



# **SCIENTIFIC** ADVICE

Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA

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This report from the European Centre for Disease Prevention and Control (ECDC) was coordinated by Teymur Noori, with the support of Marieke J. van der Werf, Tarik Derrough, Erika Duffell, Anastasia Pharris, Jonathan Suk, Helena de Carvalho Gomes, Otilia Mårdh, César Velasco Muñoz, Sara Causevic, Rikke Thoft Nielsen, Takis Panagiotopoulos, Agoritsa Baka, Andrew Amato, Johanna Takkinen, Jan Semenza, Maarit Kokki, Josep Jansa, Piotr Kramarz, Denis Coulombier and Vicky Lefevre.

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# **Abbreviations**

AIDS ART	Acquired immunodeficiency syndrome Antiretroviral therapy
BCG CDC	Bacillus Calmette–Guerin vaccine US Centers for Disease Control and Prevention
СНВ	Chronic hepatitis B
CXR	Chest X-ray
DALY	Disability-adjusted life year
DTaP-IPV-Hib	Diphtheria, tetanus, pertussis, polio, and Haemophilus influenzae type b
EACS	European AIDS Clinical Society
EASL	European Association for the Study of the Liver
EU/EEA	European Union/European Economic Area
ELISA	Enzyme-linked immunosorbent assay
GRADE	Grading of recommendations assessment, development and evaluation
HBcAb	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
HBV HCC	Hepatitis B virus Hepatocellular carcinoma
HCV	Hepatitis C virus
HIC	High-income country
HIV	Human immunodeficiency virus
ICER	Incremental cost-effectiveness ratio
INH	Izoniazid
LMIC	Low- and middle-income countries
LTBI	Latent tuberculosis infection
MMR	Measles, mumps, rubella vaccination
MSM	Men who have sex with men
MTCT	Mother-to-child transmission
NAT	Nucleic acid test
NGO	Non-governmental organization
PCR	Polymerase chain reaction
PEG-IFN PICO	Pegylated interferon Population, intervention, comparison, outcome
PMTCT	Prevention of mother-to-child transmission
PWID	People who inject drugs
QALY	Quality-adjusted life year
RBV	Ribavirin
RIF	Rifampicin
RCT	Randomised controlled trial
RDT	Rapid diagnostic test
ТВ	Tuberculosis
TST	Tuberculin skin test
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
VCT	Voluntary counselling and testing
VPD WHO	Vaccine-preventable diseases World Health Organization
WIIU	

# Glossary

Acceptability	How acceptable the intervention is to the target population in relation to the effect.
Asylum seeker	A person who awaits a decision on the application for refugee status under relevant international and national instruments.
Cost-effectiveness	The extent to which an intervention or prevention programme is effective in relation to its costs, e.g. euro cost per life-years gained.
Feasibility	Ability to implement an intervention in terms of time, money, or other circumstances.
GRADE working group	The GRADE Working Group has developed a common, sensible and transparent approach to grading quality (or certainty) of evidence and strength of recommendations. The GRADE approach is now considered the standard in guideline development.
Health	Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (1).
Health equity	Health equity is the absence of avoidable or remediable health differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically.
Irregular migrant	Is a person who, owing to unauthorised entry, breach of a condition of entry, or the expiry of his or her visa, lacks regular status in a transit or host country. The definition also covers those persons who have entered a transit or host country lawfully but have stayed for a longer period than authorised or subsequently taken up unauthorised employment.
Migrant	A migrant, as defined by the United Nations, is any individual who lives in a country temporarily or permanently apart from his or her usual place of residence for at least a year (2). In the EU/EEA context, migrants include both internal European migrants living outside of their European country of birth, and external migrants originating from outside of the EU/EEA.
Newly arrived migrants	Newly arrived migrants are defined in this guidance as individuals who have migrated to a host country within the EU/EEA in the past five years.
Pre-entry screening	Pre-entry migrant screening refers to migrant screening programmes operating in migrant departure countries, for example for migrants applying for work visas.
Refugee	A person who, owing to a well-founded fear of persecution for reasons of race, religion, nationality, membership of a particular social group or political opinions, is outside the country of his or her nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country (3).

# **Executive summary**

Increased rates of migration to and within the European Union and European Economic Area (EU/EEA) in recent years has made the development of migration policy, including health policy, a priority for the region. A migrant is defined as any individual who lives in a country temporarily or permanently away from his or her usual place of residence for at least a year. Migrants do not generally pose a health threat to the host population. However, some subgroups of migrants, including refugees, asylum seekers, and irregular migrants are particularly vulnerable to infectious diseases and may have worse health outcomes than the host population. In a number of EU/EEA Member States, subgroups of migrant populations are disproportionately affected by infectious diseases such as tuberculosis, HIV, and hepatitis B and C. Consequently, screening and vaccination programmes may be of benefit for newly arrived migrants, i.e. those who have arrived in the EU/EEA within the past five years<sup>1</sup>.

The European health policy framework 'Health 2020' aims to 'significantly improve the health and well-being of populations, reduce health inequalities, strengthen public health and ensure people-centred health systems that are universal, equitable, sustainable and of high quality'. ECDC has sought to support this aim in migrant health by developing evidence-based guidance on the prevention of infectious diseases among newly arrived migrants in the EU/EEA.

# **Objective, method and approach**

The main objective of this guidance is to provide scientific advice, based on an evidence-based assessment of targeted public health interventions, to facilitate effective screening and vaccination for priority infectious diseases among newly arrived migrant populations to the EU/EEA. It is intended to support EU/EEA Member States to develop national strategies to strengthen infectious disease prevention and control among migrants and meet the health needs of these populations.

The guidance has been developed using a series of systematic evidence reviews and the grading of recommendations assessment, development and evaluation (GRADE) evidence-to-decision framework, as well as drawing on the opinions of an ad hoc scientific panel through a consultation and assessment process. ECDC appointed a scientific panel consisting of 21 experts from EU/EEA Member States to review the evidence and express opinions on the evidence-based statements that relate to vulnerable migrant groups. None of the members of the panel declared any conflicts of interest with regard to the topic and their participation in the panel. In addition to the scientific panel, ECDC established an advisory group of experts in infectious disease, public health and migration to participate in meetings in order to select the key infectious diseases for which guidance is needed and to support the review process.

The advisory group and ad hoc scientific panel selected the following key infectious diseases for consideration: active tuberculosis (TB) and latent TB infection (LTBI), HIV, hepatitis B (HBV), hepatitis C (HCV), vaccine-preventable diseases (measles, mumps, rubella, diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type B, strongyloidiasis, and schistosomiasis.

Key overarching questions were:

- Should newly arrived migrants be offered screening for active TB, LTBI, HIV, hepatitis B, hepatitis C, strongyloidiasis, and schistosomiasis? Who should be targeted and how?
- Should newly arrived migrants be offered vaccination for measles, mumps, rubella, diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type B (HiB) and hepatitis B?
- What are the implementation considerations in EU/EEA countries?

The approach involved developing key research questions (PICO: population, intervention, comparison, outcome) and an analytic framework to identify key steps and questions related to evidence of effectiveness along the screening–intervention pathway, in order to formulate search strategies and identify relevant literature.

Search terms and strategies appropriate for each infectious disease were used to search for published literature in PubMed, the Cochrane Database of Systematic Reviews, and Embase from January 2005 to May 2016; grey literature and existing guidelines were also identified. In developing the guidance, ECDC sought to build on existing systematic reviews and randomised controlled trials; in addition, newly developed additional evidence reviews were used to address gaps in the evidence base. The systematic reviews that underpin this guidance were conducted in line with PRISMA<sup>2</sup> reporting guidelines.

<sup>&</sup>lt;sup>1</sup> Screening in this document implies a voluntary action that should be linked to an appropriate intervention; for example, treatment, vaccination, health education.

<sup>&</sup>lt;sup>2</sup> PRISMA is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses. PRISMA focuses on the reporting of reviews evaluating randomized trials, but can also be used as a basis for reporting systematic reviews of other types of research, particularly evaluations of interventions. http://www.prisma-statement.org/

The GRADE evidence-to-decision approach was used to frame evidence and develop statements, and to rate the strength of the evidence-based statements. Evidence-based statements were developed and graded through an iterative consensus process with the advisory group and ad hoc scientific panel. The ad hoc scientific panel members completed a FACE survey (feasibility, acceptability, cost and equity), which was used to inform the guidance. GRADE Pro Panel Voice Software<sup>3</sup> was used to review statements and vote on all evidence-to-decision criteria. The evidence review and guideline development process consisted of three rounds of review: of the evidence review findings, the draft evidence-based statements, and the draft guidance.

## Results

This guidance focuses on newly arrived migrants within the EU/EEA, taking into consideration country of origin, circumstances of migration, and age and gender, where relevant.

Available evidence suggests that it likely to be effective and cost-effective to screen child, adolescent and adult migrants for active TB and LTBI, HIV, HCV, HBV, strongyloidiasis and schistosomiasis, and that there is a clear benefit to enrolling migrants in vaccination programmes and ensuring catch-up vaccination where needed. This is, however, often conditional on the burden of disease in migrants' countries of origin. Box 1 summarises the key evidence-based statements.

# **Box 1. Summary of evidence-based statements for screening and vaccination for infectious diseases among newly arrived migrants**

#### **Active TB**

Offer active TB screening using chest X-ray (CXR) soon after arrival for migrant populations from high-TBincidence countries. Those with an abnormal CXR should be referred for assessment of active TB and have a sputum culture for *Mycobacterium tuberculosis*.

#### Latent TB infection<sup>4</sup>

Offer LTBI screening using a tuberculin skin test (TST) or an interferon-gamma release assay (IGRA) soon after arrival for all migrant populations from high-TB-incidence countries and link to care and treatment where indicated.

#### HIV

Offer HIV screening to migrants who have lived in communities with high HIV prevalence ( $\geq$ 1%). If HIV positive, link to care and treatment as per clinical guidelines.

Offer testing for HIV to all adolescents and adult migrants at high risk for exposure to HIV. If HIV positive, link to care and treatment as per clinical guidelines.

#### **Hepatitis B**

Offer screening and treatment for hepatitis B (HBsAg and anti-HBc, anti-HBs) to migrants from intermediate/high prevalence countries ( $\geq 2\%$  to  $\geq 5\%$  HBsAg.)

Offer hepatitis B vaccination series to all migrant children and adolescents from intermediate/high prevalence countries ( $\geq 2\%$  to  $\geq 5\%$  HBsAg) who do not have evidence of vaccination or immunity.

#### Hepatitis C

Offer hepatitis C screening to detect HCV antibodies to migrant populations from HCV-endemic countries ( $\geq 2\%$ ) and subsequent RNA testing to those found to have antibodies. Those found to be HCV RNA positive should be linked to care and treatment.

#### **Schistosomiasis**

Offer serological screening and treatment (for those found to be positive) to all migrants from countries of high endemicity in sub-Saharan Africa, and focal areas of transmission in Asia, South America and North Africa (see Figure 14).

#### Strongyloidiasis

Offer serological screening and treatment (for those found to be positive) for strongyloidiasis to all migrants from countries of high endemicity in Asia, Africa, the Middle East, Oceania and Latin America (see Figure 15).

#### Vaccine-preventable diseases

Offer vaccination against measles/mumps/rubella (MMR) to all migrant children and adolescents without immunisation records as a priority.

Offer vaccination to all migrant adults without immunisation records with either one dose of MMR or in accordance with the MMR immunisation schedule of the host country.

Offer vaccination against diphtheria, tetanus, pertussis, polio and HiB (DTaP-IPV-Hib)<sup>56</sup> to all migrant children and adolescents without immunisation records as a priority.

Offer vaccination to all adult migrants without immunisation records in accordance with the immunisation schedule of the host country. If this is not possible, adult migrants should be given a primary series of diphtheria, tetanus, and polio vaccines.

For the evidence-based statement on hepatitis B vaccination, please see Section 4.4.

<sup>&</sup>lt;sup>3</sup> Panel Voice is an add-on to the GRADEpro software that supports panel groups during the guideline development process and facilitates online and asynchronous decision making. Available from: <u>https://gradepro.org</u>

<sup>&</sup>lt;sup>4</sup> See recent ECDC guidance on programmatic management of LTBI in the European Union for further guidance on management. Available from: <u>https://ecdc.europa.eu/sites/portal/files/documents/LTBI%20cost-effectiveness%20report.pdf</u>

<sup>&</sup>lt;sup>5</sup> Diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b

<sup>&</sup>lt;sup>6</sup> Vaccination against Hib is only recommended to children up to five years of age.

# **Implementation considerations**

Infectious diseases screening and vaccination programmes for migrants to the EU/EEA should be consistent with public health principles. The success of these interventions depends on both the provision of healthcare services that are responsive to the needs of migrants and the ability of migrant populations to access key services. Key implementation considerations for infectious disease screening and vaccination programmes targeting newly arrived migrants include:

- Ensure all screening and vaccination is voluntary, confidential, non-stigmatising and carried out for the benefit of the individual.
- Provide screening, referral, and linkage to care and treatment for all individuals who require it.
- Address the individual, community and health system barriers (for example, low risk perception; diseaserelated stigma; socio-economic, cultural and linguistic barriers; lack of entitlement to healthcare or to free healthcare) that limit migrants' uptake of screening and vaccination, and subsequent uptake and completion of treatment.
- Consider the unique needs of newly arrived migrants when offering screening and vaccination, in terms of delays to presentation, follow-up appointments, and uptake and completion of treatment, and take steps to reduce post-screening/testing drop-out from care.
- Recognise that newly arrived migrants face a range of issues (for example, housing, employment, mental health problems) that may take precedence over seeking preventative healthcare and that may increase the risks or consequences of infectious diseases.

The ad hoc scientific panel members strongly supported free screening, vaccination and care for key infectious disease for all migrants in the EU/EEA, including irregular migrants.

# **Next steps**

Public health programmes have an important role in improving the health and social determinants of health for newly arrived migrants to the EU/EEA. Priority needs to be given to promoting uptake of screening and vaccination and, in particular, to monitoring uptake of TB, HIV and hepatitis testing and linkage to care and treatment in high-risk migrant populations.

Public health programmes may have to adapt their communication and approaches. Better understanding of migrant perceptions about infectious diseases, screening, testing and vaccination, and the acceptability and accessibility of healthcare services, is critical. Tailored approaches such as multiple testing, integrated care for infectious diseases and other health needs, and migrant-friendly services, are also needed.

Since the vast majority of preventative and curative healthcare for migrant populations is provided by communitybased primary care services, there is a need to ensure that health professionals have sufficient knowledge of migrant health needs and that they have skills in culturally sensitive health education, as well as access to culturally and linguistically appropriate information materials and interpretation support services. Community engagement, through culturally sensitive outreach programmes as well as community-based care, is also critical to improving awareness and uptake of services among migrant populations. Community-based care can improve trust and ease of access to screening and vaccination services. There is an opportunity to learn from the experience of EU/EEA countries that are implementing effective programmes to reach newly arrived migrants through approaches that include culturally competent health promotion and care and use of interpreters, training of community-based primary care professionals, and collaboration with public health and migrant community coalitions.

The process of developing this guidance has highlighted gaps in evidence concerning infectious disease control and vaccination in migrant populations. It has also detected limitations of the evidence on effective and cost-effective delivery of prevention interventions targeting this population. Improvements in surveillance are required to increase the completeness and quality of data and inform more accurate estimates of disease, morbidity and mortality among migrant populations. Research is needed to provide strong evidence of the impact of interventions, challenges around diagnosis and treatment, and more robust data on acceptability, effectiveness, and cost-effectiveness of screening and vaccination programmes targeting migrants. More research, including community-based participatory action research, is also needed on the determinants of health in migrant populations and migrant community perspectives, as is research into multiple-disease screening and roles for screening in community-based primary healthcare services.

# **1. Introduction**

# **1.1 Target populations and definitions**

An international migrant, as defined by the United Nations, is any individual who lives in a country temporarily or permanently apart from his or her usual place of residence for at least a year (2). Migrant populations include refugees, asylum seekers, and others who may have been forced to flee conflict, natural disasters, or economic peril, irregular migrants who reside in the EU/EEA without regular status, and voluntary migrants who seek economic opportunities (4). Some migrant populations may originate from countries where infectious diseases have a high prevalence and/or may have experienced migration journeys that increase the risk of infection. The target population for this guidance is newly arrived migrants, i.e. those who have migrated to the EU/EA within the past five years, who may benefit from being offered screening and vaccination for infectious diseases. Targeting newly arrived migrants also provides an important opportunity for public health and community interventions to prevent, detect, and treat key infectious diseases (5).

## 1.2 Rationale and objective of the guidance

Public health programmes have played an important role in assessing migrants for infectious diseases. Historically, port-of-entry authorities met ships on arrival and conducted screening and quarantine programmes (6). More recently, the number of migrants and diverse modes of travel have reduced the effectiveness of this approach (7). Consequently, evidence-based guidance focusing on migrant populations has been developed to guide and influence public health policy and primary health assessments in countries including Australia, Canada, Ireland, Italy, the United Kingdom (UK) and the United States (US) (5, 8-13). It is also clear that there is a need to improve the delivery of health services and interventions to migrant populations (14). The failure to address migrant rights to healthcare and access to health services, and to consider their unique needs, also risks undermining regional and global efforts to combat the spread of communicable diseases (15, 16).

Many EU/EEA countries have had longstanding and stable migration patterns based on past relationships with countries outside Europe. However, global migration patterns and flows are changing due to political, economic and environmental instability. Migrants to the region are a diverse group, making it hard to generalise about their health needs. However, some migrant populations are disproportionately affected by, or vulnerable to, certain infectious diseases and have low levels of vaccination – reflecting the burden of disease and weak health systems in countries of origin, exposure to infectious diseases while 'en route', and living conditions and barriers to accessing health services after arrival to the EU/EEA (17).

This guidance aims to provide an evidence-based assessment of targeted public health interventions to facilitate effective screening and vaccination for priority infectious diseases among newly arrived migrant populations to the EU/EEA (6, 17). It is intended to support EU/EEA Member States to develop national strategies to strengthen infectious disease prevention and control among migrants and to meet the health needs of this population. While this guidance focuses on screening for infectious diseases and vaccination, it should be noted that certain migrant populations also face an undue burden of non-communicable diseases, and health systems should take an integrated approach to migrant health, ensuring it is non-stigmatising and carried out for the benefit of the individual.

# **1.3 Scope of the guidance**

This guidance document covers key infectious diseases selected by an ad hoc scientific panel: active tuberculosis (TB) and latent TB infection (LTBI), HIV, hepatitis B, hepatitis C, vaccine-preventable diseases (measles, mumps, rubella, diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type B), strongyloidiasis, and schistosomiasis. The scientific panel also took into consideration the following public health values and principles in the development of the statements and guidance: relevance, effectiveness, cost-effectiveness, accessibility, acceptability, feasibility, health equity and community participation.

The following published methods and evidence reviews, many of which focus on the effectiveness and costeffectiveness of vaccination or screening for these key infectious diseases, have provided the foundation for the development of this guidance:

- Prevention and assessment of infectious diseases among children and adult migrants arriving to the EU/EEA: a protocol for a suite of systematic reviews for public health and health systems (18).
- The effectiveness and cost-effectiveness of screening for active tuberculosis among migrants in the EU/EEA: a systematic review (19).
- The effectiveness and cost-effectiveness of screening for latent tuberculosis among migrants in the EU/EEA: a systematic review (20).

- The effectiveness and cost-effectiveness of screening for HIV in migrants in the EU/EEA: a systematic review (21).
- Effectiveness and cost-effectiveness of screening for and vaccination against hepatitis B virus in migrants in the EU/EEA: a systematic review (22).
- The effectiveness and cost-effectiveness of hepatitis C screening for migrants in the EU/EEA: a systematic review (23).
- The effectiveness and cost-effectiveness of screening for schistosomiasis and strongyloidiasis in migrants in the EU/EEA: a systematic review [in press].
- Intervention to improve vaccine uptake and cost-effectiveness of vaccination strategies in newly arrived migrants in the EU/EEA: a systematic review (24).
- Evaluating the accessibility and acceptability of infectious disease interventions among migrants in the EU/EEA: a systematic review (25).
- Linkage to care is important and necessary when identifying infections in migrants: journal article (26).

This guidance has been developed using the GRADE evidence-to-decision framework; it draws on the opinions of an ad hoc scientific panel through a consultation and assessment process (18). Previous ECDC technical reports related to migrant health have addressed prevalence and scientific advice on infectious diseases and vaccinations (17, 27), but not in the form of a comprehensive evidence-based guidance document. This guidance does not cover all interventions directly related to prevention, detection, and management of the key infectious diseases; we suggest clinical guidance (i.e. WHO, EASL (European Association for the Study of the Liver), EACS (European AIDS Clinical Society), etc.) be consulted for additional information.

## **1.4 Target audience for the guidance**

The target audience for this guidance includes national, regional and international policymakers, public health and healthcare planners, health researchers, health professionals, and civil society organisations working with migrant populations. Any adaptation of this guidance should be based on a country-specific assessment that considers both the numbers and types of arriving migrants, and the legal and organisational context in which national health systems operate.

# 2. Background

## 2.1 Migrants and infectious diseases in the EU/EEA

Some migrant populations are at increased risk of specific infectious diseases, including active and latent TB, HIV, hepatitis B and hepatitis C (17, 28). In addition, immunisation coverage is low in some migrant populations, making them more susceptible to vaccine-preventable diseases (VPDs) (29-31). Factors that increase the vulnerability of migrants to infectious diseases include: demographic profile, patterns of disease and weak health systems in countries of origin, high-risk behaviour, exposure to perilous migration journeys that increase the risk of infectious diseases, living conditions in host countries (such as reception centres, overcrowding or shared accommodation), social, economic, cultural and legal barriers in host countries that limit or prevent access to and uptake of healthcare services (28, 32). Social and economic barriers include stigma, discrimination and isolation, and unemployment (4). Cultural and legal barriers include language, religion, health beliefs, and lack of entitlement to healthcare or difficulties in accessing available entitlements (33). The vulnerability of migrant populations to infectious diseases can also be exacerbated by poor living conditions and other determinants of health in the host country (34-37).

## 2.2 Recent trends in migration to the EU/EEA

The EU/EEA comprises 31 Member States, with a total population of 517 million at the end of 2017. Migrants made up 11% of this population in 2017, with 4% being born in another EU/EEA country and 7% originating from outside the EU/EEA (38). 'Short-term' migrants (residing for between 3 and 12 months) are not included in population statistics but, of all first residence permits issued in 2016, 39% were valid for less than a year (39). The above figures are averaged over the EU/EEA, but it is important to note that there are considerable variations between the Member States.

There are also fluctuations in the volume and type of migration to the EU/EEA from year to year. Figure 1 shows annual totals of first residence permits issued, distinguishing between 'routine' reasons for migration (work, family, education, 'residence only' and 'other reasons not specified') and international protection (refugee status, subsidiary and humanitarian protection, unaccompanied minors and victims of trafficking) (40).



#### Figure 1. Annual immigration to the EU/EEA, 2008–2017

Source: Eurostat, Frontex and IOM (40).

Even during the large influx of unauthorised arrivals in 2015 and 2016, most migration to the EU/EEA was for 'routine' reasons. Following the financial crisis in 2007, routine immigration declined until 2012–2013, when it started to rise again. Unauthorised landings (41) and asylum applicants (42) have increased steadily since 2012, although they decreased as a result of the EU–Turkey deal in March 2016, when the main sea route shifted to Italy (43).

As Figure 1 shows, many arrivals in 2015 did not lead to an asylum application until 2016; the backlog of applications only started to decline in 2017. Totals for asylum applications in 2015 and 2016 have been adjusted to

take account of repeat applications by the same person (estimated at 175 000 and 98 000, respectively) (44). In the three years from 2015 to 2017, approximately 56% of the 2 672 000 asylum decisions were positive (45). Of the asylum seekers whose applications were rejected, only about half can be expected to leave, adding approximately 580 000 to the EU/EEA's total number of irregular migrants (46)]. Between 2014 and 2017, 94% of all migrants to the EU28 were hosted in the EU-15 countries (47); for those given international protection, the proportion was 98% (45).

## 2.3 Origins of migrants

Patterns of recent migration to the EU/EEA reflect a range of geographical and historical factors, including European colonialism, and conflicts, for example in Syria. In the 21st century, the number of countries from which migrants to Europe originate has greatly increased. The available data (covering 56% of non-EU/EEA immigrants) show that in 2014, 2015 and 2016, the largest numbers were from Syria (94 000), China (84 000), India (77 000), Morocco (50 000) and the USA (43 000). Migrants originated from 190 different countries globally, 31 of which were the source of more than 10 000 migrants a year. Data on the main countries of birth of immigrants (Annex 1) and asylum seekers (Annex 2) arriving from outside of the EU/EEA is important to give primary healthcare workers and policymakers an indication of which infectious diseases are prevalent in the countries of origin, which can guide screening efforts at countries of destination.

As the prevalence of infectious diseases among newly arrived migrants tends to reflect the prevalence in countries of origin, information about disease patterns in these countries can determine whether screening is justified. For similar reasons, information about immunisation coverage in migrants' countries of origin is also important.

## 2.4 Migrants' access to health services

The right to health is a basic social right. Article 12 of the United Nations (UN) International Covenant on Economic, Social and Cultural Rights, which has been ratified by all EU Member States, enshrines 'the right of everyone to the enjoyment of the highest attainable standard of physical and mental health'. According to the UN Committee on Economic, Social and Cultural Rights – the body entrusted with supervising the application of the Covenant – core obligations derived from this right apply to everyone and do not depend on the regular status of the persons concerned (48). Therefore, they also apply to migrants, both regular and irregular. Target 3.8 of the UN's Sustainable Development Goal on health to provide 'access to quality essential healthcare services, and access to safe, effective, quality and affordable essential medicines and vaccines for all', also applies to migrants.

Concerning the health of migrant children, both prenatal and postnatal, Article 24 of the UN Convention on the Rights of the Child (CRC) provides specifically for children's access to health services and obliges states to 'ensure appropriate prenatal and postnatal healthcare for mothers' (49). The reference to adequate access to healthcare for mothers is motivated by the strong impact that maternal morbidity and mortality may have on children's health. The CRC requires that Member States ensure the provision of necessary medical assistance and healthcare with an emphasis on provision of primary healthcare (50). Article 12 [2] of the UN Convention on the Elimination of all Forms of Discrimination against Women provides similar healthcare rights to pregnant women (51).

At the EU level, the Charter of Fundamental Rights of the European Union (the Charter) includes the right to healthcare under Article 35, which states that 'everyone has the right of access to preventive healthcare and the right to benefit from medical treatment under the conditions established by national laws and practices' (52). The Charter's application is limited to those matters that fall within the scope of EU law. In accordance with Article 168 of the Treaty on the Functioning of the European Union, the EU's role in the field of health is limited to complementing the national policies of the EU Member States, with a focus on improving public health and increasing health security, including surveillance of communicable diseases.

EU secondary law regulates access to healthcare for a variety of categories of migrants:

- **Applicants for international protection**, commonly referred to as asylum applicants, are entitled to necessary healthcare, which must include at least emergency care and essential treatment of illness, as well as necessary medical or other assistance for those who have special needs.
- **Persons granted international protection**, namely refugees and subsidiary protection status holders, have equal access to healthcare to that of a Member State national.
- Various EU law instruments contain a duty by Member States to address the urgent medical needs of people intercepted or apprehended at the border, including those rescued at sea.
- Victims of trafficking in human beings are entitled to necessary medical treatment, including psychological assistance, counselling and information.
- People in return procedures are entitled to the same level of healthcare granted to asylum applicants namely 'emergency healthcare and essential treatment of illness' – if they have been given a period for voluntary departure or if their removal was formally postponed.

EU law does not regulate access to healthcare for migrants in an irregular situation if they do not fall under the specific categories listed above. The level of access to healthcare provided to them differs significantly between EU Member States. Evidence collected by the EU Agency for Fundamental Rights in 2010 showed that only four Member States provided cost-free emergency, primary and secondary healthcare to this group (Belgium, France, the Netherlands and Portugal). In two other countries, cost-free access was provided for emergency and primary healthcare (the UK) or emergency and secondary healthcare (Italy). In the majority of EU Member States, access to healthcare for migrants in an irregular situation is often conditional and restricted to a limited set of services ('emergency care', 'urgent medical aid', 'treatment that cannot be deferred'). Among the EU countries that provide access only to emergency healthcare for migrants, nine require payment for the cost of the emergency healthcare provided. Although in most cases emergency treatment would not be denied, the sums charged can be considerable (53).

In the case of communicable diseases, almost all European countries provide migrants in an irregular situation with access to screening services, but fewer countries provide access to state-funded treatment (54). For example, in 2017, laws and policies limited provision of HIV treatment for irregular migrants in more than half of EU/EEA countries (55). Even when cost-free access to healthcare is provided, practical barriers may prevent migrants from enjoying the right to healthcare. These include unawareness of entitlements, administrative requirements (e.g. proof of lack of financial means; requirement to register with a general practitioner) and, for migrants in an irregular situation, the fear that visits to healthcare services may be reported to immigration law enforcement authorities. In some Member States, there are additional barriers such as the requirement to provide an identity document or proof of residence in the host country or in a particular city (56).

Building on the international and European human rights law framework, the EU Agency for Fundamental Rights has recommended that migrants in an irregular situation should, as a minimum, be entitled to necessary healthcare services, which should include the option of seeing a general practitioner and receiving necessary medicines. There have been calls for a more holistic and inclusive approach to migrant health to be adopted across the EU/EEA, which recognises the health rights of migrants and works towards removing legal, social, and cultural barriers to health services to improve the health of migrants (57).

# 3. Guidance development

# 3.1 Background

The European health policy framework 'Health 2020' aims to 'significantly improve the health and well-being of populations, reduce health inequalities, strengthen public health and ensure people-centred health systems that are universal, equitable, sustainable and of high quality'. In the area of migrant health, ECDC has sought to support this through the development of evidence-based guidance for prevention of infectious diseases among newly arrived migrants to the EU/EEA. The specific objective was to systematically review and synthesise the evidence on infectious diseases screening and vaccination for newly arriving migrants. Using the newly developed GRADE 'evidence-to-decision' approach, ECDC reviewed evidence from high-quality systematic reviews on effectiveness, acceptability, feasibility, equity, resource use and cost-effectiveness of migrant screening and vaccination (18).

## 3.2 Establishment of an ad hoc scientific panel

Setting priorities for public health interventions, particularly when dealing with diverse migrant populations and limited health system resources, has been shown to improve health outcomes (58). There is no standard algorithm to determine public health priorities, although burden of illness, feasibility and economic considerations are all important factors (59, 60). At the outset, therefore, ECDC convened an advisory group consisting of EU/EEA clinical and public health stakeholders in November 2015 to explore the scope, priorities and principles for developing this guidance (61, 62).

Following this initial meeting, ECDC appointed an ad hoc scientific panel, including 21 experts from a range of EU/EEA Member States (see panel members and terms of reference in Annex 3). The main purpose of the panel was to review and assess the evidence base and provide consensus statements on good practices for interventions and service models targeting vulnerable groups. ECDC's process for setting up ad hoc scientific panels to provide independent advice follows a strict methodology and includes the following steps: identification of experts; collecting declarations of interest from experts; evaluating eligibility; and ruling out conflicts of interest of experts through clearance by the ECDC compliance officer. At the end of this process, the ECDC Director formally appoints the panel members.

The ad hoc scientific panel members for this guidance were identified through the ECDC Expert Directory, suggestions from the ECDC Advisory Forum and ECDC experts, and a literature search for experts who have published on this or related topics. Panel members were expected to have experience in critical appraisal of peer-reviewed publications, familiarity with systematic review methods, the application of evidence to decision-making, and expertise in disease prevention and health promotion. In deciding on the composition of the panel, ECDC also took into account country representativeness and the specific expertise and experience of experts. All panel members signed a declaration of interest, which was reviewed by the ECDC compliance officer. None of the members of the panel declared any interests that were considered to be a conflict with regard to the topic and their participation in the panel. Panel members were asked to provide opinions based on their professional and scientific experience, and to do so on a personal basis as an independent expert, not representing the interests of any commercial body, professional body or Member State. The ad hoc scientific panel was officially appointed by the ECDC Acting Director in October 2016.

In addition to the ad hoc scientific panel, ECDC invited experts in infectious disease, public health, and migration to participate in meetings to select the key infectious diseases and support the review process; these people, together with the ad hoc scientific panel, formed the advisory group. The advisory group included representatives from the European Commission, the WHO Regional Office for Europe, and the International Organisation for Migration (IOM).

# 3.3 Selection of key infectious diseases and key questions

The following infectious diseases were prioritised for consideration: active TB, LTBI, HIV, hepatitis B, hepatitis C, vaccine-preventable diseases (measles, mumps, rubella, diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type B), strongyloidiasis and schistosomiasis. Key overarching questions were:

- Should newly arrived migrants be offered screening for active TB, LTBI, HIV, hepatitis B, hepatitis C, strongyloidiasis, and schistosomiasis? Who should be targeted and how?
- Should newly arrived migrants be offered vaccination for measles, mumps, rubella, diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type B (HiB)?
- What are the implementation considerations in EU/EEA countries?

Additional questions of relevance to each specific infectious disease are outlined in the registered systematic review protocol (18).

## 3.4 Development of evidence reviews

With technical support from the Campbell and Cochrane Equity Methods Group

(http://methods.cochrane.org/equity/welcome) and members of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group, a series of systematic evidence reviews was undertaken for each of the prioritised infectious disease areas (see Section 1.3). A detailed description of the methods for the systematic reviews can be found in the registered systematic review protocol (18). In addition, four downloadable supplements to this guidance are available on the ECDC website: the analytic framework, characteristics of included studies for effectiveness and cost-effectiveness, PRISMA flow diagrams on (cost-)effectiveness, and the GRADE profile tables specifying the certainty of evidence.

In summary, the approach involved developing key PICO (population, intervention, comparison, outcome) questions (Table 1]. As anticipated (18) and based on previous work in developing guidance in the area of migrant health (5), migrant populations are underrepresented in randomised controlled trials and other intervention research. When available, studies on high-risk migrant groups were prioritised. However, when migrant-specific studies were lacking, indirect evidence (i.e. studies on general populations which can be extrapolated to interventions that are targeted toward migrants) was used. The GRADE method chosen to develop this guidance states that indirect population or intervention evidence is justified when serious concerns exist, but indirect evidence (63). Where evidence from non-migrant populations was used, input from the expert panel regarding the applicability and validity for migrant populations was sought, and the indirectness of the evidence was reflected in the evidence grade.

#### Table 1. Eligibility criteria used for all diseases

PICO and study characteristics inclusion criteria			
Population	Migrant-specific studies used when available. Studies of any population (e.g. children and adults) that are considered relevant, even if not migrant-specific.		
Interventions	Screening, treatment and vaccine prevention interventions and programmes for the selected diseases are evaluated.		
Comparisons	No screening or comparison of prevention interventions and/or programmes.		
Outcomes	Reduction in morbidity or mortality, including surrogate outcomes or disease transmission.		
Study characteristics	Design: systematic reviews, defined as a review with selection criteria, and search of at least one database.		

As is often the case with evidence-based prevention guidelines, there is a limited number of primary studies that assess clinical outcomes for screening versus no screening of certain conditions. For this reason, analytic frameworks to identify key steps related to evidence of effectiveness along the screening-intervention pathway were developed (all frameworks are published in the systematic reviews underpinning this guidance, see Section 1.3]. This approach guided the formulation of search strategies and identification of relevant literature for each critical step along the screening evidence chain. Search terms and strategies appropriate for each infectious disease were used to search for published literature in PubMed, the Cochrane Database of Systematic Reviews, and Embase (January 2005 to May 2016) and updated where needed up to 2018. In addition, grey literature was sourced via Google, as well as the US Centers for Disease Control and Prevention (CDC), ECDC, UNAIDS and WHO websites. No language restrictions were applied for initial searches; certain review groups restricted language to key European languages for feasibility.

Evidence was considered using a hierarchical approach, whereby meta-analyses, systematic reviews, and evidencebased guidelines were given the most weight, followed by individual randomised controlled trials (RCTs), quasiexperimental studies, observational studies and, lastly, expert opinion. The approach sought to build on existing high-quality evidence. Additional evidence reviews were conducted if gaps were noted in the evidence base.

Two independent team members manually reviewed titles, abstracts and full text of identified citations, selected evidence for inclusion, and compiled evidence reviews and PRISMA flow diagrams in accordance with PRISMA guidelines (64). The methodological quality of included systematic reviews was assessed using AMSTAR (65) and/or individual observational studies using the Newcastle Ottawa scales (66). For each cost-effectiveness study, we extracted data for three specific questions: the size of the resource requirements, the certainty of evidence around resource requirements, and whether the cost-effectiveness results favoured the intervention (67). Finally, the certainty of economic evidence in each study (using the relevant items from the 1997 Drummond checklist) was assessed (68). Tables were created that showed characteristics of included studies, rated the certainty of the effects for pre-selected outcome measures and created GRADE evidence profiles. The systematic reviews that underpin this guidance were done in line with PRISMA reporting guidelines (64) and can be found in the published systematic reviews as outlined in Section 1.3 as well as in the online supplementary material for this guidance, which is available on request.

In addition, a systematic review of qualitative outcomes was conducted to study acceptability and accessibility to screening and vaccination interventions, and to explore how migrants value such interventions (24). A team of experts used the Health Beliefs Model and graded the key findings using the GRADE CERQual method. Results are reported as implementation considerations in the sections of this guidance pertaining to each disease (69).

## **3.5 GRADE approach to develop evidence statements**

Evidence-based statements were developed and graded using the GRADE tool (67) through an iterative evidence consensus process. The review teams developed initial draft evidence-based statements using an evidence-to-decision approach and assigned initial GRADE evidence ratings, which were then revised in consultation with the ad hoc scientific panel.

An initial step was using the GRADE approach to rate the certainty of evidence starting with a simplified categorisation of study types (i.e. meta-analyses and RCTs, observational studies and expert opinion). The rating scheme allows for factors that would raise or lower a level of certainty. Factors that would lower certainty of evidence include risk of bias, inconsistency across the RCTs, indirectness and publication bias; factors that would increase certainty of evidence include large effect size and an observed dose–response effect.

The certainty of evidence rating reflects the extent to which our confidence in an estimate of the effect is adequate to support a particular option. Evidence was graded as high, moderate, low or very low certainty, based on how likely further research is to change our confidence in the estimate of effect (Table 2). Low certainty and very low certainty do not mean absence of evidence for effectiveness, but rather signal potential need for more research to improve the precision of the estimate of effect.

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

We used the GRADE evidence-to-decision approach (67) to frame evidence and develop statements, and ultimately rate the strength of the evidence-based statements. With input from the ad hoc scientific panel, agreement was made to define, assess and report vaccination and screening evidence on the following 11 GRADE evidence-to-decision criteria:

- Is the problem a priority? Assess the burden of infectious diseases in migrant populations and current approaches in the EU/EEA.
- What are the desirable and undesirable effects of the intervention?
- What is the certainty of evidence?
- Values: is there important uncertainty about or variability in how much people value the main outcomes?
- Balance of effects: does the balance between desirable and undesirable effects favour the intervention?
- Resources required: how large are the resource requirements (costs)?
- Certainty of evidence of resource requirements.
- Cost-effectiveness: does the cost-effectiveness of the intervention favour the intervention?
- Equity: What could be the impact on health equity?
- Acceptability: Is the intervention acceptable to key stakeholders?
- Feasibility: Is the intervention feasible to implement?

The evidence from the quantitative evidence reviews and qualitative synthesis was put into GRADE Pro (70) to facilitate presentation of these criteria and draft evidence-based statements (67). Evidence-to-decision criteria state that the larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong option is warranted. The narrower the difference, the higher the likelihood that a weak or conditional option is warranted. The higher the certainty of evidence, the higher the likelihood that a strong option is warranted. When an intervention improves health equity a stronger option may be warranted. The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak or conditional option is warranted. Table 3 outlines the definitions of the GRADE strength of evidence-based statements.

#### Table 3. Interpretation of GRADE strength of recommendation

Strong recommendations	Those in which we are confident that the desirable effects of an intervention outweigh its undesirable effects (strong option for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong option against an intervention). They imply that most individuals will be best served by the recommended course of action and that the recommendation can be adopted in practice or as policy in most situations.
Conditional recommendations	Those for which the desirable effects probably outweigh the undesirable effects (conditional option for an intervention) or undesirable effects probably outweigh the desirable effects (conditional option against an intervention), but appreciable uncertainty exists. Conditional statements imply that most people would want the recommended course of action, but that some would not. For clinicians, this means that they must recognise that different choices will be appropriate for each individual, and that they must help each person arrive at a management decision consistent with his/her values and preferences. Policy making will require substantial debate and involvement of various stakeholders.

## 3.6 FACE survey

The ad hoc scientific panel members completed a FACE survey (feasibility, acceptability, cost and equity). The FACE survey is designed to assess perceptions of: 1) the level of priority for the problem being addressed and 2) barriers or enablers related to the evidence-based statements' feasibility, acceptability, cost, and health equity. The findings from the survey have been incorporated into each disease section in this guidance.

Panel members were presented with 13 screening and vaccination evidence-based statements for the key infectious diseases and asked to rate implementation priorities for each disease under consideration (very low, low, moderate, high). They were then asked to indicate the level of feasibility, acceptability, cost (resource use) and equity for each option based on the FACE constructs (Table 4).

#### Table 4. Constructs of the FACE survey

Constructs	FACE questions
Feasibility	Would the option be sustainable? Would there be important barriers that are likely to limit the feasibility of implementing the option?
Acceptability	Do you feel the option would be acceptable to stakeholders (including your organisation)?
Cost (resource use)	Would the current costs of the intervention be large?
Health Equity	Do you feel the option would positively impact health equity compared to current status? Are there groups or settings (taking into account burden, access and treatment) that might be disadvantaged in relation to the option considered?

## 3.7 Evidence review process and guideline development

The evidence review and guideline development process consisted of the following steps.

First, the evidence synthesis reviews were circulated to the full ECDC advisory group (consisting of the ad hoc scientific panel, other experts, and observers) to assess and provide feedback on proposed evidence-based statements for intervention.

Second, a video conference meeting was held on 8 May 2017 during which the ad hoc scientific panel was presented with the preliminary findings of the evidence reviews for each disease and given the option to provide feedback on the evidence-based statements. The scientific panel then used the GRADE Panel Voice Software (18) to review and vote on all criteria of the evidence-to-decision summaries. Panel Voice allows each panel member to enter a judgment on the evidence and provide narrative comments. FACE categories were classified by the panel's level of agreement as follows: high agreement (>75% of ad hoc panel), medium/moderate agreement (50–75%), and low agreement (<50%). Differences in opinion or interpretation with regard to the guideline statements or the evidence review were resolved through facilitated discussions in teleconferences or direct communication.

Third, the guidance document was developed and circulated to the full advisory group in order to assess the evidence statements for intervention. Following revisions, a draft of the final guidance was sent to the ad hoc scientific panel and ECDC disease leads for final review prior to publication.

# 4. Conclusions

This chapter outlines the evidence and key areas to be taken into consideration when designing and implementing screening and vaccination programmes for key infectious diseases for newly arrived migrants in the EU/EEA. It represents a synthesis of the systematic reviews and input from the ad hoc scientific panel and the advisory group. The conclusions are presented for active TB, LTBI, HIV, hepatitis B, hepatitis C, schistosomiasis and strongyloidiasis, and VPDs, with each section following a similar structure:

- Burden of disease
- Summary of evidence, focusing on effectiveness and cost-effectiveness
- Implementation considerations
- Ad hoc scientific panel opinion
- ECDC assessment
- Evidence gaps and future research needs
- Recommendations from other national and international guidelines

Summary tables provide an overview of the evidence that informed the evidence-based statements for each disease area, with each table presenting:

- Data from publications included in the evidence review, on which conclusions have been based, under the headings of 'effectiveness' and 'cost-effectiveness'
- Strength of the body of evidence from the evidence review: certainty of evidence (GRADE)
- FACE survey results
- Strength of the recommendations
- Implementation considerations

The characteristics of included studies for effectiveness and cost-effectiveness, PRISMA flow diagrams for included studies, and the GRADE profile tables specifying the certainty of evidence for each disease are available on the ECDC website.

# 4.1 Active tuberculosis

## **Burden of disease**

TB is a public health priority in the EU/EEA, and countries have committed themselves to the WHO *End TB Strategy* and its goal of eliminating the global TB epidemic and targets of reducing TB deaths by 95%, cutting new cases by 90% between 2015 and 2035, and ensuring that no family is burdened with catastrophic expenses due to TB (71-73, 74).

The foreign-born population makes up a considerable and increasing number and proportion of all TB cases in EU/EEA countries with low TB incidence (< 10 cases/100 000 population), and this is a challenge for TB elimination efforts in the EU/EEA (72, 74). Between 2007 and 2016, the proportion of reported TB cases in the foreign-born population in the EU/EEA increased from 13.6% to 32.7% (75, 76). There are wide variations across the region: in many low-TB-incidence EU/EEA countries, more than half of all TB cases occur among foreign-born individuals (74) but in EU/EEA countries with a higher TB incidence they make up a minority of cases. A considerable proportion of internal and external migrants within the EU/EEA were born in countries with a high TB incidence (Figure 2].

#### Figure 2. WHO global map of TB incidence



\* Source: Global tuberculosis report 2017. Geneva: World Health Organization; 2017. Licence: CC BY-NCSA 3.0 IGO. Reproduced with permission.

## **Summary of evidence**

Given the disproportionate TB case notifications in migrant populations and increasing TB rates in the EU/EEA, enhanced TB control strategies among migrants will be necessary to achieve TB elimination in the EU/EEA (defined as achieving a rate of less than one case of TB per 1 000 000 population) (77, 78). There are two main approaches to TB control among migrants:

- Identification of active TB with a chest radiograph (CXR) before or soon after arrival in the host country to detect prevalent active TB cases to limit onward transmission. Many low-TB-incidence EU/EEA countries screen migrants for active TB on, or soon after, arrival (79). The migrant groups targeted for screening and the location of screening are different for each country (80, 81).
- Identifying and treating LTBI in migrants from high-TB-burden countries to prevent TB reactivation (80).

### Effectiveness

We developed an analytic framework (19) and included six systematic reviews and one ECDC report that addressed the key questions along the evidence chain for screening for active TB among migrants. These included three systematic reviews on the yield of active TB screening in migrants (82-84), two systematic reviews on the performance of CXR to detect active TB (85, 86), one systematic review on the acceptability of CXR screening (87), and one ECDC report on TB treatment outcomes in Europe among those born in (or outside) the EU/EEA (75).

Three systematic reviews assessed the yield of detecting active TB among migrant populations in CXR screening programmes performed prior to and after arrival in the EU/EEA and other low-TB-incidence countries (82-84). The yield of active TB was heterogeneous across studies and varied by migrant type, timing of screening (before/after arrival) and the setting in which the screening was done, but was consistently higher with higher TB incidence in the country of

origin. Klinkenberg et al. found that the overall yield of active TB screening programmes in migrants upon and after arrival in 26 studies done in EU/EEA countries was 350/100 000 population (82). The yield differed by migrant type (asylum seekers: median 350/100 000, (interquartile range (IQR): 250-410) and other migrants: 170 [100-630]) and by the setting where the screening was conducted (port of arrival: 360 (IQR: 100-5,200); reception/holding centres: 290 (IQR: 100-380); community post arrival: 220 (IQR: 100-380); and occasional screening: 1 720 (IQR: 730-2,740)). Arshad et al. assessed the yield of active TB screening among migrants originating from intermediate- or high-TBincidence countries upon and after entry to low-TB-incidence countries and also found a similar overall yield of active TB case detection of 349/100 000 population. The yield also varied by migrant type (refugees: 1 192 (95% confidence interval (CI): 668-1 717); regular migrants: 284 (95% CI: 204-364) and asylum seekers: 270 (95% CI: 198-342)) and TB incidence in the country of origin (Europe: 236 (95% CI: 131-340); Africa: 655 (95% CI: 319-990); and Asia: 1 117 (95% CI: 625-1 608)) (83). Finally, Aldridge et al. assessed the yield of CXR screening for active TB among migrants in the pre-entry TB screening programmes, a compulsory part of the immigration process with higher coverage than uponor after-entry programmes (84). No overall estimates were presented, but the yield increased steadily with the TB incidence in migrant country of origin. The yield was 19.6/100 000 in migrants originating from countries with a TB incidence of <50/100 000 and 336/100 000 in migrants originating from countries with a TB incidence greater than 350/100 000 (84).

Two systematic reviews addressed the performance of CXR to detect active TB in those >15 years of age. CXR is highly sensitive (98%) and moderately specific (75%) to detect active TB in the presence of any abnormality compatible with TB (85, 86, 88). Screening for TB symptoms is less reliable, with moderate sensitivity (70%) and specificity (61%) (85, 86).

An ECDC report found that TB treatment outcomes were similar or better in those born outside compared with those born inside the EU/EEA (75). More specifically, treatment success was as high in those born outside the EU/EEA (for all regions of origin) compared with those born in the EU/EEA [77.4% vs 74.6%), but their failure rates (0.2% vs 2.4%) and default rates (5.4% to 6.6%) were lower (75). Mitchell et al. conducted a review to determine the acceptability of targeted TB screening and active case finding among vulnerable and at-risk groups and found that TB screening was well accepted by the majority of risk groups, including migrants (85% range (55%-96%)). Lower acceptability was found among persons living with HIV/AIDS and individuals in refugee camps and internally displaced persons (87).

#### Cost-effectiveness

There are very little data on the cost-effectiveness of active TB screening in migrant populations as only three individual studies were identified (89-91). These studies showed a clear benefit of screening with CXR among high-prevalence groups, close contacts of those with known TB, and migrants at entry if they originate from intermediate- or high-TB-incidence countries (defined as >60/100 000 and >120/100 000, respectively) (89-91). These studies demonstrated that increased cost-effectiveness was associated with higher TB incidence in the country of origin, which suggests that programmes will be more cost-effective when targeting migrants from countries of origin with a high incidence TB.

### Implementation considerations

Migrants, particularly refugees, asylum seekers, and undocumented migrants, may be underserved and face a range of socio-economic, cultural and linguistic barriers to accessing healthcare and treatment in the EU/EEA as well as a lack of rights to free healthcare (92). Other barriers include low perception of risk, disease-related stigma, and fear of discrimination by health services (93). Although uptake of TB screening is often high in migrants, those without regular status may avoid voluntary screening programmes (33, 87); migrants may also face barriers to follow-up care and treatment. Adherence to active TB therapy may be challenging for some vulnerable migrants as it requires a minimum of six months of treatment and close follow-up to monitor for drug toxicity (94, 95).

Adherence to TB therapy among migrant populations may be enhanced by engaging non-clinical professionals who can coordinate TB care, providing reminders for clinic visits and through addressing language and cultural barriers (96-101). Front-line healthcare professionals and policymakers will need to understand and address healthcare barriers experienced by migrants to ensure uptake and completion of active TB screening and treatment.

Active screening programmes are limited by the fact that they do not capture or prevent the majority of incident TB cases occurring in the EU/EEA, which occur primarily due to reactivation of LTBI or new acquisition during travel (79, 80). Most TB screening programmes in Europe target asylum seekers and refugees and therefore miss other circulating migrant groups. Coverage is low, and the focus is around on-arrival screening, despite the fact that the risk remains high for several years after arrival (93). Pre-entry CXRs may not cover the majority of migrants in countries such as Italy or Greece, where many arrive through irregular routes. A minimum package of services for TB prevention, diagnosis, treatment, and care for migrants and refugees in the WHO European Region has recently been outlined, which highlights the importance of targeted, culturally sensitive and accessible services, of reducing stigma, and of cross-border collaboration on TB screening and care across the entire migration trajectory (57). Screening programmes for active TB in migrants will need to be tailored to the local TB epidemiology and health system context in host countries (72, 73). Programmes will also need to be adapted to the unique legal, social, and cultural needs of migrant populations, involve migrants in their set-up and delivery, alongside tailored awareness-raising about the benefits of early screening within migrant communities (93).

## Ad hoc scientific panel opinion

The ad hoc scientific panel members were in agreement that active TB case finding in migrant populations is an important TB control strategy as it allows for early detection and treatment, reduces individual morbidity, and prevents onward TB transmission. The panel concluded that the strength of the recommendation was conditional on the prevalence of TB in a migrant's country of origin, and the focus should be on screening migrants from intermediate- to high-TB-incidence countries.

The ad hoc scientific panel were asked for their opinion on the evidence relating to: feasibility, acceptability, cost (resource use), and equity of active TB screening among migrants: high level of agreement (>75% of scientific panel), medium level of agreement (50–75% of scientific panel), and low level of agreement (<50% of scientific panel). The results of the FACE survey were as follows:

- High level of agreement (87%) that active TB screening among migrants is a priority in the EU/EEA.
- Medium level of agreement (64%) that active TB screening among migrants is feasible in the EU/EEA.
- Medium level of agreement (71%) that active TB screening among migrants is acceptable in the EU/EEA.
- High level of agreement (79%) that active TB screening among migrants is equitable in the EU/EEA.

The scientific panel agreed that evidence was very low to moderate quality across all key questions. They also agreed that there were additional considerations to be taken into account when offering screening to migrants for active TB. Healthcare accessibility was considered by all to be a critical issue when designing migrant screening programmes. Programmes need to address the barriers that migrants face in accessing healthcare, including lack of entitlement to free statutory health services, in order to ensure high uptake of screening and linkage to care and TB treatment. Screening migrants increases the complexity of national TB programmes because language and cultural issues will need to be addressed and resourced.

## **ECDC** assessment

## **Evidence-based statement**

Offer active TB screening using chest X-ray (CXR) soon after arrival for migrant populations from high-TBincidence countries. Those with an abnormal CXR should be referred for assessment of active TB and have a sputum culture for *Mycobacterium tuberculosis*.

#### (Certainty of evidence: low)

Active TB case finding in at-risk populations is an important TB control strategy as it allows for early detection and treatment, reduces individual morbidity and mortality, and prevents TB spread to others. The CXR is a highly sensitive and moderately specific test to detect active TB. The yield of active TB screening among migrants and the associated cost-effectiveness consistently increases with increasing TB incidence in the country of origin. Screening uptake and treatment completion, however, may be difficult among vulnerable migrants due to barriers to accessing and remaining in healthcare. Furthermore, active TB screening is limited by the fact that it only captures or prevents a minority of migrant TB cases in the EU/EEA, as most result from reactivation of latent infection after arrival. Significant data gaps limit the ability to confidently prioritise TB control efforts for this population. Despite these limitations and data gaps, the benefits of active TB screening likely outweigh the harms and costs if targeted among migrants originating from high-TB-incidence countries. The optimal threshold of incidence in countries of origin at which to screen is yet to be defined.

Effectiveness	Cost-effectiveness	Certainty of evidence (GRADE)	FACE survey*	Strength of recommendation	Implementation considerations
The yield of active TB detected through CXR screening of migrants was heterogeneous across studies and varied by migrant type and the setting in which the screening was done, but consistently increased with higher TB incidence in a screened migrants' country of origin (82-84). CXR is highly sensitive to detect active TB but to increase specificity must be confirmed with a culture for TB. Presence of symptoms is insufficiently sensitive or specific to detect active TB (85, 86, 88). Active TB treatment is highly effective but adverse events occur in a significant number making close follow-up during therapy critical (75). The optimal threshold of incidence in countries of origin at which to screen is	in migrant populations. Increased cost- effectiveness was associated with	Low	<ul> <li>The ad hoc scientific panel rated active TB screening among migrants in the EU/EEA as follows:</li> <li>High priority</li> <li>Moderate agreement on acceptability</li> <li>Moderate agreement on feasibility</li> <li>High agreement on equitability.</li> </ul>	Conditional recommendation, based on country of origin (intermediate- to high-incidence country of origin).	Migrants face numerous barriers to accessing healthcare including socio- economic, stigma, linguistic and cultural and lack of regular status and insurance that may decrease uptake of TB screening and/or treatment. Programmes should address these barriers to ensure high uptake of screening and linkage to care and TB treatment.

#### Table 5. Evidence synthesis and guidance for active TB screening in migrants

\* FACE categories were classified by the level of agreement of the panel as follows: high (>75% of ad hoc panel), medium (50–75%), and low (<50%).

## **Evidence gaps and future research needs**

Designing highly effective active TB screening programmes requires robust population-based studies on the yield of active TB screening among migrants by age group, data on migration type, determining both the timing of screening and the optimal threshold of incidence in countries where screenings will be conducted, and data on associated cost-effectiveness. Additional studies that determine the absolute and attributable impact of active TB programmes on TB control in low-incidence EU/EEA countries and estimates of adherence to follow-up care and treatment are needed. Finally, evidence on the comparative effectiveness and cost-effectiveness of different TB control strategies (active vs. LTBI screening) for migrants are required to prioritise TB control efforts for this population.

## **Recommendations from other national and international guidelines**

#### Table 6. Active TB screening recommendations for migrants in selected low-TB-incidence countries

Country	When, how and who to test
Australia (102- 104)	<ul> <li>Pre-entry CXR screening required for permanent or provisional visa applicants and some categories of temporary visa applicants (intended duration of stay of ≥ 6 months; healthcare professionals and trainees and child care workers and trainees) if originating from a high-TB-risk country</li> <li>Age-specific requirements:</li> <li>&lt; 2 years – history and physical examination; if positive → CXR</li> <li>2–10 years – history and physical examination + TST or IGRA if coming from a higher TB burden country (not quantified); if positive → CXR</li> <li>11 years and above – history and physical examination + CXR</li> <li>If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and cultures.</li> </ul>
Canada (105- 108)	<ul> <li>Pre-entry screening required for permanent visa applicants and some categories of temporary visa applicants (intended duration of stay of ≥ 6 months) and certain professional groups and applicants; also required for extended visitors' visas ('parents and grandparents super visa') for those coming from a high TB-risk country (defined as a 3-year average TB incidence of &gt;30/100 000 cases of TB).</li> <li>Age-specific requirements: <ul> <li>0–10 years – history and physical examination; if positive → CXR</li> <li>11 years and above – history and physical examination + CXR</li> <li>If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and cultures.</li> </ul> </li> </ul>
France (109)	For all recently arrived migrants, within four months of arrival, a medical visit is recommended that includes tuberculosis screening for migrants arriving from high incidence countries (>40 /100 000].* * An update of current TBI recommendations in France is underway.
Ireland (8)	Post-arrival CXR screening for all migrants from countries with incidence ≥40 cases per 100 000 population         Age-specific requirement:         <16 years or pregnant: TST, unless medical examination → CXR + sputum examination
Italy (13)	The search of active TB diseases should be part of the initial medical assessment of migrants and for all during the reception process. Migrants should be made aware of TB symptoms and should be encouraged to report them. Migrants with cough lasting for more than two weeks should undergo CXRsor – if not available immediately – molecular rapid test to ensure detection and isolation of contagious cases. TST and IGRA are not recommended for the diagnosis of active TB disease. Routine CXR is not recommended in asymptomatic subjects. If TB disease is confirmed, complete care is to be assured, including immediate and free access to treatment and continuity of cure if the patients moves to other reception centres or countries.
UK (110-112)	<ul> <li>Pre-entry screening is required for the migrants who intend to stay in the UK for six months or longer and who come from countries with higher TB burden (not quantified, but list of countries provided). Category-specific requirements:</li> <li>Children below 11 years: symptom screen; if positive → CXR</li> <li>Applicants of 11 years and above: symptom screen + CXR</li> <li>Pregnant women: may choose to be screened with 1) symptom screen + CXR with double shielding, 2) symptom screen + sputum microscopy and cultures or 3) postpone the CXR and TB clearance until after delivery.</li> <li>If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and cultures.</li> </ul>
US (113)	<ul> <li>Pre-entry CXR screening is required for immigrant visa applicants, refugees and asylum seekers.</li> <li>Age-specific requirements:</li> <li>&lt; 2 years - history and physical examination; if positive → CXR</li> <li>2-14 years - history and physical examination + TST or IGRA if coming from a country with a TB incidence of ≥20/100 000; if positive → CXR</li> <li>15 years and above - history and physical examination + CXR</li> <li>If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and culture.</li> </ul>

CXR = chest X-ray; TB = tuberculosis; TST = tuberculin skin test; IGRA = interferon gamma release assays.

# 4.2 Latent tuberculosis infection

## **Burden of disease**

TB control programmes in the EU/EEA have successfully managed to reduce TB rates by 50% over the past 20 years (72, 73, 76, 98). However, the rate of TB decline of 4.3% per year over the past decade (2007–2016) in the region is insufficient to achieve the goal and targets of the WHO *End TB Strategy* (72, 73, 76, 98). It is projected that a mean decline of 18% per year will be necessary to meet the WHO goal and that TB control strategies must be scaled up, including addressing the burden of LTBI (72, 114, 115).

The majority of the active TB cases in migrants in the EU/EEA are due to reactivation of LTBI acquired in the country of origin. In high-TB-burden countries of origin (Figure 2), 22–31% of the population may have LTBI (76, 116, 117). High rates of LTBI, and low treatment completion rates, have been identified in data from migrant screening programmes across Europe (93).

## **Summary of evidence**

WHO has only conditionally recommended LTBI screening among migrants living in low-TB-incidence countries (<10 cases/100 000 population), owing to reservations about implementation and the low quality of evidence of the effectiveness and cost-effectiveness of LTBI programmes in these settings (118). A recent WHO Regional Office for Europe Health Evidence Synthesis Report states that there is evidence for the effectiveness of incorporating screening for LTBI into screening programmes targeting migrants from countries of high TB incidence, but there was a lack of consensus on cost-effectiveness and numerous issues regarding effective implementation (57). We present results of a systematic review on the effectiveness and cost-effectiveness of screening for LTBI among migrants to the EU/EEA.

#### Effectiveness

An analytic framework was developed (20) which included seven systematic reviews that addressed the LTBI screening chain of evidence: three on the test properties of LTBI screening tests (119-121); two on the efficacy and harms of LTBI treatments (122, 123); and two on the LTBI care cascade, including uptake of screening and treatment initiation and completion (124, 125).

Three systematic reviews assessed the properties of the diagnostic tests used in LTBI screening in *Bacillus Calmette–Guérin*) (BCG) unvaccinated populations. The tuberculin skin test (TST), at a 10 mm cut off, and interferon-gamma release assays (IGRAs) were found to have similar and good sensitivity and high specificity to detect LTBI (79% and >97%, receptively) (119, 121). TST is, however, limited by lower specificity (59%) in BCG-vaccinated populations (119). Both tests poorly predicted the development of active TB. The positive predictive value (PPV) and the pooled incidence rate ratios (IRR) estimated by comparing test-positive and test-negative cohorts, for TST and IGRA, were similar (120). The PPV (range) and the IRR (95% CI) was 1–7% and 2.07 (1.38–3.11) for the TST and 0–13% and 2.40 (1.26–4.60) for IGRAs, respectively (120).

Several different regimens to prevent the development of active TB, including rifampicin (RIF) alone or in combination with isoniazid (INH) and INH alone for 6–12 months, are equivalent and have moderate efficacy. Based on the evidence reviewed by the panel, the odds of developing active TB among those who took INH for 6 months compared with placebo was 0.64 (95% CI 0.48-0.83), and the odds of developing TB with the 3–4 months of RIF regimens compared with placebo was 0.41 (0.18-0.86) (122). Similar efficacy was found for the following three different comparisons: RIF monotherapy for 3–4 months vs. INH for 6–9 months; RIF + INH for 3 months vs. INH for 6–9 months and weekly rifapentine (RFP) + INH for 3 months vs. INH for 9 months. The comparative relative risks (RR) with 95% CI for these RIF combinations vs. INH were 0.81 (0.47 to 1.4), 1.08 (0.65 to 1.79) and 0.44 (0.18 to 1.07), respectively (123). RIF-based regimens were better tolerated with lower hepatotoxicity RR (0.15, 95% CI 0.07-0.4) and had better adherence (82% vs 69%, RR 1.19 (95% CI 1.16-1.22)) (123).

The LTBI care cascade – including the uptake of screening and treatment, and initiation (23–97%) and completion (7–86%) of therapy – varied widely among migrants (125). The review by Alsdurf et al. found that only 18.8% of all those eligible for screening completed LTBI therapy, and that this was low for all groups, including migrants (14.3%) (124). This was due to progressive losses at all stages of the care cascade; 71.9% (95% CI 71.8-72.0) completed testing, 43.7% (95% CI 42.5-44.9) completed medical evaluation, 35.0% (95% CI 33.8-36.4) were recommended treatment, and only 18.8% completed treatment (124).

### Cost-effectiveness

We included 16 cost-effectiveness analyses studies; however, the designs and outcomes for these studies were heterogeneous. These studies focused on comparisons between LTBI screening strategies (e.g. TST, IGRA or sequential TST/IGRA), or, among high-risk groups, comparisons with other screening techniques such as CXR for active TB, a combination of CXR/TST, or no screening. Eleven of 16 studies addressed an LTBI screening strategy and included a migrant group, however only three studies were specifically about migrants in EU/EEA countries

(126-128). The cost-effectiveness of screening strategies was dependent on test characteristics, which tests were being compared, the cost of tests, and whether the population was BCG vaccinated.

In four studies, screening with a single-step IGRA was less costly or more cost-effective relative to TST screening in migrants to prevent incident TB (126, 127, 129, 130). Performing an IGRA in migrants 16–35 years of age originating from countries with a TB incidence of >150/100 000 was the most cost-effective LTBI strategy, with an incremental cost-effectiveness ratio (ICER) of approximately GBP 20 000 (EUR 24 000) to GBP 30 000 (EUR 36 000) per active TB case prevented (126, 127). For migrants older than 45 years, the intervention was unlikely to be cost-effective, with an ICER for IGRAs vs. no screening between USD 103 000 and USD 283 000 per QALY gained (EUR 86 000 – EUR 236 000/QALY) (130).

In three other studies, the optimal LTBI testing strategy varied in different high-risk populations (migrants or TB contacts) and was influenced by true LTBI prevalence and prior BCG vaccination (91, 131, 132). In those with a high likelihood of a true positive TST (LTBI prevalence >5%) and who were BCG vaccinated after infancy, sequential TST/IGRA testing was preferred over single TST or IGRA (91, 131). When sequential TST-IGRA testing was compared with no testing, the ICER was EUR 560 (EUR 580) per life year gained (YLG); for IGRA compared with TST-IGRA, the ICER was EUR 730 (EUR 757)/YLG in the scenario when LTBI prevalence was >5%. This was robust across a wide range of LTBI prevalence. In contacts of active TB cases, sequential TST-IGRA testing was also more cost-effective compared with no screening or single-step TST, with an incremental cost per active case prevented of GBP 37 699 (EUR 48 020) – GBP 37 206 (EUR 47 392) (132).

### Implementation considerations

Migrants face barriers that can hinder treatment initiation and completion (125, 133-135), and this is particularly so with LTBI. Preventive treatment will likely be less of a priority compared with other competing priorities for migrants soon after arrival. Individual barriers include the stigma related to TB and its association with HIV, language and difficulties navigating the healthcare system (133). Migrants without regular status may lack the right to healthcare access in many EU/EEA countries (92). Strategies that may improve treatment completion among migrants include reminders for clinic visits, nurse counselling and addressing linguistic and cultural barriers (99-101, 136, 137). Provider barriers include inadequate knowledge of which migrants should be screened or managed, and this requires education and training (133, 138). Addressing barriers at all levels and at each step of the care cascade will be essential to ensure individual and public health benefits of LTBI programmes. Less than half of EU/EEA countries have LTBI programmes for migrants, and there are numerous challenges to developing and implementing new programmes (79, 81, 139). These include the heterogeneity of migrant populations and subgroups affected by TB in EU/EEA countries and economic and operational considerations. LTBI screening programmes will need to be tailored to the local TB epidemiology, TB risk in migrant subgroups, and economic and healthcare capacity in in host countries (72, 73).

## Ad hoc scientific panel opinion

The scientific panel members were in agreement that LTBI screening and treatment among migrant populations is an important TB control strategy and is required to achieve the WHO goal of eliminating TB. The panel concluded that the strength of the recommendation was conditional and that LTBI screening and treatment should focus on migrants from high-TB-incidence countries.

The scientific panel members were asked for their opinion on the evidence relating to: feasibility, acceptability, cost (resource use), and equity of LTBI screening among migrants. The results of the FACE survey showed:

- a high level of agreement (87%) that LBTI screening among migrants is a priority in the EU/EEA;
- a medium level of agreement (57%) that LTBI screening among migrants is feasible in the EU/EEA;
- a medium level of agreement (64%) that LTBI screening among migrants is acceptable in the EU/EEA; and
- a high level of agreement (86%) that LTBI screening among migrants is equitable in the EU/EEA.

The scientific panel agreed that the quality of the evidence was very low to moderate across all key questions. There was, however, a high level of agreement that LTBI among migrants was a priority for the EU/EEA. Given the challenges of acceptability and feasibility of implementing LTBI programmes, the panel agreed that screening and treatment for LTBI would be better targeted at high-risk groups, such as migrants coming from intermediate or high TB endemic countries. For health equity reasons, LTBI screening should be offered to migrants. Some panel members felt that investing in LTBI screening may detract from other health priorities where healthcare resources are limited.

## **ECDC** assessment

## **Evidence-based statement**

Offer LTBI screening using a tuberculin skin test (TST) or an interferon-gamma release assay IGRA soon after arrival for all migrant populations from high-TB-incidence countries and link to care and treatment where indicated.

Migrants account for a large and growing proportion of TB cases in low-TB-incidence EU/EEA countries, and most of these TB cases are due to reactivation of LTBI. Addressing LTBI among migrants will therefore be critical to achieving TB elimination. Tests to detect LTBI (TST and IGRA) when positive poorly predict the risk of developing active disease. All LTBI therapies are equivalent and have moderate efficacy, but RIF-based therapies may be preferred due to lower hepatoxicity and higher completion rates. The LTBI care cascade is weak, and only a small proportion of migrants eligible for screening complete treatment (124) due to barriers to accessing and remaining in healthcare. Limited economic analyses suggest that the most cost-effective approach may be targeting young migrants from high-TB-incidence countries. Significant data gaps limit the ability to confidently prioritise TB control efforts for this population. Widespread implementation of LTBI screening and treatment programmes is constrained by challenges including the heterogeneity of migrant populations at risk, and economic and operational considerations. Despite this, migrant-focused LTBI screening programmes may be effective and cost-effective if they are highly targeted and well implemented.

Effectiveness	Cost-effectiveness	Certainty of evidence (GRADE)	FACE survey <b>∗</b>	Strength of recommendation	Implementation considerations
TST and IGRA have high sensitivity to detect LTBI but when positive, both poorly predict the development of active TB (119-121). All LTBI therapies have low to moderate efficacy; however, RIF-based therapies may be preferred due to lower hepatoxicity and higher completion rates (122, 123). The LTBI care cascade is weak and only a small proportion (<15%) of migrants eligible for screening complete treatment (124, 125).	(>150 cases/100 000 population) (126, 127, 129, 130). Cost-effectiveness increasing TB increasing TB increasing TB	Low	<ul> <li>The ad hoc scientific panel rated LTBI screening among migrants in the EU/EEA as follows:</li> <li>High priority</li> <li>Moderate agreement on feasibility</li> <li>Moderate agreement on acceptability</li> <li>High agreement on equitability</li> </ul>	Conditional recommendation based on country of origin (intermediate- to high-TB-incidence in country of origin)	Migrants face many barriers to accessing healthcare; these socio-economic, linguistic and cultural factors need to be considered. TB-related stigma in migrant communities is an important consideration. Those with irregular status may lack the right to access to healthcare. Challenges to widespread implementation in EU/EEA countries include heterogeneous TB risk among migrants and economic and operational considerations.

 Table 7. Evidence synthesis and guidance for LTBI screening in migrants

\* FACE categories were classified by the level of agreement of the panel as follows: high (>75% of ad hoc panel), medium (50–75%), and low (<50%).

## **Evidence gaps and future research needs**

Better evidence is needed on the individual, combined and attributable population contribution of risk factors leading to progression from LTBI to active TB in migrants. Intervention studies that determine how to improve the identification of target populations and retain them in care, as well as cost-effectiveness studies that assess these interventions, will be needed to develop the highest impact programmes. Ultimately, better diagnostic tests that accurately predict those individuals who will develop active TB, shorter, better tolerated treatment courses, and more effective interventions to promote adherence, will be needed to achieve TB elimination.

## **Recommendations from other national and international guidelines**

### Table 8. LTBI screening recommendations for migrants in selected low-TB-incidence countries

Country	When, how and who to test
Australia (9)	<ul> <li>≤ 35 years of age: offer LTBI screening with TST (cut-off 10 mm) or IGRA</li> <li>&lt;5 years of age, TST preferred, 2–10 years: might have already been performed pre-entry</li> <li>&gt; 35 years of age: based on risk factors and state/territory requirements</li> </ul>
Canada (105)	<ul> <li>There are no routine post-arrival domestic LTBI screening programmes for immigrants in Canada but LTBI screening is recommended for the following groups:</li> <li>Screen immigrants with TST from countries with high TB incidence (&gt;30/100 000] if fibronodular changes on CXR (done during post landing surveillance).</li> <li>Screen all children and adolescents &lt;20 years on arrival or soon after.</li> <li>Screen all refugees aged 20–50 years.</li> <li>Screen those with underlying medical comorbidities that increase the risk of reactivation.</li> </ul>
France (140)	For all children under 15 years of age from high-incidence countries, screening by IDR for latent tuberculosis (expert opinion).*
	* An update of current LTBI recommendations in France is underway
Ireland (8)	<ul> <li>≥16 years of age: initial screen with CXR (&gt;40/100 000]</li> <li>Normal: perform TST if from sub-Saharan Africa or a high incidence country (&gt;500/100 000]</li> <li>Abnormal: rule out active disease, offer LTBI treatment</li> <li>&lt;16 years of age or pregnant: TST (&gt;40/100 000)</li> </ul>
Italy (13)	<ul> <li>Offer TST (alternatively IGRA may be used, in particular if previously vaccinated) to all migrants from high-TB-incidence countries (&gt;100/100 000 inhabitants) who are expecting to stay for at least six months</li> <li>Use TST screening test for children &lt; 5 years.</li> <li>Subjects with positive TST (cut-off ≥10 mm, use the ≥5 mm cut-off if HIV-positive or severely malnourished) or IGRA tests should be offered CXR and other diagnostic tests.</li> <li>If active disease is excluded, subjects with positive TST or IGRA tests should be offered preventive treatment.</li> </ul>
UK (141)	Migrants who are between 16 and 35 years of age and have arrived in England within the previous five years and were born or lived for more than six months in sub-Saharan Africa or countries where TB incidence is ≥150 per 100 000 population are offered LTBI screening and will be treated if positive.
US (142-144)	All newly arrived refugees are tested with TST or IGRA if not done pre-departure; if positive, treatment is offered. Other migrants: 2–14 years of age and originating from countries with a TB incidence of >20/100 000 are offered a TST or IGRA in the pre-arrival setting; if positive, treatment is offered. In the post-arrival setting, screening individuals that are likely to be infected with <i>Mycobacterium tuberculosis</i> and have an intermediate or high risk of disease progression should be prioritised for LTBI screening and treatment.

CXR = chest X-ray; LTBI = latent tuberculosis infection; TB = tuberculosis; TST: tuberculin skin test; IGRA: interferon-gamma release assay.

# 4.3 HIV

## **Burden of disease**

In the EU/EEA, 29 444 HIV diagnoses were reported in 2016 (145). An estimated 15% of people living with HIV (n = 122 000) remain unaware of their HIV-positive status (146), limiting the accuracy of data on HIV prevalence in the EU/EEA. Although the overall number of HIV diagnoses in migrants from countries where HIV is prevalent has declined in the EU/EEA over the past decade, migrants still account for 40% of reported cases (17% from sub-Saharan African countries and 23% from other countries) (145). In 2016, foreign-born cases ranged from <1% of all new HIV diagnoses (Poland, Romania) to >70% of new HIV diagnoses (Ireland, Malta, Sweden) (145). Some migrant groups have a higher frequency of delayed HIV diagnosis associated with high levels of HIV stigma (147, 148), and some subgroups of migrants may participate in high-risk behaviour for HIV, such as multiple sexual partners, low and inconsistent condom use, high alcohol consumption, and drug use (148). While some migrants may acquire HIV in their country of origin (Figure 3), new data suggest that more than half of new infections among migrants occur after their arrival in EU/EEA host countries (104, 149-152).

#### Figure 3. UNAIDS global map of HIV prevalence



\* Source: UNAIDS Report 2016. Geneva: 2016.Reproduced with permission from UNAIDS

## **Summary of evidence**

HIV testing in at-risk populations, including migrants from communities with high (>1%) HIV prevalence, migrant men who have sex with men, migrants who inject drugs, and migrants who sell sex, is an important HIV control strategy as it allows for early detection and treatment, reduces individual morbidity and mortality, and prevents onward transmission. HIV testing is highly accurate, and rapid testing strategies demonstrate acceptability and cost-effectiveness. Limited access to healthcare and HIV-related stigma pose significant barriers to testing uptake and treatment (148, 153).

In WHO's consolidated HIV testing guidelines (2017), WHO recommends community-based HIV testing services (with linkage to prevention, treatment and care services) for key populations (including migrants, refugees and displaced populations), in addition to provider-initiated testing and counselling (154). Similarly, ECDC has recommended that testing be offered to migrants from high-prevalence countries with clear referral pathways to treatment; testing should include undocumented migrants and migrants of uncertain residency status (155). Most EU/EEA countries report having national guidance on HIV testing (102, 156), and at least 22 countries acknowledge that migrants are vulnerable to HIV infection, but six of these countries do not explicitly recommend HIV testing for migrants (157). Currently, there are no EU/EEA-wide HIV testing guidelines or strategies specifically tailored for migrant populations, and questions regarding implementation of such programmes remain.

#### **Effectiveness**

As stated above (Section 3.4), studies on high-risk migrant groups were prioritised. However, when migrant-specific studies were lacking, indirect evidence [i.e. studies on general populations which can be extrapolated to interventions that are targeted toward migrants) was used. Where evidence from non-migrant populations was

used, input from the expert panel regarding the applicability and validity for migrant populations was sought, and the indirectness of the evidence was reflected in the evidence grade.

Using the analytic framework for the systematic review (21), four systematic reviews were identified relating to voluntary testing for HIV (150, 158-160) that reported on outcomes. One review studied rapid testing versus conventional testing<sup>7</sup> in populations at high risk for HIV (150), one examined universal versus selective testing (160), another considered provider-initiated testing versus conventional testing (158), and another looked at telephone outreach testing approaches (159). None of the reviews reported on post-test counselling strategies, linkage to care, or clinical outcomes.

A systematic review conducted by the US Agency for Healthcare Research and Quality reported that HIV testing was accurate (rapid test >90% sensitive, Western blot and ELISA >99% sensitive (160). However, the review found that targeted screening programmes that only test patients with identified risk factors may still miss a proportion of cases (160). The majority of included RCTs studied populations with intermediate ( $\geq$ 0.1%) or high HIV prevalence ( $\geq$ 1%). One RCT, from the USA, studied migrants (161). One meta-analysis reported that providing rapid voluntary testing improved testing uptake and receipt of results in comparison to conventional testing (RR = 2.95, 95% CI: 1.69-5.16) (150). Finally, one RCT showed repeat testing was more likely among individuals receiving community-based rapid testing (RR = 2.28, 95% CI 0.35 to 15.07) (150).

Evidence indicates that treatment reduces the risk of AIDS-defining events and mortality in persons with less advanced immunodeficiency and reduces sexual transmission in discordant couples (162-165). The US review reports universal opt-out rapid testing is associated with higher likelihood of testing compared with physiciandirected, targeted rapid testing (160). Universal testing was also associated with a higher median CD4 count and lower likelihood of CD4 count <200 cells/mm<sup>3</sup> at the time of diagnosis compared with targeted HIV testing, but these differences were not statistically significant (160).

#### Cost-effectiveness

There is very little data on the cost-effectiveness of HIV testing in migrant populations. We identified eight studies on the costeffectiveness of, and resources required for, HIV testing and care (166-173). Three studies commented on HIV testing strategies (170-172). The economic evidence suggests that rapid testing is likely to be preferable to conventional testing across a range of contexts, largely due to the ability to more effectively integrate testing and counselling. One study supports the use of a single rapid test (168), while another suggests possible cost savings with multiple rapid assays (170). Evidence supporting multiple rapid tests, rather than a single rapid test followed by later confirmatory test if positive, is mixed. In low prevalence settings (<0.1%), a single rapid assay is also likely to be cost effective.

### Implementation considerations

People living with undiagnosed HIV infection, and those diagnosed with HIV but not yet on treatment, contribute disproportionately to the number of new HIV infections (174). Uptake by migrants in EU/EEA screening programmes for HIV was found to be high (median 82.46% (range 77.06-96.77)) (167), suggesting that migrants may be proactive about screening. Screening needs to be provided in a culturally appropriate environment and efforts should be made to reduce stigma around disease screening, with more emphasis placed on tackling late presentation among migrants (175). More than half of EU/EEA countries do not provide antiretroviral therapy (ART) free of charge for undocumented migrants (176) – which will undoubtedly impact on other vulnerable migrants reducing the likelihood that these individuals will come forward for testing. Barriers to testing include perception of low risk, fear and stigma of the disease, fear of disclosure, discrimination, financial limitations, poor access to care, and lack of knowledge about where to obtain testing, and lack of entitlement to medical care due to migration status (104, 177, 178). There were low levels of HIV knowledge among certain migrants (177, 178). The most consistent benefit of testing was reassurance of negative status (177). Stigma is an overarching barrier to screening and treatment (177), as is fear that a positive test result may have a negative impact on immigration status or refugee claim (177, 179). ECDC guidance on antenatal screening for infections indicates several approaches for increasing the uptake of antenatal screening among migrant women such as offering appropriate assistance to lower communication barriers (by taking into account language, literacy levels, or individual or cultural specifics) and facilitate access to antenatal care through outreach services and informal networks (180).

<sup>&</sup>lt;sup>7</sup> Rapid voluntary counselling and testing (VCT) refers to voluntary enrolment where results are obtained within 24 hours and includes outreach counselling, results delivery and treatment options. Conventional testing for HIV is defined as traditional laboratory testing techniques for HIV in health care settings where patients have to wait for more than 1 day to receive their results. HIV testing is accurate (Rapid Test >90%, Western Blot and ELISA >99%).

## Ad hoc scientific panel opinion

The scientific panel were in agreement that offering voluntary HIV testing in migrant populations is an important HIV control strategy, and a human right, as it allows for early detection, treatment and prevention of transmission. The panel concluded that the strength of the recommendation was conditional on the prevalence of HIV in the migrants' country of origin or local regions in the EU/EEA. Voluntary HIV screening, either rapid testing or conventional testing, should focus on testing and treating migrants coming from countries with an HIV prevalence rate of  $\geq 1\%$  or migrants belonging to populations at high risk for HIV acquisition (i.e. men who have sex with men, people who inject drugs, and people who sell sex). Addressing late presentation in migrant populations and transmission after arrival was also considered a critical objective of HIV screening programmes targeting this group. Importantly, the scientific panel were in agreement that any screening initiatives need to be accompanied by access to follow-up treatment and care, provided free of charge, and that more efforts need to be made across the EU/EEA to expand access to free ART to all migrants.

The scientific panel were asked for their opinion on the evidence relating to feasibility, acceptability, cost (resource use), and equity of HIV screening among migrants. The results of the FACE survey showed a:

- a high level of agreement (87%) that HIV testing among migrants is a priority in the EU/EEA;
- a high level of agreement (80%) that HIV testing among migrants is feasible in the EU/EEA;
- a high level of agreement (93%) that HIV testing among migrants is acceptable in the EU/EEA; and
- a high level of agreement (93%) that HIV testing among migrants is equitable in the EU/EEA.

The ad hoc scientific panel also agreed that there are additional considerations that need to be taken into account when offering HIV testing to migrant populations. The panel emphasised that testing be voluntary and that access to treatment should be available as part of the testing process. Migrants may require a language interpreter and community rapid testing programmes to improve uptake and repeat of testing. Offering testing to migrants arriving from countries and populations with a high prevalence of HIV should be a priority.

### **ECDC** assessment

## **Evidence-based statement 1**

Offer HIV screening to migrants who have lived in communities with high prevalence of HIV ( $\geq$ 1%). If HIV positive, link to care and treatment as per clinical guidelines.

(Certainty of evidence: low)

### **Evidence-based statement 2**

Offer testing for HIV to all adolescents and adult migrants at high risk for exposure to HIV. If HIV positive, link to care and treatment as per clinical guidelines.

#### (Certainty of evidence: low)

Priority groups for testing include all adolescents and adults from high-prevalence countries ( $\geq 1\%$ ). As a significant proportion of diagnosed cases of mother-to-child transmission of HIV and HBV are reported among migrants from high-prevalence countries, pregnant migrant women from these countries are a priority group for screening (180). All HIV-positive patients should immediately be linked to HIV care and treatment programmes in accordance with WHO (180) and EACS clinical guidelines (181). In time-constrained settings, targeted rapid tests should be used to identify HIV-positive patients. Significant data gaps limit the ability to prioritise HIV testing in communities and primary care settings. However, despite these limitations, the benefits of HIV testing are likely to outweigh the harms and costs if targeted to migrants originating from communities with high prevalence of HIV or at high risk of exposure.

#### Table 9. Evidence synthesis and guidance for HIV testing in migrants

Effectiveness	Cost-effectiveness	Certainty of evidence (GRADE)	FACE survey*	Strength of recommendation	Implementation considerations
Laboratory testing of HIV is >99% sensitive and specific (160). Rapid HIV tests also report high screening accuracy and community effectiveness studies and a systematic review (150) have shown higher uptake for these tests, notably in communities with moderate to high HIV prevalence rates. Antiretroviral treatments are highly effective, and modern combination treatment is shown to reduce morbidity and mortality (162, 163)	data on the cost- effectiveness of HIV testing in migrant populations in the EU/EEA. Studies done in the US, Australia and Canada have demonstrated that rapid and community testing combined with HIV treatments is cost- effective in high prevalence populations >1%; some studies suggest as low as 0.1%. Programmes may use country of	Low	<ul> <li>The ad hoc scientific panel rated HIV screening among migrants in the EU/EEA as follows:</li> <li>High priority</li> <li>High agreement that screening is feasible</li> <li>High agreement that screening is acceptable</li> <li>High agreement that screening is equitable.</li> </ul>	Conditional recommendation based on prevalence in country of origin (>1%) and prevalence in migrants' community in host country.	There are gaps in HIV testing services for migrants in the EU/EEA, irregular (undocumented) migrants, in particular, face difficulties in accessing services, and all migrants may face barriers to screening and treatment. Address contributing structural/organisational barriers include lack of funding for treatment, limited availability of community-based services, limited entitlement to health services.

\* FACE categories were classified by the level of agreement of the panel as follows; high (>75% of ad hoc panel), medium/moderate (50–75%), and low (<50%).

## **Evidence gaps and future research needs**

There are few migrant-specific HIV screening and cost effectiveness studies in the EU/EEA. Future research should study testing in community and primary care settings for high-risk migrant populations. As evidence is emerging of the importance of post-migration HIV acquisition many years after arrival to the EU/EEA (106, 152, 182-184), more research is needed to understand better the determinants of risk and which migrant populations are particularly vulnerable to HIV acquisition. This information is critical to inform and tailor testing, prevention and policy programmes targeted to at-risk migrant populations.

## **Recommendations from other national and international guidelines**

#### Table 10. HIV screening recommendations for migrants in selected low-HIV-prevalence countries

Country	When, how and who to test			
Australia (9)	Offer HIV serology to all refugees greater than or equal to 15 years of age. Those with positive tests should be referred to a local HIV provider.			
Canada (5)	<ul> <li>HIV serology, pre-arrival government screening programme for all immigrants and refugees of ≥ 15 years.</li> <li>Clinical screening: offer HIV serology to high-risk migrants, with informed consent.</li> <li>All adolescents and adults from countries where HIV prevalence is ≥1% (sub-Saharan Africa, parts of the Caribbean and Thailand).</li> <li>Link HIV-positive individuals to HIV treatment programmes and post-test counselling.</li> </ul>			
France (185)	<ul> <li>Yearly HIV screening is recommended for migrants originating from countries of high prevalence, especially sub-Saharan Africa and the Caribbean.</li> <li>HIV screening recommended in association with HBV and HCV screening for migrant populations.</li> </ul>			

Country	When, how and who to test
Ireland (8)	Offer test for HIV Ag/Ab to the following groups: All women attending antenatal services. All those with risk factors for HIV, including but not limited to: - people from high-HIV-prevalence countries (>1%) - people with concurrent sexually transmitted infections - people who inject drugs - sex workers and those who have been trafficked - men who have sex with men (MSM) - people with concurrent TB infection
	Refer all positive cases to specialist services for review.
Italy (13)	<ul> <li>During the second phase of reception, offer all migrants culturally sensitive counselling for HIV.</li> <li>Offer HIV tests to: <ul> <li>all migrants aged ≥ 16 years coming from high-prevalence (1%) countries</li> <li>pregnant and breast-feeding migrant women</li> <li>those exposed to high risk (blood transfusions in country of origin, sexually abused people, or people with multiple sexual partners</li> <li>people with concomitant presence of active TB or IST.</li> </ul> </li> </ul>
	<ul> <li>Migrants &lt; 16 years should be offered an HIV test if they meet at least one of the below criteria:</li> <li>born from HIV-positive mothers</li> <li>early sexual activities</li> <li>history of sexual abuse</li> <li>concomitant presence of active TB or IST.</li> </ul>
UK (186, 187)	HIV testing in the UK is recommended in selected specialist services, in certain clinical, community and home settings where there is risk of transmission to others, and for high risk groups. High-risk groups include people born in a country of high diagnosed HIV prevalence (>1%), those reporting sexual contact with people from countries of high HIV prevalence and black African populations. For all high risk groups, routine testing is recommended annually if negative.
US (10)	<ul> <li>Post arrival (not mandatory prior to arrival)</li> <li>HIV test, universal</li> <li>Testing of all refugees is encouraged. Annual testing should be offered to all (including immigrants/migrants). Repeat testing annually for those from high-prevalence regions and those engaging in high-risk behaviours.</li> <li>Refer to specialist, post-test counselling.</li> </ul>

# 4.4 Hepatitis B

## **Burden of disease**

Hepatitis B virus (HBV) is a public health priority for the (EU/EEA). HBV is a vaccine-preventable and treatable communicable disease. In 2013, five European countries reported a high population prevalence ( $\geq$ 2%) (188) of chronic hepatitis B infection (CHB): Bulgaria (4.25%), Greece (2.33%), Romania (5.49%) (189), Lithuania (2.03%), and Slovenia (3.29%) (190).

CHB is highly prevalent in several areas of the world, notably Africa and Asia (Figure 3). Of the 49 million foreignborn people living in the EU/EEA, it is estimated that approximately 53% come from a country of intermediate/high endemicity (190). The average prevalence of CHB in migrants living in the EU/EEA that were born in an HBVprevalent country is 5.5%, compared with an overall prevalence of 1.12% in the general EU/EEA population (27). The prevalence of CHB is higher in migrants who were refugees or asylum seekers compared with all migrants (9.6% vs. 5.1%) (191). Antenatal screening programmes in Europe report that migrant women account for 1.0 to 15.4% of all antenatal diagnoses of CHB, with an average prevalence that is six times higher than the indigenous female EU/EEA population (192). ECDC estimates that migrants from countries where HBV is highly prevalent ( $\geq$ 2%) account for 25% of all HBV infections in the EU (27) (Figure 3).

Vaccination and screening practices vary across the EU/EEA. Seven of 21 EU/EEA countries for which information was available have a national policy for screening migrants for HBV (193). By contrast, universal HBV screening in antenatal screening programmes is national policy in 23 of 26 countries (194). In 27 of the 31 EU/EEA countries, universal childhood HBV vaccination is recommended, and all 31 countries recommend vaccination for children in high-risk groups.



#### Figure 3. Estimations of worldwide prevalence of chronic hepatitis B virus infection

Source: Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013 (195)

## **Summary of evidence**

### **Effectiveness**

As stated in the methods section (Section 3.4), studies on high-risk migrant groups were prioritised. When migrantspecific studies were lacking, indirect evidence (i.e. studies on general populations which can be extrapolated to interventions that are targeted toward migrants) was used. Where evidence from non-migrant populations was used, input from the expert panel regarding the applicability and validity for migrant populations was sought, and the indirectness of the evidence was reflected in the evidence grade.

Using the analytic framework for the systematic review (22), four systematic reviews (191, 196-198) and five additional studies and guidelines were identified (190, 199-202) that reported on the effectiveness of HBV screening, vaccination and treatment programmes. No RCTs on the effectiveness of screening migrants for HBV were found. Two systematic reviews (196, 197) and two clinical guidelines (200, 201) were identified that report on evidence relevant to the effectiveness of CHB treatment.

Serological tests for HBV screening are considered highly accurate (sensitivity and specificity of >98% for detecting hepatitis B surface antigen) (190). Treatment for chronic infection with interferon-alpha versus no treatment/placebo decreased hepatic events, defined as hepatocellular carcinoma (HCC), and liver-related mortality (RR 0.55 (95% CI 0.43–0.70); p<0.001)) and cirrhotic complications, defined as ascites, hepatic encephalopathy, variceal bleeding and hepatorenal syndrome (RR 0.46, 95% CI 0.32–0.67, P<0.001) (197). Treatment with nucleotide analogues resulted in improvement in intermediate markers of chronic HBV infection including loss of HBsAg compared with placebo RR 2.39 (95% CI 1.16 to 4.94) (196). The 2017 Clinical Practice Guidelines by the European Association for the Study of Liver Disease (EASL) recommends the use of the nucleotide analogues as first-line therapy for chronic HBV (200).

An effective vaccine for hepatitis B has been available for several decades and has been shown to have reduced the prevalence of HBV globally (201, 203-205).

#### Cost-effectiveness

We included nine studies on cost-effectiveness of screening and vaccination (206-214). A Dutch modelling study among a cohort of people with HBV infection comparing the natural history of infection with one-off screening for HBsAg and treating active cases of CHB with entecavir, resulted in an incremental cost-effectiveness ratio (ICER) of screening and treatment compared with no formal screening, of EUR 8 966 per quality-adjusted life year (QALY) gained, with a range of EUR 7 222 to EUR 15 694 in a sensitivity analysis. These values are well below the commonly-used Dutch cost-effectiveness threshold of EUR 20 000 per QALY gained (209).

Among the five studies of migrants to North America, the costs ranged from CAD 6 077 (192) to USD 86 620 (208) per person screened (and treated in the event of a positive result), with the majority of studies estimating programme costs of >USD 20 000 per person per year. Thus, the costs of these interventions were generally considered moderate. The ICER of screening and treatment for HBV, compared to no screening, ranged from USD 36 088 (208) to CAD 40 880 (192) and CAD 101 513 (EUR 72 508] (207) per quality-adjusted life year (QALY) gained. Screening was generally considered cost-effective at the host countries' commonly accepted willingness-to-pay thresholds. Therefore, all cost-effectiveness studies favoured screening and treatment for HBV over the status quo of no (or voluntary) screening. A study found that HBV screening was likely to be cost-effective for populations with a prevalence of HBV  $\geq 2\%$  (207). Two studies of outpatients to US hospitals found that screening may be cost-effective even in populations with a lower than 2% prevalence (0.3%) (215).

Three studies from North America reported on the cost-effectiveness of HBV vaccination compared with no vaccination in adults in mixed populations, including >50% migrants from south Asia and sub-Saharan Africa. These studies found that screening and vaccination in adults was not cost-effective or dominated by the screen and treat strategies (192, 207, 208). Vaccination provides little incremental health benefit for the additional vaccination costs, because vaccination does not change the health outcomes of persons with an existing chronic infection, and prevents only few chronic infections, as an acute HBV infection in adulthood leads to chronic hepatitis in less than 5% of cases (208).

### **Implementation considerations**

Migrants, including refugees, have been shown to accept the value of hepatitis B vaccination (93). Qualitative studies also suggest some migrants will seek HBV screening to gain reassurance or to prevent liver disease (216, 217), but that in some groups there is considerable lack of awareness of this infection (218). Fear of discrimination, stigma, loss of income or social status may, however, decrease uptake of screening and willingness to return for results and/or follow-up appointments (217); screening programmes for HBV will need to consider targeting a wider group of migrants circulating in the EU/EEA, a substantial number of whom will have come from intermediate and/or high endemic areas for HBV. HBV screening programmes have begun to consider community screening approaches and linkage to monitoring and treatment. Qualitative studies report multiple community-based testing strategies (219) for HBV; for example, mobile and home testing (220), internet-based testing (221), and testing in workplaces (222), street festivals (223), restaurants and bars (223), places of worship (224) and educational establishments (225). Recent focus has been placed on multi-disease testing in the primary care context, targeting migrants and offering one blood test for multiple infections in one appointment (HBV, HCV, HIV, latent TB) (215).

A recent systematic review found uptake by migrants to be high to HBV screening initiatives in the EU/EEA (median uptake 87.39% (range 32.34–100.00%)), suggesting acceptability towards HBV screening (93) (supported by other studies (226)). Screening uptake was highest in programmes that involved community partners or received the endorsement of local groups (219). A study of Chinese migrants in the Netherlands offered screening in schools, community centres and churches or at the local public health clinic, with support from migrants for community-based screening and outreach programmes (225).
# Ad hoc scientific panel opinion

The scientific panel was in agreement that HBV screening should be prioritised for migrants coming from highprevalence countries, as it allows for early detection and treatment, reduces individual morbidity, and prevents onward HBV transmission. The strength of the recommendation was deemed conditional on the estimated prevalence of chronic HBV in migrants' country of origin, except in the case of pregnant women, where testing is recommended for all pregnant women irrespective of the prevalence in the country of origin. The panel endorsed vaccination of migrant children and adolescents as an effective public health option to prevent HBV infection and the chronic sequelae of infection. This applied to both migrant children from HBV-endemic countries and other countries as per EU/EEA country childhood vaccination schedules.

The scientific panel were asked for their opinion on the evidence relating to: feasibility, acceptability, cost (resource use), and equity of hepatitis B screening among migrants. The results of the FACE survey showed the following:

- High level of agreement (87%) that hepatitis B screening and vaccination among migrants is a priority in the EU/EEA.
- Medium level of agreement (63%) that hepatitis B screening and vaccination among migrants is feasible in the EU/EEA.
- High level of agreement (76%) that hepatitis B screening and vaccination among migrants is acceptable in the EU/EEA.
- High level of agreement (79%) that hepatitis B screening and vaccination among migrants is equitable in the EU/EEA.

The ad hoc scientific panel agreed that the evidence was of very low to low certainty, but chronic HBV is a potentially treatable disease and the panel felt that early detection may improve outcomes. The panel agreed that vaccination is a priority and that, ideally, catch-up vaccination programmes should be implemented. Programmes should also focus on linking migrants with chronic HBV to monitoring and treatment, overcoming barriers to care such as loss of income, loss of status, and stigma.

## ECDC assessment

#### **Evidence-based statement 1**

Offer screening and treatment for hepatitis B (HBsAg and anti-HBc, anti-HBs) to migrants from intermediate-/highprevalence countries ( $\geq 2\%$  to- $\geq 5\%$  HBsAg).

(Certainty of evidence: low)

#### **Evidence-based statement 2**

Offer hepatitis B vaccination series to all migrant children and adolescents from intermediate-/high-prevalence countries ( $\geq 2\%$  to- $\geq 5\%$  HBsAg) who do not have evidence of vaccination or immunity.

#### (Certainty of evidence: low)

Chronic hepatitis B is a communicable public health priority in the EU/EEA. The disease can be prevented and treated to prevent liver cancer and cirrhosis. The WHO goal of elimination of viral hepatitis as a public health concern by 2030, which the EU has committed to achieve, requires a significant increase in the proportion of people living with CHB who are diagnosed, linked to care, and offered antiviral treatment. Available serological tests are sensitive and specific, and current therapies are effective at reducing progression to cirrhosis and liver cancer. Therefore, countries should consider screening migrants from countries with a HBsAg prevalence >2% for hepatitis B infection and immunity. Those who remain susceptible should be offered vaccination (in accordance with national guidelines), with priority for children and adolescents, and adults with additional risk factors (including people who inject drugs, MSM, people with multiple sexual partners). Testing should be offered to all household contacts and sexual partners of those diagnosed with CHB. Testing is recommended for all pregnant women irrespective of the prevalence in the country of origin.

Effectiveness	Cost-effectiveness	Certainty of evidence (GRADE)	FACE survey*	Strength of recommendation	Implementation considerations
No RCT level evidence was found on screening programs for HBV. No direct evidence was found for the effectiveness of HBV vaccine or screening programmes in migrants. Serological markers are >98% sensitive and specific for detecting hepatitis B surface antigen (190). Evidence of antiviral effectiveness at reducing progression to cirrhosis and liver cancer noted. Studies report a reduction in prevalence of HBV following vaccination in infants, children, health workers, and indigenous populations (198, 227- 229). The degree of effectiveness varied between studies.	Screening is likely to be cost-effective, even in low-prevalence populations (>0.3%) (207, 215). Vaccination of adults without additional risk factors may provide little incremental health benefit for the additional costs (208). Universal vaccination, compared to no vaccination among low- risk adult populations, does not appear to be cost-effective (192, 208, 211).	low	<ul> <li>The ad hoc scientific panel rated HBV screening, treatment and vaccination among migrants in the EU/EEA as follows:</li> <li>High priority</li> <li>Moderate agreement that screening is acceptable</li> <li>High agreement that screening is feasible</li> <li>High agreement that screening is equitable</li> </ul>	Conditional recommendation for screening migrants from intermediate and high-prevalence countries. Strong recommendation for vaccination of migrant children and adolescents.	willingness to disclose hepatitis test results (217). Screening uptake is

#### Table 11. Evidence synthesis and guidance for hepatitis B vaccination and screening in migrants

\* FACE survey high level of agreement (>75% of scientific panel), medium level of agreement (50–75% of scientific panel), and low level of agreement (<50% of scientific panel).

#### **Evidence gaps and future research needs**

Community-based screening studies and related cost-effectiveness studies on migrant populations are required to determine the optimal approach to improve uptake and linkage to monitoring and care. Studies on acceptability and feasibility in the EU/EEA on various high-risk migrant groups are needed to build trust and knowledge to support the testing approach. Research is needed to improve strategies to ensure that vaccination programmes reach all migrant children and adolescents.

# **Recommendations from other national and international guidelines**

#### Who when, how to test/assess Country Australia (9) Screening for hepatitis B infection should be offered to all refugees and for all people born in countries with a HBsAg prevalence >2%. For those diagnosed with chronic hepatitis B: linkage to care, including additional tests, monitoring and treatment. Test household and sexual contacts, vaccinate those susceptible. Canada (5) Screen adults and children from countries where the seroprevalence of chronic hepatitis B virus infection is moderate or high (i.e. ≥ 2% positive for hepatitis B surface antigen), such as Africa, Asia and eastern Europe, for hepatitis B surface antigen, anti-hepatitis B core antibody and anti-hepatitis B surface antibody. Refer to a specialist if positive for hepatitis B surface antigen (chronic infection). Vaccinate those who are susceptible (negative for all three markers). France (230) Screening for hepatitis B is recommended for migrants in association with HCV and HIV testing. Vaccinate against hepatitis B in accordance with existing French recommendations. Ireland (8) Offer testing to all new migrants originating from countries with a HBsAg prevalence of $\geq 2\%$ ; all women attending antenatal services; household or sexual contacts of cases; people who engage in high risk behaviours. Refer positive cases to specialist services; vaccinate all children <10 years of age; vaccinate all migrants from countries with a HBsAg prevalence $\geq 2\%$ ; vaccinate non-immune, high-risk persons. During the second phase of the reception, offer screening (HBsAg, HBsAb, HBcAb) to all migrants from Italy (13) countries with HBsAg prevalence >2%. Regardless of the country of origin, offer tests to migrants who meet at least one of the below criteria: concomitant HIV infection previous blood transfusion intravenous drug addiction multiple sexual partners victim of sexual abuse close contact with HBsAg-positive relatives under immunosuppressive treatment pregnancy Screening should cover HBsAg, HBcAb e HBsAb. In the case of seropositivity to HBsAg, the patient should be sent to a specialist for follow-up and treatment. UK (231-233) Pre-departure for refugees entering through resettlement programmes, and post-arrival for other migrants (including asylum seekers): Hepatitis B testing should be offered to people who were born, brought up in, or resided for a substantial amount of time in countries with an intermediate or high prevalence of chronic hepatitis B infection (2% or greater). Testing should also be offered to sexual and family contacts of persons known to be infected with hepatitis B and to people with other risk factors (such as high number of sexual exposures, illicit drug use, among others). Vaccination for newly arrived migrant infants with uncertain vaccination status is recommended up to first birthday. USA (142) Tested/vaccinated prior to and/or following arrival. Refugees or immigrants who are from, or have lived in, countries with prevalence of chronic HBV infection $\geq 2\%$ or those in high-risk groups should be tested for infection (HBsAq). If negative, vaccination should be offered or serologies should be checked, with vaccination offered to those who are non-immune. Counselling and evaluation for treatment. Vaccinate household contacts.

#### Table 12. HBV screening recommendations for migrants in selected counties

# 4.5 Hepatitis C

# **Burden of disease**

Chronic hepatitis C (CHC) is an important public health problem in the EU/EEA and a leading cause of chronic liver disease and preventable economic burden (234-236). As the infection is largely asymptomatic, people affected often remain undiagnosed and untreated, which may result in progression to cirrhosis and liver cancer (237). The recent advent of short course, orally administered and well-tolerated direct-acting antiviral (DAA) therapies that cures hepatitis C virus (HCV) infection in >95% of cases provides a historic opportunity to address the burden associated with this disease (238). An estimated 3.9 million people in the EU/EEA have CHC infection, with HCV prevalence in EU/EEA countries ranging from 0.1–5.9% (239, 240). Despite the high burden of CHC in the EU/EEA, a modelling study estimated that only 36.4% of people living with CHC have been diagnosed; of these, 12.7% have been treated (239). Europe has endorsed and is committed to the WHO goal to eliminate hepatitis C as a public health threat by 2030 (241). The European hepatitis action plan aims to achieve high uptake along all steps of the HCV 'care cascade' (diagnosis, linkage to care, treatment and cure) for all populations at risk (241).

HCV screening and control programmes in the EU/EEA primarily focus on groups with traditionally recognised risk factors such as people who inject drugs, as they experience the greatest burden of disease (239). Migrants from HCV-endemic countries (anti-HCV prevalence of  $\geq 2\%$ ) are an additional group in the EU/EEA at increased risk of CHC. Migrants from these countries have an average anti-HCV prevalence of 2% and account for a disproportionate number of all HCV cases (14%) in the EU/EAA and up to a half of those living with CHC in some low-HCV-prevalence EU/EEA countries (27). In 2016, the EU/EEA received approximately two million migrants from outside of the EU/EEA, almost 80% of whom are believed to have originated from HCV-endemic countries, with an HCV prevalence generally similar to that in their countries of origin (Figure 4) (27, 242-246).

#### Figure 4. Prevalence of anti-HCV globally in 2015



Source: (247)

#### **Summary of evidence**

Migrants bear a disproportionate burden of HCV in many EU/EEA countries. They are more likely to have been exposed to HCV in their countries of origin through unsafe injections, unsafe medical procedures, or unscreened blood products; however, they are less likely than the native-born #198; #261; #262}. Migrants are older and more likely to have advanced liver disease and hepatocellular carcinoma compared with non-migrants at the time of HCV diagnosis (248-250). This is likely to be due to missed or delayed diagnoses and possibly infection at an earlier age than is the case for other people living with CHC.

In a study from Finland, 62.5% of migrants found to be HCV positive had not been previously diagnosed. In a population-based Canadian study, it took a mean of 10 years after arrival for migrants to be diagnosed with HCV (249, 251). These data suggest that early screening based on HCV prevalence in the country of origin together with linkage to care and treatment could prevent liver-related sequelae in the migrant population. However, few EU/EEA countries have national guidance on testing migrants for HCV (193).

#### **Effectiveness**

As stated in the methods section (Section 3.4), studies on high-risk migrant groups were prioritised. However, when migrant-specific studies were lacking, indirect evidence (i.e. studies on general populations which can be extrapolated to interventions that are targeted toward migrants) was used. Where evidence from non-migrant populations was used, input from the expert panel regarding the applicability and validity for migrant populations was sought, and the indirectness of the evidence was reflected in the evidence grade.

The data identified in this review support the effectiveness and cost-effectiveness of HCV screening in populations at risk for HCV infection, including for migrants originating from intermediate and high-HCV-prevalence countries (anti-HCV  $\geq$ 2% and  $\geq$ 5%, respectively] (23). We included five systematic reviews and one set of guidelines that addressed the HCV screening chain of evidence; two assessed the performance of HCV diagnostic tests (190, 252), three assessed the impact of HCV treatment on preventing HCC and all-cause mortality (n = 3) (253-255) and one considered uptake along all steps of the HCV care continuum (256).

The performance of diagnostic testing for HCV has been summarised in the 2017 WHO Guidelines on Hepatitis B and C testing (190). In populations from low-, middle- and high-income countries WHO estimates the sensitivity and specificity of third-generation HCV EIAs to be 98% and 99%, respectively (190). Point-of-care tests, a strategy that potentially could increase screening uptake, was found to perform well in populations from low-, middle- and high-income countries (252).

The new DAA regimens are the recommended therapy for all HCV genotypes in the EU/EEA. These regimens are well tolerated and cure >95% of infections, defined as achieving sustained viral response (SVR) or negative HCV RNA, 12 weeks after completing treatment, which is considered to be a reliable surrogate outcome (200, 238).

Despite highly sensitive and specific tests to detect HCV and curative HCV therapies, the HCV care cascade in the pre-DAA era was weak (256). In a systematic review of studies of the HCV care continuum in the US from 2003–2013, for example, only 50% of cases were diagnosed and aware of their infection, 27% had HCV RNA confirmatory testing, 16% were prescribed HCV therapy, and 9% achieved SVR (256). A modelling study in Europe published after the search timeframe also demonstrated a weak HCV care continuum: in 2015, only 36.4% of all HCV cases in the EU/EEA were diagnosed, and of these, only 12.7% were treated (237).

#### Cost-effectiveness

Simplified, shorter duration (8–12 week) pangenotypic DAA regimens are now widely recommended for most HCV infections (200). We included six studies that assessed the cost-effectiveness of HCV screening followed by DAA therapy and eight studies that assessed the cost-effectiveness of DAA therapy, all conducted before our search end date in 2016.

Screening for HCV in those treated with DAAs is cost-effective, even at higher 2015 costs. A UK study found that screening pregnant women attending antenatal clinics and treating them following delivery was cost-effective (257). The incremental cost-effectiveness ratio (ICER) for screening and treatment compared with no screening and no treatment was GBP 2 400 (EUR 2 745) per QALY gained. For screening and treating with DAAs compared with no screening and no treatment, the ICER was still cost-effective at GBP 9 139 (EUR 10 455) per QALY gained. A Canadian study also found that screening for HCV in different age groups and then treating with DAAs was cost-effective (207). The ICER for IFN-free DAAs vs. older therapies ranged from CAD 34 359 (EUR 21 977) to CAD 44 034 (EUR 28 166) per QALY gained. The same group published a paper after our search timeframe and found it was cost-effective to screen immigrants from HCV-endemic countries (defined as a seroprevalence of 1.9%) with an ICER of CAD 31 468–34 600 (EUR 20 375–22 403) per QALY gained (258).

Non-pangenotypic DAA therapies were found to be moderately cost-effectiveness in France but had a large budget impact at the 2015 cost of treatment (259). Deuffic-Burban found that DAAs were moderately cost-effective for genotype 1 and 4 at a median threshold of EUR 24 000 per QALY gained and a maximum upper limit of EUR 80 000 per QALY gained; however, wide-scale introduction of these regimens would cost EUR 3.5–7.2 billion. IFN-based regimens were estimated to be more cost-effective for genotypes 2 or 3 at EUR 21 300 to EUR 19 400 per QALY gained regardless of fibrosis stage. Several US studies have also evaluated the cost-effectiveness of DAA therapies compared with older PEG-INF-RBV therapies and found that DAA therapies were moderately cost-effective at a willingness-to-pay threshold of USD 50 000 US (EUR 39 210), but varied significantly by HCV genotype, presence of liver fibrosis, and treatment history (260-265). As the cost of DAA therapies has declined in the EU/EEA over the past two years, CHC treatment is now more affordable, more widely available, and more cost-effective (266-268). With the decrease in DAA costs and the availability of highly effective pan-genotypic medications, HCV screening and DAA therapy is likely to be more cost-effective among persons with all HCV genotypes than the estimates from the studies described above.

# **Implementation considerations**

The tools to achieve HCV elimination in the EU/EEA are available although there are a number of implementation challenges, including identifying all persons at HCV risk and linking those affected to care and treatment. Migrants are disproportionately affected by HCV in some EU/EEA countries and face multiple barriers to accessing healthcare services. Barriers include lack of knowledge and awareness of risk, fear and stigma associated with blood-borne diseases, and socio-economic, linguistic and cultural barriers (177, 269, 270). Screening uptake for HCV has been found to be high in migrant populations in the EU/EEA (median 78.59% (range 32.34-96.77)) (93). HCV screening uptake and linkage to care can be improved by implementing decentralised community-based screening strategies and working with community-based organisations to overcome cultural and language barriers (271-275), or using multi-disease testing approaches whereby HCV testing is offered as a blood test alongside HBV, HIV, and latent TB (215). High rates of screening uptake and of treatment initiation and completion were observed in programmes using community-based screening strategies (272, 274). The EU-HEP SCREEN pilot project implemented community outreach and opportunistic screening in primary care to target migrants in England, Hungary, Scotland and Spain, with rates of screening uptake ranging from 33% to 80% and the highest uptake in primary care opportunistic screening (271, 276). Similarly, the CDC HEP-TLC programme and the Hepatitis Outreach Network (HONE) programme in the USA engaged community-based organisations, and employed outreach workers in non-traditional venues to reach migrant communities. These programmes achieved high levels of screening (50–60%) and linkage to care (65%) (274, 277). Furthermore, an RCT compared integrated point-of-care testing for HCV, HBV, and HIV in primary care among migrants with individual serological testing and found that testing uptake (98% vs. 62%) and linkage to care (90% vs. 83%) was higher among point-of-care testing (278).

The WHO recommends screening persons originating from countries with an intermediate ( $\geq 2\%$ ) and high ( $\geq 5\%$ ) HCV prevalence (190). Recent guidance from the WHO Regional Office for Europe has highlighted the need to increase diagnosis of people living with CHC and linkage to care while taking into consideration the local epidemiology of CHC in groups at risk, the capacity of existing systems, and leveraging already existing prevention and control efforts (204). Each country should assess its capacity to increase HCV testing in at-risk populations, link those living with CHC to care and provide access to HCV treatments. HCV screening and treatment programmes for migrants in the EU/EEA will need to be tailored to their specific needs as well as ensuring universal access to healthcare so as to enhance effectiveness along the entire HCV care continuum.

# Ad hoc scientific panel opinion

The scientific panel members agreed that screening migrant populations for HCV is an important strategy that should be considered in the EU/EEA. Feasibility, cost of new treatment options and limited evidence on migrant screening programmes were identified as concerns. The panel concluded that the strength of the recommendation for HCV screening among migrants and linking and treating those found to be positive was conditional on the prevalence of hepatitis C in the migrants' country of origin.

The scientific panel were asked for their opinion on the evidence relating to: feasibility, acceptability, cost (resource use), and equity of HCV screening among migrants. The results of the FACE survey showed a:

- Medium level of agreement (75%) that HCV testing among migrants is a priority in the EU/EEA.
- Low level of agreement (40%) that HCV testing among migrants is feasible in the EU/EEA.
- Medium level of agreement (60%) that HCV testing among migrants is acceptable in the EU/EEA.
- Medium level of agreement (67%) that HCV testing among migrants is equitable in the EU/EEA.

Although the ad hoc scientific panel agreed that hepatitis C was a priority for the EU/EEA, screening and treating migrants requires addressing cultural and language issues and may, therefore, increase the complexity of programmes. The acceptability of screening and treatment is highly dependent on the cultural sensitivity of and sense of trust in healthcare professionals and their recommendations.

## **ECDC** assessment

# **Evidence-based statement**

Offer hepatitis C screening to detect HCV antibodies to migrant populations from HCV-endemic countries ( $\geq$ 2%) and subsequent RNA testing to those found to have antibodies. Those found to be HCV RNA positive should be linked to care and treatment.

(Certainty of evidence: moderate)

Chronic hepatitis C is an important public health problem in the EU/EEA. The disease leads to cirrhosis and liver cancer in a substantial proportion of people living with undetected and untreated CHC. To address the growing burden of HCV in the EU/EEA and achieve the WHO goal of elimination of viral hepatitis as a public health concern by 2030, those affected should be diagnosed and linked to care and treatment. Migrants originating from HCV-

endemic countries have a higher prevalence for HCV than the native-born population and account for up to a half of the cases in low-HCV-prevalence EU/EEA countries. Highly sensitive and specific tests to detect HCV and curative HCV therapies, although expensive, are available but impact is limited by weaknesses in the HCV care continuum (diagnosis, linkage to care and treatment completion). Lower costs of DAA have made these treatments more available and cost-effective. Patient and provider barriers that contribute to low uptake and losses across the HCV care cascade need to be addressed. The effectiveness of HCV screening may be increased through integration with screening for other diseases, such as HIV and HBV, and through the use of community-based and culturally and linguistically adapted approaches to service delivery.

Effectiveness	Cost- effectiveness	Certainty of evidence (GRADE)	FACE survey*	Strength recommendation	Implementation considerations
Enzyme immunoassays (EIAs) are highly sensitive (98%) and specific (99%) to detect anti-HCV antibodies (190). EIA point-of-care testing is almost as sensitive and specific as blood-based testing and may be more convenient for the patient (252). Both tests need to be confirmed with a nucleic acid test (NAT) to ensure the presence of active virus (190). DAA therapy is curative in most patients (>95%) and is well tolerated but is very expensive (238). Despite excellent diagnostic tests and therapies, the HCV care cascade in the pre-DAA era was weak, with only ~35% of patients being diagnosed and 16% offered therapy (256).	genotypes 2 & 3. Introducing DAA regimens on a wide scale would have a substantial budget impact of EUR 3.5- 7.2 billion at the 2015 cost of therapy With lower DAA costs, HCV screening and DAA therapy is more cost-effective than the estimates from the included studies.	Moderate	<ul> <li>HCV screening among migrants in the EU/EEA was rated as follows:</li> <li>Medium priority</li> <li>Low agreement that screening is feasible</li> <li>Moderate agreement that screening is acceptable</li> <li>Moderate agreement that screening is equitable.</li> </ul>	Conditional recommendation based on intermediate to high HCV prevalence (≥2%) in country of origin.	Migrants bear a disproportionate burden of HCV in the EU/EEA; patient, provider and health system barriers need to be addressed to ensure high uptake along the entire HCV care continuum. At the patient level, addressing stigma and cultural and linguistic barriers will be required. Providers will need to be educated about the importance of screening migrants from intermediate- and high-HCV-endemic countries for HCV.

#### Table 13. Evidence synthesis and guidance for hepatitis C screening in migrants

\* FACE categories were classified by the level of agreement of the panel in the following manner; high (>75% of ad hoc panel), medium (50–75%), and low (<50%).

#### **Evidence gaps and future research needs**

Although DAA regimens are now recommended for all HCV genotypes in the EU/EEA (200), there is no specific data on the effectiveness or cost-effectiveness of screening and treating with these medications in migrants in the EU/EEA. There are also few studies on uptake across the HCV care continuum in different EU/EEA countries in the DAA era. Finally, there is little data on the liver-related outcomes, deaths and economic burden due to undetected/untreated HCV among migrants in the EU/EEA.

# **Recommendations from other national and international guidelines**

# Table 14. Hepatitis C screening recommendations for migrants in selected low-HCV-prevalence countries

Country	When, how and who to test
Australia (9)	Offer testing when risk factors are present or from a country with high prevalence (>3%). Test with anti-HCV antibodies; if positive, request HCV RNA test and link those positive to care.
Canada (5)	Recommendation is to screen with Anti-HCV antibodies for all immigrants from countries of high prevalence $(>3\%)$ ; if positive, link to care
Ireland (279)	<ul> <li>Offer test for anti-HCV to: <ul> <li>all migrants who originate from countries with a prevalence of chronic hepatitis C of ≥ 2%;</li> <li>those with a history of hepatitis C risk exposure/behaviour including people who inject drugs and men who have sex with men.</li> </ul> </li> <li>Offer test for HCV RNA to all those who have a positive anti-HCV result.</li> <li>Refer all positive cases to specialist services for review.</li> <li>Vaccinate those who are non-immune to hepatitis A and/or hepatitis B with hepatitis A and/or hepatitis B vaccine.</li> </ul>
Italy (13)	<ul> <li>During the second reception phase, offer screening tests (HCV-Ab) to all migrants coming from high HCV-RNA-prevalence (&gt; 3%) countries</li> <li>Regardless the country of origin, offer tests to those migrants with: <ul> <li>concomitant HIV infection</li> <li>previous blood transfusion</li> <li>intravenous drug addiction</li> <li>abnormal liver tests</li> <li>risk factors for parenteral transmission</li> </ul> </li> <li>Migrants with positive HCV-Ab test should be tested for HCV-RNA and sent to a specialised centre for follow-up of the diagnosis and, if positive, treatment.</li> </ul>
UK (232, 280)	Offer testing by Anti-HCV antibodies to people from countries where hepatitis C is endemic (prevalence 2% or greater) and confirm positive results with HCV RNA, either pre-entry or post-arrival.
US (142)	Offered to those with risk factors, no special targeting for immigrants from high-prevalence countries.
France (281, 282)	Screening is recommended for persons originating in, or receiving care, in countries known or presumed to have high prevalence of HCV (south-east Asia, Middle East, Africa, South America). Expert recommendations: screening for hepatitis C is recommended for migrants in association with hepatitis B and HIV testing.

# 4.6 Strongyloidiasis and schistosomiasis

# **Burden of disease**

The public health impact of two neglected parasitic diseases, schistosomiasis and strongyloidiasis, has increased in non-endemic regions due to increased global migration flows (283-285). Although the real burden of the disease has always been underestimated due to poorly sensitive diagnostic methods used in low-resource settings (285), recent estimates report that *Strongyloides stercoralis* infects around 370 million people globally (285). Likewise, *Schistosomiasis* spp. infects more than 200 million people, causing more than 1.53 million disability-adjusted life years (DALYs) (286-288).

Human schistosomiasis is caused by different species of the trematode *Schistosoma* spp., *S. mansoni* being the most prevalent and distributed in Africa, America, the Middle East and the West Indies, followed by *S. haematobium* in Africa and the Middle East and *S. japonicum* in east and south-east Asia (289). Strongyloidiasis is caused by the nematode *Strongyloides stercoralis* and, although it generally occurs in subtropical and tropical countries, it can be present in temperate countries with favourable conditions (290).

Of all helminthic infections, both schistosomiasis and strongyloidiasis have characteristics which make them appropriate for screening. First, most infected subjects are asymptomatic (291s) and unaware of infection (292), or complain of very mild unspecific symptoms (289). Second, both diseases are considered chronic conditions (292). *S. stercoralis* replicate indefinitely inside the human host through an auto-infective cycle, causing lifelong infection if left untreated (292). Schistosomiasis can remain as a subclinical infection for years, leading to long-term complications (293). Third, both infections can cause potentially severe conditions. *S. stercoralis* can cause disseminated infections or hyper-infections with fatal outcomes in immunosuppressed patients (293). Chronic schistosomiasis is the result of an immune-mediated granulomatous response to trapped eggs that produces organ-specific manifestations, which are mainly chronic urogenital and/or hepato-intestinal complications (289, 294, 295). There are little data on the burden of these diseases among migrants in the EU/EEA. Our estimates were derived from small observational studies from selected countries.

Few studies have assessed the prevalence rate of schistosomiasis in European countries, although a recent study shows prevalence higher than 17% in sub-Saharan African migrants (296). Prevalence of schistosomiasis in endemic countries remains high, particularly in sub-Saharan African countries, which account for around 90% of all reported cases annually (289). Prevalence rates of 10%–>50% for *S. haematobium* infections have been reported in some sub-Saharan African countries and the Middle East (287). Prevalence rates of 1%–>40% have been reported for *S. mansoni* in sub-Saharan Africa, Brazil, Suriname and Venezuela, and for *S. japonicum* in Indonesia, parts of China and south-east Asia (287-289, 296, 297) (Figure 5).

For strongyloidiasis, data derived from refugee populations originating from south-east Asia and Africa showed prevalence rates of between 0.8% and 4.3% using stool microscopy; higher rates of between 9% and 77% were reported using serum antibody-detection assays in refugees from south-east Asia (297). In the EU/EEA, prevalence rates of strongyloidiasis of 3.3%, 4.2% and 5.6% were reported in Italy, Spain and France, respectively, mainly in migrant populations or expatriates, without any reference to the diagnostic methods (297).

There are no standard EU guidelines or recommendations for the screening and treatment of schistosomiasis and strongyloidiasis and few examples of practice. Ireland and the UK are the only EU/EEA countries with a published infectious disease assessment for migrants or refugees (in the case of the UK) that includes general guidance for screening and treatment of schistosomiasis and strongyloidiasis and other intestinal parasites in asymptomatic people (8, 232, 298). Other countries with published policies include the US, Canada and Australia (5, 299, 300).



#### Figure 5. Distribution of schistosomiasis, worldwide (2012)

Source: WHO. Available from: <u>= http://www.who.int/schistosomiasis/Schistosomiasis\_2012-01.png</u>

# Summary of evidence

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#### Effectiveness

We developed an analytical evidence framework for screening and treatment of strongyloidiasis and schistosomiasis in migrants (in press). We found no studies providing direct evidence on the effectiveness of screening for strongyloidiasis or schistosomiasis among migrants, but we identified 28 studies that addressed the key question along the chain of evidence for screening for schistosomiasis and strongyloidiasis among this population. Initially, 11 systematic reviews were included, eight focusing on the effectiveness of diagnosis and treatment of schistosomiasis, and three on the same for strongyloidiasis (292, 301-310). Following a systematic update of evidence for diagnostic testing for both diseases, ten primary studies were included, seven for schistosomiasis (311, 312, 313. #331, 314-316) and three for strongyloidiasis (317-319). For the economic evidence, six studies were included, four for strongyloidiasis and two for schistosomiasis, which consisted of one systematic review, and five primary studies (three decision-analytic models for economic evaluation and two costing studies) (320-325).

#### Strongyloidiasis

Evidence from one systematic review showed that the most effective screening tests for detection of strongyloidiasis in low intensity/low endemic setting were antibody-detecting serological tests due to their higher sensitivities compared with conventional parasitological methods (292). Of all conventional methods, agar plate culture and Baermann methods were the best, with sensitivity/specificity values of 89% (95% CI; 86-92)/100% (95% CI; 100-100), and 72% (95% CI 67-76)/100% (95% CI; 100-100), respectively (292). The GRADE certainty of evidence was moderate. They were more specific in comparison to serological techniques (308, 311). However, these methods are time- and labour-intensive, require skilled personnel and are therefore not recommended as the first option for public health screening (292).

Serological antibody detection methods exhibited better sensitivity patterns than classical parasitological techniques (317). Bisoffi et al., reported the accuracy of five serological tests for detection of strongyloidiasis (317). The sensitivity and specificity values for Luciferase-immunoprecipitation system (LIPS) using 31-kD recombinants antigen from *St. stercoralis* (NIE) were 85% (95% CI; 79–92) and 100% [100-100); NIE-ELISA (using the same antigen) 75% (95% CI 66–83) and 95% (95% CI 91-99); ELISA-IVD – 91% (95% CI 86–96) and 99% (95% CI 97-100); ELISA-BORDIER 90% (95% CI 84-95) and 98% (95% CI 96-100) and indirect immunofluorescence antibody

test (IFAT) – 94% (95% CI 90–98) and 92% (95% CI 87-97), respectively (317). However, the certainty of evidence was low. The disadvantage of current serological tests based on crude antigen (ELISA-IVD and ELISA-Bordier) are 1) the huge amount of infective larvae required for their production; 2) cross–reactions with other nematode infections that have been demonstrated mostly in filariasis but also in ascariasis, hydatidosis and also toxocariasis (292); and 3) the lower sensitivity in immunosuppressed patients (292, 317).

After an effective treatment, the serology has demonstrated a seroreversion or a relevant decline between 3–12 months in a high proportion of infected individuals (326).

#### **Schistosomiasis**

The evidence from systematic reviews also showed that the most effective screening tests for detection of schistosomiasis in low intensity/low endemic setting were antibody-detecting serological tests due to higher sensitivities compared with conventional parasitological methods (301, 303, 311) such as Kato–Katz (319).

For *Schistosoma* spp. infections, the most effective screening tests were IgM-ELISA (commercial tests) (327) and indirect haemagglutination (IHA) tests in non-endemic areas. Point-of-care testing using circulating cathodic antigen (CCA) tests showed lower specificities and considerable heterogeneity compared with the antibody-detection methods (301). However, there is ample evidence that a combination of ELISA and Kato–Katz faecal examinations can improve the detection of *Schistosoma spp.* in low-intensity settings. In a recent study on the accuracy of different screening tests for schistosomiasis in African migrants, immunochromatographic IgG/IgM tests showed the best sensitivity (sensitivity: 96% (95% CI; 91-99), specificity: 83% (95% CI; 77-87)) (328).

Overall, for screening of schistosomiasis and strongyloidiasis, antibody-detecting serological tests appear to be more sensitive with a good post-test probability of a positive and negative test. However, in the case of schistosomiasis, the desirable anticipated effects for serological screening are moderate given the variability in testing methods and species involved. The optimal threshold of prevalence in countries of origin at which to screen is yet to be determined.

For treatment of schistosomiasis, praziquantel is the drug of choice; treatment with praziquantel significantly increased parasitological cure with marked reductions in micro-haematuria (304, 305). Ivermectin was more effective than albendazole in the treatment of strongyloidiasis (310). Moreover, both treatments have a very good safety profile with few exceptions: ivermectin is contraindicated in patients with a Loa-loa co-infection with high microfilarial load, and praziquantel should be avoided if there is a possibility of a concomitant neurocysticercosis.

#### Cost-effectiveness

A preliminary cost study indicated similar costs (of around USD 6–7 per test) for single Kato–Katz stool and urine tests. Another study comparing screening techniques for parasitic infections showed that eosinophil count may contribute little to the diagnosis accuracy and generate high costs (325). No studies were available on the cost of screening tests based on antibody detection in a non-endemic setting. Further economic studies are warranted to evaluate a test-and-treat strategy for schistosomiasis in non-endemic countries.

In endemic settings, double-dose praziquantel was deemed to be highly cost effective compared with a single dose (ICER of <USD 500/QALY) for schistosomiasis; the strategy was considered robust to plausible changes in parameter estimates (320). A few moderate-quality economic studies support a strategy of presumptive treatment for strongyloidiasis in migrants from high-risk backgrounds. One study showed potential cost savings of universal treatment with albendazole compared with no intervention (watchful waiting) and universal screening (321). Presumptive treatment for Strongyloides with ivermectin is cost-effective at a threshold of less than USD 10 000/QALY across a range of prevalence values. Furthermore, identified economic models with moderate quality evidence suggested that presumptive treatment with single-dose ivermectin for all immigrants was cost-effective compared to five days' treatment with albendazole and to screening (eosinophilia and/or parasitological techniques only) in the home country (322).

The certainty around several model parameters and feasibility of cost-effective strategies may limit the transferability of these results to migrants to the EU/EEA for several reasons. First, the calculation of disease progression to a severe condition and the mortality rate may be underestimated; absence of cost-effective studies based exclusively on antibody-detecting test (the promoted screening strategy in non-endemic settings); second, no studies included potential harms of large-scale administration of ivermectin, particularly in migrants coming from Loa-loa-endemic African countries; and third, ivermectin is not readily available in most endemic countries, and also not approved by regulatory authorities in the EU/EEA.

#### Implementation considerations

Screening for schistosomiasis and strongyloidiasis can easily be done with highly sensitive serological antibodydetecting tests, particularly for strongyloidiasis. For schistosomiasis, given the suboptimal sensitivity in low-intensity settings, some laboratories prefer to perform two serological tests and consider a case as positive if 'any' test is positive, whereas others undertake a combination of ELISA and Kato–Katz faecal examinations to improve accuracy for detecting *Schistosoma* spp. Serological tests are increasingly available in most laboratories. In addition, highly effective drugs with excellent tolerability are available for both infections. Screening and treatment is, therefore, feasible for migrants arriving from endemic countries, irrespective of their prevalence rates.

In the case of immunosuppressed patients with a substantial risk of hyper-infection or disseminated disease, the recommendation for screening for strongyloidiasis is stronger because the risk of developing severe complications is substantial (329). Primary care physicians and specialists should be aware of this risk when prescribing corticosteroids or other immunosuppressants. However, in immunocompromised patients, the sensitivity of serological tests may be decreased (292); therefore, if serology is negative, parasitological methods should be added (292). Whenever possible, screening should be performed before the immunosuppression, not only to preserve the high accuracy of the serological test but also, and more importantly, to minimise the risk of developing severe complications (329). Finally, and considering the high efficacy and tolerability of ivermectin, it might be probably worth treating high-risk patients preemptively if an appropriate test (stool culture or serology) is not available.

It should be noted that both ivermectin and praziquantel are not approved for human use by most national European medicine agencies. Hence, these drugs are not readily available at the primary care level, but only supplied at the hospital level (330). It should be also considered that in a particular subgroup of patients, treatment with ivermectin or praziquantel requires additional complex screening strategies to identify individuals with loiasis, or neurocysticercosis, for whom the indiscriminate use of these drugs might be deleterious (331-333).

Migrants who are at risk of strongyloidiasis and schistosomiasis face a range of barriers to accessing healthcare and treatment in the EU/EEA. Addressing these barriers, ensuring the right to healthcare for all, and tailoring programmes to address the needs of migrant populations are essential to effective screening and treatment strategies. Systematic reviews did not include data on barriers to screening that are specific to strongyloidiasis and schistosomiasis. Nevertheless, as with other infectious diseases, barriers are likely to include low risk perception, limited access to healthcare, particularly for irregular migrants, and socio-economic, cultural and language barriers.

The use of serological tests rather than the routine samples often required when using conventional methods, together with the availability of treatment, may influence the uptake of schistosomiasis and strongyloidiasis screening among migrants. In this regard, targeted screening for these infections could take place at the primary care level and in migrant health clinics, with referral to specialised infectious disease or tropical disease units for treatment and follow up, until the drugs of choice have become readily available. Physicians responsible for immunosuppressed patients or patients at risk of immunosuppression should be encouraged to screen for these infections. This risk, inherent to the underlying disease and/or to the related treatment, concerns an extensive list of conditions such as neoplasia, transplants, autoimmune and rheumatic diseases, etc. (293).

# Ad hoc scientific panel opinion

The scientific panel members were in agreement that screening for schistosomiasis and strongyloidiasis in migrant populations is an important control strategy that allows for early detection and treatment, reduces individual morbidity, and prevents onward transmission.

The scientific panel members were asked for their opinion on the evidence relating to: feasibility, acceptability, cost (resource use), and equity of screening migrants for schistosomiasis and strongyloidiasis. The results of the FACE survey were as follows:

- Medium level of agreement (73%) that screening for schistosomiasis and strongyloidiasis among migrants is a priority in the EU/EEA.
- Low level of agreement (21%) that screening for schistosomiasis and strongyloidiasis among migrants is feasible in the EU/EEA.
- Medium level of agreement (50%) that screening for schistosomiasis and strongyloidiasis among migrants is acceptable in the EU/EEA.
- Medium level of agreement (57%) that screening for schistosomiasis and strongyloidiasis among migrants is equitable in the EU/EEA.

The panel anticipated no important variability or uncertainty in patient values and preferences on being screened and treated for both infections. The panel concluded that the strength of the recommendation was conditional on the prevalence of schistosomiasis and strongyloidiasis in migrants' country of origin; the focus should be on screening of migrants from high-incidence countries. Programmes should address barriers to ensure high uptake of screening and linkage to care and treatment.

# **ECDC assessment**

# **Evidence-based statement (schistosomiasis)**

Offer serological screening and treatment (for those found to be positive) to all migrants from countries of high endemicity in sub-Saharan Africa and focal areas of transmission in Asia, South America, and North Africa (see Figure 14).

(Certainty of evidence: low)

## Evidence-based statement (strongyloidiasis)

Offer serological screening and treatment (for those found to be positive) for strongyloidiasis to all migrants from countries of high endemicity in Asia, Africa, the Middle East, Oceania and Latin America (see Figure 15).

(Certainty of evidence: low)

Screening for schistosomiasis and strongyloidiasis in migrant populations is an important control strategy as it allows for early detection and treatment, probably reduces individual morbidity, and prevents the risk of onward transmission. Although the evidence-based statements are based on indirect evidence, a very high value is placed on uncertain but potentially life-preserving benefits of screening, linkage to care, and treatment (334). In this regard, both infections are potentially severe and chronic; however, the drugs used for treatment of both are usually well tolerated and safe with few exceptions. Therefore, the health benefits are superior to the potential harms of intervention. Priority groups include immunosuppressed persons or candidates for immunosuppression. If the immunosuppression state is already established, screening should be performed with a serological test, plus parasitological tests.

#### Figure 6. Countries where schistosomiasis is endemic



Source: IAMAT. World schistosomiasis risk chart 2015. Available from: <u>https://www.iamat.org/assets/files/World%20Schistosomiasis%20Risk%20Chart\_2015.pdf</u> Note: Public health authorities should consider schistosomiasis screening of migrants from countries marked orange and dark red.

#### **Figure 7.** Countries where strongyloidiasis is endemic



High probability of being endemic for Strongyloides stercoralis based on scientific panel opinion Endemic for Strongyloides stercoralis based on prevalence studies

#### Source: ECDC expert panel

Note: According to the ECDC expert panel, migrants from countries marked orange should be considered for strongyloidiasis screening.

Effectiveness	Cost- effectiveness	Certainty of evidence (GRADE)	FACE survey*	Strength of recommendation	Implementation considerations
For the screening of schistosomiasis and strongyloidiasis, antibody- detecting serological tests identified from included primary studies were more sensitive, with very good post-test probability of a positive and negative test (292, 317). For schistosomiasis, the desirable anticipated effects for serological screening are moderate given the variations in testing methods and type of infection (301, 311). The optimal threshold of incidence in countries of origin at which to screen is yet to be determined.		Low	The ad hoc scientific panel rated the screening of strongyloidiasis and schistosomiasis among migrants in the EU/EEA as follows: • Medium priority • Low agreement that screening is acceptable • Moderate agreement of feasibility • Moderate agreement that screening is equitable	Conditional recommendation based on country of origin	In immunosuppressed patients, with a substantial risk of hyper- infection or disseminated disease, the recommendation for screening is stronger, since the risk of developing severe complications is substantial. Ivermectin and praziquantel are not readily available, and only supplied at the hospital level. Indiscriminate use of these drugs might be deleterious in patients with concomitant loiasis or neurocysticercosis. Migrants face numerous barriers to accessing healthcare, including socio-economic, stigma, linguistic and cultural barriers, and lack of regular status and insurance; this may decrease uptake of strongyloidiasis and schistosomiasis screening and/or treatment. Programmes should address these barriers to ensure high uptake of screening and linkage to care and treatment.

# Table 14. Evidence synthesis and guidance for strongyloidiasis and schistosomiasis screening in migrants

\* High (>75%), medium/moderate (50–75%) and low (50%) of ad hoc scientific panel agreed with category.

## **Evidence gaps and future research needs**

Robust population-based studies on schistosomiasis and strongyloidiasis screening among migrants by age group, migration type, timing of screening and associated cost-effectiveness are required to design the most effective programmes. High quality surveillance of migrants from highly endemic countries is needed. Also, monitoring any changes in prevalence between community and holding centres to help guide public health guidance.

# **Recommendations from other national and international guidelines**

# Table 15. Other international guideline recommendations for parasites for refugee and/or other migrant populations

Country	When, how and who to test
Australia (9)	<ul> <li>Strongyloidiasis:</li> <li>Offer blood testing for <i>Strongyloides</i> to all people; if positive, check full blood exam (FBE) for eosinophilia and perform stool microscopy for ova, cysts and parasite serology to all people.</li> <li>Treat with ivermectin. In Loa-loa-endemic countries, rule out loiasis before providing ivermectin.</li> <li>Schistosomiasis:</li> <li>Offer blood testing for schistosomiasis serology if people have lived in/travelled through endemic countries (including Africa, parts of south-east Asia and the Middle East).</li> <li>If tests are positive, treat with praziquantel, perform stool microscopy for ova and perform urine dipstick for haematuria, and end-urine microscopy for ova if haematuria.</li> </ul>
Canada (5)	<ul> <li>Strongyloidiasis:</li> <li>Screen refugees newly arriving from south-east Asia and Africa with serological tests for <i>Strongyloides</i> spp.</li> <li>If positive, treat with ivermectin.</li> <li>Schistosomiasis:</li> <li>Screen refugees newly arriving from Africa with serological tests.</li> <li>If positive, treat with praziquantel.</li> </ul>
Ireland {#8)	<ul> <li>Offer test (ova, cysts and parasites) to symptomatic migrants only, particularly those who have:</li> <li>lived or travelled in endemic regions;</li> <li>migrated from south-east Asia or sub-Saharan Africa;</li> <li>eosinophilia.</li> <li>Healthcare professionals should also be aware that those with concurrent immunosuppression are at increased risk of developing disseminated parasitic infections, especially <i>Strongyloides</i>, as this auto-infects and disseminates widely in those who are immunosuppressed.</li> </ul>
Italy (13)	<ul> <li>At initial medical assessment, pay attention to symptoms (diarrhoea, abdominal pain, nausea, vomiting, pruritus, haematuria) and biochemical markers (eosinophilia) that may be suggestive of parasitosis.</li> <li>If symptoms or eosinophilia is present, offer stool examination test for parasitosis.</li> <li>Regardless of the presence of symptoms, offer serological tests to all migrants coming from endemic areas (<i>Schistosoma spp.</i> or <i>Strongyloides</i>). Migrants with a positive serological test should be treated, unless there is already evidence of recent completed treatment.</li> </ul>
France (335, 336)	<ul> <li>Strongyloidiasis screening for target populations (ELISA + stool examination test for parasitosis):</li> <li>Immigrants or refugees from endemic areas, upon arrival.</li> <li>All patients originating from, or having lived in, an endemic area prior to commencing immunosuppressive therapy.</li> <li>Schistosomiasis screening for target populations (serology +/- testing for schistosome eggs in urine or faeces) :</li> <li>All migrants from endemic areas.</li> </ul>
UK (232, 298)	<ul> <li>For refugees, pre-entry: Helminthic infections:</li> <li>Refugees who come from, or reside in, the Middle East, Africa, Asia, Latin America and the Caribbean should be offered stool test (for ova, cysts and parasites) and serology for strongyloidiasis and schistosomiasis. Refugees should be treated based on test results.</li> <li>Exceptionally, if testing is not available or is logistically impractical and depending on the epidemiological situation, presumptive treatment with albendazole is indicated during the pre-departure checks for refugees coming from the Middle East, Africa, Asia, Latin America and the Caribbean. <ul> <li>A single dose of albendazole 400 mg for all refugees except pregnant women and children &lt; 2 years of age;</li> <li>Children 12 – 23 months of age should have a single dose of albendazole 200 mg.</li> </ul> </li> <li>For migrants, post-arrival: <ul> <li>The UK has guidance on the investigation of helminth infections for general practices, which should be considered in migrant patients with unexplained symptoms (especially gastrointestinal) and eosinophilia.</li> <li>For migrants from sub-Saharan Africa, screening is recommended for patients with eosinophilia (&gt;0.4 x 10<sup>9</sup> per litre), by</li> </ul> </li> </ul>
USA (142)	<ul> <li>stool microscopy, urine microscopy, strongyloides serology and schistosoma serology</li> <li>For migrants from anywhere in the tropics, screening is recommended for patients with eosinophilia (&gt;0.4 x 10<sup>9</sup> per litre), by stool microscopy and strongyloides serology.</li> <li>Treatment is according to testing results.</li> <li>Official guidelines only for refugees and international adoptees. Pre-departure testing or presumptive treatment is recommended for all categories for strongyloidiasis; testing or presumptive treatment is recommended for schistosomiasis in all migrants/refugees from sub-Saharan Africa. Testing and/or treatment is generally provided prior to migration. When not provided pre-departure, post-arrival testing or treatment is recommended.</li> </ul>
	Refugees from sub-Saharan Africa should receive presumptive therapy for <i>Strongyloides</i> spp. infection with ivermectin if they resided in, or came from, countries or areas not considered endemic for Loa. Refugees from sub-Saharan Africa should receive presumptive pre-departure therapy with praziquantel for schistosomiasis

# 4.7 Vaccine-preventable diseases

# **Burden of disease**

Control of vaccine-preventable diseases (VPDs) is a priority in the EU/EEA (337). Although national surveillance systems for VPDs are in place and regular reporting is done, surveillance is incomplete for data on migrants such as country of birth and time since arrival in the host country and very little information is available on the occurrence of VPDs among newly arrived migrant populations in the EU/EEA.

Seroprevalence studies have demonstrated suboptimal immunity to VPD among adult and child migrants (29, 338-345). Some outbreaks of measles and polio in the EU/EEA have been related to under-immunised migrant populations (346-350), but outbreaks have also occurred in non-migrant populations (30, 351-353). The 2017– 2018 pan-European measles epidemic involved internal EU/EEA migrants moving between countries, so it is important to also consider this group alongside migrants arriving from outside of the EU/EEA (354) (Figure 13].

WHO data report suboptimal immunisation among the general population worldwide, with global coverage ranging from 47–85%, depending on the vaccine and the geographical region (355). This includes the EU/EEA, where some countries have not achieved target vaccine coverage with regard to, for example, first-dose measles (Figure 14). Among the top ten source countries for migrants to the EU/EEA, the range of age-appropriate (i.e. 2-dose) measles vaccination coverage ranges from 31–99% (356). Suboptimal immunisation coverage has implications for maintaining herd immunity in order to minimise outbreaks, which requires seropositivity thresholds of 80–94% (357, 358). Collective immunity below these thresholds, whether in the native-born population, newly arrived migrants or a combination of both, carries the inherent risk of disease transmission and outbreak.

A recent cross-sectional survey of EU/EEA countries' 'immigrant' measles vaccination policies found that nine of the 31 countries had no policy and considerable diversity in strategies in the 22 countries that had a policy (359). Vaccination policies concerning migrants and refugees are heterogenous across the wider WHO European Region (360). Data on VPDs and vaccination coverage for the EU/EEA demonstrate ongoing transmission in the context of vaccine coverage below the threshold for herd immunity (361-366). We found no specific data on effective vaccination implementation strategies for migrants to the EU/EEA.

The evidence review focused on the following VPDs: measles, mumps, rubella, polio, tetanus, diphtheria, pertussis, and *Haemophilus influenzae* type b (Hib) disease. Vaccination for hepatitis B is covered in Section 4.4. Varicella and newer vaccines were not within the scope of this work.



#### Figure 8. Distribution of measles cases by country, EU/EEA, 1 January–31 December 2017

ECDC. Map produced on: 14 Feb 2018 ECDC map maker: https://emma.ecdc.europa.eu



# **Summary of evidence**

#### **Effectiveness**

The systematic review identified ten primary studies (367-376). These studies reported on interventions to increase vaccine uptake among international migrants (369) and internally displaced people, as both populations face barriers to vaccination programmes (367, 368, 370-373). Interventions included social mobilisation and community outreach (368, 370, 371), planned vaccination programmes (369, 373), and education campaigns (367, 368). All studies were non-randomised and reported an increase in vaccinations. Social mobilisation and outreach programmes (370-372) appeared to be associated with the greatest increases in vaccination rates.

A study on asylum seekers in Germany reported on a vaccination strategy using some of these approaches (376). The local public health office informed asylum seekers about relevant VPDs through direct mail, posters, and in person, and invited them to on-site vaccinations in their housing areas. General practitioners carried out the vaccinations. Information about vaccination was provided in various languages and by interpreters. Vaccination certificates were also provided. In areas using this strategy, vaccination rates of 58% were achieved, compared with 6% in areas that did not offer comparable services. Of 642 vaccinated asylum seekers, 86% were immunised right in their housing area. There was a particular focus on male adults, among whom an eight-fold increase in vaccination uptake was recorded. A second European study involved Roma children and women of childbearing age in a nomadic camp in Rome. As part of a TB outbreak assessment, a monthly vaccination day led to a 56% coverage of hexavalent vaccines and a 58% coverage of MMR vaccines, a 30% increase in vaccinated subjects compared with the previous year (368, 370, 371, 373).

#### Cost-effectiveness

The systematic review identified 26 studies on cost-effective approaches to vaccinations, but only one was focused on migrants (377). It compared pre-vaccination serotesting with presumptive immunisation for polio, diphtheria, and tetanus in internationally adopted and immigrant infants to the US (377). It showed that, compared with presumptive immunisation, pre-vaccination serotesting for polio increased the cost per patient from USD 57 to USD 62 and decreased the percentage of patients protected against polio from 95.3% to 94.0%. Presumptive immunisation was more effective and less expensive than pre-vaccination serotesting when seroprevalence was <69%. Presumptive immunisation was the preferred method unless vaccination compliance was extremely high (>96% completion rate) (377). Results for diphtheria, tetanus and pertussis (DTaP) were less definitive. Pre-vaccination serotesting for diphtheria and tetanus increased the cost per patient from USD 62 to USD 119 and increased the percentage of patients protected against both diphtheria and tetanus from 91.5% to 92.3% (377).

Presumptive immunisation was the preferred strategy with an ICER of USD 7 148 per infant protected in populations with poor vaccine compliance (where >80% of patients did not complete the full catch-up vaccine series), or populations with low seroprevalence (<51%) of antibodies to diphtheria and tetanus (377).

Two US studies that were published after the systematic review was performed, examined different costs associated with pre-departure vaccinations, one in the context of a response to an outbreak (378) and one evaluating the US Vaccination Program for US-bound Refugees (VPR) (379). The first study showed that pre-departure vaccination of all US-bound refugees would not only improve health and reduce importations of VPD, but would also be cost saving when considering all the resources required for response to outbreaks (378). The second study demonstrated that – compared with post-arrival vaccinations – the initiation of the pre-departure VPR where the refugees received one or two doses of selected vaccines before departure and completed the series after arrival, demonstrated a net savings per person of USD 225.93 (a 29% decrease in vaccination costs). The cost savings were sensitive to different variables, but demonstrated cost savings across all estimates.

## **Implementation considerations**

Engaging migrant populations in preventive health services remains a challenge in view of the barriers they face in accessing healthcare (177, 380). A recent consensus statement on access to health services in the EU/EEA by IOM's EQUI-HEALTH project (381) highlights the discrepancies in entitlements to statutory health services for migrants; irregular migrants often have highly restrictive access. Barriers to immunisations for migrants include: use of traditional healthcare (382), socio-economic status (382), language (383), distance to immunisation service (383, 384), continued migration (384), fear of arrest (384), necessity of work (384), lack of vaccination knowledge (383, 385, 386), cost (386) and lack of healthcare provider recommendation (387). Well-informed migrants routinely accept vaccination, sometimes at a rate higher than the native population (388).

Bundling of primary care services for migrants may prevent further barriers to vaccination, diagnosis, and care. Clinicians should assess immunisation documentation and provide migrants with documentation of vaccines administered. Social mobilisation appears promising to increase vaccination coverage in migrant populations (368, 370, 371). Multiple opportunities for vaccinations occur at different points in the migration trajectory. Information regarding immunisation should be available in multiple languages, particularly those most commonly spoken by arriving migrants.

Italy, Ireland, Australia, Canada the UK and the US have all published migrant-specific VPD guidelines (see Table 17), yet concerns have been raised as to the extent such guidelines are implemented in practice and the need to consider wider groups of migrants beyond refugees and asylum seekers in catch-up vaccination programmes (360, 389). The WHO, UNHCR and UNICEF have published a joint statement on general principles on vaccination of refugees, asylum-seekers and migrants in the WHO European Region (390). In 2015, ECDC suggested vaccinations for newly arriving migrants be offered in accordance with the national immunisation guidelines of the host country (61). These migrant guidelines recommend assessing the immunisation record of the migrants and not pursuing serology testing. WHO has published a framework for decision-making about vaccinations for migrants in acute humanitarian emergencies. This framework looks at epidemiological risk assessments, vaccine characteristics, and contextual factors in a three-step process of decision-making (390).

# Ad hoc scientific panel opinion

The ad hoc scientific panel members were in agreement that vaccination in migrant populations is important in terms of VPD control and equity. The panel concluded that the strength of the recommendation was strong for child and adolescent migrants and conditional on health system resources for adult migrants.

The scientific panel members were asked for their opinion on the evidence relating to feasibility, acceptability, cost (resource use), and equity of vaccinations among migrants. The results of the FACE survey showed the following:

- High level of agreement (80%) that providing vaccinations to migrants is a priority in the EU/EEA.
- High level of agreement (93%) that providing vaccinations to migrants is feasible in the EU/EEA.
- High level of agreement (100%) that providing vaccinations to migrants is acceptable in the EU/EEA.
- High level of agreement (100%) that providing vaccinations to migrants is equitable in the EU/EEA.

The ad hoc scientific panel agreed that there are additional considerations to take into account when proposing vaccination of adult migrants. Healthcare accessibility was considered by all as a critical issue, given the barriers that migrants often face. Integrating migrants into primary care and public health programmes would increase feasibility. The panel agreed that it is important to ensure that migrant children and adults receive vaccination coverage similar to that of EU/EEA citizens. However, it also recognises that immunisation of migrants increases the complexity of vaccination programmes because of the need to address language and cultural differences.

# **ECDC** assessment

# **Evidence-based statement 1**

Offer vaccination against measles/mumps/rubella (MMR) to all migrant children/adolescents without immunisation records as a priority.

(Certainty of evidence: low)

# **Evidence-based statement 2**

Offer vaccination to all migrant adults without immunisation records with either one dose of MMR or in accordance with the MMR immunisation schedule of the host country.

(Certainty of evidence: very low)

# **Evidence-based statement 3**

Offer vaccination against diphtheria, tetanus, pertussis, polio and HiB (DTaP-IPV-Hib) to all migrant children/and adolescents without immunisation records as a priority.

(Certainty of evidence: low)

# **Evidence-based statement 4**

Offer vaccination to all adult migrants without immunisation records in accordance with the immunisation schedule of the host country. If this is not possible, adult migrants should be given a primary series of diphtheria, tetanus, and polio vaccines.

(Certainty of evidence: very low).

For the evidence-based statement on hepatitis B vaccination, please see Section 4.4.

Control of VPDs is an important priority for the EU/EEA. Migrants have been shown to have suboptimal immunity against VPDs and outbreaks of VPDs have occurred in migrant populations living in the EU/EEA. All migrant children and adolescents should be vaccinated in accordance with the host countries' vaccine schedules to support health equity. Migrant adults without prior vaccination records should be vaccinated in accordance with the host countries' vaccine schedules to support health equity. Migrant adults without prior vaccination records should be vaccinated in accordance with the host country vaccine schedule. In the case of migrant children and/or incomplete records, age-appropriate catch-up schedules are recommended. MMR and DTaP-IPV-Hib vaccines should be prioritised for children and adolescents. In adults without an immunisation record or with incomplete immunisations, MMR and diphtheria, pertussis, tetanus immunisation is recommended. Migrants face many barriers to accessing healthcare that can lead to low uptake of vaccinations. Social mobilisation and culturally and linguistically appropriate community outreach paired with planned vaccination programmes have been shown to increase vaccine uptake among migrants internationally and in the European context; more evaluation to identify effective implementation strategies in the EU/EEA is required.

#### Table 16. Evidence synthesis and guidance for VPDs in migrant populations

Effective implementation strategies	Cost- effectiveness	Certainty of evidence (GRADE)	FACE survey*	Strength of recommendation	Implementation considerations
All guidelines recommend assessing a migrant's immunisation record and not pursuing serology testing. Vaccination is to be offered in accordance with the national immunisation guidelines of the host country. Social mobilisation and outreach programmes appear to be associated with the most significant increases in vaccination rates (370-372).	There are very little data on the cost-effectiveness of vaccination strategies in migrant populations. Serological testing was less cost- effective than presumptive immunisation of internationally adopted children. Pre-departure vaccination of refugees was cost- saving and decreased vaccine- preventable diseases.	Very low to moderate.	The ad hoc scientific panel rated immunisation against VPDs among migrants in the EU/EEA as follows: • High agreement around priority • High agreement of acceptability • High agreement around feasibility • High agreement that vaccination migrants is equitable	Strong recommendation for children/adolescents. Conditional recommendation for adults.	All migrant children/ adolescents should be vaccinated according to the host country's vaccine schedules. Adult migrants without vaccination records should be offered catch-up vaccination in accordance with the host country vaccine schedule. Measles/mumps/rubella (MMR) and diphtheria, tetanus and polio vaccines should be prioritised. Provide migrants with documentation of vaccines administered to prevent vaccination duplication. Social mobilisation could be used to increase vaccination coverage in migrant populations. Primary healthcare interactions remain an important opportunity for assessing vaccinations. Information regarding immunisation should be available in multiple languages, particularly those most commonly spoken by newly arriving migrants.

\* High (>75%), medium (50–75%) and low (50%) of ad hoc panel agreed with category

## **Evidence gaps and future research needs**

National immunisation guidelines, plans and programmes should include a specific focus on migrants, considering both internal migrants within the EU/EEA and external migrants to the EU/EEA. Robust surveillance data on VPDs and vaccine coverage in migrant populations by age group, migration type, source country, and duration of presence in the EU/EEA are required to design the most effective programmes (391). This will require standardisation of migrant definitions and variables. Evidence on the effectiveness and cost-effectiveness of different immunisation strategies for migrants is required as is specific research on vaccination uptake and immunisation coverage in adults vs. children to inform prioritisation and guidelines. The optimal approach to document immunisations and share immunisation data concerning mobile populations across jurisdictions to avoid vaccination duplication is an understudied area (392).

# **Recommendations from other national and international guidelines**

# Table 17. International guideline VPD recommendations for refugees and/or other migrant populations

Country	How and who to vaccinate
Australia (9)	<ul> <li>Assess availability of immunisation records; plan vaccination based on age.</li> <li>Provide catch-up immunisation so people from refugee-like backgrounds are immunised equivalent to an Australian-born person of the same age.</li> <li>Full catch-up if records are not available</li> </ul>
Canada (5)	Measles, mumps and rubella
	<ul> <li>Vaccinate all adult immigrants without immunisation records using one dose of measles-mumps- rubella vaccine.</li> </ul>
	Diphtheria, pertussis, tetanus, polio
	<ul> <li>Vaccinate all adult immigrants without immunisation records using a primary series of tetanus, diphtheria and inactivated polio vaccine (three doses), the first of which should include a cellular pertussis vaccine.</li> </ul>
Ireland (8)	Assess all migrants for previous measles vaccination.
	MMR
	All migrants without documented evidence of previous measles vaccination should be offered MMR vaccination as follows:
	<ul> <li>All children in accordance with the routine childhood immunisation schedule at 12 months and 4– 5 years of age (2 doses)</li> </ul>
	<ul> <li>All others according to the 'late entrants catch-up schedule' for children and adults, as follows:</li> <li>12 months to 4 years, 1 dose MMR, 2nd dose at 4–5 years of age</li> </ul>
	<ul> <li>4 years to &lt;18 years of age, 2 doses MMR at one month interval</li> <li>Adulta age of 19 years and older 2 doses MMD at one month interval</li> </ul>
	<ul> <li>Adults aged 18 years and older, 2 doses MMR at one month interval DTaP-IPV</li> </ul>
	<ul> <li>Vaccinate all adult immigrants without immunisation records using a primary series of tetanus, diphtheria and inactivated polio vaccine (three doses), the first of which should include acellular pertussis vaccine.</li> <li>Vaccinate all immigrant children with missing or uncertain vaccination records using age-</li> </ul>
Italy (13, 393)	appropriate vaccination for diphtheria, pertussis, tetanus and polio. Primary prevention interventions (vaccinations) as well as secondary prevention interventions are recommended in the second reception phase.
	Children (0–14 years) never vaccinated or with uncertain or unknown vaccination status: vaccinations in accordance with the national schedule, depending on age.
	Adults with uncertain or no vaccination history: • polio
	<ul> <li>measles, mumps, rubella, chickenpox; excluding pregnant women</li> <li>diphtheria, tetanus, pertussis, HBV for the entire adult population screened in accordance with guideline recommendations (migrants from HBV incidence of HBsAg &gt;2%, migrants with risk factors, and pregnant women) and negative for serological markers.</li> </ul>
UK (232, 233)	The UK offers vaccinations in line with the national immunisation schedule to any migrant whose immunisation status is uncertain or incomplete, in accordance with guidance for individuals with uncertain or incomplete immunisation status.
	<ul> <li>All migrants are eligible for vaccines through the National Immunisation Programme and can access immunisation services the same way as the rest of the population.</li> <li>Refugees who are to be resettled in the UK through a formal refugee resettlement scheme are</li> </ul>
	<ul> <li>offered vaccination pre-departure, in line with the national immunisation schedule.</li> <li>Asylum seekers in initial accommodation centres in the UK are offered vaccination as part of their initial health assessment.</li> </ul>
USA (394)	<ul> <li>Immigrants are required to show proof that they have received certain vaccines prior to arrival.</li> <li>If an applicant does not have proof of having received the required vaccines, the law states that the initial doses vaccines must be given at the time of the medical examination.</li> </ul>
	<ul> <li>Refugees and international adoptees are exempt from this requirement, however they are offered 1–3 doses of each vaccine series (394).</li> <li>Following arrival, all immigrants are recommended that they have their vaccinations updated in</li> </ul>
	accordance with national guidelines (ACIP) (395, 396).

# **5. Implications for public health practice and research**

# 5.1 Public health practice

This ECDC guidance provides evidence-based assessments on public health interventions – vaccination, screening and linkage to treatment and care – in order to decrease the burden of disease among migrant populations in the EU/EEA and promote health in these population groups. It addresses infectious diseases that disproportionately affect migrants and focuses on interventions for newly arrived migrants to the EU/EEA. The guidance is intended to inform public health policy and programmes and aims to improve implementation and service delivery; it does not provide detailed clinical recommendations.

The evidence cited in this document is overwhelmingly based on data and lessons from high-risk non-migrant populations and approaches used in low- and middle-income countries. Further input was received through the views of a range of experts. Although the quality of some of the evidence for effectiveness and cost-effectiveness is low, this guidance identifies potential approaches to improve health outcomes for migrants in the EU/EEA.

Available evidence suggests that the screening of migrants is likely to be both effective and cost-effective for active TB, LTBI, HIV, HCV, HBV, strongyloidiasis and schistosomiasis. There are clear benefits to be derived from enrolling migrants in vaccination programmes and ensuring catch-up vaccinations. Screening for priority infectious diseases is, however, conditional on the prevalence of the disease in a migrant's country of origin.

# 5.2 Linkage to care

Although identifying infectious diseases early through testing is a critical clinical and public health intervention, it is only one element of the care pathway (26). Integral to the development of this guidance is an understanding of the importance of, and interventions for, each element of the care pathway, from access to appropriate health services to testing/screening and adherence to/completion of treatment.

Experience relating to a range of infections shows that post-testing losses occur at all stages of the clinical care pathway. These include failure to get results after testing, failure to attend specialist services to commence treatment, and failure to complete or adhere to treatment (124, 397-400). Although data for migrants are less clear (401), the same principle of minimising dropout across the cascade following screening/diagnostic testing applies.

Dropouts at each stage of the care pathway can be due to a number of personal and system-level barriers that migrants may face in accessing statutory health/appropriate health services on arrival and after, for example due to the lack of clarity about the organisation and financing of care, compounded by linguistic and cultural barriers (402-404). Many vulnerable migrant groups are not entitled to free statutory healthcare on arrival, which will undoubtedly impact on uptake of screening and attendance at specialist services (404). Additional concerns for new migrants to European countries include competing psycho-social priorities such as housing, employment, concerns about family reunion, mental health issues and chronic diseases. These problems not only interfere with testing, but also have the potential to increase the risks or consequences of infectious diseases. This synergistic interaction linked to socially disadvantaged circumstances, known as syndemics, calls for an integrated approach of public health and primary care, addressing biomedical as well as psychosocial problems (405).

Therefore, it is important that ease of access, making health services responsive, and engaging migrant communities is considered at an early stage when developing clinical pathways relating to screening for infection and appropriate vaccination (406). Engagement includes providing the necessary information and tailoring services to the needs and possibilities of the migrants involved (104, 407, 408). While this early work may seem less important, it likely sets in motion the basis for future community engagement and the co-development of services, which are critical to reaching individuals from often marginalised and neglected communities (409).

It is also important to consider the way in which screening/testing is framed and offered, as this can have an impact on whether individuals from migrant communities accept testing, how they view the results, and whether they attend for follow-up care and complete treatment. Testing is only one element of the care pathway and, without follow-up case and treatment, has limited individual or public health benefit. A decision to test should equate to an intention to refer for assessment and, if required, treatment. Particular attention, therefore, needs to be given to the linkage between testing and referral and specialist care when designing programmes and services for migrants and providing education and information to migrants and health professionals. Ease of access and responsiveness can be enhanced by offering integrated services that consider multiple infections, rather than just screening for TB, for example. This will require working more closely with migrant communities to ascertain their view and concerns, but certain elements should be incorporated including (410):

- Collaboration between public health, primary care and specialist care in order to ensure continuity of care tailored to all the needs of the person involved.
- Single point-of-referral to a migrant-friendly clinical service with culturally competent staff who can manage infectious diseases and other health needs alongside interpreters and other support services to enhance treatment adherence and completion.
- Robust data collection to facilitate sharing of best practice with respect to linkage to care and treatment completion for migrants with infectious diseases.

# 5.3 Research gaps

The process of developing this guidance has highlighted gaps in knowledge concerning infectious disease interventions targeting migrant populations.

Research is needed to provide strong evidence on how best to deliver screening and vaccination to migrant populations, challenges around diagnosis and treatment, and on the impact of interventions. More robust data are needed on the acceptability, effectiveness, and cost-effectiveness of screening and vaccination programmes targeting migrants. Large linked datasets studies or multi-country and multi-ethnic group studies are needed to improve the precision of estimates of disease, morbidity, and mortality. More research, including community-based participatory action research, is also needed on the determinants of health in migrant populations and migrant community perspectives on screening and vaccination. Research into multiple disease screening (i.e. screening concomitantly for HIV, TB and hepatitis and intestinal parasites when indicated) (93) and roles for screening in community-based primary healthcare services should be a priority.

Furthermore, countries should consider research and innovations in public policy and migration, new forms of EU/EEA cooperation and governance, programmes to empower migrants and technology to support integration and communications.

# 6. Next steps

Public health programmes have an important role in improving the health and social determinants of health for newly arriving migrant populations to the EU/EEA. This ECDC guidance provides the evidence base to enable EU/EEA Members States to develop and adapt their own public health and clinical guidance on screening and vaccination for newly arrived migrant populations.

Public health programmes need to target screening and vaccination programmes towards high-risk migrant populations and take steps to increase uptake of screening and vaccination, to improve linkage to care and treatment, and to improve retention across the cascade of care for infectious diseases. Health programmes and services will need to adapt their approaches to optimise public health benefits and meet the needs of migrant populations, including providing culturally and linguistically sensitive services and offering integrated screening, vaccination and care services. For example, using rapid HIV tests can dramatically improve uptake of testing; multiple test approaches are often preferred by migrants who may require serology testing for multiple infectious diseases.

Since the majority of preventive and curative healthcare for migrants is provided by community-based primary care services, there is a need to improve health professionals' awareness and skills with respect to migrant health needs and ensure delivery of non-stigmatising services that respect privacy and confidentiality. Community engagement, through outreach and community-based care, is also critical to improving awareness and uptake among migrant populations. Community-based care can improve trust and ease of access to screening and vaccination services. There is an opportunity to learn from the experience of EU/EEA countries that are implementing effective programmes to reach newly arrived migrants through approaches that include culturally sensitive health promotion, use of interpreters, training of community-based primary care professionals, and collaboration with public health and migrant community coalitions.

The guidelines also highlight the need to address the various socio-economic, cultural, legal and other barriers that limit access to, and uptake of, healthcare services. Particular attention needs to be given to ensuring that economic barriers do not inhibit or prohibit migrants from seeking or obtaining vaccination, screening and treatment for infectious diseases.

Better understanding is needed of migrant perceptions about infectious diseases, disease susceptibility, benefits of screening, testing and vaccination, and the acceptability and accessibility of healthcare services, as well as better monitoring of uptake of services. In addition, improvements in surveillance are required to increase the completeness and quality of data and inform more accurate estimates of disease prevalence, morbidity and mortality among migrant populations.

This guidance will be reviewed five years after publication to determine whether it requires updating in light of new evidence and developments in migrant health and migrant demographics in the EU/EEA.

# References

- 1. Preamble to the Constitution of World Health Organization, (adopted 1946, entered into force 7 April 1948). Available at: http://apps.who.int/gb/bd/PDF/bd47/EN/constitution-en.pdf.
- 2. United Nations. United Nations Statistics Division Demographic and Social Statistics. 2017. Available at: https://unstats.un.org/unsd/demographic-social/index.cshtml.
- Convention relating to the Status of Refugees United Nations Conference of Plenipotentiaries on Status of Refugees and Stateless Persons; 1950. Available at: https://www.ohchr.org/EN/ProfessionalInterest/Pages/StatusOfRefugees.aspx.
- International Organization for Migration. World Migration Report 2015. Migrants and Cities: New Partnerships to Manage Mobility 2015. Available at: https://www.iom.int/world-migration-report-2015.
- 5. Pottie K, Greenaway C, Feightner J, Welch V, Swinkels H, Rashid M, et al. Evidence-based clinical guidelines for immigrants and refugees. CMAJ. 2011;183:E824-E925.
- 6. Gushulak BD, Pottie K, Hatcher Roberts J, Torres S, DesMeules M, Canadian Collaboration for I, et al. Migration and health in Canada: health in the global village. CMAJ. 2011;183(12):E952-8.
- 7. Thiel de Bocanegra H, Carter-Pokras O, Ingleby JD, Pottie K, Tchangalova N, Allen SI, et al. Addressing refugee health through evidence-based policies: a case study. Annals of Epidemiology. 2017.
- 8. Health Protection Surveillance C. Infectious Disease Assessment for Migrants. Dublin, Ireland: 2015. Available at: https://www.hpsc.ie/a-z/specificpopulations/migrants/guidance/File,14742,en.pdf.
- Chaves NJ, Paxton G, Biggs BA, Thambiran A, Smith M, Williams J, et al. on behalf of the Australasian Society for Infectious Diseases and Refugee Health Network of Australia Guidelines writing group. Recommendations for comprehensive postarrival health assessment for people from refugee-like backgrounds. Australasian Society for Infectious Diseases Inc., 2016. Available at: https://www.asid.net.au/documents/item/1225.
- US Centers for Disease Prevention and Control (US CDC). Immigrant and Refugee Health. Guidelines for the U.S. Domestic Medical Examination for Newly Arriving Refugees 2018 [cited 2018]. Available at: https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/domestic-guidelines.html.
- Public Health England. Assessing new patients from overseas: migrant health guide. Public Health England, 2014 31 July 2014. Available at: https://www.gov.uk/guidance/assessing-new-patients-from-overseas-migrant-health-guide#history.
- Pre-entry health assessments for UK-bound refugees. Home Office; Public Health England; International Organization for Migration, 2017 August 2017. Available at: https://www.england.nhs.uk/south/wpcontent/uploads/sites/6/2014/06/refugee-health-protocal.pdf.
- INMP, SIMM controlli alla frontiera. La frontiera dei controlli. Controlli sanitari all'arrivo e percorsi di tutela per i migranti ospiti nei centri di accoglienza. Sistema Nazionale per le Linee-guida. June 2017. Available at: <u>http://www.inmp.it/lg/LG\_Migranti-integrata.pdf</u>.
- 14. Mipex. Migrant Integration Policy Index. Brussels: Migration Policy Group in collaboration with the Barcelona Centre for International Affairs (CIDOB); 2015.
- 15. Dara M, de Colombani P, Petrova-Benedict R, Centis R, Zellweger J-P, Sandgren A, et al. Minimum package for cross-border TB control and care in the WHO European Region: a Wolfheze consensus statement. The European Respiratory Journal. 2012;40(5):1081-90.
- 16. Heldal E, Kuyvenhoven JV, Wares F, Migliori GB, Ditiu L, Fernandez de la Hoz K, et al. Diagnosis and treatment of tuberculosis in undocumented migrants in low- or intermediate-incidence countries. The International Journal of Tuberculosis and Lung Disease: the official journal of the International Union against Tuberculosis and Lung Disease. 2008;12(8):878-88.
- 17. European Centre for Disease Prevention and Control Asessing the burden of key infectious diseases affecting migrant populations in the EU/EEA. Stockholm: ECDC; 2014. Available at: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/assessing-burden-disease-migrant-populations.pdf.
- Pottie K, Mayhew AD, Morton RL, Greenaway C, Akl EA, Rahman P, et al. Prevention and assessment of infectious diseases among children and adult migrants arriving to the European Union/European Economic Association: a protocol for a suite of systematic reviews for public health and health systems. BMJ Open. 2017;7(9).
- Greenaway C, Pareek M, Abou Chakra CN, Walji M, Makarenko I, Alabdulkarim B, et al. The effectiveness and costeffectiveness of screening for active tuberculosis among migrants in the EU/EEA: a systematic review. Euro Surveill. 2018;23(14).
- 20. Greenaway C, Pareek M, Abou Chakra CN, Walji M, Makarenko I, Alabdulkarim B, et al. The effectiveness and costeffectiveness of screening for latent tuberculosis among migrants in the EU/EEA: a systematic review. Euro Surveill. 2018;23(14).
- 21. Pottie K, Lotfi T, Kilzar L, Howeiss P, Rizk N, Akl E, et al. The Effectiveness and Cost-Effectiveness of Screening for HIV in Migrants in the EU/EEA: A Systematic Review. Int J Environ Res Public Health. 2018;15(8):1700.
- Myran D, Morton R, Biggs B-A, Veldhuijzen I, Castelli F, Tran A, et al. The Effectiveness and Cost-Effectiveness of Screening for and Vaccination Against Hepatitis B Virus among Migrants in the EU/EEA: A Systematic Review. Int J Environ Res Public Health. 2018;15(9):1898.
- 23. Greenaway C, Makarenko I, Abou Chakra C, Alabdulkarim B, Christensen R, Palayew A, et al. The Effectiveness and Cost-Effectiveness of Hepatitis C Screening for Migrants in the EU/EEA: A Systematic Review. Int J Environ Res Public Health. 2018;15(9):2013.
- 24. Hui C DJ, Morton R, et al. Interventions to Improve Vaccine Uptake an Cost-Effectiveness of Vaccination Strategies in Newly Arrived Migrants in the EU/EEA: A Systematic Review. It J Environ Res Pub Health. 2018;15:2065.
- Driedger M, Mayhew A, Welch V, Agbata E, Gruner D, Greenaway C, et al. Accessibility and Acceptability of Infectious Disease Interventions Among Migrants in the EU/EEA: A CERQual Systematic Review. Int J Environ Res Public Health. 2018;15(11):2329. https://www.mdpi.com/1660-4601/15/11/2329/htm.
- 26. Pareek M, Noori T, Hargreaves S, van den Muijsenbergh M. Linkage to Care Is Important and Necessary When Identifying Infections in Migrants. Int J Environ Res Public Health. 2018;15(7):1550.

- European Centre for Disease Prevention and Control. Epidemiological assessment of hepatitis B and C among migrants in the EU/EEA. Stockhlom: ECDC, 2016. Available at: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/epidemiological-assessment-hepatitis-B-and-Camong-migrants-EU-EEA.pdf.
- Gushulak B, Pace P, Weekers J. Poverty and social exclusion in the WHO European Region: health systems respond. In: Koller T, editor: World Health Organization; 2010. p. 257-81.
- 29. Mipatrini D, Stefanelli P, Severoni S, Rezza G. Vaccinations in migrants and refugees: a challenge for European health systems. A systematic review of current scientific evidence. Pathogens and Global Health. 2017;111(2):59-68.
- Grammens T, Maes V, Hutse V, Laisnez V, Schirvel C, Trémérie JM, et al. Different measles outbreaks in Belgium, January to June 2016–a challenge for public health. Eurosurveillance. 2016;21(32).
- 31. Tavares AM, Fronteira I, Couto I, Machado D, Viveiros M, Abecasis AB, et al. HIV and tuberculosis co-infection among migrants in Europe: A systematic review on the prevalence, incidence and mortality. PloS one. 2017;12(9):e0185526.
- 32. Stronks K, Snijder MB, Peters RJG, Prins M, Schene AH, Zwinderman AH. Unravelling the impact of ethnicity on health in Europe: the HELIUS study. BMC Public Health. 2013;13:402.
- 33. Tankimovich M. Barriers to and interventions for improved tuberculosis detection and treatment among homeless and immigrant populations: a literature review. Journal of Community Health Nursing. 2013;30(2):83-95.
- 34. Norredam M, Agyemang C, Hoejbjerg Hansen OK, Petersen JH, Byberg S, Krasnik A, et al. Duration of residence and disease occurrence among refugees and family reunited immigrants: test of the 'healthy migrant effect' hypothesis. Tropical Medicine & International Health. 2014;19(8):958-67.
- 35. Padilla B, Miguel JP. Health and Migration in the European Union: Better Health for All in an Inclusive Society: Chapter 1: Health and Migration in the European Union: Building a Shared Vision for Action. 2009. p. 15-22. Available at: http://www.academia.edu/3757255/Health and migration in the European Union Good practices.
- 36. Semenza JC, Carrillo-Santisteve P, Zeller H, Sandgren A, van der Werf MJ, Severi E, et al. Public health needs of migrants, refugees and asylum seekers in Europe, 2015: Infectious disease aspects. European Journal of Public Health. 2016;26(3):372-3.
- 37. Migration and health: a complex relation. The Lancet. 2006;368(9541):1039.
- Eurostat. Population statistics. Migrant population. Eurostat migr\_pop3ctb. Available at: <u>http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=migr\_pop3ctb&lang=en%20</u>.
   Eurostat. Population statistics. Migrant population. Eurostat migr\_resfirst. Available at:
- http://appso.eurostates.europa.eu/nui/show.do?dateset=mig\_\_resfirst.elang=el
   http://appso.eurostates.europa.eu/nui/show.do?dateset=mig\_\_resfirst.elang=el
   http://appso.eurostates.europa.eu/nui/show.do?dateset=mig\_\_resfirst.elang=el
- 40. Eurostat. Population statistics. Migrant population. Eurostat migr\_resfirst, migr\_resoth. Available at: <a href="http://ec.europa.eu/eurostat/statistics-explained/index.php/Residence">http://ec.europa.eu/eurostat/statistics-explained/index.php/Residence</a> permits statistics#First residence permits by reason.
- 41. Frontex. Data from Frontex. Available at: https://frontex.europa.eu/assets/Migratory\_routes/Detections\_of\_IBC\_2018\_05\_07.xlsx.
- 42. Eurostat. Population statistics. Migrant population. Eurostat migr\_asyappctza. . Available at: <u>http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=migr\_asyappctza&lang=EN</u>.
- 43. European Parliament. EU-Turkey Statement and Action Plan, 2016. Available at: <u>http://www.europarleuropaeu/legislative-train/theme-towards-a-new-policy-on-migration/file-eu-turkey-statement-action-plan.</u>
- 44. Eurostat. Statistics explained. Asylum statistics. Eurostat tps00192, tps00193. Available at: http://ec.europa.eu/eurostat/statistics-explained/index.php?title=Asylum statistics.
- 45. Eurostat. Statistics explained. Asylum statistics. Eurostat migr\_asydcfsta, tps00193. Available at:
- <u>http://ec.europa.eu/eurostat/statistics-explained/index.php?title=Asylum\_statistics.</u>
  46. European Parliament. EU Migrant Crisis: facts and figures. 2017. Available at:
- <u>http://wwweuroparleuropaeu/news/en/headlines/society/20170629ST078630/eu-migrant-crisis-facts-and-figures.</u>
  47. Eurostat. Population by age group, sex and citizenship. Eurostat migr\_pop1ctz. Available at:
- http://appsso.eurostat.ec.europa.eu/nui/show.do?wai=true&dataset=miqr\_pop1ctz.
  48. Committee on Economic Social and Cultural Rights. General Comments No. 14: The Right to the Highest Attainable Standard of Health (Art. 12). 2009. Available from:
- https://tbinternet.ohchr.org/ layouts/treatybodyexternal/TBSearch.aspx?Lang=en&TreatyID=9&DocTypeID=11
   United Nations. Convention on the Rights of the Child, Nov. 20, 1989, 28 I.L.M. 1448 (1989), corrected at 29 I.L.M. 1340 (1990) (entered into force 2 September 1990), Article 24(2)(d). 1989.
- 51. United Nations. Convention on the Elimination of All Forms of Discrimination Against Women. Dec. 18, 1979, 1249 U.N.T.S. 13, 19 ILM. 33 (entered into force 3 September 1981), Article 12(2).
- European Union. Charter of Fundamental Rights to the European Union, Article 35. Official Journal of the European Communities. 2012/C(364/01). Available at: European Union. Charter of Fundamental Rights to the European Union, Article 35. Official Journal of the European Communities.2012/C(364/01).
- 53. European Union Agency for Fundamental Rights. Fundamental Rights Report 2016. Available at: http://fra.europa.eu/en/publication/2016/fundamental-rights-report-2016.
- 54. Amets Suess IRP, Ainhoa Ruiz Azarola, Joan Carles March Cerdà. The right of access to healthcare for undocumented migrants: a revision of comparative analysis in the European context. European Journal of Public Health. 2014;24(5):712-20.
- 55. European Centre for Disease Prevention and Control. HIV and laws and policies in Europe: Monitoring implementation of the Dublin Declaration on partnership to fight HIV/AIDS in Europe and Central Asia. 2017. Available at: https://ecdc.europa.eu/en/publications-data/evidence-brief-hiv-and-laws-and-policies-europe.
- Medecins du Monde. 2017 Observatory report Falling through the cracks: the failure of universal coverage in Europe. 2017. Available at: https://www.medecinsdumonde.org/en/actualites/publications/2017/11/08/falling-through-cracksfailure-universal-healthcare-coverage-europe.
- 57. Hargreaves S, Rustage K, Nellums LB, Powis Jaynaide, Milburn J, Severoni S, et al. What constitutes an effective and efficient package of services for the prevention, diagnosis, treatment and care of tuberculosis among refugees and migrants in the WHO European Region? Themed issues on migration and health, VIII. Health Evidence Network Synthesis Report 56. Copenhagen: WHO Regional Office for Europe, 2018. Available at: <a href="http://www.euro.who.int/">http://www.euro.who.int/</a> data/assets/pdf file/0003/371145/who-hen-report-56.pdf?ua=1

- 58. Schünemann HJ, Hill SR, Kakad M, Vist GE, Bellamy R, Stockman L, et al. Transparent Development of the WHO Rapid Advice Guidelines. PLoS Medicine. 2007;4(5):e119-e.
- 59. Battista RN, Hodge MJ. Setting priorities and selecting topics for clinical practice guidelines. CMAJ. 1995;153(9):1233-7.

60. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 2. Priority setting. Health Research Policy and Systems. 2006;4(1):14.

- European Centre for Disease Prevention and Control. Infectious diseases of specific relevance to nearly-arrived migrants in the EU/EEA. Stockholm: ECDC, 2015. Available at: <u>https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Infectious-diseases-of-specific-relevance-to-newly-arrived-migrants-in-EU-EEA.pdf.</u>
- European Centre for Disease Prevention and Control. Meeting report: Evidence-based guidance for the prevention of infectious diseases among newly arrived migrants to the EU/EEA. Stockholm: ECDC, 2015.
- Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 8. Rating the quality of evidence—indirectness. Journal of Clinical Epidemiology. 2011;64(12):1303-10.
- 64. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic Reviews. 2015;4(1):1.
- 65. Shea BJ, Grimshaw JM, Well GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7:10.
- 66. Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. 2011. Available at: <u>http://www.ohri.ca/programs/clinical\_epidemiology/oxford.asp</u>.
- Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well-informed healthcare choices. 1: Introduction. Br Med J. 2016;353.
- 68. Drummond M, Methods for the economic evaluation of health care programmes: Oxford University Press; 2005. p.379.
- Lewin S, Glenton C, Munthe-Kaas H, Carlsen B, Colvin CJ, Gulmezoglu M, et al. Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). PLoS Med. 2015;12(10):e1001895.
- 70. McMaster University, Gradepro tool. GRADEpro GDT. 2017. Available at: https://cebgrade.mcmaster.ca/gradepro.html.
- 71. European Centre for Disease Prevention and Control. Guidance on tuberculosis control in vulnerable and hard-to-reach populations. Stockholm: European Centre for Disease Prevention and Control. 2016. Available at: <a href="https://ecdc.europa.eu/en/publications-data/public-health-guidance-tuberculosis-control-vulnerable-and-hard-reach-populations">https://ecdc.europa.eu/en/publications-data/public-health-guidance-tuberculosis-control-vulnerable-and-hard-reach-populations</a>
- Lönnroth K, Migliori GB, Abubakar I, D'Ambrosio L, de Vries G, Diel R, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. The European Respiratory Journal. 2015;45(4):928-52.
- 73. European Centre for Disease Prevention and Control. Progressing towards TB elimination. Stockholm: ECDC, 2010. Available at: <u>https://ecdc.europa.eu/en/publications-data/progressing-towards-tb-elimination</u>.
- 74. European Centre for Disease Prevention and Control and World Health Organization Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2017. Stockholm ECDC, 2017. Available at: <u>https://ecdc.europa.eu/en/publications-data/tuberculosis-surveillance-and-monitoring-europe-2017</u>.
- 75. Ködmön C, Zucs P, van der Werf M. Migration-related tuberculosis: epidemiology and characteristics of tuberculosis cases originating outside the European Union and European Economic Area, 2007 to 2013. Euro Surveill. 2016;21:12.
- 76. European Centre for Disease Prevention and Control and World Health Organization Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2018 – 2016 data. Stockholm: ECDC, 2018. Available at: <u>https://ecdc.europa.eu/en/publications-data/tuberculosis-surveillance-and-monitoring-europe-2018</u>.
- 77. Hollo V, Beauté J, Ködmön C, van der Werf MJ. Tuberculosis notification rate decreases faster in residents of native origin than in residents of foreign origin in the EU/EEA, 2010 to 2015. Eurosurveillance. 2017;22(12):30486.
- Hollo V, Kotila S, Kodmon C, Zucs P, Van der Werf MJ. The effect of migration within the European Union/European Economic Area on the distribution of tuberculosis, 2007-2013. Euro Surveill. 2016;21(12):pii=30171.
- 79. Dara M, Solovic I, Sotgiu G, D'Ambrosio L, Centis R, Tran R, et al. Tuberculosis care among refugees arriving in Europe: An ERS/WHO Europe Region survey of current practices. European Respiratory Journal. 2016;48(3):808-17.
- 80. Pareek M, Greenaway C, Noori T, Munoz J, Żenner D. The impact of migration on tuberculosis epidemiology and control in high-income countries: a review. BMC Medicine. 2016;14(1):48.
- 81. Pareek M, Baussano I, Abubakar I, Dye C, Lalvani A. Evaluation of Immigrant Tuberculosis Screening in Industrialized Countries. Emerging Infectious Diseases. 2012;18:1422-9.
- Klinkenberg E, Manissero D, Semenza J, Verver S. Migrant tuberculosis screening in the EU/EEA: yield, coverage and limitations. European Respiratory Journal. 2009;34(5):1180-9.
- Arshad S, Bavan L, Gajari K, Paget SN, Baussano I. Active screening at entry for tuberculosis among new immigrants: a systematic review and meta-analysis. European Respiratory Journal. 2010;35(6):1336-45.
- 84. Aldridge RW, Yates TA, Zenner D, White PJ, Abubakar I, Hayward AC. Pre-entry screening programmes for tuberculosis in migrants to low-incidence countries: a systematic review and meta-analysis. The Lancet Infectious Diseases. 2014;14(12):1240-9.
- 85. Van't Hoog A, Langendam M, Mitchell E, Cobelens F, Sinclair D, Leeflang M, et al. A systematic review of the sensitivity and specificity of symptom-and chest-radiography screening for active pulmonary tuberculosis in HIV-negative persons and persons with unknown HIV status. Systematic Review #2 for WHO Document- Systematic screening for active tuberculosis: principles and recommendations.Geneva, Switzerland: WHO, 2013.
- 86. Pinto LM, Pai M, Dheda K, Schwartzman K, Menzies D, Steingart KR. Scoring systems using chest radiographic features for the diagnosis of pulmonary tuberculosis in adults: a systematic review. Eur Resp J. 2013;42(2):480-94.
- Mitchell EMH, Shapiro A, Golub J, Kranzer K, Portocarrero AV, Najlis CA, et al. Acceptability of TB Screening Among At-Risk and Vulnerable Groups: A Systematic Qualitative/Quantitative Literature Metasynthesis Systematic Review #4a for WHO. Systematic screening for active tuberculosis: principles and recommendations. Geneva, Switzerland: World Heatlh Organization, 2013.
- World Health Organization. Systematic Screening for Active Tuberculosis: Principles & Recommendations. Geneva, Switzerland: World Health Organization, 2013.

- 89. Schwartzman K, Menzies D. Tuberculosis screening of immigrants to low-prevalence countries: a cost-effectiveness analysis. American Journal of Respiratory and Critical Care Medicine. 2000;161(3):780-9.
- Dasgupta K, Schwartzman K, Marchand R, Tennenbaum TN, Brassard P, Menzies D. Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. American Journal of Respiratory and Critical Care Medicine. 2000;162(6):2079-86.
- Oxlade O, Schwartzman K, Menzies D. Interferon-gamma release assays and TB screening in high-income countries: a costeffectiveness analysis. The International Journal of Tuberculosis and Lung Disease. 2007;11(1):16-26.
- Rechel B, Mladovsky P, Ingleby D, Mackenbach JP, McKee M. Migration and health in an increasingly diverse Europe. The Lancet. 2013;381:1235-45.
- Seedat F, Hargreaves S, Nellums LB, Ouyang J, Brown M, Friedland JS, et al. How effective are approaches to migrant screening for infectious diseases in Europe? A systematic review. The Lancet Infectious Diseases. 2018 Sep;18(9):e259-e271.
- 94. Menzies D, Benedetti A, Paydar A, Martin I, Royce S, Pai M, et al. Effect of duration and intermittency of rifampin on tuberculosis treatment outcomes: a systematic review and meta-analysis. PLoS Med. 2009;6(9):e1000146.
- 95. Yee D, Valiquette C, Pelletier M, Parisien I, Rocher I, Menzies D. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. Am J Respir Crit Care Med. 2003;167(11):1472-7.
- European Centre for Disease Prevention and Control (ECDC)/World Health Organization Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2017. Stockholm: ECDC, 2017.
- Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clinical Infectious Diseases. 2016;63(7):e147-e95.
- European Centre for Disease Prevention and Control. Guidance on tuberculosis control in vulnerable and hard-to-reach populations. Stockholm: ECDC, 2016. Available at: https://www.ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/TB-guidance-interventions-vulnerablegroups.pdf.
- Liu Q, Abba K, Alejandria MM, Sinclair D, Balanag VM, Lansang MAD. Reminder systems to improve patient adherence to tuberculosis clinic appointments for diagnosis and treatment. The Cochrane Library. 2014. Cochrane Database Syst Rev. 2014 Nov 18;(11):CD006594.
- 100. Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. The Cochrane Library. 2015. Cochrane Database Syst Rev. 2015 Sep 3;(9):CD007952.
- Nglazi MD, Bekker L-G, Wood R, Hussey GD, Wiysonge CS. Mobile phone text messaging for promoting adherence to antituberculosis treatment: a systematic review. BMC Infectious Diseases. 2013;13(1):1.
- 102. European Centre for Disease Prevention and Control. HIV and migrants. Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia. Stockholm: 2017. Available at: https://ecdc.europa.eu/sites/portal/files/documents/HIV%20and%20migrants.pdf.
- 103. Australian Panel Member Instructions: Immigration Medical Examinations. Australian Government Department of Home Affairs, July 2018.
- 104. Fakoya I, Reynolds R, Caswell G, Shiripinda I. Barriers to HIV testing for migrant black Africans in Western Europe. HIV Medicine. 2008;9:23-5.
- 105. Public Health Agency of Canada. Canadian Tuberculosis Standards. Chapter 13: Tuberculosis Surveillance and Screening in Selected High-Risk Populations. 2014. Available at: https://www.canada.ca/en/public-health/services/infectiousdiseases/canadian-tuberculosis-standards-7th-edition/edition-9.html.
- 106. Fakoya I, Álvarez-del Arco D, Woode-Owusu M, Monge S, Rivero-Montesdeoca Y, Delpech V, et al. A systematic review of post-migration acquisition of HIV among migrants from countries with generalised HIV epidemics living in Europe: implications for effectively managing HIV prevention programmes and policy. BMC Public Health. 2015;15(1):561.
- 107. Panel Members' Handbook. Government of Canada, 2013. Immigration Medical Examination Instructions: Tuberculosis. Government of Canada, November 2013.
- 108. Government of Canada. Operations Directorate, health Branch, Immigration Medical Examination Instructions: Tuberculosis. 01 November 2013. Available at: https://www.canada.ca/content/dam/ircc/migration/ircc/english/department/partner/pp/pdf/imei\_tuberculosis.pdf
- 109. La ministre des solidarités et de la santé. Direction générale de la santé. Instruction No.
   DGS/SP1/DGOS/SDR4/DSS/SD2/DGCS/2018/143 du 8 juin 2018 relative à la mise en place du parcours de santé des migrante prime arrivate.
- migrants primo-arrivants. [Instructions relating to the implementation of health examinations for newly-arrived migrants]. Available at: <u>http://circulaires.legifrance.gouv.fr/pdf/2018/07/cir\_43755.pdf</u>.
- 110. Public Health England. UK Visas and Immigration UK tuberculosis technical instructions (UKTBTI) Version 6. 2013 September 2013.
- 111. Kunst H, Burman M, Arnesen TM, Fiebig L, Hergens MP, Kalkouni O, et al. Tuberculosis and latent tuberculous infection screening of migrants in Europe: comparative analysis of policies, surveillance systems and results. The International Journal of Tuberculosis and Lung Disease. 2017;21(8):840-51.
- 112. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. Geneva: 2014. Available at: http://www.unaids.org/sites/default/files/media\_asset/90-90-90\_en.pdf.
- 113. US Centers for Disease Control and Prevention. CDC Immigration Requirements: Technical Instructions for Tuberculosis Screening and Treatment Using Cultures and Directly Observed Therapy In: Technical Instructions for Medical Examination of Aliens. 2009.
- van der Werf MJ, Zellweger JP. Impact of migration on tuberculosis epidemiology and control in the EU/EEA. Eurosurveillance. 2016;21(12):30174.
- 115. Getahun H, Matteelli A, Abubakar I, Aziz MA, Baddeley A, Barreira D, et al. Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries. European Respiratory Journal. 2015;46(6):1563-76.
- 116. Eurostat. European social statistics 2013. Available at: https://ec.europa.eu/eurostat/web/products-pocketbooks/-/KS-FP-13-001.
- 117. Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. PLoS Med. 2016;13(10):e1002152.

- 118. World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization, 2018.
- 119. Pai M, Zwerling A, Menzies D. Systematic review: T-cell–based assays for the diagnosis of latent tuberculosis infection: an update. Ann Intern Med. 2008;149(3):177-84.
- 120. Kik SM RM. Predictive utility of the tuberculin skin test and interferon-gamma release assay among individuals who are not prescribed tuberculosis preventive therapy. Systematic Review # 4 for WHO Document "Guidelines on the management of latent tuberculosis infection". Geneva, Switzerland: World Health Organization, 2014.
- 121. Kahwati LC, Feltner C, Halpern M, Woodell CL, Boland E, Amick HR, et al. Primary care screening and treatment for latent tuberculosis infection in adults: evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2016;316(9):970-83.
- 122. Stagg HR, Zenner D, Harris RJ, Munoz L, Lipman MC, Abubakar I. Treatment of latent tuberculosis infection: a network meta-analysis. Ann Inter Med. 2014;161(6):419-28.
- 123. Sharma SK, Sharma A, Kadhiravan T, Tharyan P. Rifamycins (rifampicin, rifabutin and rifapentine) compared to isoniazid for preventing tuberculosis in HIV-negative people at risk of active TB. Evidence-Based Child Health: A Cochrane Review Journal. 2014;9(1):169-294.
- 124. Alsdurf H, Hill PC, Matteelli A, Getahun H, Menzies D. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. The Lancet Infectious Diseases. 2016;16(11):1269-78.
- 125. Sandgren A, Noordegraaf-Schouten MV, van Kessel F, Stuurman A, Oordt-Speets A, van der Werf MJ. Initiation and completion rates for latent tuberculosis infection treatment: a systematic review. BMC Infectious Diseases. 2016;16(1):1.
- 126. Pareek M, Watson JP, Ormerod LP, Kon OM, Woltmann G, White PJ, et al. Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis. The Lancet Infectious Diseases. 2011;11(6):435-44.
- 127. Pareek M, Bond M, Shorey J, Seneviratne S, Guy M, White P, et al. Community-based evaluation of immigrant tuberculosis screening using interferon-release assays and tuberculin skin testing: observational study and economic analysis.. Thorax. 2013 Mar;68(3):230-9.
- 128. Hardy AB, Varma R, Collyns T, Moffitt SJ, Mullarkey C, Watson JP. Cost-effectiveness of the NICE guidelines for screening for latent tuberculosis infection: the QuantiFERON-TB Gold IGRA alone is more cost-effective for immigrants from high burden countries. Thorax. 2010;65(2):178-80.
- 129. Iqbal AZ, Leighton J, Anthony J, Knaup RC, Peters EB, Bailey TC. Cost-effectiveness of Using Quantiferon Gold (QFT-G)® versus Tuberculin Skin Test (TST) among US and Foreign Born Populations at a Public Health Department Clinic with a Low Prevalence of Tuberculosis. Public Health Nursing. 2014;31(2):144-52.
- 130. Linas BP, Wong AY, Freedberg KA, Horsburgh Jr CR. Priorities for screening and treatment of latent tuberculosis infection in the United States. Am J Respir Crit Care Med. 2011;184(5):590-601.
- 131. Deuffic-Burban S, Atsou K, Viget N, Melliez H, Bouvet E, Yazdanpanah Y. Cost-effectiveness of QuantiFERON®-TB test vs. tuberculin skin test in the diagnosis of latent tuberculosis infection. The International Journal of Tuberculosis and Lung Disease. 2010;14(4):471-81.
- 132. Pooran A, Booth H, Miller RF, Scott G, Badri M, Huggett JF, et al. Different screening strategies (single or dual) for the diagnosis of suspected latent tuberculosis: a cost effectiveness analysis. BMC Pulmonary Medicine. 2010;10(1):1.
- 133. Greenaway C, Sandoe A, Vissandjee B, Kitai I, Gruner D, Wobeser W, et al. Tuberculosis: evidence review for newly arriving immigrants and refugees. Canadian Medical Association Journal. 2011;183(12):E939-E51.
- 134. Munro SA, Lewin SA, Smith HJ, Engel ME, Fretheim A, Volmink J. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. PLoS Med. 2007;4(7):e238.
- 135. Tomás BA, Pell C, Cavanillas AB, Solvas JG, Pool R, Roura M. Tuberculosis in migrant populations. A systematic review of the qualitative literature. PLOS one. 2013;8(12):e82440.
- 136. Stuurman AL, Noordegraaf-Schouten MV, van Kessel F, Oordt-Speets AM, Sandgren A, van der Werf MJ. Interventions for improving adherence to treatment for latent tuberculosis infection: a systematic review. BMC Infectious Diseases. 2016;16(1):1.
- 137. M'Imunya JM, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis. The Cochrane Library. 2012(5). Available at: <u>https://www.cap-</u>

tb.org/sites/default/files/documents/Cochrane.PatientAdherence.Counselling.TB.pdf

- 138. Griffiths C, Sturdy P, Brewin P, Bothamley G, Eldridge S, Martineau A, et al. Educational outreach to promote screening for tuberculosis in primary care: a cluster randomised controlled trial. The Lancet. 2007;369(9572):1528-34.
- 139. D'Ambrosio L, Centis R, Dara M, Solovic I, Sulis G, Zumla A, et al. European policies in the management of tuberculosis among migrants. Inter J Infect Dis. 2017.56, 85–89.
- 140. La ministre des solidarités et de la santé. Recommandations relatives à la lutte antituberculeuse chez les migrants en France, 2005. [Recommendations to prevent tuberculosis among migrants in France.] Available at: https://solidarites-sante.gouv.fr/IMG/pdf/Avis\_30\_septembre\_2005\_relatif\_aux\_recommandations\_relatives\_a\_la\_lutte\_antituberculeuse\_chez \_\_les\_migrants\_en\_France.pdf.
- 141. Public Health England. Guidance: Tuberculosis Screening, Latent TB infection (LTBI) 2014 [10 April 2018]. Available at: https://www.gov.uk/guidance/tuberculosis-screening#latent-tb-infection-ltbi.
- 142. US Centers for Disease Control and Prevention. Refugee Health Guidelines. Immigrant and Refugee Health. CDC. 2013. Available at: https://www.cdc.gov/immigrantrefugeehealth/guidelines/refugee-guidelines.html.
- 143. US Centers for Disease Control and Prevention. Chapter-8 Newly Arrived Immigrants & Refugees. CDC 2017. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2018/advising-travelers-with-specific-needs/newly-arrived-immigrants-refugees.
- 144. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official American Thoracic Society/Infectious Diseases Society of America/US Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin Infect Dis. 2017;64(2):e1-e33.
- 145. European Centre for Disease Prevention and Control/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2017 – 2016 data. Stockholm: ECDC, 2017. Available at: <u>https://ecdc.europa.eu/en/publications-data/hivaids-surveillanceeurope-2017-2016-data</u>
- 146. Pharris A, Quinten C, Noori T, Amato-Gauci AJ, van Sighem A. Estimating HIV incidence and number of undiagnosed individuals living with HIV in the European Union/European Economic Area, 2015. Eurosurveillance. 2016;21(48):30417.

- 147. World Health Organization. HIV assays: laboratory performance and other operational characteristics: rapid diagnostic tests (combined detection of HIV-1/2 antibodies and discriminatory detection of HIV-1 and HIV-2 antibodies): Report 18. Geneva: WHO, 2015.
- Alvarez-del Arco D, Monge S, Azcoaga A, Rio I, Hernando V, Gonzalez C, et al. HIV testing and counselling for migrant populations living in high-income countries: a systematic review. European Journal of Public Health. 2013;23:1039-45.
   Salama P, Dondero, TJ. HIV surveillance in complex emergencies. AIDS. 2001;15(Supplement 3):S4-S12.
- 150. Pottie K, Medu O, Welch V, Dahal GP, Tyndall M, Rader T, et al. Effect of rapid HIV testing on HIV incidence and services in populations at high risk for HIV exposure: an equity-focused systematic review. BMJ Open. 2014;4(12).
- 151. Rice BD, Elford J, Delpech VC. A new method to assign country of HIV infection among heterosexuals born abroad and diagnosed with HIV. AIDS. 2012;26(15):1961-6.
- 152. Alvarez-del Arco D, Fakoya I, Thomadakis C, Pantazis N, Touloumi G, Gennotte A-F, et al. High levels of postmigration HIV acquisition within nine European countries. AIDS. 2017;31(14):1979-88.
- 153. Pottie K, Vissandjée B, Grant J. Human immunodeficiency virus. Evidence review for newly arriving immigrants and refugees: Appendix to Pottie K, Greenaway C, Feightner J, et al. Evidence-based clinical guidelines for immigrants and refugees. CMAJ 2011 Sep 6; 183(12): E824–E925.
- 154. World Health Organization. Consolidated guidelines on HIV testing services. Geneva: WHO, 2015.
- 155. European Centre for Disease Prevention and Control. HIV Testing: increasing uptake and effectiveness in the European Union. Stockholm: ECDC, 2010. Available at:
- https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/101129\_GUI\_HIV\_testing.pdf
- Mounier-Jack S, Nielsen S, Coker RJ. HIV testing strategies across European countries. HIV Medicine. 2008;9(2):13-9.
   Alvarez-Del Arco D, Monge S, Caro-Murillo AM, Ramirez-Rubio O, Azcoaga-Lorenzo A, Belza MJ, et al. HIV testing policies for migrants and ethnic minorities in EU/EFTA Member States. European Journal of Public Health. 2014;24:139-44.
- Kennedy CE, Fonner VA, Sweat MD, Okero FA, Baggaley R, O'Reilly KR. Provider-Initiated HIV Testing and Counseling in Low- and Middle-Income Countries: A Systematic Review. AIDS and Behavior. 2013;17(5):1571-90.
- 159. Desai M, Woodhall SC, Nardone A, Burns F, Mercey D, Gilson R. Active recall to increase HIV and STI testing: a systematic review. Sexually Transmitted Infections. 2015;91(5):314-23.
- 160. Chou R, Selph S, Dana T, et al. Screening for HIV: Systematic review to update the 2005 U.S. Preventive Services Task Force Recommendation. Annals of Internal Medicine. 2012;157(10):706-18.
- 161. Walensky RP, Morris BL, Reichmann WM, Paltiel AD, Arbelaez C, Donnell-Fink AL, et al. Counselor-Versus Provider-Based HIV Screening in the Emergency Department: Results From the Universal Screening for HIV Infection in the Emergency Room (USHER) Randomized Controlled Trial. Annals of Emergency Medicine. 2011;58(Supplement 1):s126-S32.
- 162. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 Infection with Early Antiretroviral Therapy. New England Journal of Medicine. 2011;365(6):493-505.
- 163. Lundgren JD, Babiker AG, Gordin F, Emery S, Grund B, Sharma S, et al. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. New England Journal of Medicine. 2015;373(9):795-807.
- 164. World Health Organization. Guidelines on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Geneva, Switzerland: WHO; 2015.
- Muessig KE, Smith MK, Powers KA, Lo Y-R, Burns DN, Grulich AE, et al. Does ART prevent HIV transmission among MSM? AIDS (London, England). 2012;26(18):2267-73.
- 166. Farnham PG, Gorsky RD, Holtgrave DR, Jones WK, Guinan ME. Counseling and testing for HIV prevention: costs, effects, and cost-effectiveness of more rapid screening tests. Public Health Reports. 1996;111(1):44-54.
- 167. Kassler WJ, Dillon BA, Haley C, Jones WK, Goldman A. On-site, rapid HIV testing with same-day results and counseling. AIDS. 1997;11(8):1045-51.
- 168. Wilkinson D, Wilkinson N, Lombard C, Martin D, Smith A, Floyd K, et al. On-site HIV testing in resource-poor settings: is one rapid test enough? AIDS. 1997;11(3):377-81.
- Kallenborn JC, Price TG, Carrico R, Davidson AB. Emergency Department Management of Occupational Exposures: Cost Analysis of Rapid HIV Test. Infection Control and Hospital Epidemiology. 2001;22(5):289-93.
- 170. Ekwueme DU, Pinkerton SD, Holtgrave DR, Branson BM. Cost comparison of three HIV counseling and testing technologies. American Journal of Preventive Medicine. 2003;25(2):112-21.
- 171. Doyle NM, Levison JE, Gardner MO. Rapid HIV versus enzyme-linked immunosorbent assay screening in a low-risk Mexican American population presenting in labor: A cost-effectiveness analysis. American Journal of Obstetrics and Gynecology. 2005;193(3):1280-5.
- 172. Paltiel AD, Weinstein MC, Kimmel AD, Seage GR, Losina E, Zhang H, et al. Expanded Screening for HIV in the United States — An Analysis of Cost-Effectiveness. New England Journal of Medicine. 2005;352(6):586-95.
- 173. Vickerman P, Terris-Prestholt F, Delany S, Kumaranayake L, Rees H, Watts C. . Are targeted HIV prevention activities costeffective in high prevalence settings? Results from a sexually transmitted infection treatment project for sex workers in Johannesburg, South Africa. Sexually transmitted diseases. Transmitted Diseases. 2006;33(10):S122-S32.
- 174. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS. 2006;20:1447-50.
- 175. Hernando V, Alvárez-del Arco D, Alejos B, Monge S, Amato-Gauci AJ, Noori T, et al. HIV Infection in Migrant Populations in the European Union and European Economic Area in 2007–2012: An Epidemic on the Move. Journal of Acquired Immune Deficiency Syndromes. 2015;70(2).
- 176. European Centre for Disease Prevention and Control. Evidence brief: Impact of stigma and discrimination on access to HIV services in Europe. Monitoring implementation of the Dublin Declaration on partnership to fight HIV/AIDS in Europe and Central Asia. Stockholm: ECDC; 2017. Available at: <a href="https://ecdc.europa.eu/sites/portal/files/documents/Dublin-EB-Stigma%20and%20discrimination%202017">https://ecdc.europa.eu/sites/portal/files/documents/Dublin-EB-Stigma%20and%20discrimination%202017</a> final.pdf
- 177. Blondell SJ, Kitter B, Griffin MP, Durham J. Barriers and Facilitators to HIV Testing in Migrants in High-Income Countries: A Systematic Review. AIDS and Behavior. 2015;19(11):2012-24.
- 178. Deblonde J, De Koker P, Hamers FF, Fontaine J, Luchters S, Temmerman M. Barriers to HIV testing in Europe: a systematic review. European Journal of Public Health. 2010;20(4):422-32.
- 179. Arco DAD, Monge S, Caro-Murillo AM, Ramïrez-Rubio O, Azcoaga-Lorenzo A, Belza MJ, et al. HIV testing policies for migrants and ethnic minorities in EU/EFTA Member States. European Journal of Public Health. 2014;24(1):139-44.

- 180. European Centre for Disease Prevention and Control. Antenatal screening for HIV, hepatitis B, syphilis and rubella susceptability in the EU/EEA. Stockholm: ECDC, 2017. Available at: <u>https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/antenatal-screening-HIV-hepatitis-B-syphilis-rubella-EU.pdf</u>
- 181. European AIDS Clinical Society. European guidelines for the treatment of HIV-positive adults in Europe. Version 9.1, October 2018. Available at: http://www.eacsociety.org/files/2018\_guidelines-9.1-english.pdf
- 182. Rice BD, Elford J, Yin Z, Delpech VC. A new method to assign country of HIV infection among heterosexuals born abroad and diagnosed with HIV. AIDS. 2012;26(15):1961-6.
- Desgrees-du-Lou A, Pannetier J, Ravalihasy A, Gosselin A, Supervie V, Panjo H, et al. Sub-Saharan African migrants living with HIV acquired after migration, France, ANRS PARCOURS study, 2012 to 2013. Euro Surveill. 2015;20(46).
- 184. Desgrees-du-Lou A, Pannetier J, Ravalihasy A, Le Guen M, Gosselin A, Panjo H, et al. Is hardship during migration a determinant of HIV infection? Results from the ANRS PARCOURS study of sub-Saharan African migrants in France. AIDS. 2016;30(4):645-56.
- 185. Réévaluation de la stratégie de dépistage de l'infection à VIH en France. Haute Autorité de Santé; 2017 March 2017.
- 186. HIV: Migrant Health Guide: Public Health England; London: PHE, 2014 [updated 31 July 2014 and 18 July 2018]. Available from: https://www.gov.uk/guidance/hiv-migrant-health-guide.
- 187. HIV Testing in England: 2017 report. Public Health England; London: PHE 2017. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\_data/file/666478/HIV\_testing\_in \_England\_2017\_report.pdf.
- 188. World Health Organization. Global hepatitis report. Geneva: WHO, 2017.
- 189. Pitigoi D, Rafila A, Pistol A, Arama V, Molagic V, Streinu-Cercel A. Trends in hepatitis B incidence in Romania, 1989-2005. Eurosurveillance. 2008;13(2):11-2%P 8012.
- 190. World Health Organization. Guidelines on Hepatitis B and C testing. Geneva: WHO, 2017.
- 191. Rossi C, Shrier I, Marshall L, Cnossen S, Schwartzman K, Klein MB, et al. Seroprevalence of Chronic Hepatitis B Virus Infection and Prior Immunity in Immigrants and Refugees: A Systematic Review and Meta-Analysis. PLoS ONE. 2012;7(9):e44611-e.
- 192. Rossi C, Schwartzman K, Oxlade O, Klein MB, Greenaway C, et al. Hepatitis and Vaccination Strategies for Newly Arrived Adult Canadian Immigrants and Refugees: Analysis. PLoS One 2013 Oct 18;8(10).
- 193. European Centre for Disease Prevention and Control. Hepatitis B and C testing activities, needs, and priorities in the EU/EEA. Stockholm: ECDC, 2017. Available at: https://ecdc.europa.eu/en/publications-data/hepatitis-b-and-c-testing-activities-needs-and-priorities-eueea.
- 194. European Centre for Disease Prevention and Control. Antenatal screening approaches effective in preventing mother-childtransmission of HIV, hepatitis B, syphilis and rubella in vulnerable populations. Stockholm: ECDC; 2017. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/antenatal-screening-approaches-to-prevent-MTCT-of-HIV-HBV-syphilis-rubella-lit-review-2017.pdf
- 195. Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ, et al. Estimations of worldwide prevalence of chronic hepatitis C virus infection: a systematic review of data published between 1965 and 2013. The Lancet Infectious Diseases. 2015;386 (10003):1546-55.
- 196. Chou R, Dana T, Bougatsos C, Blazina I, Zakher B, Khangura J. Screening for Hepatitis B Virus Infection in Nonpregnant Adolescents and Adults: Systematic Review to Update the 2004 U.S. Preventive Services Task Force Recommendation. Rockville (MD): Agency for Healthcare Research and Quality, 2014.
- 197. Wong GLH, Yiu KKL, Wong VWS, Tsoi KKF, Chan HLY. Meta-analysis: Reduction in hepatic events following interferon-alfa therapy of chronic hepatitis B. Aliment Pharmacol Ther. 2010;32(9):1059-68.
- 198. Graham S, Guy RJ, Cowie B, Wand HC, Donovan B, Akre SP, et al. Chronic hepatitis B prevalence among Aboriginal and Torres Strait Islander Australians since universal vaccination: a systematic review and meta-analysis 2013. BMC Infect Dis. 2013 08 31;13(1):403.
- 199. European Centre for Disease Prevention and Control. Epidemiological assessment of hepatitis B and C among migrants in the EU/EEA. Stockholm: ECDC; 2016. <u>https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/epidemiological-assessment-hepatitis-B-and-C-among-migrants-EU-EEA.pdf</u>
- 200. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2016. Journal of Hepatology. 2017;66(1):153-94.
- 201. World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: WHO, 2015.
- 202. Chang MH, You SL, Chen CJ, Liu CJ, Lee CM, Lin SM, et al. Decreased incidence of hepatocellular carcinoma in hepatitis B vaccinees: A 20-year follow-up study. Cancer Inst. 2009;101:1348-55.
- Blachier M, Leleu H, Peck-Radosavljevic M, Valla D, Roudot-Thoraval F, J. C, The burden of liver disease in Europe: A review of available epidemiological data 2009. J Hepatol. 2013 Mar; 58(3):593-608.
- 204. Duffell E, Hedrich D, Mardh O, Mozalevskis A. Towards Elimination of hepatitis B and C in European Union and European Economic Area Countries: Monitiroing World Health Organization's global health sector strategy core indicators and scaling up key interventions. Euro Surveill 2017;22(9):pii=30476.
- 205. LeFevre ML. Screening for hepatitis B virus infection in nonpregnant adolescents and adults: U.S. preventive services task force recommendation statement. Vol Annals of Internal Medicine 2014;161:58-66.
- 206. Rossi C, Schwartzman K, Oxlade O, Klein MB, Greenaway C. Hepatitis B Screening and Vaccination Strategies for Newly Arrived Adult Canadian Immigrants and Refugees: A Cost-Effectiveness Analysis. PLOS ONE. 2013;8(10):e78548.
- Wong WWL, Woo G, Heathcote E, Krahn M. Cost effectiveness of screening immigrants for hepatitis B. Liver Int. 2011;31(8):1179-90.
   Hutton DW, Tan D, So SK, Brandeau ML. Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B. Ann Intern Med. 2007;147(7):460-9.
- Veldhuijzen IK, Toy M, Hahne SJ, De Wit GA, Schalm SW, de Man RA, et al. Screening and Early Treatment of Migrants for Chronic Hepatitis B Virus Infection Is Cost-Effective. Gastroenterology. 2010;138(2):522-30.
- Rein DB, Lesesne SB, Smith BD, Weinbaum CM. Models of community-based hepatitis B surface antigen screening programs in the U.S. and their estimated outcomes and costs. Public health reports (Washington, DC: 1974). 2011;126(4):560-7.

- Jazwa A, Coleman MS, Gazmararian J, Wingate LMT, Maskery B, Mitchell T, et al. Cost-benefit comparison of two proposed overseas programs for reducing chronic Hepatitis B infection among refugees: is screening essential? Vaccine. 2015;33(11):1393-9.
- Ruggeri M, Cicchetti A, Gasbarrini A. The cost-effectiveness of alternative strategies against HBV in Italy. Health policy (Amsterdam, Netherlands). 2011;102(1):72-80.
- 213. Eckman MH, Kaiser TE, Sherman KE. The cost-effectiveness of screening for chronic hepatitis B infection in the United States. Clin Infect Dis. 2011;52(11):1294-306.
- 214. Li S Onder FO, Xie Q, Liu Y, Toy M. Cost-effectiveness of Early Detection of Inactive and Treatment of Active Cases in a High Endemic Chronic Hepatitis B Region. J Antivir Antiretrovir. 2013;5:154-9.
- 215. Hargreaves S, Seedat F, Car J, Escombe R, Hasan S, Eliahoo J, et al. Screening for latent TB, HIV, and hepatitis B/C in new migrants in a high prevalence area of London, UK: a cross-sectional study. BMC Infect Dis, 2014:14,657.
- 216. Do TN, Nam S. Knowledge, Awareness and Medical Practice of Asian Americans/Pacific Islanders on Chronic Hepatitis B Infection: Review of Current Psychosocial Evidence. Pogon sahoe yon'gu. 2011;31(3):341.
- 217. Owiti JA, Greenhalgh T, Sweeney L, Foster GR, Bhui KS. Illness perceptions and explanatory models of viral hepatitis B & C among immigrants and refugees: a narrative systematic review. BMC Public Health. 2015;15(1):151.
- 218. Lee A, Vedio A, Lio EZH, Horsley J, Jesurasa A, Salway S, et al. Determinants of uptake of heptitis B testing and healthcare access by migrant Chinese in England: a qualitative study. BMC Public Health. 2017;17:747.
- 219. Robotin MC, George J. Community-based hepatitis B screening: what works? Hepatology International. 2014;8:478-92.
- 220. Herman A, Bullen C, Finau S, Ofanoa M. Mobilising Pacific people for health: insights from a hepatitis B screening programme in Auckland, New Zealand. Pacific health dialog. 2006;13(2):9-15.
- van der Veen YJ, van Empelen P, de Zwart O, Visser H, Mackenbach JP, Richardus JH. Cultural tailoring to promote hepatitis B screening in Turkish Dutch: a randomized control study. Health promotion international. 2014;29(4):692-704.

222. World Health Organization. Enter the Hepatitis Testing Innovation Contest: WHO; Geneva 2016 [cited 12 June 2017]. Available from: <u>http://www.who.int/hepatitis/news-events/hepatitis-innovation-contest/en</u>

- 223. Gish RG, Cooper SL. Hepatitis B in the Greater San Francisco Bay Area: An Integrated Programme to Respond to a Diverse Local Epidemic. Journal of Viral Hepatitis. 2011;18(4):e40-51.
- 224. Richter C, Beest GT, Sancak I, Aydinly R, Bulbul K, Laetemia-Tomata F, et al. Hepatitis B prevalence in the Turkish population of Arnhem: implications for national screening policy? Epidemiology and Infection. 2012;140(4):724-30.
- Veldhuijzen IK, Wolter R, Rijckborst V, Mostert M, Voeten HA, Cheung Y, et al. Identification and treatment of chronic hepatitis B in Chinese migrants: Results of a project offering on-site testing in Rotterdam, the Netherlands. [cited 12 June 2018]. Journal of Hepatology. 2012;57(6):1171-6. Available from: <u>http://www.ncbi.nlm.nih.gov/pubmed/22885717</u>
- 226. El-Hamad I, Pezzoli MC, Chiari E, Scarcella C, Vassallo F, Puoti M, et al. Point-of-care screening, prevalence, and risk factors for hepatitis B infection among 3,728 mainly undocumented migrants from Non-EU countries in northern Italy. Med. 2015;22(2):78-86.
- 227. Chang MH, Chen CJ, Lai MS, Hsu HM, Wu TC, Kong MS, et al. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. Taiwan Childhood Hepatoma Study Group. 1997;336:1855-9.
- Ni YH, Chang MH, Huang LM, Chen HL, Hsu HY, Chiu TY, et al. Virus infection in children and adolescents in a hyperendemic area: 15 years after mass hepatitis B vaccination. Ann Intern Med. 2001;135(9):796-800.
- 229. Jefferson T, Demicheli V, Deeks J, MacMillan A, Sassi F, Pratt M. Vaccines for preventing hepatitis B in health-care workers. Nurs Times. 2001 Nov 15-21;97(46):39.
- 230. Dhumeaux Daniel DJ-F, Yeni Patrick. Prise en charge thérapeutique et suivi de l'ensemble des personnes infectées par le virus de l'hépatite C Rapport de recommandations 2016. Conseil national du sida; Agence nationale de recherche sur le SIDA et les hepatites virales (France); 2018 October 2016.
- 231. Hepatitis B: migrant health guide: Public Health England. London: PHE, 2014 [updated 28 June 2017]. Available from: https://www.gov.uk/guidance/hepatitis-b-migrant-health-guide.
- 232. Public Health England. Health protocol: pre-entry health assessments for UK-bound refugees. UK Visas and Immigration, August 2017. Available at:
  - https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\_data/file/638386/protocolguidance.pdf
- Public Health England. Vaccination of individuals with uncertain or incomplete immunisation status. London: PHE, 2017.
   Mühlberger N, Schwarzer R, Lettmeier B, Sroczynski G, Zeuzem S, Siebert U. HCV-related burden of disease in Europe: a
- systematic assessment of incidence, prevalence, morbidity, and mortality. BMC Public Health. 2009;9(34). 235. Mathurin P. HCV burden in Europe and the possible impact of current treatment. Dig Liver Dis. 2013;45 Suppl 5:S314-7.
- El Khoury AC, Wallace C, Klimack WK, Razavi H. Economic burden of hepatitis C-associated diseases: Europe, Asia Pacific, and the Americas. J Med Econ. 2012;15(5):887-96.
- Razavi H, Robbins S, Zeuzem S, Negro F, Buti M, Duberg A-S, et al. Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study. The Lancet Gastroenterology & Hepatology. 2017;2(5):325-36.
- 238. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, Fried MW, Segal JB, Sulkowski MS. Oral direct-acting agent therapy for hepatitis c virus infection: A systematic review. Annals of Internal Medicine. 2017.
- 239. European Centre for Disease Prevention and Control. Systematic review on hepatitis B and C prevalence in the EU/EEA. Stockholm: ECDC, 2016. Available at:
- https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/systematic-review-hepatitis-B-C-prevalence.pdf 240. Hofstraat S, Falla A, Duffell E, Hahne S, Amato-Gauci A, Veldhuijzen I, et al. Current prevalence of chronic hepatitis B and C
- virus infection in the general population, blood donors and pregnant women in the EU/EEA: a systematic review. Epidemiology & Infection. 2017;145(14):2873-85.
- 241. World Health Organization Regional Office for Europe. Action plan for the health sector response to viral hepatitis in the WHO European Region. Copenhagen: WHO/Europe, 2016.
- 242. International Organization for Migration. Europe/Mediterranean Mixed Flows in the Mediterranean and Beyond Flows Compilation Overview 2015. OiM 2016. Available at: https://www.iom.int/sites/default/files/situation\_reports/file/Mixed-Flows-Mediterranean-and-Beyond-Compilation-Overview-2015.pdf.
- 243. International Organization for Migration. Migration flows- Europe. 2016. Available at: <a href="http://migration.iom.int/europe?type=arrivals">http://migration.iom.int/europe?type=arrivals</a>.

- 244. Eurostat. Migration and Migrant Population Statistics. 2017. Available at: https://ec.europa.eu/eurostat/statisticsexplained/index.php/Migration\_and\_migrant\_population\_statistics.
- 245. Falla A, Ahmad A, Duffell E, Noori T, Veldhuijzen I. Estimating the scale of chronic hepatitis C virus infection in the EU/EEA: a focus on migrants from anti-HCV endemic countries. BMC Infect Dis 2018;18(42).
- 246. Greenaway C, Ma AT, Kloda LA; Klein M; Cnossen S; Schwarzer G. The Seroprevalence of Hepatitis C Antibodies in Immigrants and Refugees from Intermediate and High Endemic Countries: A Systematic Review and Meta-Analysis. PLoS ONE. 2015;10:e0141715.
- Sharma S, Carballo M, Feld JJ, Janssen HL. Immigration and viral hepatitis. Journal of Hepatology. 2015;63(2):515-22.
   Chen W, Tomlinson G, Krahn M, Heathcote J. Immigrant patients with chronic hepatitis C and advanced fibrosis have a higher risk of hepatocellular carcinoma. Journal of Viral Hepatitis. 2012;19(8):574-80.
- 249. Greenaway C, Azoulay L, Allard R, Cox J, Tran VA, Chakra CNA, et al. A population-based study of chronic hepatitis C in immigrants and non-immigrants in Quebec, Canada. BMC Infectious Diseases. 2017;17(1):140.
- 250. Nguyen L, Nguyen M. Systematic review: Asian patients with chronic hepatitis C infection. Alimentary Pharmacology & Therapeutics. 2013;37(10):921-36.
- 251. Tiittala P, Ristola M, Liitsola K, Ollgren J, Koponen P, Surcel H-M, et al. Missed hepatitis b/c or syphilis diagnosis among Kurdish, Russian, and Somali origin migrants in Finland: linking a population-based survey to the national infectious disease register. BMC Infectious Diseases. 2018;18(1):137.
- 252. Khuroo MS, Khuroo NS, Khuroo MS. Diagnostic accuracy of point-of-care tests for hepatitis C virus infection: a systematic review and meta-analysis. PLoS ONE. 2015;10:e0121450.
- 253. Kimer N, Dahl EK, Gluud LL, Krag A. Antiviral therapy for prevention of hepatocellular carcinoma in chronic hepatitis C: systematic review and meta-analysis of randomised controlled trials. BMJ Open. 2012;2.
- 254. Simmons B, Saleem J, Heath K, Cooke GS, Hill A. Long-Term Treatment Outcomes of Patients Infected With Hepatitis C Virus: A Systematic Review and Meta-analysis of the Survival Benefit of Achieving a Sustained Virological Response. Clin Infect Dis. 2015;61(5):730-40.
- 255. Public Health Agency of Canada. Treatment for Hepatitis C Virus: a Systematic Review and Meta-Analysis. Ottawa: Canadian Preventative Task Force, 2016.
- 256. Yehia BR, Schranz AJ, Umscheid CA, Lo Re V, 3rd. The treatment cascade for chronic hepatitis C virus infection in the United States: a systematic review and meta-analysis. PLoS ONE. 2014;9(7):e101554.
- 257. Selvapatt N, Ward T, Bailey H, Bennett H, Thorne C, See L-M, et al. Is antenatal screening for hepatitis C virus costeffective? A decade's experience at a London centre. Journal of Hepatology. 2015;63(4):797-804.
- Wong WW, Erman A, Feld JJ, Krahn M. Model-based projection of health and economic effects of screening for hepatitis C in Canada. CMAJ Open. 2017;5(3):E662.
- 259. Deuffic-Burban S, Obach D, Canva V, Pol S, Roudot-Thoraval F, Dhumeaux D, et al. Cost-effectiveness and budget impact of interferon-free direct-acting antiviral-based regimens for hepatitis C treatment: the French case. Journal of Viral Hepatitis. 2016;23(10):767-79.
- 260. Chhatwal J, Kanwal F, Roberts MS, Dunn MA. Cost-effectiveness and budget impact of hepatitis C virus treatment with sofosbuvir and ledipasvir in the United States. Annals of Internal Medicine. 2015;162(6):397-406.
- 261. Hagan LM, Sulkowski MS, Schinazi RF. Cost analysis of sofosbuvir/ribavirin versus sofosbuvir/simeprevir for genotype 1 hepatitis C virus in interferon-ineligible/intolerant individuals. Hepatology. 2014;60(1):37-45.
- 262. Najafzadeh M, Andersson K, Shrank WH, Krumme AA, Matlin OS, Brennan T, et al. Cost-effectiveness of novel regimens for the treatment of hepatitis C virus. Annals of Internal Medicine. 2015;162(6):407-19.
- 263. Rein DB, Wittenborn JS, Smith BD, Liffmann DK, Ward JW. The cost-effectiveness, health benefits, and financial costs of new antiviral treatments for hepatitis C virus. Clinical Infectious Diseases. 2015;61(2):157-68.
- Saab S, Gordon S, Park H, Sulkowski M, Ahmed A, Younossi Z. Cost-effectiveness analysis of sofosbuvir plus peginterferon/ribavirin in the treatment of chronic hepatitis C virus genotype 1 infection. Alimentary Pharmacology & Therapeutics. 2014;40(6):657-75.
- 265. Younossi Z, Park H, Saab S, Ahmed A, Dieterich D, Gordon S. Cost-effectiveness of all-oral ledipasvir/sofosbuvir regimens in patients with chronic hepatitis C virus genotype 1 infection. Alimentary Pharmacology & Therapeutics. 2015;41(6):544-63.
- Iyengar S, Tay-Teo K, Vogler S, Beyer P, Wiktor S, de Joncheere K, et al. Prices, costs, and affordability of new medicines for hepatitis C in 30 countries: an economic analysis. PLoS Medicine. 2016;13(5):e1002032.
- 267. Marshall AD, Cunningham EB, Nielsen S, Aghemo A, Alho H, Backmund M, et al. Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe. The Lancet Gastroenterology & Hepatology. 2018;3(2):125-33.
- 268. Marshall AD, Pawlotsky J-M, Lazarus JV, Aghemo A, Dore GJ, Grebely J. The removal of DAA restrictions in Europe–one step closer to eliminating HCV as a major public health threat. Journal of Hepatology. 2018.
- 269. In: Institute of Medicine (US) Committee on the Prevention and Control of Viral Hepatitis Infection; Colvin HM, Mitchell AE, editors. Washington (DC): National Academies Press (US); 2010.
- 270. Ferrante JM, Winston DG, Chen P-H, de la Torre AN. Family physicians' knowledge and screening of chronic hepatitis and liver cancer. Family Medicine. 2008;40(5):345-51.
- Fernandez M, Manzanares S, Jacques C, Caylá J, Kunkel J, Foster G. Screening for chronic viral hepatitis in migrant populations -- Report on Four HEPscreen Pilot Studies screening for chronic viral hepatitis in migrant populations. EU-HEP-SCREEN, Project No 20101105. 2014. Available at: <u>http://hepscreen.eu/wp-content/uploads/2014/12/HEPscreen\_Final-WP6-report\_Pilot-studies.pdf</u>.
- 272. Jafferbhoy H, Miller MH, McIntyre P, Dillon JF. The effectiveness of outreach testing for hepatitis C in an immigrant Pakistani population. Epidemiology and infection. 2012;140:1048-53.
- 273. Perumalswami PV, DeWolfe Miller F, Orabee H, Regab A, Adams M, Kapelusznik L, et al. Hepatitis C screening beyond CDC guidelines in an Egyptian immigrant community. Liver international: Official Journal of the International Association for the Study of the Liver. 2014;34:253-8.
- 274. Perumalswami PV, Factor SH, Kapelusznik L, Friedman SL, Pan CQ, Chang C, et al. Hepatitis Outreach Network: a practical strategy for hepatitis screening with linkage to care in foreign-born communities. Journal of Hepatology. 2013;58:890-7.
- 275. Zuure FR, Bouman J, Martens M, Vanhommerig JW, Urbanus AT, Davidovich U, et al. Screening for hepatitis B and C in first-generation Egyptian migrants living in the Netherlands. Liver International. 2013;33:727-38.

- 276. Falla AM, Rossi MK, Thomson R, Fernandez M, Cayla J, Csohán A, et al. Screening for chronic hepatitis B and C among migrants: outcomes and costs of different screening models. European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2015.
- 277. Linde AC, Sweet KA, Nelson K, Mamo B, Chute SM. Impact of the Hepatitis Testing and Linkage to Care (HepTLC) Initiative on Linkage to Care for Minnesota Refugees with Hepatitis B, 2012-2014. Public health reports (Washington, DC: 1974). 2016;131 Suppl 2:112-8.
- 278. Bottero J, Boyd A, Gozlan J, Carrat F, Nau J, Pauti M-D, et al. Simultaneous Human Immunodeficiency Virus-Hepatitis B-Hepatitis C Point-of-Care Tests Improve Outcomes in Linkage-to-Care: Results of a Randomized Control Trial in Persons Without Healthcare Coverage. Open Forum Infectious Diseases. 2015;2:162.
- 279. Hepatitis C Screening (NCEC National Clinical Guideline No. 15). Department of Health (Ireland), 2017.
- 280. Public Health England. Hepatitis C: migrant health guide: London: PHE, 2017. Available from:
- https://www.gov.uk/guidance/hepatitis-c-migrant-health-guide#testing.
- 281. Population à dépister et modalités du dépistage. Recommandations du comité d'experts réuni par l'Anaes. Agence nationale d'accréditation et d'évaluation en santé. Dépistage de l'hépatite C 2000. Haute autorité de santé: 2000 Available at: https://www.has-sante.fr/portail/jcms/c\_271987/fr/depistage-de-l-hepatite-c-populations-a-depister-et-modalites-dudepistage-recommandations-du-comite-d-experts-reuni-par-l-anaes.
- 282. Dhumeaux Daniel DJ-F, Patrick Y. Prise en charge thérapeutique et suivi de l'ensemble des personnes infectées par le virus de l'hépatite C Rapport de recommandations 2016. Conseil national du SIDA; Agence nationale de recherche sur le SIDA et les hepatites virales (France), October 2016. Available at: https://solidarites-sante.gouv.fr/IMG/pdf/rapport\_.pdf.
- Hotez PJ, Brindley PJ, Bethony JM, King CH, Pearce EJ, Jacobson J. Helminth infections: the great neglected tropical diseases. Journal of Clinical Investigation. 2008;118(4):1311-21.
- Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2197-223.
- Puthiyakunnon S, Boddu S, Li Y, Zhou X, Wang C, Li J, et al. Strongyloidiasis--an insight into its global prevalence and management. PLoS Negl Trop Dis. 2014;8(8):e3018.
- 286. Berry A, Paris L, Boissier J, Caumes E. Schistosomiasis Screening of Travelers to Corsica, France. Emerging Infectious Diseases. 2016;22(1):159.
- 287. King CH. Parasites and poverty: the case of schistosomiasis. Acta Trop. 2010;113(2):95-104.
- Zoni AC, Catalá L, Ault SK. Schistosomiasis Prevalence and Intensity of Infection in Latin America and the Caribbean Countries, 1942-2014: A Systematic Review in the Context of a Regional Elimination Goal. PLoS Neglected Tropical Diseases. 2016;10(3):e0004493.
- Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. The Lancet. 2014;383(9936):2253-64.
   World Health Organization. Strongyloidiasis (Fact sheet). WHO. 2016. Available at:
  - http://www.who.int/intestinal\_worms/epidemiology/strongyloidiasis/en.
- 291. González A, Gallo M, Valls ME, Muñoz J, Puyol L, Pinazo MJ, et al. Clinical and epidemiological features of 33 imported Strongyloides stercoralis infections. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2010;104(9):613-6.
- Requena-Mendez A, Chiodini P, Bisoffi Z, Buonfrate D, Gotuzzo E, Munoz J. The laboratory diagnosis and follow up of strongyloidiasis: a systematic review. PLoS Negl Trop Dis. 2013;7(1):e2002.
- 293. Buonfrate D, Requena-Mendez A, Angheben A, Munoz J, Gobbi F, Van Den Ende J, et al. Severe strongyloidiasis: a systematic review of case reports. BMC Infect Dis. 2013;13:78.
- 294. Deniaud F, Rouesse C, Collignon A, Domingo A, Rigal L. [Failure to offer parasitology screening to vulnerable migrants in France: Epidemiology and consequences]. Sante. 2010;20(4):201-8.
- 295. Hotez PJ, Alvarado M, Basanez MG, Bolliger I, Bourne R, Boussinesq M, et al. The global burden of disease study 2010: interpretation and implications for the neglected tropical diseases. PLoS Negl Trop Dis. 2014;8(7):e2865.
- 296. Beltrame A, Buonfrate D, Gobbi F, Angheben A, Marchese V, Monteiro GB, et al. The hidden epidemic of schistosomiasis in recent African immigrants and asylum seekers to Italy. Eur J Epidemiol. 2017.
- Khan K, Sears J, Chan A, Rashid M, Greenaway C, Stauffer W, et al. Strongyloides and Schistosoma: evidence review for newly arriving immigrants and refugee. The Canadian Collaboration for Immigrant and Refugee Health Appendix 8: Intestinal parasites 2011. Available at: <u>http://www.cmaj.ca/content/suppl/2010/06/07/cmaj.090313.DC1/imm-para-8-at.pdf</u>
   Public Health England. Helminth infections: migrant health guide. London: PHE, 2017.
- Chaves NJ, Paxton G, Biggs BA, Thambiran A, Smith M, Williams J. Recommendations for comprehensive post-arrival health assessment for people from refugee-like backgrounds. Surry Hills. Australia: Australasian Society for Infectious Diseases and Refugee Health Network, 2016.
- 300. Chaves NJ, Paxton GA, Biggs BA, Thambiran A, Gardiner J, Williams J, et al. The Australasian Society for Infectious Diseases and Refugee Health Network of Australia recommendations for health assessment for people from refugee-like backgrounds: an abridged outline. Med J Aust. 2017;206(7):310-5.
- Ochodo EA, Gopalakrishna G, Spek B, Reitsma JB, van Lieshout L, Polman K, et al. Circulating antigen tests and urine reagent strips for diagnosis of active schistosomiasis in endemic areas. Cochrane Database of Systematic Reviews. 2015(3).
- 302. King CH, Bertsch D. Meta-analysis of Urine Heme Dipstick Diagnosis of Schistosoma haematobium Infection, Including Low-Prevalence and Previously-Treated Populations. PLoS Negl Trop Dis. 2013;7(9):e2431.
- 303. Wang W, Li Y, Li H, Xing Y, Qu G, Dai J, et al. Immunodiagnostic efficacy of detection of *Schistosoma japonicum* human infections in China: a meta analysis. Asian Pacific Journal of Tropical Medicine. 2012;5(1):15-23.
- 304. Danso-Appiah A, Olliaro PL, Donegan S, Sinclair D, Utzinger J. Drugs for treating *Schistosoma mansoni* infection. Cochrane Database of Systematic Reviews. 2013(2).
- 305. Kramer CV, Zhang F, Sinclair D, Olliaro PL. Drugs for treating urinary schistosomiasis. Cochrane Database Syst Rev. 2014(8):CD000053.
- 306. Pérez del Villar L, Burguillo FJ, López-Abán J, Muro A. Systematic Review and Meta-Analysis of Artemisinin Based Therapies for the Treatment and Prevention of Schistosomiasis. PLoS ONE. 2012;7(9):e45867.
- 307. Yang F, Tan XD, Liu B, Yang C, Ni ZL, Gao XD, et al. Meta-analysis of the diagnostic efficiency of the questionnaires screening for schistosomiasis. Parasitol Res. 2015;114(9):3509-19.

- 308. Campo Polanco L, Gutierrez LA, Cardona Arias J. [Diagnosis of Strongyloides Stercoralis infection: meta-analysis on evaluation of conventional parasitological methods (1980-2013)]. Rev Esp Salud Publica. 2014;88(5):581-600.
- 309. Henriquez-Camacho C, Gotuzzo E, Echevarria J, White Jr AC, Terashima A, Samalvides F, et al. Ivermectin versus albendazole or thiabendazole for Strongyloides stercoralis infection. Cochrane Database of Systematic Reviews. 2016(1).
- Danso-Appiah A, Minton J, Boamah D, Otchere J, Asmah RH, Rodgers M, et al. Accuracy of point-of-care testing for circulatory cathodic antigen in the detection of schistosome infection: systematic review and meta-analysis. Bull World Health Organ. 2016;94(7):522-33A.
- 311. Kinkel HF, Dittrich S, Baumer B, Weitzel T. Evaluation of eight serological tests for diagnosis of imported schistosomiasis. Clin Vaccine Immunol. 2012;19(6):948-53.
- 312. Lodh N, Mwansa JC, Mutengo MM, Shiff CJ. Diagnosis of *Schistosoma mansoni* without the stool: comparison of three diagnostic tests to detect Schistosoma [corrected] mansoni infection from filtered urine in Zambia. Am J Trop Med Hyg. 2013;89(1):46-50.
- 313. Espirito-Santo MC, Alvarado-Mora MV, Dias-Neto E, Botelho-Lima LS, Moreira JP, Amorim M, et al. Evaluation of real-time PCR assay to detect Schistosoma mansoni infections in a low endemic setting. BMC Infect Dis. 2014;14:558.
- 314. da Frota SM, Carneiro TR, Queiroz JA, Alencar LM, Heukelbach J, Bezerra FS. Combination of Kato-Katz faecal examinations and ELISA to improve accuracy of diagnosis of intestinal schistosomiasis in a low-endemic setting in Brazil. Acta Trop. 2011;120 Suppl 1:S138-41.
- 315. Silveira AM, Costa EG, Ray D, Suzuki BM, Hsieh MH, Fraga LA, et al. Evaluation of the CCA Immuno-Chromatographic Test to Diagnose Schistosoma mansoni in Minas Gerais State, Brazil. PLoS Negl Trop Dis. 2016;10(1):e0004357.
- Espirito-Santo MC, Sanchez MC, Sanchez AR, Alvarado-Mora MV, Castilho VL, Goncalves EM, et al. Evaluation of the sensitivity of IgG and IgM ELISA in detecting *Schistosoma mansoni* infections in a low endemicity setting. Eur J Clin Microbiol Infect Dis. 2014;33(12):2275-84.
- Bisoffi Z, Buonfrate D, Sequi M, Mejia R, Cimino RO, Krolewiecki AJ, et al. Diagnostic accuracy of five serological tests for Strongyloides stercoralis infection. PLoS Negl Trop Dis. 2014;8(1):e2640.
- 318. Rascoe LN, Price C, Shin SH, McAuliffe I, Priest JW, Handali S. Development of Ss-NIE-1 recombinant antigen based assays for immunodiagnosis of strongyloidiasis. PLoS Negl Trop Dis. 2015;9(4):e0003694.
- Knopp S, Becker SL, Ingram KJ, Keiser J, Utzinger J. Diagnosis and treatment of schistosomiasis in children in the era of intensified control. Expert Rev Anti Infect Ther. 2013;11(11):1237-58.
- 320. King CH, Olbrych SK, Soon M, Singer ME, Carter J, Colley DG. Utility of Repeated Praziquantel Dosing in the Treatment of Schistosomiasis in High-Risk Communities in Africa: A Systematic Review. PLoS Negl Trop Dis. 2011;5(9):e1321.
- Muennig P, Pallin D, Sell RL, Chan M-S. The Cost Effectiveness of Strategies for the Treatment of Intestinal Parasites in Immigrants. New England Journal of Medicine. 1999;340(10):773-9.
- 322. Muennig P, Pallin D, Challah C, Khan K. The cost-effectiveness of ivermectin vs. albendazole in the presumptive treatment of strongyloidiasis in immigrants to the United States. Epidemiology and Infection. 2004;132(6):1055-63.
- 323. Maskery B, Coleman MS, Weinberg M, Zhou W, Rotz L, Klosovsky A, et al. Economic Analysis of the Impact of Overseas and Domestic Treatment and Screening Options for Intestinal Helminth Infection among US-Bound Refugees from Asia. PLoS Negl Trop Dis. 2016;10(8):e0004910.
- 324. Worrell CM, Bartoces M, Karanja DM, Ochola EA, Matete DO, Mwinzi PN, et al. Cost analysis of tests for the detection of Schistosoma mansoni infection in children in western Kenya. Am J Trop Med Hyg. 2015;92(6):1233-9.
- 325. Libman MD, MacLean JD, Gyorkos TW. Screening for schistosomiasis, filariasis, and strongyloidiasis among expatriates returning from the tropics. Clin Infect Dis. 1993;17(3):353-9.
- 326. Buonfrate D, Sequi M, Mejia R, Cimino RO, Krolewiecki AJ, Albonico M, et al. Accuracy of five serologic tests for the follow up of Strongyloides stercoralis infection. PLoS neglected tropical diseases. 2015;9(2):e0003491.
- 327. Espirito-Santo MC, Alvarado-Mora MV, Pinto PL, Sanchez MC, Dias-Neto E, Castilho VL, et al. Comparative Study of the Accuracy of Different Techniques for the Laboratory Diagnosis of Schistosomiasis Mansoni in Areas of Low Endemicity in Barra Mansa City, Rio de Janeiro State, Brazil. Biomed Res Int. 2015;2015:135689.
- 328. Beltrame A, Guerriero M, Angheben A, Gobbi F, Requena-Mendez A, Zammarchi L, et al. Accuracy of parasitological and immunological tests for the screening of human schistosomiasis in immigrants and refugees from African countries: An approach with Latent Class Analysis. PLoS Neglected Tropical Diseases. 2017;11(6):e0005593.
- 329. Requena-Méndez A, Buonfrate D, Gomez-Junyent J, Zammarchi L, Bisoffi Z, Muñoz J. Evidence-based guidelines for screening and management of strongyloidiasis in non-endemic countries. The American Journal of Tropical Medicine and Hygiene. 2017;97(3):645-52.
- 330. Albonico M, Becker SL, Odermatt P, Angheben A, Anselmi M, Amor A, et al. StrongNet: an international network to improve diagnostics and access to treatment for strongyloidiasis control. PLoS Neglected Tropical Diseases. 2016;10(9):e0004898.
- Boussinesq M, Gardon J, Gardon-Wendel N, Chippaux J-P. Clinical picture, epidemiology and outcome of Loa-associated serious adverse events related to mass ivermectin treatment of onchocerciasis in Cameroon. Filaria Journal. 2003;2(1):S4.
- 332. Garcia HH, Del Brutto OH, Peru CWGi. Antiparasitic treatment of neurocysticercosis-The effect of cyst destruction in seizure evolution. Epilepsy & Behavior. 2017.
- 333. Vanijanonta S, Bunnag D. Treatment of cysticercosis with praziquantel at the Bangkok Hospital for Tropical Diseases. The Southeast Asian Journal of Tropical Medicine and Public Health. 1985;16(3):435-40.
- Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ (Clinical research ed). 2004;328(7454):1490.
- 335. Update of laboratory medicine procedures related to the diagnosis of strongyloidiasis. French National Authority for Health (HAS), April 2017.
- 336. Assessement of laboratory medicine procedures related to the diagnosis of schistosomiasis (bilharzia). French National Authority for Health (HAS), January 2017.
- 337. World Health Organization. European Vaccine Action Plan 2015-2020. Copenhagen: WHO Regional Office for Europe, 2014.
- Barnett ED, Christiansen D, Figueira M. Seroprevalence of measles, rubella, and varicella in refugees. Clin Infect Dis. 2002;35(4):403-8.
- 339. Greenaway C, Dongier P, Boivin JF, Tapiero B, Miller M, Schwartzman K. Susceptibility to measles, mumps, and rubella in newly arrived adult immigrants and refugees. Ann Intern Med. 2007;146(1):20-4.
- Toikkanen SE, Baillot A, Dreesman J, Mertens E. Seroprevalence of Antibodies against Measles, Rubella and Varicella among Asylum Seekers Arriving in Lower Saxony, Germany, November 2014-October 2015. Int J Environ Res Public Health. 2016;13(7).
- Freidl GS, Tostmann A, Curvers M, Ruijs WLM, Smits G, Schepp R, et al. Immunity against measles, mumps, rubella, varicella, diphtheria, tetanus, polio, hepatitis A and hepatitis B among adult asylum seekers in the Netherlands, 2016. Vaccine. 2018;36(12):1664-72.
- 342. Ceccarelli G, Vita S, Riva E, Cella E, Lopalco M, Antonelli F, et al. Susceptibility to measles in migrant population: implication for policy makers. Journal of Travel Medicine. 2018;25(1).
- Nakken CS, Skovdal M, Nellums LB, Friedland JS, Hargreaves S, Norredam M. Vaccination status and needs of asylumseeking children in Denmark: a retrospective data analysis. Public Health. 2018;158:110-6.
- 344. Hübschen JM, Charpentier E, Weicherding P, Muller CP. IgG antibody prevalence suggests high immunization needs in newcomers to Luxembourg, 2012. Vaccine. 2018;36(6):899-905.
- 345. Roberton T, Weiss W, Doocy S, Team JHAS, Team LHAS. Challenges in estimating vaccine coverage in refugee and displaced populations: results from household surveys in Jordan and Lebanon. Vaccines. 2017;5(3):22.
- 346. Filia A, Amendola A, Faccini M, Del Manso M, Senatore S, Bianchi S, et al. Outbreak of a new measles B3 variant in the Roma/Sinti population with transmission in the nosocomial setting, Italy, November 2015 to April 2016. Euro Surveill. 2016;21(20).
- 347. Williams GA, Bacci S, Shadwick R, Tillmann T, Rechel B, Noori T, et al. Measles among migrants in the European Union and the European Economic Area. Scand J Public Health. 2016;44(1):6-13.
- 348. Jones G, Haeghebaert S, Merlin B, Antona D, Simon N, Elmouden M, et al. Measles outbreak in a refugee settlement in Calais, France: January to February 2016. Euro Surveill. 2016;21(11):30167.
- 349. Khetsuriani N, Perehinets I, Nitzan D, Popovic D, Moran T, Allahverdiyeva V, et al. Responding to a cVDPV1 outbreak in Ukraine: Implications, challenges and opportunities. Vaccine. 35(36): 2017.
- 350. Werber D, Hoffmann A, Santibanez S, Mankertz A, Sagebiel D. Large measles outbreak introduced by asylum seekers and spread among the insufficiently vaccinated resident population, Berlin, October 2014 to August 2015. Euro Surveill. 2017;22(34).
- 351. Derrough T, Salekeen A. Lessons learnt to keep Europe polio-free: a review of outbreaks in the European Union, European Economic Area, and candidate countries, 1973 to 2013. Euro Surveill. 2016;21(16).
- 352. Woudenberg T, van Binnendijk RS, Sanders EAM, Wallinga J, de Melker HE, Ruijs WLM, et al. Large measles epidemic in the Netherlands, May 2013 to March 2014: changing epidemiology. Euro Surveill. 2017;22(3).
- 353. Antona D, Lévy-Bruhl D, Baudon C, Freymuth F, Lamy M, Maine C, et al. Measles elimination efforts and 2008–2011 outbreak, France. Emerging Infectious Diseases. 2013;19(3):357.
- 354. Hargreaves s NL, Ramsay M, et al. Who is responsible for the vaccination of migrants in Europe? The Lancet Infectious Diseases. 2018;391.
- 355. World Health Organization. Immunization coverage 2018. Available at: <a href="http://www.who.int/news-room/fact-sheets/detail/immunization-coverage">http://www.who.int/news-room/fact-sheets/detail/immunization-coverage</a>.
- 356. World Health Organization. Global Health Observatory data repository: Immunization: WHO [19 July 2018]. Available at: http://apps.who.int/gho/data/view.main.uhcimmunization
- 357. Anderson RM. The concept of herd immunity and the design of community-based immunization programmes. Vaccine. 1992;10(13):928-35.
- 358. Plotkin, SA. In: Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's Vaccines (Seventh Edition): Elsevier; 2018. p. iv.
- 359. Bica MA, Clemens R. Vaccination policies of immigrants in the EU/EEA Member States-the measles immunization example. European Journal of Public Health. 2018;28(3):439-44.
- 360. De Vito E, Parente P, De Waure C, Poscia A, Ricciardi W. A review of evidence on equitable delivery, access and utilization of immunization services for migrants and refugees in the WHO European Region. 2017. Available at: http://www.euro.who.int/ data/assets/pdf file/0005/351644/HEN53.pdf.
- 361. European Centre for Disease Prevention and Control. Diptheria. In: ECDC. Annual epidemiological report for 2015. Stockoholm: ECDC; 2017.
- 362. European Centre for Disease Prevention and Control. Risk of measles transmission in the EU/EEA, 21 March 2018. Stockholm: ECDC; 2018.
- 363. European Centre for Disease Prevention and Control. Pertussis. In: ECDC. Annual epidemiological report for 2015. Stockholm: ECDC; 2017.
- European Centre for Disease Prevention and Control. Tetanus. In: ECDC. Annual epidemiological report for 2015. Stockholm: ECDC; 2017.
- 365. European Centre for Disease Prevention and Control. *Haemophilus influenzae*. In: ECDC. Annual epidemiological report for 2015. Stockholm: ECDC; 2017.
- 366. European Centre for Disease Prevention and Control. Bi-annual measles and rubella monitoring report, October 2017. ECDC: Stockholm, 2017. Available at: https://ecdc.europa.eu/sites/portal/files/documents/Biannual%20measles%20rubella%20monitoring-OCT-2017.pdf.
- 367. Adam IF, Nakamura K, Kizuki M, Al Rifai R, Vanching U. Relationship between implementing interpersonal communication and mass education campaigns in emergency settings and use of reproductive healthcare services: evidence from Darfur, Sudan. BMJ Open. 2015;5(9):e008285.
- 368. Hu Y, Luo S, Tang X, Lou L, Chen Y, Guo J, et al. Does introducing an immunization package of services for migrant children improve the coverage, service quality and understanding? An evidence from an intervention study among 1548 migrant children in eastern China. BMC Public Health. 2015;15:664.
- 369. Milne B, Raman S, Thomas P, Shah S. Immunisation of refugee and migrant young people: can schools do the job? Aust N Z J Public Health. 2006;30(6):526-8.
- 370. Ndiaye SM, Ahmed MA, Denson M, Craig AS, Kretsinger K, Cherif B, et al. Polio outbreak among nomads in Chad: outbreak response and lessons learned. J Infect Dis. 2014;210 Suppl 1:S74-84.
- 371. Sengupta P, Benjamin AI, Myles PR, Babu BV. Evaluation of a community-based intervention to improve routine childhood vaccination uptake among migrants in urban slums of Ludhiana, India. J Public Health (Oxf). 2016.

- 372. Sheikh MA, Makokha F, Hussein AM, Mohamed G, Mach O, Humayun K, et al. Combined use of inactivated and oral poliovirus vaccines in refugee camps and surrounding communities Kenya, December 2013. MMWR Morb Mortal Wkly Rep. 2014;63(11):237-41.
- Spadea A, Semyonov L, Unim B, Giraldi G, Corda B, D'Amici AM, et al. Action against vaccine-preventable infectious diseases and tuberculosis in Nomad Camps: the experience of a Local Health Unit in Rome. Ann Ig. 2014;26(2):176-80.
  Kaji A, Parker DM, Chu CS, Thayatkawin W, Suelaor J, Charatrueangrongkun R, et al. Immunization coverage in migrant
- school children along the Thailand-Myanmar border. Journal of Immigrant and Minority Health. 2016;18(5):1038-45.
- 375. Fang H, Yang L, Zhang H, Li C, Wen L, Sun L, et al. Strengthening health system to improve immunization for migrants in China. International Journal for Equity in Health. 2017;16(1):19.
- 376. Brockmann SO, Wjst S, Zelmer U, Carollo S, Schmid M, Roller G, et al. ÖGD-Initiative zur Verbesserung der Durchimpfung bei Asylsuchenden. Bundesgesundheitsblatt-Gesundheitsforschung-Gesundheitsschutz. 2016;59(5):592-8.
- 377. Cohen AL, Veenstra D. Economic analysis of prevaccination serotesting compared with presumptive immunization for polio, diphtheria, and tetanus in internationally adopted and immigrant infants. Pediatrics. 2006;117(5):1650-5.
- 378. Coleman MS, Burke HM, Welstead BL, Mitchell T, Taylor EM, Shapovalov D, et al. Cost analysis of measles in refugees arriving at Los Angeles International Airport from Malaysia. Human Vaccines & Immunotherapeutics. 2017;13(5):1084-90.
- Joo H, Maskery B, Mitchell T, Leidner A, Klosovsky A, Weinberg M. A comparative cost analysis of the Vaccination Program for US-bound Refugees. Vaccine. 2018;36(20):2896-901.
- Agudelo-Suárez AA, Gil-González D, Vives-Cases C, Love JG, Wimpenny P, Ronda-Pérez E. A metasynthesis of qualitative studies regarding opinions and perceptions about barriers and determinants of health services' accessibility in economic migrants. BMC Health Serv Res. 2012;12:461.
- 381. Ingleby, D. and Petrova-Benedict, R. (2016) Recommendations on access to health services for migrants in an irregular situation: an expert consensus. Brussels: International Organization for Migration (IOM) Regional Office Brussels, Migration Health Division. Available at: <u>http://equi-health.eea.iom.int/index.php/9-uncategorised/336-expert-consensus</u>.
- 382. Baker DL, Dang MT, Ly MY, Diaz R. Perception of barriers to immunization among parents of Hmong origin in California. American Journal of Public Health. 2010;100(5):839-45.
- Harmsen IA, Bos H, Ruiter RAC, Paulussen TGW, Kok G, de Melker HE, et al. Vaccination decision-making of immigrant parents in the Netherlands; a focus group study. BMC Public Health. 2015;15:1229.
- 384. Canavati S, Plugge E, Suwanjatuporn S, Sombatrungjaroen S, Nosten F. Barriers to immunization among children of migrant workers from Myanmar living in Tak province, Thailand. Bulletin of the World Health Organization. 2011;89(7):528-31.
- 385. Kowal SP, Jardine CG, Bubela TM. "If they tell me to get it, I'll get it. If they don't...": Immunization decision-making processes of immigrant mothers. Can J Public Health. 2015;106(4):e230-5.
- Wang LDL, Lam WWT, Wu JT, Liao Q, Fielding R. Chinese immigrant parents' vaccination decision making for children: a qualitative analysis. BMC Public Health. 2014;14:133.
- 387. Devroey D, Riffi A, Balemans R, Van De Vijver E, Chovanova H, Vandevoorde J. Comparison of knowledge and attitudes about vaccination between Belgian and immigrant adolescents. Journal of Infection and Public Health. 2013;6(1):1-9.
- 388. Guttmann A, Manuel D, Stukel TA, Desmeules M, Cernat G, Glazier RH. Immunization coverage among young children of urban immigrant mothers: findings from a universal health care system. Ambul Pediatr. 2008;8(3):205-9.
- 389. Hargreaves S, Nellums L, Ramsay M, Saliba V, Majeem A, Mounier-Jack S, et al. Who is responsible for the vaccination of migrants in Europe? The Lancet. 2018;391.
- 390. World Health Organization. Vaccination in acute humanitarian emergencies: a framework for decision making: WHO; 2017 [19 July 2018]. Available from: http://apps.who.int/iris/bitstream/10665/255575/1/WHO-IVB-17.03-eng.pdf.
- Bozorgmehr K, Samuilova M, Petrova-Benedict R, Girardi E, Piselli P, Kentikelenis A. Infectious disease health services for refugees and asylum seekers during a time of crisis: A scoping study of six European Union countries. Health Policy (Amsterdam, Netherlands). 2018.
- 392. Giambi C, Del Manso M, Dalla Zuanna T, Riccardo F, Bella A, Caporali MG, et al. National immunization strategies targeting migrants in six European countries. Vaccine. 2018.
- 393. Linee Guida Salute Migranti. I controlli alla frontiera. La frontiera dei controlli. Controlli sanitari all'arrivo e percorsi di tutela per i migranti ospiti nei centri di accoglienza. 2017.
- 394. Guidelines for evaluating and updating immunizations during the domestic medical examination for newly arrived refugees. U.S. Department of Health and Human Services, US Centers for Disease Control and Prevention; 2015.
- 395. US CDC. Recommended Immunizations for Adults by Age in Easy-to-read Format: US Centers for Disease Control and Prevention; 2018. Available at: https://www.cdc.gov/vaccines/schedules/easy-to-read/adult-easyread.html.
- 396. US CDC. 2018 Recommended Immunizations For Infants and Children (Birth through 6 Years) in Easy-to-read Format: US Centers for Disease Control and Prevention; 2018 [19 July 2018]. Available at: https://www.cdc.gov/vaccines/schedules/easy-to-read/child-easyread.html.
- 397. Simmons R, Ireland G, Irving W, Hickman M, Sabin C, Ijaz S, et al. Establishing the cascade of care for hepatitis C in England—benchmarking to monitor impact of direct acting antivirals. Journal of Viral Hepatitis. 2018.
- Anderson LF, Tamne S, Watson JP, Cohen T, Mitnick C, Brown T, et al. Treatment outcome of multi-drug resistant tuberculosis in the United Kingdom: retrospective-prospective cohort study from 2004 to 2007. Eurosurveillance. 2013;18(40):20601.
- 399. Coppola N, Alessio L, Gualdieri L, Pisaturo M, Sagnelli C, Minichini C, et al. Hepatitis B virus infection in undocumented immigrants and refugees in Southern Italy: demographic, virological, and clinical features. Infectious Diseases of Poverty. 2017;6(1):33.
- 400. Ross J, Cunningham CO, Hanna DB. HIV outcomes among migrants from low-income and middle-income countries living in high-income countries: a review of recent evidence. Current Opinion in Infectious Diseases. 2018;31(1):25-32.
- Nellums LB, Rustage K, Hargreaves S, Friedland JS. Multidrug-resistant tuberculosis treatment adherence in migrants: a systematic review and meta-analysis. BMC Medicine. 2018;16(1):27.
- 402. Stanicole AE, Huber M. Access to Health Care for Migrants, Ethnic Minorities, and Asylum Seekers in Europe. Vienna: European Centre for Social Welfare Policy and Research; 2009.
- 403. van Loenen T, van den Muijsenbergh M, Hofmeester M, Dowrick C, van Ginneken N, Mechili EA, et al. Primary care for refugees and newly arrived migrants in Europe: a qualitative study on health needs, barriers and wishes. European Journal of Public Health. 2018;28(1):82-7.

- 404. Aldridge RW, Miller AK, Jakubowski B, et al. Falling through the Cracks: The Failure of Universal Healthcare Coverage in Europe, European Network to Reduce Vulnerabilities in Health Observatory Report. London 2017.
- Singer M, Bulled N, Ostrach B, Mendenhall E. Syndemics and the biosocial conception of health. The Lancet. 2017;389(10072):941-50.
  Bulled N, Ostrach B, Mendenhall E. Syndemics and the biosocial conception of health. The Lancet.
- 406. Seedat F, Hargreaves S, Friedland JS. Engaging New Migrants in Infectious Disease Screening: A Qualitative Semi-Structured Interview Study of UK Migrant Community Health-Care Leads. PLOS ONE. 2014;9(10):e108261.
- 407. van den Muijsenbergh M, van Weel-Baumgarten E, Burns N, O'Donnell C, Mair F, Spiegel W, et al. Communication in crosscultural consultations in primary care in Europe: the case for improvement. The rationale for the RESTORE FP 7 project. Primary Health Care Research & Development. 2013;15(2):122-33.
- 408. O'Reilly de Brún M, Brún T, O'Donnell CA, et al. Material practices for meaningful engagement: An analysis of participatory learning and action research techniques for data generation and analysis in a health research partnership. Health Expectations. 2018;21(1):159-70.
- 409. Lionis C, Papadakaki M, Saridaki A, Dowrick C, O'Donnell CA, Mair FS, et al. Engaging migrants and other stakeholders to improve communication in cross-cultural consultation in primary care: a theoretically informed participatory study. BMJ Open. 2016;6(7).
- 410. Pareek M. NIHR: Impact, acceptability and cost-effectiveness of identifying infectious diseases amongst migrants in primary care. London: NIHR; 2016.

# Annex 1. Top ten countries of birth of immigrants to the EU/EEA (average of 2014, 2015 and 2016)

	EU/EEA*			Austria			Belgium	
Total	1 226 859	%	Total	64 258	%	Total	59 971	%
Syria	94 356	8	Syria	11 745	18	Morocco	6 310	11
China	83 883	7	Afghanistan	9 158	14	Syria	5 800	10
India	77 002	6	Serbia	5 693	9	Afghanistan	3 629	6
Morocco	50 469	4	Bosnia & H.	4 986	8	Iraq	3 616	6
United States	43 132	4	Iraq	3 746	6	India	2 324	4
Pakistan	35 764	3	Turkey	2 895	5	DR Congo	2 154	4
Ukraine	35 384	3	Iran	2 829	4	United States	2 142	4
Moldova	29 606	2	Russia	2 178	3	Turkey	2 087	3
Russia	24 976	2	Ukraine	1 415	2	Cameroon	1 603	3
Brazil	24 915	2	China	1 359	2	China	1 398	2
Other	727 371	59	Other	18 255	28	Other	28 908	48

	Bulgaria	
Total	12 373	%
Syria	3 563	29
Russia	3 234	26
Turkey	1 314	11
Ukraine	1 122	9
FYR Macedonia	351	3
Kazakhstan	298	2
Serbia	233	2
Moldova	225	2
United States	198	2
China	184	1
Other	1 652	13

	Czech Republic	
Total	17 464	%
Ukraine	5 643	32
Russia	1 571	9
United States	1 267	7
Vietnam	1 252	7
Moldova	989	6
Mongolia	593	3
India	466	3
Kazakhstan	416	2
Turkey	315	2
China	314	2
Other	4 639	27

Total	59 971	%
Morocco	6 310	11
Syria	5 800	10
Afghanistan	3 629	6
Iraq	3 616	6
India	2 324	4
DR Congo	2 154	4
United States	2 142	4
Turkey	2 087	3
Cameroon	1 603	3
China	1 398	2
Other	28 908	48

	Croatia	
Total	7 242	%
Bosnia & H.	4 656	64
Serbia	674	9
Kosovo	308	4
FYR Macedonia	268	4
Russia	160	2
Ukraine	135	2
United States	128	2
China	89	1
Switzerland	86	1
Montenegro	56	1
Other	682	9

	Denmark			Estonia			Finland	
Total	30 996	%	Total	3 531	%	Total	16 384	%
Syria	9 228	29	Russia	1 371	39	Iraq	1 613	10
India	1 549	26	Ukraine	931	26	Russia	987	6
Philippines	1 361	11	Belarus	116	3	Syria	930	6
China	1 307	9	United States	110	3	China	775	5
Eritrea	1 284	3	India	72	2	India	772	5
United States	1 279	2	Georgia	72	2	Afghanistan	708	4
Ukraine	1 251	2	Nigeria	72	2	Vietnam	703	4
Greenland	954	2	Kazakhstan	68	2	Somalia	638	4
Iran	947	2	Turkey	55	2	Thailand	566	3
Nepal	768	1	China	48	1	Iran	563	3
Other	11 067	13	Other	617	17	Other	8 128	50

4 019 12

	11						the last second	
-	Hungary		-	Iceland			Italy	
Total	25 465	%	<b>Total</b> United	1 047	%	Total	201 426	%
Ukraine	8 326	29	States	162	16	Morocco	15 600	8
Serbia	3 555	26	Philippines	78	7	China	13 446	7
China	3 230	11	Thailand	51	5	Bangladesh	11 871	6
United States	1 108	9	Vietnam	47	5	Pakistan	11 837	6
Russia	637	3	China	44	4	Albania	11 618	6
Turkey	617	2	Syria	37	4	India	10 711	5
Iran	511	2	Canada	34	3	Brazil	9 986	5
Japan	488	2	Ukraine	31	3	Nigeria	9 311	5
India	483	2	Russia	29	3	Egypt	7 549	4
South Korea	362	1	Serbia	27	3	Senegal	7 345	4
Other	6 146	13	Other	506	48	Other	92 151	46
	Latvia			Liechtenstein			Lithuania	
Total	3 365	%	Total	332	%	Total	5 213	%
Russia	1 511	45	Switzerland	195	59	Ukraine	1 656	32
Ukraine	689	20	Brazil	18	5	Russia	1 391	27
Belarus	391	12	Turkey	10	3	Belarus	757	15
Uzbekistan	143	4	Ukraine	9	3	India	147	3
Kazakhstan	85	3	China	8	3	Kazakhstan	139	3
China	62	2	Syria	7	2	Georgia	114	2
Philippines	53	2	Bosnia & H. Dominican	7	2	Moldova	107	2
India	51	2	Rep.	6	2	Azerbaijan	84	2
United States	44	1	Kosovo	5	2	Iran	69	1
Onited States	44	T	KUSUVU	_	2	United	05	T
Azerbaijan	38	1	Philippines	5	2	States	65	1
Other	298	9	Other	62	19	Other	683	13
	Luxembourg			Norway			Romania	
Total	7 084	%	Total	31 279	%	Total	32 920	%
United States	580	8	Syria	6 016	19	Moldova	23 282	71
China	436	6	Eritrea	2 659	9	Ukraine	2 166	7
Syria	382	5	Philippines	2 166	7	Turkey	673	2
Cape Verde	339	5	Somalia	1 469	5	China	559	2
India	330	5	India	1 407	4	Israel	457	1
Brazil	302	4	Afghanistan	1 239	4	Russia	363	1
Russia	288	4	Thailand United	1 195	4	Syria	358	1
Morocco	239	3	States	1 003	3	Serbia United	349	1
Iraq	225	3	China	783	3	States	349	1
Serbia	183	3	Pakistan	714	2	Iraq	347	1
Other	2 7 0 4	- -	011	12 020	40	0.1	4 0 4 0	42

	Slovakia			Slovenia			Spain	
Total	1 178	%	Total	10 443	%	Total	224 131	%
Ukraine	365	31	Bosnia & H.	4 513	43	Morocco	24 661	11
United States	100	9	Kosovo	1 533	15	Venezuela	20 462	9
Serbia	87	7	Serbia	1 445	14	Colombia	15 404	7
Switzerland	69	6	FYR Macedonia	1 199	11	China	9 527	4
Russia	61	5	Russia	543	5	Argentina	8 897	4
Iraq	52	4	Ukraine	280	3	Dominica	8 829	4
Vietnam	31	3	United States	99	1	Brazil	8 762	4
Canada	30	3	China	92	1	Ecuador	8 513	4
China	29	2	Montenegro	82	1	Honduras	8 144	4
FYR Macedonia	24	2	Switzerland	38	0	Cuba	8 106	4
Other	331	28	Other	619	6	Other	102 826	46

12 626 40

Other

3 781 53

Other

Other

	Sweden			United Kingdom	
Total	94 774	%	Total	294 284	%
Syria	36 081	38	India	45 754	16
Eritrea	6 247	7	China	42 957	15
Iraq	4 125	4	United States	19 988	7
India	3 639	4	Pakistan	12 713	4
Afghanistan	3 339	4	Nigeria	8 842	3
China	2 514	3	Canada	8 770	3
Iran	2 337	2	South Africa	7 815	3
United States	1 639	2	Malaysia	7 305	2
Thailand	1 600	2	Thailand	7 182	2
Turkey	1 505	2	Saudi Arabia	6 820	2
Other	31 748	33	Other	126 139	43

Source: Eurostat migr\_imm3ctb

Data disaggregated by all countries of birth are not available for Germany, Ireland, Greece, Spain, France, Cyprus, Malta, Poland, Portugal, and the United Kingdom.

Spain and the UK submitted only data on major countries of birth. These are also included in this table.

Note: Some countries include asylum seekers in the total number of immigrants, others do not. The metadata do not allow for the differentiation of national approaches.

Includes only 23 countries (see above), accounting for 56% of non-EU/EEA migrants. The figure for Syria would be far greater if Germany were included.

# Annex 2. Top ten origins (nationalities) of asylum seekers in the EU/EEA (average of applications in 2015, 2016 and 2017)

EU/EEA						
Total	1 037 378	%				
Syria	270 728	26				
Afghanistan	137 500	13				
Iraq	99 930	10				
Pakistan	41 447	4				
Albania	39 595	4				
Nigeria	38 535	4				
Eritrea	31 682	3				
Iran	28 159	3				
Kosovo	27 200	3				
Russia	18 121	2				
Other	304 482	29				

	Austria
Total	49 063
Syria	13 538
Afghanistan	13 295
Iraq	5 765
Pakistan	2 250
Iran	2 243
Somalia	1 400
Nigeria	1 342
Stateless	1 273
Russia	1 203
Kosovo	857
Other	5 897

	Belgium	
Total	22 240	%
Syria	5 052	23
Afghanistan	3 650	16
Iraq	3 525	16
Somalia	1 010	5
Guinea	702	3
Unknown	685	3
Albania	643	3
DR Congo	560	3
Russia	445	2
Eritrea	443	2

	Bulgaria	
Total	14 203	%
Afghanistan	5 287	37
Iraq	4 368	31
Syria	3 160	22
Pakistan	850	6
Iran	228	2
Stateless	68	0
Sri Lanka	35	0
Ukraine	33	0
Bangladesh	33	0
Algeria	18	0
Other	122	1

Cro	oatia	
Total	1 032	%
Afghanistan	292	28
Syria	167	16
Iraq	125	12
Pakistan	98	10
Iran	70	7
Algeria	63	6
Turkey	50	5
Morocco	35	3
Libya	17	2
Bangladesh	15	1
Other	100	10

Other	5 525	25
	Cyprus	
Total	3,130	%
Syria	1 282	41
India	240	8
Vietnam	208	7
Pakistan	172	5
Bangladesh	153	5
Egypt	147	5
Somalia	135	4
Palestine	90	3
Sri Lanka	88	3
Cameroon	68	2
Other	547	17

% 

	Czech Republic		
Total	1 175	%	Total
Ukraine	405	34	Syria
Syria	88	8	Afghanistan
Cuba	87	7	Iran
Iraq	73	6	Stateless
Armenia	65	6	Eritrea
Azerbaijan	58	5	Iraq
Georgia	57	5	Morocco
Vietnam	57	5	Somalia
Russia	40	3	Algeria
China	35	3	Libya
Other	210	18	Other

	Denmark			Estonia
	9 902	%	Total	
	3 533	36	Syria	
anistan	1 165	12	Ukraine	
	1 068	11	Iraq	
less	765	8	Russia	
ea	750	8	Georgia	
	678	7	Afghanistan	
оссо	267	3	Palestine	
alia	197	2	Albania	
ia	108	1	Iran	
l	98	1	Armenia	
r	1 272	13	Other	

%

	Finland	
Total	13 863	%
Iraq	7 493	54
Afghanistan	2 060	15
Somalia	833	6
Syria	738	5
Albania	312	2
Iran	282	2
Eritrea	260	2
Russia	245	2
Unknown	158	1
Nigeria	137	1
Other	1 345	10

	Greece	
Total	39 238	%
Syria	15 420	39
Pakistan	4 757	12
Afghanistan	4 440	11
Iraq	4 405	11
Albania	1 520	4
Bangladesh	948	2
Iran	857	2
Palestine	737	2
Turkey	680	2
Georgia	622	2
Other	4 853	12

	Ireland		
Total	2	782	%
Pakistan		590	21
Syria		305	11
Albania		242	9
Zimbabwe		185	7
Nigeria		183	7
Georgia		140	5
Bangladesh		130	5
Afghanistan		105	4
South Africa		87	3
Iraq		75	3
Other		740	27

Fi	rance	
Total	73 298	%
Albania	7 197	10
Afghanistan	5 008	7
Syria	4 695	6
Haiti	4 692	6
DR Congo	3 663	5
Kosovo	2 952	4
Guinea	2 938	4
Bangladesh	2 802	4
Iraq	2 672	4
Algeria	2 618	4
Other	34 062	46

H	ungary	
Total	68 413	%
Syria	23 173	34
Afghanistan	19 233	28
Kosovo	7 933	12
Pakistan	6 253	9
Iraq	4 442	6
Bangladesh	1 423	2
Iran	1 043	2
Unknown	512	1
Palestine	407	1
Morocco	398	1
Other	3 595	5

	Germany	
Total	451 675	%
Syria	157 958	35
Afghanistan	58 272	13
Iraq	49 277	11
Albania	24 145	5
Iran	13 477	3
Eritrea	13 318	3
Kosovo	13 233	3
Unknown	12 597	3
Pakistan	8 785	2
Nigeria	8 575	2
Other	92 038	20

	Iceland	
Total	1 053	%
FYR		
Macedonia	253	24
Albania	240	23
Georgia	165	16
Iraq	90	9
Syria	33	3
Pakistan	25	2
Somalia	25	2
Iran	23	2
Afghanistan	20	2
Nigeria	15	1
Other	165	16

98 30

42 13

32 10

8 3

50 15

%

	Italy			Latvia
Total	109 563	%	Total	
Nigeria	23 093	21	Syria	
Pakistan	11 075	10	Vietnam	
Gambia The	8 522	8	Iraq	
Bangladesh	8 237	8	Afghanistan	
Senegal	7 405	7	Russia	
Mali	6 415	6	Ukraine	
Côte d'Ivoire	6 300	6	Georgia	
Guinea	5 173	5	Eritrea	
Eritrea	4 822	4	Tajikistan	
Ghana	4 363	4	India	
Other	24 158	22	Other	

	Liechtenstein	
Total	60	%
Serbia	15	25
Ukraine	10	17
Albania	5	8
Georgia	5	8
Syria	5	8
Somalia	5	8
Eritrea	5	8
Belarus	5	8
China	5	8
FYR Macedonia	0	0
Other	0	0

Malta		
Total	1 657	%
Libya	653	39
Syria	372	22
Somalia	197	12
Eritrea	130	8
Ukraine	63	4
Iraq	35	2
Nigeria	18	1
Egypt	18	1
Venezuela	18	1
Ethiopia	17	1
Other	135	8

	Poland		
Total	7	660	%
Russia	5	513	72
Ukraine		823	11
Tajikistan		480	6
Armenia		182	2
Syria		122	2
Georgia		102	1
Kyrgyzstan		57	1
Vietnam		48	1
Iraq		45	1
Turkey		42	1
Other		247	3

	Lithuania		
Total	40	0	%
Syria	11	.3	28
Russia	5	5	14
Ukraine	4	2	10
Afghanistan	2	25	6
Tajikistan	2	25	6
Iraq	2	2	5
Georgia	2	20	5
Belarus	2	20	5
Armenia	1	.5	4
Eritrea	1	.0	3
Other	5	3	13

	Netherlands	
Total	25 757	%
Syria	8 157	32
Eritrea	3 615	14
Iraq	1 605	6
Afghanistan	1 298	5
Iran	1 163	5
Albania	1 012	4
Stateless	975	4
Morocco	777	3
Algeria	638	2
Serbia	518	2
Other	5 998	23

Por	tugal		
Total	842	%	То
Ukraine	210	25	Ira
DR Congo	75	9	Syı
Angola	57	7	Af
Guinea	43	5	Pa
Congo	40	5	Ira
Mali	40	5	Tu
Pakistan	37	4	Sta
China	28	3	Eri
Iraq	23	3	Pa
Sierra			
Leone	23	3	Uk
Other	265	31	Ot

	Luxembourg	
Total	2 172	%
Syria	457	21
Iraq	288	13
Albania	160	7
Kosovo	150	7
Eritrea	130	6
Serbia	128	6
Afghanistan	107	5
Morocco	98	5
Algeria	87	4
Georgia	75	3
Other	492	23

	Norway	
Total	12 177	%
Syria	4 025	33
Afghanistan	2 470	20
Eritrea	1 390	11
Iraq	1 093	9
Iran	503	4
Stateless	460	4
Ethiopia	298	2
Somalia	227	2
Albania	213	2
Pakistan	163	1
Other	1 333	11

	Romania	
Total	2 570	%
Iraq	1 113	43
Syria	758	30
Afghanistan	140	5
Pakistan	123	5
Iran	80	3
Turkey	43	2
Stateless	33	1
Eritrea	22	1
Palestine	20	1
Ukraine	18	1
Other	218	8

	Slovakia		
Total	SIOVAKIA	150	0/
Total		158	%
Iraq		63	40
Afghanistan		20	13
Ukraine		12	7
Pakistan		10	6
Syria		8	5
Vietnam		7	4
Iran		5	3
Cuba		5	3
Unknown		5	3
Algeria		3	2
Other		20	13

	Slovenia	
Total	973	%
Afghanistan	343	35
Syria	125	13
Pakistan	90	9
Algeria	77	8
Iraq	60	6
Turkey	55	6
Iran	52	5
Kosovo	30	3
Morocco	28	3
Eritrea	22	2
Other	92	9

	Spain	
Total	20 058	%
Venezuela	4 957	25
Syria	4 263	21
Ukraine	2 692	13
Colombia	1 047	5
Algeria	838	4
Palestine	762	4
El Salvador	550	3
Honduras	498	2
Morocco	413	2
Cameroon	333	2
Other	3 705	18

	Sweden	
Total	66 540	%
Syria	20 283	30
Afghanistan	14 860	22
Iraq	7 903	12
Stateless	3 130	5
Eritrea	2 932	4
Somalia	2 187	3
Iran	2 037	3
Albania	1 327	2
Georgia	808	1
Ukraine	780	1
Other	10 293	15

	United Kingdom	
Total	35 220	%
Iran	3 867	11
Pakistan	3 422	10
Iraq	3 215	9
Afghanistan	2 627	7
Eritrea	2 048	6
Albania	1 858	5
Bangladesh	1 852	5
Syria	1 720	5
India	1 717	5
Nigeria	1 688	5
Other	11 207	32

Source: Eurostat migr\_asyappctza

# Annex 3. Terms of reference of the ad hoc scientific panel

## Background

The European health policy framework 'Health 2020' aims to 'significantly improve the health and well-being of populations, reduce health inequalities, strengthen public health and ensure people-centred health systems that are universal, equitable, sustainable and of high quality'. In the area of migrant health, ECDC will work towards this aim by embarking on a project to develop evidence-based guidance for prevention of infectious diseases among newly arrived migrants to the EU/EEA.

The objective of this project is to systematically review and synthesize the evidence on infectious diseases considering emergency public health and longer-term preventive actions for newly arriving migrants within existing EU/EEA health systems. Using the newly developed GRADE 'evidence to decision' framework, ECDC will search for evidence and update high quality systematic reviews on effectiveness, acceptability, feasibility, equity, resource use and cost effectiveness of migrant screening. This review will inform the deliberation of the evidence and subsequent development of an evidence-based guidance document, which will serve as a European guidance for key migrant health infectious diseases. A scientific panel will be set up to oversee the process.

## Process to establish an ad hoc scientific panel

ECDC has the possibility to establish ad hoc scientific panels that will aid ECDC and provide independent advice on a topic during a limited time and with a specific scope. The process to set up such an ad hoc scientific panel follows a strict methodology and includes the following main steps: Identification of experts; collecting declarations of interests of experts; evaluating the eligibility and rule out conflict of interests of experts through clearance by the ECDC compliance officer; formal appointment of panel members by the ECDC Director.

The identification of experts can be done in several ways: inventory of key experts that publish scientific literature in the area, request for suggestions of experts by the ECDC Advisory Forum, and through other means that involve contacting our network and partners for suggestions. It is for ECDC to decide on the composition of the panel, taking into account for example country/setting representativeness, and balance of specific expertise and experience of panel members.

## **Observers**

The scientific panel will also be complemented with observers from key stakeholders, such as the European Commission, WHO Regional Office of Europe, the International Organisation for Migration and representatives from EU Commission-funded projects. The role of the observers will be to provide scientific advice prior to, during and after the scientific panel meeting. However, the final formulation of the statements in the ECDC guidance will be determined by the officially appointed scientific panel for eventual ECDC approval.

## Purpose and role of the scientific panel

The scientific panel will follow the Institute of Medicine Standards for Systematic Reviews and Guidelines (2011) to ensure a rigorous and transparent scientific process.

- The panel will be responsible for thoroughly reviewing the proposed methodology, subsequent evidence reviews and the final guidance document.
- A review of the proposed methodology will include an assessment of whether the proposed guideline development process is consistent with the steps described in methods process.
- The panel will also review the options for interventions based on the scientific evidence.
- A review of the final guidance document will ensure that the approved process has been followed.
- The panel will ensure that the final output contains clear and actionable guidance.

#### Table A-1. Composition of the ad hoc scientific panel

Name	Country	Affiliation
Angel Kunchev	Bulgaria	Ministry of Health, Chief State Health Inspector
Gabrielle Jones	France	Santé publique France, Epidemiologist
Anna Kuehne	Germany	Robert Koch Institute, Epidemiologist
Agoritsa Baka	Greece	Hellenic Centre for Disease Control and Prevention (KEELPNO), Office for Scientific Advice
Apostolos Veizis	Greece	MSF, Director Medical Operational Support Unit

Name	Country	Affiliation
Lelia Thornton	Ireland	HSE Health Protection Surveillance Centre, Specialist in Public Health Medicine
Silvia Declich	Italy	Istituto Superiore di Sanità (ISS), National Centre for Global Health, senior epidemiologist
Francesco Castelli	Italy	University of Brescia, Professor
Pierluigi Lopalco	Italy	University of Pisa, Full Professor of Hygiene and Preventive Medicine
Machiel Vonk	Netherlands	RIVM/LCI, Public health doctor
Maria Van Den Muijsenbergh	Netherlands	Pharos/Radboud University Medical centre Nijmegen, senior researcher and general practitioner
Sonia Dias	Portugal	National School of Public Health, Universidade Nova de Lisboa, Professor of Public Health
Henrique Dias Pinto De Barros	Portugal	University of Porto, MD, PHD
Manuel Carballo	Spain	Executive Director, ICMHD
Maria Axelsson	Sweden	Public Health Agency of Sweden, epidemiologist
Dominik Zenner	United Kingdom	Public Health England, Head of TB screening
Ines Campos-Matos	United Kingdom	Public Health England, Consultant Epidemiologist, acting head of Travel and Migrant Health section
Manish Pareek	United Kingdom	University of Leicester, Department of Infection and HIV Medicine, DR
Rebecca Hall	United Kingdom	Mawbey Group Practice Darzi Fellow, North West London Collaboration of CCGs Clinical Support Fellow, RCGP, GP

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