Universitat Autònoma de Barcelona

Migrant Health Evidence: a critical analysis of systematic reviews and guidelines

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DOCTORAL THESIS

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List of abbreviations

- AMSTAR: A MeaSurement Tool to Assess systematic Reviews
- CPG: Clinical Practice Guidelines
- EtD: Evidence to Decision
- FACE: Feasibility, Acceptability, Cost-effectiveness and Equity issues
- G-I-N: Guidelines International Network
- GRADE: Grading of Recommendations Assessment, Development and Evaluation
- IOM: Institute of Medicine
- MeSH: Medical Subject Headings
- NICE: National Institute for Health and Care Excellence
- PICO: Patient, Intervention, Comparison, Outcome
- RCT: Randomised Controlled Trial
- ROBINS-I: Risk of Bias in Non-randomised Studies - of Interventions
- SR: Systematic Review
- WHO: World Health Organisation

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1. Abstract

Abstract

Background: Increased migration is a global public health concern and presents an urgent need for evidence-based health guidance, which highlights the many contextual factors affecting the implementation of existing guidance and the provision of health services.

Objective: To identify and evaluate evidence in relation to the quality of clinical practice guidelines (GCPs) and systematic reviews (SRs) on migrant health and to develop evidence-based recommendations.

Methods: The first study focused on the evaluation of the quality of GPCs on the health of migrants with the AGREE II instrument. The second study evaluated the methodological quality, bias risk, and RS information using the AMSTAR-2, ROBIS, and PRISMA instruments, respectively. The third study assessed the available evidence regarding the detection and treatment of schistosomiasis and strongyloidiasis in newly arrived migrants from EU and EEA endemic countries. In the fourth study, we made recommendations using the GRADE method.

Results: We identified 32 CPGs; nine (28%) were considered “recommended”, six (19%) “recommended with modifications”, and seventeen (53%) “not recommended.” The lowest average scores observed for the AGREE II domains were in the domains. “Rigor of development” (34%), “applicability” (40%) and “editorial independence” (27%) In the second study, we included 57 RS. The methodological quality in 30 (52.6%) SRs was low/critically low. The risk of bias

of included SR was high in 23 (40.4%) and the quality of reporting in 36 (63.2%) SRs was moderate. In the third study, we included 27 RS. The certainty of the detection techniques was low, and the certainty of the treatment was moderate to high. The serological tests for

antibody detection were the most effective screening tests in low endemicity settings. Short courses of praziquantel and ivermectin were safe, highly effective, and cost-effective. For schistosomiasis, the panel recommended serological testing and treatment to all migrants from highly endemic countries in sub-Saharan Africa and focal areas of transmission in Asia, South America and North Africa. The panel recommended serological screening and treatment for strongyloidiasis to all migrants from highly endemic countries in Asia, Africa, the Middle East, Oceania, and Latin America (conditional recommendations based on low-quality evidence).

Conclusions: 1) Most GPCs on migrant health have a suboptimal quality with much room for improvement, especially in the areas of development rigor, applicability, and editorial independence. 2) The methodological quality, the risk of bias and the information of the RS on the health of migrants are still suboptimal, with gaps related to the low registration of protocols, the assessment of the risk of bias and the publication bias, the additional analysis and funding. 3) The certainty of the evidence on the effectiveness of the screening techniques was low and the certainty supporting the effectiveness of the treatment for the two parasitic infections was moderate to high. 4) Newcomer immigrants from EU and EEA endemic countries should be offered the detection and treatment of schistosomiasis and strongyloidiasis adapted to their region.

(Word count- 473 words)

Resumen

Antecedentes: El incremento de la migración es una preocupación global para la salud pública y presenta una necesidad imperiosa de orientación sanitaria basada en la evidencia, que pone de manifiesto los numerosos factores contextuales que afectan la implementación de la orientación existente y la prestación de servicios de salud.

Objetivo: Identificar y evaluar la evidencia en relación con la calidad de las guías de práctica clínica (CPG) y de las revisiones sistemáticas (RS) sobre la salud de los migrantes y desarrollar recomendaciones basadas en la evidencia.

Métodos: El primer estudio, se centró en la evaluación de la calidad de las GPC sobre la salud de los migrantes con el instrumento AGREE II. El segundo estudio evaluó la calidad metodológica, el riesgo de sesgo y la información de RS mediante los instrumentos Amster-2, rubí y PRISMA, respectivamente. El tercer estudio evaluó la evidencia disponible en relación con la detección y el tratamiento de la esquistosomiasis y del estrongiloidiasi en migrantes recién llegados de países endémicos de la UE y el EEE. En el cuarto estudio, formulamos recomendaciones mediante el método GRADE.

Resultados: Identificamos 32 CPG; nuevo (28%) se consideraron "recomendadas", seis (19%) "recomendadas con modificaciones", y diecisiete (53%) "no recomendadas". Las puntuaciones medias más bajas observadas para los dominios AGREE II fueron en los dominios "rigor del desarrollo" (34%), "aplicabilidad" (40%) y "independencia editorial" (27%). en el segundo estudio, incluimos 57 RS. La calidad metodológica en 30 RS (52,6%) va a ser baja o muy baja. el riesgo de sesgo fue elevado en 23 (40,4%), mientras que la calidad de la información en 36 (63,2%) fue moderada. En el tercer estudio, incluimos 27 RS. La certeza de las técnicas de detección fue baja y la certeza del tratamiento fue de

moderada a alta. Las pruebas serológicas de detección de anticuerpos fueron las pruebas de cribado más eficaces en entornos de baja endemicidad. Los cursos cortos de praziquantel y ivermectina fueron seguros, altamente eficaces y rentables. Para la esquistosomiasis, el grupo recomendó pruebas serológicas y tratamiento a todos los migrante s de países de alta endemicidad en el África subsahariana y áreas focales de transmisión en Asia, América del Sur y el norte de África. El grupo recomendó pruebas serológicas y tratamiento para la estrongiloidiasi a todos los migrantes procedentes de países de alta endemicidad en Asia, África, Oriente Medio, Oceanía y América Latina (recomendaciones condicionales basadas en evidencias de baja calidad).

Conclusiones: 1) La mayor parte de las GPC sobre la salud de los migrantes tienen una calidad subóptima con mucho margen de mejora, especialmente en los dominios del rigor del desarrollo, la aplicabilidad y la independencia editorial. 2) La calidad metodológica, el riesgo de sesgo y la información de las RS sobre la salud de los migrantes todavía son subóptimas, con lagunas relacionadas con el bajo registro de protocolos, la evaluación del riesgo de sesgo y el sesgo de publicación, el análisis adicional y la financiación. 3) La certeza de la evidencia sobre la eficacia de las técnicas de cribado fue baja y la certeza de que apoyaba la eficacia del tratamiento para ambas infecciones parasitarias fue de moderada a alta. 4) A los inmigrantes recién llegados procedentes de países endémicos de la UE y el EEE les debería ofrecer la detección y el tratamiento de la esquistosomiasis y del estrongiloidiasi adaptados a su región.

(Word count – 555 words)

Resum

Antecedents: L'increment de la migració és una preocupació global per a la salut pública i presenta una necessitat imperiosa d'orientació sanitària basada en l'evidència, que posa de manifest els nombrosos factors contextuals que afecten la implementació de l'orientació existent i la prestació de serveis de salut.

Objectiu: Identificar i avaluar l'evidència en relació amb la qualitat de les guies de pràctica clínica (CPG) i de les revisions sistemàtiques (RS) sobre la salut dels migrants i desenvolupar recomanacions basades en l'evidència.

Mètodes: El primer estudi, es va centrar en l'avaluació de la qualitat de les GPC sobre la salut dels migrants amb l'instrument AGREE II. El segon estudi va avaluar la qualitat metodològica, el risc de biaix i la informació de RS mitjançant els instruments AMSTAR-2, ROBIS i PRISMA, respectivament. El tercer estudi va avaluar l'evidència disponible en relació amb la detecció i el tractament de l'esquistosomiasi i de l'estrongiloidiasi en migrants nouvinguts de països endèmics de la UE i l'EEE. En el quart estudi, vam formular recomanacions mitjançant el mètode GRADE.

Resultats: Vam identificar 32 CPG; nou (28%) es van considerar "recomanades", sis (19%) "recomanades amb modificacions", i disset (53%) "no recomanades". Les puntuacions mitjanes més baixes observades per als dominis AGREE II van ser en els dominis "rigor del desenvolupament" (34%), "aplicabilitat" (40%) i "independència editorial" (27%). En el segon estudi, vam incloure 57 RS. La qualitat metodològica en 30 RS (52,6%) va ser baixa o molt baixa. El risc de biaix va ser elevat en 23 (40,4%), mentre que la qualitat de la informació en 36 (63,2%) va ser moderada. En el tercer estudi, vam incloure 27 RS. La certesa de les tècniques de detecció va ser baixa i la certesa del tractament va ser de moderada a alta. Les proves serològiques de detecció d'anticossos van ser les proves de

cribratge més eficaces en entorns de baixa endemicitat. Els cursos curts de praziquantel i ivermectina van ser segurs, altament eficaços i rendibles. Per a l'esquistosomiasi, el grup va recomanar proves serològiques i tractament a tots els migrants de països d'alta endemicitat a l'Àfrica subsahariana i àrees focals de transmissió a Àsia, Amèrica del Sud i el nord d'Àfrica. El grup va recomanar proves serològiques i tractament per a l'estrongiloidiasi a tots els migrants procedents de països d'alta endemicitat a Àsia, Àfrica, Orient Mitjà, Oceania i Amèrica Llatina (recomanacions condicionals basades en evidències de baixa qualitat).

Conclusions: 1) La major part de les GPC sobre la salut dels migrants tenen una qualitat subòptima amb molt marge de millora, especialment en els dominis del rigor del desenvolupament, l'aplicabilitat i la independència editorial. 2) La qualitat metodològica, el risc de biaix i la informació de les RS sobre la salut dels migrants encara són subòptimes, amb llacunes relacionades amb el baix registre de protocols, l'avaluació del risc de biaix i el biaix de publicació, l'anàlisi addicional i el finançament. 3) La certesa de l'evidència sobre l'eficàcia de les tècniques de cribratge va ser baixa i la certesa que recolzava l'eficàcia del tractament per a les dues infeccions parasitàries va ser de moderada a alta. 4) Als immigrants nouvinguts procedents de països endèmics de la UE i l'EEE se'ls hauria d'oferir la detecció i el tractament de l'esquistosomiasi i de l'estrongiloidiasi adaptats a la seva regió.

(Word count – 544)

2. Introduction

2.1 Background

In recent years, migrant health has become a major global public health problem, due to the significant increase in cross-border migrations in multiple regions of the world. This requires an effective and timely national and global collaboration, as well as a need to adapt the clinical care and health systems to these migrant populations (1-4). Human mobility across international borders usually due to travel, trade, globalization, in addition to conflicts and climatic disasters have a profound impact in transmission, prevention and control of numerous diseases (5, 6). Similarly, the population of refugees and asylum seekers has increased to approximately 26 million people in 2020 – about one in every ten migrants compared to one in seven migrants in 2015 (7, 8). Almost 1% of the world's population representing a record 65 million individuals are forcibly displaced globally (8), and approximately 272 million persons live outside their home country, representing an increase of 50 per cent, compared to 150 million persons in year 2000 (9, 10).

According to the United Nations Department of Economic and Social Affairs (UN DESA), international migrants constitute about 10% of the total population in the European Region and roughly one-third of total international migrants worldwide (11, 12). According to the office of the United Nations High Commissioner for Refugees (UNHCR) there are nearly 5.2 million refugees (including people in refugee-like situations), and 1.4 million asylum seekers presently living in the Region (9, 13). While the reported surge in international migrant flow happened across Asia, Europe and Northern America, most of the relocations occur in countries within similar geographic regions (7, 12). Notably, emigration of refugees and asylum seekers into the European area in recent years is through the Mediterranean Sea. This is one of the deadliest migration routes with reported total deaths of 3139 and 5143 refugee and migrants in 2016 and 2017 respectively (8, 14). Consequently, these large relocation or population movements of refuges and other migrants create new and increasing challenges

for the host's national health systems. Challenges are amplified in settings with limited resources and limited technical expertise. These significant increases in refugees and other migrants result in demographic changes with much slower growth of the host population, reflected by declining birth rates and ageing populations. (15). Annual changes in migrant populations compared to the total host population in the European region is shown in **Figure 1**. Since, 2015, majority of these refugees and other migrants are young adults in their mid-twenties and thirties, the number of elderly and disabled persons, as well as minors (in addition to unaccompanied, minors), are increasing (16).

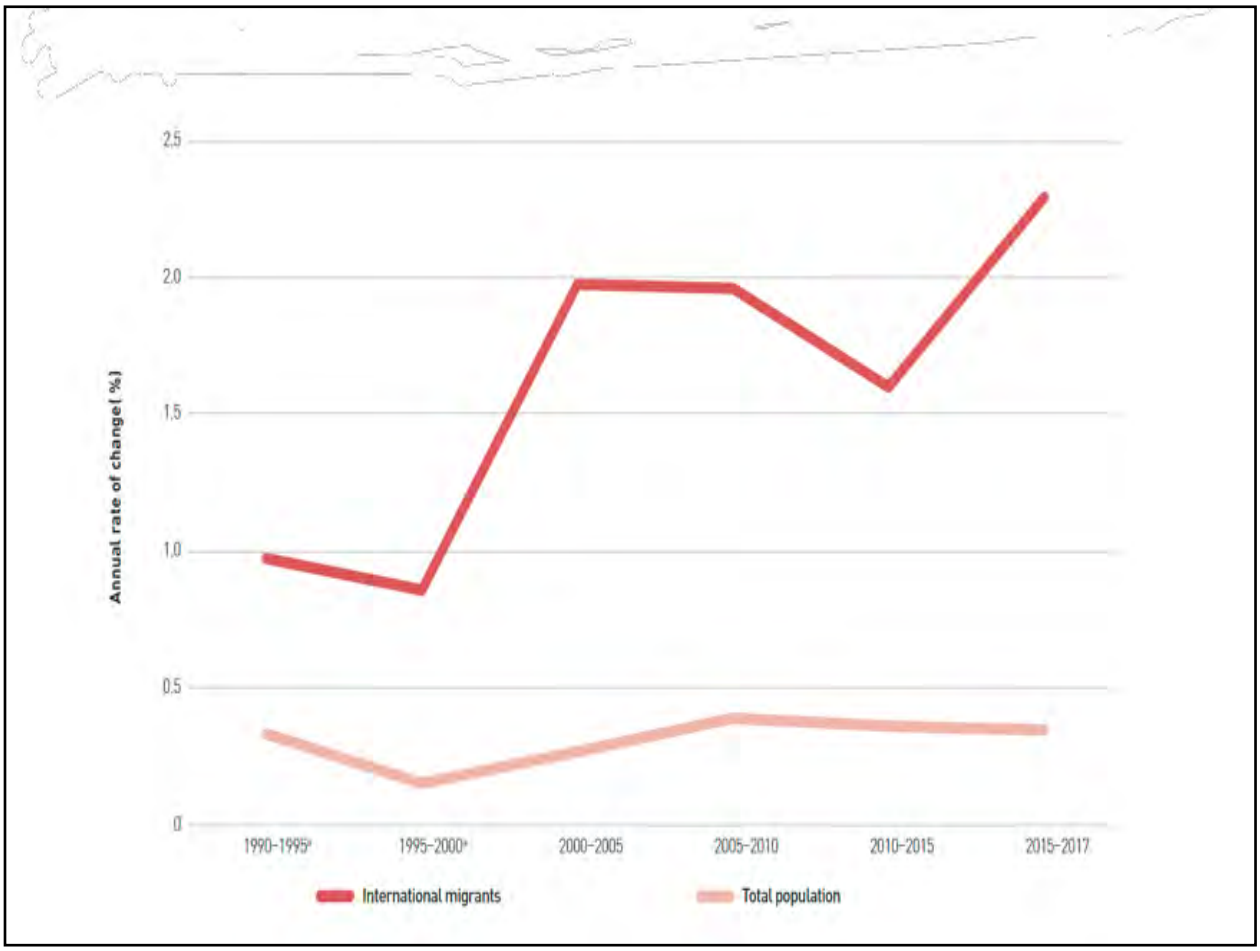

Figure 1: Annual rate of change in migrant populations compared to the total host population in WHO European Region, 1990–2017.

2.2 International migrants and rights to Health

Describing what constitutes an international migrant population can be challenging. Different and diverse terms and dynamic categorizations of these groups of people sometimes overlap. In general, migrant populations represent a diverse groups of regular or irregular and undocumented migrants, including economic migrants, refugees, asylum seekers, and unaccompanied minors (6, 17, 18).

According to the Special Rapporteur of the Commission on Human Rights, three main factors determine the categorization or migration status of an individual as a migrant; 1) to be residing outside the territory of the State in which they are nationals or citizens, not subject to its official protection; 2) not experiencing the general inherent legal recognition of rights, such as being granted the status of refugee, naturalised person or other status, and; 3) individuals without general legal protection of their fundamental rights under diplomatic agreements, visas, or other agreements (18, 19).

Refugees are legally owed protection and access to health services, by their first country of asylum registration (15). Nevertheless, the European Union (EU) Agency for Fundamental Rights states the fundamental rights of refugees and other migrants remain under threat across most member states; these rights are characteristically denied even at the stage at which asylum is determined (15, 19).

2.3 Public health implications of migration

International migration has public health consequence due to the potential risk of transmission of diseases especially from high to lower-risk countries. These risks impact surveillance, prevention strategies, health promotion, service needs, use and uptake, as well as health care cost in the host nations (20-24). Recent experience of pandemics and epidemic of influenza A/H1N1, Ebola fever, COVID-19 support the need for specific measures to combat these outbreaks in destination countries, addressing local concerns of new infectious

diseases or the re-emergence of previously controlled ones (25, 26). Considerable population immigration creates rapid changes in local health services, challenging national health systems, increasing healthcare costs due to the higher burden of latent or poorly managed communicable and non-communicable diseases in migrants (7, 17, 27).

Furthermore, migration-related consequences contribute to some shifts in the patterns of disease-specific morbidity and mortality in refugees and migrants (28). For instance, the lack of adequate immunization records contributes to migrants vulnerability to new health risk while on transit, and current evidence suggest changing patterns in the migration-linked health risks at different phases of migrations, e.g. from pre-departure to destination (11).

Other associated health risk factors for migrant populations in the destination countries include socio-economic deprivation or limitation, lack of access to care provision, issues about legal status, occupational risks and exposure to risky behaviours, alcohol abuse, injection drug use, and criminal organizations (11). In the EU region, assessment and prevention of infectious diseases in newly arrived migrants is one of the prioritized strategies employed to determine their health needs (29, 30). Unfortunately, there is limited access to health care services, lack of continuity exacerbating existing acute and chronic health conditions in migrant populations (30). (See Table 1).

Table 1: Health risk factors associated with migration

Migratory phase	Health risk factors
Pre-departure	• Biological characteristics • Local patterns of chronic conditions (communicable and non-communicable) • Pathogens' distribution • Environmental factors • Political and socio-economic circumstances • Depletion of healthcare workers
Travel	• Transports and travel conditions • Epidemiological characteristics of transit areas • Sexual violence • Human trafficking
Interception	• Poor living conditions • Human rights violations • Inadequate medical care
Destination	• Socio-economic deprivation • Access to care • Legal status • Occupational risks • Exposure to risk behaviours (alcohol abuse, injection drug use and criminal organizations)
Return	• Pre-travel advice • Poor medical assistance • Reduced immunity against local pathogens

Source: Zimmerman et al., PloS Med (2011).

2.4 Migrants and refugees right and access to healthcare

The right to health and provision of adequate healthcare for refugees and other migrants is a programmatic goal in the international framework of human rights (7, 31). Although emphasized within international human rights law, national constitutions and local legislation, they remain constrained by the availability of resources and each member states' developmental context (7, 31-33).

The World Health Organization (WHO) encourages incorporating evidence-based interventions toward addressing international healthcare challenges, informs current priorities, and reaffirms a commitment towards principles that promote refugees' and migrant's health in member states; principles essentially shared by other global institutions. (7, 31, 33, 34).

Despite the EU Charter of Fundamental Rights establishing the right to health as a human right irrespective of immigration status, local practices deviate from these obligations/ difficult the implementation of the law in some member countries (11, 31, 32, 35, 36). Unfortunately, the legal status of international migrants and refugees determines their access to health care, being the provision of healthcare for irregular migrants mainly restricted (7, 33, 37). Some studies reported evidence that asylum-seeking and refugee children in some European countries have higher rates of infectious diseases and dental problems compared to their counterparts in the host country population (11, 20, 38, 39). Legal entitlement to health does not guarantee access. Even if it is established for specific groups and regulations permit access, there are further barriers such as healthcare organization, inadequate awareness of entitlements and health staff expertise, linguistic and cultural challenges, and migration governance (1, 5, 7).

2.5 Migrant health guidelines and recommendations

Clinical practice guidelines (CPGs) are sets of recommendations based on systematic reviews of the evidence intended to promote recommended practices in health care (40). Practice guidelines aim at ensuring the planning of workplace practices with minimal variations, as well as improve effectiveness and excellence (41-46). Over the years, several global and national organizations and countries like the EU/EEA, USA, Canada, Australia have developed CPGs explicit for migrant populations or have guidelines in which refugees and other migrants may as sub-populations of vulnerable persons benefit from their extensive guidelines or recommendations (2, 47-50). These clinical or healthcare guidelines or policy documents have the singular purpose of providing clear-cut routes towards appropriate, accessible and acceptable health care provision for international migrants (2, 49).

However, poor adherence and implementation of most guidelines or recommendations have resulted from formal and informal barriers, which include a lack of legal protection, limited access to the health system, inadequate knowledge of the health system and the lack of a social network [4, 5]. Other factors include practice difficulties compounded by language and communication difficulties and experiences of marginalization and discrimination (1, 27, 51-54). Furthermore, in some regions, complex regulatory frameworks, along with ambiguous or substandard guidelines, may result in unnecessary internal restrictions, uncertainties, short-term emergency measures and inequalities with negative consequences of poor access to health and poorer health outcomes among international migrants (55, 56).

Over the past two decades, systematic evaluations of clinical practice guidelines have generally revealed low to moderate quality scores due to poor compliance in domains crucial to methodological quality; however, since 2011, some improvement has been reported. (57-59). With more than 250 million migrants globally with varied contextual health issues in their destination countries, there is now an increase in the number of researches on migrant-

specific healthcare (screening, treatment, and prevention services) and the development of relevant clinical and public health practice guidelines. (1, 5, 35, 39, 60-63).

2.6 Migrant health systematic reviews and evidence

Systematic reviews (SRs) are considered the gold standard for healthcare decision-making because they help in identifying and appraising available evidence in a specific field; evaluate its quality in addressing particular health questions for improving healthcare services and outcomes (64-68). Systematic reviews have detailed and comprehensive research plans and search strategies from a priori geared towards identifying, appraising, and synthesizing all relevant studies on a particular topic with minimal bias (69). Accordingly, the quality of a systematic review portrays the range of standards and best practices adhered to ensure the integrity of the research processes and avoid systematic, unsystematic, and inferential errors (70-72). Conversely, poorly conducted SRs can introduce biases, thereby diminishing their utility in healthcare decision (64, 72).

According to the WHO European region, evidence of increased interest in migrant health correlates with an increase in a different body of evidence; nevertheless, studies on International migrant health report a lack of evidence (15). However, most migrant related studies use assorted terms to group this heterogeneous set which differs either by their stage or process of migration, making the concept of a shared definition rather challenging (15). Moreover, studies assessing international migrant's health vary in their methods and designs, which impacts the analysis of findings, reliability, generalizability and utility in healthcare decisions (15). Other possible challenges in research evidence include limited information on health status, clarity on migrant's position, whether documented and irregular migrants.

2.7 Justification of the thesis research topic and publications

In the last ten year, there is an increase in the number of systematic reviews published in different health areas related to migrant or international migrants (73-75). Systematic

reviews of the literature constitute a good compilation of all the empirical evidence that answers a specific research question following a strict scientific design based on explicit, pre-specified, and reproducible methods (68, 69). However, systematic reviews on migrant health appear limited in scope, with a significant proportion of them focused on topics related to screening of infectious diseases, prevalence rates, the therapeutic efficacy of drugs for interventions, as well as access to maternal health care delivery (68). Similarly, studies assessing international migrant's health vary in their methods and designs, which may impact on the quality of analysis in terms of findings, reliability, generalizability and utility in making healthcare decisions (15). Also, other possible challenges in the synthesis of research evidence include limited information on health status, clarity on migrant's status, i.e., whether documented and irregular migrants. Evaluations of reporting and methodological quality of systematic reviews are now available in most research areas (73, 76-79). Evaluating methodological quality captures accuracy in the systematic design and conduct, with an assessment of the risk of bias of systematic reviews (77, 79-82), whereas, the reporting quality evaluates the transparent depiction of the methodology and findings by authors of SRs (72, 76, 83). However, our knowledge on quality assessments of systematic reviews in the area of migrant health is insufficient.

As previously mentioned, systematic evaluations of guidelines in healthcare interventions revealed some gaps in quality, with a substantial prospect for improvement in the last two decades (57-59). While both clinical and public health guidelines for migrants have become increasingly available (1, 11, 84). We are not aware of the quality of migrants' specific health guidelines, in terms of relevance, appropriateness and usability in addressing migrant health (28).

As part of this thesis, we also developed evidence-based recommendation on the topic of screening and treatment evidence of two neglected intestinal parasitic infections -

schistosomiasis and strongyloidiasis in migrants in the EU/EEA region. This work included a review of the public health impact of two global health neglected parasitic diseases, schistosomiasis and strongyloidiasis, in the European Union/European Economic Area (EU/EEA) and it was part of European Public health guidance on screening and vaccination for infectious diseases in newly arrived refugees and other migrants (50). The review of the evidence was essential, especially with the increased flow of migrants from high endemic settings. Both infections may become life-threatening under a specific circumstance, and evidence on prevalence, morbidity and mortality in the EU/EEA is very limited. Therefore, the evaluation of existing evidence on the screening and management of schistosomiasis and strongyloidiasis in migrants from endemic countries arriving in the EU/EEA was indispensable. For the development of the reviews of the evidence and the formulation, we used the GRADE approach. This work has the potential to inform policymakers on an integrative migrant health policy to ensure early detection and treatment, reduce individual morbidity and prevent an onward risk of transmission.

The collection of evidence in this thesis will present information for clinicians, patients, caregivers and health administrators, among others, regarding the quality of existing migrant health care guidelines, quality of evidence reviews on migrant health interventions, as well as guide the development of recommendations for practice.

3. Objectives

3.1 General objective

- To collect, appraise and develop migrant healthcare evidence synthesis products, including systematic reviews and clinical practice guidelines

3. 2. Specific objectives

- To generate new knowledge about the quality of available migrant related CPGs
- To generate new knowledge about the quality of migrant health systematic reviews
- To develop rigorous evidence-based recommendation on migrant health

4. Methods

4.1. Article 1. "Migrant health clinical practice guidelines and recommendations – a systematic quality assessment of using the AGREE II tool."

4.1.1 Design

Systematic review

4.1.2 Search Strategy and Study Selection

We conducted a systematic search of scientific literature to identify eligible CPGs, health guidelines and consensus documents relevant to international migrants' health care access and service provisions. We searched the following electronic databases - PubMed, MEDLINE, CINHAL, Psych info, guideline/guideline- developers' databases and websites such as TRIP (Turning Research into Practice) database, guidelines compiler entities or clearinghouses, and project-based websites for evidence-based guidelines. We also examined grey literature sources for relevant materials. The search was restricted to CPGs, recommendations or reports that were published between March 2006 and March 2016. All sources of evidence, as well as the electronic search strategies, are described in Supplement A1 in the published article (85)

We performed a calibration exercise of the selection process and conducted a pilot using five records from our search to ensure the validity and consistency of the selection process. Two team members independently evaluated all search results to determine the inclusion and exclusion of the references. Disagreements were resolved by discussion with a fourth reviewer (PF). We included documents that contained explicit recommendations about migrants' health access and/or health care provision in health care systems, which were published in the last ten years. We omitted CPGs that addressed the host population only. CPGs or health guidance for migrant health in English, Spanish, French, German and Dutch languages were included.

4.1.3 Appraisal of Included CPGs

Three reviewers (EA, IA, LH) independently assessed the methodological quality of CPGs, health guidelines, consensus documents using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument across the six domain of the 23 items - scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence (86, 87). To ensure standardization of each reviewer's approach, all reviewers completed the online training tutorial (87) before starting the project. Each appraiser rated all individual items on a seven-point Likert scale from 1 ('Strongly Disagree') to 7 ('Strongly Agree'); and judged the guideline. We used the standardized electronic form on the AGREE II website (www.agreetrust.org) to compile the data (88).

The total score for each domain was calculated by summing up all the scores of the individual items in a domain for each reviewer and then standardizing this total as a percentage of the maximum possible score for that domain as follows (87).

We determined the agreement between reviewers using the intraclass correlation coefficient between the scores with their corresponding confidence interval. SPSS Version 23.0 was used to make these estimates. Subsequently, the three reviewers used the concordance calculator developed by McMaster University (88) to obtain accurate quality scores for each domain. Where there are significant variations in scored points between appraisers (more than three points), or if the standard deviation (SD) for a particular item was greater than or equal to 1.5 SD, all the domains were re-assessed independently.

The overall quality rating of assessed CPGs were classified according to a three-point recommendation scale as "recommended", "recommended but with modifications" or "not recommended" (86, 87). Recommendations for the use of CPGs were either deemed 'recommended for practice', 'recommended but with modifications' or 'not recommended for practice'. We based the recommendations on a CPG being judged as both internally and

externally valid and feasible for practice if the different items addressed in the AGREE II domains were sufficiently addressed [(86). We categorized as high-quality CPGs in migrant health in practice as those that scored above 60% of the maximum score in at least three domains, one of which must be “rigour of development” (86, 87, 89).

Also, for each CPG selected, the three reviewers extracted title, the scope of the guideline, year of publication, organization and other information was available. The extracted data were analysed using a descriptive approach, and tables were used to illustrate the differences between the different CPGs. The Kendall tau_b non-parameter correlation was used to analyse the associates between variables using the statistical package IBM SPSS (version 23.0).

4.2 Article 2. “Quality Assessment of Systematic Reviews on International Migrant Healthcare Interventions: A Systematic Review.”

4.2.1 Design

Systematic review

4.2.2 Search Strategy and Study Selection

We searched for systematic reviews in five electronic databases - MEDLINE -OVID, EMBASE, COCHRANE LIBRARY, CINAHL, and LILACS; also, we reviewed SRs published in the World Health Organization (WHO) website. All sources of evidence, as well as the electronic search strategies, are described in Appendix 1 in the published article (90).

We performed a calibration exercise of the selection process and conducted a pilot using five records from our search to ensure the validity and consistency of the selection process. Two team members independently screened the titles and abstracts, followed by full-text assessments for eligibility of studies on prevalence, screening and treatment effectiveness, and related key questions. We included SRs about cross-country adult migrants or refugees as population but excluded aborigine or local minority population. We restricted

the search to reviews published between January 2007 and November 2017 and published in English Language. Disagreements were resolved by consensus or the involvement of a third author. We retrieved all citations and accompanying abstracts from the electronic searches and downloaded to an online referencing manager – Endnote X8. The list of excluded studies with reasons for exclusion is included in Appendix 2 in the published article.(90)

Two independent reviewers performed data extraction using a pre-defined and pilot-tested data extraction form. If more than one comparison reported the same number of trials, reviewers would select the comparison that includes the largest number of outcomes. The detailed list of items extracted from the reviews is included in Appendix 3 in the published article (90).

4.2.3 Quality assessment of included systematic reviews

4.2.3.1 Assessment of reporting quality using PRISMA Checklist

Two independent reviewers evaluated the reporting quality of the systematic reviews using the PRISMA checklist (20). The response options on 27 checklist items were answered with ‘yes’, ‘partly’, ‘no’, ‘unclear’, or ‘not applicable’ (72, 91, 92). The results of the completed PRISMA checklist for each of the reviews were compiled into a table. The total number of items that were answered (‘yes’) was calculated as the overall score out of a possible count of 27 (71, 92).

4.2.3.2. Assessment of methodological quality using AMSTAR 2

Two reviewers independently assessed the quality of systematic reviews using Assessing Methodological Quality of Systematic Reviews - 2 tool (AMSTAR 2) (78, 80). AMSTAR 2 is a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. Each question in the AMSTAR tool was answered as either “yes”, “partial yes”, “no”, “cannot answer”, or “unable to assess” (78).

For each systematic review, overall confidence in the quality ratings was classified as high, moderate, low, or critically low depending on the presence of critical and non-critical flaws in items 2, 4, 7, 9, 11, 13 and 15 in the checklist (80). We resolved any disagreements via a consensus decision by a third reviewer.

4.2.3.3 Assessment of risk of bias using ROBIS tool

Two reviewers independently evaluated the risk of bias and methodological quality of the selected SRs using the Risk of Bias of Systematic Reviews tool – ROBIS (82). We assess the fulfilment of the criterion per domain by responding 'yes', 'probably yes', 'probably no', 'no', or 'no information. A judgement on the overall rating of either 'low risk of bias', 'high risk of bias', or 'unclear risk of bias' was assigned after considering the degree to which each criterion per domain was fulfilled, or there was not enough evidence to support the ROBIS domain. Any disagreements were resolved by a consensus decision or via third reviewer (77, 82).

4.2.4 Data analysis

Two reviewers independently collated and verified data extracted. We summarised the extracted data from the included SRs as frequencies and percentages for the reported characteristics. We reported important outcomes in the included SRs in the following categorises – access and uptake of health services and maternal health; screening programmes – prevalence/ incidence rates, health care delivery, barriers and facilitators, mental health-related and health needs or behaviour. We compiled the result of the completed assessment of each SR using AMSTAR, ROBIS and PRISMA tools concerning adequately satisfied items. We reported the mean numbers of items completed appropriately across all included SRs (overall and by domain), and then stratified by year of publication and type of intervention for exploratory analysis (79, 91, 92). The overall agreement between reviewers was assessed between ROBIS and AMSTAR-2 using intra-class coefficient (ICC) at 95%

confidence interval (CI) as an indicator (93). Data were analysed using the statistical package SPSS version 25.0.

4.3 Article 3. "Effectiveness and cost-effectiveness of screening for schistosomiasis and strongyloidiasis in migrants in the EU/EEA - a systematic review."

4.3.1 Design

Systematic review. The review was one of six systematic reviews conducted under the auspices of a European Centre for Disease Prevention and Control (ECDC) project to develop guidance on screening for parasitic infections in newly arrived migrants to the EU/EEA and the protocol published (94, 95). We followed the PRISMA reporting guidelines (96).

4.3.2 Search strategy for the review

We searched for systematic reviews in MEDLINE, EMBASE-ELSEVIER, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Epistemonikos, the Database of Abstracts of Reviews of Effects (DARE) and the Cochrane Database of Systematic Reviews (CDSR) for evidence on effectiveness, respectively. We used a combination of the key terms: 'Immigrant', *'Strongyloides'*, 'Schistosomiasis', 'endemicity', 'prevalence', 'screening', 'migrant screening', 'mass screening', 'early detection', 'health impact assessment' and 'cost-effectiveness'. We searched grey literature sources for published guidelines, and reports on screening and prevention programme from the United States (US) Centres for Disease Control and Prevention, ECDC, and the World Health Organization (WHO).

We searched the National Health System (NHS) Economic Evaluation Database, the Health Economic Evaluations Database, the Cost-Effectiveness Analysis Registry and Google Scholar for evidence on cost-effectiveness. We used a combination of the key terms ("costs and cost analysis"; "cost-effectiveness analysis"; "costs.tw"; "cost$.mp."; "cost effective$.tw"; "cost-benefit analys$.mp" "health care costs.mp") combined with clinical criteria.

Due to the limited evidence obtained from the initial search, we conducted an updated search of six databases (MEDLINE, EMBASE-ELSEVIER, CINAHL, CDSR, DARE, Cochrane CENTRAL and Latin American Literature in Health Sciences - LILACS) for additional primary studies on diagnostic or screening tools for schistosomiasis. Also, we searched the references of the included primary studies to identify other relevant studies.

4.3.3 Inclusion criteria and study selection

The primary populations were migrants and refugees. We considered as key outcomes: cure, mortality, morbidity, adverse effects, health equity, quality of life and test accuracy measures (sensitivity and specificity). We restricted the search to studies published between January 1993 and May 2016 for studies on screening for schistosomiasis and strongyloidiasis. We also identified reviews on prevalence of the two infections. For the primary studies on diagnostic or screening tools, we included studies published between January 2010 and February 2017 for schistosomiasis, and between January 2012 and February 2017 for strongyloidiasis due to a lack of systematic reviews in this area. We did not apply language restrictions, and when we identified more than one version of a systematic review, we included the most recent. For evidence on cost-effectiveness, we included studies that reported resource use, costs and cost-effectiveness on schistosomiasis and strongyloidiasis.

4.3.4 Data extraction and synthesis

Two authors independently screened the titles and abstracts, followed by full-text assessments. For systematic reviews, we extracted the following data – study design, population, intervention, comparison and outcomes - prevalence, screening accuracy (sensitivity and specificity) and treatment effectiveness, and cost-effectiveness. We resolved any disagreements by consensus or by the involvement of a third author.

For cost-effectiveness studies, we extracted the following data: economic study design (e.g., cost-utility analysis, Markov model), description of the case base population, the intervention and comparator, the absolute and relative difference in resource use and cost-effectiveness (e.g., incremental net benefit (INB) or incremental cost-effectiveness ratio (ICER).

4.3.5 Quality assessment

We assessed the methodological quality of included reviews using AMSTAR (80), Newcastle–Ottawa Scale (97) for observational studies and evaluated the methodological quality of included primary studies on diagnostic effectiveness using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS 2) tool (98). We assessed the of certainty of the evidence for systematic reviews and individual studies using GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria. The GRADE rating was based on assessments of the following vital factors - the risk of bias, heterogeneity of studies, indirectness, imprecision, and effect size and publication bias in the included studies. The quality of evidence was downgraded if there were serious or very serious concerns related to any GRADE criteria (99).

4.2.4 Data analysis

Two authors independently collated and verified data extracted. We summarised the extracted data from the included reviews and primary studies the reported the study characteristics. We entered all the key data into the GRADEpro software, and produced GRADE evidence profile tables, summary of findings tables and evidence to decision tables.

4.4. Article 4. “Public health guidance on screening for Strongyloidiasis and Schistosomiasis in newly arrived migrants within the EU/EEA.”

4.4.1 Setting up an ad hoc scientific panel

This public health guidance for screening and vaccination was produced under the European Centre for Disease Prevention and Control (ECDC) - ECDC Framework Service Contract Number ECDC/2015/016 with Euro Health Group A/S which led by team of independent consultants. The duration of the contract was from January 2016 to December 2018. Eric Agbata led the systematic review and provided an initial draft of the chapter on schistosomiasis and strongyloidiasis as the emerging guideline synthesis; in addition, he is a member of the Cochrane and Campbell Equity Methods Group, which supported the development of the systematic reviews, the GRADE evidence profiles and the GRADE evidence to decision tables in all the disease groups. As part of the project, members of the ad hoc panel were appointed through the following steps identification of experts; collecting declarations of interest from experts; evaluating eligibility; and ruling out conflicts of interest of experts and then appointed (50). Firstly, ECDC convened an advisory group to explore the scope, priorities and principles for developing in six infectious disease areas. Thereafter, ECDC appointed an ad hoc scientific panel of 21 experts from a range of EU/EEA Member States to review and assess the evidence base and provide consensus statements on good practices for interventions and service models targeting refugees and other migrants(50). Finally, 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, as well as invited stakeholders from European Commission, the WHO Regional Office for Europe, and the International Organisation for Migration (IOM)(50).

4.4.2 Selection of key questions

Strongyloidiasis and schistosomiasis were prioritised in addition to other infectious diseases - active TB, LTBI, HIV, hepatitis B, hepatitis C, vaccine-preventable diseases (measles, mumps, rubella, diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type B).

The key questions for screening priorities were:

- Should newly arrived migrants be offered screening for strongyloidiasis, and schistosomiasis? Who should be targeted and how?
- What are the implementation considerations about screening in EU/EEA countries?(95)

4.4.3 Systematic evidence review

We developed a systematic evidence review on the screening and treatment priorities for schistosomiasis and strongyloidiasis with technical support from the Campbell and Cochrane Equity Methods Group and members of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. A detailed description of the methods for the systematic reviews can be found in the registered systematic review protocol (95).

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 (71). The methodological quality of eligible systematic reviews was assessed using AMSTAR (99); the quality of individual observational studies was assessed using the Newcastle Ottawa scales (100). For cost-effectiveness studies, we extracted key data including the size of the resource requirements, the certainty of evidence around resource requirements, and whether the cost-effectiveness results favoured the intervention (101). We analysed the evidence from the quantitative evidence review and qualitative synthesis; rated the certainty of the effects for

pre-selected outcome measures; created GRADE evidence profile, and draft evidence-based statements using the GRADEPro platform (101).

4.4.4 Developing evidence statements using GRADE approach

We developed evidence-based statements for screening and treatment options for two intestinal parasite - schistosomiasis and Strongyloidiasis using the GRADE approach (102). The final evidence synthesis was circulated to an expert panel (ad hoc scientific panel, other experts, and observers) for assessment and feedback on proposed evidence-based statements. We presented the preliminary findings via video conference to the scientific panel, who reviewed and voted on all criteria of the evidence-to-decision summaries.

4.4.5 FACE Survey

We conducted a face survey of ad hoc scientific panel members and experts to assess their perceptions on potential feasibility, acceptability, cost and equity issues related (FACE) to screening and treatment according to the GRADE approach. Panel members were presented with 13 screening and vaccination evidence-based statements for the key infectious diseases, including schistosomiasis and strongyloidiasis and asked to rate implementation priorities for each condition under consideration (very low, low, moderate, high). Then, they were then asked to indicate the level of feasibility, acceptability, cost (resource use) and equity for each option based on the FACE constructs.

We categorised the FACE results based on the panel's level of agreement as follows: high agreement (>75% of ad hoc panel), medium/moderate agreement (50–75%), and low agreement (<50%). We resolved any differences by facilitated discussions or consensus. After that, we developed the final recommendations, and the *ad hoc* scientific panel reviewed a final draft and ECDC disease leads for schistosomiasis and strongyloidiasis for final review prior to publication.

5. Results

5.1. Article 1: "Migrant Healthcare Guidelines: A Systematic Quality Assessment."

Summary of the results

Of the 2620 citations obtained from our systematic searches, 2563 citations were obtained after de-duplication. Based on title and abstract review, 2518 citations were excluded because they did not fulfil the inclusion criteria. Forty-five full-text articles were assessed for eligibility, and 13 were excluded: five were not relevant guidelines, policy or consensus recommendations, four papers were not relevant to the population, two were not specific to the population of interest, while two were excluded because of lack of access to credible translation.

In total, we included 32 migrant healthcare guidelines. Fourteen HGs were from the United States, five from Europe in liaison with European based health societies. Also, four HGs were from Australia, three from global supranational bodies such as the World Health Organization, two each were from the United Kingdom and Ireland, and one each from Canada and Italy, respectively.

In terms of the overall appraisals and interpretation of domain scores for included migrant guidelines and recommendations, the overall agreement between appraisers using with AGREE II instrument was excellent (ICC: 0.954; 95% CI: 0.924 - 0.984). The overall mean scores for the six domains were as follows – Scope and Purpose - 84.81% ± 19.02% (range 13%-100%); Stakeholder involvement and intended user representation - 84.81% ± 19.02% (range 13%-100%); Rigour of development - 33.91% ± 31.98% (range 4%-100%); Clarity of Presentation- 88.53% ± 7.34% (range 67%-100%); Applicability of guideline - 40.4% ± 23.6% (range 0%-94%); and for editorial independence - mean score for the selected guidelines was 26.6% ± 38.5% (range 0%-100%). For the overall recommendation of included guidelines,

nine out of thirty-two migrant guidelines evaluated (28.1%) were deemed “recommended” by the reviewers; six (18.6%) were “recommended with modifications”; while seventeen (53.1%) were “not recommended”. The nine “recommended “guidelines scored ≥ 60% in at least four of the domains (including “rigour of development), whereas the seventeen “Not recommended” guidelines (53.1%) had scores below 40% in at least four domains (including the “rigour of development” domain). The overall quality in guideline development and reporting appeared to have improved slightly in the last four years (2013-16) compared to previous years (2006 to 2012) (P = 0.04).

5.2. Article 2: “Quality Assessment of Systematic Reviews on International Migrant Healthcare Interventions: A Systematic Review.”

Summary of the results

A total of 1614 citations, reduced to 1456 citations, after duplicates were removed — that were title-and-abstract screened. Of 71 full-text documents selected for review, 32 were excluded, leaving 39 eligible SRs. The updated systematic literature search for migrant health systematic reviews yielded after de-duplication 555 citations for the screening of titles and abstracts. Of the 72 articles selected for full-text screening, we included 18 SRs. Overall, we included 57 systematic reviews. The characteristics of the included studies showed that more than half of the SRs were conducted in high-income countries, specifically Australia, Canada, US, UK, and European states, whereas only SRs were from LMICs. Fifty-one (89.5%) of the SRs were published between 2014 – April 2020. Thirty-one SRs included quantitative studies only (54.4%), 18 SR included mixed methods studies (31.6%), and eight SRs focused on qualitative studies. Migrant populations in included SRs were - all migrants - 23 SRs; women migrants only - 12 SRs, refugees and asylum seekers or IDPs - 12 SRs; ethnic migrants (Arab, Asians, Chinese or Latin American) – five SRs; migrant and refugee populations – three SRs, and three SRs on undocumented migrants.

Using the AMSTAR- 2 tool, the quality in 30 SRs (56.1%) was either low or critically low due to limitations in AMSTAR- 2 items 4, 7, 8, 10-16. Approximately 40% of the SRs had "high" concerns for risk of bias, directly linked to the ROBIS domains on - "study identification," "data collection and study appraisal," and "synthesis and findings," respectively. Finally, with the PRISMA Checklist, the quality of reporting in 36 SRs (63.2%) was moderate, with 19.74 ± 4.67 mean number of items fulfilled, however 16 SRs (28.1%) reported research protocol and registration.

5.3. Article 3: “Effectiveness of Screening and Treatment Approaches for Schistosomiasis and Strongyloidiasis in Newly Arrived Migrants from Endemic Countries in the EU/EEA: A Systematic Review.”

Summary of the results

The systematic search yielded, after removal of duplicates, 662 systematic reviews for which we screened titles and abstracts. Of the 26 systematic reviews selected for full-text screening, we included 11 systematic reviews, which focused on the efficacy of diagnosis and treatment of schistosomiasis (n = 8) and strongyloidiasis (n = 3). The search for additional diagnostic testing accuracy studies for schistosomiasis yielded 1,961 citations for the screening of titles and abstracts. Of the 30 articles selected for full-text screening, we finally included eight individual studies. Similarly, the search for diagnostic testing accuracy evidence for strongyloidiasis yielded 497 records; titles and abstracts were screened, and of the 24 studies were selected for full-text screening. We finally included three individual studies.

For the economic evidence, the search strategy yielded 160 studies. We retrieved 20 studies after title and abstract screening, of which six (four decision-analytic models for economic evaluation and two costing studies) were finally included—four for strongyloidiasis and two for schistosomiasis. Overall, we included 11 systematic reviews, 11 individual studies, and six economic studies on economic evidence in this systematic review.

ELISA (Enzyme-linked immunosorbent assay) was the most sensitive test for Schistosoma spp. , while ELISA Recombinant Ag (NIE) and Immunofluorescence antibody test (IFAT) were the most sensitive screening tests for *St. stercoralis.* The GRADE certainty of evidence on effectiveness of screening techniques for Schistosoma Spp and St. stercoralis was low.

For Schistosomiasis, praziquantel (single 40 mg/kg dose) achieved 60% reduction in parasitic ova in urine in 4 – 8 weeks while for strongyloidiasis parasitological cure was higher with

ivermectin (RR 1.79) compared with albendazole or thiabendazole. The GRADE certainty of evidence was moderate to high.

The economic evidence on the screening and treatment intervention for both infections were moderate quality.

Antibody-detecting serological tests were the most effective screening tests for detection of both schistosomiasis and strongyloidiasis in low-endemicity settings. The serological screening tests showed higher sensitivity than conventional parasitological methods. Short courses of praziquantel and ivermectin were safe and highly effective and cost-effective in treating schistosomiasis and strongyloidiasis, respectively.

5.4. Article 4: "Evidence to Decision (EtD) Framework for screening for schistosomiasis and strongyloidiasis in migrants in the EU/EEA."

Summary of the results

After conducting the systematic search of evidence on major databases and grey literature, we did not find studies providing direct evidence on the effectiveness of screening for strongyloidiasis or schistosomiasis among migrants. However, we identified 28 studies that partially addressed some issues around the screening for schistosomiasis and strongyloidiasis among this population. We included for analysis 11 systematic reviews (SRs), eight of them focusing on the effectiveness of diagnosis and treatment of schistosomiasis, and three on strongyloidiasis. When possible we updated the results of these SRs, including ten additional primary studies: seven for schistosomiasis and three for strongyloidiasis. For the economic evidence, we identified six studies (four for strongyloidiasis and two for schistosomiasis), which consisted of one SR and five primary studies (three decision-analytic models for economic evaluation and two costing studies).

Regarding strongyloidiasis screening, the 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. While traditional methods such as agar plate culture and Baermann methods were the best techniques 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) (GRADE certainty of evidence = moderate); serological antibody detection methods exhibited better sensitivity patterns than classical parasitological techniques. The sensitivity and specificity values were: 85% (95% CI: 79–92) and 100% (95% CI: 100–100) for the luciferase-immunoprecipitation system (LIPS); 91% (95% CI: 86–96) and 99% (95% CI: 97–100) for IVD-ELISA; 90% (95% CI: 84–95) and 98% (95% CI: 96–100) for

Bordier-ELISA; and 94% (95% CI: 90–98) and 92% (95% CI: 87–97) for the indirect fluorescent antibody technique (IFAT) (low certainty of evidence).

Regarding schistosomiasis screening, the evidence from systematic reviews showed that the most effective screening tests for schistosomiasis spp. in low intensity/low endemic setting were the antibody-detecting serological tests - IgM-ELISA (commercial tests) and the indirect hemagglutination (IHA) tests, due to higher sensitivities compared with conventional parasitological methods such as Kato–Katz technique.

In terms of cost-effectiveness of management of those with positive screening results, double dose of praziquantel was highly cost-effective compared with a single dose (ICER of <USD 500/QALY) for schistosomiasis in endemic settings. For strongyloidiasis, presumptive treatment for strongyloidiasis with ivermectin is cost-effective at a threshold of less than USD 10 000/QALY across a range of prevalence values. In addition, a few moderate-quality economic studies support a strategy of presumptive treatment for strongyloidiasis in migrants from high-risk backgrounds. Finally, presumptive treatment with single-dose ivermectin for all immigrants was cost-effective compared to five days' treatment with albendazole and screening (eosinophilia and/or parasitological techniques only) in the home country.

The opinion of the ad hoc scientific panel members on the evidence relating to feasibility, acceptability, cost (resource use), and equity of screening migrants for schistosomiasis and strongyloidiasis were as follows - medium level of agreement (73%) on the priority of screening; low level of agreement (21%) on the feasibility of screening; medium level of agreement (50%) on acceptability of screening; medium level of agreement (57%) on equitability of screening, for schistosomiasis and strongyloidiasis among migrants is equitable in the EU/EEA, respectively.

The final recommendations developed by the scientific panel after discussion are listed as follow:

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. (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. (Certainty of evidence: low)

Public Health Considerations: Schistosomiasis and strongyloidiasis are preventable diseases with low-cost screening and cost-effective treatment to reduce the impact of chronic infections. Routine screening aligned with national recommendations makes sense for public health. Migrant at high risk stands to benefit from treatment resulting in the improved quality of life.

5. 5. Publications included in the Thesis

5.5.1 First publication

- Agbata EN, Padilla PF, Agbata IN, Armas LH, Solà I, Pottie K, Alonso-Coello P. Migrant Healthcare Guidelines: A Systematic Quality Assessment. Journal of immigrant and minority health. 2018 May 21:1-3. D.O.I 10.1007/s10903-018-0759-9. Impact factor: 1.425.

- Journal of immigrant and minority health 2018: Impact factor: (1.425; Second Quarter (Q2) (194/500 Medicine: Public Health, Environmental and Occupational Health; 65/89 Medicine: Epidemiology).

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REVIEW PAPER

Migrant Healthcare Guidelines: A Systematic Quality Assessment

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Abstract

Significant international and cross-border migration has led to a growing availability of migrant healthcare guidelines (MHGs), which we systematically reviewed for quality. PubMed, MEDLINE, CINHAL, PsychINFO and guideline developer/guideline databases were searched for MHGs published 2006–2016. Three independent reviewers assessed eligible MHGs using the Appraisal of Guidelines, Research and Evaluation II instrument (AGREE II). MHGs were identified as high quality if they had a score of ≥60% in at least three of the six domains, including "rigour of development", and overall quality was assessed on a seven-point Likert scale. We included 32 MHGs. Overall agreement between reviewers was very good. Mean scores for each AGREE II domain were as follows: 85 ± 19.0% for "scope and purpose"; 51 ± 30.5% for "stakeholder involvement"; 34 ± 31.9% for "rigour of development"; 86 ± 7.3% for "clarity of presentation"; 40 ± 23.6% for "applicability"; and 27 ± 38.5% for "editorial independence". Nine and six MHGs were deemed "recommended" or "recommended with modifications", respectively, and 17 were "not recommended". Our review of MHGs has highlighted critical deficiencies in rigour of development, applicability, editorial independence and stakeholder involvement that point to the need for improvements in future MHGs.

Keywords Migrant health · Refugee health · Practice guidelines · AGREE II tool · Quality assessment

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Introduction

Substantial attention is being paid to the public health crisis associated with international cross-border migration, which has increased in recent years due to conflict, climatic disasters and globalization [1, 2]. Migrant populations represent a diverse group of frequently irregular and undocumented migrants, including economic migrants, refugees, asylum seekers and unaccompanied minors [2, 3]. Often considered a potential health risk, migrants also represent a burden on healthcare resources, given the higher prevalence of latent or poorly managed communicable and non-communicable diseases in this population [3, 4].

Supranational health bodies and a number of European Union (EU) states have identified key areas regarding the promotion of migrants' right to health, aimed at ensuring accessible and acceptable quality in healthcare provision to international migrants [5–8]. While many developed countries have health recommendations, guidelines and policy documents that refer to foreign migrants [6, 9], poor adherence and implementation have resulted from formal and informal barriers [4, 5]. The barriers include a lack of legal protection, limited access to the health system, inadequate knowledge of the health system and the lack of a social network. These difficulties are further compounded by language and communication difficulties and experiences of marginalization and discrimination [4, 5, 10–13]. Furthermore, in most EU countries, complex regulatory frameworks, along with ambiguous or substandard guidelines, may result in unnecessary internal restrictions, uncertainties, short-term emergency measures and inequalities [14, 15]. Altogether, therefore, the result is one of poor access to health and poorer health outcomes among international migrants.

Healthcare guidelines (HGs) in health care are sets of recommendations based on systematic reviews of the evidence intended to promote recommended practices [16]. They are aimed to ensure planning and minimal variations in work practices and improved efficiency and quality [17–22]. High-quality HGs should be specific and evidence-based, should have been critically reviewed by experts and should, furthermore, reflect the perspectives of stakeholders and provide clear guidance for implementation [23, 24]. However, the fact that most HGs do not as yet adequately accommodate the health requirements of migrants—and so impact negatively on migrants' rights to health and to health equity [6, 7, 11]—may reflect poor quality [6, 24, 25].

Over the last two decades, systematic evaluations of HGs in healthcare have revealed some gaps in methodological quality, with considerable potential for improvement [26–28]. The Appraisal of Guidelines for Research and Evaluation II instrument (AGREE II) was developed as is a validated, reliable, international instrument that provides with an established framework for the development and quality appraisals and development of HGs in healthcare [25, 29].

While both clinical and public health guidelines for migrants have become increasingly available [2, 4, 5, 8], to our knowledge, no migrant healthcare guidelines (MHGs) have been systematically evaluated in terms of quality. In view of this gap in the literature, using the AGREE II tool, we conducted a systematic evaluation of the quality of MHGs.

Methods

Study Design

Systematic Review of Published MHGs

Search Strategy and Selection of MHGs We searched for MHGs in PubMed, MEDLINE, CINHAL and PsycINFO, in guideline and guideline developer databases, in the TRIP database, in guideline compilation bodies and clearinghouses and in project-based websites. We also explored grey literature from the International Federation of Red Cross and Red Crescent Societies, the Migration Policy Institute, Organization for Economic Cooperation and Development and relevant US public health organizations. The search was limited to the 10-year period March 2006 to March 2016 (see Supplement A1 for sources and search strategies).

Eligibility Criteria

As MHGs we included all documents that included health care recommendations, including policy documents, published in English that contained explicit recommendations on migrants' access to health and healthcare provision by healthcare systems. Our definition of migrants was that of the Health Protection Surveillance Centre (HPSC) Scientific Advisory Committee (Ireland), as this definition includes cross-country or international migrants residing in a destination country, irrespective of their legal status [30]. We excluded HGs that only addressed local or native populations in migrant-receiving countries. Three reviewers (EA, IA, LH) independently determined whether inclusion and exclusion criteria were met. Differences in opinion were resolved by discussion with a fourth reviewer (PF).

Quality Evaluation

To evaluate quality, we used AGREE II (http://www.agreetrust.org; see Supplement A2), an internationally endorsed 23-item tool that evaluates six domains, namely, "scope and purpose", "stakeholder involvement", "rigour of development", "clarity of presentation", "applicability" and "editorial independence" [29, 31]. AGREE II provides a framework for (1) assessing the quality of practice guidelines, (2) guiding methodological strategies for the development of guidelines, and (3) determining what information is reported in guidelines [25, 31]. Using AGREE II, three reviewers (EA, IA, LH) independently assessed the methodological quality of retrieved HGs. To ensure a standardized approach, all reviewers previously completed the AGREE II online training tutorial [25, 31]. Reviewers performed a calibration exercise to ensure the validity and consistency of the rating process. Individual items were rated on a seven-point Likert scale scored from 1 (strongly disagree) to 7 (strongly agree). Quality appraisal took into consideration all the appraisal items. A standardized electronic form available from the AGREE II website was used to compile the data [31].

Data Analysis

We calculated domain scores by summing scores for individual items in a domain and scaling this total as a percentage of the maximum possible score for that domain. We standardized domain scores using the following formula: (obtained score—minimum possible score), (maximum possible score—minimum possible score) × 100. The maximum possible score was obtained by multiplying the maximum score for each domain (strongly agree) by the number of domain items and the number of reviewers; likewise, the minimum possible score was obtained by multiplying the minimum score for each domain (strongly disagree) by the number of domain items domain and the number of reviewers. The range of standardized scores for each domain was 0–100%. We used the Rater Concordance Calculator developed by McMaster University to obtain accurate quality scores for each domain [32]. When there was a score variation of more than three points between reviewers or of 1.5 or more in the standard deviation (SD), each one of the domains was independently re-assessed by the reviewers. We evaluated whether MHGs quality improved over time using the Student *t* test. The P-value was set to $\alpha = 0.05$ (2-tailed) for all tests. The intra-class coefficient (ICC) for a 95% confidence interval (CI) was used as an overall indicator of agreement between reviewers, rated as slight (0.01–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), or very good (0.81–1.00) [33, 34]. Data was analysed using the statistical package SPSS version 23.0.

The overall quality of each HG was rated using a seven-point Likert scale (scored from 1 for lowest quality to 7 for highest quality) [29, 31]; scores of 6–7, 4–5 and 3 and below reflected high quality, moderate quality and low quality, respectively. On the basis of the overall quality rating, MHGs were classified according to a three-point recommendation scale as "recommended", "recommended but with modifications" or "not recommended" [29, 31]. Recommendations were based on a MHGs being judged as both internally and externally valid and feasible for practice if the different items addressed in the AGREE II domains were sufficiently addressed [29, 31, 35]. Categorized as high-quality MHGs were those that scored above 60% of the maximum score in at least three domains, one of which had to be "rigour of development" [34].

Results

A total of 2620 citations were located in the systematic search, reduced to 2563 citations—after duplicates were removed—that were title-and-abstract screened. Of 45 full-text documents selected for review, 13 were excluded, leaving 32 eligible MHGs (Fig. 1). In terms of origin, 14 (43.7%) were from the USA [36–49], four (12.5%) were published by WHO [50–52], four (12.5%) were published by Europe/European-based health bodies [53–57], four (12.5%) were from Australia [58–61], and the remaining six guidelines were from the UK [62, 63], Ireland [3, 64], Canada [65] and Italy [66] (Table 1). In terms of type of document, 24 (75.0%) guidelines, five (15.6%) were recommendations, two (6.3%) consensus statements and one (3.1%) policy recommendation.

We classified the scope of the included MHGs—29 (90.6%) of which were published during or after 2011—in four categories: screening, screening and treatment, immunization, and communication (Fig. 2). Of the 32 MHGs, 18 (56.3%) focused on screening and treatment strategies for infectious and some non-infectious diseases [38, 39, 44, 49–51, 53–56, 58, 59, 61, 65, 66], 11 (31.2%) focused on screening strategies for specific conditions such as hepatitis, tuberculosis, HIV, STIs, mental health, lead and nutritional status [3, 37, 40–43, 45–47, 52, 60], and one each focused on immunization/immunization updates [36], preventing hepatitis A [48] and communication in cross-cultural general practice consultations [64].

Appraisal and Interpretation of Domain Scores

Overall agreement between reviewers was very good (ICC 0.95; 95% CI: 0.92–0.98). Standardized AGREE II scores per domain for the recommended HGs (see Sect. "Overall MHG Assessment") are summarized in Table 2

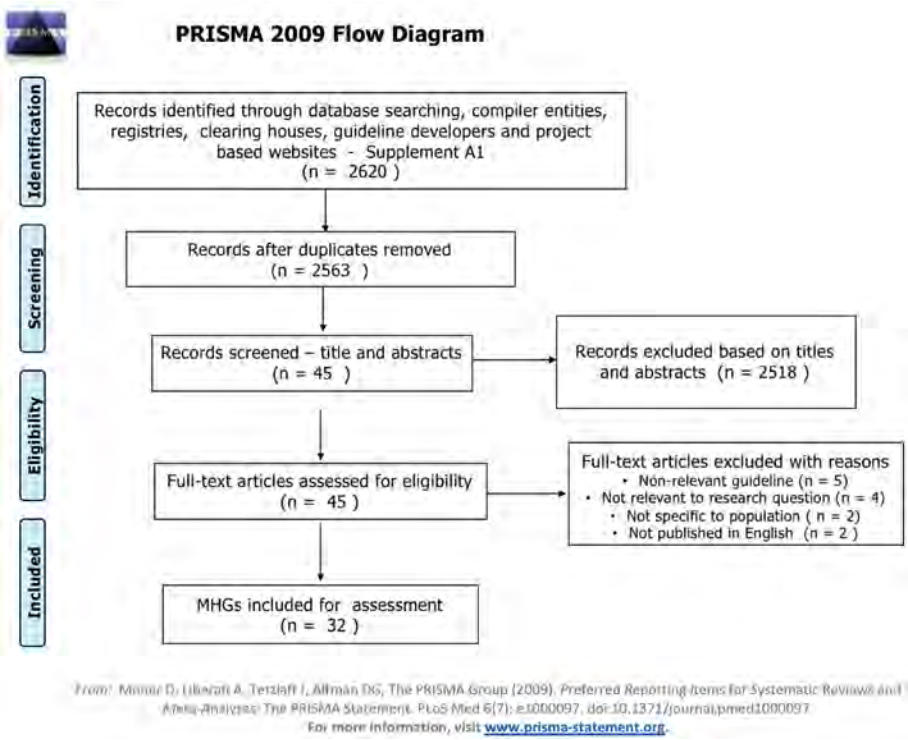

Fig. 1 Literature search and inclusion flowchart (PRISMA model).

(non-recommended HGs are not listed) and mean scores for all 32 HGs by domain are summarized in Fig. 3.

Scope and Purpose

The mean score for this domain was 85 ± 19.0% (range 39–00%), indicating that, on average, MHGs attained 85% of the maximum possible score. A single guideline [46] scored under 60% for this domain.

Stakeholder Involvement

The mean score for this domain was 51 ± 30.5% (range 6–100%). While 12 (37.5%) MHGs [3, 36, 50–52, 54–56, 58, 59, 64, 65] demonstrated stakeholder involvement by scoring over 60% in this domain, in the 20 (62.5%) CPGs [37–49, 57, 60–64, 66] that scored below 60%, there was no clear description of the process for obtaining the views and preferences of migrants or their representatives.

Rigour of Development

The mean score for this domain was 34 ± 31.9% (range 4–100%). Only 9 (28.2%) MHGs scored above 60%; seven (21.8%) of these [50–56, 58, 65] rated the quality of the evidence and five (15.6%) of these [50–52, 55, 56] described a procedure for updating. Conversely, the 23 (71.8%) remaining HGs lacked details on systematic methods for searching for evidence, selecting evidence, formulating recommendations or arranging external review by experts before publication.

Clarity of Presentation

The mean score for this domain was 89 ± 7.3% (range 67–100%). All 32 included MHGs received scores above 60% [3, 36–66].

Applicability

The mean score for this domain was 40.4 ± 23.6% (range 0–94%). While eight of the 32 included MHGs (25.0%) [3, 36, 50–52, 54–56] had mean scores above 60%, only four (12.5%) [50, 51, 55, 56] clearly reported monitoring or auditing criteria.

Editorial Independence

The mean score in this domain was 26.6 ± 38.5% (range 0–100%), with most MHGs (62.5%) scoring zero [3, 36–47, 49, 57, 60–64]. Only eight (25.0%) HGs [50–53, 58, 59, 65] scored over 60%, given that they had included information on potential conflicts of interest among guideline group members or institutions and sources of funding for the guideline development.

Table 1 Included MHGs (n = 32)

Title	ID	Organization (country/region)	Published	Scope
Guidance on tuberculosis control in vulnerable and hard-to-reach populations. Stockholm: ECDC	ECDC_TB1 [49]	European Centre for Disease Prevention and Control (Europe)	2016	Screening, treatment
Recommendations for comprehensive post-arrival health assessment for people from refugee-like backgrounds	ASID_Health [55]	Australasian Society for Infectious Diseases and Refugee Health Network of Australia (Australia)	2016	Screening
Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries	WHO_TB1 [59]	European Respiratory Society/World Health Organization (supranational)	2015	Screening, treatment
Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection, 2015	WHO_HepB [58]	World Health Organization (supranational)	2015	Screening, treatment
Infectious disease assessment for migrants	HPSC_Inf [3]	Health Protection Surveillance Centre (Ireland)	2015	Screening
Guidelines for evaluating and updating immunizations during the domestic medical examination for newly arrived refugees	CDCORR_Immun [35]	Centres for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2015	Screening
Guidelines for Mental Health Screening during the Domestic Medical Examination for Newly Arrived Refugees	CDCORR_Mental [36]	Centres for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2015	Screening
Policy recommendation: latent tuberculosis infection screening and treatment in children in immigration detention	NTDoH_TB [57]	Centre for Disease Control, Department of Health, Northern Territory Government (Australia)	2015	Screening, treatment
Screening for Sexually Transmitted Diseases during the Domestic Medical Examination for Newly Arrived Refugees	CDCORR_STI [41]	Centres for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2014	Screening
Screening for hepatitis during the domestic medical examination for newly arrived refugees	CDCORR_Hep [40]	Centres for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2014	Screening
Tuberculosis control in big cities and urban risk groups in the European Union—A Consensus Statement	ECDC_TB2 [50]	European Centre for Disease Prevention and Control/ Euro surveillance (Europe)	2014	Screening, treatment
EPA Guidance mental health care of migrants	EPA_Mental [51]	European Psychiatric Association (EPA) (Europe)	2014	Screening, treatment
National Evidence-Based Antenatal Care Guidelines—Module II	AUGOV_Antenatal [54]	Australian Government Department of Health (Australia)	2014	Screening, treatment
Systematic screening for active tuberculosis: principles and recommendations	WHO_TB2 [60]	World Health Organization (supranational)	2013	Screening
Guidelines for overseas presumptive treatment of strongyloidiasis, schistosomiasis, and soil-transmitted helminth infections for refugees resettling to the United States	CDCORR_Hel [37]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2013	Screening
Lead Screening during the Domestic Medical Examination for Newly Arrived Refugees	CDCORR_Pb [42]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2013	Screening
Intestinal parasite guidelines for domestic medical examination for newly arrived refugees	CDCORR_Par [43]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2013	Screening
Guidelines for Evaluation of the Nutritional Status and Growth in Refugee Children During Domestic Medical Screening Examination	CDCORR_Nutr [45]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2013	Screening
Minimum package for cross-border TB control and care in the WHO European region: a Wolfheze consensus statement	WHO_TB3 [52]	World Health Organization/Wolfheze Transborder Migration Task Force (Europe)	2012	Screening, treatment
Screening guidelines for the initial health assessment of newly arrived refugees in the Northern Territory	NTDoH_Health [56]	Centre for Disease Control, Department of Health, Northern Territory Government (Australia)	2012	Screening

Table 1 (continued)

Title	ID	Organization (country/region)	Published	Scope
Guideline for Communication in Cross-Cultural General Practice Consultations	HSE_Comm [63]	Health Services Executive/ Health Research Board (Ireland)	2012	Communication
Overseas refugee health guidelines: Malaria	CDCORR_Mal1 [38]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2012	Screening, treatment
Guidelines for screening for tuberculosis infection and disease during the domestic medical examination for newly arrived refugees	CDCORR_TB [39]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2012	Screening
Screening for HIV Infection During the Refugee Domestic Medical Examination	CDCORR_HIV [44]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2012	Screening
Guidelines and discussion of the history and physical examination	CDCORR_Exam [46]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2012	Screening
Domestic refugee health guidelines: malaria	CDCORR_Mal2 [48]	Centre for Disease Control and Prevention (CDC)/Office of Refugee Resettlement (ORR) Health Work Group (USA)	2012	Treatment
Evidence-based clinical guidelines for immigrants and refugees	CCIRH_Imm [64]	Canadian Collaboration for Immigrant and Refugee Health (Canada)	2011	Screening, treatment
Recommendations for the prevention, diagnosis, and treatment of chronic hepatitis B and C in special population groups (migrants, intravenous drug users and prison inmates)	IT_HepB/C [65]	Italian Association for the Study of the Liver (AISF), Italian Society of Infectious and Tropical Diseases (SIMIT), Italian Federation Department's Operators and Addiction Services (FederSerD), Italian Prison Medicine and Healthcare Society (SIMSPe) (Italy)	2011	Screening, treatment
Recommendations for Administering Hepatitis A Vaccine to Contacts of International Adoptees	AAP_HepA [47]	Centre for Disease Control and Prevention and the American Academy of Pediatrics (AAP) (USA)	2011	Immunization
Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management	BIA_Eos [61]	British Infection Association Guidelines Group (UK)	2010	Screening, treatment
UK National Guidelines for HIV Testing 2008	UK_HIV [62]	British HIV Association, British Association for Sexual Health and HIV; British Infection Society (UK)	2008	Screening
EAU Guidelines for the Management of Urogenital Schistosomiasis	EAU_Schist [53]	European Association of Urology (Europe)	2006	Treatment

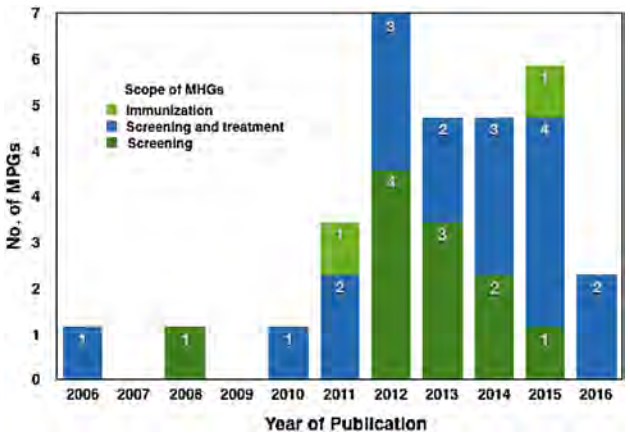

Fig. 2 Scope of MHGs published in the period 2006–2016. A single MHG whose scope is communication is not included (HSE [63], published 2012).

Overall MHG Assessment

In terms of reviewer recommendations of the 32 MHGs (Table 2), nine (28.1%) were "recommended" [50–56, 58, 65]; six (18.6%) were "recommended with modifications" [3, 36, 59, 62, 64, 66] and 17 (53.1%) were "not recommended". All the "recommended" HGs scored at least 60% in at least four of the six domains (including "rigour of development") and achieved a high overall quality score (6 or 7 of a maximum of 7 on the Likert scale). The HGs that were "recommended with modifications" had scores below 60% in three or four domains (including "rigour of development"), and although one HG [58] achieved good scores for the other five domains, it failed to be rated as recommended because it underachieved in the "rigour of development" domain. These HGs achieved a moderate overall quality score (4 or 5 on the Likert scale). The HGs that were "not recommended" scored below 40% in 5 or all 6 domains (including "rigour of development") and achieved a low overall quality score (1–3 on the Likert scale).

There were minimal improvements over time in domain mean scores except in one domain ("applicability"), whose mean score increased from 29.6 ± 13.8 for HGs published 2006–2012 to 49.9 ± 26.5 ($P < 0.01$) for MHGs published 2013–2016. However, the overall assessment resulting in a recommendation category in the timeline assessment was well below 60%, with only a amarginal improvement in the mean per-item score for MHGs published 2013–2016 compared to MHGs published 2006–2012 (3.89 ± 1.3 vs. 4.76 ± 1.7; $P = 0.12$) (Table 3).

Discussion

Main Findings

Our assessment of MHGs showed that the overall quality was suboptimal, with only nine (28%) HGs recommended for use without modifications: four by the WHO (WHO_HB, WHO_TB1, WHO_TB2 and WHO_TB3); two by the ECDC (ECDC_TB1 and ECDEC_TB2); and one each Australian (AUGOV_Antenatal), Canadian (CCIRH_Imm) and European (EPA_Mental). In general, the highest scores were achieved for the "clarity of presentation" and "scope and purpose" domains, and the lowest scores were obtained for "editorial independence", "applicability" and "stakeholder involvement". MHGs published by supranational bodies accounted for six of the nine recommended MHGs, and generally obtained higher quality scores across all six domains than HGs published by state-owned organizations. There was no significant improvement in the quality of MHGs s over time.

Our Results in the Context of Previous Research

Our findings are comparable to those for other reviews of clinical practice guidelines (CPGs) that used the AGREE II tool, in that the overall quality of CPGs was deemed suboptimal [30, 67]. CPGs in clinical areas such as pain management and survivorship care planning, for instance, failed to score over 60% in any of the six domains [18, 68]. However, five (16%) of the 32 MHGs (WHO_HB, WHO_TB1, WHO_TB2, ECDC_TB1 and AUGOV_Antenatal) evaluated scored more than 60% in all domains. Our result regarding marginal improvements in quality over time also agreed with results reported for practice guidelines in other clinical areas [18, 27, 30, 69, 70].

The "rigour of development" domain is critical in HGs appraisal, as it reflects an assessment of the methods used to identify and synthesize evidence for MHG development, the formulation of recommendations and strategy updates [25, 29]. The low mean score (34%) for this domain obtained in our evaluation suggests a lack of methodological proficiency in MHG developing groups. It also points to the possibility of limited resources available for MHG development. In comparison, the mean score (43%) reported across a wide range of healthcare topics in a quality appraisal of practice guidelines, was mainly linked to flaws in reporting [69–71]. Domain scores seem to have improved marginally in recent years, as noted in other practice guidelines appraisal studies [18, 70].

The "applicability" domain addresses crucial features necessary for implementation such as potential

Table 2 Standardized domain scores for recommended MHGs (n = 15)

CPG ID	CPG title	Scope and purpose %	Stakeholder involvement %	Rigour of development %	Clarity of presentation %	Applicability %	Editorial independence %	Overall recommendation
ECDC_TB1 [49]*	Guidance on tuberculosis control in vulnerable and hard-to-reach populations. Stockholm: ECDC; 2016	100	93	98	89	60	78	Recommended
WHO_HB [58]*	Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection, 2015	100	91	92	93	86	94	Recommended
WHO_TB1 [59]*	Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries, 2015	96	87	70	85	71	94	Recommended
ECDC_TB2 [50]	Tuberculosis control in big cities and urban risk groups in the European Union, 2014	100	81	60	91	78	42	Recommended
EPA_Mental [51]	EPA Guidance mental health care of migrants, 2014	75	61	67	93	24	47	Recommended
AUGOV_Antenatal [54]*	National Evidence-Based Antenatal Care Guidelines — Module II, 2014	100	94	94	94	69	100	Recommended
WHO_TB2 [60]*	Systematic screening for active tuberculosis: principles and recommendations, 2013	100	91	100	100	94	94	Recommended
WHO_TB3 [52]	Minimum package for cross-border TB control and care in the WHO European region: a Wolfheze consensus statement, 2012	93	85	63	91	42	39	Recommended
CCIRH_Imm [64]	Evidence-based clinical guidelines for immigrants and refugees, 2011	91	93	77	100	46	83	Recommended
ASID_Health [55]	Recommendations for comprehensive post-arrival health assessment for people from refugee-like backgrounds, 2016	98	98	46	97	71	86	Recommended with modifications
HPSC_Inf [3]	Infectious Disease Assessment for Migrants, 2015	100	65	41	100	46	0	Recommended with modifications
CDCORR_Immun [35]	Guidelines for evaluating and updating immunizations during the domestic medical examination for newly arrived refugees, 2015	81	30	6	86	63	0	Recommended with modifications
HSE_Comm [63]	Guideline for Communication in Cross-Cultural General Practice Consultations, 2012	100	100	35	93	43	0	Recommended with modifications
IT_HepB/C [65]	Recommendations for the prevention, diagnosis, and treatment of chronic hepatitis B and C in special population groups (migrants, intravenous drug users and prison inmates), 2011	83	43	15	85	40	17	Recommended with modifications

Table 2 (continued)

CPG ID	CPG title	Scope and purpose %	Stakeholder involvement %	Rigour of development %	Clarity of presentation %	Applicability %	Editorial independence %	Overall recommendation
BIA_Eos [61]	Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management, 2010	98	56	22	93	40	0	Recommended with modifications

MHGs that scored over 60% in all six domains are indicated with an asterisk. MHGs deemed "Not recommended" are excluded

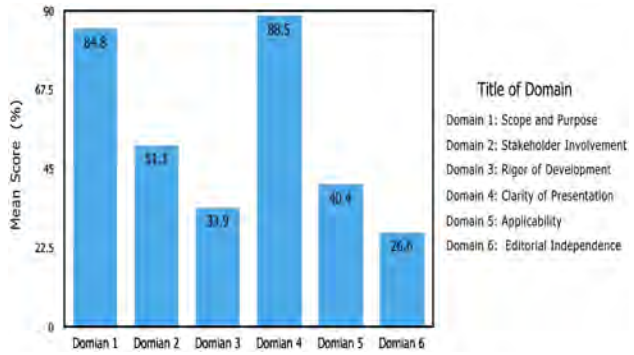

Fig. 3 Mean quality score for each domain of MHGs

Table 3 AGREE II quality assessment of MHGs over time

Domain	CPGs from 2006 to 2012 (n = 15)	CPGs from 2013 to 2016 (n = 17)	P-value
Scope and purpose	77.87 ± 24.34	90.9 ± 9.88	0.06
Stakeholder involvement	45.00 ± 27.02	56.76 ± 32.99	0.28
Rigor of development	23.20 ± 20.53	43.35 ± 37.56	0.07
Clarity of presentation	86.80 ± 8.31	90.06 ± 6.21	0.22
Applicability	29.60 ± 13.81	49.94 ± 26.55	0.01
Editorial independence	14.67 ± 29.30	37.18 ± 43.30	0.09
Overall quality	3.89 ± 1.36	4.76 ± 1.72	0.12

organizational, behavioural, and resource implications [29, 72]. Our study reports similar low-level compliance with the AGREE II criteria in the majority of the MHGs. Organizational barriers and facilitators, cost implications and monitoring and auditing criteria [27, 29, 68, 73] were not reported in most of the evaluated HGs, consistently with previous general evaluations [26, 27, 70]. It is plausible that the type of developer or particular areas of emphasis in the 32 selected MHGs may have contributed to the low quality scores [70].

The "editorial independence" domain in our 32 MHGs obtained the lowest mean domain score (27%); there was little or no evidence of descriptions of competing interests, of procedures implemented to account for this or of their impact on MHG development and reporting processes. In most MHGs (over 60%) published by national governments or agencies, editorial independence requirements were overlooked. Thus, our observation is in agreement with the significant underreporting, and poor compliance with editorial independence criteria reported for other HGs authored by national bodies or agencies [27, 70, 73–75]. Our findings were not at variance with the lack of clarity regarding potential conflicts of interest frequently reported for published HGs [74].

Limitations and Strengths

There is a possibility that we failed to identify some MHGs, as these are often not indexed. Nevertheless, we also searched for HGs in the grey literature. Moreover, it would be reasonable to assume that HGs not indexed in electronic databases nor available as grey literature, would probably be of lower quality than those included in our assessment. On that basis, our conclusions would be strengthened. Similarly there is no reason to expect that those published in languages other than English would be of higher quality.

The main strengths of our review are that we performed an exhaustive search, that we used three independent reviewers to perform the quality evaluations, that inter-rater agreement was good, and that we used a standardized, reliable instrument. Finally, our team included clinical experts and a methodologist with extensive experience with the AGREE II tool.

Implications for Practice and Research

Guideline users need to be mindful of the low rigour of most published MHGs. Improved rigour in evidence development processes requires sufficient resources to support migrant health recommendations [75]. MHGs developers need to adhere to systematic and established methods as published by guideline institutions (e.g. the National Institute for Health and Care Excellence (NICE) or the Scottish Intercollegiate Guidelines Network (SIGN)) [76, 77]. Also integral to the MHGs development process is the use of checklists for development and reporting, as advocated by the AGREE II tool and the GIN-McMaster checklist [75, 77, 78]. Furthermore, the new, widely implemented and rigorous Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach would likely help improving the quality MHGs, and specifically the communication between MHGs users and developers [79, 80].

To improve the applicability MHGs, developers would need to construct support tools that facilitate implementation, such as summary documents, links to checklists, algorithms and solutions linked to barrier analysis [29, 31]. Furthermore, vital features in the assessment of outcomes include adequate stakeholder involvement through consultation, identification of values and preferences of migrants, and review of MHGs by external experts before publication [26, 73, 75].

In general, MHGs should, moreover, be subjected to standard conflict of interest policies during development, in order to reduce the risk of associated bias and improve transparency. Any potential deficiency in this area may undermine guideline users' trust, due to possible perceptions of covert or overt influences arising as the result of conflicts of interest originating in institutional, financial, academic or educational affiliations.

Regarding research development, more effort geared towards developing and consolidating networks for researchers would facilitate evaluation and synthesis of all available evidence for MHG development. We suggest that there needs to be more collaborative efforts by supranational bodies, national agencies and professional societies in developing practice guidelines for migrant healthcare, and establishing and implementing optimal conflict of interest policies, all of which would require more resources to be made available.

Conclusions

Our review of MHGs published in the last decade has highlighted critical deficiencies in quality standards—in domains as crucial as rigour of development, applicability, editorial independence and stakeholder involvement—that point to the need for improvements in those areas in future MHGs.

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Author Contributions EA and PAC contributed to the conceptualization, design and conduct of the study. EA, IS and PF contributed to the search strategy design, searching and screening. EA and IA performed data extraction with input from PF. EA, IA and LH evaluated the MHGs using the AGREE II tool. EA performed data analysis with input from PF and PAC. EA, IS, PF and PAC interpreted the data. EA wrote the initial draft of the manuscript, which was then added to and edited in subsequent iterations with PAC, PF, KP. All authors reviewed and approved the final manuscript.

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Data Availability The data that support the findings of this study are available from the figshare https://figshare.com/s/349171b21d21be08b985.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no competing interests.

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Supplement A1: Lists of sites and search strategy.
The used search strategies for the identification of CPGs are listed in this supplement.

1. **Generic databases or search engines:**

A. PubMed : (http://www.ncbi.nlm.nih.gov/pubmed)
(((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline")) OR (((((migrant*) OR refugee*) OR immigrant*)) AND "recommendation")) OR (((((migrant*) OR refugee*) OR immigrant*)) AND "consensus") AND ("last 10 years"[PDat] AND Humans[Mesh])

#	Query	Result
#14	Search (((((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") OR "practice guideline"[Publication Type])))) AND "consensus") AND "recommendation" Filters: Guideline; Practice Guideline; published in the last 10 years; Humans	239
#13	Search (((((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") OR "practice guideline"[Publication Type])))) AND "consensus") AND "recommendation" Filters: Guideline; Practice Guideline; Humans	312
#12	Search (((((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") OR "practice guideline"[Publication Type])))) AND "consensus") AND "recommendation" Filters: Guideline; Practice Guideline	320
#11	Search (((((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") OR "practice guideline"[Publication Type])))) AND "consensus") AND "recommendation" Filters: Guideline	320
#10	Search (((((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") OR "practice guideline"[Publication Type])))) AND "consensus") AND "recommendation"	320
#9	Search ((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") OR "practice guideline"[Publication Type])	21444
#8	Search ((((migrant*) OR refugee*) OR immigrant*)) AND "consensus"	190
#7	Search ((((migrant*) OR refugee*) OR immigrant*)) AND "recommendation"	136
#6	Search (((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline") AND "practice guideline"[Publication Type]	20
#5	Search "practice guideline"[Publication Type]	21440
#4	Search "consensus"	131039
#3	Search "recommendation"	28250
#2	Search "practice guideline"	24158
#1	Search ((migrant*) OR refugee*) OR immigrant*	44645

B. CINAHL Database – (EBSCOhost Research Databases).

(((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline")) OR (((((migrant*) OR refugee*) OR immigrant*)) AND "recommendation")) OR (((((migrant*) OR refugee*) OR immigrant*)) AND "consensus") AND ("last 10 years"[PDat] AND Humans[Mesh])

#	Query	Results
S17	S14 OR S15 - Limiters - Published Date: 20010101-20161231	425
S16	S14 OR S15	468
S15	S4 AND S8	405
S14	S11 OR S12 OR S13	73
S13	S3 AND S7	50
S12	S2 AND S7	26
S11	S1 AND S7	12

S10	S8 OR S9	46,936
S9	consensus statement*	1,273
S8	recommendation*	45,958
S7	S5 OR S6	42,564
S6	practice guideline*	42,564
S5	"practice guideline"	1,397
S4	S1 OR S2 OR S3	15,630
S3	immigrant*	10,026
S2	refugee*	3,956
S1	migrant*	3,263

C. EMBASE Database - (EBSCOhost Research Databases)

((migrant* or refugee* or immigrant*) and ('practice guidelines' or 'recommendations' or 'consensus')) and 'practice guideline'/de and (2006:py or 2007:py or 2008:py or 2009:py or 2010:py or 2011:py or 2012:py or 2013:py or 2014:py or 2015:py or 2016:py)

#	Query	Result
#11	#10 AND ('human'/de OR 'practice guideline'/de) AND (2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py)	789
#10	#4 AND #9	1,261
#9	#6 OR #7 OR #8	370,224
#8	'consensus'	165,310
#7	'recommendations'	205,177
#6	'practice guidelines'	20,852
#5	'practice guidelines as topic'	120
#4	#1 OR #2 OR #3	46,967
#3	immigrant*	25,254
#2	Refugee*	10,665
#1	Migrant*	11, 048

D. PsycARTICLES;PsycINFO – Database

(((((((migrant*) OR refugee*) OR immigrant*)) AND "practice guideline")) OR (((((migrant*) OR refugee*) OR immigrant*)) AND "recommendation")) OR (((((migrant*) OR refugee*) OR immigrant*)) AND "consensus") AND ("last 10 years"[PDat] AND Humans[Mesh])

#	Query	Results
S7	(practice guidelines OR recommendations OR consensus) AND (S2 AND S5)	1,211
S6	(practice guidelines OR recommendations OR consensus) AND (S2 AND S5)	1,226
S5	practice guidelines OR recommendations OR consensus	104,742
S4	practice guidelines OR recommendations	83,389
S3	practice guidelines	5,934
S2	migrant* OR refugee* OR immigrant*	32,408
S1	Migrant*	7,264

E. Turning Research into Practice (TRIP) (http://www.tripdatabase.com)

No.	Query	Source	Result
#1	Migrant* OR Refugee* OR Immigrant*AND Practice guideline*OR Recommendation* OR Consensus*	All sources	2,417

#2	"practice guidelines and migrant*" by quality	All sources	239
#3	"practice guidelines and migrant*" By Evidence type	Guidelines	178

Keyword: Migrant* OR Refugee* OR Immigrant*

2. Compiler Entities, Registries or Clearinghouses

a) National Guideline Clearinghouse (http://www.guideline.gov).
   i. Keywords: "migrant" or "immigrant" or "refugee"

b) Guideline International Networks (GIN): (http://www.g-i-n.net/library/international-guidelines-library).
   a. Keywords: "migrant" or "immigrant" or "refugee"

c) Agency for Healthcare Research and Quality (AHRQ) (http://www.ahrq.gov/).
   a. Keywords: "migrant" or "immigrant" or "refugee"

d) Canadian Medical Association: InfoBase: Clinical Practice Guidelines. (www.cma.ca/)
   a. Keywords: "migrant" or "immigrant" or "refugee"

e) Global health Library and Information Networks for Knowledge –– Global Index Medicus – Medline http://search.bvsalud.org/ghl/?lang=en&submit=Search&where=MEDLINE.

   a. (tw:((tw:("migrant")) OR (tw:("refugee")) OR (tw:("immigrant")))) AND (tw:((tw:("practice guideline")) OR (tw:("recommendation"))))

3. Guidelines developers:

Keywords: "Migrant" or "Immigrant" or "Refugee"

a) Institute for Clinical Systems Improvement (ICSI) (https://www.icsi.org).
b) National Health and Medical Research Council (NHMRC) Guidelines Group (http://www.nhmrc.gov.au/).
c) Health Information and quality assurance Ireland – (https://www.hiqa.ie/standards).
d) National Clinical Guideline Centre (NCGC) (http://www.ncgc.ac.uk).
e) National Institute for Health and Care Excellence (NICE) (https://www.nice.org.uk/guidance)
f) New Zealand Guidelines Group (http://www.health.govt.nz/).
g) Partnership for Health Equity- Ireland. (http://www.healthequity.ie).
h) World Health Organization (WHO)(http://www.who.int/hac/techguidance/health_of_migrants).
i) Canadian Medical Association Journal (CMAJ) (http://www.cmaj.ca/site/misc/service/guidelines.xhtml).
j) Department of Health - Common Wealth of Australia – (http://www.health.gov.au/Internet/main/publishing.nsf/content/health-publicat.htm).
k) The Royal Australian College of General Practitioners (RACGP) – (http://www.racgp.org.au/your-practice/guidelines/national-guide).

4. Project based websites

Keywords: "Migrant" or "Immigrant" or "Refugee

a) Centre for Disease and control - (http://www.cdc.gov).
b) European Union agency for fundamental human right - (http://fra.europa.eu/en/search/node/Migrant%20health).
c) EU-Level Consultations on Migration Health – (http://www.migrant-health-europe.org.)
d) European Centre for Disease and Control – (http://ecdc.europa.eu/en/publications/guidance/Pages/index.aspx).
e) Equity Health – Europe - (http://equi-health.eea.iom.int/index.php/migrant-health/background-mh).
f) International Organization for Migration – (http://iom.by/en/activities/migration-health).
g) Migrant Health Subgroup of the Campbell and Cochrane Equity Methods Group - (http://methods.cochrane.org/equity/migrant-health.)

5.5.2. Second publication

- Agbata EA, Buitrago-Garcia D, Nunez-Gonzalez S, Hashmi SS, Pottie K, Alonso-Coello P, Arevalo-Rodriguez I. Quality Assessment of Systematic Reviews on International Migrant Healthcare Interventions: A Systematic Review. Journal of Public Health (Springer Nature). (Accepted – 2020 September 21) D.O. I: 10.1007/s10389-020-01390-0.

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REVIEW ARTICLE

Quality assessment of systematic reviews on international migrant healthcare interventions: a systematic review

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Abstract

Aim The significant increase in international cross-border migrations remains a global public health concern; therefore, the need for migrant-specific evidence-based interventions is critical. We assessed the methodological and reporting quality of systematic reviews (SRs) focused on migrant healthcare interventions.

Methods We systematically searched in five electronic databases from 2007 to April 2020 to identify SRs on migrant health. Two independent reviewers assessed risk of bias, methodological and reporting quality in included systematic reviews (SRs) using ROBIS, AMSTAR-2 and PRISMA checklist, respectively.

Results We included 57 systematic reviews. The quality in 30 SRs (52.6%) was either low or critically low due to limitations in AMSTAR-2 items 4, 7, 8 and 10–16. The overall risk of bias was high in 23 SRs (40.4%), particularly in domains—data collection and study quality—20 SRs (35.1%), synthesis and findings—19 SRs (33.3%), and study identification and selection 13 SRs (22.8%). The quality of reporting in 36 SRs (63.2%) was moderate, with 19.74 ± 4.67 items fulfilled. While 19 SRs (33.3%) had 10–18 PRISMA items satisfied. Sixteen SRs (28.1%) reported a research protocol and registration.

Conclusions The overall quality of migrant SRs is suboptimal, with critical gaps linked to low protocol registrations, assessment of risk of bias and publication bias, additional analysis of synthesized evidence and available funding. These findings reflect current deficiencies in the development of SR on migrant healthcare.

Keywords Migrant healthcare · Quality assessment, AMSTAR-2 tool · ROBIS · PRISMA checklist · Systematic reviews

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Introduction

Migrant populations represent a diverse group frequently comprising irregular and undocumented migrants, including economic migrants, refugees, asylum seekers and unaccompanied minors (Zimmerman et al. 2011). As a consequence of their displacements and adaptation, some migrant populations have a higher burden of diseases, in addition to severe physical, emotional and psychological stress (Antoniades et al. 2014; Penelope 2014). However, lower morbidity, especially in newly arrived economic migrants, have been reported (Pavli and Maltezou 2017). Compared to the local populations, migrants often lack access to local healthcare services due to formal and informal barriers (Kontunen et al. 2014). These include the lack of legal protection, access to the entire health system, knowledge of the health system or social networks; as well as language and communication issues (Penelope 2014; Suphanchaimat et al. 2015; Zimmerman et al. 2011). Furthermore, it has been reported that their experiences of marginalization and discrimination result in poorer health outcomes (Antoniades et al. 2014; Penelope 2014; Suphanchaimat et al. 2015; Syed and Mobayed 2017).

In recent years, migrant healthcare has become a major global public health problem, due to the significant increase in cross-border migrations in multiple regions of the world that requires national and global collaboration (Kontunen et al. 2014; Syed and Mobayed 2017). Several healthcare guidelines or policy documents developed by global and national organizations offer pathways to an accessible and acceptable quality of health care provision for migrants (Agbata et al. 2019b). Given the complexity of determinants affecting migrants' health in their destination countries, there is an increased interest in migrant population health-related topics, with studies accumulating on different health interventions or services delivery (Agudelo-Suárez et al. 2012; Bradby et al. 2015; Kontunen et al. 2014; Suphanchaimat et al. 2015; Wickramage et al. 2018).

Systematic reviews (SRs) are considered the most reliable method to synthesize evidence used in decision-making scenarios for addressing specific health questions and improving healthcare services and outcomes (Antoniades et al. 2014; Nellums et al. 2018; Peters et al. 2015). Quality in SRs describe the range of measures employed to "protect all aspects of research design and implementation from all source of bias as a result of systematic error, unsystematic error, and inferential error" (Pieper et al. 2019; Seo and Kim 2012). For optimal development of SRs, researchers must follow best practices in the synthesis of evidence to reduce potentially inherent biases (Liberati et al. 2009; Moher et al. 2009). In contrast, poorly conducted SRs can introduce bias due to inadequate methodological rigour, missing data, weak or inconsistent reporting, or where quality assessment tools not used in the inclusion or exclusion of methodologically deficient SRs diminish their utility in healthcare decisions (Liberati et al. 2009; Tacconelli 2010).

Since 2000, there has been a significant increase in number of systematic reviews published in different health areas (Duncan et al. 2017; Graetz et al. 2017; Winters et al. 2018). In addition, an increased number of evaluations of reporting and methodological quality of SRs are now available following the development and validation of assessment tools (Agbata et al. 2019b; Banzi et al. 2018; Bühn et al. 2017; Duncan et al. 2017; Pollock et al. 2017; Pussegoda et al. 2017; Tian et al. 2017). While methodological quality assesses the accuracy in the design and conduct of systematic reviews, including the assessment of the risk of bias (Pollock et al. 2017; Shea et al. 2017; Smith et al. 2011; Viswanathan et al. 2012; Whiting et al. 2016), the reporting quality evaluates the transparent depiction of the methodology and findings by authors of SRs (Liberati et al. 2009; Page and Moher 2017; Pussegoda et al. 2017).

To our knowledge, the quality assessment of systematic reviews in the area of migrant health is lacking, coupled with the existing evidence of suboptimal quality in migrant healthcare guidelines and recommendations (Agbata et al. 2019b). Because of the link between the quality of migrant health guidelines and the systematic evidence base for its development, differences in risk of bias (RoB), methodological and reporting quality in individual SRs in migrant health may be responsible for the observed overall suboptimal quality in migrant healthcare guidelines and recommendations. Therefore, we conducted a systematic assessment to assess their risk of bias, methodological and reporting quality in systematic reviews focused on migrant healthcare interventions.

Methods

We performed a systematic review focused on migrant health care. The study protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO) database (CRD42018104454).

Search strategy and selection criteria

We searched for SRs in electronic databases—Medline-Ovid, EMBASE, COCHRANE LIBRARY, CINAHL, and LILACS. We restricted the search to reviews published between January 2007 and November 2017, published in English, as in our published systematic quality assessment of migrant healthcare guidelines. In addition, we reviewed SRs published in the World Health Organization (WHO) website—http://www.who.int/migrants/publications/en/. We used a combination of key MESH terms such as—"Refugees" or "refugee*" or "Emigrants and Immigrants" OR "asylum seeker" OR "asylum seeker*" OR

"Immigration "OR "Immigrant"; 'health service' OR 'health services' OR 'health care delivery' OR 'health care accessibility'; and 'quality' OR 'health care quality.' All sources of evidence, together with the electronic search strategies, can be accessed in Appendix 1.

Based on the eligibility criteria Participants–Intervention–Comparison–Outcome–Study (PICOS), criteria for the study were as follows: We included SRs about cross-country adult migrants or refugees as population but excluded aborigine or local minority population. We will include systematic reviews on health interventions (pharmacological and non-pharmacological, prevention or treatment), either compared with another or no intervention in humans.

We will extract the primary outcome specified in the included SRs. If no primary outcome was assessed, then the most important health outcome will be selected, e.g. health service coverage, access, uptake, utilization as well as screening outcomes and quality of life. We excluded articles that were not an SR, not specific to the population of interest or focused on health intervention and where the full-text is unavailable. All citations and accompanying abstracts retrieved from the electronic searches were downloaded to an online referencing manager – Endnote X9 ®.

Additional systematic searches

Due to time lapses in the evidence obtained from the initial search, we conducted an updated systematic search of five databases (Medline-Ovid, EMBASE ELSEVIER, COCHANE LIBRARY, CINAHL and Latin American Literature in Health Sciences - LILACS). SRs focused on healthcare interventions, including both prevention and treatment (December 201– April 2020). References of included SRs were searched to identify other relevant studies, as well as grey literature for relevant studies. We did not apply language restrictions, and where we identified more than one version of a systematic review, we included the most recent.

Selection process

Two reviewers independently screened the titles and abstracts, followed by full-text assessments for eligibility of studies. Disagreements were resolved by consensus or the involvement of a third author. We used the PRISMA flowchart to illustrate the steps taken in the selection process (Moher et al. 2009). The list of excluded studies with reasons for exclusion are included in Appendix 2.

Data extraction

Two reviewers performed data abstraction independently from included SRs using a pre-defined and pilot-tested data extraction form. We have a detailed list of items extracted from the reviews in Appendix 3.

Assessment of risk of bias using ROBIS tool

Two reviewers independently evaluated the risk of bias and methodological quality of the selected systematic reviews using the Risk of Bias of Systematic Reviews tool – ROBIS (Whiting et al. 2016). Each domain was assessed to determine if the study fulfilled the domain's specific criterion by answering 'yes', 'probably yes', 'probably no', 'no', or 'no information'. Judgement on the overall rating of 'low risk of bias', 'high risk of bias', or 'unclear risk of bias' was assigned after considering the extent to which each criterion in each domain were fulfilled or there was not enough evidence to support the ROBIS domain. Any disagreements were resolved by a consensus decision or via third reviewer (Viswanathan et al. 2012; Whiting et al. 2016).

Assessment of methodological quality using AMSTAR-2

Two reviewers independently assessed the quality of systematic reviews using Assessing Methodological Quality of Systematic Reviews - 2 tool (AMSTAR-2) (Shea et al. 2017; Tian et al. 2017). Each question in the AMSTAR tool were answered as either "yes", "partial yes", "no", "cannot answer", or "unable to assess" (Shea et al. 2017). Overall confidence in the quality rating in the SRs were classified as high, moderate, low, or critically low depending on the presence of critical and non-critical flaws in items 2, 4, 7, 9, 11, 13 and 15 (Shea et al. 2017). We resolved any disagreements via a consensus decision by a third reviewer.

Assessment of reporting quality using PRISMA checklist

Two independent reviewers evaluated the reporting quality of the systematic reviews using the PRISMA checklist (Moher et al. 2009). The response options for the 27 checklist items were answered with 'yes', 'partly', 'no', 'unclear', or 'not applicable' (Kelly et al. 2016; Liberati et al. 2009; Shamseer et al. 2015). The total number of items answered 'yes' was calculated as the overall score out of a possible count of 27 (Moher et al. 2009; Shamseer et al. 2015). PRISMA items reported were grouped into three categories: 1–9, 10–18 and 20–27 items reported for the descriptive analysis. We resolved any disagreements via a consensus decision by a third reviewer.

Data analysis

Two reviewers independently collated and verified data extracted. We summarized the extracted data from the included

SRs as frequencies and percentages for the reported characteristics. We reported important outcomes in the included SRs in the following categories – access and uptake of health services and maternal health; screening programmes – prevalence/incidence rates, health care delivery, barriers and facilitators, mental health related and health needs or behaviour. We compiled the results of the completed assessment for each SR using AMSTAR, ROBIS and PRISMA tools concerning adequately satisfied items. We reported the mean numbers of items completed appropriately across all included SRs (overall and by domain); we then stratified them by year of publication and type of intervention for exploratory analysis. (Kelly et al. 2016; Pollock et al. 2017; Shamseer et al. 2015). The overall agreement between reviewers was assessed between ROBIS and AMSTAR-2 using intra-class coefficient (ICC) at 95% confidence interval (CI) as an indicator (Landis and Koch 1977). Data was analysed using the statistical package SPSS version 25.0.

Results

A total of 1614 citations, reduced to 1456 citations—after duplicates were removed—that were title-and-abstract screened. Of 71 full-text documents selected for review, 32 were excluded, leaving 39 eligible SRs (Fig. 1).

The updated systematic literature search for migrant health systematic reviews yielded after de-duplication 555 citations for the screening of titles and abstracts. Of the 72 articles selected for full-text screening, we included 18 SRs. Overall, we included 57 systematic reviews (Fig. 2).

The details of the included migrant SRs and a descriptive summary of the included studies are presented in Tables 1 and 2. In terms of the source of SRs, more than half of the SRs were published in high-income countries, specifically Australia, Canada, the United States of America (USA), Germany, and the United Kingdom (UK) (Agbata et al. 2019a; Al Abed et al. 2014; Anderson de Cuevas et al. 2018; Bellamy et al. 2015; Bhargava et al. 2018; Chen et al. 2019; Conners et al. 2016; Driedger et al. 2018; Gieles et al. 2019; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hadgkiss and Renzaho 2014; Hargreaves et al. 2019; Higginbottom et al. 2015; Hui et al. 2018; Joo 2014; Klein and von dem Knesebeck 2018; Mosdol et al. 2017; Myran et al. 2018; Pottie et al. 2018; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Slewa-Younan et al. 2015; Vedio et al. 2017; Winters et al. 2018), and European states (Agbata et al. 2019a; Almeida et al. 2013; Balaam et al. 2013; Carmona et al. 2014; Chernet et al. 2017; de Jong et al. 2017; de Vries et al. 2017; Driedger et al. 2018; Fair et al. 2020; Gieles et al. 2019; Graetz et al. 2017; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hui et al. 2018; Klein and von dem Knesebeck 2018; Myran et al. 2018; Norredam et al. 2010; Pottie et al. 2018; Requena-Mendez et al. 2015; Satinsky et al. 2019; Spallek et al. 2015; Tavares et al. 2017; Winters et al. 2018). In contrast, only three SRs were from low–middle income countries (LMICs) (Bogic et al. 2015; Hendrickx et al. 2019; Warren et al. 2015).

Fifty-one (89.5%) of the SRs were published between 2014 and April 2020. Thirty-one SRs included quantitative studies only (54.4%) (Agbata et al. 2019a; Aldridge et al. 2014; Almeida et al. 2013; Anderson de Cuevas et al. 2018; Bhargava et al. 2018; Carmona et al. 2014; Chernet et al. 2017; Conners et al. 2016; Ehiri et al. 2014; Falah-Hassani et al. 2015; Greenaway et al. 2015; Joo 2014; Lindert et al. 2009; Mosdol et al. 2017; Norredam et al. 2010; Nosè et al. 2017; Requena-Mendez et al. 2015; Slewa-Younan et al. 2015; Spallek et al. 2015; Tavares et al. 2017; Uiters et al. 2009), 18 SRs included mixed methods studies (31.6%) (Al Abed et al. 2014; Bogic et al. 2015; de Jong et al. 2017; Driedger et al. 2018; Fair et al. 2020; Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Hadgkiss and Renzaho 2014; Higginbottom et al. 2015; Horyniak et al. 2016; Myran et al. 2018; Olaussen et al. 2016; Pottie et al. 2018; Santiago Mda and Figueiredo 2015; Suphanchaimat et al. 2015); and eight SRs were focused on qualitative studies (Balaam et al. 2013; Bellamy et al. 2015; Chen et al. 2019; de Vries et al. 2017; Joshi et al. 2013; Nilaweera et al. 2014; Robertshaw et al. 2017; Small et al. 2014). Migrant populations in included SRs were: all migrants – 23 SRs (Agbata et al. 2019a; Aldridge et al. 2014; Bhargava et al. 2018; Carmona et al. 2014; Conners et al. 2016; Driedger et al. 2018; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hargreaves et al. 2019; Hui et al. 2018; Klein and von dem Knesebeck 2018; Myran et al. 2018; Norredam et al. 2010; Olaussen et al. 2016; Pottie et al. 2018; Spallek et al. 2015; Suphanchaimat et al. 2015; Tavares et al. 2017; Uiters et al. 2009); women migrants only - 12 SRs (Almeida et al. 2013; Anderson de Cuevas et al. 2018; Balaam et al. 2013; Chen et al. 2019; Fair et al. 2020; Falah-Hassani et al. 2015; Gagnon and Redden 2016; Higginbottom et al. 2015; Nilaweera et al. 2014; Santiago Mda and Figueiredo 2015; Small et al. 2014; Warren et al. 2015), refugees and asylum seekers or IDPs – 12 SRs (Bellamy et al. 2015; Bogic et al. 2015; Hadgkiss and Renzaho 2014; Hendrickx et al. 2019; Joshi et al. 2013; Nosè et al. 2017; Robertshaw et al. 2017; Slewa-Younan et al. 2015); ethnic migrants (Arab, Asians, Chinese or Latin American) – five SRs (Al Abed et al. 2014; Joo 2014; Mosdol et al. 2017; Requena-Mendez et al. 2015; Vedio et al. 2017); migrant and refugee populations – three SRs (Chernet et al. 2017; Greenaway et al. 2015; Joshi et al. 2013); and three SRs on undocumented migrants (de Jong et al. 2017; Gieles et al. 2019; Winters et al. 2018). Consequently, the scope of included SRs were focused mostly on studies of access and uptake of health services (Bellamy

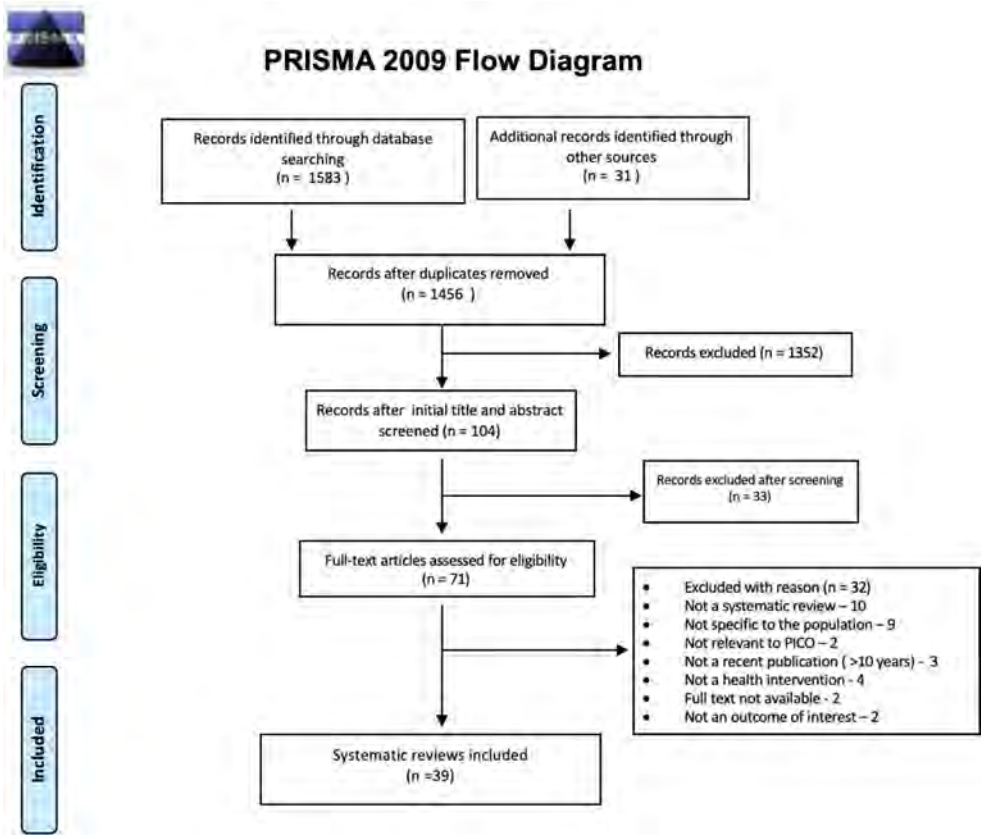

Fig. 1 PRISMA flow diagram of Systematic reviews selection on migrant health care interventions — 2007 – December 2017

et al. 2015; Carmona et al. 2014; de Vries et al. 2017; Driedger et al. 2018; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Hadgkiss and Renzaho 2014; Hui et al. 2018; Joshi et al. 2013; Norredam et al. 2010; Robertshaw et al. 2017; Suphanchaimat et al. 2015; Uiters et al. 2009; Winters et al. 2018), infectious disease screenings (Aldridge et al. 2014; Chen et al. 2019; Chernet et al. 2017; Conners et al. 2016; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Greenaway et al. 2015; Lindert et al. 2009; Myran et al. 2018; Nilaweera et al. 2014; Pottie et al. 2018; Requena-Mendez et al. 2015), maternal health services (Almeida et al. 2013; Balaam et al. 2013; de Jong et al. 2017; Fair et al. 2020; Gieles et al. 2019; Higginbottom et al. 2015; Klein and von dem Knesebeck 2018; Small et al. 2014; Warren et al. 2015) and mental health related (Bogic et al. 2015; Falah-Hassani et al. 2015; Hendrickx et al. 2019; Horyniak et al. 2016; Nosè et al. 2017; Santiago Mda and Figueiredo 2015; Satinsky et al. 2019; Slewa-Younan et al. 2015; Spallek et al. 2015), health needs/promotion (Al Abed et al. 2014; Gagnon and Redden 2016; Joo 2014; Mosdol et al. 2017; Olaussen et al. 2016), occupational health (Hargreaves et al. 2019) and training (Ehiri et al. 2014).

In terms of funding, 20 SRs (35.1%) did not explicitly report their funding source (Al Abed et al. 2014; Almeida et al. 2013; Bellamy et al. 2015; Bradby et al. 2015; Carmona et al. 2014; Chernet et al. 2017; Ehiri et al. 2014; Fair et al. 2020; Falah-Hassani et al. 2015; Graetz et al. 2017; Greenaway et al. 2015; Hendrickx et al. 2019; Joo 2014; Klein and von dem Knesebeck 2018; Mosdol et al. 2017; Nilaweera et al. 2014; Norredam et al. 2010; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Satinsky et al. 2019; Spallek et al. 2015); whereas 14 SRs (24.6%) were funded by governmental organizations (Agbata et al. 2019a; Driedger et al. 2018; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hui et al. 2018; Joshi et al. 2013; Olaussen et al. 2016; Pottie et al. 2018; Requena-Mendez et al. 2015; Suphanchaimat et al. 2015; Tavares et al. 2017; Uiters et al. 2009), a research body (Anderson de Cuevas et al. 2018; Chen et al. 2019; Conners et al. 2016; Gil-Gonzalez et al. 2015; Hargreaves et al. 2019; Higginbottom et al. 2015; Nosè et al. 2017; Slewa-Younan et al. 2015; Small et al. 2014; Winters et al. 2018), or both (Aldridge et al. 2014; Balaam et al. 2013; Bhargava et al. 2018; Gieles et al. 2019; Horyniak et al. 2016; Lindert et al. 2009; Vedio et al. 2017; Warren et al. 2015).

In 15 SRs (26.3%), there was no risk of bias assessment performed (Al Abed et al. 2014; Almeida et al. 2013; Anderson de Cuevas et al. 2018; Conners et al. 2016; Ehiri et al. 2014; Klein and von dem Knesebeck 2018; Lindert et al. 2009; Mosdol et al. 2017; Norredam et al. 2010; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Small et al. 2014; Spallek et al. 2015; Tavares et al. 2017; Uiters et al.

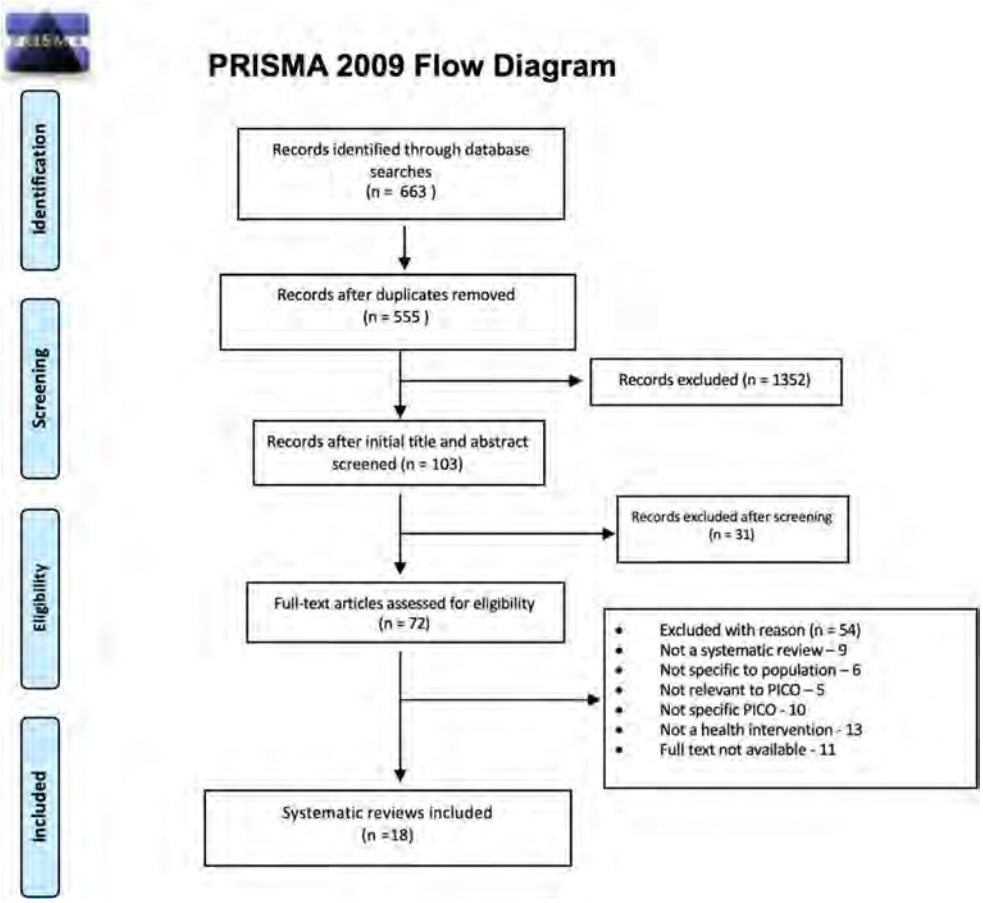

Fig. 2 PRISMA flow diagram of Systematic reviews selection on migrant health care interventions — December 2017 – April 2020

2009), while the primary studies included employed a variety of quality assessment tools in their synthesis of evidence. The two main quality assessment tools used in the selected SRs were Critical Appraisal Skills Program (CASP) checklist for risk of bias (Anderson de Cuevas et al. 2018; Bellamy et al. 2015; de Jong et al. 2017; Gil-Gonzalez et al. 2015; Horyniak et al. 2016; Satinsky et al. 2019; Winters et al. 2018), and the GRADE approach for assessment of the quality of evidence (Agbata et al. 2019a; Aldridge et al. 2014; Chernet et al. 2017; Driedger et al. 2018; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Greenaway et al. 2015; Hui et al. 2018; Myran et al. 2018; Nosè et al. 2017; Pottie et al. 2018). Other assessment tools used in the included SRs were also identified.

PRISMA evaluation

The mean number of items reported was 19.74 ± 4.67 (Table 3). Only two SRs had all 27 PRISMA items reported (Mosdol et al. 2017; Nosè et al. 2017). Thirty-six SRs (63.2%) had 19–27 items reported (Agbata et al. 2019a; Carmona et al. 2014; Chernet et al. 2017; de Vries et al. 2017; Driedger et al. 2018; Ehiri et al. 2014; Gieles et al. 2019; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hargreaves et al. 2019; Higginbottom et al. 2015; Horyniak et al. 2016; Joo 2014; Joshi et al. 2013; Klein and von dem Knesebeck 2018; Myran et al. 2018; Nosè et al. 2017; Olaussen et al. 2016; Pottie et al. 2018; Requena-Mendez et al. 2015; Robertshaw et al. 2017; Satinsky et al. 2019; Small et al. 2014; Suphanchaimat et al. 2015; Uiters et al. 2009; Vedio et al. 2017; Warren et al. 2015; Winters et al. 2018); 19 SRs had 10–18 items reported (Aldridge et al. 2014; Anderson de Cuevas et al. 2018; Balaam et al. 2013; Bellamy et al. 2015; Bhargava et al. 2018; Chen et al. 2019; Conners et al. 2016; de Jong et al. 2017; Fair et al. 2020; Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Hadgkiss and Renzaho 2014; Klein and von dem Knesebeck 2018; Lindert et al. 2009; Nilaweera et al. 2014; Santiago Mda and Figueiredo 2015; Slewa-Younan et al. 2015; Spallek et al. 2015; Tavares et al. 2017), whereas two SRs had 1–9 items reported (Al Abed et al. 2014; Almeida et al. 2013), respectively. The following eight PRISMA items—rationale and objective, study characteristics, title (reported as SRs), information sources and eligibility criteria, study selection criteria, discussion and conclusion—were reported in all the selected SRs, while PRISMA items 15, 'Risk bias in individual studies' was reported in 24 included SRs (42.1%). Furthermore, 12 SRs (21.1%) did not report a structured summary or

Table 1 Characteristics of included systematic reviews

Author/year of publication	Population	Intervention	Outcome	Source of funding	No. of included studies	Type of studies included	Quality assessment tools used	Country/region
Agbata et al. 2019a	Migrants/refugees	Screening and treatment	Public health screening/-treatment	European Centre for Disease Prevention and Control	28	Quantitative SR, RCTs, primary studies – cross-sectional, retrospective	AMSTAR, Newcastle–Ottawa Scale and QUADAS-II tools/ GRADE	HIC - Global
Al Abed et al. 2014	Older Arab migrants	Healthcare needs	Health care needs - Culturally competent aged care services for older people	None	16	Mixed – survey, literature review, census data analysis, interviews	Not assessed	HIC – Australia
Aldridge et al. 2014	All migrants	TB pre-entry screening	TB detection rates	Welcome Trust, UK National Institute for Health Research, Medical Research Council, Public Health England."	15	Quantitative – observational studies	GRADE	Global – HIC &LMIC
Almeida et al. 2013	Migrant women – pregnant	Maternal care	Maternal care and risks	None	30	Quantitative – retrospective cross-sectional, prospective cohort, observational study, survey, population-based register, Longitudinal	Not assessed	HIC (Europe) - Portugal
Anderson de Cuevas et al. 2018	South Asian women (migrants)	Asymptomatic breast or cervical screening	Uptake of screening; barriers and enablers	Part funded - National Institute for Health Research Collaboration for Leadership	51	Mixed	Critical Appraisal Skills Programme	HIC
Balaam et al. 2013	Migrant women	Pregnancy and childbirth.	Experience of maternal care	EU, COST Action No. IS0907, and Vestfold University College, Norway	29	Qualitative – semi-structured tape--recorded interviews, focus groups, field notes	Eight essential criteria - Walsh and Downe's (2006)	HIC (Europe)
Bellamy et al. 2015	Resettled refugees	Access to medication and pharmacy services	Access and uptake of pharmacy services	None	16	Qualitative	modified CASP (Critical Appraisal Skills Program & JBI	HICs - Australia, UK, USA.
Bhargava et al. 2018	Immigrant women	Mammographic screening	Uptake of screening	Norwegian Breast Cancer Society	33	Quantitative	Not assessed	HIC
Bogic et al. 2015	War refugees	Long-term mental health	Prevalence	Partly funded - Queen Mary University of London	9	Mixed - descriptive, cross-sectional; focus groups, semi-structured interviews, and cohort	Adapted	HICs (Global)
Carmona et al. 2014	Immigrants	Use of health services	Access and uptake rates	None	44	Quantitative – surveys, comparative studies	STROBE initiative	HIC (EU)

Table 1 (continued)

Author/year of publication	Population	Intervention	Outcome	Source of funding	No. of included studies	Type of studies included	Quality assessment tools used	Country/region
Chen et al. 2019	Chinese immigrant women	Maternal mental health	Postpartum depression		4	Quantitative		HIC
Chernet et al. 2017	African migrants and refugees	Screening of six infectious diseases	Prevalence rates	None	96	Quantitative studies	GRADE	HIC (EU)
Conners et al. 2016	Migrants	Chagas disease screening	Prevalence rates	Centre for AIDS Research (CFAR), an NIH-funded program (P30 AI036214)	23	Quantitative	None	HICs
de Jong et al. 2017	Undocumented migrants	Use of maternal and child healthcare services	Outcomes of maternal and child healthcare services	Part support - Maastricht University travel grant to the lead author.	33	Mixed – quantitative and qualitative studies	CASP, National Heart LaBi - Quality assessment tool	HIC (EU)
de Vries et al. 2017	Hard to reach population (includes migrants and refugees).	What factors help or hinder the uptake of tuberculosis diagnostic and treatment services	Barriers and facilitators	National Institute for Health and Care Excellence (NICE)	37	Qualitative studies	NICE Quality Assessment Tools for qualitative research	HIC (EU)
Driedger et al. 2018	Migrants/refugees	Infectious disease interventions	Accessibility and acceptability	European Centre for Disease Prevention and Control	11	Mixed	GARDE, GRADE CERQual tool	HIC
Ehiri et al. 2014	Lay refugees/ internally displaced persons (IDPs).	Basic health training & deployment	Provision of Basic Health service	None	10	Quantitative – cohort and cross sectional – five cross-sectional, four pre-post, and one post-test only	None	LMIC (Guinea, Belize, Myanmar, Thailand border)
Fair et al. 2020	Migrant women	Maternal health care	Access/ uptake/ experience	None	59	Mixed	NICE	HIC
Falah-Hassani et al. 2015	Immigrant women	Postpartum depression	Prevalence/ risk factors for postpartum depressive symptoms	None	22	Cross-sectional and prospective cohort studies	Effective Public Health Practice Project Quality Assessment Tool	Global (HIC&LMIC)
Gagnon and Redden 2016	Migrants women	Refining the clinical lens	Evidence Reproductive health research	Student support to KR through McGill University's Mr. and Mrs. Henry Collins Memorial Bursary.	47	Mixed	US Preventive Services Task Force (USPSTF) criteria for cohort and case-control studies	Global (HIC&LMIC)
Gieles et al. 2019	Migrants/refugees	Maternal and perinatal care	Access and uptake	Royal Netherlands Academy of Arts and Sciences	28	Mixed -Retrospective cohort, cross--sectional, mixed, qualitative	Newcastle-Ottawa Scale (NOS)	HIC – Europe
Gil-Gonzalez et al. 2015	Migrants	Access to health services	Barriers to access to health services	CIBER Epidemiología y Salud Pública (CIBERESP), Spain	9	Mixed – qualitative and quantitative studies	Critical appraisal criteria (Bambra 2009)	Global (HIC&LMIC)

Table 1 (continued)

Author/year of publication	Population	Intervention	Outcome	Source of funding	No. of included studies	Type of studies included	Quality assessment tools used	Country/region
Graetz et al. 2017	Migrants	Patterns of utilization of health care services	Utilization - uptake/ access	None	39	Mixed – cross-sectional, cohort, retrospective observational, feasibility study	Standardized quality assessment tool from the National Heart, Lung and Blood Institute (NHLBI)	HIC – Europe
Greenaway et al. 2015	Immigrants and Refugees	Hepatitis C Antibodies	Estimated - Seroprevalence	None	50	Quantitative	GRADE	Global - HIC/LMIC
Greenaway et al. 2018a	Migrants	Screening - latent tuberculosis	Public health screening	European Centre for Disease Prevention and Control	23	Quantitative – RCT/ non-RCT	GRADE/AMSTAR	HIC
Greenaway et al. 2018b	Migrants	Screening - active tuberculosis	Public health screening	European Centre for Disease Prevention and Control	11	Quantitative – RCT/ non-RCT	GRADE/AMSTAR	HIC
Greenaway et al. 2018c	Migrants	Screening – Hep C	Public health screening	European Centre for Disease Prevention and Control	20	Quantitative – RCT/ non-RCT	GRADE/AMSTAR	HIC
Hadgkiss et al. 2014 (Hadgkiss and Renzaho 2014)	Asylum seekers	Physical health status, service utilization and barriers to accessing care	Access and Uptake of services	ARC Future Fellowship (Part funded - one of the authors)	32	Mixed methods – quantitative, qualitative, mixed methods studies	Adapted – Consolidated criteria for reporting qualitative research (COREQ) for qualitative.	HIC – Australia
Hargreaves et al. 2019	Migrant workers	Occupational health	Quality of life	Wellcome Trust, UK	36	Quantitative – cross-sectional studies	Joanna Briggs Institute Checklist for Prevalence Studies	HIC – global
Hendrickx et al. 2019	Syrian refugees	Mental health and psychosocial	Access	None	28	Quantitative – RCT/ non-RCT, cross-sectional studies	Newcastle-Ottawa scale (NOS), Consolidated Standardsof Reporting Trials (CONSORT)	LMIC
Higginbottom et al., 2015 (Higginbottom et al. 2015)	Immigrant women	Maternity-care/services Canada	Experiences/ accessibility and acceptability	Canadian Institutes for Health Research	24	Qualitative and quantitative	Joanna Briggs Institute (JBI), Critical Skills Appraisal Programme (CASP) and Crombie tools for survey	HIC – Canada
Hui et al. 2018	Migrants/Immigrants	Vaccination	Access and uptake	European Centre for Disease Prevention and Control	3	Quantitative – Cross-sectional, cohort	GRADE/AMSTAR	HIC
Horyniak et al. 2016	Forced Migrants/ IDP	Substance use	Use	Australian National Health & Medical Research Council Early Career Fellowship, UCSD Centre for	63	Qualitative and quantitative methods- 16 studies utilized qualitative methods	Critical Appraisal Skills Programme (CASP)	Global – LMIC

Table 1 (continued)

Author/year of publication	Population	Intervention	Outcome	Source of funding	No. of included studies	Type of studies included	Quality assessment tools used	Country/region
				US-Mexican Studies; NIDA Merit Award R37DA019829		and three studies used mixed-methods		
Joo 2014	Asian Immigrants	Culturally tailored diabetes interventions	Improved Baseline A1C, Lipids, Psychological behaviour	Not reported	9	Quantitative - 5RCT, 4 quasi-experimental	Amsterdam-Maastricht Consensus List for Quality Assessment	HIC- US
Joshi et al. 2013	Refugees	primary health care delivery models	Access, quality and coordination	Australian Primary Health Institute (APHCRI), Commonwealth Department of Health	25	Narrative synthesis	National Collaborating Centre for Methods and Tools: Quality assessment tool for quantitative studies	Global-HIC
Klein and von dem Knesebeck 2018		Health care utilization	Access and uptake	None	63	Quantitative	Not assessed	HIC
Lindert et al. 2009	labour migrants and refugees	Depression and anxiety	Prevalence of depression and anxiety depressive symptoms	Intramural Research Program at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD	35	Quantitative cross-sectional studies	Not assessed	Global- HIC, LMICs
Mosdol et al. 2017	Ethnic minorities (include Latino or Chinese immigrants)	Targeted mass media	Healthy behaviour	Not reported	6	RCTs	GRADE	HIC- US
Myran et al. 2018	Migrant	Screening and vaccination – hepatitis B virus	Access and uptake	European Centre for Disease Prevention and Control	18	Mixed	AMSTAR, GRADE	HIC
Nilaweera et al. 2014	Women Migrants	Postpartum mental health problems	Prevalence, nature and determinants	None	15	Qualitative Studies (5); Quantitative (10)	Adapted - Consolidated criteria for reporting qualitativeresearch (COREQ) for qualitative	Global - Australia, Canada, Norway and other countries
Norredam et al. 2010	Migrants	Use of somatic health services	Uptake of services	None	21	Surveys	None	HIC – Europe
Nosè et al. 2017	Refugees and asylum seekers	Psychosocial interventions for post-Traumatic stress disorder	Post-traumatic stress	Internal funding - University of Verona	12	Intervention- FGI, NET, CBT, TFP etc.	GRADE	Global HIC – EU and non-EU.
Olaussen et al. 2016	Migrants with disability	Cultural competence healthcare models	Better care/ Health care needs	Australian Research Council Future Fellowship	11	Quantitative and qualitative	None	Global HICs – US, Canada,

Table 1 (continued)

Author/year of publication	Population	Intervention	Outcome	Source of funding	No. of included studies	Type of studies included	Quality assessment tools used	Country/region
								England, Australia
Pottie et al. 2018	Migrants	Screening for HIV	Access and uptake	European Centre for Disease Prevention and Control	12	Qualitative and quantitative	AMSTAR, GRADE	HiC
Requena-Mendez et al. 2015	Latin-American migrants	Chagas disease screening	Prevalence of Chagas depressive symptoms	EC within the 7th Framework Program under grant agreement no. FP7? GA-261495."	18	Prospective, retrospective, multicentre	MOOSE guidelines.	HIC (Europe) – Spain, France, Germany, Italy and Switzerland.
Robertshaw et al., 2017 (Robertshaw et al. 2017)	Refugees and asylum seekers	Primary health care delivery	Challenges and facilitators	None	26	Qualitative		HICs- Australia, Canada, Denmark, Ireland, Netherlands, UK, USA
Santiago Mda and Figueiredo 2015	Immigrant women	Prenatal and postpartum care	Opinion	None	11	Qualitative and quantitative	Not assessed	Global – HIC & LMICs
Satinsky et al. 2019	Refugees	Mental health care	Access and uptake	None	27	Qualitative and quantitative		
Slewa-Younan et al. 2015	Iraqi refugees	Post-traumatic Stress disorder and depression	Incidence/ prevalence rate	Summer scholarship - School of Medicine, The University of Western Sydney	8	Quantitative cross-sectional studies	Adapted - from Reijnder et al.	HICs –Australia, The Netherlands, Sweden, USA
Small et al. 2014	Immigrant women	Maternity care	Experiences/opinions	William Dawson Scholar award.	34	Qualitative based studies	Not assessed	HIC – 5 countries -Australia, Canada, Sweden, UK, USA
Spallek et al. 2015	Immigrants	Suicide	Prevalence/ Incidence rate	None	24	Quantitative – Registry-based	Not assessed	HIC – Europe wide
Suphanchaimat et al. 2015	Migrants	Migrant healthcare services	Challenges and facilitators	Health Insurance System Research Office, Thailand (letter no.: 58-ko-009)	37	Mixed methods – quantitative and qualitative	Spencer et al. for quantitative; CASP checklist for qualitative	HIC (EU and non-EU)
Tavares et al. 2017	Migrants	HIV and tuberculosis co-infection	Prevalence/ Incidence rates	Portuguese Foundation for Science and Technology	27	Quantitative – prospective, cohort, retrospective, quasi--experimental	Not assessed	HIC – Europe
Uiters et al. 2009	Immigrant				37	Quantitative		

Table 1 (continued)

Author/year of publication	Population	Intervention	Outcome	Source of funding	No. of included studies	Type of studies included	Quality assessment tools used	Country/region
		Use of primary medical care	Access and uptake rate	Netherlands Organisation for Scientific Research [NWO] Social cohesion Programme; sub-programme, the Dutch Multicultural and Pluriform Society (MPS)			Not assessed/ mentioned	Global – US and Non-US
Vedio et al. 2017	Migrant Chinese	Health care for chronic hepatitis B	Improving access to health care	US Department of Health, Policy Research Programme, Grant/Award Number: 015/0313	48	Quantitative and qualitative	Systematic Approaches to a Successful Literature Review; Leeds Consensus Statement.	HIC – Australia, Canada, UK, USA
Warren et al. 2015	Migrant women (refugees and asylum seekers)	Sexual and reproductive health	Social determinants – Health promotions	Wellcome Trust and DFID	15	Qualitative and quantitative studies	STROBE checklist	Global – LMICs
Winters et al. 2018	Undocumented migrants	Healthcare services	Access and uptake	Maastricht University	29	Qualitative and quantitative studies	CASP	HIC

Table 2 Descriptive summary of the main characteristics included in migrant systematic reviews

Population ($N = 57$)	Migrants/immigrants	22 (38.6%)	Scope of interventions ($N = 57$)	Healthcare access & uptake	14 (24.6%)
	Refugees/asylum seekers/IDPs	12 (21.1%)		Maternal/reproductive health	9 (15.8%)
	Migrants & refugees	3 (7.0%)		Mental health	9 (15.8%)
	Undocumented migrants	3 (3.5%)		Infectious disease/screening	18 (31.6%)
	Women migrants/immigrants	12 (21.1%)		Health needs/promotion	5 (8.8%)
	Ethnic migrants (Arabs, Asians or Chinese)	5(8.8%)		Health needs	3 (7.7%)
Outcomes in included SRs ($N = 57$)	Maternal care	9 (15.8%)		Occupational health	1 (1.8%)
	Health care delivery	5 (8.8%)		Training	1 (1.8%)
	Access and uptake	14 (24.6%)	Country/region ($N = 57$)	HIC	15 (26.3%)
	Prevalence/incidence rates	14 (24.6%)		LMIC	3 (5.3%)
	Barriers & facilitators	5 (8.8%)		Global	15 (26.3%)
	Mental health	2 (3.5%)		HIC-EU	24 (42.1%)
	Health needs	2 (3.5%)	Research funding ($N = 57$)	Government	14 (24.6%)
	Screening/treatment	6 (10.5%)		Regulatory body	3 (5.3%)
Year of publication ($N = 57$)	2009	2 (3.5%)		Research organization	10 (17.5%)
	2010	1 (1.8%)		Mixed	6 (10.5%)
	2013	3 (5.3%)		Part funded	4 (7.0%)
	2014	8 (14.0%)		None	20 (35.1%)
	2015	11 (19.3%)	Type of studies included ($N = 57$)	Quantitative	14 (24.6%)
	2016	5 (8.8%)		Qualitative	31 (54.4%)
	2017	9 (15.8%)		Mixed (both)	8 (14.0%)
	2018	12 (21.1%)		Mixed	18 (31.6%)
	2019	5 (8.8%)	Conflict of interest ($N = 57$)	Reported	50 (87.7%)
	2020	1 (1.8%)		Not reported	31 (54.4%)

abstract (Almeida et al. 2013; Balaam et al. 2013; Bellamy et al. 2015; Bogic et al. 2015; Bradby et al. 2015; Chernet et al. 2017; Conners et al. 2016; Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Lindert et al. 2009; Santiago Mda and Figueiredo 2015; Slewa-Younan et al. 2015; Spallek et al. 2015), while 16 SRs (28.1%) reported research protocol and registration (Agbata et al. 2019a; Anderson de Cuevas et al. 2018; de Vries et al. 2017; Driedger et al. 2018; Gieles et al. 2019; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hargreaves et al. 2019; Hui et al. 2018; Klein and von dem Knesebeck 2018; Mosdol et al. 2017; Myran et al. 2018; Nosè et al. 2017; Pottie et al. 2018; Satinsky et al. 2019). Figure 3 shows the summary of quality of reporting in included SRs.

ROBIS evaluation

The concerns for bias in the ROBIS domain "study eligibility" wwere considerably low in 45 SRs (78.9%) (Fig. 4). There were concerns of "high RoB" in the domain "identification and selection of studies" in 13 (22.8%) SRs (Al Abed et al. 2014; Bellamy et al. 2015; Carmona et al. 2014; Chernet et al. 2017; Conners et al. 2016; Joo 2014; Lindert et al. 2009; Nilaweera et al. 2014; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Spallek et al. 2015; Tavares et al. 2017; Vedio et al. 2017), and "unclear" concerns of RoB in six selected SRs (Aldridge et al. 2014; Bhargava et al. 2018; Gieles et al. 2019; Gil-Gonzalez et al. 2015; Slewa-Younan et al. 2015; Warren et al. 2015). Regarding the methods of data collection or extraction, the number of reviewers, assessment of the RoB and the quality assessment tools employed, 20 (35.1%) of the SRs had "high" concern for bias (Al Abed et al. 2014; Almeida et al. 2013; Balaam et al. 2013; Bellamy et al. 2015; Bhargava et al. 2018; Conners et al. 2016; Gil-Gonzalez et al. 2015; Hadgkiss and Renzaho 2014; Horyniak et al. 2016; Joo 2014; Klein and von dem Knesebeck 2018; Lindert et al. 2009; Nilaweera et al. 2014; Norredam et al. 2010; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Small et al. 2014; Spallek et al. 2015; Tavares et al. 2017). Subsequently, in the domain "synthesis of findings", 27 (47.4%) had "low" concerns for RoB; 19 SRs (33.3%) had "high" concerns for RoB (Almeida et al. 2013; Balaam et al. 2013; Bellamy et al. 2015; Carmona et al. 2014; Chen et al. 2019; Gagnon and Redden 2016; Graetz et al. 2017; Hadgkiss and Renzaho 2014; Joo 2014; Norredam et al. 2010; Santiago Mda and Figueiredo 2015; Satinsky et al. 2019; Slewa-Younan et al. 2015; Small et al. 2014; Spallek et al. 2015; Suphanchaimat et al. 2015; Tavares et al. 2017; Uiters et al.

Table 3 PRISMA checklist assessment of migrant systematic reviews

PRISMA checklist items	Yes (%)
Title – reported as a systematic review, meta-analysis, or both.	55 (96.5%)
Abstract – structure summary	45(78.9%)
Introduction – rationale and objectives	57 (100%)
Methods	
Protocol and registration	16 (28.1%)
Eligibility	52 (91.2%)
Information sources	56 (98.2%)
Searches – present full electronic search strategy, etc.	44 (77.2%)
Study selection process stated	51 (89.5%)
Data collection process described	39 (68.4%)
Data items listed and defined	41 (71.9%)
Methods use for risk of bias in individual studies listed	42 (73.7%)
Summary measures	41 (71.9%)
Synthesis of results – methods of handling data etc.	32 (56.1%)
Risk of bias across studies – specified	24 (42.1%)
Describe methods of additional analyses (subgroup analysis)	16 (28.1%)
Result	
Study selection	53 (92.9%)
Study characteristics	57 (100.0%)
Risk of bias within studies for each study and, if available,	28 (49.1%)
Results of individual studies for all outcomes considered	42 (73.7%)
Synthesis of results (if meta-analysis is done)	30 (52.6%)
Risk of bias across studies results presented	23 (40.3%)
Additional analysis	20 (35.1%)
Discussion	
Summary of evidence	55 (96.5%)
Limitations	54 (94.7%)
Conclusions	56 (98.2%)
Funding – source and role of funders described	42 (73.7%)
Summary of PRISMA Items satisfied – 1–9 items	2 (3.5%)
10–18 items	19 (33.3%)
19–27 items	36(63.2%)

2009; Vedio et al. 2017), while "unclear" concerns for RoB were observed in 11 SRs (Aldridge et al. 2014; Anderson de Cuevas et al. 2018; Bhargava et al. 2018; Conners et al. 2016; de Jong et al. 2017; Driedger et al. 2018; Fair et al. 2020; Gieles et al. 2019; Gil-Gonzalez et al. 2015; Hendrickx et al. 2019; Klein and von dem Knesebeck 2018; Winters et al. 2018). The overall judgement on the RoB was "high" in 23 SRs (Al Abed et al. 2014; Almeida et al. 2013; Balaam et al. 2013; Bellamy et al. 2015; Bhargava et al. 2018; Carmona et al. 2014; Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Hadgkiss and Renzaho 2014; Joo 2014; Lindert et al. 2009; Nilaweera et al. 2014; Norredam et al. 2010; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Slewa-Younan et al. 2015; Small et al. 2014; Spallek et al. 2015; Suphanchaimat et al. 2015; Tavares et al. 2017; Vedio et al. 2017; Warren et al. 2015); "low" in 27 SRs (Agbata et al. 2019a; Bogic et al. 2015; Chernet et al. 2017; de Jong et al. 2017; de Vries et al. 2017; Driedger et al. 2018; Ehiri et al. 2014; Fair et al. 2020; Falah-Hassani et al. 2015; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Greenaway et al. 2015; Hargreaves et al. 2019; Higginbottom et al. 2015; Horyniak et al. 2016; Hui et al. 2018; Joshi et al. 2013; Klein and von dem Knesebeck 2018; Mosdol et al. 2017; Myran et al. 2018; Nosè et al. 2017; Olaussen et al. 2016; Pottie et al. 2018; Requena-Mendez et al. 2015; Uiters et al. 2009) and "unclear" in seven SRs (Aldridge et al. 2014; Anderson de Cuevas et al. 2018; Chen et al. 2019; Gieles et al. 2019; Hendrickx et al. 2019). In summary, approximately 40% of the SRs had "high" concerns for risk of bias, directly linked to the ROBIS domains regarding "study identification", "data collection and study appraisal" and "synthesis and findings", respectively.

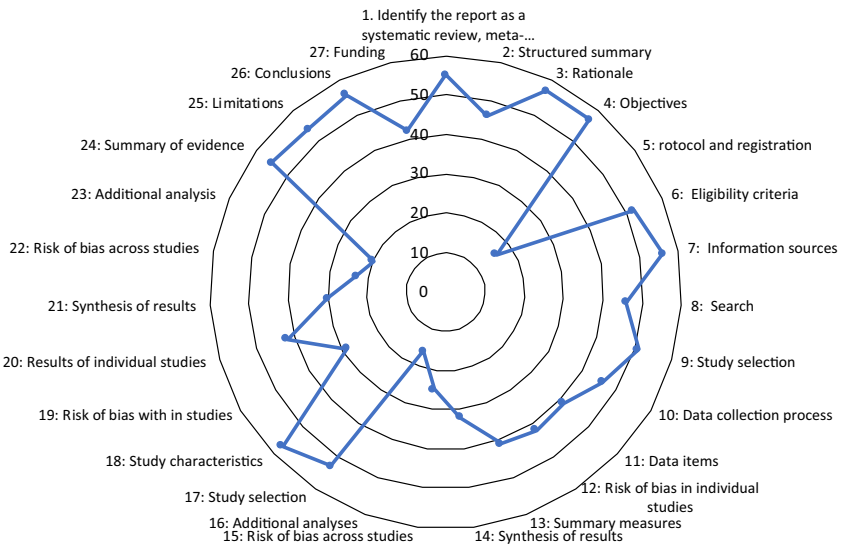

Fig. 3 Summary of the quality of PRISMA items in included SRs

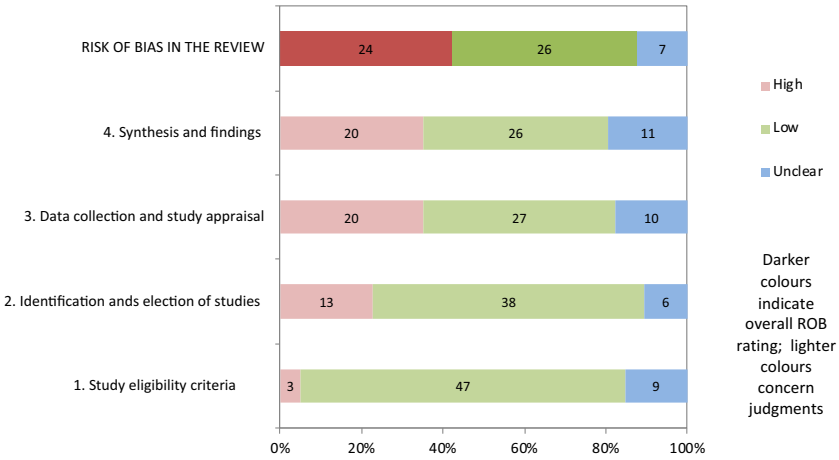

Fig. 4 ROBIS assessment of the included systematic reviews on migrant healthcare

AMSTAR-2 evaluation

The total mean score for the items completed in the 16 items AMSTAR-2 checklist was 9.1 ± 3.2 (Table 4). Five SRs (12.8%) reported that the review methods had established priori (Gil-Gonzalez et al. 2015; Hadgkiss and Renzaho 2014; Mosdol et al. 2017; Nilaweera et al. 2014; Uiters et al. 2009), while approximately half of the SRs did not report a stated priori design or registered protocol (Al Abed et al. 2014; Aldridge et al. 2014; Almeida et al. 2013; Balaam et al. 2013; Bellamy et al. 2015; Carmona et al. 2014; Conners et al. 2016; de Jong et al. 2017; Ehiri et al. 2014; Gagnon and Redden 2016; Lindert et al. 2009; Norredam et al. 2010; Olaussen et al. 2016; Robertshaw et al. 2017; Slewa-Younan et al. 2015; Small et al. 2014; Tavares et al. 2017; Warren et al. 2015). Five selected SRs (8.8%) did not use a comprehensive literature search strategy (Carmona et al. 2014; de Vries et al. 2017; Joo 2014; Small et al. 2014; Spallek et al. 2015); 17 SRs (29.8%) did not perform dual study selection and data extraction stages (Al Abed et al. 2014; Aldridge et al. 2014; Balaam et al. 2013; Bellamy et al. 2015; Chernet et al. 2017; Conners et al. 2016; de Jong et al. 2017; Gagnon and Redden 2016; Hadgkiss and Renzaho 2014; Joo 2014; Joshi et al. 2013; Nilaweera et al. 2014; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Spallek et al. 2015; Tavares et al. 2017; Uiters et al. 2009); and 19 SRs (40%) did not include a list of excluded studies with reasons (Al Abed et al. 2014; Almeida et al. 2013; Anderson de Cuevas et al. 2018; Bellamy et al. 2015; Bhargava et al. 2018; de Jong et al. 2017; de Vries et al. 2017; Gil-Gonzalez

Table 4 AMSTAR-2 assessment of migrant systematic reviews

#Items	Description	YES (%)	No (%)	Partial yes
1	Research questions and inclusion criteria – contains PICO	53 (93.0%)	4 (7.0%)	–
2	Contained statement that review methods were established prior	34 59.6%)	23 (40.4%)	–
3	Study designs selection for inclusion explained	48 (84.2%)	9 (15.8%)	–
4	Use of Comprehensive literature search strategy	29 (50.9%)	5 (8.8%)	23 (40.4%)
5	Study selection process in duplicates	40 (70.2%)	17 (29.8%)	–
6	Data extraction was done in duplicates	39 (68.4%)	18 (31.6%)	–
7	List of excluded studies with reason	13 (22.8%)	19 (33.3%)	25 (43.9%)
8	Included studies described in detail	33 (57.9%)	4 (7.0%)	20 (35.1%)
9	Use of technique to assess the risk of bias (RoB) in included studies	20 (35.1%)	15 (26.3%)	22 (38.6%)
10	Sources of funding reported	7 (12.3%)	50 (87.7%)	–
11	If meta-analysis was performed using appropriate statistical methods	7 (12.3%)	50 (87.7%)	–
12	If meta-analysis was performed, potential impact of RoB on included studies assessed	9 (15.8%)	48 (84.3%)	–
13	RoB in individual studies when interpreting/ discussion accounted for by authors	34 (59.6%)	23 (40.4%)	–
14	Explanation/discussion for Heterogeneity	26 (45.6%)	31 (54.4%)	–
15	Investigation of publication bias done	10 (17.5%)	47 (82.4%)	–
16	Reported sources of conflict of interest/funding received	51 (89.5%)	6 (10.5%)	–
	Overall confidence	High 5 (8.8%)	Moderate 22 (38.6%)	Low 13 (22.8%) Critically low 17 (29.8%)

et al. 2015; Graetz et al. 2017; Hadgkiss and Renzaho 2014; Joshi et al. 2013; Lindert et al. 2009; Nilaweera et al. 2014; Norredam et al. 2010; Small et al. 2014; Suphanchaimat et al. 2015; Vedio et al. 2017; Warren et al. 2015; Winters et al. 2018). Furthermore, 23 SRs (40.4%) did not addressed the risk of bias in individual studies when interpreting or discussing the result of the review (Al Abed et al. 2014; Aldridge et al. 2014; Almeida et al. 2013; Balaam et al. 2013; Bellamy et al. 2015; Bhargava et al. 2018; Bogic et al. 2015; Carmona et al. 2014; Chen et al. 2019; Chernet et al. 2017; Conners et al. 2016; de Jong et al. 2017; de Vries et al. 2017; Ehiri et al. 2014; Falah-Hassani et al. 2015; Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Graetz et al. 2017; Greenaway et al. 2015; Hadgkiss and Renzaho 2014; Hendrickx et al. 2019; Higginbottom et al. 2015; Horyniak et al. 2016; Joo 2014; Joshi et al. 2013; Lindert et al. 2009; Mosdol et al. 2017; Nilaweera et al. 2014; Norredam et al. 2010; Nosè et al. 2017; Olaussen et al. 2016; Requena-Mendez et al. 2015; Robertshaw et al. 2017; Santiago Mda and Figueiredo 2015; Slewa-Younan et al. 2015; Small et al. 2014; Spallek et al. 2015; Suphanchaimat et al. 2015; Tavares et al. 2017; Uiters et al. 2009; Vedio et al. 2017; Warren et al. 2015); and 26 SRs (45.6%) explained heterogeneity of the included studies (Agbata et al. 2019a; Aldridge et al. 2014; Bhargava et al. 2018; Bogic et al. 2015; Chernet et al. 2017; Driedger et al. 2018; Falah-Hassani et al. 2015; Gagnon and Redden 2016; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Greenaway et al. 2015; Hadgkiss and Renzaho 2014; Hargreaves et al. 2019; Higginbottom et al. 2015; Hui et al. 2018; Joshi et al. 2013; Klein and von dem Knesebeck 2018; Lindert et al. 2009; Mosdol et al. 2017; Myran et al. 2018; Nilaweera et al. 2014; Nosè et al. 2017; Pottie et al. 2018; Requena-Mendez et al. 2015; Vedio et al. 2017). Ten SRs (17.5%) reported the potential evidence of publication bias (Bogic et al. 2015; Chernet et al. 2017; Falah-Hassani et al. 2015; Gagnon and Redden 2016; Greenaway et al. 2015; Hargreaves et al. 2019; Lindert et al. 2009; Mosdol et al. 2017; Nilaweera et al. 2014; Nosè et al. 2017), while six SRs (10.5%) did not report conflict of interest or funding sources (Aldridge et al. 2014; Carmona et al. 2014; Chen et al. 2019; Conners et al. 2016; Fair et al. 2020; Horyniak et al. 2016; Mosdol et al. 2017; Nosè et al. 2017; Requena-Mendez et al. 2015; Santiago Mda and Figueiredo 2015; Spallek et al. 2015). Judgments on the overall confidence in the methodological quality of the assessed SRs were: five (10.3%) "high" quality SRs (Carmona et al. 2014; Greenaway et al. 2015; Hargreaves et al. 2019; Mosdol et al. 2017; Nosè et al. 2017); 22 (38.6%) "moderate" quality SRs (Agbata et al. 2019a; Aldridge et al. 2014; Bogic et al. 2015; Chernet et al. 2017; Driedger et al. 2018; Fair et al. 2020; Falah-Hassani et al. 2015; Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Greenaway et al. 2018a; Greenaway et al. 2018b; Greenaway et al. 2018c; Hadgkiss and Renzaho 2014; Hendrickx et al. 2019; Higginbottom et al. 2015; Hui et al. 2018; Klein and von dem Knesebeck 2018; Myran et al. 2018; Olaussen et al. 2016; Pottie et al. 2018; Requena-Mendez et al. 2015; Robertshaw et al. 2017); 13 (22.8%) "low" quality SRs (de Vries et al. 2017; Ehiri et al. 2014; Gagnon and Redden 2016; Graetz et al. 2017; Horyniak et al. 2016; Lindert et al. 2009; Nilaweera et al. 2014; Norredam et al. 2010; Satinsky et al. 2019; Suphanchaimat et al. 2015; Uiters et al. 2009; Vedio et al. 2017; Winters et al. 2018), and 17 (33.3%) were "critically low" quality SRs (Al Abed et al. 2014; Almeida et al. 2013; Anderson de Cuevas et al. 2018; Balaam et al. 2013; Bellamy et al. 2015; Bhargava et al. 2018; Chen et al. 2019; Conners et al. 2016; de Jong et al. 2017; Gieles et al. 2019; Joo 2014; Santiago Mda and Figueiredo 2015; Slewa-Younan et al. 2015; Small et al. 2014; Spallek et al. 2015; Tavares et al. 2017; Warren et al. 2015). No included SRs satisfied all items of the AMSTAR-2 checklist (Table 4 and Fig. 2).

Overall summary of quality measures

Overall agreement between the reviewers was very good for AMSTAR-2, ROBIS and PRISMA tool evaluations (ICC 0.84 to 0.99; 95% CI: 0.78–0.99). The agreement in terms of the assessment outcome between the three tools varied. In ten SRs (25.6%), the assessments were similar in terms of the total number of PRISMA reported items, low risk of bias (ROBIS tool) and moderate or high overall quality (AMSTAR-2). For SRs with moderate to high overall confidence in quality (AMSTAR-2) and low risk of bias (ROBIS), the primary study outcome was prevalence or incidence rate of tuberculosis (Aldridge et al. 2014; de Vries et al. 2017; Greenaway et al. 2018b; Greenaway et al. 2018c), infectious diseases (Chernet et al. 2017), Chagas disease (Requena-Mendez et al. 2015), hepatitis C (Greenaway et al. 2015), PTSD, depression/mental health, (Bogic et al. 2015; Falah-Hassani et al. 2015; Nosè et al. 2017), access/experience/uptake of maternal health/child services/screening (Agbata et al. 2019a; Driedger et al. 2018; Higginbottom et al. 2015; Myran et al. 2018; Pottie et al. 2018) and health promotion or training (Mosdol et al. 2017; Olaussen et al. 2016). Finally, the outcome of the quality ratings using PRISMA, AMSTAR-2 and ROBIS tools was not consistent.

Discussion

Our findings showed that the overall quality of SRs on migrant health interventions published from 2007 to 2017 was suboptimal, irrespective of the study design, migrant population or the country or the region of the systematic review published. Most of the included systematic reviews originated from research studies in high-income countries such as the

USA, UK, Australia and most European states, compared to only two SRs carried out in low–middle income countries (Xing et al. 2017). Often significant cross-border migrations from low-income to these high-income countries present a problem for governments, researchers and policies as a result of unknown variables, such as potential population health risk, weak link between migrant and health outcome, the resulting health system burden as other socioeconomic factors, not clearly understood in host countries (Bradby et al. 2015; Kontunen et al. 2014; Wickramage et al. 2018).

The assessment of SRs on international migrant healthcare interventions showed that the overall confidence in methodological quality using AMSTAR-2 was either low or critically low in approximately half (52.6%) of the included reviews. The shortcomings observed in the included migrant healthcare SRs appear linked to the following methodological factors—a lack of a statement of priority, study selection process and data analysis, source of funding, analysis of the risk of bias, study heterogeneity and assessment of publication bias, respectively. Although none of the included SRs satisfied all the AMSTAR-2 items, there were slight improvements in the quality of SRs published from 2014 compared to before 2013. Our team noted a similar observation in our previously published systematic assessment of migrant healthcare guidelines (Agbata et al. 2019b). Our assessment revealed that a high number of the migrant health SRs (>50%) had low methodological quality or high risk of bias which agrees with a previously reported poor compliance with AMSTAR and PRISMA checklists in other evaluations in other fields (Kelly et al. 2016).

Conversely, the quality of reporting in most of the migrant SRs (>60%) was good, with a mean of 19.74 ± 4.67 PRISMA items satisfied which was better than the mean of 13.2 (SD 6.0) or 18 ± 4 PRISMA items reported in rapid reviews or SRs (Page and Moher 2017). Additionally, the lack of research protocol and registration found in the majority of the included migrant health SRs matches the overall suboptimal reporting quality reported in a pooled assessment of SRs adherence to the PRISMA statement (Kelly et al. 2016; Nawijn et al. 2019; Page and Moher 2017). Despite the overall improvement in the quality of reporting observed over time in published migrant health SRs, it was not significant.

Furthermore, considerations of the assessment outcomes of both ROBIS and AMSTAR-2 tools revealed some inconsistencies, emanating from the specific concerns associated with the multi-part and highly divided rating scale inherent in the domains, and particularly for the ROBIS tool (Whiting et al. 2016). In some cases, SRs with "high" RoB also had "high" overall confidence (Carmona et al. 2014; Nosè et al. 2017); "moderate" overall confidence with "high" RoB (Gagnon and Redden 2016; Gil-Gonzalez et al. 2015; Hadgkiss and Renzaho 2014; Higginbottom et al. 2015; Robertshaw et al. 2017); or "low" overall confidence in quality AMSTAR-2 and "low" RoB (de Jong et al. 2017; de Vries et al. 2017; Ehiri et al. 2014; Horyniak et al. 2016; Joshi et al. 2013; Small et al. 2014; Uiters et al. 2009). A similar pattern of inconsistencies in outcome assessment was reported in another study using the ROBIS tool (Yiu et al. 2018). Roughly 40% of the included SRs, published from 2015 onwards, showed some consistency in the quality of SRs with higher number of PRISMA items reported, with "low" RoB (ROBIS tool), and "moderate" to "high" overall confidence (AMSTAR −2) in methodological quality, respectively. The appraisal tools' consistency in the outcome quality across the included SRs was low and varied in terms of topics investigated and important outcome reported. However, there was no linear association between improvements in quality. A related study reported poor compliance with both PRISMA and AMSTAR checklists with only selected items in both instruments adequately addressed in a rapid review (Kelly et al. 2016). When compared to two recent studies (Banzi et al. 2018; Pieper et al. 2019), our study showed a slightly negative relationship between AMSTAR-2 with ROBIS and PRISMA checklist, but a positive correlation between reports of "low" concerns of risk of bias (ROBIS tool) and higher PRISMA checklist items reported. Consequently, the use of ROBIS and PRISMA checklist may be a more suitable bouquet of quality tools for the future assessment of non-randomized systematic SRs. Our results highlighted the potential impact of the inadequate funding devoted to migrant health research.

Regarding the limitations and strengths of our study, there is a possibility that we failed to identify some relevant migrant health SRs because we only included SRs published in the English language; and the search duration was limited to 2007 to 30 November 2017 to match the period in our published assessment of migrant healthcare guidelines (Agbata et al. 2019b). However, we also performed an updated literature search for December 2017 to April 2020 to include more recent studies in the field. While our sample of 57 SRs were obtained from at least five different databases, the context, scope or topics covered varied widely. Likewise, the inclusion of different study designs with the heterogeneous populations of migrants captured may have impacted on the quality of SRs in this field. We highlight the need for more extensive research on the health concerns of subpopulations of migrants, and particularly for migrant workers with similar health concerns, of which we found only one systematic review; hence, this is not well-represented in our sample (Hargreaves et al. 2019).

Our study offered a comparative assessment of the methodological quality of SRs using ROBIS and AMSTAR-2 which although related have distinctive rating components and criteria in selected domains resulting in variations in

overall judgement of bias in some studies. In addition, we found that the "synthesis and findings" domain (ROBIS tool) contained criteria that did not apply to most of the included migrant SRs because the study designs were mostly qualitative, mixed studies or quantitative studies with no meta-analysis.

The main strengths of our review were as follows: we had a priori design with a registered protocol, an exhaustive systematic search, and used four independent reviewers with substantial experience in the quality evaluations of systematic reviews. Additionally, we utilized standardized, validated and reliable instruments for the quality assessments; performed a rigorous calibration of reviewers as well as piloted the tools; we used consensus procedure to obtain final ratings when required. The inter-rater agreement was excellent. Furthermore, using ROBIS/AMSTAR-2 tools ensured that we employed rigour in compliance with the instruments' criteria, which included the use of specific predefined objectives and eligibility criteria, duplicate study selection and data extraction processes to minimize the risk of errors.

In summary, SRs provides relevant evidence essential in developing guidelines and guiding public health decision-making (Agbata et al. 2019a; Agbata et al. 2019b; Xing et al. 2017). We, at this moment, caution end-users of SRs to consider the less than optimum quality and rigour associated with a large number of published migrant health SRs. Hence, improvements in methodological rigour in the evidence development processes are needed. We suggest that migrant health researchers should adhere to using either ROBIS or AMSTAR-2 in addition to the PRISMA checklist due to their robust construct and method applicability. Additionally, the inclusion of a method expert with considerable experience and links with migrant research groups and networks such as the Cochrane network, Migration Health and Development Research Initiative (MHADRI) and global south research is vital. Also, we advocate for more collaborative efforts between supranational bodies, national agencies, professional societies and researchers in the area of migrant health. Hence, the need for increased funding is paramount.

In addition, we suggest an expansion in the scope of systematic reviews on migrant health beyond primary healthcare services or infectious disease screenings to other clinical areas available to the host population. Also, a focus on a specific subpopulation of migrants and interventions may be beneficial.

Furthermore, we highlight future research directions based on gaps in knowledge and the existing limited evidence base in the scope of migrant health area. Our research strengthens the argument for more funding for improving the research rigour, guidance on designing health interventions, as well as enhancing migrant access to health interventions and services for migrants. Finally, we anticipate that our findings will aid healthcare practitioners and policymakers towards developing more comprehensive migrant healthcare guidelines.

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Author's contributions EA, DB, SN, SSH and IA contributed to the analysis of systematic reviews, and participated and assisted in the data review, as well as in the writing and editing of the manuscript. DB, SN and SSH participated and assisted in the data review, while IA and KP contributed to the design, review and editing of the final manuscript. EA, IA and PAC contributed to the conceptualization, design and conducting of the study. EA, KP, PAC and AI contributed to the review and approved the final manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no competing interests.

Consent for publication Not applicable.

Ethics approval and consent to participate The study did not require any ethical approval because there were no requirement or involvement of vulnerable subjects. However, the study protocol was submitted for consideration, comments, and approved by the postgraduate/doctoral research review board of the University.

Abbreviations AMSTAR, A Measurement Tool to Assess systematic Reviews; CASP, Critical Appraisal Skills Program checklist; CINAHL, Cumulative Index to Nursing and Allied Health Literature; EMBASE, Excerpta Medica database; LILACS, Latin American & Caribbean Health Sciences Literature; MeSH, Medical Subject Headings; MHADRI, Migration Health and Development Research Initiative; NICE, National Institute for Health and Care Excellence; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, Prospective Register of Systematic Reviews database; ROBIS, Risk of Bias Assessment Tool for Systematic Reviews; STROBE, Strengthening the Reporting of Observational studies in Epidemiology; SR, Systematic Reviews.; UK, United Kingdom; USA, United States of America

Appendix 1: Sources and search strategies

1. Literature search strategy for systematic review

A. MEDLINE-OVID

1	Refugees/.
2	refugee.mp.
3	"Emigrants and Immigrants"/.
4	asylum seeker.mp.
5	asylum seeker*.mp.
6	Immigration.mp.
7	Immigrant.mp.
8	or/1–7.
9	Health Services Accessibility/.
10	health access.mp.
11	health services.mp.
12	immigrant health access.mp.
13	(Health adj2 access).mp. [mp = title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms].
14	or/9–13.
15	8 and 14.
16	limit 15 to humans.
17	quality.mp.
18	Quality Assurance, Health Care/.
19	or/17–18.
20	15 and 19.

B. EMBASE ELSEVIER

C. ID Search

#1	'refugee'/exp. OR 'refugee'.
#2	'refugees'.
#3	'migrant'.
#4	migrant*.
#5	'asylum seeker'.
#6	'asylum seekers'.
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6.
#8	'health service'.
#9	'health services'.
#10	'health care delivery'.
#11	'health care accessibility'.
#12	health NEAR/2 services.
#13	#8 OR #9 OR #10 OR #11 OR #12.
#14	'quality'.
#15	'health care quality'.
#16	#14 OR #15.
#17	#7 AND #16.
#18	#17 AND [embase]/lim NOT [medline]/lim.
#19	#17 AND [embase]/lim NOT [medline]/lim AND 'human'/de

C. COCHRANE LIBRARY

ID	Search.
#1	MeSH descriptor: [Refugees] explode all trees.
#2	refugee*.
#3	MeSH descriptor: [Emigrants and Immigrants] explode all trees.
#4	asylum seeker*.
#5	Immigration.
#6	Immigrant.
#7	#1 or #2 or #3 or #4 or #5 or #6.
#8	MeSH descriptor: [Health Services Accessibility] explode all trees.
#9	health access.
#10	health services.
#11	health near/2 access.
#12	#8 or #9 or #10 or #11.
#13	MeSH descriptor: [Quality of Health Care] explode all trees.
#14	quality.
#15	#13 or #14.
#16	#7 and #12 and #15

D. CINAHL

ID	Search.
S1	refugee.
S2	refugee*.
S3	Emigrants and Immigrants.
S4	asylum seeker.
S5	asylum seeker policies.
S6	immigration.
S7	immigrants.
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7.
S9	health services accessibility.
S10	health services.
S11	immigrant healthcare.
S12	S9 OR S10 OR S11.
S13	quality.
S14	quality healthcare.
S15	S13 OR S14.
S16	S8 AND S12 AND S15.

E. LILACS

(tw:(refugee)) OR (tw:(migrant)) OR (tw:(migrant*)) OR (tw:(asylum seeker)) OR (tw:(asylum seeker*))AND (tw:(health services)) OR (tw:(health access)) OR (tw:(Health Services Accessibility))AND (tw:(quality)) OR (tw:(quality health))

2. Additional update literature search for systematic review (December 2017 – April 2020)

A MEDLINE-OVID

1	Refugees/.
2	refugee.mp.
3	asylum seeker.mp.
4	asylum seeker*.mp.
5	Immigration.mp.
6	Immigrant.mp.
7	"Emigrants and Immigrants"/.
8	or/1–7.
9	Health Services Accessibility/.
10	health access.mp.
11	health services.mp.
12	immigrant health access.mp.
13	(Health adj2 access).mp.
14	or/9–13.
15	8 and 14.
16	limit 15 to humans.
17	quality.mp.
18	Quality Assurance, Health Care/.
19	or/17–18.
20	15 and 19.
21	limit 20 to yr = "2017 -Current".

B. EMBASE OVID Database: Embase <1974 to 2020 April 23>

Search Strategy:	
1	Refugees/.
2	refugee.mp.
3	asylum seeker.mp.
4	asylum seeker*.mp.
5	Immigration.mp.
6	Immigrant.mp.
7	"Emigrants and Immigrants"/.
8	or/1–7.
9	Health Services Accessibility/.
10	health access.mp.
11	health services.mp.
12	immigrant health access.mp.
13	(Health adj2 access).mp.
14	or/9–13.
15	8 and 14.
16	limit 15 to humans.
17	quality.mp.
18	Quality Assurance, Health Care/.
19	or/17–18.
20	15 and 19.
21	limit 20 to yr = "2017–Current"

C. COCHRANE LIBRARY

ID	Search Hits.
ID	Search Hits.
#1	MeSH descriptor: [Refugees] explode all trees.
#2	refugee*.
#3	MeSH descriptor: [Emigrants and Immigrants] explode all trees.
#4	asylum seeker*.
#5	Immigration.
#6	Immigrant.
#7	#1 or #2 or #3 or #4 or #5 or #6.
#8	MeSH descriptor: [Health Services Accessibility] explode all trees.
#9	health access.
#10	health services.
#11	health near/2 access.
#12	#8 or #9 or #10 or #11.
#13	MeSH descriptor: [Quality of Health Care] explode all trees.
#14	quality.
#15	#13 or #14.
#16	#7 and #12 and #15 Online Publication Date from Nov 2017 to April 2020 (Word variations have been searched).

D. CINAHL

S17	S8 AND S12 AND S15.
S16	S8 AND S12 AND S15.
S15	S13 OR S14.
S14	quality healthcare.
S13	quality.
S12	S9 OR S10 OR S11.
S11	immigrant healthcare.
S10	health services.
S9	health services accessibility.
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7.
S7	immigrants.
S6	immigration.
S5	asylum seeker policies.
S4	asylum seekers.
S3	Emigrants and Immigrants.
S2	refugee*.
S1	refugee.

E. LILACS

tw:((tw:((tw:((tw:(migrant)) OR (tw:(migrant*)) OR (tw:(asylum seeker)) OR (tw:(asylum seeker*)) OR (tw:(refugee)))) AND (tw:((tw:(health services)) OR (tw:(health access)) OR (tw:(health services accessibility)))) AND (tw:((tw:(quality)) OR (tw:(quality health))))))) AND (db:("LILACS" OR "PAHOIRIS")) AND (year_cluster:[2017–2020]).

Appendix 2

Table 5 List of excluded studies along with reasons for exclusion

Study	Reason for exclusion
Abuhaloob et al., 2018	Not a systematic review
Agbata et al., 2019	Not a health intervention (guidelines)
aïeb et al., 2008	Not a systematic review
Alawa, Zarei & Khoshnood, 2019	Not a systematic review
Araujo et al., A, 2019	Not a health intervention (Portuguese language).
Bal et al., 2019	Full-text unavailable
Batista et al., 2018	Full-text unavailable
Batra, Gupta & Erbas, 2019	Not a health intervention
Baumeister et al., 2019	Full-text unavailable
Blackmore et al., 2019	Full-text unavailable
Brady et al. 2015	Not a systematic review
Brandenberger et al., 2019	Not a health intervention
Chen et al., 2009	Full-text not available
Chiarenza et al., 2019	Not a systematic review
Claassen et al., 2005	Not a systematic review
Curtis, Thompson & Fairbrother, 2018	Not specific to population criteria (Children) or health intervention
Dahlan et al., 2019	Not a health intervention
Dare et al., 2019	Not a relevant to PICO
De Freitas et al., 2020	Not a systematic review
Dywili et al., 2012	Not specific to migrant population.
Forster et al., 2007	Not specific to the population of interest

Table 5 (continued)

Study	Reason for exclusion
Ekezie et al., 2020	Not specific to population – focuses on internally displaced persons (not cross country)
Ferdous et al., 2018	Not a systematic review
Fitzgeral et al., 2013	Not specific to population (*not cross-country migrants; internal rural migrants)
Gagnon et al., 2004	Not recent (> 10 years); and Not a review of health interventions
Garner-Purkis et al., 2019	Not a health intervention (assessing policies for screening)
Garrett at al., 2010	Not a health intervention
Gao and McGrath 2011	Not specific to population
Gea-Sanchez et al., 2017	Full text unavailable
Giorgio et al., 2017	Not a systematic review
Hahn et al., 2019	Not a health intervention
Heuvelings et al., 2017	Full text unavailable
Heuvelings et al., 2018	Not specific to population
Heslehurst et al., 2018	Not a health intervention
Horyniak et al., 2016	Not specific to population
Ivanova et al., 2018	Not a health intervention
Iwelunmor et al., 2014	Not relevant to the population of interest.
Jia et al., 2014	Not relevant to the population
Keboa et al., 2016	Not a systematic review
Kien et al., 2019.	Not specific to population
Klinkenberg et al., 2019	Not a health intervention
Larenas – rosa & Valdes, 2019	Not a systematic review
Liu et al., 2009	Full-text not available
Luiking et al., 2019	Not a systematic review
Markkula et al., 2018	Not specific to population
Martinez et al., 2015	Not focused on a health intervention
McGrath et al., 2004	Not a recent publication (> 10 years)
McKnight et al., 2019	Not specific to PICO
Mcmichael & Healy, 2017	Not specific to PICO
Meyer et al., 2011	Not a systematic review.
Mill et al., 2005	Not a recent publication (> 10 years)
Miller et al., 2019	Not Specific to PICO
Nellums et al., 2011	Not relevant to the population (population interpreters)
Nellums et al., 2018	Not specific to PICO
Ngongalah et al., 2018	Not specific to PICO
Otts et al., 2004	Not a health intervention study
Pangas et al., 2019	Not specific to PICO
Parajuli & Horey, 2020	Not specific to PICO
Patel et al., 2017	Not a systematic review
Pulver et al., 2016	Not a systematic review
Phung et al., 2020	Not specific to PICO
Pocock et al., 2018	Not specific to PICO
Ponte et al., 2019	Not specific to PICO
Quosh et al., 2013	Not specific to the population of interest
Roura et al., 2015	Not a systematic review
Sadarangani & Murali, 2018	Not a systematic review
Schmied et al., 2017	Not a relevant to PICO
Seedat et al., 2018	Full text-unavailable
Tay et al., 2019	Not a health intervention
Tobin et al., 2018	Not a health intervention

Table 5 (continued)

Study	Reason for exclusion
Tribe et al.,2017	Full text-unavailable
Turkmani, Homer & Dawson, 2019	Full text-unavailable
Turrini et al., 2017	Not a systematic review
Vang et al., 2015	Not a health intervention
Vang et al., 2017	Not relevant to PICO
Van Wyk and Schweitzer 2014	Not relevant to PICO
Villa-Torres et al., 2017	Not an outcome of interest
von Werthern et al., 2018	Not specific to population
Wanden-Berghe et al., 2013	Not an outcome of interest
Ward, Kristiansen & Sorensen, 2019	Full text-unavailable
Win, Hetherington & Tough, 2017	Not a health intervention
Wittkowski, Patel & Fox, 2017	Full text-unavailable
Yazdani et al., 2018	Not a systematic review
Yeheskel & Rawal, 2019	Not a relevant to PICO

Appendix 3: Data extraction

1. Objective of the review.
2. Type of intervention (pharmacological or non-pharmacological).
3. Population—Refugees or migrant or both, asylum seekers, undocumented migrants or immigrants.
4. Risk of bias assessment of the primary studies included in the review (Yes/No/Unclear), including assessment method (e.g. Jadad tool, RoB Cochrane Tool, etc.).
5. Use of GRADE to assess the certainty about the body of evidence (Yes, No, Unclear).
6. Assessed study specific outcomes (Primary and/or secondary outcomes). We will extract the primary outcome specified in the included SRs. If no primary outcome was assessed, then the most important patient outcome will be selected.
7. Source of funding: government, academic, private organization (for profit or not) and or scientific society.
8. Reported conflict of interest (YES, No, Not assessed).
9. Number of included studies overall and total of participants /patients included.
10. Design of the included studies of each review (randomized controlled trials, non-randomized-observational, etc., or both).

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5.5.3 Third publication

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Review

Effectiveness of Screening and Treatment Approaches for Schistosomiasis and Strongyloidiasis in Newly-Arrived Migrants from Endemic Countries in the EU/EEA: A Systematic Review

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Abstract: We aimed to evaluate the evidence on screening and treatment for two parasitic infections—schistosomiasis and strongyloidiasis—among migrants from endemic countries arriving in the European Union and European Economic Area (EU/EEA). We conducted a systematic search of multiple databases to identify systematic reviews and meta-analyses published between 1 January 1993 and 30 May 2016 presenting evidence on diagnostic and treatment efficacy and cost-effectiveness. We conducted additional systematic search for individual studies published between 2010 and 2017. We assessed the methodological quality of reviews and studies using the

AMSTAR, Newcastle–Ottawa Scale and QUADAS-II tools. Study synthesis and assessment of the certainty of the evidence was performed using GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. We included 28 systematic reviews and individual studies in this review. The GRADE certainty of evidence was low for the effectiveness of screening techniques and moderate to high for treatment efficacy. Antibody-detecting serological tests are the most effective screening tests for detection of both schistosomiasis and strongyloidiasis in low-endemicity settings, because they have higher sensitivity than conventional parasitological methods. Short courses of praziquantel and ivermectin were safe and highly effective and cost-effective in treating schistosomiasis and strongyloidiasis, respectively. Economic modelling suggests presumptive single-dose treatment of strongyloidiasis with ivermectin for all migrants is likely cost-effective, but feasibility of this strategy has yet to be demonstrated in clinical studies. The evidence supports screening and treatment for schistosomiasis and strongyloidiasis in migrants from endemic countries, to reduce morbidity and mortality.

Keywords: migrant populations; schistosomiasis/schistosoma; strongyloidiasis/strongyloides; screening/diagnosis; treatment; public health; GRADE

1. Introduction

The public health importance of schistosomiasis and strongyloidiasis has increased in non-endemic regions as a result of growing global migration [1,2]. Schistosomiasis is caused by species of the trematode *Schistosoma* spp. *Sc. mansoni* is the most prevalent in Africa, the Americas, the Middle East and the West Indies, followed by *Sc. haematobium* in Africa and the Middle East and *Sc. japonicum* in east and south-east Asia [3]. Sub-Saharan African countries account for 90% of reported cases globally [3]. Prevalence rates of 10–50% for *Sc. haematobium* infections have been reported in some countries in sub-Saharan Africa and the Middle East [4], and prevalence rates of 1–40% have been reported for *Sc. mansoni* in sub-Saharan Africa and South America and for *Sc. japonicum* in Indonesia, parts of China and south-east Asia [5].

Strongyloidiasis is caused by the nematode *Strongyloides stercoralis* and, although it generally occurs in sub-tropical and tropical countries, it can be present in temperate countries where conditions are favourable [6]. The global burden of both diseases has been underestimated because of the poor sensitivity of diagnostic methods used in low-resource settings [6], but recent estimates indicate that around 370 million people are infected with *St. stercoralis* [7] and more than 200 million are infected with schistosomiasis causing a loss of more than 1.53 million disability-adjusted life years (DALYs) [4,5,8,9].

Few studies have assessed the prevalence schistosomiasis in European countries, but recent data show rates above 17% in migrants from sub-Saharan Africa [10]; prevalence of strongyloidiasis among refugee populations originating from south-east Asia and Africa was reported to be between 0.8% and 4.3% using microscopy; higher rates of between 9% and 77% using antibody detection assays were reported among refugees from south-east Asia [11]. Prevalence rates of 3.3%, 4.2% and 5.6% were reported in Italy, Spain and France, respectively, mainly in migrant populations or expatriates, without specifying diagnostic methods [6].

From all parasitic infections that may be highly prevalent among migrants, schistosomiasis and strongyloidiasis have several characteristics which support the rationale for screening based on the classical principles of Wilson and Jungner [12]. First, both infections are of particular importance, besides being as highly prevalent as other parasitic infections, they can cause long-term complications and severe consequences. Schistosomiasis is associated with chronic urogenital, hepato-intestinal and central nervous system complications [9,13–15]. *St. stercoralis* can cause disseminated infections or hyper infections with fatal outcomes in immunosuppressed patients (e.g., transplant recipients, those on corticosteroid therapy, with malignancies or co-infections with human T-cell lymphotropic virus-1 (HTLV-1)) [16]. In addition, there is a potential risk of transmission in the EU/EEA, either through organ transplantation in the case of strongyloidiasis [17] or through a favourable environment for the intermediate host, as in recent autochthonous cases of urinary schistosomiasis in Corsica, France

which is not the case from many other parasitic infections [11,18]. Second, most infections are asymptomatic [13,19,20] and those infected are either unaware of their infection [19] or have very mild unspecific symptoms [3]. Third, both are chronic infections if untreated [19]. Schistosomiasis can remain as a sub-clinical infection for many years [3], and *St. stercoralis* replicates indefinitely inside the human host, causing lifelong infection if untreated [19].

Fourth, screening could be based on a simple and widely accessible technology, including commercially available serological test with a reasonable cost. In this sense, diagnosis of both infections based on microscopy has high specificity but low sensitivity [19,21,22]. Antibody-detecting serological tests offer higher sensitivity, at the expense of specificity, and have been shown to be useful in countries with low endemicity [19,22,23]. Finally, treatments for both infections are universally accepted with a high efficacy rate and low rate of adverse events. Praziquantel and ivermectin are the drugs of choice for treating schistosomiasis and strongyloidiasis, respectively [7,13].

In the last ten years, there has been a significant increase in migration patterns to the EU/EEA with some fluctuations in the volume and type of migration from year to year [24,25]. In 2017, migrants, here defined as being born abroad, made up 11% of this population, with 4% being born in another EU/EEA country and 7% originating from outside the EU/EEA [26]. There is an increased number of asylum applications with 56% of the 2,672,000 asylum decisions being positive between 2015 to 2017 [27]. Half of those denied asylum can be expected to leave, adding 580,000 to the EU/EEA's total number of irregular migrants [28].

There is a notable gap in data collection on the disease burden, public health management, and in the surveillance for imported diseases in migrants arriving from endemic areas to EU/EEA. Geographic differences in disease distribution between global regions, influenced by increasing migration and population mobility from high endemic to non-endemic areas, remains an ongoing challenge to surveillance programmes and hampers the implementation of health policies concerning migrant health screening strategies [29,30].

There have been several systematic reviews addressing how effective are approaches to migrant screening infectious diseases in Europe [31–33], however parasitic infections are not adequately covered. Therefore, given the recent increase in migrants to the EU/EEA from endemic countries, there is a need for public health guidelines on the optimal approach to screening for schistosomiasis and strongyloidiasis [34–36]. In this systematic review, we assessed the effectiveness (and cost-effectiveness) of screening and management of these two parasitic infections in migrant populations.

2. Methods

The review was one of six systematic reviews conducted under the auspices of a European Centre for Disease Prevention and Control (ECDC) project to develop guidance on screening for hepatitis C, hepatitis B, HIV, tuberculosis, vaccine-preventable diseases and parasitic infections in newly-arrived migrants to the EU/EEA [37]. The review group followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for the reporting of this systematic review [38]. The review protocol and methods assembled by a team of methodologists and clinicians with disease expertise was registered in Prospero (CRD42016045798) and published [39].

Our key research question was:

What are the most effective screening and treatment options for schistosomiasis and strongyloidiasis in migrant populations arriving from endemic regions in the EU/EEA?

To address this, we developed a logic model, prioritised outcomes important for the patient, and developed key questions along the evidence pathway (Appendix 1). These key questions included:

(i) What are the best diagnostic tests to detect these infections non-endemic settings?
(ii) How effective are the drugs to treat them and what are the associated adverse events?
(iii) What are the most cost-effective screening and treatment options for schistosomiasis and strongyloidiasis in migrant populations from endemic regions in the EU/EEA?

2.1. Search Strategy and Selection Criteria

We searched for systematic reviews and meta-analyses in MEDLINE, Embase-ELSEVIER, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Epistemonikos, the Database of Abstracts of Reviews of Effects (DARE) and the Cochrane Database of Systematic Reviews (CDSR) for evidence on effectiveness. Our search used a combination of the key terms: 'Immigrant', *'Strongyloides'*, 'Schistosomiasis', 'endemicity', 'prevalence', 'screening', 'migrant screening', 'mass screening', 'early detection', 'health impact assessment' and 'cost-effectiveness' (Appendix 2). The primary inclusion populations were migrants and refugees. We considered as main outcomes: cure, mortality, morbidity, adverse effects, health equity, quality of life and test accuracy measures (sensitivity and specificity). Also, we searched the National Health System (NHS) Economic Evaluation Database, the Health Economic Evaluations Database, the Cost Effectiveness Analysis Registry and Google Scholar for evidence on cost-effectiveness. We also identified any reviews on prevalence of the two infections. We restricted the search to studies published between 1 January 1993 and 30 May 2016. We did not apply language restrictions, and where we identified more than one version of a systematic review, we included the most recent. For the economic evidence, systematic reviews and primary studies of resource use, costs or cost-effectiveness of screening for schistosomiasis or strongyloidiasis with or without treatment were identified using specific search terms including ("costs and cost analysis"; "cost effectiveness analysis"; "costs.tw"; "cost$.mp"; "cost effective$.tw"; "cost-benefit analys$.mp" "health care costs.mp") combined with clinical criteria. We reported all the costs in the local currency of the study setting or country, and in Euros using the Cochrane methods group purchasing power parity currency conversion calculator for the given year [40]. We also searched grey literature for published guidelines and reports on screening and prevention programme from the United States (U.S.) Centers for Disease Control and Prevention, ECDC, Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO).

2.2. Additional Included Studies

Due to the limited evidence obtained from the initial search, we conducted an updated systematic search of six databases (MEDLINE, Embase-ELSEVIER, CINAHL, CDSR, DARE, Cochrane CENTRAL and Latin American Literature in Health Sciences—LILACS). We included relevant primary studies on diagnostic or screening tools for schistosomiasis (January 2010–February 2017) and strongyloidiasis (January 2012–February 2017). References of included primary studies were searched to identify other relevant studies.

2.3. Study Selection, Quality Assessment, and Synthesis

We included systematic reviews and evidence-based review guidelines which addressed each key question. When no systematic review was identified, we used primary studies. Two team members independently screened the titles and abstracts, followed by full-text assessments for eligibility of studies on prevalence, screening and treatment effectiveness, and related key questions (Eric Agbata, Nadia Montero) and of studies on cost-effectiveness (Nick Rowbotham, Rachael Morton). Disagreements were resolved by consensus or the involvement of a third author (AR). We assessed the methodological quality of reviews using AMSTAR [41] or Newcastle–Ottawa Scale [42] for reviews and observational studies respectively. We assessed the methodological quality of included primary studies on diagnostic effectiveness using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS II) tool [43]. Synthesis of the studies and assessment of the certainty of the evidence for systematic reviews and individual studies was performed using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methods, including Summary of Findings tables and Evidence to Decision tables [37]. For cost-effectiveness studies, we extracted the following data: economic study design (e.g., cost–utility analysis, Markov model), description of the case base population, the intervention and comparator, the absolute and relative difference in resource use and cost-effectiveness (e.g., incremental net benefit (INB) or incremental cost-effectiveness ratio (ICER).

3. Results

The first systematic search yielded, after removal of duplicates, 662 systematic reviews for which we screened titles and abstracts. Of the 26 systematic reviews selected for full-text screening, we included 11 systematic reviews which focused on the efficacy of diagnosis and treatment of schistosomiasis ($n = 8$) and strongyloidiasis ($n = 3$) (Figure 1) [19,44–53]. The updated systematic search for diagnostic testing accuracy studies for schistosomiasis yielded after de-duplication 1961 citations for the screening of titles and abstracts. Of the 30 articles selected for full-text screening, we included seven primary studies (Figure 2) [54–60]. One more primary research was identified later and included [61]. Another systematic search performed for diagnostic testing accuracy evidence for strongyloidiasis yielded 497 records after de-duplication; titles and abstracts were screened, and of the 24 papers selected for full-text screening, we included three primary studies (Figure 3) [62–64]. For the economic evidence, the search strategy yielded 160 studies after de-duplication. We retrieved 20 studies after title and abstract screening, of which six studies (four decision-analytic models for economic evaluation and two costing studies) were finally included—four for strongyloidiasis and two for schistosomiasis (Figure 4) [65–70]. Overall, we included 28 reviews and studies in this systematic review (Tables 1–3).

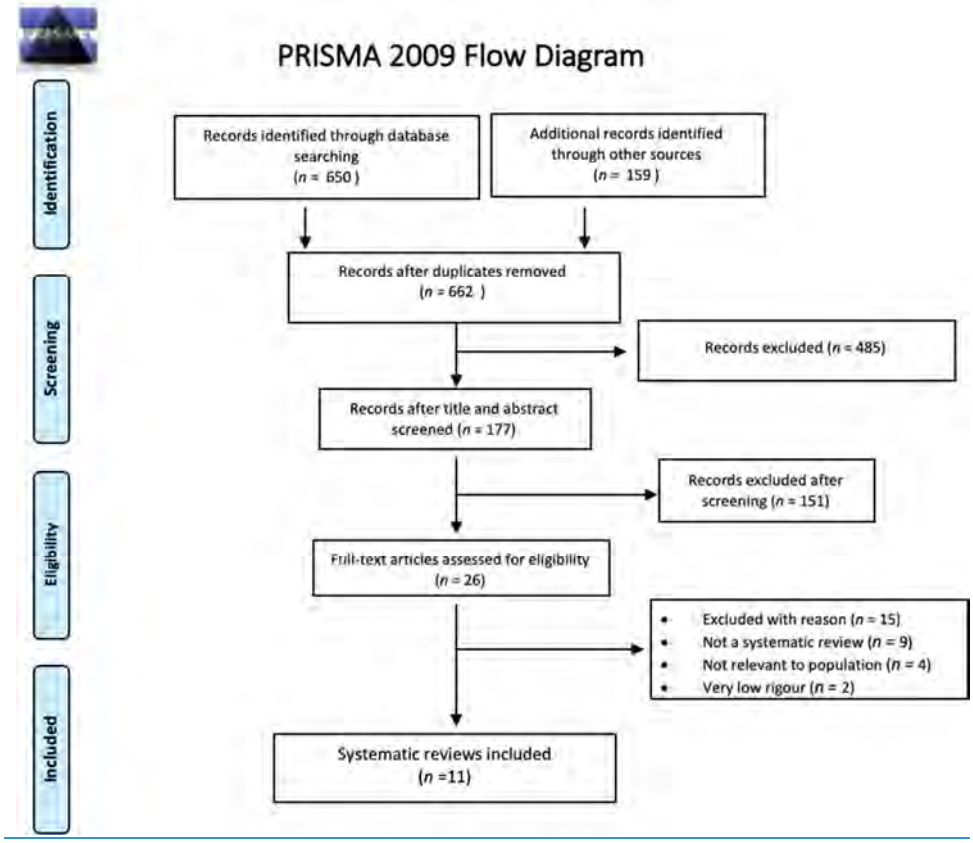


Figure 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for selection of systematic reviews on diagnostic accuracy and treatment efficacy for schistosomiasis and strongyloidiasis, (January 1993–May 2016)

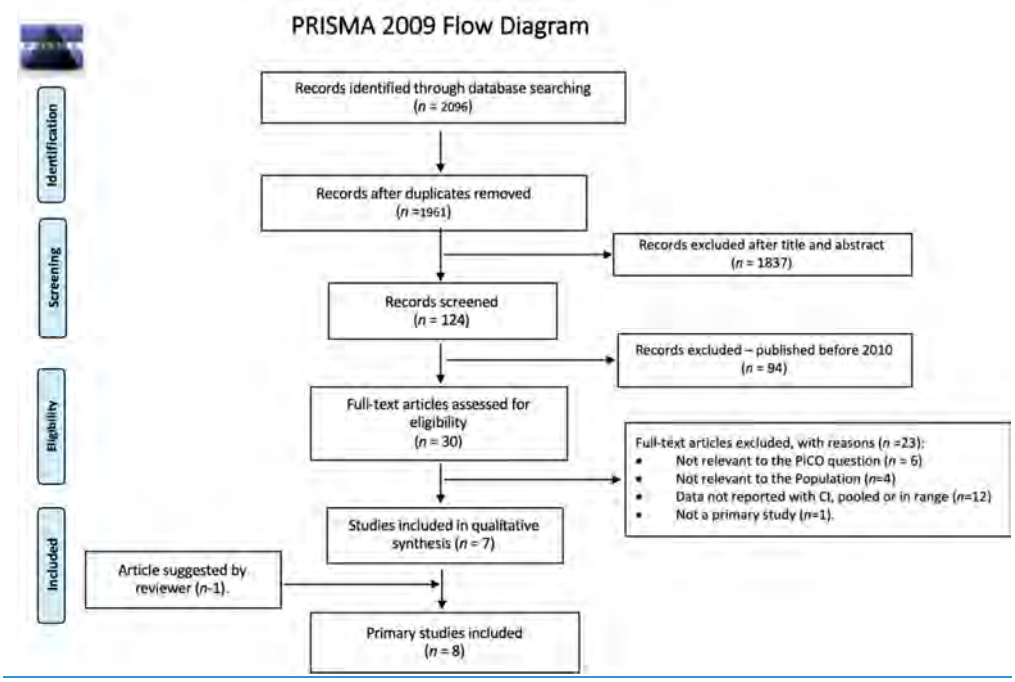


Figure 2. PRISMA flow diagram for selection of primary studies on diagnostic accuracy for schistosomiasis, January 2010–February 2017

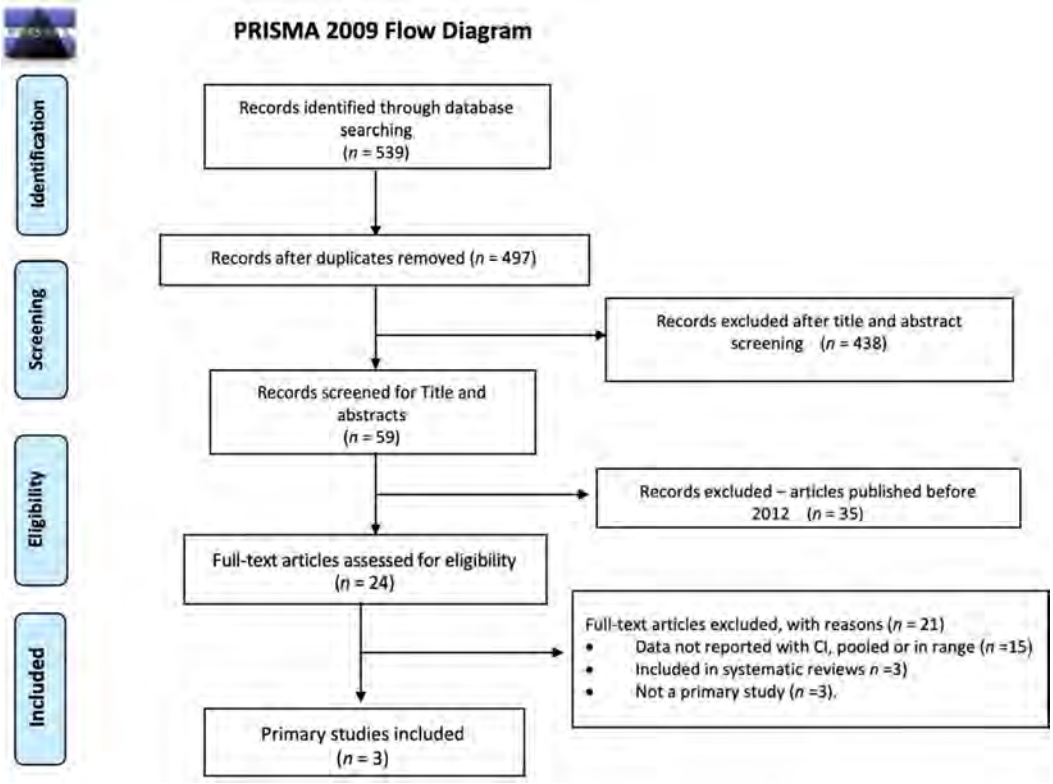


Figure 3. PRISMA flow diagram for selection of primary studies on diagnostic accuracy on strongyloidiasis, (January 2012–February 2017).

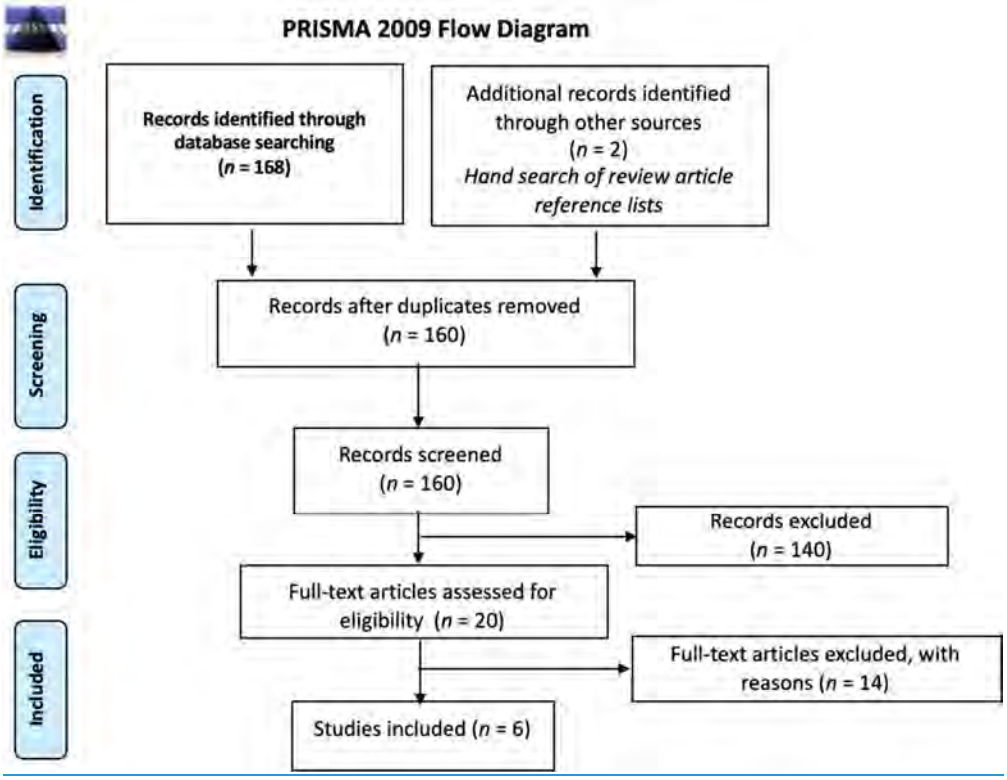


Figure 4. PRISMA flow diagram for selection of cost-effectiveness studies for schistosomiasis and strongyloidiasis, 1993–2016. DARE: Database of Abstracts of Reviews of Effects; NHS EED: National Health Service Economic Evaluation Database; Tufts CEA: Tufts Medical Centre Cost-Effectiveness Analysis Registry.

Table 1. Characteristics of included studies on diagnostic test effectiveness for schistosomiasis and strongyloidiasis, January 1993–February 2017.

Study	Quality	Design	Population	Intervention/Outcomes	Results
Included systematic reviews of diagnostic tests to detect schistosomiasis					
Danso Appiah et al., 2016 [53]	AMSTAR: 11/11 GRADE: low to moderate-quality evidence	Systematic review and meta-analysis	Preschool children and infants, school-aged children or adults from high-/low-prevalence locations	Intervention: POC CCA for *Sc. mansoni* Outcomes: detection of egg-positive urine—sensitivity/specificity (95% CI:)	Sensitivity/specificity (95% CI) POC CCA (single standard) 90% (84–94)/56% (39–71); POC CCA (duplicate standard) 85% (80–88)/66% (53–76); POC CCA (triplicate standard) 91% (84–95)/56% (39–72)
Yang et al., 2015 [50]	AMSTAR: 11/11 GRADE: low to moderate-quality evidence	Meta-analysis	Patients infected with schistosomiasis in endemic areas; mainly school children, Africa and China	Intervention: questionnaire screening for Schistosoma species. Outcomes: sensitivity/specificity (95% CI:)	Sensitivity/specificity (95%CI: *Sc. haematobium* 85% (84–86)/94% (94–94); *Sc. mansoni* 46% (45–47)/81% (80–82); *Sc. japonicum* 82% (79–85)/59% (57–60)
Ochodo et al., 2015 [44]	AMSTAR: 11/11 GRADE: very low to low-quality evidence	Systematic review and meta-analysis of RCTs	Individuals with active infection with S. haematobium	Intervention: urine reagent strip tests; circulating antigen tests in urine/serum Outcomes: sensitivity/ specificity (95% CI:)	Sensitivity/specificity (95% CI) *Sc. haematobuim*: microhaematuria 75% (71–79)/87% (84–90); proteinuria 61% (53–68)/82% (77–88); leukocyturia 58% (44–71)/61% (34–88); *Sc. mansoni* (CCA test) 89% (86–92)/55% (46–65)
King and Bertsch, 2013 [45]	AMSTAR: 11/11 GRADE: low-quality evidence	Systematic review and meta-analysis of surveys	Schools, communities with high/low prevalence, low intensity groups in Africa	Intervention: dipstick test *Sc. haematobium*. Outcomes: sensitivity and specificity (95% CI:), diagnostic odds ratio (DOR)	Sensitivity/specificity (95% CI) Detection of egg-positive urine 81% (79–83)/89% (87–92). In high-prevalence settings 80% (78–83)/86% (82–90); lower in treated population 72% (61–78)/87% (81–94); in lower intensity population subgroups 65% (58–72)/82% (76–90)
Wang, et al., 2012 [46]	AMSTAR: 7/11 GRADE: very low- to low-quality evidence	Systematic review and meta-analysis of RCTs, retro-/pro-observational studies	Infected patients with schistosomiasis in control programmes in China	Intervention: IHA and ELISA. Outcomes: true positive rates, sensitivity/specificity (95% CI:), DOR	Sensitivity/specificity (95% CI) IHA 75.6% (74–77)/73% (72–74) ELISA 84.9% (83–87)/50.4% (49.2–51.6) The DOR of IHA was 9.41 (95% CI: 5–18), and ELISA 4.78 (95% CI: 3.21–7.13)
Included primary studies of diagnostic tests to detect schistosomiasis					
Espirito-Santo et al., 2015 [57]	QUADAS-2-11/14 GRADE: very low- to low-quality evidence	Cross-sectional epidemiological survey in areas of low prevalence of *Sc. Mansoni*	The estimated sample size required was 650 individuals; Barra Mansa City, Rio de Janeiro State, Brazil	Intervention: diagnostic assays: ELISA-IgG/ELISA-IgM/IFT-IgM/qPCR in faeces. Outcomes: sensitivity/ specificity (95% CI:)	Sensitivity/specificity (95% CI) KK 13.8% (4–32)/99.8% (99.0–100); ELISA-IgG 66.7% (48–82)/91.5% (89–94); ELISA-IgM 81.8% (64–93)/82% (79–85); IFT-IgM 78.8% (61–91)/87.7% (84.8–90); qPCR in faeces 51.7% (32–71)/92.6% (90–95); qPCR in serum 12.1% (3–28)/99.1% (98–99)
Espirito-Santo et al., 2014a [60]	QUADAS-2-12/14 GRADE: very low- to low-quality evidence	Cross-sectional study	City of Barra Mansa, Rio de Janeiro State, Brazil, with an estimated prevalence of 1%	Intervention: diagnostic assays: ELISA-IgG and ELISA-IgM. Outcomes: sensitivity/specificity (95% CI:); PPV, NPV	Sensitivity/specificity (95%CI) ELISA-IgG 60.0% (15–95) /89.1% (86.2–91.5); ELISA-IgM 60.0(15–95)/79.2% (75.6–82.5) PPV/NPV (95%CI):

					ELISA-IgG 4.6% (1–13) /99.6% (98–100); ELISA-IgM 2.5% (0.5–7); NPV 99.6% (98.4–100.0)
Espirito-Santo et al., 2014b [56]	QUADAS-2-13/14 GRADE: very low- to low-quality evidence	Cross-sectional epidemiological survey	7000 inhabitants located in the outskirts of Barra Mansa, Rio de Janeiro, Brazil	Intervention: qPCR in serum or faeces. Outcomes: sensitivity/ specificity (95% CI:); PPV, NPV	Sensitivity/specificity (95% CI) qPCR in faeces 80.0% (28–99)/92.4% (90–94); qPCR in serum 20.0% (0.5–71.6)/98.8(97–99) PPV/NPV (95% CI:): qPCR in faeces 8.0% (2–19)/99.8% (99–100); qPCR in serum 12.5% (0.3–52.7)/99.3% (98.2–99.8)
Lodh et al., 2013 [55]	QUADAS-2-12/14 GRADE: very low- to low-quality evidence	Cross-sectional case study	Filtered urine specimens from infected and not-infected patients in Zambia	Intervention: qPCR ELISA IgG in serum or faeces; filtered Urine PCR. Outcomes: sensitivity/specificity (95% CI:); PPV, NPV	Sensitivity/specificity (95%CI) KK test 57% (45–68)/100% (69–100); CCA rapid test 65% (56–77)/60% (26–88); PCR 100% (95–100)/100% (69–100) PPV/NPV: KK test 100%/23%; CCA rapid test 93%/19%; PCR 100%/100%.
Kinkel et al., 2012 [54]	QUADAS-2-12/14 GRADE: very low- to low-quality evidence	Retrospective comparative diagnostic study: performance of 8 serological tests for Schistosoma spp	Serum specimens from infected patients and those without the infection in low-prevalence locations or non-endemic settings (Germany)	Intervention: serological assays: IFAT, ELISA-CA, ELISA-AWA, ELISA-SEA, IHA, ELISA-NovaTec, ELISA-DRG and ELISA-Viramed. Outcomes: sensitivity and specificity (95% CI:)	Sensitivity/specificity-(95% CI): IFAT 75.7% (58–98)/98.1% (92–99); ELISA-CA 40.5% (25–59)/95.2% (89–98); ELISA-AWA 54.1% (37–70)/100% (95.6–100); ELISA-SEA-75.7% (58–98)/97.1% (91–99); IHA 73.0% (55.6–85.6)/99.0% (94.0–100); ELISA-NovaTec 64.9% (47–79)/99 (94–100); ELISA-DRG 78.3% (61.3–89.6)/88.4 (80–94); ELISA-Viramed 67.6% (50–81)/76.9% (67–84).
De Frotas et al., 2011 [58]	QUADAS-2-12/14 GRADE: very low- to low-quality evidence	Cross-sectional survey	Stool and serum specimens from infected and not infected patients, low-endemic setting in Brazil	Intervention: serological assays, ELISA IgG Outcomes: sensitivity and specificity (95%CI)	Sensitivity/specificity (95% CI): ELISA-IgG 100% (68–100)/72.9% (67–78). PPV/NPV (95% CI): ELISA-IgG 26.0% (18–36) /100% (97–100).
Silveira et al., 2016 [59]	QUADAS-2-12/14 GRADE: very low- to low-quality evidence	Evaluation of the CCA test to diagnose *Sc. mansoni* in Minas Gerais State, Brazil.	Infected individuals in regions with moderate to high prevalence	Intervention: CCA-immuno-chromatographic test. Outcomes: sensitivity/specificity (95% CI:)	Sensitivity/specificity (95% CI): CCA-ICT 68.7% (54–81)/97.6% (87–99)
Beltrame et al., 2017 [61]	QUADAS-2-12/14 GRADE: very low- to low-quality evidence	Accuracy of parasitological and immunological tests for the screening of human schistosomiasis in immigrants and refugees from African countries	Frozen serum specimens from recent African asylum seekers that were routinely screened for schistosomiasis in Italy	Intervention: urine CCA; Bordier-ELISA, Western Blot IgG, ICT IgG-IgM, microscopy compared with composite reference standard. Outcomes: sensitivity/specificity (95% CI:)	Sensitivity/specificity (95% CI): Urine CCA 29% (22–37)/95% (91–97); Bordier-ELISA 71% (63–78)/99.6% (98–100); Western blot IgG 92% (86–96)/94% (90–97); ICT IgG-IgM 96% (91–99)/83% (77–87); microscopy 45% (37–54)/100%
Included systematic reviews for diagnostic effectiveness for strongyloidiasis					

Campo Polanco et al., 2014 [51]	AMSTAR: 11/11 GRADE: moderate-quality evidence	Systematic review and meta-analysis	Individuals with active/chronic infection	Intervention: Baermann method, agar plate, direct faecal smear examination and formol-ether concentration technique. Outcome: sensitivity and specificity (95% CI:)	Sensitivity: Baermann method (72%) with LR+ 228 and LR−0.32; APC 89%, LR+ 341 and LR−0.11; stool microscopy 21%, LR+ 67 and LR−0.67; formol-ether concentration 48%, LR+ 110 and LR−0.59. Specificity: 100% in all four tests. APC and Baermann method are best.
Requena-Méndez et al., [19]	AMSTAR: 7/11 GRADE: low- to moderate-quality evidence	Systematic review	Individuals with active/chronic infection	Intervention: Baermann method, agar plate, direct faecal smear examination and formol-ether concentration technique, serological techniques. Outcome: sensitivity and specificity (95% CI:)	No meta-analysis was undertaken. Sensitivity and specificity of different techniques were individually reported.
Included primary studies for diagnostic effectiveness for strongyloidiasis					
Bisofi et al., 2014 [62]	QUADAS-2: 13/14 GRADE: low-quality evidence	Retrospective comparative diagnostic study to evaluate the performance of 5 tests for *St. stercoralis.*	Serum specimens from subjects with *St. stercoralis*; healthy people and patients with previous exposure	Intervention: IFAT, NIE-LIPS NIE-ELISA, IVD-ELISA- and Bordier-ELISA Outcome: sensitivity and specificity (95% CI:)	Sensitivity/specificity (95% CI): NIE-ELISA 75.4% (67–83)/94.8% (91–99); NIE-LIPS 85.1% (78–92)/100% (100–100); IFAT 93.9% (89–98)/92.2% (87–97); IVD-ELISA 91.2% (86–96)/99.1% (97.4–100.0); Bordier-ELISA 89.5% (84–95) 98.3% (96–100).
Rascoe et al., 2015 [63]	QUADAS-2: 10/14 GRADE: low-quality evidence	Retrospective comparative diagnostic study of 5 tests for the follow-up of patients infected with *St. stercoralis*	Serum samples positive for *St. stercoralis* and negative samples from United States residents with no history of foreign travel	Intervention: Ss-NIE-1 ELISA, Ss-NIE-1 Luminex. Outcome: sensitivity and specificity (95% CI:)	Sensitivity/specificity (95% CI): SS-NIE-1 ELISA 95% (92–97)/93% (90–96); Ss-NIE-1 Luminex 93% (88–96)/95% (93–97). The inter-assay coefficient of variation was determined to be 22% for the low-positive control serum and 10% for the medium-positive control serum.
Knopp et al., 2014 [64]	QUADAS-2: 11/14 GRADE: low-quality evidence	International standard randomised controlled trial	Children and adults residing in rural villages in the Baga moyo District, Tanzania (endemic areas)	Intervention: Real-time PCR, FLOTAC technique, KK method. Outcome: sensitivity and specificity (95% CI:)	Sensitivity/specificity (95% CI): PCR + pseudo-standard PCR 17.4 (8–31)/3.9 (89–97); Baermann + pseudo-standard 47 (23–72)/78.4 (72 -84); PCR + multiple gold standard 30.9 (19.1–44.8)/100 (100–100); Baermann + multiple gold standard 83.6 (71.2–92.2)/100 (100–100)

AWA: adult worm antigen; AMSTAR: a tool for assessing the methodological quality of systematic reviews ; APC: agar plate culture; CA: Cercarial antigen; CCA: circulatory cathodic antigen; CI: confidence interval; DOR: diagnostic odds ratio; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; ELISA: enzyme-linked immunosorbent assay; FLOTAC: novel multivalent faecal egg count method; ICT: Immuno chromatographic test; IFAT: indirect fluorescent antibody technique; IHA: indirect haemagglutination: In Vitro Diagnostic kit; KK: Kato–Katz method; LIPS: luciferase immunoprecipitation system; LR+: positive likelihood ratio; LR−: negative likelihood ratio; NIE: a 31-kDa recombinant antigen; NovaTec: NovaTec Immundiagnostica, Dietzenbach,Germany; NPV: negative predictive value; POC: point-of-care; qPCR: quantitative PCR (real-time polymerase chain reaction); PPV: positive predictive value; RCT: randomised controlled trial; SEA: soluble egg antigen; Ss-NIE-1: a luciferase tagged recombinant protein of *St. stercoralis* for IgG and IgG_4 specific antibodies; QUADAS-2: a tool for the quality assessment of diagnostic accuracy studies; Viramed®: Viramed Biotech, Planegg, Germany).

Table 2. Characteristics of included studies about efficacy of treatment for schistosomiasis and strongyloidiasis, 1993–2016.

Study	Quality	Design	Population	Intervention/Outcomes	Results
Treatment efficacy of anti-Schistosoma drugs					
Kramer et al., 2014 [48]	AMSTAR: 11/11 Data in study: GRADE: high-quality evidence	Systematic review, fixed effects meta-analysis; Embase, MEDLINE (1966 to 2014), LILACS, Cochrane library, Cochrane infectious disease (1980–2014)	School-aged and young adults: 6–20 years (16 trials); 2–23 years (5 trials); Adults (2 trials). Participants setting: Rural areas in 15 sub-Saharan African countries; an urban setting in Saudi Arabia	Interventions: drugs used to treat urinary schistosomiasis: praziquantel, metrifonate, artesunate and/or in combination Outcome: parasitological cure or failure at 4 weeks; % egg reduction rate at 4 weeks	Praziquantel (single dose 40 mg/kg), egg reduction (60%) in urine achieved in 4–8 weeks (38 per 100 (95% CI: 26–54). Treatment failure: RR 0.42, (95% CI: 0.29–0.59), 864 participants, 7 trials Metrifonate (single dose 10 mg/kg) reduced egg excretion only marginally in comparison to placebo (RR 0.63, 95% CI: 0.54 to 0.73) 210 participants, 1 trial, at 8 months
Danso-Appiah et al., 2013 [47]	AMSTAR: 11/11 Data in study: GRADE: low- to moderate-quality evidence	Systematic review and meta-narrative of RCTs, RTCs of anti-Schistosoma drugs	Trials conducted in Africa (n = 36), South America (n = 15; all in Brazil) and the Middle East (n = 1). 52 trials enrolling 10,269 participants in endemic areas	Intervention: praziquantel 40 mg/kg, oxamniquine 40 mg/kg	Praziquantel (single dose 40 mg/kg) vs placebo: reduced parasitological treatment failure at 1 month (69/100; RR = 3.13, 2 trials, 414 participants). Praziquantel (single dose 30 mg/ kg): RR = 1.52, 3 trials, 521 participants. Higher doses: no significant difference. Oxamniquine (single dose 40 mg /kg) vs Placebo: reduced parasitological treatment failure at 3 months in 2 trials (68/100; RR = 8.74).
Pérez del Villar et al., 2012 [49]	AMSTAR: 11/11 Data in study: not reported. GRADE: Moderate-quality evidence	Quantitative systematic review and meta-analysis	Healthy villagers who live in areas in Africa endemic for *Sc. haematobium* and *Sc. mansoni* and in China for *Sc. Japonicum*	Intervention: prophylactic effect of artesunate or artemether vs placebo against *Sc. haematobium*, *Sc. mansoni* and *Sc. japonica* infections. Outcomes: parasitological cure rate at 3–8 weeks; infection rate at 3–4 weeks after treatment.	Artesunate treatment (single dose: significantly lower cure rates than with praziquantel. Combined therapy of artesunate plus sulfadoxine-pyrimethamine: significantly less effective than praziquantel treatment Combination of artemisinin derivatives and praziquantel: higher cure rate than praziquantel monotherapy Artesunate or artemether: significantly better than a placebo.
Treatment efficacy of drugs for strongyloidiasis					
Henriquez-Camacho et al., 2016 [52]	AMSTAR: 11/11 GRADE: Moderate-quality evidence	Systematic review of RCTs, controlled or uncontrolled interventional studies.	Individuals with chronic infections of *St. stercoralis*; Immuno-competent patients. All ages	Intervention: ivermectin (single/double dose) vs albendazole or thiabendazole. Outcome: elimination of infection; parasitological cure (> 2 negative stool samples, 5 weeks).	Ivermectin (single/double dose) vs albendazole: parasitological cure was higher with ivermectin, 84/100 vs 48/100 ivermectin (RR = 1.79). Ivermectin vs thiabendazole: little or no difference in parasitological cure, 74/100 vs 68/100), but adverse events were less common with ivermectin (RR = 0.31) than albendazole. No serious adverse events or death reported

AMSTAR: a tool for assessing the methodological quality of systematic reviews; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; LILACS: Latin American Literature in Health Sciences; RCT: randomized clinical trial; RR: Relative Risk.

Table 3. Characteristics of included studies on cost-effectiveness of screening and treatment of schistosomiasis and strongyloidiasis, 1993–2016.

Study	Quality	Design	Population	Intervention/Outcomes	Results
Libman et al., 1993 [70]	NA	Retrospective-cross-sectional study with cost analysis	Cohort of individuals returning from the tropics and screened in a Canadian clinic 1981–1987 Costs in 1988 CAD	Stool examination + eosinophil count + serological studies for filariasis and schistosomiasis (gold standard); vs stool examination + eosinophil count; vs stool examination alone; vs stool examination + serological studies; vs eosinophil counts only Outcome: difference in cost or resource use/cost effectiveness	Difference in resource use/costs: high-/low-prevalence locations Costs per case of schistosomiasis and/or strongyloidiasis diagnosed for each strategy: (i) CAN$4674[€3693]; (ii) CAN$6111[€4829]; (iii) CAN$4788[€3783]; (iv) CAN$3737[€2953]; (v) CAN$3307[€2613] Cost-effectiveness (ICER or INB): no ICER calculated. Study did not include a decision analytic model
Muennig et al., 1999 [66]	NA	Decision analytic model	Large immigrant populations in which *St. stercoralis* is not endemic (one third of the sample population was from the state of New York) Costs in 1997 USD	No preventive intervention (watchful waiting) vs universal screening vs presumptive treatment with albendazole Outcome: difference in cost or resource use/cost effectiveness (ICER or INB) per DALY averted	Difference in resource use/costs: gross costs: USD 11,086,181 [€7,228,785] for no intervention, USD 7,290,624 [€40,203,726] per year for treatment with albendazole, USD 40,547,651[€40,203,726] for universal screening Cost-effectiveness (ICER or INB): treatment with albendazole was cost saving compared with no intervention, universal screening had ICER of USD 159,236/DALY [€157,885/DALY] averted
Muennig et al., 2004 [67]	NA	Decision analytic model (Markov)	California and New York, two states with large immigrant populations in which *St. stercoralis* is not endemic Costs in 2000 USD	Intervention: no intervention (watchful waiting) vs 3 or 5 days of albendazole vs eosinophil screening vs ivermectin Outcome: difference in cost or resource use/cost effectiveness (ICER or INB)	Difference in resource use/costs: costs per person: no intervention USD 1666[€1611], albendazole 3 days USD 1674[€1618], albendazole 5 days USD 1680 [€1624], screening USD 1684 [€1628], ivermectin USD 1688 [€1632] Cost-effectiveness (ICER or INB): ICERs varied based on prevalence: albendazole USD 155–1584/QALY gained [€150–1531], albendazole 5 days USD 314–3175/QALY gained [€304-3069], ivermectin USD 848–8514/QALY gained [€820-8231]. Eosinophil was documented among all prevalence groups
King et al., 2011 [65]	AMSTAR	Systematic review of efficacy of schistosomiasis treatment with praziquantel (by dose), with a Markov model estimating cost-effectiveness of various dosing strategies	Non-migrants in endemic setting; population-based or sub-population-based (e.g., schools) drug treatment of *Sc. haematobium* or *Sc. Mansoni*. Costs in 2002 & 2008 USD	Intervention: No treatment vs single dose of praziquantel per annual treatment vs double dose Outcome: difference in cost or resource use/cost effectiveness (ICER or INB)	Difference in resource use/costs: single dose lifetime cost: USD 23 [€19] per person; double dose: USD 46 [€35] per person. Cost-effectiveness (ICER or INB): single dose: ICER of USD 48 [€39] and USD 46[€37] per QALY gained *for Sc. mansoni* and *Sc. haematobium*, respectively, compared with no treatment; double dose: ICERs of USD 291 [€236] and USD 433 [€351] per QALY gained respectively compared with single dose

Worrell et al., 2015 [69]	NA	Cost analysis study	Cohort of children in Kenya assessed 2010–2011. Non-migrant settings. Costs in 2010 USD	Intervention: single KK (stool examination) vs triplicate KK vs POC CCA (urine dipstick) Outcome: difference in cost or resource use/cost effectiveness (ICER or INB)	Difference in resource use/costs: total costs per test: single KK USD 6.89[€5], triplicate KK USD 17.54[€14], POC CCA USD 7.26[€6] Cost-effectiveness (ICER or INB): no ICER calculated, this was not a decision analysis study.
Maskery et al., 2016 [68]	NA	Cost analysis study; Markov model: discount rate of 3% over 60-year time horizon; costs in 2013 USD	Average annual cohort of 27,700 Asian refugees based on Department of Homeland Security data for 2002–2011, primarily from south-east Asia and the Middle East	Intervention: no screening or treatment vs overseas albendazole and ivermectin treatment vs domestic screening and treatment vs overseas albendazole and domestic screening for strongyloidiasis. Outcome: difference in cost or resource use/cost effectiveness (ICER or INB)	Difference in resource use/costs, total costs per migrant (strongyloidiasis.): no treatment USD 5.99[€5], overseas albendazole and ivermectin USD 15.12[€12], domestic screening and treatment USD 138.36[€108], overseas albendazole and domestic screening for Strongyloides infection USD 78.79[€61]. Cost-effectiveness: ICERs per QALY gained: USD 2219 for "overseas albendazole and ivermectin", USD 32,706[€25,422] for domestic screening and treatment, USD 18,167[€14,121] for overseas albendazole followed by domestic screening for strongyloidiasis. All vs no screening or treatment [€1723]

AMSTAR: A measurement tool to assess systematic reviews; CAD: Canadian dollars; CCA: circulatory cathodic antigen; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; ICER: incremental cost-effectiveness ratio, INB: incremental net benefit; NA: Not Applicable KK: Kato–Katz; POC: point-of-care; USD: United States dollars.

3.1. Screening: Diagnostic Test Accuracy for Schistosomiasis

We assessed diagnostic and screening tools for *Schistosoma* spp. in five included systematic reviews [44–46,50,53] and eight individual studies [54–61]. The best performing tests were included in the GRADE summary of finding on diagnostic tools for screening schistosomiasis (Tables 4 and Figure 5).

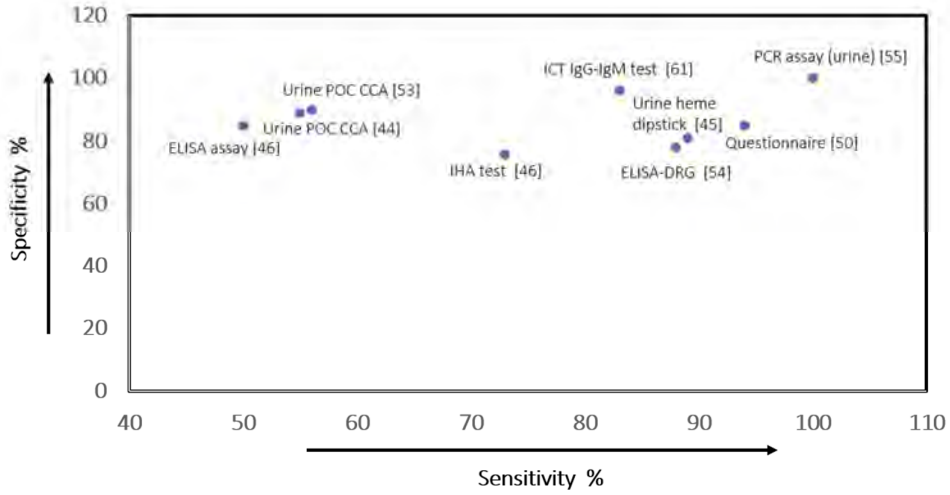


Figure 5. Scatter plot of sensitivity versus specificity values of the Index diagnostic tools for screening schistosomiasis.

3.1.1. *Schistosoma Mansoni*

A meta-analysis reported estimated sensitivity and specificity values of 89% (95% CI: 86–92) and 55% (95% CI: 46–55) respectively, for the urinary circulating cathodic antigen (CCA) assay that detects *Sc. mansoni* in endemic areas [44]. Another urinary CCA test for *Sc. mansoni* [53] reported sensitivity and specificity values of 90% (95% CI: 84–94) and 56% (95% CI: 39–71), respectively compared with the duplicate Kato–Katz (KK) test (moderate-quality evidence) (Table 4). From the included primary studies, PCR assay in urine was the best-performing diagnostic test for *Sc. mansoni* with a sensitivity of 100% (95% CI: 95–100) compared with the CCA test—65% (95% CI: 56–77) and KK test—57% (95% CI: 46–68) [55] (very low-quality evidence); the specificity of PCR assay in urine was 100% (95% CI: 69–100) (Table 4) [55]. Espírito-Santo et al. reported sensitivity and specificity of 80% (95% CI: 28–99) and 92.4% (95% CI: 90–94), respectively for quantitative PCR (qPCR) in faeces compared with the KK test (not included in the GRADE Summary of findings) [56].

In low-endemic settings, the best-performing diagnostic test was the IgM-ELISA assay with sensitivity and specificity values of, respectively, 82% (95% CI: 64–93) and 82% (95% CI: 79–85)-low-quality evidence (Table 1) [57]. In another study, the ELISA-DRG kit showed the best accuracy with sensitivity and specificity values of, respectively, 78% (95% CI: 61–90) and 95% (95% CI: 89–98) (Table 4) [54]. In a recent study on the accuracy of different screening tests for schistosomiasis in African migrants, the immuno chromatographic test (ICT) IgG-IgM showed the best accuracy, with sensitivity and specificity values of 96% (95% CI: 91–99) and 83% (95% CI: 77–87) (Table 4) [61]. In all the individual studies, the certainty of evidence was very low to low.

3.1.2. *Schistosoma Haematobium*

The urine heme dipsticks for the diagnosis of *Sc. haematobium* showed a mean sensitivity and specificity of 81% (95% CI: 73–83) and 89% (95% CI: 87–92), respectively, and were more accurate in high-prevalence than in low-prevalence settings -low-quality evidence (Table 4) [45]. Similarly, Ochodo et al. reported sensitivity and specificity values of 75% (95% CI: 71–79) and 87% (95% CI: 84–90)-

low-quality evidence (Table 1) [44]. Furthermore, a meta-analysis on the diagnostic efficiency of questionnaire screening for schistosomiasis reported sensitivity and specificity values of 85% (95% CI: 84–86) and 94% (95% CI: 94–94) for *Sc. haematobium* infections (low-quality evidence) (Table 4) [50].

Kinkel et al. evaluated the accuracy of antibody-detection tests for diagnosis of imported *Sc. haematobium* [54]. The indirect haemagglutination (IHA) test with a sensitivity of 73% (95% CI: 56–86) and specificity of 99% (95% CI: 94–100) and the ELISA-DRG with a sensitivity of 78% (95% CI: 61–90) and specificity of 95% (95% CI: 89–98) demonstrated the best accuracy (certainty of evidence low) (Table 4) [54]. In another study, the ICT IgG-IgM test showed the best accuracy with sensitivity of 96% (95% CI: 91–99) and specificity of 83% (95% CI: 77–87) (Table 4) [61].

3.1.3. *Schistosoma Japonicum*

In a meta-analysis of the accuracy of antibody detection of *Sc. japonicum* infection in humans, pooled sensitivities and specificities were 76% (95% CI: 74–77) and 73% (95% CI: 72–74) for the IHA test and 85% (95% CI: 83–87) and 50% (95% CI: 49–52) for ELISA (Table 4) [46].

The evidence also suggests that accuracy of diagnostic tests for schistosomiasis depends on pre-test prevalence (Table 5). As prevalence increased (from 2.5% to 30%), the estimated number of false-positives per 1000 migrants tested decreased with all tests—from 47 to 34 (*Sc. haematobium*/*Sc. mansoni*) [54], 58 to 42 (*Sc. haematobium*) [44], 107 to 77 (*Sc. Haematobium*) [45] and 166 to 119—(*Sc. haematobium*/*Sc. mansoni*) [61] per 1000 for ELISA-DRG, questionnaire screening, urine heme dipsticks and ICT IgG-IgM, respectively. The estimated false-negative tests were between 0–6 and 0–73 per 1000 at 2.5% and 30% prevalence for all the tests. At 2.5% pre-test prevalence, the proportion of correctly diagnosed schistosomiasis infections in migrant populations was 100% for the urine PCR assay, 96% for the ICT IgG-IgM test, 90% for the urine POC CCA, 85% for the questionnaire screening and 84.9% for *Sc. japonicum* ELISA (Table 5).

3.2. Screening: Diagnostic Test Accuracy for Strongyloidiasis

We assessed diagnostic and screening tools for *St. stercoralis* in two included systematic reviews [19,51] and three individual studies (Tables 1 and 6) [62–64].

Table 4. GRADE summary of findings on diagnostic tools for screening schistosomiasis, 1993–2017

Index Test at Median Test Prevalence in Study *	Sensitivity (95% CI)	Specificity (95% CI)	Post-Test Probability of a Positive Result (95% CI)	Post-Test Probability of a Negative result (95% CI)	Number of Studies/ Participants	Certainty of Evidence (GRADE)	Reference Standard
PCR assay (filtered urine) at 89% prevalence—*Sc. mansoni* [55]	1.00 (0.95–1.00)	1.00 (0.69–1.00)	100% (96–100)	0% (37–0)	1/89	Very Low [a,b,c]	KK test—duplicate smears
Urine POC CCA test at 36% prevalence—*Sc. mansoni* [44]	0.89 (0.86–0.92)	0.55 (0.46–0. 65)	53% (47–60)	10% (15–7)	15/6091	Very Low [a,b,c]	Stool microscopy
Urine POC CCA test at 30% prevalence—*Sc. mansoni* [53]	0.90 (0.84–0.94) [d]	0.56 (0.39–0.71) [d]	47% (37–58)	7% (15–3)	7/4584	Moderate [a,b]	KK test
Questionnaire screening 30% prevalence—*Sc. haematobium* [50]	0.85 (0.84–0.86) [d]	0.94 (0.94–0.94) [d]	86% (86–86)	6% (7–6)	12/41,412	Low [c,e]	Urine filtration/microscopy
ELISA-DRG (commercial kit) at 26% prevalence—All cases [54]	0.78 (0.61–0.90)	0.88 (0.80–0.94)	85% (65–95)	7% (13–4)	1/37	Very Low [c,e,f]	Stool/urine microscopy
Urine heme dipstick at 27% prevalence—*Sc. haematobium* [45]	0.81 (0.73–0.83) [d]	0.89 (0.87–0.92) [d]	73% (67–79)	7% (10–6)	98/126,119	Low [a,f,g]	Urine microscopy
ELISA at 24% prevalence—*Sc. japonicum* [46]	0.85 (0.83–0.87)	0.50 (0.49–0.52)	35% (34–36)	9% (10–7)	10/9014	Low [a,f,g]	KK and Miracidium hatching test
IHA at 12% prevalence—*Sc. japonicum* [46]	0.76 (0.72–0.74) [d]	0.73 (0.72–0.74) [d]	28% (26–28)	4% (5–5)	15/23,411	Low [a,b]	KK and Miracidium hatching test
ICT IgG-IgM test at 17% prevalence *Sc. mansoni* and *Sc. haematobium* [61]	0.96 (0. 91–0.99)	0.83 (0.77–0.87)	13% (9–16)	0% (0–0)	1/373	Low [b,c]	Stool/urine microscopy/ composite standard.

Population: patients with schistosomiasis or stored sera; Settings: high-/low-endemic settings; Target condition: Schistosoma spp. Infections. GRADE: Grading of Recommendations, Assessment, Development and Evaluation. Tests—CCA: circulating cathodic antigen; CI: confidence interval; DRG: DRG Instruments, Marburg, Germany; ELISA: enzyme-linked immunosorbent assay; IHA: indirect haemagglutination; KK: Kato–Katz; POC: point-of-care. *Post-test probability of test was calculated at median test prevalence obtained from individual studies.

a. Heterogeneity across similar studies because of several factors; downgraded because of serious inconsistency.
b. Use of intermediate or surrogate outcomes rather than health outcomes, hence a source of serious indirectness.
c. Single study design, not a randomised control trial.
d. Sensitivity and specificity values obtained from multiple-field study.
e. Use of indirect comparisons; sample population not migrants, another source of indirectness.
f. Very low-quality of evidence (downgraded by 1) because of serious indirectness.
g. Studies were insufficient to provide summary estimates for CAA tests.

Table 5. Accuracy of diagnostic tools for schistosomiasis at different pre-test prevalence levels, January 2010–February 2017

Index Test	True Positives Pre-Test Probability *			False Positives Pre-Test Probability *			True Negative Pre-Test Probability *			False Negative Pre-Test Probability			% Infected Correctly Diagnosed
Test % Prevalence [a]	**2.5%**	**10%**	**30%**	**2.5%**	**10%**	**30%**	**2.5%**	**10%**	**30%**	**2.5%**	**10%**	**30%**	
PCR assay (filtered urine)—Sc. mansoni [55]	25	100	300	0	0	0	975	900	700	0	0	0	100%
ICT IgG-IgM test—*Sc. haematobium*/ *Sc. mansoni* [61]	24	96	288	166	153	119	809	747	581	1	4	12	96%
Urine POC CCA test—*Sc. mansoni* [53]	23	90	270	429	396	308	546	504	392	2	10	30	90%
Questionnaire screening—Sc. haematobium [50]	21	85	255	58	54	42	917	846	658	4	15	45	85%
ELISA-DRG (commercial kit) – *Sc. haematobuim*/ Sc. mansoni [54]	20	78	235	47	43	34	928	857	666	5	22	65	78.3%
Urine heme dipstick—*Sc. haematobium* infections [45]	20	81	243	107	99	77	868	801	623	5	19	57	81.0%
ELISA—Sc. japonicum [46]	21	85	255	484	446	347	491	454	353	4	15	45	84.9%
IHA—Sc. japonicum [46]	19	76	227	263	243	189	712	657	511	6	24	73	75.6%

[a] Different pre-test prevalence or probability of having schistosomiasis in an at-risk population.

* Data reported as effect per 1,000 migrants tested. Tests: DRG: DRG Instruments, Marburg, Germany; ELISA: enzyme-linked immunosorbent assay; ICT: Immuno chromatographic test; IHA: Indirect haemagglutination; PCR: Polymerase chain reaction assay; POC: Point of care.

Table 6. GRADE summary of findings on diagnostic tools for screening strongyloidiasis, January 1993–February 2017

Index Test—at 10% Prevalence *	Sensitivity (95% CI)	Specificity (95% CI)	Post-Test Probability of a Positive Result (95% CI)	Post-Test Probability of a Negative Result (95% CI)	Number of Studies/ Participants	Certainty of Evidence (GRADE)	Reference Standard
Baermann method [51]	0.72 (0.67–0.76) [a]	1.00 (1.00–1.00) [a]	100% (100–100)	3% (4–3)	9/2459	Moderate [b,c]	Combination of diagnostic tests
Agar plate—10% prevalence [51]	0.89 (0.86–0.92) [a]	1.00 (1.00–1.00) [a]	100% (100–100)	1% (2–1)	10/3,563	Moderate [b,c]	Combination of diagnostic tests
NIE LIPS [62] [d]	0.85 (0.79–0.92)	0.95 (0.93–0.98)	65% (56–84)	2% (2–1)	1/399	Low [e,f,g]	Stool microscopy or culture
IVD ELISA—commercial test [62]	0.92 (0.87–0.97)	0.97 (0.96–0.99)	77% (71–92)	1% (1–0)	1/399	Low [e,f,h]	Stool microscopy
IFAT [62]	0.94 (0.90–0.98)	0.87 (0.83–0.91)	45% (37–55)	1% (1–0)	1/399	Low [e,f,h]	Stool microscopy and culture
Bordier-ELISA—commercial kit [62]	0.91 (0.86–0.96)	0.94 (0.91–0.96)	63% (52–77)	1% (2 –0)	1/193	Low [e,f,h]	Kato–Katz, Flotac, and Baermann method
SS-NIE-1 ELISA [63]	0.95 (0.92–0.97)	0.93 (0.90–0.96)	60% (71–73%)	1% (1–0)	1/583	Low [f,g,i]	Stool microscopy and culture

Notes: Population: patients with strongyloidiasis or sera infected with *St. stercoralis*; Settings: low-/high-endemic areas; Target condition: strongyloidiasis (test prevalence 10%). Cost effectiveness: serological testing may be cost-effective relative to stool and eosinophil testing for both strongyloidiasis and schistosomiasis, because of superior test performance characteristics.

Tests: ELISA: enzyme-linked immunosorbent assay; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; IFAT: indirect fluorescent antibody technique; IVD: Invitro diagnostic test; LIPS: luciferase immunoprecipitation system; NIE: a 31-kDa recombinant antigen from *St. stercoralis*. *Post-test probability of test was calculated at 10% prevalence for all the tests.

a. Sensitivity and specificity values obtained from a multiple-field study.
b. Evidence was downgraded because of serious inconsistencies and heterogeneity.
c. Heterogeneity between studies; use of intermediate or surrogate outcomes rather than health outcomes.
d. Test result with a primary standard.
e. Absence of a reliable gold standard for diagnosis of *S. stercoralis* infection. The review did not describe the specific gold standard used in the included studies for each test.
f. Single study design.
g. Samples were classified according to a composite reference standard, a procedure suggested for evaluation of diagnostic tests when there is no gold standard.
h. Use of intermediate or surrogate outcomes rather than health outcomes.
i. The inter-assay coefficient of variation was determined to be 22% for the low-positive control serum and 10% for the medium-positive control serum.

The best conventional diagnostic tools for *St. stercoralis* have been agar plate culture with a sensitivity and specificity of 89% (95% CI: 86–92) and 100% (95% CI: 100–100) respectively, and the Baermann method with a sensitivity and specificity of 72% (95% CI: 67–76) and 100% (95% CI: 100–100) respectively (moderate certainty of evidence) [51]. Knopps et al. reported a much lower sensitivity value of 31% (95% CI: 19.1–44.8) for PCR in stools compared with a combination of stool-based methods as the gold standard; specificity was 100% (95% CI: 100–100) [64].

Serological antibody detection methods have demonstrated greater sensitivity compared with classical parasitological techniques [19]. Bisoffi et al. reported the accuracy of five serological tests for detection of strongyloidiasis [62]. The sensitivity and specificity values were: 85% (95% CI: 79–92) and 100% (95% CI: 100–100) for the luciferase-immunoprecipitation system (LIPS) using 31-kD recombinants antigen from *St. stercoralis* (NIE); 75% (95% CI: 66–83) and 95% (95% CI: 91–99) for the NIE-ELISA (using the same antigen); 91% (95% CI: 86–96) and 99% (95% CI: 97–100) for the IVD-ELISA; 90% (95% CI: 84–95) and 98% (95% CI: 96–100) for the Bordier-ELISA; and 94% (95% CI: 90–98) and 92% (95% CI: 87–97) for the indirect fluorescent antibody technique (IFAT) (low certainty of evidence) [62] (Figure 6). Rascoe et al. reported comparable values for two new recombinant antigens in antibody detection assays: SS-NIE-1 ELISA with sensitivity of 95% (95% CI: 92–97) and specificity of 93% (95% CI: 90–96), and Ss-NIE-1 Luminex with sensitivity of 93% (95% CI: 86–96) and specificity of 95% (95% CI: 93–97) (Table 6) [63].

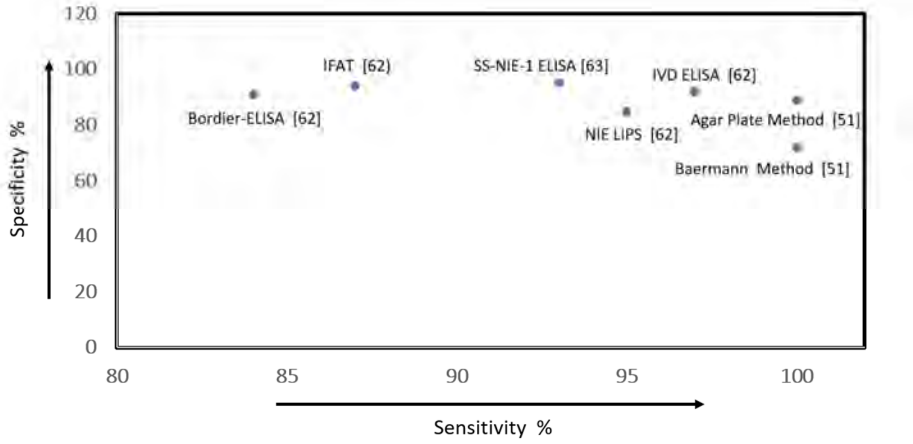


Figure 6. Scatter plot of sensitivity versus specificity values of the Index diagnostic tools for screening strongyloidiasis

As with schistosomiasis, estimates of false-positive tests per 1000 tested decreased with increasing pre-test prevalence, from 29 to 21, 58 to 42 and 68 to 49 for IVD-ELISA, Bordier-ELISA and SS-NIE-1 ELISA assays, respectively [62,63]. The estimated number of false-positive tests for the Baermann and Agar plate methods was 0 at all pre-test prevalence levels. Lower numbers of false-negatives were estimated for all the serological tests, for example, 1 and 15, and 2 and 24, per 1000 tests for SS-NIE-1 and IVD-ELISA at 2.5% and 30% prevalence levels compared with 3 and 33, and 7 and 84, per 1000 for the Agar plate and Baermann methods. At 2.5% pre-test prevalence, the proportion of correctly diagnosed *Strongyloides* infections in migrant populations was 95% for the SS-NIE-1 ELISA, 93.8% for IFAT, 92% for IVD-ELISA and 90.7% for Bordier-ELISA, compared with 72% and 89% for the Baermann and Agar plate methods (Table 7).

3.3. Treatment Efficacy: Schistosomiasis and Strongyloidiasis

We evaluated four included systematic reviews on treatment of schistosomiasis and strongyloidiasis (Tables 8 and 9) [47–49,52]. In a Cochrane review, the efficacy of praziquantel (single 40 mg/kg dose) showed much lower parasitological failure in urine (<53%) at 1 to 2 months (RR = 0.42;

95% CI: 0.29–0.58) compared with placebo [48]. The proportion of people cured with praziquantel varied substantially between trials, from 22.5% to 83.3%, but was higher than 60% in five of the seven trials [48]. Similarly, in another Cochrane review, parasitological cure rate for *Sc. mansoni* infection at one month with praziquantel (single 40 mg/kg dose) varied substantially across studies, ranging from 52% to 92% in Brazil in 2006 and 2007, for example parasitological cure 66% more in intervention group compared with placebo (RR 3.13; 95% CI: 1.03–9.53) (Table 8) [47]. Pérez del Villar et al. compared the efficacy of praziquantel and artemisinin derivatives and reported that artesunate showed significantly lower cure rates than praziquantel 30% vs 61% (RR 0.49 (0.28–0.75)) [49]. Artemeter monotherapy (6mg/kg single dose) reduced *Sc. Japonicum* infection rates in patients (RR = 0.25; 95% CI: 0.16–0.40). However, a combination of artemisinin derivatives plus praziquantel showed higher cure rates than praziquantel monotherapy (RR = 1.25; 95% CI: 1.09–1.37) in areas with intense transmission (moderate certainty of evidence) (Table 8) [49]. No significant adverse events were reported.

Table 7. Accuracy of diagnostic tools for strongyloidiasis at different pre-test prevalence levels, 2012–February 2017

Index tests	True-Positives Pre-Test probability [a]			False-Positives Pre-Test probability [a]			True-Negatives Pre-Test probability [a]			False-Negatives Pre-Test probability [a]			% Infected Correctly Diagnosed
Test % prevalence [b]	**2.5%**	**10%**	**30%**	**2.5%**	**10%**	**30%**	**2.5%**	**10%**	**30%**	**2.5%**	**10%**	**30%**	
Baermann method [51]	18	72	216	0	0	0	975	900	700	7	28	84	72%
Agar plate [51]	22	89	267	0	0	0	975	900	700	3	11	33	89%
NIE -LIPS [62]	21	85	255	49	45	35	926	855	665	4	15	45	85.1%
IVD-ELISA (commercial test) [62]	23	92	276	29	27	21	946	873	679	2	8	24	92%
IFAT [62]	23	94	282	127	117	91	848	783	609	2	6	18	93.8%
Bordier- ELISA (commercial kit) [62]	23	91	272	58	54	42	917	846	658	2	9	28	90.7%
SS-NIE-1 ELISA [63]	24	95	285	68	63	49	907	837	651	1	5	15	95%

ELISA: enzyme-linked immunosorbent assay; IFAT: indirect fluorescent antibody technique; IVD: Invitro diagnostic test; LIPS: luciferase immunoprecipitation system; NIE: 31-kDa recombinant antigen from *St. stercoralis.*

a. Data reported as effect per 1,000 migrants tested.

b. pre-test prevalence or probability of having schistosomiasis in an at-risk population.

Table 8. GRADE summary of findings of different schistosomiasis treatments vs placebo, 2010–2016

Outcomes	Anticipated Absolute Effects [a] (95% CI)		Relative Chance of Cure (95% CI)	Number of Participants/Studies	Certainty of the Evidence (GRADE)
	Risk with Placebo per 1000	Cure with Intervention Drug			
Parasitological failure at 1 to 2 months (praziquantel 40 mg/kg single dose) [48]	908	381 (263–562)	RR 0.42 (0.29 to 0.58)	864/7 RCTs	High
Parasitological cure at 1 month b—Sc. mansoni infections (praziquantel 40 mg/kg single dose) [47]	337	1000 (347–1000)	RR 3.13 (1.03–9.53)	414/2 RCTs	Moderate c
Microhaematuria at 8 weeks (praziquantel 40 mg/kg single dose) [48]	281	149 (93–236)	RR 0.53 (0.33–0.84)	119/1 RCT	Low [d,e,f]
Infection rate of *Sc. japonicum* (artemether monotherapy 6 mg/kg) [49]	175	44 (28–70)	RR 0.25 (0.16–0.40)	8051/13 RCTs	Moderate [c]
Parasitological cure rate of *Schistosoma species*. (Artesunate—monotherapy (4 mg/kg daily for three consecutive days)) [49]	615 *	302 (172–459)	RR 0.49 (0.28–0.75)	800/7 RCTS	Moderate [c]
Adverse events, minor (praziquantel 40 mg/kg single dose) [49]	None	None	Not estimable	1591/9 RCTs	Low [d]

CI: confidence interval; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; RR: risk ratio; RTC: randomized controlled trial.
* praziquantel 40 mg/kg once.

a. The risk in the intervention group per 1000 persons treated (95% CI) was based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
b. Treatment of only *Sc. mansoni* infections reported.
c. Downgraded by 1 for indirectness: only two trials from limited settings evaluated this comparison.
d. The trial was under-powered; downgraded by 1.
e. Only a single trial reported this outcome.
f. Publication bias was unclear.

Table 9. GRADE summary of findings on ivermectin (200 mg/kg) vs albendazole or thiabendazole for the treatment of strongyloidiasis, and certainty of evidence on treatment efficacy, benefits and harms, 2010–2016

Outcomes	Anticipated Absolute Effects (95% CI)		Relative Chance of Cure (95% CI) [b]	Number of Participants /Studies	Certainty of the Evidence (GRADE)
	Cure with Comparator Drug per 1000 [a]	Cure with Intervention Drug—Ivermectin (200 mg/kg) [b]			
Cure overall assessed at 5 weeks—albendazole [52]	480	840 (720–980)	RR 1.79 (1.55–2.08)	478/4 RCTs	Moderate [d]
Adverse events assessed at 5 weeks—albendazole [52]	260	210 (150–290)	RR 0.80 (0.59–1.09)	518/4 RCTs	Low [c,g]
Cure overall assessed at 11 weeks—thiabendazole [52]	690	740 (660–820)	RR 1.07 (0.96–1.20)	467/3 RCTs	Moderate [e]
Adverse events assessed at 11 weeks—thiabendazole [52]	730	230 (150–360)	RR 0.31 (0.20–0.50)	507/3 RCTs	Moderate [f]

PICO—Patient or population: sersons with Strongyloides stercoralis infection; Setting: south-east-Asia, America and Europe; Intervention: ivermectin; Comparison: albendazole and thiabendazole. CI: confidence interval; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; RR: risk ratio; RTC: randomized controlled trial.

a. Albendazole or thiabendazole.
b. The risk in the intervention group per 1000 persons treated (95% CI) was based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
c. No method of allocation concealment in two trials and no method of allocation described.
d. Two trials did not conceal allocation and no method of allocation was described.
e. Two trials did not conceal allocation and no method of allocation was described in one trial.
f. Two trials did not conceal allocation and no method of allocation was described.
g. Wide range of estimates in three trials could include substantive fewer events.

Only one systematic review was included which addressed the efficacy of ivermectin vs albendazole or thiabendazole for treating chronic strongyloidiasis infection (Table 9) [52]. Parasitological cure determined with both serological and conventional techniques was higher with ivermectin (single-/double-dose) treatment than with albendazole 84% vs 48% (RR = 1.79; 95% CI: 1.55–2.08) (moderate-quality evidence) [52]. When ivermectin was compared with thiabendazole, there was no distinction in parasitological cure, i.e. 74% vs 68% (RR = 1.07; 95% CI: 0.96–1.2), but adverse events were less frequent with ivermectin (RR = 0.31; 95% CI: 0.20–0.50) than with thiabendazole [52] (moderate certainty of evidence). No serious adverse events or deaths were reported with either ivermectin or thiabendazole.

3.4. Resource use, Costs and Cost-Effectiveness

3.4.1. Strongyloidiasis

Three economic studies of moderate quality support a strategy of presumptive treatment for strongyloidiasis in migrants from high-risk backgrounds [66–68]. One study showed potential cost savings of universal treatment with albendazole compared with i) no intervention (watchful waiting); and compared with ii) universal stool-based screening; in migrant populations in the U.S. [66]. Sensitivity analyses indicated a best-case scenario of large savings from presumptive treatment, and a worst-case scenario in which treatment was still cost effective at the $30,000/QALY threshold (1997 U.S. dollars).

The second study on presumptive treatment for strongyloidiasis in migrants living in the U.S. in California and New York compared: i) presumptive treatment with albendazole for 3 or 5 days; ii) presumptive treatment with one dose of ivermectin; iii) treatment in those with documented eosinophilia; and iv) no intervention [67]. It indicated that presumptive treatment with ivermectin was cost-effective at a threshold of less than USD 10,000 (EUR 9667) per QALY across a range of prevalence values in migrants living in the U.S. [67]. This study did not include antibody detection among the diagnostic tools. At a prevalence higher than 10%, treatment with ivermectin cost less than USD 2000 (EUR 1983) per QALY. These results were robust across a wide range of sensitivity analyses [67].

The third more recent study on presumptive treatment for hookworm and strongyloidiasis in U.S.-bound Asian populations indicated that treatment in the destination country with albendazole and ivermectin was likely to be cost-effective relative to no screening or screening and treatment strategies in the country of origin among refugees from high-prevalence countries [68]. For strongyloidiasis, overseas treatment cost less than USD 40,000 (EUR 31,092) per QALY gained at prevalence greater than 1% and fell to less than USD 18,000 (EUR 13,991) per QALY gained at prevalence greater than 3%.

3.4.2. Schistosomiasis

There were no cost-effectiveness studies of screening and presumptive treatment in migrants at risk of schistosomiasis. In non-migrant populations, a recent costing study compared the costs of single and double KK tests with a urine dipstick test [69] for *Sc. haematobium* diagnosis in areas of high endemicity. The results of this preliminary costing study indicated similar costs of around USD 6–7 (EUR 5–6) per test for single KK stool and urine tests; however, the quality of evidence for resource use was low. A cost-effectiveness study by King et al. compared single-dose (40 mg/kg body weight) and double-dose (40 mg/kg doses separated by 2–8 weeks) presumptive treatment with praziquantel for schistosomiasis in high-prevalence (>40%) settings in Africa [65]. Double-dose praziquantel was found deemed to be highly cost-effective (ICER of less than USD 500 (EUR 471)/QALY) compared with single-dose treatment.

4. Discussion

The rationale for screening for strongyloidiasis and schistosomiasis in the EU/EEA and not other parasitic infections is based on the estimated prevalence of these parasitic infections among migrants

from endemic countries; potential prevention of fatal complications through early case detection and treatment, and secondary transmission in asymptomatic patients based on a highly sensitive test and very effective and safe treatment [11,35,36,71]. Therefore, the implementation of a screening programme would allow early detection of the infection in individuals at risk, before they develop a severe condition which may justify the screening itself.

Although quality data on the prevalence of schistosomiasis and strongyloidiasis among migrant populations in the EU/EEA is limited, available data from endemic regions shows that prevalence of schistosomiasis is between 20% and 40% and prevalence of strongyloidiasis is between 10% and 40% [3–5]. However, there is a rationale for public health surveillance for schistosomiasis and strongyloidiasis to inform proper surveillance of mobile population from the regions [30]

Overall, systematic reviews showed that antibody-detecting serological tests are the most effective screening tests for detection of schistosomiasis and strongyloidiasis in low-endemicity settings, because they have higher sensitivity than conventional parasitological methods [19,44,45,50,53]. Newer serological tests were shown to be more effective than conventional techniques such as agar plate culture and the Baermann method for strongyloidiasis and KK for *Sc. mansoni*. These conventional techniques, as well as PCR, failed to detect infections of very low intensity [64] although they were more specific than serological techniques [51,54]. They are also labor-intensive and require skilled personnel and are therefore not recommended as the first option for screening [19]. In contrast, serological testing is easier to perform in health facilities than collecting and testing faecal samples and can also be combined with other infectious disease screening tests.

One limitation of antibody-detecting serological tests, particularly with schistosomiasis, is that they cannot differentiate current from past infections; however, with strongyloidiasis, antibody titres decline after treatment over time in most patients [62,72]. In addition, in immuno-compromised patients, the sensitivity of serological tests may be reduced, and other additional screening methods may be needed if serology is negative. In this regard, the utility of PCR assay as an alternative screening method in immunosuppressed patients deserves further investigation.

Specifically, for *Schistosoma spp*. infections, available evidence shows that the IgM-ELISA [57], IHA [46] and ICT IgG-IgM [61] tests were the most effective screening tests in low-endemicity countries. In some low endemicity settings, two serological tests are performed, and a case is considered to be positive if either test is positive; in others, a combination of ELISA testing and KK faecal examinations is used to improve the accuracy of detection. However, Beltrame et al. advocate the use of the ICT IgG-IgM test as a single screening test (negative predictive value >97%) [61].

For strongyloidiasis, available evidence (of very low to low quality) shows that antibody-detecting blood tests using a variety of antigen preparations have a better detection rate than conventional parasitological methods, with IVD-ELISA, Bordier-ELISA and NIE LIPS being the most accurate tests [62]. Limitations of these serological tests include the large number of infective larvae required, cross–reactions with other nematode infections and lower sensitivity in immuno-compromised patients [19,62]. New tests based on the recombinant antigen Ss-NIE-1, although slightly less sensitive, but currently considerably more expensive than other serological techniques, show excellent specificity [62,63] and, although not widely available, they may be useful when designing rapid tests [63].

For treatment of schistosomiasis, single-dose praziquantel is the drug of choice. Evidence from systematic reviews shows that treatment with praziquantel significantly increased parasitological cure and, achieved marked reductions in microhaematuria compared with placebo; praziquantel also has a very good safety profile [47,48]. For treatment of strongyloidiasis, there is evidence (of low to moderate quality) that ivermectin is more effective than albendazole [52] and evidence (of moderate quality) that ivermectin is as effective as thiabendazole, but much better tolerated; no difference in the efficacy of ivermectin was observed between endemic and non-endemic populations [52]. However, there are no studies on the potential harms of large-scale administration of ivermectin (although widespread experience with filariasis control is reassuring).

Implementing presumptive treatment either with ivermectin or praziquantel requires additional complex screening strategies to identify individuals with loiasis or neurocysticercosis for whom these drugs might be inappropriate [70,71] and recently published recommendations specify that immigrants arriving from endemic areas should undergo a thorough clinical screening before being given either praziquantel or albendazole [73]. In addition, ivermectin is not readily available in most endemic and non-endemic countries and has limited approval by regulatory authorities in the EU/EEA.

We found no studies evaluating the cost-effectiveness of schistosomiasis screening and treatment interventions in migrant populations. For schistosomiasis, no studies were available on the cost of screening tests based on antibody detection in the non-endemic setting. In endemic settings, double-dose praziquantel was deemed to be highly cost-effective compared with a single dose and was considered robust to plausible changes in parameter estimates [65]. Further economic studies are required to provide better data on the cost-effectiveness of a test-and-treat strategy for schistosomiasis in non-endemic countries. For strongyloidiasis, three studies indicated that presumptive treatment with albendazole or ivermectin was cost-saving or cost-effective, in migrants to the U.S. or in endemic settings [66–68]. The limitations of these studies may decrease the relevance of the results for migrant populations in the EU/EEA. Most of the economic studies identified were limited to Asian populations and not based on screening with antibody testing in a non-endemic setting. However, where the prevalence of schistosomiasis and strongyloidiasis is greater than 1% and the price of presumptive treatment is similar to that used in the economic evaluations identified in this review, presumptive treatment with ivermectin or albendazole is likely to be cost-effective for migrants to the EU/EEA.

The strengths of our study include the use of the GRADE methodology to evaluate the quality and strength of the evidence and effect size in the included studies. The primary outcomes—parasitological cure or failure for efficacy of treatment and accuracy for screening—were objective measures. The individual studies in the included systematic reviews originated from different regions and countries with moderate to high endemicity for both parasites, increasing the generalizability of the results.

We did not identify any systematic reviews or RCTs on screening for schistosomiasis and strongyloidiasis in newly arrived migrants to EU/EEA. RCTs on preventive screening are rare, and so we used a logic model approach, as recommended at US Task Force on Preventive Health Care, and present data on population prevalence, diagnostic accuracy, treatment effectiveness and cost-effectiveness [70,74]. Other limitations include the lack of accurate data on the prevalence of schistosomiasis and strongyloidiasis among migrants from endemic countries entering the EU/EEA and the lack of data on the cost-effectiveness of screening and treating migrants for these parasitic infections. Further studies evaluating the effectiveness and cost-effectiveness of screening intervention in migrant populations are warranted.

The results of this systematic review indicate that although the certainty of desirable over undesirable effects of screening mobile and high-risk migrant populations from endemic areas is low to moderate, there is a rationale for screening, particularly in immunosuppressed patients since there is a high value placed on uncertain but potentially life-preserving benefits as suggested elsewhere [75]. Both schistosomiasis and strongyloidiasis can become chronic and cause severe long-term complications if untreated and the health benefits of intervention therefore outweigh its potential harms. Effective diagnostic tests are available and treatments for both infections are efficacious, well tolerated and safe with few exceptions [48,52,54,62].

Presumptive single-dose therapy of strongyloidiasis with ivermectin for all migrants is likely to be cost-effective; however, the feasibility of this measure has not been demonstrated in clinical studies in non-endemic settings. Importantly, implementing presumptive treatment either with ivermectin for strongyloidiasis or praziquantel for schistosomiasis requires additional screening strategies to identify individuals for whom these drugs might be harmful.

The evidence suggest screening should target people arriving from endemic areas, but national screening strategies will need to be tailored to the specific context of individual EU/EEA countries and, in particular, the countries of origin of migrants to those countries. Although, there are no

studies on the extent to which multiple screening tests for infectious diseases in migrants can improve cost-effectiveness, integrating innovative public health screening strategies for schistosomiasis and strongyloidiasis with other infectious diseases will improve surveillance data as well as reduce costs.

However, the optimal approach to delivery of screening will need to consider a global perspective, as well as depend on the health system context in individual EU/EEA countries. In this regard, addressing lack of access to healthcare for migrants, heterogeneity of screening strategies applicable in member states, and improving health professionals' knowledge and training of migrant related infectious diseases should improve the responsiveness of the public health care system with regards to coverage and uptake of screening at the level of primary health care.

Finally, although we consider that sufficient evidence exists to justify screening for strongyloidiasis and schistosomiasis immigrants coming to the EU/EEA from endemic areas, further assessment of the benefits and risks of screening and treatment is needed. More specifically, additional economic analysis is required, in particular to evaluate the costs of a test and treat strategy and to compare the cost-effectiveness of screening and of presumptive treatment.

5. Conclusions

This systematic review provides a compendium of indirect evidence that support the screening for strongyloidiasis and schistosomiasis in migrants coming from endemic areas to the EU/EEA, and particularly in immunosuppressed or at-risk-of immunosuppression patients.

Screening for strongyloidiasis and schistosomiasis should be considered based on serological testing in the absence of immunosuppression. Ivermectin and praziquantel have demonstrated a high efficacy, an excellent safety profile, and a potentially easy schedule for the treatment of strongyloidiasis and schistosomiasis. Economic modelling suggests presumptive single-dose treatment of strongyloidiasis with ivermectin for all migrants is likely cost-effective, but the feasibility of this strategy has yet to be demonstrated in clinical studies in non-endemic settings.

Appendix

Appendix 1: Logic Model—Analytic framework for screening and treatment for schistosomiasis and Strongyloidiasis in migrants.

Figure A1. Analytic framework for screening and treatment of schistosomiasis in migrants.

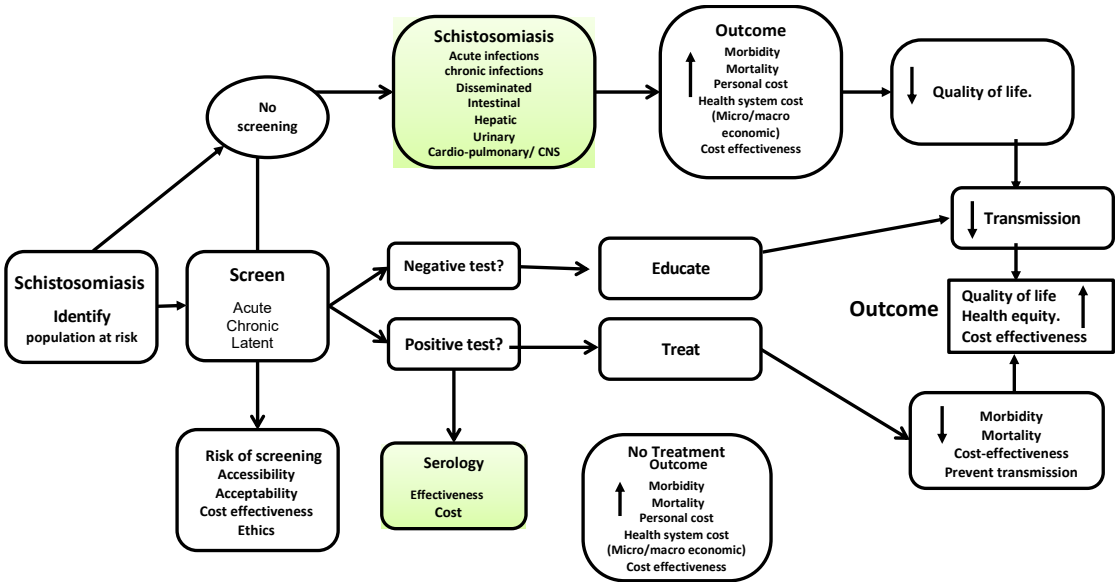
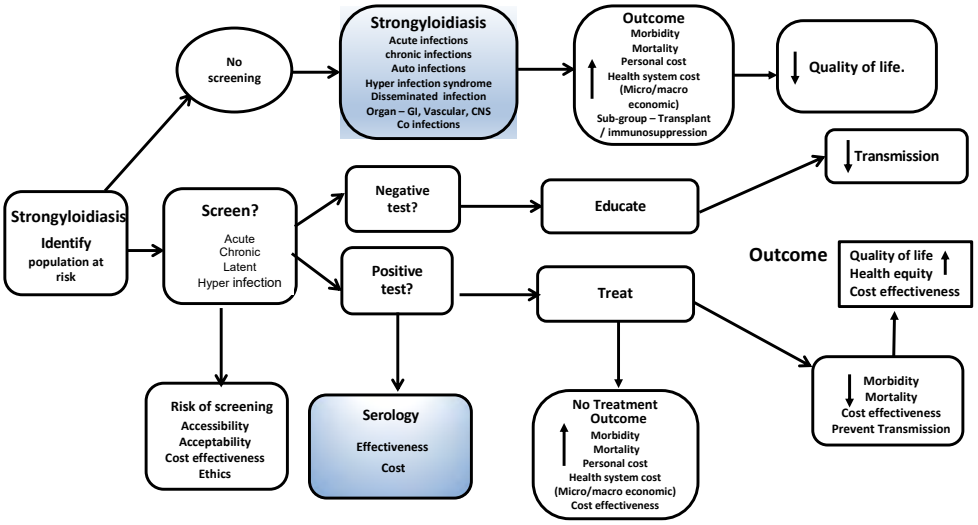


Figure A2. Analytic framework for screening and treatment of strongyloidiasis in migrants.



Appendix 2: List of sites and literature search strategy

1. Literature search strategy for systematic review

The used search strategies for the identification of systematic reviews are listed here.

A. Database: Ovid MEDLINE(R) 1946 to Present with Daily Update

Search Date: 15 April 2016

---

1. exp Schistosoma/ (15595)
2. bilharzia$.tw. (2431)
3. exp Schistosomiasis/ (21432)
4. schistosom$.tw. (25367)
5. katayama fever$.tw. (30)
6. or/1–5 (30014)
7. Strongyloides/ (985)
8. Strongyloides stercoralis/ (1044)
9. Strongyloidiasis/ (3301)
10. strongyloid$.tw. (3988)
11. or/7–10 (4959)
12. 6 or 11 (34621)
13. exp Mass Screening/ (107821)
14. (screened or screening?) tw. (417896)
15. Early Diagnosis/ (19041)
16. (detected or detection? or diagnos$ or discover$ or indentif$) tw. (2972048)
17. exp Population Surveillance/ (56090)
18. (disease? adj2 surveillance) tw. (4053)
19. Contact Tracing/ (3521)
20. contact tracing tw. (1152)
21. or/13–20 (3301561)
22. meta analysis mp, pt. (91365)
23. review pt. (2035657)
24. search$ tw. (253765)
25. or/22–24 (2222329)
26. animals/ not (humans/ and animals/) (4194238)
27. 25 not 26 (2065589)
28. 12 and 21 and 27 (711)

29. 28 and (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$ or 2016$) ed. (222)
30. remove duplicates from 29 (218)

****

B. Database: Embase <1980 to 2016 April 14>

Search Date: 15 April 2016

---

1. exp Schistosoma/ (19846)
2. bilharzia$.tw. (2115)
3. exp schistosomiasis/ (20241)
4. schistosom$.tw. (26744)
5. katayama fever$.tw. (40)
6. or/1–5 (33204)
7. Strongyloides/ (1220)
8. Strongyloides stercoralis/ (2315)
9. strongyloidiasis/ (3835)
10. strongyloid$.tw. (4704)
11. or/7–10 (6600)
12. 6 or 11 (39071)
13. exp mass screening/ (178654)
14. (screened or screening?).tw. (614882)
15. early diagnosis/ (82347)
16. parasite identification/ (13161)
17. ((case? or early or parasit$) adj5 (detected or detection? or diagnos$ or discover$ or egg or indentif$)).tw. (385884)
18. exp health survey/ (182738)
19. (disease? adj2 surveillance).tw. (5156)
20. contact examination/ (2830)
21. contact tracing.tw. (1448)
22. or/13–21 (1237076)
23. meta analys$.mp. (167508)
24. search$.tw. (362044)
25. review.pt. (2131214)
26. or/23–25 (2472677)
27. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans) ti.) (5499319)
28. 26 not 27 (2251777)
29. 12 and 22 and 28 (455)
30. 29 and (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$ or 2016$) dd. (195)
31. remove duplicates from 30 (190)

****

C. Database: EBSCO CINAHL <1970 to April 2016>

Search Date: 15 April 2016

#	Query	Limiters/Expanders	Last Run Via	Results
S28	S24 AND S27			129
S27	S25 OR S26			2,596,403
S26	EM 2010 or EM 2011 or EM 2012 or EM 2013 or EM 2014 or EM 2015 or EM 2016			2,415,478
S25	PY 2010 or PY 2011 or PY 2012 or PY 2013 or PY 2014 or PY 2015 or PY 2016			2,346,296
S24	S9 AND S17 AND S23			253
S23	S18 OR S19 OR S20 OR S21 OR S22			221,252
S22	(TI meta analy * or AB meta analy *)			29,697
S21	(MH “Meta-Analysis”)			24,939

S20 PT review 141,448
S19 PT systematic review 53,358
S18 (MH "Systematic Review") 37,435
S17 S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 1,246,183
S16 TX contact tracing 2230
S15 TX (disease * or population) N2 surveillance 23,893
S14 (MH "Population Surveillance+") 5949
S13 TX (detected or detection * or diagnos * or discover * or indentif *) 1,184,038
S12 (MH "Early Diagnosis") 4472
S11 TI ((screened or screening *) OR AB (screened or screening *)) 78,236
S10 (MH "Health Screening+") 62,744
S9 S5 OR S8 5460
S8 S6 OR S7 4460
S7 TX strongyloid * 529
S6 (MH "Helminthiasis+") 4132
S5 S1 OR S2 OR S3 OR S4 1931
S4 TX katayama fever 25
S3 TX bilharzia * 175
S2 TX schistosome * 1871
S1 (MH "Schistosomiasis+") 756
****

D. Databases: Database of Abstracts of Reviews of Effects (DARE) and Cochrane Database of Systematic Reviews (CDSR)
Search Date: 15 April 2016

ID Search
#1 MeSH descriptor: [Schistosoma] explode all trees
#2 bilharzia *
#3 MeSH descriptor: [Schistosomiasis] explode all trees
#4 schistosom *
#5 katayama fever
#6 #1 or #2 or #3 or #4 or #5
#7 MeSH descriptor: [Strongyloides] this term only
#8 MeSH descriptor: [Strongyloides stercoralis] this term only
#9 MeSH descriptor: [Strongyloidiasis] this term only
#10 strongyloid *
#11 #7 or #8 or #9 or #10
#12 #6 or #11
#13 #12 in Other Reviews
#14 #12 in Cochrane Reviews (Reviews and Protocols)
****

2. Literature search strategy for systematic search for cost-effectiveness studies

The used search strategies for the identification of systematic reviews on cost-effectiveness are listed here.

A. Database: Ovid MEDLINE(R) Epub Ahead of Print <May Week 3 2016>, Ovid MEDLINE(R) 1946 to Present with Daily Update

Search Date: 31 May 2016

---

1. exp Schistosoma/ (15714)
2. bilharzia$.tw. (2438)

3. exp Schistosomiasis/ (21583)
4. schistosom$.tw. (25722)
5. katayama fever$.tw. (30)
6. or/1–5 (30381)
7. Strongyloides/ (990)
8. Strongyloides stercoralis/ (1056)
9. Strongyloidiasis/ (3319)
10. strongyloid$.tw. (4079)
11. or/7–10 (5051)
12. 6 or 11 (35067)
13. exp Mass Screening/ (108535)
14. (screened or screening? or tested or testing or tests).tw. (1734474)
15. Early Diagnosis/ (19350)
16. (detected or detection? or diagnos$ or discover$ or indentif$).tw. (3053822)
17. exp Population Surveillance/ (56687)
18. (disease? adj2 surveillance).tw. (4195)
19. Contact Tracing/ (3563)
20. contact tracing.tw. (1176)
21. or/13–20 (4387118)
22. meta analysis.mp,pt. (96759)
23. review.pt. (2060867)
24. search$.tw. (266775)
25. guideline.pt. (15780)
26. guideline/ (15780)
27. guidelines as topic/ (34071)
28. practice guideline.pt. (21216)
29. practice guideline/ (21216)
30. practice guidelines as topic/ (91792)
31. (CPG or CPGs or guidance or guideline? or recommend$ or standard?).ti. (147179)
32. exp clinical pathway/ (5273)
33. exp clinical protocol/ (139345)
34. ((care or clinical) adj2 pathway?).tw. (5129)
35. or/22–34 (2572065)
36. 12 and 21 and 35 (960)
37. animals/ not (humans/ and animals/) (4215704)
38. 36 not 37 (838)
39. 38 and (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$ or 2016$).ed. (271)
40. remove duplicates from 39 [reviews and guidelines] (261)
41. exp "costs and cost analysis"/ (197942)
42. cost$.mp. (467877)
43. cost effective$.tw. (83090)
44. cost benefit analys$.mp. (67319)
45. health care costs.mp. (37157)
46. or/41–45 (477217)
47. 12 and 21 and 46 (260)
48. animals/ not (humans/ and animals/) (4215704)
49. 47 not 48 (222)
50. 49 and (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$ or 2016$).ed. (82)
51. remove duplicates from 50 (78)

****

B. Database: Embase <1974 to 2016 Week 22>

Search Date: 31 May 2016

---

1. exp Schistosoma/ (21727)
2. bilharzia$.tw. (2492)
3. exp schistosomiasis/ (21930)
4. schistosom$.tw. (29047)
5. katayama fever$.tw. (42)
6. or/1–5 (36157)
7. Strongyloides/ (1229)
8. Strongyloides stercoralis/ (2447)
9. strongyloidiasis/ (3986)
10. strongyloid$.tw. (4977)
11. or/7–10 (6962)
12. 6 or 11 (42352)
13. exp mass screening/ (182895)
14. (screened or screening? or tested or testing or tests).tw. (2429856)
15. early diagnosis/ (83110)
16. parasite identification/ (13222)
17. ((case? or early or parasit$) adj5 (detected or detection? or diagnos$ or discover$ or egg or indentif$)).tw. (405389)
18. exp health survey/ (184236)
19. (disease? adj2 surveillance).tw. (5253)
20. contact examination/ (2867)
21. contact tracing.tw. (1512)
22. or/13-21 (2999272)
23. meta analys$.mp. (170914)
24. search$.tw. (371898)
25. review.pt. (2163187)
26. guideline.pt. (0)
27. guideline/ (144)
28. guidelines as topic/ (229895)
29. practice guideline.pt. (0)
30. practice guideline/ (275502)
31. practice guidelines as topic/ (171091)
32. (CPG or CPGs or guidance or guideline? or recommend$ or standard?).ti. (203285)
33. exp clinical pathway/ (6983)
34. exp clinical protocol/ (75932)
35. ((care or clinical) adj2 pathway?).tw. (9455)
36. or/23–35 (2900847)
37. 12 and 22 and 36 (824)
38. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.) (5865460)
39. 37 not 38 (678)
40. 39 and (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$ or 2016$).dd. (304)
41. remove duplicates from 40 [reviews and guidelines] (295)
42. cost effectiveness analysis/ (114264)
43. cost.tw. (387431)
44. costs.tw. (208732)
45. or/42–44 (544771)
46. 12 and 22 and 45 (274)
47. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.) (5865460)
48. 46 not 47 (223)

49. 48 and (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$ or 2016$).dd. (115)
50. remove duplicates from 49 [costing] (111)

****

C. Databases: Database of Abstracts of Reviews of Effects (DARE) and Cochrane Database of Systematic Reviews (CDSR) and NHS EED
Search Date: 31 May 2016

ID Search
#1 MeSH descriptor: [Schistosoma] explode all trees
#2 bilharzia*
#3 MeSH descriptor: [Schistosomiasis] explode all trees
#4 schistosom*
#5 katayama fever
#6 #1 or #2 or #3 or #4 or #5
#7 MeSH descriptor: [Strongyloides] this term only
#8 MeSH descriptor: [Strongyloides stercoralis] this term only
#9 MeSH descriptor: [Strongyloidiasis] this term only
#10 strongyloid*
#11 #7 or #8 or #9 or #10
#12 #6 or #11
#13 #12 in Other Reviews
#14 #12 in Cochrane Reviews (Reviews and Protocols)
#15 #12 in Economic Evaluations

****

D. Database: EBSCO CINAHL <1970 to May 2016>

Search Date: 31 May 2016

Query Limiters/Expanders Last Run Via Results
S38 S32 AND S3738
S37 S9 AND S17 AND S3676
S36 S34 OR S35 139,767
S35 TI (cost OR costs) OR AB (cost OR costs)89,616
S34 (MH "Costs and Cost Analysis+") 82,915
S33 S29 AND S32164
S32 S30 OR S31 2,653,954
S31 EM 2010 or EM 2011 or EM 2012 or EM 2013 or EM 2014 or EM 2015 or EM 2016 2,445,432
S30 PY 2010 or PY 2011 or PY 2012 or PY 2013 or PY 2014 or PY 2015 or PY 2016 2,403,611
S29 S9 AND S17 AND S28307
S28 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 348,353
S27 TX (care or clinical) N2 pathway * 15,555
S26 TI (CPG or CPGs or guidance or guideline * or recommend * or standard *) 79,261
S25 (MH "Critical Path") 4120
S24 PT Practice Guidelines 9487
S23 (MH "Practice Guidelines") 53,690
S22 (TI meta analy * or AB meta analy *) 30,542
S21 (MH "Meta Analysis") 25,200
S20 PT review 144,019
S19 PT systematic review 53,350
S18 (MH "Systematic Review") 37,846
S17 S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 1,801,344

S16 TX contact tracing 2236
S15 TX (disease * or population) N2 surveillance 24,089
S14 (MH "Population Surveillance+") 6026
S13 TX (detected or detection * or diagnos * or discover * or indentif *) 1,195,388
S12 (MH "Early Diagnosis") 4553
S11 TX (screened or screening * or tested or testing or tests) 1,102,848
S10 (MH "Health Screening+") 63,147
S9 S5 OR S8 5501
S8 S6 OR S7 4500
S7 TX strongyloid * 537
S6 (MH "Helminthiasis+") 4167
S5 S1 OR S2 OR S3 OR S4 1942
S4 TX katayama fever 24
S3 TX bilharzia * 175
S2 TX schistosome * 1881
S1 (MH "Schistosomiasis+") 764
****

E. Databases: PubMed

Search Date: 31 May 2016

((((((((schistosome * or bilharzia * or katayama or strongyloid *))) AND ((screened or screening * or tested or testing or tests)))) AND (((CPG or CPGs or guidance or guideline * or metaanalysis or meta-analysis or recommend * or review or standard or standards)))) AND ((publisher [3])))))) (8)
((((((((schistosome * or bilharzia * or katayama or strongyloid *))) AND ((screened or screening * or tested or testing or tests)))) AND (((cost or costs)))) AND ((publisher [3])))))) (2)
****

3. Update Literature strategy for primary studies on diagnostic or screening tools for schistosomiasis.

A. Database: Ovid MEDLINE(R)—1946 to February 2017.

1. Schistosomiasis/ (13485)
2. Schistosomiasis.mp. (24533)
3. snail fever.mp. (10)
4. schistosome *.mp. (5528)
5. exp "Sensitivity and Specificity"/ (495027)
6. sensitivity.tw. (638974)
7. specificity.tw. (379605)
8. ((pre-test or pretest) adj probability).tw. (1695)
9. post-test probability.tw. (441)
10. predictive value$.tw. (85102)
11. likelihood ratio$.tw. (11639)
12. or/5–11 (1217873)
13. or/1–4 (26340)
14. 12 and 13 (1493)
15. limit 14 to humans (1112)
16. from 15 keep 1001–1112 (112)

A. Database: EMBASE—up to February 2017
#16 #14 AND 'human'/de AND [embase]/lim NOT [medline]/lim 308
#15 #14 AND 'human'/de 1489
#14 #5 AND #13 2534

#13 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 1688887
#12 'sensitivity and sensibility' 982
#11 'sensitivity' 1132406
#10 'specificity' 719846
#9 'pretest posttest design' 2331
#8 'predictive value' 161458
#7 'likelihood ratio' 11832
#6 'diagnostic accuracy' 220669
#5 #1 OR #2 OR #3 OR #4 35984
#4 'snail fever' 9
#3 'schistosome' 4643
#2 'schistosoma' 25091
#1 'schistosomiasis'/exp 22890

B. Database: COCHRANE LIBRARY- up to February 2017
ID Search Hits
#1 MeSH descriptor: [Schistosomiasis] explode all trees 295
#2 Schistosomiasis 497
#3 snail fever 3
#4 schistosome * 50
#5 #1 or #2 or #3 or #4 506
#6 MeSH descriptor: [Diagnosis] explode all trees 298999
#7 diagno * 129750
#8 #6 or #7 367644
#9 #5 and #8 220

C. Database: CINAHL—up to February 2017
S12 S4 AND S11
S11 S5 OR S6 OR S7 OR S8 OR S9 OR S10
S10 likelihood ratio$
S9 predictive value$
S8 post-test probability
S7 sensitivity and specificity
S6 specificity
S5 sensitivity
S4 S1 OR S2 OR S3
S3 schistosoma
S2 schistosome *
S1 Schistosomiasis
D. Database: LILACS – up to February 2017
(tw:((tw:(esquistosomiasis)) OR (tw:(bilharziasis)) OR (tw:(schistosoma)))) AND
(tw:((tw:(diagnostico)) OR (tw:(deteccion)))) AND (instance:"regional") AND (db:("LILACS" OR
"colecionaSUS" OR "IBECS" OR "SES-SP" OR "MedCarib" OR "CUMED") AND
clinical_aspect:("diagnosis") AND limit:("humans"))
****

4. Update Literature strategy for primary studies on diagnostic or screening tools for strongyloidiasis

A. Database: Ovid MEDLINE(R)—1946 to February 2017
1. Strongyloidiasis/ (3403)
2. Strongyloidiasis.mp. (3747)
3. Strongyloides stercoralis/ (1098)

4. Strongyloides stercoralis.mp. (2142)
5. or/1–4 (4376)
6. exp "Sensitivity and Specificity"/ (494358)
7. sensitivity.tw. (637846)
8. specificity.tw. (379066)
9. ((pre-test or pretest) adj probability).tw. (1689)
10. post-test probability.tw. (438)
11. predictive value$.tw. (84929)
12. likelihood ratio$.tw. (11613)
13. or/6–12 (1216076)
14. 5 and 13 (247)
15. limit 14 to humans (207)

B. Database: EMBASE—up to February 2017

No.	Query	Results
#14	#12 AND [embase]/lim NOT [medline]/lim AND 'human'/de	136
#13	#12 AND [embase]/lim NOT [medline]/lim	156
#12	#3 AND #11	472
#11	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	1686971
#10	'diagnostic accuracy'	220414
#9	'likelihood ratio'	11815
#8	'predictive value'	161090
#7	'pretest posttest design'	2315
#6	'specificity'	719056
#5	'sensitivity'	1131076
#4	'sensitivity and sensibility'	981
#3	#1 OR #25662	
#2	'strongyloides stercoralis'	3193
#1	'strongyloidiasis'/exp	4162

C. Database: COCHRANE LIBRARY—up to February 2017

ID	Search	Hits
#1	MeSH descriptor: [Strongyloidiasis] explode all trees	28
#2	Strongyloidiasis	53
#3	MeSH descriptor: [Strongyloides stercoralis] explode all trees	12
#4	Strongyloides stercoralis	47
#5	#1 or #2 or #3 or #4	72
#6	MeSH descriptor: [Diagnosis] explode all trees	298999
#7	diagno *	129739
#8	#6 or #7	367633
#9	#5 and #8	38

D. Database: CINAHL—up to February 2017

Términos de la búsqueda	Opciones de búsqueda
S11	(S4 OR S5 OR S6 OR S7 OR S8 OR S9) AND (S3 AND S10)
S10	S4 OR S5 OR S6 OR S7 OR S8 OR S9
S9	likelihood ratio$
S8	predictive value$
S7	post-test probability
S6	sensitivity and specificity
S5	specificity
S4	sensitivity
S3	S1 OR S2

S2 strongyloides stercoralis
S1 strongyloidiasis

E. Database: LILACS—up to February 2017

(tw:((tw:(estrongiloidiasis)) OR (tw:(Strongyloides stercoralis)))) AND (tw:((tw:(diagnostico)) OR (tw:(deteccion))))

****

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5.5.4 Fourth publication

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

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Abbreviations

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
BCG	Bacillus Calmette–Guerin vaccine
CDC	US Centers for Disease Control and Prevention
CHB	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	Hepatitis B virus
HCC	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	Pegylated interferon
PICO	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
TB	Tuberculosis
TST	Tuberculin skin test
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
VCT	Voluntary counselling and testing
VPD	Vaccine-preventable diseases
WHO	World Health Organization

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[1].

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[2] reporting guidelines.

[1] Screening in this document implies a voluntary action that should be linked to an appropriate intervention; for example, treatment, vaccination, health education.

[2] 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[3] 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-TB-incidence 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[4]

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 (≥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 (≥2% to ≥5% HBsAg.)

Offer hepatitis B vaccination series to all migrant children and adolescents from intermediate/high prevalence countries (≥2% to ≥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 (≥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)[5][6] 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.

[3] 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: https://gradepro.org

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

[5] Diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b

[6] 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; disease-related 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 community-based 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 cost-effectiveness 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

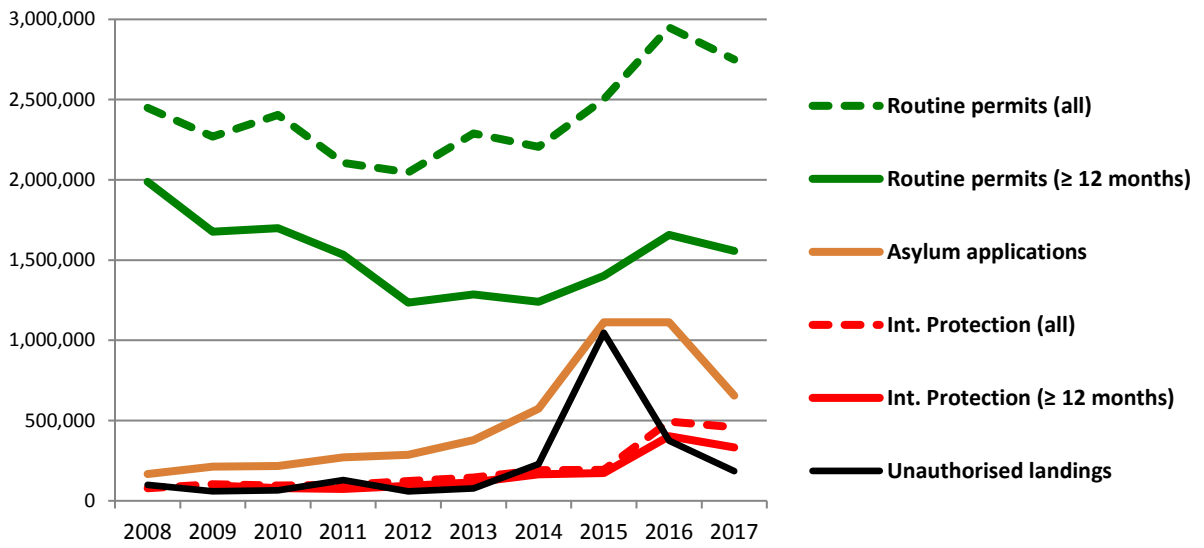
Some migrant populations are at increased risk of specific infectious diseases, including active and latent TB, HIV, hepatitis B and hepatitis C (17, 28). In addition, immunisation coverage is low in some migrant populations, making them more susceptible to vaccine-preventable diseases (VPDs) (29-31). 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 must be downgraded (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 evidence-based guidelines were given the most weight, followed by individual randomised controlled trials (RCTs), quasi-experimental 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.

Table 2. Interpretation of GRADE certainty of evidence

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.

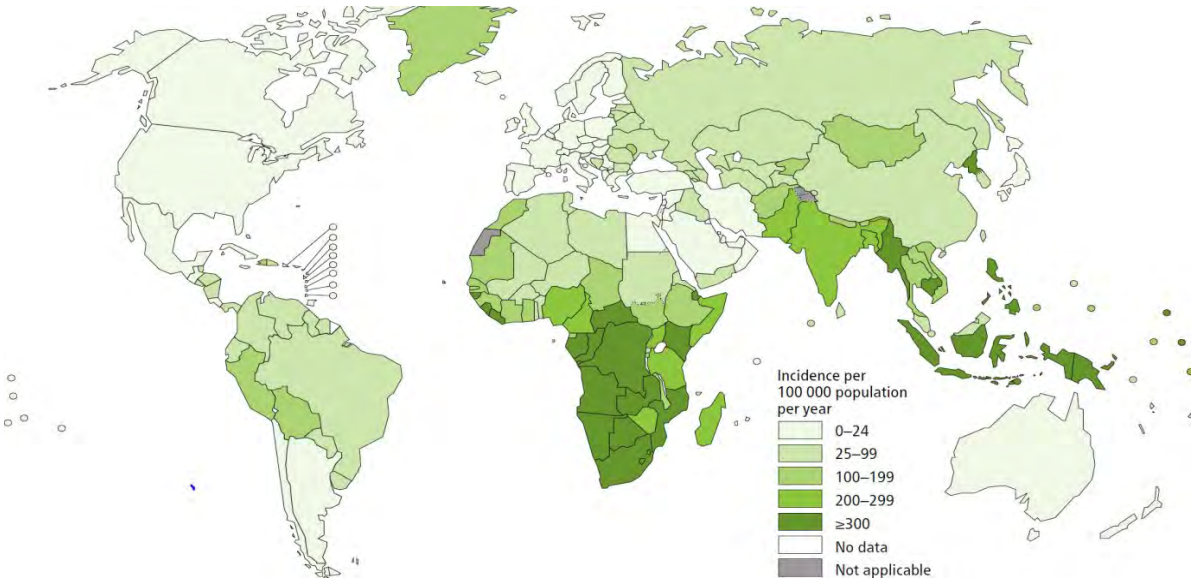
4.1 Active tuberculosis

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-TB-incidence 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 upon- or 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-TB-incidence 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.

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

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 yet to be defined (89-91).	There is very little data on the cost-effectiveness of active TB screening in migrant populations. Increased cost-effectiveness was associated with higher TB incidence in the country of origin, which suggests that programmes are more cost-effective when targeting migrants from intermediate and high-incidence TB countries of origin (89-91).	Low	The ad hoc scientific panel rated active TB screening among migrants in the EU/EEA as follows: • High priority • Moderate agreement on acceptability • Moderate agreement on feasibility • High agreement on equitability.	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.

** 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)	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 Age-specific requirements: • < 2 years – history and physical examination; if positive → CXR • 2–10 years – history and physical examination + TST or IGRA if coming from a higher TB burden country (not quantified); if positive → CXR • 11 years and above – history and physical examination + CXR • If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and cultures.
Canada (105-108)	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 >30/100 000 cases of TB). Age-specific requirements: • 0–10 years – history and physical examination; if positive → CXR • 11 years and above – history and physical examination + CXR • If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and cultures.
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 • ≥16 years: CXR • 16–35 years of age from sub-Saharan Africa or country incidence >500/100 000: CXR +TST • If CXR is suggestive of TB or if there are signs and symptoms of pulmonary TB → sputum microscopy and cultures
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)	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: • Children below 11 years: symptom screen; if positive → CXR • Applicants of 11 years and above: symptom screen + CXR • 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. • If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and cultures.
US (113)	Pre-entry CXR screening is required for immigrant visa applicants, refugees and asylum seekers. Age-specific requirements: • < 2 years – history and physical examination; if positive → CXR • 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 • 15 years and above – history and physical examination + CXR • If CXR is suggestive of TB or there are signs and symptoms of pulmonary TB → sputum microscopy and culture.

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 dependant 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.

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

Effectiveness	Cost-effectiveness	Certainty of evidence (GRADE)	FACE survey*	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).	Limited economic analyses suggest that the most cost-effective approach may be targeting young migrants (<35 years of age) from high-TB-incidence countries (>150 cases/100 000 population) (126, 127, 129, 130). Cost-effectiveness increased with increasing TB incidence in the country of origin.	Low	The ad hoc scientific panel rated LTBI screening among migrants in the EU/EEA as follows: • High priority • Moderate agreement on feasibility • Moderate agreement on acceptability • High agreement on equitability	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.

** 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)	• ≤ 35 years of age: offer LTBI screening with TST (cut-off 10 mm) or IGRA • <5 years of age, TST preferred, 2–10 years: might have already been performed pre-entry • > 35 years of age: based on risk factors and state/territory requirements
Canada (105)	There are no routine post-arrival domestic LTBI screening programmes for immigrants in Canada but LTBI screening is recommended for the following groups: • Screen immigrants with TST from countries with high TB incidence (>30/100 000] if fibronodular changes on CXR (done during post landing surveillance). • Screen all children and adolescents <20 years on arrival or soon after. • Screen all refugees aged 20–50 years. • Screen those with underlying medical comorbidities that increase the risk of reactivation.
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)	≥16 years of age: initial screen with CXR (>40/100 000] • Normal: perform TST if from sub-Saharan Africa or a high incidence country (>500/100 000] • Abnormal: rule out active disease, offer LTBI treatment <16 years of age or pregnant: TST (>40/100 000)
Italy (13)	• Offer TST (alternatively IGRA may be used, in particular if previously vaccinated) to all migrants from high-TB-incidence countries (>100/100 000 inhabitants) who are expecting to stay for at least six months • Use TST screening test for children < 5 years. • 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. • If active disease is excluded, subjects with positive TST or IGRA tests should be offered preventive treatment.
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 *Mycobacterium tuberculosis* and have an intermediate or high risk of disease progression should be prioritised for LTBI screening and treatment.

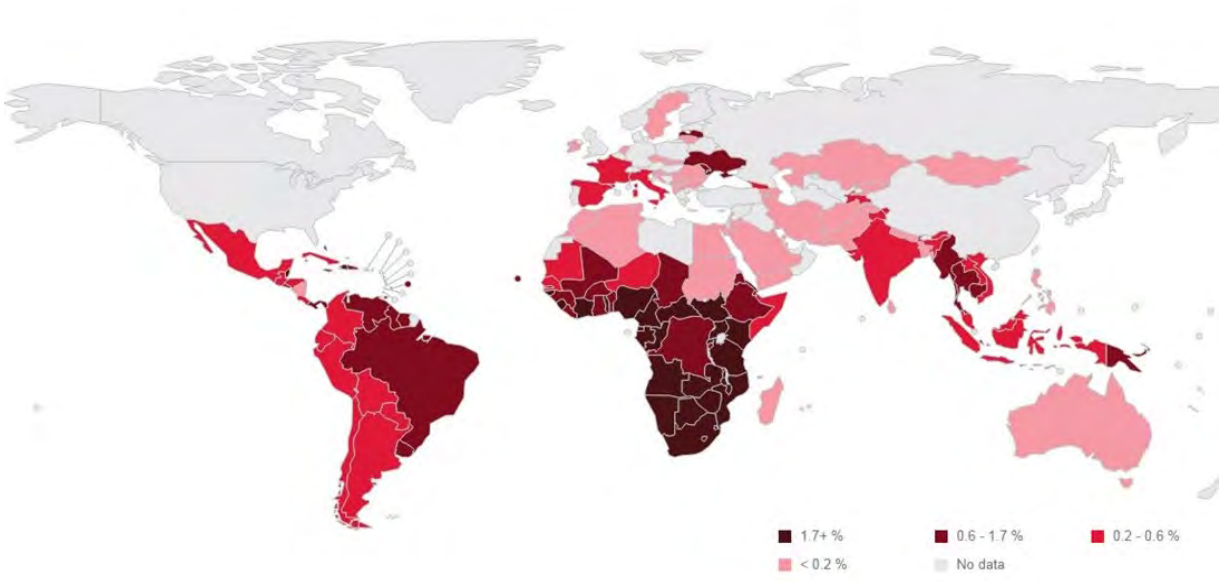
CXR = chest X-ray; LTBI = latent tuberculosis infection; TB = tuberculosis; TST: tuberculin skin test; IGRA: interferon-gamma release assay.

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[7] 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 (≥0.1%) or high HIV prevalence (≥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 physician-directed, targeted rapid testing (160). Universal testing was also associated with a higher median CD4 count and lower likelihood of CD4 count <200 cells/mm^3 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 cost-effectiveness 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).

[7] 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 ≥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 (≥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 (≥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)	There is very little 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 origin prevalence as guide (see Figure 4).	Low	The ad hoc scientific panel rated HIV screening among migrants in the EU/EEA as follows: • High priority • High agreement that screening is feasible • High agreement that screening is acceptable • High agreement that screening is equitable.	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)	• HIV serology, pre-arrival government screening programme for all immigrants and refugees of ≥ 15 years. • Clinical screening: offer HIV serology to high-risk migrants, with informed consent. • All adolescents and adults from countries where HIV prevalence is ≥1% (sub-Saharan Africa, parts of the Caribbean and Thailand). • Link HIV-positive individuals to HIV treatment programmes and post-test counselling.
France (185)	• Yearly HIV screening is recommended for migrants originating from countries of high prevalence, especially sub-Saharan Africa and the Caribbean. • HIV screening recommended in association with HBV and HCV screening for migrant populations.

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)	During the second phase of reception, offer all migrants culturally sensitive counselling for HIV. Offer HIV tests to: • all migrants aged ≥ 16 years coming from high-prevalence (1%) countries • pregnant and breast-feeding migrant women • those exposed to high risk (blood transfusions in country of origin, sexually abused people, or people with multiple sexual partners • people with concomitant presence of active TB or IST. Migrants < 16 years should be offered an HIV test if they meet at least one of the below criteria: • born from HIV-positive mothers • early sexual activities • history of sexual abuse • concomitant presence of active TB or IST.
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)	• Post arrival (not mandatory prior to arrival) • HIV test, universal • 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. • Refer to specialist, post-test counselling.

4.4 Hepatitis B

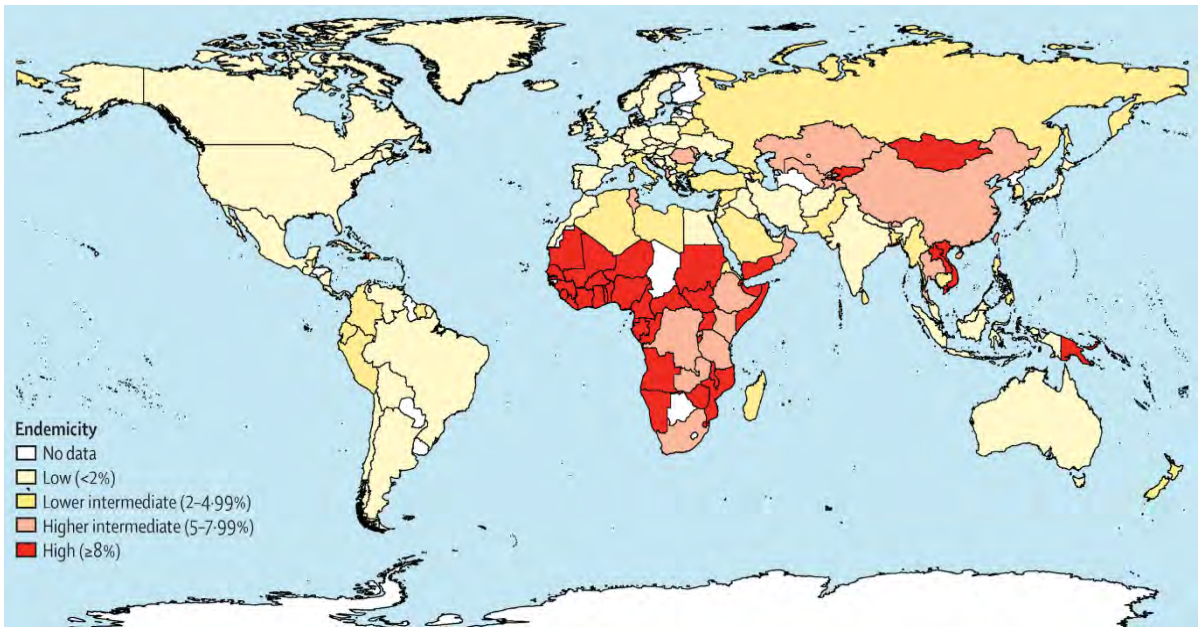
Burden of disease

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 (≥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 foreign-born 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 HBV-prevalent 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 (≥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 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 (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 ≥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 high-prevalence 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-/high-prevalence countries (≥2% to– ≥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 (≥2% to– ≥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.

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

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	The ad hoc scientific panel rated HBV screening, treatment and vaccination among migrants in the EU/EEA as follows: • High priority • Moderate agreement that screening is acceptable • High agreement that screening is feasible • High agreement that screening is equitable	Conditional recommendation for screening migrants from intermediate and high-prevalence countries. Strong recommendation for vaccination of migrant children and adolescents.	Migrant barriers in accessing healthcare contribute to decrease screening uptake and willingness to disclose hepatitis test results (217). Screening uptake is highest in programmes that involve community partners or the endorsement of local groups (219). Programmes screening for CHB should consider linkage of cases to monitoring and treatment. Migrant women should be screened in existing antenatal programmes.

** 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

Table 12. HBV screening recommendations for migrants in selected counties

Country	Who when, how to test/assess
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 ≥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 ≥2%; vaccinate non-immune, high-risk persons.
Italy (13)	During the second phase of the reception, offer screening (HBsAg, HBsAb, HBcAb) to all migrants from 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 ≥2% or those in high-risk groups should be tested for infection (HBsAg). 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.

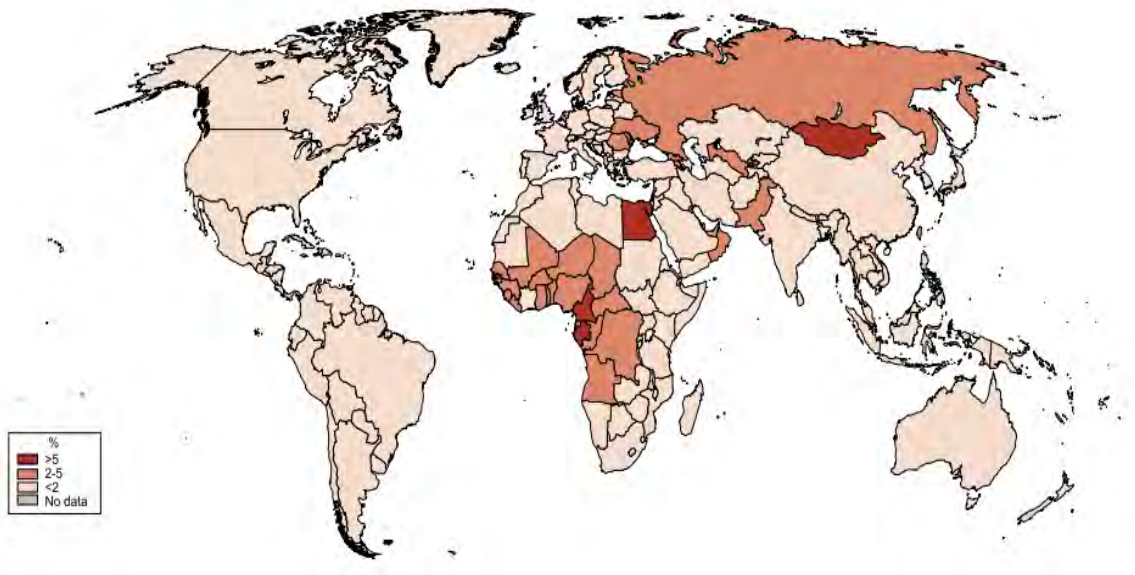
4.5 Hepatitis C

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 ≥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 ≥2% and ≥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 (≥2%) and high (≥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 (≥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.

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

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).	In France, DAAs were moderately cost-effective for genotypes 1 & 4, ranging from EUR 40 000 to EUR 88 000 per QALY gained, whereas IFN-RBV was more cost-effective for 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	HCV screening among migrants in the EU/EEA was rated as follows: • Medium priority • Low agreement that screening is feasible • Moderate agreement that screening is acceptable • Moderate agreement that screening is equitable.	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.

** 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)	• Offer test for anti-HCV to: – all migrants who originate from countries with a prevalence of chronic hepatitis C of ≥ 2%; – those with a history of hepatitis C risk exposure/behaviour including people who inject drugs and men who have sex with men. • Offer test for HCV RNA to all those who have a positive anti-HCV result. • Refer all positive cases to specialist services for review. • Vaccinate those who are non-immune to hepatitis A and/or hepatitis B with hepatitis A and/or hepatitis B vaccine.
Italy (13)	During the second reception phase, offer screening tests (HCV-Ab) to all migrants coming from high HCV-RNA-prevalence (> 3%) countries • Regardless the country of origin, offer tests to those migrants with: – concomitant HIV infection – previous blood transfusion – intravenous drug addiction – abnormal liver tests – risk factors for parenteral transmission • 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.
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).

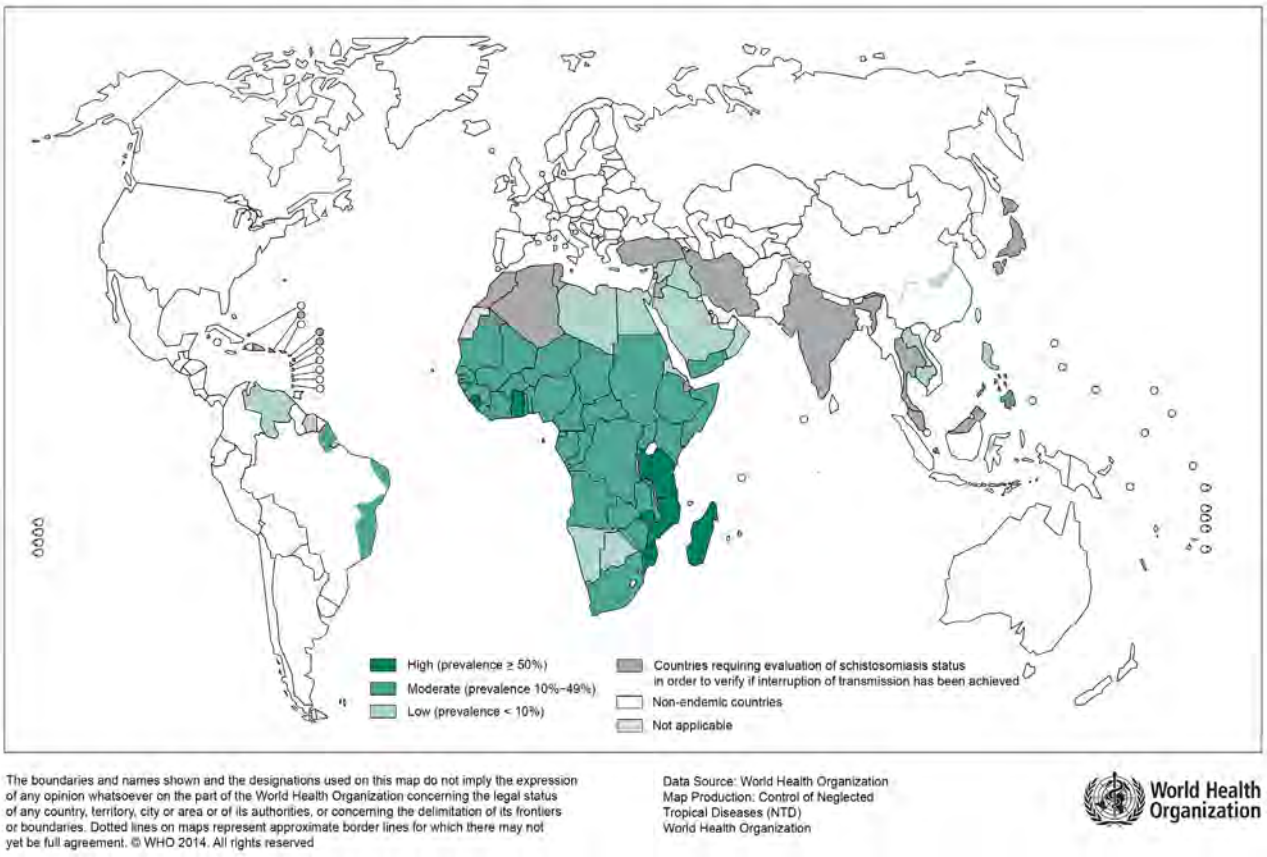
Of all helminthic infections, both schistosomiasis and strongyloidiasis have characteristics which make them appropriate for screening. First, most infected subjects are asymptomatic (291s) and unaware of infection (292), or complain of very mild unspecific symptoms (289). Second, both diseases are considered 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: = http://www.who.int/schistosomiasis/Schistosomiasis_2012-01.png

Summary of evidence

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 antibody-detecting 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)

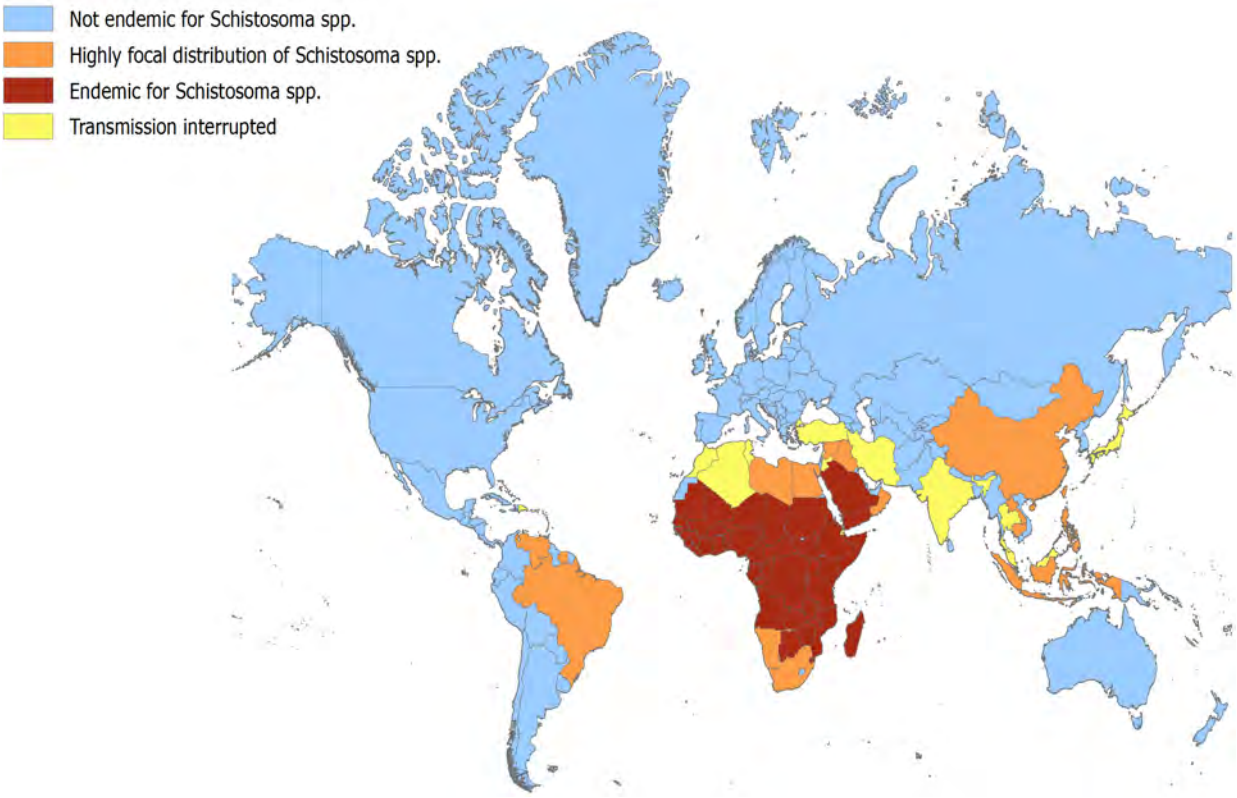
Evidence-based statement (strongyloidiasis)

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)

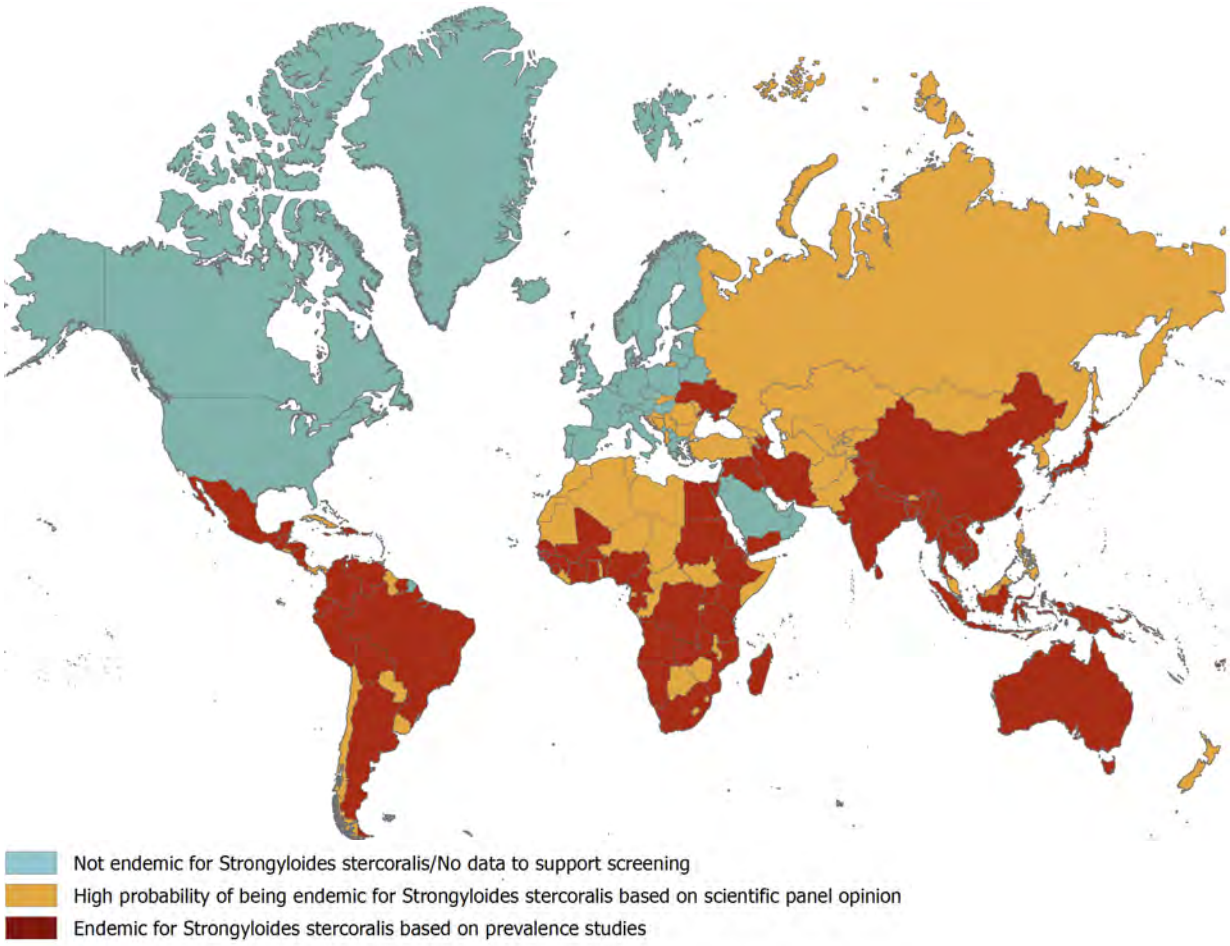
Screening for schistosomiasis and strongyloidiasis in migrant populations is an important control strategy as it allows for early detection and treatment, probably reduces individual morbidity, and prevents the risk of onward transmission. Although the evidence-based statements are based on indirect 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: https://www.iamat.org/assets/files/World%20Schistosomiasis%20Risk%20Chart_2015.pdf
Note: Public health authorities should consider schistosomiasis screening of migrants from countries marked orange and dark red.

Figure 7. Countries where strongyloidiasis is endemic



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

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

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.	There is very little data on the cost-effectiveness of strongyloidiasis screening in migrant populations. There is no data on cost-effectiveness of schistosomiasis screening Limited available evidence suggests that presumptive treatment would be the most cost-effective strategy. However, the uncertainty 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.	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.

** 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)	Strongyloidiasis: • Offer blood testing for *Strongyloides* 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. • Treat with ivermectin. In Loa-loa-endemic countries, rule out loiasis before providing ivermectin. Schistosomiasis: • 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). • 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.
Canada (5)	Strongyloidiasis: • Screen refugees newly arriving from south-east Asia and Africa with serological tests for *Strongyloides* spp. • If positive, treat with ivermectin. Schistosomiasis: • Screen refugees newly arriving from Africa with serological tests. • If positive, treat with praziquantel.
Ireland {#8)	Offer test (ova, cysts and parasites) to symptomatic migrants only, particularly those who have: • lived or travelled in endemic regions; • migrated from south-east Asia or sub-Saharan Africa; • eosinophilia. Healthcare professionals should also be aware that those with concurrent immunosuppression are at increased risk of developing disseminated parasitic infections, especially *Strongyloides*, as this auto-infects and disseminates widely in those who are immunosuppressed.
Italy (13)	• 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. • If symptoms or eosinophilia is present, offer stool examination test for parasitosis. • Regardless of the presence of symptoms, offer serological tests to all migrants coming from endemic areas (*Schistosoma spp.* or *Strongyloides*). Migrants with a positive serological test should be treated, unless there is already evidence of recent completed treatment.
France (335, 336)	Strongyloidiasis screening for target populations (ELISA + stool examination test for parasitosis): • Immigrants or refugees from endemic areas, upon arrival. • All patients originating from, or having lived in, an endemic area prior to commencing immunosuppressive therapy. Schistosomiasis screening for target populations (serology +/- testing for schistosome eggs in urine or faeces) : • All migrants from endemic areas.
UK (232, 298)	For refugees, pre-entry: Helminthic infections: • 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. • 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. – A single dose of albendazole 400 mg for all refugees except pregnant women and children < 2 years of age; – Children 12 – 23 months of age should have a single dose of albendazole 200 mg. For migrants, post-arrival: • 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. • For migrants from sub-Saharan Africa, screening is recommended for patients with eosinophilia (>0.4 x 10^9 per litre), by stool microscopy, urine microscopy, strongyloides serology and schistosoma serology • For migrants from anywhere in the tropics, screening is recommended for patients with eosinophilia (>0.4 x 10^9 per litre), by stool microscopy and strongyloides serology. • Treatment is according to testing results.
USA (142)	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. Refugees from sub-Saharan Africa should receive presumptive therapy for *Strongyloides* 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

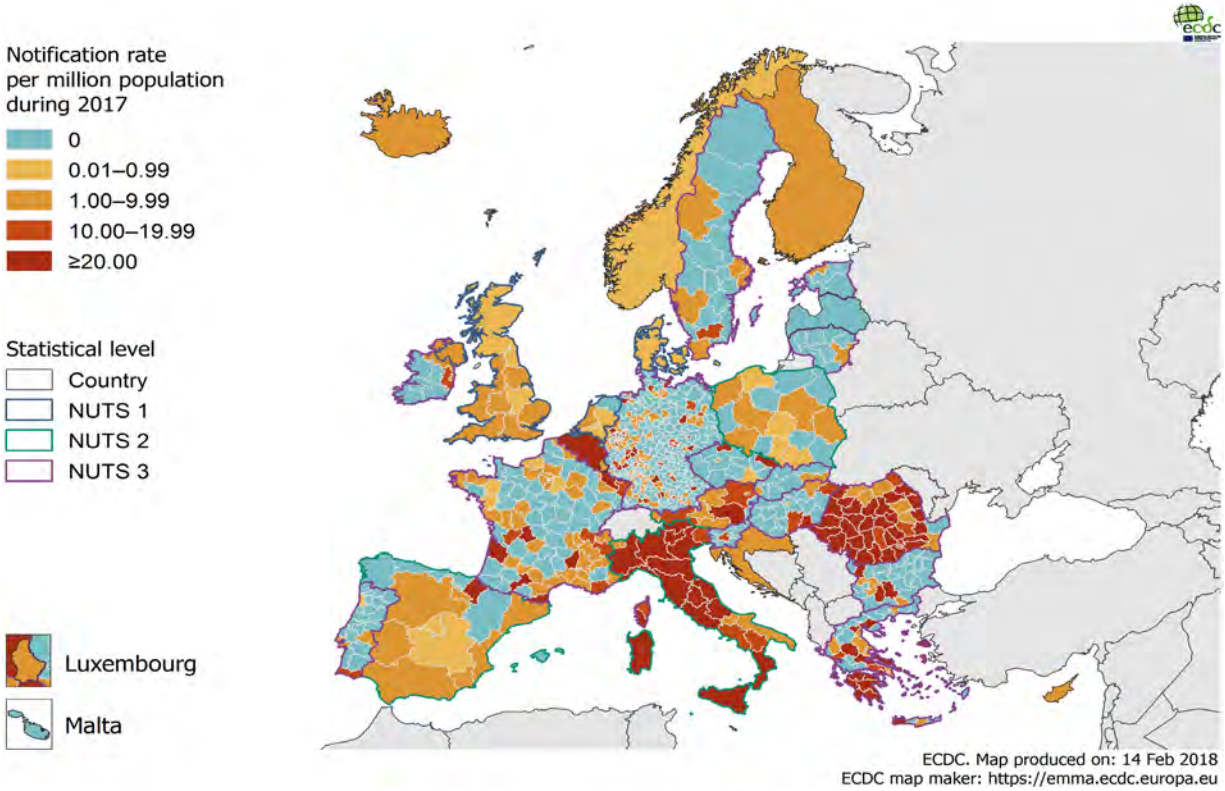
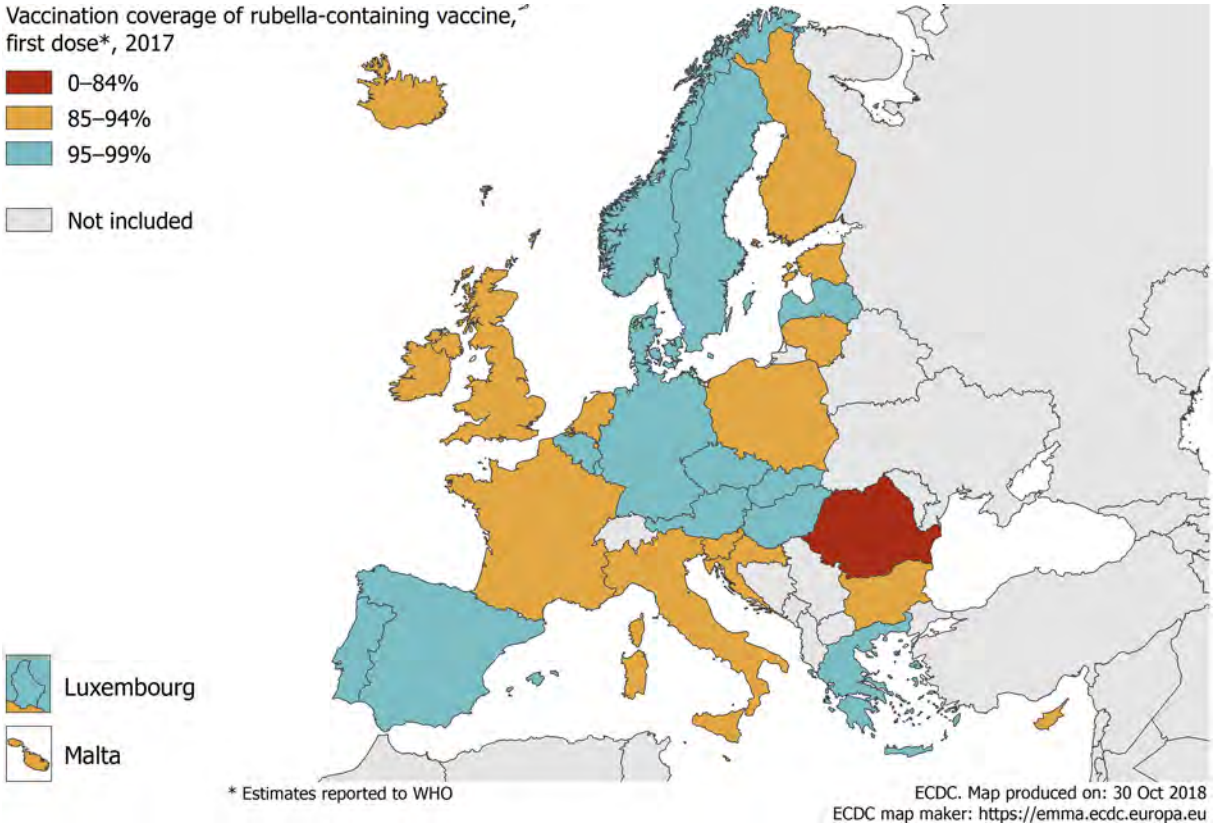


Figure 9. Measles vaccination coverage by country, EU/EEA countries, 2017



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 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 vaccination status and offering 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)	• Assess availability of immunisation records; plan vaccination based on age. • Provide catch-up immunisation so people from refugee-like backgrounds are immunised equivalent to an Australian-born person of the same age. • Full catch-up if records are not available
Canada (5)	Measles, mumps and rubella • Vaccinate all adult immigrants without immunisation records using one dose of measles–mumps–rubella vaccine. Diphtheria, pertussis, tetanus, polio • 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.
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: • All children in accordance with the routine childhood immunisation schedule at 12 months and 4–5 years of age (2 doses) • All others according to the 'late entrants catch-up schedule' for children and adults, as follows: – 12 months to 4 years, 1 dose MMR, 2nd dose at 4–5 years of age – 4 years to <18 years of age, 2 doses MMR at one month interval – Adults aged 18 years and older, 2 doses MMR at one month interval DTaP-IPV • 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. • Vaccinate all immigrant children with missing or uncertain vaccination records using age-appropriate vaccination for diphtheria, pertussis, tetanus and polio.
Italy (13, 393)	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 • measles, mumps, rubella, chickenpox; excluding pregnant women • diphtheria, tetanus, pertussis, HBV for the entire adult population screened in accordance with guideline recommendations (migrants from HBV incidence of HBsAg >2%, migrants with risk factors, and pregnant women) and negative for serological markers.
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. • 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. • Refugees who are to be resettled in the UK through a formal refugee resettlement scheme are offered vaccination pre-departure, in line with the national immunisation schedule. • Asylum seekers in initial accommodation centres in the UK are offered vaccination as part of their initial health assessment.
USA (394)	• Immigrants are required to show proof that they have received certain vaccines prior to arrival. • 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. • Refugees and international adoptees are exempt from this requirement, however they are offered 1–3 doses of each vaccine series (394). • Following arrival, all immigrants are recommended that they have their vaccinations updated in 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.

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

	EU/EEA*	
Total	1 226 859	%
Syria	94 356	8
China	83 883	7
India	77 002	6
Morocco	50 469	4
United States	43 132	4
Pakistan	35 764	3
Ukraine	35 384	3
Moldova	29 606	2
Russia	24 976	2
Brazil	24 915	2
Other	727 371	59

	Austria	
Total	64 258	%
Syria	11 745	18
Afghanistan	9 158	14
Serbia	5 693	9
Bosnia & H.	4 986	8
Iraq	3 746	6
Turkey	2 895	5
Iran	2 829	4
Russia	2 178	3
Ukraine	1 415	2
China	1 359	2
Other	18 255	28

	Belgium	
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

	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

	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	
Total	30 996	%
Syria	9 228	29
India	1 549	26
Philippines	1 361	11
China	1 307	9
Eritrea	1 284	3
United States	1 279	2
Ukraine	1 251	2
Greenland	954	2
Iran	947	2
Nepal	768	1
Other	11 067	13

	Estonia	
Total	3 531	%
Russia	1 371	39
Ukraine	931	26
Belarus	116	3
United States	110	3
India	72	2
Georgia	72	2
Nigeria	72	2
Kazakhstan	68	2
Turkey	55	2
China	48	1
Other	617	17

	Finland	
Total	16 384	%
Iraq	1 613	10
Russia	987	6
Syria	930	6
China	775	5
India	772	5
Afghanistan	708	4
Vietnam	703	4
Somalia	638	4
Thailand	566	3
Iran	563	3
Other	8 128	50

Hungary		
Total	25 465	%
Ukraine	8 326	29
Serbia	3 555	26
China	3 230	11
United States	1 108	9
Russia	637	3
Turkey	617	2
Iran	511	2
Japan	488	2
India	483	2
South Korea	362	1
Other	6 146	13

Iceland		
Total	1 047	%
United States	162	16
Philippines	78	7
Thailand	51	5
Vietnam	47	5
China	44	4
Syria	37	4
Canada	34	3
Ukraine	31	3
Russia	29	3
Serbia	27	3
Other	506	48

Italy		
Total	201 426	%
Morocco	15 600	8
China	13 446	7
Bangladesh	11 871	6
Pakistan	11 837	6
Albania	11 618	6
India	10 711	5
Brazil	9 986	5
Nigeria	9 311	5
Egypt	7 549	4
Senegal	7 345	4
Other	92 151	46

Latvia		
Total	3 365	%
Russia	1 511	45
Ukraine	689	20
Belarus	391	12
Uzbekistan	143	4
Kazakhstan	85	3
China	62	2
Philippines	53	2
India	51	2
United States	44	1
Azerbaijan	38	1
Other	298	9

Liechtenstein		
Total	332	%
Switzerland	195	59
Brazil	18	5
Turkey	10	3
Ukraine	9	3
China	8	3
Syria	7	2
Bosnia & H.	7	2
Dominican Rep.	6	2
Kosovo	5	2
Philippines	5	2
Other	62	19

Lithuania		
Total	5 213	%
Ukraine	1 656	32
Russia	1 391	27
Belarus	757	15
India	147	3
Kazakhstan	139	3
Georgia	114	2
Moldova	107	2
Azerbaijan	84	2
Iran	69	1
United States	65	1
Other	683	13

Luxembourg		
Total	7 084	%
United States	580	8
China	436	6
Syria	382	5
Cape Verde	339	5
India	330	5
Brazil	302	4
Russia	288	4
Morocco	239	3
Iraq	225	3
Serbia	183	3
Other	3 781	53

Norway		
Total	31 279	%
Syria	6 016	19
Eritrea	2 659	9
Philippines	2 166	7
Somalia	1 469	5
India	1 407	4
Afghanistan	1 239	4
Thailand	1 195	4
United States	1 003	3
China	783	3
Pakistan	714	2
Other	12 626	40

Romania		
Total	32 920	%
Moldova	23 282	71
Ukraine	2 166	7
Turkey	673	2
China	559	2
Israel	457	1
Russia	363	1
Syria	358	1
Serbia	349	1
United States	349	1
Iraq	347	1
Other	4 019	12

Slovakia		
Total	1 178	%
Ukraine	365	31
United States	100	9
Serbia	87	7
Switzerland	69	6
Russia	61	5
Iraq	52	4
Vietnam	31	3
Canada	30	3
China	29	2
FYR Macedonia	24	2
Other	331	28

Slovenia		
Total	10 443	%
Bosnia & H.	4 513	43
Kosovo	1 533	15
Serbia	1 445	14
FYR Macedonia	1 199	11
Russia	543	5
Ukraine	280	3
United States	99	1
China	92	1
Montenegro	82	1
Switzerland	38	0
Other	619	6

Spain		
Total	224 131	%
Morocco	24 661	11
Venezuela	20 462	9
Colombia	15 404	7
China	9 527	4
Argentina	8 897	4
Dominica	8 829	4
Brazil	8 762	4
Ecuador	8 513	4
Honduras	8 144	4
Cuba	8 106	4
Other	102 826	46

	Sweden	
Total	94 774	%
Syria	36 081	38
Eritrea	6 247	7
Iraq	4 125	4
India	3 639	4
Afghanistan	3 339	4
China	2 514	3
Iran	2 337	2
United States	1 639	2
Thailand	1 600	2
Turkey	1 505	2
Other	31 748	33

	United Kingdom	
Total	294 284	%
India	45 754	16
China	42 957	15
United States	19 988	7
Pakistan	12 713	4
Nigeria	8 842	3
Canada	8 770	3
South Africa	7 815	3
Malaysia	7 305	2
Thailand	7 182	2
Saudi Arabia	6 820	2
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	28
Afghanistan	13 295	27
Iraq	5 765	12
Pakistan	2 250	5
Iran	2 243	5
Somalia	1 400	3
Nigeria	1 342	3
Stateless	1 273	3
Russia	1 203	2
Kosovo	857	2
Other	5 897	12

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
Other	5 525	25

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

Croatia		
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

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	%
Ukraine	405	34
Syria	88	8
Cuba	87	7
Iraq	73	6
Armenia	65	6
Azerbaijan	58	5
Georgia	57	5
Vietnam	57	5
Russia	40	3
China	35	3
Other	210	18

Denmark		
Total	9 902	%
Syria	3 533	36
Afghanistan	1 165	12
Iran	1 068	11
Stateless	765	8
Eritrea	750	8
Iraq	678	7
Morocco	267	3
Somalia	197	2
Algeria	108	1
Libya	98	1
Other	1 272	13

Estonia		
Total	172	%
Syria	47	27
Ukraine	37	21
Iraq	13	8
Russia	13	8
Georgia	8	5
Afghanistan	7	4
Palestine	7	4
Albania	5	3
Iran	5	3
Armenia	5	3
Other	25	15

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

France		
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

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

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

Hungary		
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

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

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

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

Latvia		
Total	332	%
Syria	98	30
Vietnam	42	13
Iraq	32	10
Afghanistan	28	9
Russia	20	6
Ukraine	18	6
Georgia	15	5
Eritrea	10	3
Tajikistan	10	3
India	8	3
Other	50	15

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

Lithuania		
Total	400	%
Syria	113	28
Russia	55	14
Ukraine	42	10
Afghanistan	25	6
Tajikistan	25	6
Iraq	22	5
Georgia	20	5
Belarus	20	5
Armenia	15	4
Eritrea	10	3
Other	53	13

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

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

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

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

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

Portugal		
Total	842	%
Ukraine	210	25
DR Congo	75	9
Angola	57	7
Guinea	43	5
Congo	40	5
Mali	40	5
Pakistan	37	4
China	28	3
Iraq	23	3
Sierra Leone	23	3
Other	265	31

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	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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6. Discussion

6. Discussion

This doctoral thesis integrates four research papers based on three independent and specific objectives, united by their commonalities in public and global health and methodological aspects and implications. The common public health aspect in this work included: the critical appraisal of migrant health evidence, including a compendium of clinical or healthcare guidelines, recommendations or consensus statements about migrant healthcare; the appraisal of systematic reviews on migrant health interventions; the systematic assessment of screening alternatives and treatments for two neglected parasitic infections, and; the formulation of recommendations as scientific advice towards better health policy.

Our systematic quality assessment of available guidelines revealed a collection of resources on guidelines explicitly designed for migrants or inclusive of refugees and migrants as a unique population for consideration. The evaluation required the use of sufficient, valid and reliable evidence in all development processes and implementation considerations of the guideline. This appraisal work reported nine “recommended” guidelines. However, the overall quality in the development processes and reporting quality of migrant healthcare CPGs published from March 2006 to March 2016 was suboptimal. The recommendations underscored weaknesses observed in three domains of the guidelines, i.e., rigour of development, stakeholder participation, and editorial independence, needing significant improvements. Rigour of development ensures adequate inclusion and synthesis of evidence, stakeholder participation plays a critical role in equity and implementation, and editorial independence ensures the recommendations are emerging from the evidence-based process.

In the second work, we found that systematic reviews of health interventions for migrants published from January 2007 to April 2020 have important shortcomings, regardless the type of eligible study design, migrant subgroups included or region of the publication. The quality

of reporting was good in most of the included SRs on migrant healthcare; however, the lack of research protocol registration remained a significant issue. On the contrary, the methodological quality using AMSTAR-2 criteria was either low or critically low in approximately half of the included reviews. Regarding the risk of bias assessment under the ROBIS checklist, approximately 40% of the SRs had “high” concerns for risk of bias, related to flaws in the “study identification”, “data collection and study appraisal” and “synthesis and findings” domains.

In the third work, we found evidence from diagnostic systematic reviews showing that antibody-detecting serological tests were the most effective screening tests for schistosomiasis and strongyloidiasis in low intensity or low endemic setting; this was due to higher sensitivities and showed good post-test probabilities for positive and negative tests in comparison to the conventional parasitological methods. We also concluded that treatment of both infections was cost-effective.

We included a published protocol in the thesis which provided the rationale for developing evidence-based guidance for voluntary screening, treatment and vaccine prevention of common infectious diseases for newly arriving migrants to the European Union/European Economic Area (EU/EEA) (95). The protocol detailed the methods used in the identification, appraisal and synthesis of the best available evidence on prevention and assessment (95). Also, we included a systematic review on the accessibility and acceptability of Infectious Disease Interventions among Migrants in the EU/EEA(103) The study utilised a framework analysis based on the Health Beliefs Model that underlie preventive health behaviour, including knowledge of risk factors, perceived susceptibility, severity and barriers, and facilitators.

Finally, our fourth work focused on the development of evidence-based statements on screening and treatment of schistosomiasis and strongyloidiasis with considerations for cost,

feasibility and equity using the GRADE evidence to decision framework. According to the GRADE evidence-to-decision criteria, 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.

Thus, we addressed all the objectives, we employed systematic and transparent methods, including: the search for the available evidence, appraisal of retrieved documents using validated instruments, analysis of the findings, and reaching conclusions.

6.1 Findings on migrant public health and clinical care guidelines and recommendations evaluation and its significance.

In this context, the research question sought to report on the quality of the evidence in the currently published migrant health-related guideline and recommendations. Specifically, this research addressed the first of the three objectives of the thesis – to generate new knowledge on the quality of available migrant related CPGs.

From this research process, my overall understanding of clinical practice guidelines as "systematically developed statements to assist practitioner and patient in the decisions on suitable health care specific clinical circumstances" has significantly improved (104, 105). While, we can take for granted that CPGs employ clearly defined methods to establish reliable recommendations; in reality, however, some healthcare guidelines with poorly defined developmental processes, content and quality, which varies widely between and within

developing institutions, often resulting in inconsistencies in application and poorer outcomes (105).

Most guidelines for refugees and other migrants in our assessment were either developed explicitly for refugees or migrants by countries USA, Canada, Australia, while other guidelines particularly by global international organizations identified refugees and other migrants as subpopulations in their overall recommendations.

Our evaluation of CPGs for migrant health revealed that overall quality in the development processes and reporting was suboptimal with less than 30% of the CPGs evaluated as “recommended” for use [29-37]. We observed the highest quality score in guidelines authored by supranational bodies that were typically not specific to migrant populations, and a few specifically about migrants from countries like Canada, Australia and the USA (106-109). The domains with the lowest scores were “Editorial independence”, “Applicability” and “Stakeholder involvement”. Rigour of development ensures adequate inclusion and synthesis of evidence, stakeholder participation play a critical role in equity and implementation, and editorial independence ensures the recommendations are emerging from the evidence-based process. Our findings were comparable with other reviews of CPGs about other topics using the AGREE II tool, where the overall quality of guidelines was deemed suboptimal, or varied from low to moderate (110-113). This generally agreed with our assessment of the overall quality of migrant healthcare. Deficiencies in AGREE II domains highlight a lack of transparency in the guidelines development process and increase potential variabilities in such guidelines' intended results

CPGs in clinical areas such as pain management and survivorship care planning, for instance, failed to score over 60% in any of the six domains (42, 114). However, five (16%) of the 32 migrant healthcare CPGs evaluated scored more than 60% in all domains (85). Our result regarding marginal improvements in quality over time also agreed with results reported

for practice guidelines in other health areas(110, 111, 115, 116). The field of migrant health has significantly improved over the years because of available and applicable rating scales developed by organizations and some countries (48). Still, there is not an international society of migrant health research as such, other than practical field operations guidelines (e.g. UNHCR), which that can set methods and create quality criteria specifically for refugees and other migrants (117).

Typically, high-quality health guidelines are specific and unambiguous and developed based on empirical evidence which reflects the perspectives of relevant stakeholder (118). Our results showed that currently available public health guidelines appear not to accommodate the health requirements of migrants adequately (119). Still, the lack of effective global governance for migrant health persists due to varied, persistent and evolving issues affecting individual national health systems and beyond the present capacities of such supranational bodies like the WHO (119).

In terms of “rigour of development” in evaluated guidelines, a domain considered critical in guidelines’ appraisal for assessing methods used to identify and synthesize evidence, as well as processes relevant to the CPG development, formulation of the specific recommendations, and updating strategy (120), this was worryingly low. The domain scores for most migrant CPGs evaluated, appear not to have improved significantly even in recent years which suggest a significant lack of methodological proficiency in the guideline developing groups, or limitation in resources available in this area. Similar findings of low mean scores in “rigour of development’ linked to reporting flaws in the methods were observed in guidelines in other areas (57, 111, 121). The implication of this outcome is the need for migrant health recommendations to be supported by sufficient resources, for rigour in evidence synthesis in their development as well as incoproated the use of GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (115, 122).

Furthermore, our study reported overall low-level compliance with the AGREE criteria, which was similar in another assessment guideline using the AGREE tool (57). Typically, items relevant to the implementation of guidelines such as organisation barriers and facilitators, the resource implications, monitoring and auditing criteria were usually not reported in most of the guidelines (111, 123-126). The nature of the guideline developer, available resources and the field or topic covered in guidelines may have been some of the influencing factors. Hence, to boost the applicability of guidelines, developers need to incorporate support tools like summary documents, checklists, algorithms, solutions linked to barrier analysis as well as other tools for guideline facilitation (123, 124). Furthermore, stakeholders' involvement and values and preferences of the target population via consultations, panel participation or external reviews are essential elements for assessment of the central outcomes of guidelines are fundamental (57, 122, 126). While relevant professional groups were included and explicitly reported in most high quality guidelines focused on infectious diseases including migrants, whereas guidelines with specific focus on migrant screening scored low on criteria – "target population's views and preferences sought".

Lastly, the domain "editorial independence", returned the lowest overall mean score of 26.6% $\pm$ 38.5% attained in our study with generally little or no evidence of the description of the nature of competing interests, procedures undertaken, and their impact on guideline development and reporting processes (123, 127). Our observations agree with the reports of significant lack of clarity regarding the potential conflict of interests (COI) in published guidelines (112), and findings of significant underreporting and low compliances to "editorial independence" standards in migrant healthcare guidelines authored by national bodies or agencies (111, 112, 122). The danger inherent in this limitation may undermine the awareness and consideration of covert or overt influences on conflicts of interest (e.g. institutional,

financial, academic or educational) by guideline readers, hence the lack of credibility in the guidelines. Possibly, the requirements for “editorial independence” domain were unintentionally overlooked in a larger proportion of the evaluated guidelines and probably authored by the national governments or agencies. Hence, for migrant CPGs, national governments and all developers should be subjected to standard COI policies during their development to reduce risk of bias associated with conflict of interest, and improve transparency.

6.2 Findings on quality of migrant health systematic reviews and its significance.

In this context, the research question sought to report n the quality of migrant health systematic reviews used to support the development of migrant health guidelines, which addressed the second objective of the thesis – to critically appraise the quality of migrant health systematic reviews. This systematic appraisal of systematic reviews in this area using validated tools for risk of bias, methodological and reporting quality. Our main findings show that the overall quality of SRs on migrant health interventions published from January 2007 to April 2020 was suboptimal, regardless the study design, nature of the migrant population, or country/region in which the systematic review was published.

The assessment of the general methodological quality using the AMSTAR – 2 tool showed that approximately half of the included reviews have either low or critically low quality. The major shortcomings observed in these SRs are related to critical methodological factors, such as a lack of priori design, weaknesses in the study selection process and data analysis, absence in the identification of source of funding and their influence in the development of the review, flaws in the risk of bias assessment, presence of study heterogeneity not fully explained and presence of publication bias, among others. Although none of the included SRs

fulfilled? all the AMSTAR-2 items, we observed a slight improvement in the quality of SRs published from the year 2014 compared to those published before the year 2013.

Regarding the assesment of risk of bias using the ROBIS tool, our study identified that approximately 40% of the SRs had high concerns on the risk of bias directly related to the domains of study identification, data collection and study appraisal and synthesis and findings, respectively. Comparing the risk of bias assessment and the methodological quality, we observed some inconsistencies in assessment outcomes between AMSTAR-2 and ROBIS tools due to their multiple and highly divided rating measures within domains (82). Some SRs with high RoB under ROBIS had high or moderate overall confidence under AMSTAR-2 (128) (129-132), while other reviews with low overall confidence underAMSTAR-2 were classified as with low RoB following the ROBIS tool (133-139). A similar pattern of inconsistencies in outcome assessment was reported in a previous study using ROBIS and AMSTAR tools. The tools were not appraising the same issues - the risk of bias versus methodological quality in general.(140).

In contrast, the quality of reporting in most migrant SRs following the PRISMA statement showed that more than 60% had 20 – 27 items satisfied ~ mean: 20 ± 5.24.This was better than the reported mean of PRISMA 13.2 (SD 6.0) or 18 ± 4 items satisfied in rapid reviews or SRs in other health areas (83). However, the lack of research protocol and registration in the majority of the included migrant health SRs matches the overall suboptimal reporting quality reported in a pooled assessment of SRs adherence to the PRISMA statement (83, 91).

The appraisal tools' consistency in the outcome in quality across the included SRs was low and varied in terms of topics investigated and important outcome reported. However, there was no linear association between improvements in quality. A related study reported poor

compliance with both PRISMA and AMSTAR checklists with only selected items in both instruments adequately addressed in a rapid review (91).

SRs provide evidence essential in developing guidelines and guiding public health decision (85, 141, 142). Since clinical practice guidelines in this area will base their decisions on the evidence collected in systematic reviews of the literature, we judge that the significant differences or inconsistencies in the quality of the migrant guidelines may drop as the quality of the systematic reviews increases. We caution end-users of SRs to consider the less than optimum quality and rigour associated with a large number of published migrant health SRs. (119). Therefore, improvements in methodological rigour in the synthesis of evidence in migrant health area are urgently needed. Migrant health researchers should adhere to using either ROBIS or AMSTAR-2 in addition to PRISMA checklist due to their robust construct and methodological applicability. Furthermore, the participation of a methodological expert with considerable experience in both SR development and migrant research (for instance, involvement in relevant, as well network and groups such as Cochrane network, Migration Health and Development Research Initiative (MHADRI) and Global South Research) is essential for future high-quality SRs. Finally, there is a need for more collaborative efforts between supranational bodies, national agencies, professional societies and researchers in migrant health. Hence, the need for increased funding for the research in this field is paramount.

6.3 Findings on systematic reviews on the effectiveness of screening and treatment options for schistosomiasis and strongyloidiasis in migrants from endemic countries in the EU/EEA.

In this context, the research question posed was what the evidence on the most effectiveness and cost-effectiveness of screening and treatment for schistosomiasis and

strongyloidiasis is for migrants from endemic countries recently arriving in the EU/EEA region. We conducted a systematic review of literature on the efficacy of screening and treatment of both infections, and cost-effectiveness to generate new knowledge on migrant health, in line with the third objective of the thesis.

Although, several systematic reviews are addressing how effective are approaches to migrant screening infectious diseases in Europe, parasitic infections are not adequately covered (143) (39). Also, the recent increase in migrants to the EU/EEA from endemic countries, highlights the need for public health guidelines and recommendations on the optimal approach to screening for schistosomiasis and strongyloidiasis (30, 144). Furthermore, the rationale for screening for strongyloidiasis and schistosomiasis in the EU/EEA and not other parasitic infections is based on the estimated prevalence of these parasitic infections among migrant from high endemic areas; possible prevention of severe complications via early detection and treatment and prevention of secondary infections is based on the use of sensitive tests and safe treatment (30, 144). The goal to detect at-risk individuals may justify the screening since available data from endemic regions shows that prevalence of schistosomiasis is between 20% and 40% and prevalence of strongyloidiasis is between 10% and 40% (145, 146).

Overall, systematic reviews showed that antibody-detecting serological tests are the most effective screening tests for detection of schistosomiasis and strongyloidiasis in low-endemicity settings because they have higher sensitivity than conventional parasitological methods. For Schistosoma spp. infections, evidence from our review indicated that IgM-ELISA (147), IHA (148) and ICT IgG-IgM (149) tests were the most effective screening tests in low-endemicity countries (low certainty of evidence). According to protocols, in some low endemicity settings a case is considered to be positive if the serological test is positive; in others, a combination of ELISA testing and KK faecal examinations is used to improve

accuracy. However, Beltrame et al. advocate the use of the ICT IgG-IgM test as a single screening test because it showed the best accuracy (negative predictive value >97%) (149).

For strongyloidiasis, our results (very low to low certainty of evidence) indicate that antibody-detecting blood tests using a variety of antigen preparations have a better detection rate than conventional parasitological methods, with IVD-ELISA, Bordier-ELISA and NIE LIPS being the most accurate (150). However, the limitations of these serological tests include the large number of infective larvae required, cross-reactions with other nematode infections, and lower sensitivity in immunocompromised patients (150, 151). New tests based on the recombinant antigen Ss-NIE-1, although slightly less sensitive, but currently considerably more expensive and not widely available, show excellent specificity and may be useful when designing rapid tests(150, 152).

The conventional techniques, as well as PCR despite better specificity than serological techniques failed to detect infections of very low intensity (153-155); and are labour-intensive, requiring skilled personnel (151). In contrast, serological testing is easier to perform in health facilities and can also be combined with other infectious disease screening tests. However, the lack of differentiation between current and past infections is associated with the? detection of schistosomiasis, whereas with strongyloidiasis, antibody titres decline following treatment in most patients (150, 156). In immuno-compromised persons, the sensitivity of serological tests may be reduced, thus requiring additional assessment methods. The use of PCR assay may be an alternative screening method in immunosuppressed patients but deserves further investigation.

In terms treatment of schistosomiasis, single-dose praziquantel is the drug of choice. Evidence from systematic reviews show that treatment with praziquantel significantly increased parasitological cure and, achieved marked reductions in microhaematuria compared with placebo; praziquantel also has an excellent safety profile (157, 158). For

strongyloidiasis, there was low to moderate quality evidence that ivermectin is more effective than albendazole (159) and moderate quality that ivermectin is as effective as thiabendazole, but much better tolerated; no difference in the efficacy of ivermectin was observed between endemic and non-endemic populations (159). However, there are no studies on the potential harms of large-scale administration of ivermectin, though overall experience with filariasis control is reassuring. Considerations of presumptive treatment either with ivermectin or praziquantel requires complex screening strategies to identify individuals with loiasis or neurocysticercosis for whom these drugs might be inappropriate (160, 161). Recent recommendations for immigrants arriving from endemic areas specify a thorough clinical screening to be performed before the commencement on courses of praziquantel or albendazole (162). Besides, ivermectin is not readily available in most endemic and non-endemic countries and has limited approval by regulatory authorities in the EU/EEA.

On cost-effectiveness, we did not retrieve any studies evaluating the cost-effectiveness of schistosomiasis screening and treatment interventions in migrant populations. For schistosomiasis, no studies were available on the cost of screening tests based on antibody detection in the non-endemic setting. However, in endemic settings, double dose praziquantel was deemed to be highly cost-effective compared with a single dose (163). However, more economic analyses are required to provide better information on the cost-effectiveness of a test-and-treat strategy for schistosomiasis in non-endemic countries.

For strongyloidiasis, we retrieved three studies indicated that presumptive treatment with albendazole or ivermectin was cost-saving or cost-effective in migrants to the U.S. or in endemic settings (164-166). However, the limitations of these studies may decrease the relevance of the results for migrant populations in the EU/EEA. Again, most of the economic studies identified were limited to Asian populations, and not based on screening with antibody testing in a non-endemic setting. Regardless, where the prevalence of schistosomiasis and

strongyloidiasis is greater than 1% and the price of presumptive treatment is similar to that used in the economic evaluations identified in this review, presumptive treatment with ivermectin or albendazole is likely to be cost-effective for migrants to the EU/EEA.

6.4 Developing evidence-based recommendations for screening for schistosomiasis and strongyloidiasis in migrants from endemic countries in the EU/EEA.

Based on the evidence from a conducted systematic review of literature on the efficacy of screening and treatment of both infections and cost-effectiveness, we participated in the development of evidence-based recommendation using GRADE Evidence to Decision (EtD) framework, in line with the fourth objective of the thesis.

Of all helminthic infections, both schistosomiasis and strongyloidiasis can cause potentially severe consequences; however, they possess singular characteristics appropriate for population screening. First, most infected subjects are asymptomatic (167) and unaware of infection (151), or affected by very mild unspecific symptoms (168). Second, both diseases are considered as chronic conditions (151). *S. stercoralis* replicate indefinitely inside the human host through an auto-infective cycle, causing lifelong infection if left untreated (151). Schistosomiasis can remain as a subclinical infection for years, resulting in long-term complications (169). Furthermore, *S. stercoralis* can cause disseminated infections or hyper-infections with fatal outcomes in immunosuppressed patients (169). In contrast, chronic schistosomiasis can result from an immune-mediated granulomatous response to trapped eggs that produce organ-specific manifestations, which are mainly chronic urogenital and/or hepato-intestinal complications (168, 170, 171). However, there are very little data on the burden of these diseases among migrants in the EU/EEA, and prevalence estimates are derived from small observational studies from selected countries.

In the EU, there are few standard guidelines or recommendations for the screening and treatment of schistosomiasis and strongyloidiasis. Ireland and the UK are the only EU/EEA countries 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 (172, 173). Other non-EU countries with published guidelines on screening, treatment and vaccination against of infectious diseases include the US, Canada and Australia (48, 49).

Based on collated evidence using GRADE approach, we conducted a FACE survey of scientific panel/ expert members the EtD framework, there was an overall medium level 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 panel anticipated no significant 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 data on schistosomiasis and strongyloidiasis in migrants' country of origin; and to 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.

Screening for schistosomiasis and strongyloidiasis in migrant populations would be an important control strategy as it allows early detection and treatment of both infectious diseases, probably having an important impact in the individual morbidity, and preventing the risk of onward transmission. Although the evidence-based statements are based on indirect evidence, a very high value is placed on potentially life-preserving benefits of screening, linkage to care, and treatment (174). In this regard, both infections are potentially severe and chronic; however, the drugs used for the treatment of both are usually well-tolerated and safe

with few exceptions. Therefore, the health benefits are superior to the potential harms of the intervention. Priority groups should 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.

In terms of gaps in evidence and future research needs, there is a need for robust population-based studies on schistosomiasis and strongyloidiasis screening among migrants by age group, migration type, the timing of screening and associated cost-effectiveness is required to design the most effective programmes. Furthermore, high-quality surveillance of migrants from highly endemic countries is urgently needed. Also, monitoring any changes in prevalence between the community and holding centres for migrants in destination countries may help guide public health measures.

6.5 Strengths and limitations of this thesis

Systematic reviews constitute studies that collect all the scientific evidence that answers a specific research question. For its development, it uses systematic methods that allow minimization of bias in order to provide reliable conclusions for its users (70). Because the methodology of the three studies was based on the collection and evaluation of the scientific evidence of different types of studies, their application represented a challenge for the authors.

First, in the review and critical evaluation of migrant healthcare guidelines, it is possible that we did not identify some migrant HGs because they are often not indexed. Nonetheless, it is reasonable to accept that migrant public health guidelines or CPGs which are not indexed in electronic databases searched were probably of lower quality than those that we included in our assessment, hence, strengthening our conclusions.

However, the strength of the critical appraisal of guidelines includes the use of an exhaustive search for migrant health guidelines; independent assessment by three reviewers using a standardized instrument with very good concordance, and the absence of restriction by language, thus giving a more representative international view.

Regarding the quality of SRs**,** the limitations of our study include the possibility that we failed to identify some relevant migrant health SRs because we only included SRs published in the English language; and the search duration was limited to the period 2007-2017 (85). However, we also performed a search of individual studies from 2017 to 2020 to include. While our sample of 57 SRs was obtained from at least five different databases, the context, scope or topics covered varied widely. Likewise, the inclusion of different study designs, with heterogeneous populations may have impacted on the quality of SRs in this field.

Our study offered a comparative assessment of the methodological quality of SRs using ROBIS and AMSTAR-2, which although related have distinctive rating components and criteria in selected domains resulting in variations in overall judgement of bias in some studies. We also found that the "synthesis and findings" domain (ROBIS tool) contained criteria that did not apply to most of the included migrant SRs because the study designs were mostly qualitative, mixed studies or quantitative studies with no metanalysis.

The main strengths of our review were as follows - we had a priori design with a registered protocol, an exhaustive search, and used four independent reviewers with substantial experience in the quality evaluations of systematic reviews. Also, we used standardized, validated, and reliable instruments; performed a rigorous calibration of reviewers, as well as piloted the tools; and we used consensus procedures to obtain final ratings when required. The inter-rater agreement was excellent. Furthermore, using PRISMA, ROBIS and AMSTAR-2 ensured that we employed rigour in compliance to the instruments criteria, such using explicit

predefined objectives and eligibility criteria, duplicate selection of studies, and data extraction processes to minimize the risk of errors.

Regarding the evaluation of systematic reviews on the efficacy of screening and treatment of schistosomiasis and strongyloidiasis, we believe that the main limitation is that we did not identify any systematic reviews or RCTs on screening for schistosomiasis and strongyloidiasis in newly arrived migrants to EU/EEA. Randomized trials on screening are rare, and therefore we used a logic model approach, as recommended at US Task Force on Preventive Health Care, and presented data on population prevalence, diagnostic accuracy, treatment effectiveness and cost-effectiveness (160, 175). Other limitations include the lack of accurate data on the prevalence of schistosomiasis and strongyloidiasis among migrants from endemic countries entering the EU/EEA, and the lack of data on the cost-effectiveness of screening and treating migrants for these parasitic infections. We believe these factors may decrease the relevance of the results for migrant populations in the EU/EEA, even in the face of a strong rationale for screening and treatment.

However, the strengths of our study include the use of the GRADE methodology to evaluate the certainty of evidence, the inclusion of objective outcomes —parasitological cure or failure for the efficacy of treatment and accuracy for screening—and the inclusion of studies from different regions and countries with moderate to high endemicity for both parasites, increasing the generalizability of the results.

Although migrant health evidence is mostly support by evidence based on indirect outcome, however using the GRADE certainty estimate methods, indirect evidence may be more useful than low quality direct evidence. In the case of indirect evidence, the guideline panel must determine the significance of the indirectness considering population, intervention, comparison and outcomes indirectness to determine if it is necessary to decrease the certainty rating or not (176). While identifying infectious diseases early through testing is a critical

clinical and public health intervention, it is only one element of the care pathway (177). Integral to the development of guidelines is an understanding of the importance of, and interventions for, each element of the healthcare pathway, i.e., from access to appropriate health services to testing/screening and adherence, to/completion of treatment. Although the evidence suggests screening should target people arriving from endemic areas, tailored national screening strategies should consider the specific context for individual countries in the EU/EEA and the migrants' countries of origin.

Finally, given the developed recommendations on screening options, we suggest that the optimal approach to the delivery of screening should consider a global perspective but one that is dependent on the health system context. In this regard, addressing lack of access to healthcare for migrants, heterogeneity of screening strategies applicable in member states, and improving health professionals' knowledge and training of migrant related infectious diseases should improve the responsiveness of the public health care system with regards to coverage and uptake of screening.

6.6. Implications

6.6.1.Implications for practice

There is need for more collaboration between supranational bodies, national agencies and professional societies in developing practice guidelines for migrant healthcare and establishing and implementing optimal conflict of interest policies, all of which would require more resources to be made available.

- Of critical importance is ensuring that assessment of guideline outcomes in practice include adequate stakeholder involvement, identification of values and preferences of migrants, and review of MHGs by external experts before publication (178)

- Integration of the GRADE(Grading of Recommendations Assessment, Development and Evaluation) by developers and researchers in evidence synthesis could significantly impact the rigour in methods and reporting, and therefore, recommendations in this field. (115).
- High quality surveillance of migrants from highly endemic countries is needed. Also, monitoring any changes in prevalence between community and holding centres in destination countries to better adapt public health measures.
- Integrating a health equity consideration as well as improving cultural competence in the health professionals and in institutions working with refugees and other migrants will be beneficial.

6.6.2. Implications for research

- This thesis highlights progress made in improving health access and quality of care for refugees and other migrants, but inconsistencies, gaps in knowledge in existing evidence base in this health area remain
- An over-representation of research evidence and guidelines in migrant health focuses on infectious disease screening and treatment compared to other neglected aspects such as mental health.
- There need to consciously expand the scope of systematic reviews on migrant health beyond routine primary healthcare services or infectious disease screenings to other clinical or healthcare interventions accessible to the host population.
- There is a need for more extensive research on the health concerns of subpopulations of migrants, and particularly in the category of migrant workers, of which we found only one systematic review, not well-represented in our sample (179).

- Robust population-based studies on schistosomiasis and strongyloidiasis screening among migrants by age group, migration type, the timing of screening and associated cost-effectiveness will improve the future designing of effective programmes.
- More evaluations of the effectiveness and cost-effectiveness of screening intervention in migrant populations coming to the EU/EEA from endemic areas are needed. Additionally, in host countries, we need economic analysis on the costs of a test and treat strategy compared to the cost-effectiveness of screening and presumptive treatment.

7. CONCLUSION

7. Conclusion

- Few migrant guidelines were "recommended." The quality in most published guidelines for refugees and other migrants was suboptimal quality with much room for improvement, especially in the domains of rigour of development, stakeholder participation, and editorial independence
- Current CPGs for refugees and other migrants are either explicitly designed for migrants or infectious diseases recommendations inclusive of refugees and migrants as a unique population for consideration.
- The overall quality of migrant health SRs is suboptimal, with critical gaps linked to low protocol registration, inadequate assessment of the risk of bias and publication bias, no additional analysis of synthesized evidence and limited funding resource.
- Current deficiencies in systematic evidence on migrant healthcare, in terms of focus and quality, reveal an academic field that is still at the early stages of development; and highlight the present limited funding scope devoted to migrant health research.
- Based on a compendium of indirect evidence on screening outcomes (low -certainty of evidence), we suggest offering serological testing for strongyloidiasis and schistosomiasis in the absence of immunosuppression to all migrants coming from endemic areas into the EU/EEA.
- Ivermectin and praziquantel demonstrated high efficacy, an excellent safety profile, and with potentially easy schedule for the presumptive treatment of strongyloidiasis and schistosomiasis.
- The findings of this thesis will aid guideline developers, healthcare practitioners and policymakers in developing more comprehensive migrant healthcare guidelines.

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Related Publication 1

- Pottie K, Mayhew AD, Morton RL, Greenaway C, Akl EA, Rahman P, Zenner D, Pareek M, Tugwell P, Welch V, Meerpohl J. 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 Sep 1;7(9):e014608.

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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

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ABSTRACT

Introduction The European Centre for Disease Prevention and Control is developing evidence-based guidance for voluntary screening, treatment and vaccine prevention of infectious diseases for newly arriving migrants to the European Union/European Economic Area. The objective of this systematic review protocol is to guide the identification, appraisal and synthesis of the best available evidence on prevention and assessment of the following priority infectious diseases: tuberculosis, HIV, hepatitis B, hepatitis C, measles, mumps, rubella, diphtheria, tetanus, pertussis, poliomyelitis (polio), *Haemophilus influenza* disease, strongyloidiasis and schistosomiasis.

Methods and analysis The search strategy will identify evidence from existing systematic reviews and then update the effectiveness and cost-effectiveness evidence using prospective trials, economic evaluations and/or recently published systematic reviews. Interdisciplinary teams have designed logic models to help define study inclusion and exclusion criteria, guiding the search strategy and identifying relevant outcomes. We will assess the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Ethics and dissemination There are no ethical or safety issues. We anticipate disseminating the findings through open-access publications, conference abstracts and presentations. We plan to publish technical syntheses as GRADEpro evidence summaries and the systematic reviews as part of a special edition open-access publication on refugee health. We are following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols reporting guideline. This protocol is registered in PROSPERO: CRD42016045798.

Strengths and limitations of this study

- ► Explicit, transparent and trustworthy review method.
- ► Pragmatic approach builds on existing systematic reviews and permits de novo reviews when warranted.
- ► International team with guideline, Grading of Recommendations Assessment, Development and Evaluation migrant health, and infectious disease experts.
- ► There will be less emphasis on synthesis of local and contextual data in this portion of the project.
- ► Synthesis of data from various systematic reviews will require close focus on research questions.
- ► Updates and de novo synthesis will need to focus on the most substantive evidence gaps.

INTRODUCTION

The increase in refugees and other migrants from low-income and middle-income countries (LMICs) to the European Union/European Economic Area (EU/EEA) since 2011[1] has made the development of infectious disease guidance a public health priority for EU/EEA Member States. High mobility, poor living conditions, barriers to accessing healthcare and potential public health risks for newly arriving migrant populations and host populations are leading public health concerns. As a result, the European Centre for Disease Prevention and Control (ECDC) called for evidence-based guidance to support tailored public health approaches to health

assessment (voluntary screening) and prevention (vaccination) among newly arrived migrants. This guidance aims to support public health and health system professionals to screen and treat international migrants.[2]

Migrant populations include economic migrants, refugees, asylum seekers and irregular migrants who may have been forced to flee conflict, natural disasters or economic peril.[3] For the purposes of this evidence-based project, we define the target migrant population using health risk associated with recent arrival (eg, within 5 years of arrival in EU/EEA), country of origin, gender, and unaccompanied minors and other circumstances of migration.[3] Scoping literature reviews and a consensus meeting in Stockholm have selected a series of infectious diseases for systematic reviews: tuberculosis (TB) (active and latent), HIV, hepatitis B, hepatitis C, measles, mumps, rubella, diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b, strongyloidiasis and schistosomiasis.

Infectious diseases endanger the health of both migrant and host populations. Interventions targeting both public health and health systems levels are needed to address these threats. The Migration Integration Policy Index health system survey showed that policies and programmes relevant for migrants are underdeveloped in many European countries.[2] Key challenges identified by the survey include inadequate entitlements to healthcare, poor accessibility of services, lack of responsiveness to migrants' specific needs, absence of interpretation services and lack of local health professional training.[4]

For decades, public health programmes have played an important role in assessing migrants for infectious diseases. Historically, port-of-entry approaches met ships on arrival and conducted screening and quarantine programmes.[5] In recent decades, the sheer number of migrants and diverse modes of travel have reduced the effectiveness of this approach.[6] Evidence from a series of evidence reviews in Canada on recent migrants showed that age, gender, forced migration and migrant country of origin often modified disease risk and helped guide assessment and prevention priorities.[3] Evidence from international migrant health reviews have begun to influence public health policy and primary health clinical assessments, as seen in Ireland, Canada, Australia and the USA, for example.[3 5–7]

The objective of this suite of systematic reviews is to guide the identification, appraisal and synthesis of best available quantitative and qualitative evidence on prevention and assessment (voluntary screening) of priority infectious diseases. This protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols (PRISMA-P) guideline.

RATIONALE

The ECDC has invested in systematic reviews of public health voluntary screening and prevention for newly arriving migrants.[8 9] Systematic reviews play an important role in synthesising evidence to address important questions in health and social programmes. Using standardised methods, review findings can contribute to new recommendations, trustworthiness of existing evidence and the identification of gaps in knowledge. Systematic review protocols serve as explicit and transparent templates for the final review. Protocols minimise bias by determining the content of the process and content of the review. Publishing the protocol demonstrates to the reader that the methods have been thought out in advance and provides the reader with an opportunity to confirm the authors made critical decisions a priori.[10] Following the protocol accordingly and performing the review properly will identify the effects of interventions on the benefits and harms of health assessment (voluntary screening, treatment and vaccine prevention) in migrants. Below, we provide context overviews of each selected infectious disease; additional details on rationale, key questions and logic models for each infectious disease review can be found in the online supplementary appendices.

Tuberculosis

TB causes significant morbidity and mortality in high-income countries. Migrants from high TB incidence countries account for the vast majority of the TB case burden.[1 11 12] Migrants originating from intermediate and high TB incidence countries are at increased risk of exposure to TB and increased risk of developing active TB.[6] Individuals and overcrowded populations exposed to TB have an increased lifetime risk of developing active TB through reactivation of latent TB infection (LTBI) after arrival. Screening and treatment of active and latent TB are often components of TB control and elimination strategies. Most Western European countries screen migrants for active TB on or soon after their arrival. However, for the migrant groups targeted, the TB incidence in migrant source countries and the setting vary.[13–16] The effectiveness and cost-effectiveness of these strategies are unclear. Given the relatively low yield of active TB screening programmes, there is a growing interest in latent TB screening and treatment for migrants to prevent the development of active TB.[17] It is also unclear which migrants may benefit from LTBI screening and treatment and what would be the impact on health system's resource use and costs. The ECDC continues to work on TB elimination strategies and these include screening guidance[17] (see online supplementary appendix 1, supplementary appendix 1 figure 1 and supplementary appendix 1 figure 2).

HIV

By the end of 2014, approximately 36.9 million people were living with HIV and/or AIDS, 2.6 million of whom were children under the age of 15 years. Sub-Saharan Africa bears the largest burden of HIV, where the number of HIV-infected people had reached 25.8 million in 2014[18] and only 54% of infected people were aware of their positive status for HIV. In the same year, 1.2 million persons

around the world died due to HIV-related causes. In 2014, almost 30 000 people were diagnosed with HIV in EU/EEA Member States, a rate of 6.4 cases in every 100 000 people.[19] In the EU, an estimated 30% of people living with HIV are unaware of their HIV infection.[20] This is thought to be mainly due to the low uptake of and access to voluntary HIV testing and counselling. HIV is disproportionately prevalent in LMICs, and thus refugees and other migrants coming from HIV endemic countries are at increased risk for this infection. The stigma attached to HIV and the potential for exclusion from immigration by some countries pose additional barriers and concerns for the migrants. Migrants face fears of HIV transmission, and impact of seropositive status on family, community and individual/family costs, including loss of work time related to screening and treatment. This fear and stigma forces migrants to avoid HIV testing and to seek treatment.[21 22] There is a need for evidence-based guidance for screening approaches and treatment of migrant populations coming to the EU/EEA from HIV endemic areas (see online supplementary appendix 2 and supplementary appendix 2 figure 1).

Hepatitis B

Hepatitis B virus (HBV) infection is an important global health problem that affects an estimated 240 million people worldwide and approximately 13 million in the WHO European region.[5 23] Chronic HBV infection is frequently asymptomatic, but 20%–30% of patients with chronic hepatitis B (CHB) will develop complications, including liver cirrhosis and hepatocellular carcinoma (HCC). These complications result in 650 000 premature global deaths annually.[24–26] An effective vaccine for hepatitis B has existed for several decades. In addition, new treatment options are increasingly effective at reducing the incidence of cirrhosis and HCC in patients with CHB.[6] Although global vaccination rates have increased, the prevalence of CHB remains high in certain LMICs.[7 26] Migrants to EU/EEA carry a disproportionate burden of CHB-related morbidity and mortality. Practices in screening and treatment for hepatitis B vary by country across Europe, with no standard EU/EEA guidance for screening, vaccination and treatment.[24] Impact on resource use and costs varies by country. Studying the effectiveness of screening and developing appropriate guidance for hepatitis B in migrants to Europe for whom to screen, vaccinate and treat are a priority for migrant health (see online supplementary appendix 3 and supplementary appendix 3 figure 1).

Hepatitis C

Worldwide, between 120 and 170 million people are living with hepatitis C virus (HCV), with 15 million in the WHO European region.[24] HCV is the leading cause of chronic liver disease, end-stage cirrhosis and liver cancer.[6] It is estimated that between 2 and 6.6 million individuals in the EU/EEA are infected with chronic HCV. HCV is one of the leading causes of chronic liver disease and cirrhosis, and the most common indication for liver transplantation in most European countries. Patients in early stages of the disease are generally asymptomatic, and therefore most patients present in the late stages of HCV disease, when treatments are less effective and complications or death are unavoidable.[27] In recent years, highly effective but very expensive curative treatments have emerged. Early diagnosis and treatment may limit the burden of the disease in the EU/EEA, for example, screening migrants when HCV prevalence in their countries of origin is higher than those of European settlement countries.[28] Defining high prevalence regions and determining the effectiveness, acceptability, cost and affordability of screening and treatment from both an EU/EEA migrant and a public health perspective are necessary (see online supplementary appendix 4 and supplementary appendix 4 figure 1).

Vaccine-preventable diseases (measles, mumps, rubella (MMR vaccines), and diphtheria, tetanus, polio and pertussis, *Haemophilus influenzae* type b (DTPP-Hib vaccines))

In 2011, evidence-based clinical guidelines for migrants and refugees recommended vaccination for all adult immigrants without immunisation records with one dose of measles, mumps and rubella vaccine, and a primary series of tetanus, diphtheria and polio vaccines, to reduce associated morbidity and mortality.[6] For children, the guidelines propose age-appropriate vaccination for those with absent or uncertain vaccination records.[6] The low cost of vaccination is strongly favoured against potential morbidity and mortality costs associated with measles complications, congenital rubella syndrome, tetanus and severe pertussis in infants.[29–33] Despite this recommendation, engaging migrant populations in preventative health services remains a challenge. Factors include barriers to accessing healthcare, lack of health coverage in public programmes, inability to obtain private health insurance and documented immigration status, among others. Organisational barriers include availability of interpreters and cultural mediators, hours of operation, lack of information regarding services provided, as well as geographical and transportation challenges.[34] Individual-level barriers that include social isolation and lack of support networks, cultural aspects of belonging to an ethnic group, language barriers and discrimination were factors that migrants identified as making them vulnerable, hindering access to care.[34] This review will synthesise evidence on safety, resource use including type of personnel (eg, nurses and health workers) and models of administering vaccinations, cost and implementation for EU/EEA (see online supplementary appendix 5 and supplementary appendix 5 figure 1).

Intestinal parasites

Schistosomiasis and strongyloidiasis affect between 30 and 250 million persons in endemic regions. The health impact of these neglected intestinal parasitic diseases has recently gained prominence due to increased global migration and resettlement. For example, strongyloidiasis

and schistosomiasis both have the peculiarity of leading to severe chronic infections years after leaving endemic regions. Strongyloidiasis may be life-threatening in immunocompromised patients, and schistosomiasis may lead to chronic and fatal complications such as cancer. The rates have significantly increased in previously non-endemic regions.[6] *Schistosoma haematobium* can infest bodies of water in Southern Europe where intermediate competent host Bulinus (molluscum) is present. This could theoretically lead to foci of transmission in the EU.[35] Thus, there is a need to provide evidence-based guidance for voluntary testing and treatment that will reduce morbidity and mortality in high-risk migrant populations, in order to reduce transmission and out-of-pocket and health system costs, and to prevent the transmission of the infection. Defining high prevalence regions and determining the effectiveness, acceptability, resource use and cost-effectiveness from both a migrant and an EU/EEA public health perspective are necessary (see online supplementary appendix 6, supplementary appendix 6 figure 1 and supplementary appendix 6 figure 2).

OBJECTIVE

The objective of this systematic review is to identify, appraise and synthesise the best available evidence on prevention and health assessment of selected infectious diseases among migrants to the EU/EEA. It will use a Cochrane-based approach and report on clinically important outcomes and Grading of Recommendations Assessment, Development and Evaluation (GRADE) summary of findings tables and cost-effectiveness of interventions.[36] We provide detailed key questions and outcomes for each of the disease reviews in the online supplementary appendices.

METHODS

The Cochrane methodological approach described in this protocol for evidence-based literature searching conforms to the PRISMA for systematic review protocols (PRISMA-P) as closely as possible.[10] This suite of systematic reviews aims to conduct systematic reviews and to inform ECDC public health guidance. We will update and enhance anchoring evidence-based migrant evidence.[36] This protocol outlines the methods approach to the systematic review. This approach follows the new GRADE Adolopment Approach, a systematic guideline development approach that combines adoption, adaptation, and as needed de novo development of reviews to address elements of the GRADE evidence to decision (EtD) framework.[3 36–38]

Within this overall systematic review, there are six infectious diseases working groups, each one evaluating the evidence for one or more infectious disease topics. Each working group has developed key questions and prioritised clinically important outcomes. Groups then constructed a logic model considering children and adult migrant populations to explicitly outline the evidence pathway to guide the search and synthesis (see online supplementary appendices). All six subgroups will follow the review methods as described in this protocol. Each interdisciplinary group includes disease content experts, a European public health context expert and a GRADE methodologist; some groups include community organisations. The process is divided into four phases:

- Phase 1: conduct systematic review and appraisal of effectiveness reviews and evidence-based guidelines (ie, linked to systematic reviews).
- Phase 2: conduct systematic search and appraisal for economic evaluations on resource use and cost-effectiveness, on each topic.
- Phase 3: update systematic reviews of effectiveness: search for, select, appraise and synthesise new trials and systematic reviews to update the existing systematic review.
- Phase 4: supplement with de novo systematic reviews: we will conduct new focused systematic reviews if there is promising evidence but no existing systematic reviews on a critical topic or question. These searches will focus on randomised and non-randomised trials.

Phase 1: conduct a systematic review of reviews and guidelines

Eligible studies for this review will include systematic reviews that meet the criteria described in table 1. We will not apply a language restriction in this protocol, and when we identify more than one version of a systematic review, the most recent one will be considered.

Table 1 Eligibility criteria used for all diseases

Study characteristics	Inclusion criteria
Population	We will consider studies of any population, children and adults, which may be considered indirect evidence. We will use migrant data if available.
Interventions	Screening, treatment and vaccine prevention interventions and programmes for one of the selected diseases being evaluated.
Comparisons	No screening or prevention intervention/programmes comparison.
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 searching of at least one database.

Search strategy

An experienced health information specialist with expertise in systematic review searching will develop electronic literature search strategies in consultation with infectious disease working groups (see online supplementary appendix 7 for an example of a draft search strategy for one disease for one database). We will search Medline, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Epistemonikos and Cochrane Central. The literature search will be restricted to studies published from 1 January 2010 to present. Our group published migrant health guidelines based on systematic reviews in 2011,[6] and we will use these as anchoring evidence-based guidelines to supplement with new systematic review evidence. The search strategy will use a combination of indexed terms and free text words. Our previous searches[6] demonstrated that refugees and other migrants are under-represented in randomised controlled trials and other intervention research. Migrants represent a very heterogeneous international population. When appropriate, we will consider studies on high-risk migrant groups, but in estimating effectiveness of interventions we will also consider studies on general populations. Later as we develop guidance, we will also collect evidence as we study migrant values on outcomes, acceptability, feasibility and equity.

In addition, we will search grey literature for published guidelines and reports on screening and prevention programme on relevant organisations' websites (eg, Centers for Disease Control and Prevention (CDC), ECDC, The Joint United Nations Programme on HIV/AIDS (UNAIDS), WHO). The literature search results will be uploaded to a reference manager software package, to facilitate the study selection process.

Study screening and selection

Prior to the screening process, the review teams will undergo an exercise to facilitate consistency in study selection. The trained reviewers will screen in duplicate and independently screen the titles and abstracts of all retrieved citations to identify the eligible reviews. The full texts of potentially eligible citations (systematic reviews) will then be retrieved and screened independently in duplicate. During the systematic review, citations that are not reviews will be catalogued so they are available if needed at a later stage. The reviewers will compare the results and resolve disagreement by discussion or with help of third reviewer. We will contact authors of reviews once for missing information. If the reviewers are unable to find a meta-analysis relevant to the research question, but do find relevant individual studies within the review, then they will consider assessing the studies for inclusion.

Data extraction

We will develop a standardised extraction sheet for each condition-specific subgroup. We anticipate some consistency across groups, especially with respect to how data are extracted, but there will be unique content aspects to each disease-specific data extraction as well. Prior to data extraction, reviewers will undergo a calibration exercise to ensure consistency. Teams of two reviewers will extract data in duplicate and independently. They will compare results and resolve disagreements by discussion or with help from a third reviewer. At a minimum we will extract (1) population, intervention, comparison and outcome elements of the research questions for interventional systematic reviews; (2) databases searched; (3) number of studies included in the systematic review; and (4) results (see online supplementary appendix 8 table 1). Data extraction will be modified if individual studies are found and included at this stage.

Risk of bias

We will assess the quality of the included systematic reviewers using the Scottish Intercollegiate Guidelines Network (SIGN 50) and 'A Measurement Tool to Assess the Methodological Quality of Systematic Reviews (AMSTAR)' tools (see online supplementary appendix 8 table 2).[39] Two reviewers will independently assess the quality in duplicate and disagreements will be resolved by discussion or using a third reviewer. We will also consider reporting of other forms of bias for systematic reviews of observational studies based on recommendations from the draft AMSTAR II (B Shea, personal communication, 2016). Quality assessment criteria will not be used to include or exclude studies but will be used to assess certainty in the findings. GRADE requires an assessment of the risk of bias. Information on the risk of bias for the individually included studies will be extracted according to the reporting in the included systematic reviews. Any individual studies will be assessed using Cochrane Risk of Bias tool or Newcastle-Ottawa Scale as appropriate.

Assessing the quality and certainty of the evidence

The GRADE criteria will be applied to assess the quality and certainty of evidence for the included studies. The rating is based on an assessment of (1) risk of bias (study limitation); (2) inconsistency (heterogeneity) in the direction and/or size of the estimates of effect; (3) indirectness of the body of evidence to the populations, interventions, comparisons and/or outcomes; (4) imprecisions of results (few participant/events/observations and/or wide CIs); and (5) other considerations (effect size and publication bias). The quality of evidence may be downgraded if there are serious or very serious concerns related to any of the GRADE criteria (see online supplementary appendix 8 table 3). All key data will be entered in the GRADEpro software. This software will be used to produce GRADE evidence profile tables and summary of findings tables. If relevant, we will use the GRADE-CERQual approach for summary of findings for outcomes for qualitative systematic reviews.[40–42]

Ranking of outcomes

In this protocol, we have identified and ranked all potential patient important outcomes (see online supplementary

appendix 8 table 4). Outcomes are ranked as critical, important but not critical, or limited importance for decision making. Only evidence on critical and important outcomes will be considered.

Phase 2: conduct a systematic search and selection for economic evaluations on resource use, costs and cost-effectiveness

We will use cost-effectiveness studies identified from phase 1, and a librarian scientist will systematically search for economic evidence including resource use, costs and cost-effectiveness studies using Medline and Embase relating to our priority interventions. In addition, two health economists will systematically search the National Health System Economic Evaluation Database, the Cost-Effectiveness Analysis Tuft's registry and Google Scholar databases for economic studies. A sample PRISMA flow chart is provided for economic studies for TB (see online supplementary appendix 9). The health economists will screen the results for systematic reviews and primary studies of resource use, costs or cost-effectiveness of screening and treating each of the priority infectious diseases, then independently screen the full-text articles and assess the systematic reviews for quality using AMSTAR. Studies will not be excluded on the basis of AMSTAR scores. Data will be independently extracted from primary studies of resource use, costs or cost-effectiveness aligned with the disease group's aims, including GRADE EtD considerations around size of resource requirements, certainty of evidence of resources and cost-effectiveness favouring the intervention or comparator. A one-page narrative summary of the economic evidence will be written, and evidence about the resource use and costs will be incorporated into the GRADE evidence profiles and summary of findings tables where appropriate.[43]

As economic evidence has not previously been reported in guidelines, we will systematically search all databases from inception to June 2016. Two reviewers will independently select, appraise and extract data. In case of disagreement, we will use discussion or a third reviewer. Evidence will be summarised for each of the infectious disease conditions. We will use AMSTAR for quality assessment of systematic reviews and GRADE to appraise certainty of evidence in the primary economic evaluations.

Phase 3: update systematic reviews of effectiveness

We will search for, select, appraise and synthesise new prospective trials and systematic reviews to update the existing systematic reviews. We will use the same search strategies as used in phase 1, but will consider trials as well as systematic reviews. We will search for intervention effectiveness dating 1 year prior to the publication of the most recent systematic reviews. We will appraise and evaluate the new evidence and we will integrate new evidence into the evidence summaries when feasible.

Phase 4: supplement with de novo systematic reviews

If no reviews are identified in phase 1 to address a critical disease or care delivery question, then a new systematic review will be performed to develop the guidance. Studies identified in this stage will be evaluated and synthesised using similar methods described previously. We will conduct a quality assessment using tools designed for individual studies, such as the Cochrane Risk of Bias tool for randomised trials[44] or the Newcastle-Ottawa Scale for non-randomised studies.[45] We will not use quality as sole eligibility criteria.

When possible, we will conduct a meta-analysis as part of the creation of GRADE summary of findings table. When not appropriate due to high levels of heterogeneity, we will synthesise and report the evidence using a narrative summary of findings format. The objective will be to report on the preselected benefits and harms associated with the interventions of interest.

Developing guidance using evidence

All existing evidence selected and synthesised for interventions, including both benefits and harms, will be identified as evidence for GRADE summary of findings tables. We will select the most recent, the most relevant (based on European context and our logic model and questions) and the highest quality evidence. Evidence will come from systematic reviews and cost-effectiveness studies updates with randomised controlled trials. Where important gaps exist, we will address them with focused de novo systematic reviews.

DISSEMINATION

We will publish the separate systematic review in an open-access journal for public health stakeholders and/or the GRADEpro database of evidence profiles (dbep.gradepro.org). We will make the results available to panels of experts to use the evidence to develop international guidelines for migration. ECDC will publish a technical report, and we plan to submit a final guideline summary paper to a European clinical journal, for example, the *British Medical Journal*. We will use the ECDC, the International Conference on Ethnicity, Race and Migrant Health, our Campbell and Cochrane Collaboration Equity Methods website, and other social media to push out results.

DISCUSSION

During the past 50 years, many national and some international disease detection and control, immunisation, and communicable disease prevention strategies have been successful. Refugees and other migrants originating from countries with a high infectious disease burden could pose a challenge for national disease control and/or elimination strategies. Evidence-based guidelines are required to guide public health, non-governmental organisations and clinical sectors in the assessment and prevention of

infectious diseases for child and adult migrants to Europe. The results of our systematic review(s) will be of interest to a broad group of stakeholders, including policymakers, healthcare practitioners and members of international health organisations. Accessing and summarising the data using explicit, consistent and transparent methods provide a foundation for public health policy and guidelines.[6] High-quality synthesis and dissemination of the evidence and updating and enhancing the 2011 systematic review[6] will support a more coordinated approach to voluntary screening and treatment of infectious diseases in migrants in EU/EEA Member States. Our reviews will facilitate evidence-based management of migrants with the studied infectious diseases, and will likely identify key areas for future research, and provide a framework for conducting overviews of systematic reviews on causation.

We will use the evidence from these reviews to inform GRADE EtD criteria.[38–42 46] These EtD summaries will also include data on migrants' preferences, stakeholder acceptability and feasibility and health equity. These summaries will support an ECDC scientific panel in developing guidance statements on infectious diseases for newly arriving migrants to the EU/EEA. Details on GRADE EtD methods process will be published separately.

CONCLUSIONS

In this protocol, we detail a suite of linked systematic reviews of infectious disease conditions that may benefit from assessment for newly arriving child and adult migrants. The four-phase approach aims to identify, appraise and update existing systematic reviews, and identify critical gaps leading to opportunities for syntheses and de novo reviews. This review will provide high-quality evidence for the forthcoming ECDC Evidence-Based Guidance on Prevention and Assessment of Infectious Diseases for Migrants to the EU/EEA .

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Related Publication 2

- Driedger, M., Mayhew, A., Welch, V., Agbata, E., Gruner, D., Greenaway, C., Noori, T., Sandu, M., Sangou, T., Mathew, C., Kaur, H., Pareek, M., & Pottie, K. (2018). Accessibility and Acceptability of Infectious Disease Interventions Among Migrants in the EU/EEA: A CERQual Systematic Review. International journal of environmental research and public health, 15(11), 2329.

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Review

Accessibility and Acceptability of Infectious Disease Interventions Among Migrants in the EU/EEA: A CERQual Systematic Review

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Abstract: In the EU/EEA, subgroups of international migrants have an increased prevalence of certain infectious diseases. The objective of this study was to examine migrants' acceptability, value placed on outcomes, and accessibility of infectious disease interventions. We conducted a systematic review of qualitative reviews adhering to the PRISMA reporting guidelines. We searched MEDLINE, EMBASE, CINAHL, DARE, and CDSR, and assessed review quality using AMSTAR. We conducted a framework analysis based on the Health Beliefs Model, which was used to organize our preliminary findings with respect to the beliefs that underlie preventive health behavior, including knowledge of risk factors, perceived susceptibility, severity and barriers, and cues to action. We assessed confidence in findings using an adapted GRADE CERQual tool. We included 11 qualitative systematic reviews from 2111 articles. In these studies, migrants report several facilitators to public health interventions. Acceptability depended on migrants' relationship with healthcare practitioners, knowledge of the disease, and degree of disease-related stigma. Facilitators to public health interventions relevant for migrant populations may provide clues for implementation. Trust, cultural sensitivity, and communication skills also have implications for linkage to care and public health practitioner education. Recommendations from practitioners continue to play a key role in the acceptance of infectious disease interventions.

Keywords: access to care; disease prevention; public health; stigma; refugees; migrants

1. Introduction

Migrant populations often come from or travel through low- and middle-income countries where the prevalence and burden of infectious diseases differs from the European Union/European Economic Area (EU/EEA) [1]. Migrant populations include immigrants, refugees, asylum-seekers, displaced persons, undocumented migrants, and other foreign-born residents. In the EU/EEA, for example, subgroups of migrants have a higher prevalence of HIV, tuberculosis (TB), hepatitis B (HBV), and hepatitis C (HCV), and have lower rates of childhood vaccinations compared to native-born populations [1].

Evidence-based guidelines can direct public health and healthcare practitioners in the screening and treatment of such diseases. These guidelines include information on testing and vaccination and may also consider culturally sensitive ways to approach migrants. For example, existing guidelines for HIV among migrant populations [2–4] synthesize evidence on benefits, harms and cost effectiveness, and also provide some interpretation on qualitative data relevant to HIV related stigma and strategies to link patients for treatment. To implement public health guidelines, an understanding of migrant populations' perceptions and fears is needed [5]. Thus, to ethically offer interventions, we need to understand the perspective of migrants regarding the acceptability of interventions, value placed on outcomes, and accessibility of screening and treatment of infectious disease interventions in the EU/EEA [6,7].

The acceptability of infectious disease interventions influences the readiness of migrants and clinicians to incorporate guidelines into practice, as seen in the case of HIV screening [8]. Insufficient knowledge among clinicians about the acceptability of interventions may inhibit them from offering screening to migrants [9]. How patients value the disease-related outcomes of interventions (e.g., perception of risk of disease, diagnoses, symptoms, or disease resolution), or other outcomes (e.g., time away from work, stigma, side effects, or adverse events) can create barriers to the uptake of guideline recommendations [5]. For example, one qualitative study on developing decision aids for HIV testing for newly arrived Sub-Saharan African women to Canada demonstrated how the provision of accurate HIV information can reduce stress [10]. Existing strategies to improve access to healthcare for migrants include support for transportation, interpreters, and cultural brokers [11].

The objective of this study is to understand the acceptability, the value placed on outcomes and the accessibility of infectious disease interventions and other health services among recently arrived EU/EEA migrants. We focused specifically on tuberculosis, HIV, HBV, HCV, vaccine-preventable diseases (VPD), and parasitic diseases; diseases that were selected during an ECDC consensus meeting in Stockholm [12]. We also aimed to explore how the GRADE CERQual tool can appraise qualitative research on implementation considerations.

2. Materials and Methods

2.1. Search Strategy and Selection Criteria

We conducted a systematic review of qualitative reviews, and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline [13]. A team of experts with qualitative research expertise developed a protocol that considered implementation for public health interventions relevant to migrant populations in EU/EEA. We registered the protocol on Prospero (CRD42016045798) and published our detailed review methods in BMJ Open [12,14].

We searched MEDLINE, MEDLINE In-Process, MEDLINE Ahead of Print, EMBASE, CINAHL, DARE, and CDSR for articles published between 1 January 2010 and 29 July 2016. The full search strategy is provided in Supplementary File S1. We also searched grey literature for published reports that met our inclusion criteria from the CDC, ECDC, UNAIDS, EU, and WHO, and scanned references to identify additional qualitative systematic reviews. We included qualitative systematic reviews that reported on values, perceptions on access, and acceptability of infectious disease interventions (see Appendix A). We restricted our inclusion to studies published in English. We included reviews if

search and selection strategy methods were explicitly provided, and if the review included qualitative evidence. We focused on migrant and forcibly displaced populations, including children, adolescents, pregnant women, and adults. See Appendix B for full inclusion and exclusion criteria.

2.2. Study Selection and Data Extraction

Three independent team members (MD, MS, TS) screened title and abstracts in duplicate, followed by full-text assessments for eligibility. Conflicts were resolved through discussion or the involvement of a fourth reviewer (AM). Data were downloaded into EndNote reference software [15]. We assessed the methodological quality of included reviews using the Assessing Methodological Quality of Systematic Reviews tool (AMSTAR) [16] but did not exclude any studies based on quality.

The same team members extracted data from the included reviews in duplicate. We used a calibration exercise prior to data extraction and discrepancies were resolved through discussion. We designed our data extraction form using the Jacob's accessibility framework [17]. The Jacob's accessibility framework highlights barriers to accessing health services from both the supply and demand side, and as such recognizes that determinants of geographic accessibility, acceptability, availability, and affordability play a critical role in access. The framework focusses more on accessibility rather than appraising the acceptability and attitudes towards these services. However, adapting this framework to create an inclusive data extraction form (see Appendix C) allowed us to capture all relevant data, which was subsequently contextualized with respect to our research objectives.

2.3. Data Synthesis

We contextualized the preliminary findings on migrant populations using the Health Belief Model framework (HBM) [18]. The HBM is a commonly used model of the beliefs, expectations, and values that underlie preventive health behavior [19], and was therefore selected for its clear alignment with our stated research objectives involving the values and acceptability of interventions. HBM suggests that six factors predict health behavior: perceived susceptibility, perceived severity, benefits to action, barriers to action, self-efficacy, and cues to action [18].

We applied a qualitative lens considering saturation (200 studies were identified within the reviews) and triangulation of data between different diseases, migrant populations, and destination countries to identify preliminary findings. We consulted clinicians (KP, MP, DG, CG) with expertise and experience in migrant health to identify and corroborate the credibility, transferability, confirmability, and dependability to establish the trustworthiness of these findings. Of note, while many reviews discussed how knowledge of risk factors influences health behavior, only two reviews [20,21] commented specifically on how susceptibility, in itself, determines health behavior, which is how "perceived susceptibility" is classically theorized in the HBM [18]. Given the strong cognitive component of susceptibility within the HBM [22], we opted to include the knowledge data in our main findings, yet we typified this as "knowledge of risk factors" to maintain accuracy.

Five of the 12 preliminary findings were selected as "key findings" to be further analyzed with the Confidence in the Evidence from Reviews of Qualitative research (CERQual) tool. These were selected by consensus among three authors (MD, KP, AM), based on their respective strength of evidence, the number of reviews supporting the finding, the level of variability in review findings, and the significance of the findings as stated in the included reviews.

We used the CERQual tool to assess the confidence of our findings. CERQual is a new method for assessing the confidence of qualitative review evidence, similar to how the GRADE approach assesses the certainty of quantitative evidence [23]. CERQual bases this evaluation on four criteria: (a) methodological limitations of included studies supporting a review finding, (b) the relevance of included studies to the review question, (c) the coherence of the review finding, and (d) the adequacy of the data contributing to a review finding. To our knowledge, CERQual has not been used in a review of reviews to date. To apply the principles of CERQual to a review of reviews, we needed to make

minor adjustments, such as considering the number of primary studies within a given review to assess the adequacy criterion.

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3. Results

3.1. Study Selection

The formal search identified 2108 articles. Reference scanning identified three additional reviews. We screened 87 full-text articles and 11 qualitative systematic reviews met our inclusion criteria. All reviews examined populations migrating from low- and middle-income countries to high-income countries. See PRISMA Flow Sheet showing selection, Figure 1.

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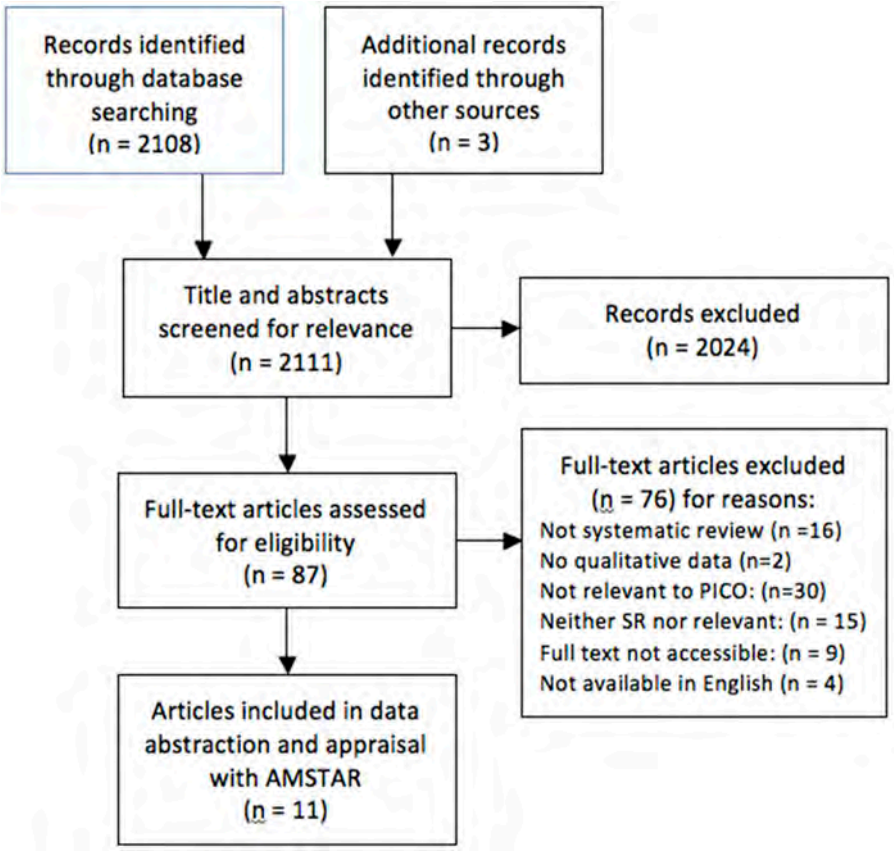

Figure 1. PRISMA Flow Diagram.

Three of the systematic reviews focused exclusively on migrant populations [24–26]. Other reviews examined migrant populations as subgroups within the general populations [21,27,28]. The host population countries were predominantly in Western Europe and the United States. Participants mostly consisted of Latino, Hispanic, or sub-Saharan African migrants, but also included South East Asian and Middle Eastern migrants. Most reviews included both quantitative cohort and cross-sectional studies as well as qualitative data from focus groups and interviews. Three reviews focused on HIV, three on HBV/HCV, and five on TB. No reviews specifically addressed vaccine-preventable or parasitic diseases. See characteristics of included studies in Table 1.

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Table 1. Characteristics of Included Studies.

Citation	Years Searched	Population	Intervention/ Service Setting	Analysis/ Synthesis Approach	EU/EEA Settings Included?	1′ Study Design	# of 1′ Studies	AMSTAR Score (/11)
Alvarez-del Arco et al. [20]	2005–2009	Migrants and ethnic minorities populations living in high-income countries Migrants were largely from sub-Saharan Africa and Latin America, (1) and other regions.	HIV testing and/or counselling in health and community settings	None specified-Narrative	Yes	Quantitative (25); mixed-methods (2); qualitative (6); literature reviews (4)	37	1
Blondell et al. [24]	1997–2014	Foreign-born: African, particularly Sub-Saharan, and Hispanic/Latino migrants were the most studied populations.	HIV screening, testing	None specified - narrative	Yes	quantitative (n = 21) (descriptive/non-randomized) and qualitative (n = 10).	31	3
de Vries et al. [29]	2010–2017 (OECD countries); or 1990–2017 (EU, EEA, EU candidate countries)	Hard-to-reach populations including homeless, migrants, travelers (including Roma), refugees, others. 7/10 studies were of migrants only. One study included homeless, migrants, and drug users.	TB services of any kind	Thematic and content analysis	Yes	Qualitative: Interviews (6), focus groups (2), both Interviews and Focus groups (3) multi-method participatory research (1)	12	7
Do et al. [30]	2002–2009	Asian Americans and Pacific Islanders (69% foreign-born).	Health education, screening, and vaccination for HBV	None specified - narrative	No	Cross-sectional (13); RCT (1); quasi-experimental (1); Longitudinal (1)	20	1
Greenaway et al. [27]	1950 to 17 December 2008) *	Immigrants (subgroup).	Screening and treatment of latent TB	Summary of findings table (GRADE)	Not specified	SRs (7) and guidelines (2)	9	2
Mitchell et al. [28]	1985–April 2011	30 individual risk groups * Data extracted from two groups only—Internally Displaced Populations (IDPs), and "Migrants/Immigration"	TB screening (CXR, Mantoux TST)	Metasynthesis	Yes	Qualitative and Quantitative literature.	21	2

Table 1. *Cont.*

Citation	Years Searched	Population	Intervention/ Service Setting	Analysis/ Synthesis Approach	EU/EEA Settings Included?	1′ Study Design	# of 1′ Studies	AMSTAR Score (/11)
Nguyen-Truong et al. [31]	1998–2012	Vietnamese Americans—most studies report that majority of sample are immigrants, but most aggregated immigrant and native-born.	Screening (HBV and Colorectal cancer)	None specified	No	Descriptive (15); Interventional (2); Qualitative (3); Chart/medical record review (2); Mixed-method (1)	23	2
Owiti et al. [25]	1970–2014 **	High-risk 1st- or 2nd-gen immigrants from high-prevalence countries or intermediate prevalence countries who migrated to traditionally low prevalence countries.	Knowledge of HBV and/or HCV infections and/or with targeted screening, vaccination, and treatment	Narrative synthesis	Yes	Quantitative surveys (39) and qualitative studies (11); mixed-methods (1)	51	6
Pottie et al. [21]	1995–2008	Immigrants and refugees (subgroup).	HIV Screening and treatment	Summary of findings table (GRADE)	Not specified	SRs (7) and guidelines (2)	8	4
Tankimovich et al. [32]	1998–2012	Homeless and immigrants with TB.	TB detection and treatment (active and latent)	None specified—narrative	Yes	Quantitative (17); Qualitative (5); Intervention studies (10)	22	2
Tomas et al. [26]	1995–2011	Immigrants, and intra-national migrants and including migrants, asylum-seekers, refugees.	Screening and treatment of TB (active and latent)	Meta-ethnography	Yes	In-depth interviews (24); focus groups (12); participant observation (5); case studies (1); Other (6) Many combined qualitative and quantitative methods.	30	3

* Includes primary studies from 1995 onwards; ** Includes primary studies from 1999 onwards.

3.2. Methodological Quality

We assessed methodological quality using the AMSTAR tool. AMSTAR was originally designed for quantitative reviews but many of the criteria are applicable to qualitative reviews, such as, a priori design, duplicate selection, comprehensive search, criteria, and characteristics of included and excluded studies and consideration of scientific quality. The authors have used AMSTAR for qualitative systematic reviews [33,34]. AMSTAR scores were distributed fairly evenly between one and seven points out of a possible 11, with a median score of 2/11. AMSTAR items varied significantly with respect to the proportion of reviews meeting that item.

3.3. Migrants' Perceptions of Acceptability

We organized the findings using the Health Beliefs Model (HBM) [19]. Through our framework analysis, we identified 12 preliminary findings from the data. See Table 2 for a detailed description of these findings.

Three reviews reported on acceptability of interventions [25,26,28]. Tomas et al. found that the TB screening process was generally well-received among migrants [26]. According to Mitchell et al. [28], the overall acceptability of TB screening among migrants was considered to be high, yet migrants' perception of TB as a severe disease was associated with screening refusal. Owiti et al., reported that some migrants expressed motivation to or actively sought screening for HBV/HCV, and that certain populations were receptive to HBV vaccination [25].

Furthermore, peer support and the influence of family members promotes self-efficacy in seeking healthcare and improves the acceptability of interventions, yet there are also instances in which these social connections may introduce other barriers [20,24,25]. For example, family support would improve adherence to TB treatment, but the need for women, at times, to request their partner's approval to seek screening acted as a barrier [20,24]. Cultural and family beliefs that differ from those of the host nation may present a perceived barrier, and may lead to other barriers, such as disease-related stigma, that can influence acceptability of care [21,26,27,30–32]. In addition, various attitudes towards an intervention itself, especially side effects and cultural taboos, may influence its acceptability among migrants [24,26,27].

The patient-practitioner relationship was consistently emphasized as an important cue to action in seeking further care. Trust, cultural sensitivity, and communication skills can greatly improve the acceptability of infectious disease interventions [20,25–31]. Therefore, recommendations from healthcare practitioners can influence migrants' health seeking behavior [25,30,31].

Social determinants also influenced the acceptability of interventions. The number of years of formal education was positively correlated with HIV screening [21,24], HBV/HCV knowledge [25], testing and vaccination [30] and TB screening and treatment [27]. In one review, older age was associated with HBV/HCV knowledge [25], but another review, among Asian Americans/Pacific Islanders [30] showed younger age was associated with HBV/HCV knowledge. Gender also played a role, as females were more receptive to HIV screening [20,24], but males were more likely to be screened for HBV [30,31].

3.4. Migrants' Values on Outcomes of Interventions

Traditional beliefs of migrants may play a role in the value placed on outcomes of infectious disease interventions. The reviews report that migrants' perceived severity of and susceptibility to infectious diseases influences their uptake of testing and treatment interventions. Reviews of TB, HIV and hepatitis reported a low level of western knowledge and understanding of risk factors and transmission of disease among migrants, and this may make them less likely to seek screening, vaccination, or treatment [20,21,24,25,27,29–31]. While the degree of knowledge varied among studies, it was consistently associated with the uptake of interventions.

Migrants reported certain perceived benefits as valued outcomes of screening, vaccination, and treatment. The most consistently valued outcomes included reassurance of disease-free status and thus prevention of transmission to others [21,24,26,30]. Uptake of interventions was associated with perceptions of negative disease-related outcomes among migrants. Stigma, and its related connotation, acts as a large barrier to screening and treatment [20,21,24–27,29,32]. Indirect costs, such as loss of employment and loss of migration status and social status, reduced the value placed on interventions [20,24,25,29,32]. For example, certain migrants feared that a positive test result would have a negative impact on their immigration status or refugee claim. Symptoms were consistently reported as an important cue for health actions; for example, migrants value screening or treatment of symptomatic diseases over asymptomatic diseases and often wait until they are symptomatic before seeking care [24,26,29–31].

3.5. Accessibility of Health Services

Barriers to accessibility were reported at both structural and community levels. Structural barriers to care for migrants include cultural and language barriers [35], inadequate practitioner cultural competencies [36], disease-related stigma and discrimination [20], perceptions of health and healthcare [37], and legal status of migrants [24]. Community-level barriers include the availability and awareness of services such as transportation, economic barriers including healthcare coverage and cost of services, and policy barriers such as the healthcare system capacity and coverage. These barriers interact with poverty, inequality, and power, further exacerbating the poor health of the migrants [38]. Time spent accessing healthcare can incur a significant opportunity cost for migrants, especially when they have insecure employment or cannot meet basic needs during their settlement process [20,24,26–29]. Furthermore, barriers related to the migration process, including language proficiency, cultural barriers, and navigation of the healthcare system, can make interventions less acceptable or accessible for migrants [20,21,24–27,29,30]. While interpreters may improve accessibility, their presence may introduce new potential barriers surrounding confidentiality [24,26,30].

3.6. Confidence in Findings

We analyzed the confidence of our five findings using CERQual (see Table 3). Three findings were assigned a moderate confidence rating, and two were assigned a low confidence rating. See Table 4 for a detailed explanation of confidence ratings.

Table 2. Preliminary Findings from Health Belief Model Framework Analysis.

	Main Theme	Reviews Cited (Lead Authors)	Disease-Specific Supporting Examples
Knowledge of Risk Factors	Low level of knowledge of risk factors and transmission of disease may make migrants less likely to seek screening, immunization, or treatment.	(5) de Vries, Owiti, Lee, Nguyen, Blondell	TB: • Underestimated risk of acquiring TB due to poor understanding of transmission and false beliefs, e.g. that TB is not present in US. (de Vries) HBV/HCV • HBV screening is associated with better knowledge of HBV and specific modes of transmission (Owiti, Lee, Nguyen) HIV: • Migrants with greater knowledge of HIV and its risk factors were more likely to be screened (Blondell)
Perceived Susceptibility	Low perceived personal risk of acquiring an infectious disease may make migrants less likely to seek screening	(3) Greenaway, Pottie, Alvarez	• Perceived low risk of progressing from latent to active infection is a barrier to screening/treatment of latent TB (Greenaway) HIV • Low perceived personal risk is a barrier to screening (Pottie, Alvarez)
Perceived Severity	The severity and consequences (medical, social, economic) of diseases varied between studies, were generally well understood. However, the literature is divided on whether this is a motivating factor, or a perceived barrier to screening (i.e. risk of realizing the negative consequences through screening).	(4) Blondell, Lin, de Vries, Owiti)	Tuberculosis: • TB was thought to be important, potentially fatal disease; participants afraid of disease's severity (Tomas) • Varying perception on TB severity included: very serious, lethal disease, a long-lasting but curable disease, fear of dying from incurable disease (de Vries) HBV/HCV: • Perceived outcomes of HepB and C: Poor health; discrimination/stigma; loss of income; loss of social status; liver disease (Owiti) • On the other hand, belief that HBV infection is transient could lead to it not being taken seriously (Owiti) HIV: • Concerns regarding the logistical consequences of living with a positive status, and fear of a future with a positive result, reduced the acceptability of screening among African migrants (Blondell)

Table 2. *Cont.*

	Main Theme	Reviews Cited (Lead Authors)	Disease-Specific Supporting Examples
Perceived Benefits	Several distinct, tangible benefits to screening, vaccination, and treatment were reported by reviews, especially reassurance of negative status and prevention of spread to others.	(4) Tomas, Do, Pottie Blondell,	Tuberculosis: • In some communities, benefits of treating latent TB were well understood, including efficacy of medication, avoidance of stigma, and reducing risk of transmission to others (Tomas) HBV/HCV: • Primary motivations for hepatitis B vaccination were protection of future health and avoidance of hepatitis B (Do) HIV: • "Just wanted to find out" was a motivator among Latino migrants; "ensure they were healthy and clean" (Blondell) • Refugees and refugee claimants might be reluctant to accept screening tests because they fear limited access to antiretroviral treatment and thus do not see a perceived benefit to screening (Pottie)
Perceived Barriers	Stigma is an overarching barrier to screening and treatment that was reflected in most diseases and reviews. Stigma is also related to other perceived barriers (e.g. confidentiality issues with interpreters, hesitancy to report symptoms to family/healthcare providers)	(8) Tomas, Tankimovich, de Vries, Greenaway, Pottie, Owiti, Blondell, Alvarez,	Tuberculosis: • Feelings of stigma influenced immigrants' attitudes towards prevention and diagnosis and could prevent them from sharing relevant information with their doctors. Medical interpreters often posed a problem due to the perceived sensitivity of the information, loss of privacy, and stigmatization (Tomas) HBV/HCV: • Shame and stigma of hepatitis may negatively uptake screening; may dissuade migrants from disclosing test results (Owiti) HIV: • Stigma, discrimination related to HIV described as most important impediment to HIV testing, treatment (Pottie) • Stigma is not significant across all studies, which may be explained by population characteristics or definitions of stigma. The few quantitative studies on stigma failed to show a statistically significant association with testing (Blondell)

Table 2. *Cont.*

Main Theme	Reviews Cited (Lead Authors)	Disease-Specific Supporting Examples
Time spent accessing healthcare can incur a significant opportunity cost on migrants, especially when they are in a precarious employment situation or do not have basic needs met in their settlement process.	(6) Tomas, Greenaway, de Vries, Mitchell, Blondell, Alvarez	Tuberculosis: • Missed days at work is a barrier to TB screening and treatment adherence (Greenaway) • Reasons for refusing TB screening were predominantly a lack of time (Mitchel) HIV: • Provision of rapid testing outside normal working hours may improve uptake by eliminating the opportunity cost of missed work (Blondell, Alvarez)
Indirect costs that may be unique to migrants can reduce the value placed on these screening and treatment interventions. The most prominent of these was that a positive test result may have a negative impact on the migrant's immigration status or refugee claim.	(5) Lin, Tankimovich, Blondell, Alvarez de Vries,	Tuberculosis: • Undocumented status was consistently correlated with non-adherence to treatment (Lin) • Migrants may not seek treatment due to fear of revealing their illegal immigration status (Tankimovich) HIV: • Migrants placed their legal status as among their highest priorities, and fears on the implications of testing positive on their visa/residency application or deportation were main barriers in several studies (Alvarez). However, this was not a barrier in all studies (Blondell)
Factors inherent to the migration process, including language proficiency, cultural barriers, and navigation of the healthcare system, can create barriers for migrants. However, reviews reported conflicting results regarding the influence of acculturation and language proficiency	(9) Tomas, Lin, Do, Owiti, Pottie, Blondell, Greenaway, de Vries, Alvarez,	Tuberculosis • Years spent in host country inconsistently associated with treatment completion/outcomes. Two studies found that immigrants with better English proficiency were at increased risk of not completing treatment (Lin) • Lack of familiarity with the local language was a barrier to screening (Tomas) HBV/HCV • Access to interpreter services increased odds of testing (Do, Owiti) • One study reported an associated between lower English proficiency and higher likelihood of being tested for HBV, while another found that not needing an interpreter was associated with getting tested (Owiti) HIV • Non-integration of health services was a key barrier to HIV screening • Inability to communicate in the host country's language was a prominent barrier to screening (Pottie) • While language services increase uptake, translators may introduce confidentiality concerns (Blondell)

Table 2. *Cont.*

	Main Theme	Reviews Cited (Lead Authors)	Disease-Specific Supporting Examples
	Various attitudes and expectations of the intervention itself (the procedure or its side effects) may influence its acceptability among migrants	(4) Greenaway, Lin, Blondell, Tomas	Tuberculosis • Barriers to TB screening included fear of a painful test (Tomas) and venipuncture (Greenaway) • Side effects are inconsistently associated with treatment adherence. Quantitative studies found no significant correlations in multivariate analysis (Lin) HIV • Some African migrants felt that too much blood was taken during screening (Blondell)
Cues to Action	Recommendation from healthcare providers can influence healthcare seeking by migrant patients.	(3) Owiti, Do, Nguyen	HBV/HCV • Recommendation by healthcare professionals was positively associated with uptake of screening and vaccination (Owiti, Do, Nguyen)
	The importance of the patient-physician relationship was consistently emphasized. Trust, cultural sensitivity, and communication skills can act as facilitators to the acceptability of infectious disease interventions, whereas a negative relationship can serve as a barrier.	(7) Tomas, Greenaway, Mitchel, de Vries, Do, Nguyen, Owiti	Tuberculosis • Using a dedicated nurse and cultural interpreter to provide a "transcultural" approach increased screening acceptability within one year (Mitchell) • Health staff can improve adherence to treatment by providing personal advice with sensitivity and "the ability to establish a personal relation on the same cultural terms". Positive relationships with health staff are perceived as "a crucial element" (Tomas) HCV/HBV • Poor patient-doctor communication, and reliance on professional opinion, discouraged testing and vaccine uptake (Do, Nguyen)
	The presence of symptoms can be a necessary cue to seeking healthcare among migrants who may not understand or value the importance of treating asymptomatic disease	(5) Tomas, Do, Blondell, de Vries, Nguyen	TB • A lack of symptoms despite contact with infected persons can lead migrants to place less value on prevention and screening (Tomas) HBV/HCV • Apparent good health and personal preferences of migrants may discourage screening and vaccination (Do) HIV • African and Latin migrants reported waiting until health crises, symptoms, or being extremely sick before seeking formal healthcare (Blondell) • Feeling healthy and a lack of symptoms were consistently cited as barriers to HIV screening (Blondell)

Table 3. GRADE CERQual Evidence Profile.

Key Finding	Studies Supporting Key Finding	Methodological Quality	Relevance-Research Question	Relevance-Population	Coherence	Adequacy-Reviews	Adequacy-Primary Studies	Overall Assessment of Confidence	Explanation of Judgement
Subjects may be reluctant to undergo screening due to negative indirect costs of having a positive result—on employment status, immigration status, and social status	[20,21,24,26, 29,32]	Moderate methodological concerns	No relevance concernsFull (6/6)	Moderate relevance concerns Full (3/6) partial (3/6)	Minor coherence concerns Coherent (5/6) Among Latino migrants in Spain, legal and administrative fears were not found to be significant barriers [29]	Minor adequacy concerns 6 reviews	20 studies	Low confidence	Lack of adequate evidence, including contradictory evidence, in addition to methodological concerns among reviews reporting this finding.
Patients value testing and treatment less if they are asymptomatic	[24,26,29–31]	Moderate methodological concerns	Minor relevance concerns Full (4/5) Indirect (1/5)	Moderate relevance concerns Full (2/5) Partial (3/5)	No coherence concerns Coherent (5/5)	Minor adequacy concerns 5 reviews	25 studies	Low confidence	Methodological concerns, indirect/partial relevance of reviews supporting key finding.
Incorrect knowledge of infectious diseases and low self-perceived risk are barriers to acceptability of screening and vaccination	[20,21,24–32]	Moderate methodological concerns	Minor relevance concerns Full (8/11) Indirect (3/11)	Moderate relevance concerns Full (8/11) Partial (3/11)	Minor coherence concerns Coherent (10/11) Perceiving tuberculosis as a severe disease (OR 0.29, 95% CI 0.09-0.91) was associated with refusal of TST screening [28]	Minor adequacy concerns11 reviews	81 studies	Moderate confidence	Some reviews have significant methodological concerns, yet the key finding is consistently supported by directly relevant data in reviews with only minor methodological concerns.
The acceptability of screening and treatment interventions is highly dependent on the cultural sensitivity and relationship with healthcare professionals	[20,21,24–32]	Moderate methodological concerns	Minor relevance concerns Full (10/11) Indirect (1/11)	Minor relevance concerns Full (8/11) Partial (3/11)	No coherence concerns Coherent (11/11)	Minor adequacy concerns 11 reviews	67 studies	Moderate confidence	Supported by all reviews. Although some reviews have significant methodological concerns, reviews with few methodological concerns report directly relevant data.

Table 3. *Cont.*

Key Finding	Studies Supporting Key Finding	Methodological Quality	Relevance-Research Question	Relevance-Population	Coherence	Adequacy-Reviews	Adequacy-Primary Studies	Overall Assessment of Confidence	Explanation of Judgement
Stigma associated with infectious diseases is a barrier to the acceptability of screening interventions	[20,21,24–27,29]	Moderate methodological concerns	No relevance concerns Full (7/7)	Minor relevance concerns Full (6/7) Partial (1/7)	Minor coherence concerns Coherent (6/7) Stigma is not a significant factor in all studies. Two quantitative studies on stigma found it was not a significant deterrent to testing	Minor adequacy concerns 7 reviews	71 studies	Moderate confidence	Well-supported by review data that is directly relevant. Direct support from reviews with few methodological concerns.

Objective: To identify, appraise and synthesize review level evidence on values and preferences for infectious disease interventions among migrants in Europe. Perspectives: Experience and attitudes of migrant population regarding ID interventions in the EU/EEA? Included programs: Reviews of programs of testing and prevention of infectious diseases in migrants where values and preferences are evaluated.

Table 4. Summary CERQual Confidence Ratings.

Key Finding	CERQual Assessment Rating for Assessment of Confidence	Explanation of Confidence Rating
Incorrect knowledge of infectious diseases and low self-perceived risk are barriers to acceptability of screening and vaccination	Moderate confidence	Some reviews have significant methodological concerns, yet the key finding is consistently supported by directly relevant data in reviews with only minor methodological concerns.
The acceptability of screening and treatment interventions is highly dependent on the cultural sensitivity and sense of trust in healthcare professionals and their recommendations	Moderate confidence	Supported by all reviews. Although some reviews have significant methodological concerns, reviews with few methodological concerns report directly relevant data.
Stigma associated with infectious diseases is a barrier to the acceptability of screening interventions	Moderate confidence	Well-supported by review data that is directly relevant. Direct support from reviews with only mild methodological concerns.
Subjects may be reluctant to undergo screening due to negative indirect costs of having a positive result—on employment status, immigration status, and social status	Low confidence	Lack of adequate evidence, including contradictory evidence, in addition to methodological concerns among reviews reporting this finding.
Patients value testing and treatment less if they are asymptomatic	Low confidence	Methodological concerns, indirect/partial relevance of reviews supporting key finding.

4. Discussion

We identified 11 systematic reviews that addressed factors influencing acceptability, the value placed on outcomes, and accessibility of screening and treatment of infectious diseases among migrants. Using the framework of the Health Belief Model, we found factors that influenced healthcare engagement and intervention uptake in each disease group, i.e., TB, HIV, HBV, and HCV. This analysis supports the role of the HBM in identifying and organizing implementation considerations in public health guidelines for migrants. We also assessed the confidence in five key findings using the CERQual tool. Three findings were rated as moderate confidence, and two were rated as low confidence (See GRADE CERQual Table 4).

The findings of this review suggest that disease-related stigma, and inaccurate knowledge related to certain infectious diseases, continue to be major deterrents for screening among migrants. However, ongoing education of migrant patients and their physicians may increase adherence to TB screening and treatment [27]. Stigma relates to traditional and western beliefs concerning disease outcomes, and these beliefs interact with longstanding cultural and social barriers [37]. Stigma can manifest in family and community life and may impact employment as well as healthcare. Addressing stigma will require a multi-faceted approach that involves engagement of affected communities as well as efforts to reduce structural barriers [24], as exemplified by the integration efforts taking place in Germany [39].

Migrant populations face screening at the political, public health and primary health care levels. We found that migrants consider the indirect costs that potentially accompany disease results, such as loss of employment and loss of migration status and social status. These negative outcomes may vary across the EU/EEA. On the contrary, migrants value screening, post hoc, when they do not have a disease.

Migrants consistently identify trust in practitioners as a key determinant to accepting infectious disease interventions [40]. Various organizations have developed cultural competency [41], cultural humility [42] programs to build trust for newly arrived migrants. In the context of cultural sensitivity, practitioners' approach may play an important role for linkage to care for migrants. More research, including participatory research, is needed to engage migrants in implementation strategies [43,44]. For example, one qualitative study used interviews with migrant leaders in community health to not only identify barriers to disease screening, but also identify innovative approaches to mitigate barriers by combining screening for all relevant diseases into one standardized check-up, thereby improving accessibility and further reducing disease-related stigma [45].

4.1. Implications for Practice

The qualitative data from our 11 reviews reports a compelling story of migrant access to care issues and acceptability issues related to stigma, indirect costs, and health system barriers. When migrants experienced disease symptoms or were able to perceive benefits from screening and/or trusted their practitioners, they were more likely to value, accept, and access infectious disease interventions. These findings tap into the lived experience of many migrants and may have relevance for screening programs; however, these findings cannot be generalized across all populations and diseases.

4.2. Strengths and Limitations

Traditionally, the GRADE CERQual tool is used to assess confidence in the evidence of synthesized qualitative studies. This paper is the first to adapt the CERQual tool to assess the confidence of systematic review level qualitative evidence. We also directed our findings and applied our confidence ratings as evidence in the ECDC Guidance development process, including values on intervention outcomes and acceptability of screening and treatment interventions of infectious diseases among migrant populations. These findings were implemented into evidence to decision tables and helped to develop ECDC guidance and implementation considerations for migrants.

According to the AMSTAR scores, the quality of eligible systematic reviews was low, highlighting a need for more rigorous evidence on the acceptability and accessibility of interventions among migrants. Specifically, the methods used to combine findings were generally appropriate, yet only two reviews [24,29] assessed and documented the quality of the primary studies included. While this may impact the validity of our findings, we demonstrated how the CERQual methodology can be used to account for the quality of the included reviews to generate sound assessments of the strength of qualitative evidence.

Our systematic review of reviews approach allowed us to use data that summarized findings from over 200 primary studies and supported the assessment of adequacy, consistency, and coherence. However, this approach also created some methodological challenges. We were obliged to report the findings without additional interviews and triangulation. Second, while we used the number of reviews and primary studies supporting a finding as evidence for the robustness of a finding, the precise relevance of these findings varied.

We began with six infectious disease interventions, which were consistent with those prioritized by the EU/EEA guidance work. This allowed us to consider consistencies across different individual diseases and provided more data to synthesize into findings. However, examining the data in aggregate may mask differences between these diseases. For example, most of the evidence on stigma comes from reviews on HIV and TB, and thus may not be generalizable to HBV or HCV or diseases not represented in the included reviews. We were unable to find qualitative systematic reviews that addressed vaccine-preventable diseases or intestinal parasites. While some of the evidence is likely relevant to these diseases, we accept that some of the barriers may be different. For example, VPDs are likely more relevant for migrant children and parents/caregivers, for whom the barriers and facilitators differ from adult migrants.

We were able to look at the findings from various migrant population and destination country perspectives. We chose to group the priority infectious diseases together, demonstrating that migrant perspectives varied across these diseases. We were unable to effectively rule out outliers on all the priority conditions and our findings are more aligned with migrant populations than destination countries.

5. Conclusions

Our review highlights migrants' perspectives on screening and treatment of infectious diseases, and as such, provides insight as to why migrants may accept or reject screening and treatment. Addressing disparities in prevalence and treatment rates of diseases between and within migrant populations will require implementation strategies that address migrant and practitioner knowledge, fear, and access barriers to health services. The acceptability, value of main outcomes and accessibility of screening and treatment interventions among migrants is highly dependent on the cultural sensitivity, relationship with healthcare professionals, disease-related stigma, and the degree of knowledge and self-perceived risk of diseases. Migrants may fear negative outcomes of screening including indirect costs related to the employment and immigration status, and they value screening and treatment less when asymptomatic. While our findings demonstrate similarities and differences across several infectious diseases, the available data was not sufficient for a complete analysis of factors that are specific to individual diseases or to migrant sub-populations. This highlights a need for ongoing implementation research involving individual populations and diseases to address this important public health and primary care topic.

Supplementary Materials: The following are available online at http://www.mdpi.com/1660-4601/15/11/2329/s1, Table S1: Search Strategy.

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Appendix A Determinants of Interest

We analyzed data on three overarching determinants of intervention uptake—values of main outcomes, acceptability, and accessibility. These are defined below:

Values of Main Outcomes of Infectious Disease Interventions:

- The importance placed upon the main outcomes of an intervention. These outcomes include those directly related to the disease (e.g., cure, symptom reduction, diagnosis), or costs or benefits resulting from the downstream effects of the intervention (e.g., side effects, time spent at the hospital, stigma, disclosure of disease status, cultural beliefs)

Acceptability of Infectious Disease Interventions:

- The willingness of the patient to request or adhere to the intervention based on their subjective attitudes and preferences towards the intervention itself or the process of receiving it (e.g., adherence challenges, social/cultural attitudes, fears about the procedure)

Accessibility of Infectious Disease Interventions:

- The ease with which patients use an infectious disease intervention. Determinants of accessibility include policies, community factors, healthcare service organization, or the delivery of the intervention itself.

Appendix B Determinants of Interest

- Study design: Systematic reviews (qualitative or qualitative/quantitative) defined as any review that includes selection criteria, search strategy, and use of at least one database
- Time: Published after 1 January 2010
- Language: English language
- Relevant to the PICO question:
    - Population: Migrants from Low- and Middle-Income Countries residing in High-Income Countries (i.e., permanent resettlement countries)
    - Intervention: Prevention, screening, and treatment interventions for infectious diseases (tuberculosis, hepatitis, VPDs, HIV, parasitic diseases)
    - Comparison: No intervention
    - Outcome: Valuation of outcomes, views about acceptability and accessibility of interventions

Appendix C Data Abstraction Tables

Table A1. Value of Outcomes.

Citation
Disease
Knowledge of Disease Status
Behavioral Prevention
Vaccination
Treatment of Asymptomatic Disease
Cure of Symptomatic Disease

Table A2. Acceptability.

Citation
Demand-Side Determinants
User's attitudes and Expectations
Household attitudes and expectations
Information on healthcare choice/providers
Disease-related knowledge
Intervention-related knowledge
Stigma
Indirect costs
Acculturation
SocialSupply-Side Determinants
Characteristics of the Health Services
Management/Staff Efficiency
Technology
Staff Interpersonal Skills, Including Trust
Wages and Quality of Staff
Language Barriers

Table A3. Accessibility.

Citations
Demand-Side Determinants
Indirect costs to household (e.g. transport, legal status)
Household income and willingness to pay
Opportunity costs
Means of transport available
System navigation
Low self-esteem and little assertivenessSupply-Side Determinants
Service/household location
Availablity of health workers, drugs, equipment
Direct price of service, including informal fees
Waiting time
Unqualified health woerks, absenteeism
Non-integration of health services
Lack of opportunity (exclusion from services)
Late or no referral

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