pregnant women in LVR (2) EUR 107 800 and all non-vaccinated pregnant women (3) EUR 266 600. • Preventing a complication of rubella infection during pregnancy leads to an average of 22.9 QALYs gained. • The screening and vaccination programme during lifelong scenarios 2 and 3 would have a cost-effectiveness ratio of between EUR 26 900 and EUR 28 100/QALY gained. • The 16-year period would be cost-effective if targeted at non-vaccinated women in LVR (EUR 1100/QALY gained).

4. Discussion

Very few articles in the literature were found that met the inclusion criteria assessing increased participation of the vulnerable population groups to antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility. This reveals a gap in the research and calls for future efforts to gather more evidence on successful ways of reaching groups currently considered vulnerable. On the other hand, many of the cited studies identified challenges and hurdles in reaching vulnerable groups. Turning these hurdles around and transforming them into goals could help ECDC in the production of a guidance document on strengthening of antenatal screening.

4.1 Limitations

In the literature review for groups vulnerable to MTCT of HIV, hepatitis B, syphilis and rubella, the searches were limited to publications in the English and Nordic languages. This choice was justified by the desire to reduce bias by including several languages, as the language skills of the study group did not cover all languages in the EU/EEA area. Nevertheless, the bias caused by limiting only to English was not considered a major factor since only one of the 426 identified publications (0.2%) were excluded based on language restrictions.

During the course of the project it was decided to keep the focus of this literature review on antenatal screening and not to include antenatal care as a whole. By including antenatal care as an entity and by including the observed perceptions of the users, more relevant challenges and issues could have been found.

Any literature review is dependent on the quality of the search strategies and the ability to find all relevant articles addressing the questions under review. Screening the search results for relevance is always a somewhat subjective process, even when performed in accordance with predefined inclusion criteria. In the process of producing this report, selection of the articles included followed predefined steps and was always carried out by two people. Several search strategies were tested in the various databases, and final strategies were decided upon when no additional significant publications were retrieved by further modification of the algorithms.

The ability of this project to comprehensively identify grey literature (reports and other types of publications not indexed in databases) even in the English and Nordic languages is doubtful. Ancestry searches were used to identify such materials and although this did provide some new references, it is inevitable that there may be other very relevant material which was not identified.

5. Conclusions

This literature review shows a gap in the availability of high-quality evidence (i.e. comparative studies) for interventions to increase the effectiveness of antenatal screening among groups vulnerable to MTCT. Instead, the publications included in this report provide a detailed description of factors that hindering effective antenatal screening among pregnant migrant women, pregnant women with high-risk behaviour or those refusing testing or vaccinations. The authors' recommendations are formulated to address these challenges.

Many of the challenges identified (i.e. communication issues, lack of knowledge and understanding of the importance of antenatal screening) were mentioned repeatedly in several publications. They were also found to be common across the vulnerable population groups and the infections studied.

The prevalence of HIV, hepatitis B, syphilis and rubella susceptibility is often higher among migrant/foreign-born pregnant women and women from ethnic groups than among the general population. These women are often unaware of their infectious disease status and may be newly diagnosed through antenatal screening testing. Having less access to antenatal care services and specific prevention/treatment intervention further adds to the risk of perinatal transmission. Cultural behaviour that inhibits access to sexual health services, fear of stigma and discrimination and restrictive immigration policies were all cited as barriers to antenatal testing. Most studies recommended a universal antenatal screening approach in order to better identify women at risk. Targeted screening or screening by risk mapping would be administratively difficult, politically sensitive and unlikely to achieve satisfactory testing uptake rates.

As expected, exercising high-risk behaviour (i.e. injecting drug use during pregnancy), was shown to predict a diagnosis of infection later during the course of the pregnancy and a lower use of preventive interventions, hence a higher risk of vertical transmission. Women with high-risk sexual behaviour (or with a partner at risk) were more likely to become infected later during pregnancy even if they tested negative during a first trimester screening. Prompt identification of infectious status and appropriate case management for IDU women and repeat testing for women with an increased risk of sexually transmitting infections were suggested as actions which could help minimise the risk of vertical transmission.

Practices that increase uptake of antenatal screening among risk groups are:

- Eliminating communication/linguistic hurdles
- Giving due consideration to cultural sensitivity
- Reducing fear of stigma, criminal convictions and immigration restrictions
- Increasing awareness of the risk of infections for the mother and the newborn and the benefit of antenatal screening.

The review also emphasises the need to identify country- or region-specific vulnerable groups as they may differ across countries.

6. Next steps

The results of this literature review will serve as a basis for ECDC guidance on strengthening antenatal screening programmes in the EU/EEA Member States.

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Appendix 1. Example of the search strategy

Search strategy for Ovid MEDLINE (R)

1. exp Mass Screening/
2. exp Prenatal Diagnosis/
3. exp Neonatal Screening/
4. exp Diagnosis/
5. 1 or 2 or 3 or 4
6. exp Pregnancy/
7. exp Pregnancy Complications/
8. exp Fetus/
9. 6 or 7 or 8
10. ((prenatal or pre-natal or antenatal or ante-natal or pregnan* or fetus or fetal) adj2 (diagnos* or screen*)).ti,ab.
11. 5 and 9
12. 10 or 11
13. exp Syphilis/
14. (syphilis or "great pox").ti,ab.
15. 13 or 14
16. exp HIV Infections/
17. exp Hepatitis B/
18. exp Rubella/
19. (rubella* or "three day measles" or "german measles").ti,ab.
20. 18 or 19
21. 15 or 16 or 17 or 20
22. 12 and 21
23. not (news or comment or letter or editorial or interview).pt.
24. 22 not 23
25. exp Gypsies/
26. exp "Emigrants and Immigrants"/
27. exp Minority Groups/
28. exp Minority Health/
29. exp Ethnic Groups/
30. (migrant* or immigrant* or refugee* or "roma people" or "roma population" or gipsy or gypsies or gipsy or gipsies or romani or romany or romanies or "mobile population*" or traveller* or traveler* or homeless* or "undocumented population*" or "without documentation").ti,ab.
31. 25 or 26 or 27 or 28 or 29 or 30
32. 24 and 31
33. exp Sex Workers/
34. exp Unsafe Sex/
35. exp Substance Abuse, Intravenous/
36. exp Religion/
37. exp Vulnerable Populations/
38. (intravenous drug* adj2 (user* or abuser*)).ti,ab.
39. (prostitute or prostitutes or "sex worker*" or "unsafe sex" or "risk behaviour*" or "risk behaviour*" or "intravenous drug users" or "people who inject drugs" or IDU or "religion and medicine").ti,ab.
40. (vulnerable or disadvantaged or underserved or "sensitive populations" or "sensitive group*" or "hard to reach" or "refusing testing" or "presenting late in pregnan*" or "first pregnan*").ti,ab.
41. 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42. 24 and 41
43. (non-vaccinat* or anti-vaccin* or antivaccin* or "vaccine criticism" or "vaccine hesitancy" or "don't vaccinate" or "do not vaccinate" or "not vaccinated" or "intention to vaccinate" or "willingness to vaccinate").ti,ab.
44. ((refuse* or refusal) adj2 vaccin*).ti,ab.
45. 43 or 44
46. 24 and 45

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