

# Reducing burden from respiratory infections in refugees and immigrants: a systematic review of interventions in OECD, EU, EEA and EU-applicant countries

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## Research article

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## Abstract

**Background** Respiratory diseases are a major reason for recently arrived migrants seeking health care in countries of arrival. The burden of respiratory diseases in refugees is exacerbated by poor living conditions and crowding. The lack of synthesised evidence and guideline-relevant information to reduce morbidity and mortality from respiratory infections endangers this population.

**Methods** A systematic review of all controlled and observational studies assessing interventions targeting the treatment, diagnosis and management of respiratory infections in refugees and immigrants in OECD, EU, EEA and EU-applicant countries published between 2000 and 2019 in MEDLINE, CINAHL, PSYINDEX and Web of Science.

**Results** Nine of 5779 identified unique records met our eligibility criteria. Seven studies reported an increase in vaccine coverage from 2% – 52% after educational multilingual interventions for respiratory-related childhood diseases (4 studies) and for influenza (5 studies). There was limited evidence in one study that hand sanitiser reduced rates of upper respiratory infections and when provided together with face masks also the rates of influenza-like-illness in a hard to reach migrant neighbourhood. In outbreak situations of vaccine-preventable diseases, secondary cases and outbreak hazards were reduced by general vaccination strategies early after arrival but not by serological testing after exposure (1 study). We identified evidence gaps regarding interventions assessing housing standards, reducing burden of bacterial pneumonia and implementation of operational standards in refugee care and reception centres.

**Conclusions** Multilingual health literacy interventions should be considered to increase uptake of vaccinations in refugees and immigrants. Well designed controlled studies on housing and operational standards in refugee population early after arrival as well as adequate ways to gain informed consent for early vaccinations in mass housing is required to inform guidelines.

## Background

Worldwide, more than 60 million people were fleeing from war, violence, climate catastrophes, human rights violations and other circumstances at the end of 2017 [1]. Difficult living conditions, the context of having fled from hardship and cultural and language barriers can limit health care access and uptake, as well as result in missed opportunities for prevention, vaccination and treatment [2, 3].

Respiratory infections are a major reason why refugees and asylum seekers seek healthcare [4, 5]. There is agreement that refugees and asylum seekers are not a notable source of transmission of respiratory disease to the general population [5–7]. However, due to difficult living and housing conditions refugees and asylum seekers are not only at higher risk of respiratory infections [8], but also at higher risk of critical illness from vaccine preventable diseases [9] than non-migrant populations. This makes respiratory tract-related infections and vaccine-preventable diseases particularly important health issues in this population [4, 4, 8, 10–12].

Concerning respiratory infections, national guidelines mostly focus on vaccine-preventable diseases and to our knowledge no specific guidelines on reducing the overall burden of respiratory infectious diseases in refugees and asylum seekers exist. There is little consensus across different guidelines on which strategies should be applied [13–21] (see Table 2 at the end of the manuscript).

Table 2

National and international guidelines with recommendations regarding infectious diseases, including respiratory infectious diseases

Guideline		Main recommendations regarding particular issues			
Region/Country	Guideline	Vaccinations	Screening or other diagnostic assessment	Health-literacy	Housing
Europe[13]	European Centers for Disease Control and Prevention (ECDC) / WHO regional office for Europe	<ul style="list-style-type: none"> <li>-country-specific vaccination schedule should be implemented for all refugees/asylum seekers/migrants staying for one week or more</li> <li>-main priority should be MMR and Polio-vaccines</li> <li>-vaccination should not be implemented at border crossings unless in the presence of an outbreak</li> </ul>	<ul style="list-style-type: none"> <li>-Regarding less of their legal status equitable and non-discriminatory access to essential health care services with preventive and curative interventions should be granted to all refugees and asylum seekers</li> <li>-all member countries should be prepared at any time to epidemiologically assess and adequately react to any outbreak situation</li> </ul>	none	<ul style="list-style-type: none"> <li>- overcrowding should be avoided (not giving numbers)</li> <li>-clean sanitary institutions and clothing should be available</li> </ul>
Switzerland[14]	Schweizerische Gesellschaft für Infektionskrankheiten	<ul style="list-style-type: none"> <li>-Following the same vaccination schedule as for indigenous previously unimmunised adults/children</li> <li>-Vaccination only valid when written documentation is available</li> </ul>	<ul style="list-style-type: none"> <li>-all refugee children under 5 y.o. should be screened for TB using tuberculin skin test regardless of BCG-vaccination status and country of origin</li> <li>-all adults and children &gt; 5 y.o. should be screened for TB only in case of symptoms using IGRA or TST on</li> <li>-Syphilis Screening for all children &lt; 2 y.o. and all juvenile refugees 12–15 y.o.</li> </ul>	none	none
Germany[15, 16]	Robert-Koch-Institut	<ul style="list-style-type: none"> <li>-Documentation of vaccination status</li> <li>-valid documentation leads to enrolment of national vaccination schedule for all residents</li> <li>-invalid documentation leads to accomplishment of separate minimum-vaccination schedule</li> <li>-all refugees should be vaccinated against influenza not only high-risk-population</li> </ul>	<ul style="list-style-type: none"> <li>-Examination not focussing on personal health status but on outbreak prevention in the first line</li> <li>-general anamnesis focussing on infectious diseases</li> <li>-full body examination including vital parameters focussing on infectious diseases and rashes</li> <li>-screening for active lung TB by x-ray (exceptions for pregnant women and children under 15 y.o.)</li> </ul>	none	none

Guideline		Main recommendations regarding particular issues			
Australia[17]	Australian Government - Departement of Health	<p>-Vaccination status of refugees is not routinely assessed, differing by states</p> <p>-all refugees arriving to Australia should receive vaccination catch-up vaccinations</p> <p>-predeparture vaccinations and valid documentations of previous vaccinations should be considered and all vaccinations to children under 7 y.o. should be reported to ACIR (Australian Childhood Immunisation Register)</p>	<p>-in all arriving people with refugee-like background a general assessment regarding HIV, disability, strongyloides serology and other should be conducted</p> <p>-some assessments like syphilis serology, vitamin- or ferritin status should be conducted by individual risk.</p> <p>-some assessments like Malaria status, Hepatitis C and Schistosoma serology should be conducted by respective country of origin</p>	none	none
USA[18]	Centers for Disease Control and prevention	<p>- Vaccination only valid when written documentation is available</p> <p>-Overseas vaccination program implemented by registered physicians before departure to US consisting of two doses of several vaccines with 1–2 months of time in between</p> <p>-post-arrival after assessment of immunization status an age-adjusted vaccination schedule will be implemented. Serologic testing may be used for evaluating vaccination-status</p>	<p>-If possible medical examination by special physicians will be implemented before departure from overseas. Except from vaccination status assessment there will be also presumptive treatment with albendazole enrolled</p> <p>-Broad medical examination by special physicians implemented during the first months after arrival in the US. Physical status as well as nutritional status, lead-test, laboratory testing and age adjusted TB screening will be assessed. Vaccination coverage is assessed and records from former overseas examination will be checked and completed</p>	none	none
Canada[19]	<p>-National Advisory Committee on Immunization (NACI)</p> <p>-Committee to Advise on Tropical Medicine and Travel (CATMAT)</p> <p><a href="https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html">https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html</a></p>	<p>-Vaccination status is assessed prior to arrival with only documented proof of vaccination accepted as valid</p> <p>-catch-up schedule is oriented to country of origin and age of individual</p> <p>-MMR and Varicella vaccination should not be given in case of suspected active tuberculosis</p>	<p>-before arriving in Canada refugee claimants are enrolled in Immigration Medical Examinations</p> <p>-TB-screening using TST is implemented to migrants from high-risk countries</p> <p>-Laboratory examinations are implemented after arrival in Canada checking for full blood cell count, sickle cell status, HIV status (when coming from high-burden countries) and other</p>	none	none

Guideline		Main recommendations regarding particular issues			
United Kingdom[20]	National Institute for Health Care Excellence <a href="https://www.gov.uk/government/collections/migrant-health-guide-countries-a-to-z">https://www.gov.uk/government/collections/migrant-health-guide-countries-a-to-z</a>	-vaccination status of refugees residing in the UK should always be assessed by physicians. Age adjusted national catch-up-schedule is implemented	-existing assessment guidelines for many different countries: every country of origin has its respective schedule for migrant health -newly arriving migrants are evaluated by assessing their psychosocial status, sexual-behaviour, ethnicity and risk of communicable diseases, as well as personal health issues such as hearing, seeing and risk factors for chronic diseases. -LTBI screening is implemented for all immigrants having spent significant time or being born in high-risk areas using TST or IGRA -active TB screening is implemented to all immigrants migrating from high incidence countries using chest x-ray	Newly arriving migrants should be informed how the NHS works and how it differs to health systems they are used to	none

Several recent reviews have criticised national screening guidelines as too restrictive, focussed on single diseases [22] and failing to cover the targeted populations [4, 22, 23], failing to provide information on how to improve screening and treatment coverage and completion [23], and being insufficiently based on evidence and evidence synthesis [24] (see Table 3 at the end of the manuscript). Previous studies of refugee/asylum seeker populations have mainly been concerned with screening and treatment strategies, as well as the cost-effectiveness of tuberculosis prevention in immigrants from high to lower-incidence regions [25–27]. Studies of respiratory infections other than tuberculosis shows that more resources for prevention and control of acute respiratory infections (ARI) are needed [8] and that there should be a particular focus on vaccine-preventable infections [9] (see Table 3). Despite prevalence assessments of disease spectrums in migrant and refugee health and evaluations of implemented screening strategies[4, 5, 8], effective strategies and recommendations to reduce the burden of respiratory infections are lacking [9, 24, 28–30]. Healthcare providers often have insufficient training and are confronted with specific ethical, institutional and cultural issues as well as unfamiliar spectrums of diseases and symptoms [31–33]. Overviews and syntheses of evidence regarding effective interventions to reduce mortality and morbidity from respiratory tract infections in refugees and asylum seekers are scarce, especially in industrial nations [24, 34, 35]. Yet evidence is urgently needed to inform recommendations for treatment, diagnostics, screening and effective prevention of infectious diseases [22, 28] in national and international guidelines.

Table 3

Previous or ongoing systematic reviews regarding infectious diseases and respiratory infections in refugees and asylum seekers

Authors (Year)	Name of review	N references	Population	Infection(s)	Intervention(s) /Exposure(s)	Main findings
Dasgupta, et al. (2005) [25]	Cost-effectiveness of tuberculosis control strategies among immigrants and refugees.	72	Immigrants, refugees from high to low incidence-countries	tuberculosis	All Tb- related diagnostics*	1) previously used chest-x-ray has minimal impact 2) ideal control strategy would be global investment in high-incidence countries 3) cell-mediated strategies are expensive and were not evaluated for screening purposes
Aldridge et al. (2014) [26]	Pre-entry screening programmes for tuberculosis in migrants to low-incidence countries	15	Migrants to low-incidence-countries	tuberculosis	Pre-entry-screening (All Tb- related diagnostics*)	1) biggest yield for culture- and smear-based screening for individuals from high-incidence-countries 2) ideal control strategy would be domestic returns for investment in tuberculosis control programs overseas
Campbell et al. (2015) [27]	A Systematic Review on TST and IGRA Tests Used for Diagnosis of LTBI in Immigrants	51	immigrants	tuberculosis	TST and IGRA in low-incidence countries	1) TST and IGRA present similar sensitivity and specificity for active TB – IGRA may be preferred in immigrants 2) positive test prevalence was lower for individuals < 18 years old and individuals from low-incidence countries
de-Vries et al. (2017) [41]	Barriers and facilitators to the uptake of tuberculosis diagnostic and treatment services by hard-to-reach	12	Hard-to-reach (mainly migrants)	tuberculosis	risk-factors for limited uptake of Tb treatment and diagnostic	1) tuberculosis-related stigmatisation was perceived as a major barrier 2) institutional barriers main factors for delay to diagnosis 3) no strong evidence on facilitators found 4) cultural and language barriers main factors for health-care providers
Heuvelings et al. (2017) [29]	Effectiveness of interventions for diagnosis and treatment of tuberculosis in hard-to-reach populations in countries of low and medium tuberculosis incidence	19	Hard-to-reach	tuberculosis	Treatment of active Tb in OECD, EU, EEA and EU-applicant countries	1) Mobile chest-x ray units are an effective and easy way of diagnosing active Tb, because of poor follow-up in this population 2) active referral to Tb clinics has been shown to be effective in migrants for the uptake of treatment 3) community DOT by non-family members seem to be most effective, some contradictions 4) incentives are a valuable intervention to increase uptake of screening, diagnosis and adherence to treatment in homeless people and drug abusers
Bellos et al. (2010) [8]	The burden of acute respiratory infections in crisis-affected populations	36	Health-crises affected populations	Acute respiratory infections	Affected by health crises	1) high burden of ARI even increases during crises 2) older children should be more integrated in vaccination strategies 3) more resources should be invested for ARI prevention and control

Authors (Year)	Name of review	N references	Population	Infection(s)	Intervention(s) /Exposure(s)	Main findings
Bozorgmehr et al. (2017) [24]	Infectious disease screening in asylum seekers - Range, coverage and economic evaluation in Germany, 2015	n.a.	Refugees	Screened infectious diseases	Health screening implemented by German states	1) newly arrived refugees are mainly affected by screening for active Tb, STI and stool parasites 2) expenses for screening using private fees could be 30% higher 3) high costs in diseases with low yield argue for more evidence-based approaches in screening methods
Crocker-Buque et al. (2017) [79]	Immunization, urbanization and slums - a systematic review of factors and interventions	63	Hard-to-reach neighbourhood mostly in middle and low-income countries	VPD***	Living in difficult conditions	1) many different factors associated with immunization status strongly varying by investigated area 2) community involvement has shown to face several factors for low immunization at the same time 3) physical distance to health services should be reduced 4) maternal education has shown to be effective
Eiset et al. (2017) [5]	Review of infectious diseases in refugees and asylum seekers-current status and going forward	51	Refugees and other migrants	Infectious diseases	Migrant status (prevalence studies)	1) prevalence of tb is rising 2) infectious diseases are important in refugees 3) risk of transmission to autochthonous population is low 4) refugee status and context of flight is rarely considered in studies
Hvass et al. (2017) [22]	Systematic health screening of refugees after resettlement in recipient countries	53	refugees	Screened infectious diseases	Implemented health screenings	1) circumstances of screening strongly depend on recipient country 2) most common screened diseases are tb, parasites, hepatitis and anaemia 3) Though important – mental health issues and chronic diseases were only screened in a few studies
Mipatrini et al. (2017) [9]	Vaccinations in migrants and refugees - A challenge for European health systems	58	Migrants and refugees in Europe	VPD***	Strategies for assessment and immunisation	1) health systems of countries of origin often are disrupted from war, leading to risk of critical infection with VPD*** 2) Polio and MMR-vaccines should be prioritised, Tetanus, Diphtheria and Hep. B. as well

The objective of this systematic review is to collect and synthesize evidence on the effect of interventions to diagnose, treat and manage respiratory-tract infections in refugees/asylum seekers and disadvantaged immigrants in OECD, EU, EEA and EU-applicant countries.

## Methods

This review was carried out in accordance with the PRISMA Statement [36] and the Cochrane Handbook [37, 38]. (PROSPERO: CRD42018074338) [39].

## Eligibility for inclusion

We included controlled studies (including non-randomised intervention studies and longitudinal studies with pre-test/post-test designs) published between 1 January 2000 and 1 October 2019. Study populations were refugees [40], asylum seekers [40] or immigrant hard-to-reach populations (e.g. Sinti and Roma, sex workers, drug abusers, prisoners, homeless people and people living with HIV [29, 41]). Place of intervention was a member country of the OECD [42], the European Union [43, 44], the European Economic Area (EEA) [45] or an European Union applicant country [46] (**For full list of included countries see Additional file 1**). Included were interventions to reduce incidence, prevalence, mortality, delay to diagnosis and treatment and transmission from respiratory infections, including lower and upper respiratory infections of unknown aetiology, acute respiratory infections and respiratory infections with pathogens listed in (**Full PICOS Table can be found in Additional File 2**). Also included were interventions to improve vaccination coverage for respiratory-related vaccine-preventable

diseases. We excluded interventions to reduce tuberculosis incidence due to the existence of several recently-published systematic reviews [25–27, 29, 41]. Studies with any type of individual- or group-level interventions were included: outbreak prevention, any type of vaccination campaign, health literacy interventions, pharmaceutical and non-pharmaceutical prevention and treatment strategies, housing interventions and local health care arrangements.

Outcomes were change in diseases incidence, prevalence or mortality, delay to diagnosis or treatment, transmission rates, number of secondary cases and vaccination coverage.

## Search strategy, study selection and data collection

The database search was conducted following the Cochrane Collaboration guideline for systematic literature searches [47, 48]. The following databases were searched in June 2017. The search was updated in May 2018 and October 2019:

- MEDLINE® using OvidSP (including: Ovid MEDLINE® Epub Ahead of Print, In-Process & Non-Indexed Citations, Ovid MEDLINE® Daily)
- Web of Science by Clarivate Analytics using All Databases
- CINAHL using EBSCOhost
- PSYINDEX using EBSCOhost.

The search terms in the literature review included specific terms for respiratory infections, unspecific terms for infections and inflammation in general, terms for anatomic and topographic localisations, and terms for refugees, asylum seekers and migrants. The Medline® search was complemented by a Mesh Term search. The full search strategy can be found in **Additional file 3**.

References were screened by title and abstract by two reviewers (JFL and AB) independently, consensus was reached via consultation with a third reviewer (BL). For all selected abstracts full texts were obtained. We extracted information on study characteristics, study population, study design and outcome measures. In cases of incomplete or inconsistent data, authors were contacted.

After extraction, data was summarised and represented in tabular form by outcomes and outcome measures: Incidence rate, outbreak measures in number of secondary cases per exposed individual and vaccination coverage as percentage of being vaccinated. Further outcome measures were not found, i.e. mortality rate, delay to diagnosis and treatment. Whenever possible, we calculated risk or rate ratios comparing intervention and control groups to achieve better comparability.

## Risk of bias assessment

Risk of bias assessment was carried out using the ROBINS-I tool for cohort-style non-randomised trials of interventions for all included non-randomised trials [49] and using RoB2.0 for all included randomised controlled trials [50]. Risk of bias across studies was evaluated for publication and language bias and following the GRADE recommendations in the range of outcome subgroups across studies [51–55].

## Results

### Study Selection and characteristics

After manual deduplication 5779 of 10242 abstracts remained for screening. After title and abstract screening 105 full texts were assessed of which 9 studies were included in the review. Inter-reviewer reliability was high (>90%). The PRISMA flowchart is displayed in **Figure 1**.

## Risk of bias

Table 5  
Risk of bias assessment of included studies

Larson et al., USA, 2010 [64]	Impact of non-pharmaceutical interventions on URIs and influenza in crowded, urban households	Randomised controlled trial	Door-to-door informational campaign and provision of face masks and/or alcohol based hand sanitiser	Allocated by residency, random sampling	Influenza vaccination, prevention of URI, ILI and influenza (Vaccination coverage against influenza after intervention period (%), Incidence of URI, ILI and influenza (N/1000 person-weeks) during intervention period	All residents with indication	Group E only provided with information material	904	Immigrant and hard-to-reach	hard-to-reach- neighbourhood Upper Manhattan (New York)
							Group 1 additionally provided with hand sanitiser	946		
							Group 2 additionally provided with face masks and hand sanitiser	938		

The most important sources of bias among studies targeting vaccination coverage of respiratory tract-related infections were confounding bias in seven [56–62], reporting bias in six [57–62] and bias due to the measurement of outcomes in six studies [57–62]. The most important non reported confounding factors were length of travel in seven [56–64], period of stay in seven [56–61, 64] and health literacy in seven studies [56–59, 61, 62, 65]. The main source of bias among studies targeting prevention of upper respiratory tract infections, influenza-like illness, influenza and vaccination coverage for influenza was social desirability bias in three studies [56, 59, 64]. In two studies the risk of bias was rated as critical; one because of missing data [58], and the other mainly due to incorrect classification of interventions [61].

Across studies the heterogeneous outcome measures could be an important source of bias, especially among the studies on influenza vaccination uptake, as interest in being vaccinated [56] or the presence of a vaccinated person in a household [59] may not be valid measures of actual vaccination coverage [58, 64] in the examined population. Publication bias may also be an important source of bias, because with only two exceptions ([57], [64]), no negative intervention effect was described. Therefore, the findings regarding the overall effect of these interventions should be interpreted with caution [51] and evidence across all outcomes is evaluated as „low“ following the GRADE approach.

Since the included studies have heterogeneous study designs, characteristics and outcome measures, no pooled analysis in the form of a meta-analysis was performed.

## Results of individual studies

Table 4  
Characteristics of included studies

Pavli et al. (2017) [4]	Health problems of newly arrived migrants and refugees in Europe	n.i.	Refugees and migrants in Europe	Infectious and other diseases	Migrant status (prevalence studies)	1) prevalence and disease-spectrums vary by country of origin 2) respiratory diseases are the most common health issue at the Greek-Turkish border 3) access to health care is often influenced by legal limitations for refugees
Pottie et al. (2017) [80]	[Review-Protocol] Prevention and assessment of infectious diseases among children and adult migrants arriving to the European Union/European Economic Association	n.a.	Migrants in Europe	Tuberculosis Hepatitis B and C VPD*** HIV Intestinal parasites	Being targeted by any prevention and assessment strategy considered	-Data not yet published-
Chernet et al. (2018) [81]	Prevalence rates of six selected infectious diseases among African migrants and refugees	113	Migrants/refugees of African origin	Hepatitis B and C Intestinal parasites Syphilis	Migrant status (prevalence studies)	1) blood-borne infections are more relevant in refugees than intestinal parasitic infections 2) transmission cycle of parasitic infections is interrupted in recipient countries 3) geographic region of origin shows correlation with disease-spectrum
Nellums et al. (2018) [6]	Antimicrobial resistance among migrants in Europe	23	Migrants in Europe	Infection with AMR°	Migrant status (observational studies)	1) prevalence of AMR in migrants is about 25% overall 2) prevalence of AMR higher in refugees/asylum seekers than other migrants 3) no data found on transmission to autochthonous population
Seedat et al. (2018) [23]	How effective are approaches to migrant screening for infectious diseases in Europe?	47	Migrants in Europe	Screened infectious diseases	Implemented health screenings	1) innovative strategies should be implemented for completion of screening and treatment 2) coverage of screening is low 3) EU/EEA approach of screening is too restrictive/focussed on single diseases
<p>* (= radiological), cell-mediated, serological, microbiological, microscopical)          *** vaccine preventable diseases          ° antimicrobial resistant pathogens</p>						

Table 6  
Results of included studies

Using ROBINS-I-tool for non-randomised studies of cohort-type // Risk of bias due to:								
Author (year of publication)	Confounding	Selection of participants	Classification of interventions	Deviation from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall judgement
De Vallière et al. (2011) [63]	Low	Low	Low	Low	Low	Low	Low	Low
Pallasch et al. (2005) [65]	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Brockmann et al. (2016) [62]	Serious	Moderate	Low	Low	Moderate	Moderate	Serious	Serious
Koop et al. (2001) [57]	Serious	Low	Moderate	Moderate	Low	Low	Serious	Serious
Coady et al. (2008) [56]	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
Hoppe et al. (2011) [58]	Serious	Serious	Low	Low	Critical	Serious	Serious	Critical
Rodriguez-Rieiro et al. (2011) [61]	Critical	Critical	Critical	Serious	Moderate	Moderate	Critical	Critical
Larson et al. (2009) [59]	Serious	Low	Moderate	Low	Serious	Serious	Serious	Serious
Using RoB 2.0 for cluster-randomised parallel group trials of intervention // Risk of bias due to								
	Randomisation process	Timing of identification and recruitment of individual participants in relation to timing of randomisation		Deviations from intended interventions	Missing outcome data	Measurement of outcomes	Selection of reported result	Overall judgement
Larson et al. (2010) [64]	Low [01-04]	Low [01-04]		Some concerns [01-04]	Low [01-04]	Some concerns [01-04]	Low [01-04]	Some concerns [01-04]

## Influenza vaccination/interest in vaccination informational campaigns

Three studies assessed influenza vaccination in hard-to-reach neighbourhoods in New York City with an immigrant proportion of more than 70% [56, 59, 64]. Each evaluated multilingual information campaigns in various forms such as comic strips, informational talks, and community events responding to common myths about vaccinations and advising on locations of free vaccination clinics. One study of 3744 participants conducted in East Harlem and The Bronx measured interest in getting vaccinated against influenza [56], finding an increase after a 10-month intervention period from 80% among those surveyed pre-intervention (95%CI: 78.7–81.3%) to 94% (95%CI: 93.1–94.8%) among those surveyed post-intervention. Two studies were conducted in Upper Manhattan; one a randomised controlled trial including 2788 individuals from 509 households over 19 intervention months [64], the other a non-randomised intervention study including 422 households each represented by one person [59]. The non-randomised intervention study measured the probability of a person vaccinated against influenza living in the same household as the respondent, which increased from 63.7% (95%CI: 58.9–68.3%) to 73.9% (95%CI: 69.5–78.1%). The randomised controlled study compared health literacy campaign with added non-pharmaceutical prevention strategies against influenza and upper respiratory infections: one group (Group E) received only the informational campaign, another (Group 1) received additional alcohol-based hand sanitiser, and a third group (Group 2) received additional hand sanitiser and face masks. Influenza vaccination coverage improved in all groups after the intervention period from 21.1% (95%CI: 18.5–23.9%) to 40.8% (95%CI: 37.6–44.1%) in Group E, from 19% (95%CI: 16.6–21.7%) to 57.1% (95%CI: 53.9–60.3%) in Group 1 and from 22.4% (95%CI: 19.8–25.2%) to 43.5% (95%CI: 40.3–46.7%) in Group 2.

One study retrospectively evaluated the effect of the national vaccination campaigns against influenza in Spain in 2008/2009 and 2009/2010 in 51,666 individuals including 3426 immigrants [61]. There was no evidence of an increase in vaccination coverage in immigrants; the odds of vaccination for immigrants was 1.10 (95%CI: 0.97–1.25), and the proportion of vaccinated immigrants increased slightly from 7.9% (95%CI: 6.8–9.2%) pre-intervention to 10% (95%CI: 8.5–11.8%) post-intervention. We were unable to identify the main content of the campaign interventions. We found no official records of the interventions and received no answer to our requests for information.

In a birth clinic in Seattle in 157 pregnant, women of varying ethnicities [58], influenza vaccination coverage increased from 48.8% (95%CI: 47.9–49.7%) to 76% (95%CI: 69.0–82.8%) pre- to post-intervention, which compares to data from the Pregnancy Risk Assessment Monitoring System (PRAMS) from separate studies [66–70]. The intervention in this study comprised three months of multi-language information and video material in the waiting room as well as personal talks and “flu-packs” consisting of face masks, hand sanitiser and thermometers [58].

# Vaccination campaigns for respiratory tract-related childhood diseases

Three studies evaluated different vaccination campaigns for respiratory tract-related childhood diseases [57, 62, 65]. One compared the effectiveness of two consecutive vaccination campaigns in recently-arrived refugee children under 4 years of age fleeing from the Kosovo Crisis (1998/1999) in Macedonian refugee camps with high and low turnover [57], showing a benefit for more stable populations with less turnover: in a camp with high population turnover vaccination coverage rates dropped from 93% (95%CI: 91.9%-93.4%) after the first campaign to 73% (95%CI: 70.9-74.9%) after the second campaign three weeks later, while in a stable population camp vaccination coverage stayed constant at 91% (95%CI: 89.9-91.9%) after both campaigns.

A second study, conducted by the Ministry of Health in German reception centres, demonstrated the benefit of vaccination education among 2256 newly-arrived refugees. During a 6-month intervention period, a vaccination campaign for MMR and DPPT was implemented which involved vaccine doses, informational material and interpreters to ensure informed consent. The percentage of refugees with at least one vaccination increased from 10% (95%CI: 7.9-12.7%) prior to the intervention to 36.8% (95%CI: 33.8-39.9%) afterwards.

The third study evaluated the effect of the „keyperson” principle enhancing the effectiveness of a MMR vaccination campaign for 344 children under 10 years of age during a 2-year intervention period [65]. Keypersons are defined as trained persons from similar living conditions and ethnicities. In this study, they assisted in a door-to-door vaccination campaign in German hard-to-reach and broad-spectrum immigrant neighbourhoods with refugee proportions of about 30%. The risk of receiving at least one dose of vaccination increased from 55% (95%CI: 38.3-71.3%) to 84% (95%CI: 69.3-93.1%), while the risk of receiving two doses increased from 8% (95%CI: 1.6-21.1%) to 60% (95%CI: 44.4-75.0%).

## Outbreak prevention

In a Swiss interventional study, two varicella outbreak response strategies were evaluated in 1824 newly arrived refugees, each for twelve months [63]. The first (“rapid”) response strategy, evaluated in 858 new asylum seekers lodged in seven housing facilities, involved the isolation of index cases and serotesting and, if necessary, vaccination of people in the same housing facility. This was found to lower the proportion of infected persons from 12.8% (95%CI: 7.4-19.8%) to 2.8% (95% CI: 1.1-5.7%) compared to an outbreak series in 2007 with no previously defined response strategy. The second (“general”) response strategy involved the strict vaccination of 966 arriving refugees aged 15 to 39 years without a history of varicella, leading to no varicella infections in any refugee shelter (0.004%, 95%CI: 0.0002-0.066%).

## URI/ILI/Influenza Prevention

The previously-described randomised controlled trial by Larson et al. in hard-to-reach Manhattan neighbourhoods also assessed rates of upper respiratory infections (URI), influenza and influenza-like illness (ILI) [64]. It was found that the URI rate/1000 person-weeks in the control group E (informational campaign only) was 35.38, 95%CI: 33.7-37.1, in Group 1 (additional hand sanitiser) it was 29.06, 95%CI: 27.6-30.6 and in Group 2 (hand sanitiser and face masks) it was 38.91, 95%CI: 37.2-40.7. ILI rates/1000 person-weeks were 2.26, 95%CI: 1.8-2.7 in Group E, 1.93, 95%CI: 1.6-2.4 in Group 1, and 1.56, 95%CI: 1.2-1.9 in Group 2. Influenza rates/1000 person-weeks were 0.52, 95%CI: 0.33-0.77 in Group E, 0.60, 95%CI: 0.39-0.85 in Group 1, and 0.49, 95%CI: 0.32-0.73 in Group 2.

## Discussion

### Key results

In this systematic review of controlled studies we collected evidence on interventions aiming to reduce morbidity or mortality from respiratory infections and to improve vaccination coverage among refugees and migrants in hard-to-reach neighbourhoods. In six studies, we found evidence for the effectiveness of multilingual informational campaigns to increase the uptake of vaccination [56, 58, 59, 62, 64, 65].

There was limited evidence in one study that hand sanitiser reduced rates of upper respiratory infections and when provided together with face masks also the rates of influenza-like-illness in a hard to reach migrant neighbourhood [64].

To reduce secondary cases in outbreak situations, one study reported that in the case of vaccine-preventable diseases, general vaccination strategies implemented in refugees immediately after arrival have a large effect in reducing secondary cases. Evaluation of a positive history of infection or vaccination is sufficient, but serological testing after potential exposure is not necessary [63]. The hazard of outbreak situations is also lowered by this strategy. [63]

The main evidence gaps include a lack of data on housing arrangement standards, interventions to reduce rates of bacterial pneumonia, and evidence for the efficacy of operating standards in refugee health care and reception centres (Table 1).

Table 1  
Evidence gaps identified in this systematic review

Outcome	Type of intervention	TB	Influenza	Bacterial Pneumonia and lower respiratory infections	Other
Reducing morbidity or mortality	Information campaigns	+	-	-	-
	Housing standards	-	-	-	-
	Health literacy campaigns	+	-	-	-
	Operational standards for health care	-	-	-	-
	Personal Hygiene	+	+	-	+
Increasing vaccination coverage	Information campaigns	+	+	-	+
	Housing standards	-	-	-	-
	Health literacy campaigns	+	+	-	-
	Operational standards for health care	-	-	-	-

## Evidence rarely reflected in international standards

Five informational campaigns assessed in this review integrated the cultural and educational background of the targeted population [56, 58, 59, 64, 65], either by recruiting keypersons supporting the campaign staff [65], or by directly addressing common cultural myths about vaccinations [56, 64]. The efficacy of this strategy is not currently reflected in national or international guidelines, but is congruent with evidence that informational campaigns, community and culturally-oriented health literacy interventions are effective in improving vaccination coverage in autochthonous populations [71–73].

Currently, only NICE recommends institutional health literacy interventions in immigrant populations, however these are not clearly defined. Other European guidelines for refugee health care do not address this issue (Table 2).

European guidelines explicitly recommend against implementation of vaccination strategies at border crossings because informed consent is difficult to obtain [21]. However, a timely vaccination strategy has been shown to reduce the potential for outbreaks in particular for highly transmissible diseases [63]. Research is needed to determine the optimal strategies for obtaining informed consent in this situation. [74–76]

No evidence could be found for interventions targeting housing facilities for refugees, although they play an important role in the transmission and spreading of infectious diseases [21]. The effect of turn-over of refugees on vaccination coverage in refugee camps shows that it is easier to implement vaccination campaigns during the first months after arrival in more stable camps, but this study did not investigate overall housing conditions or number of housing units [57]. We did not find any controlled studies of interventions to reduce morbidity and mortality from relevant severe respiratory diseases such as bacterial pneumonia or interventions affecting the latency to diagnosis in airway infections.

## Limitations

Migration status was not always clear for all participants in the identified studies. While most of the studies indicated the ethnic or geographical origin of the participants [56, 58, 59, 64, 65], only two primarily represented refugee populations [57, 63]. However, interventions in the context of having fled from hardship, forced migration and life as a refugee are possibly presenting an important independent factor [5]. Countries of origin were not always clearly indicated, especially for Latin American and African populations. In addition, the heterogeneous outcome measures among the included studies made it difficult to obtain concrete effect estimates for refugee populations. Some of the findings should be interpreted with caution due to methodological issues in several of the studies (see Table 5).

The countries of origin of refugees and asylum seekers have shifted in the last 10 years [77, 78], therefore we included a longer time-span to provide a broader overview and context in relation to refugee health.

## Conclusions

Respiratory infections continue to be a major contributor to the poor health status of refugees and asylum seekers and currently interventions to lower this burden are not adequately reflected in national guidelines. This evidence synthesis shows that while there is some low-quality evidence for the effect and timing of multilingual vaccination campaigns that involve the community, there is little high-quality research on housing standards or operational standards needed to prevent respiratory infections in this population. Similar to other reviews of refugee and hard-to-reach populations for tuberculosis [29, 41], vaccine-preventable diseases [79] and respiratory infections [8], we conclude that it is important to incorporate cultural aspects in informational and community-involving campaigns and that more controlled operational research is needed. New methods of ensuring informed consent for early vaccinations must also be established.

## Abbreviations

Tb	tuberculosis
VPD	vaccine preventable diseases
AMR	antimicrobial resistant pathogens

## Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable. Full search strategy in Additional file 3

Competing interests

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Authors' contributions

- Idea: BL, KS, J-FL, MB
- Conception and design: BL, MB, J-FL, KS,
- Data extraction and screening: J-FL, AB, BL
- Interpretation of the findings: J-FL, BL, JB, WK, SR
- First draft: J-FL, BL
- Commented and revised first draft: MB, KS, AB, JB, SR, WK
- All authors read and approved the final version of the manuscript.

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## Figures

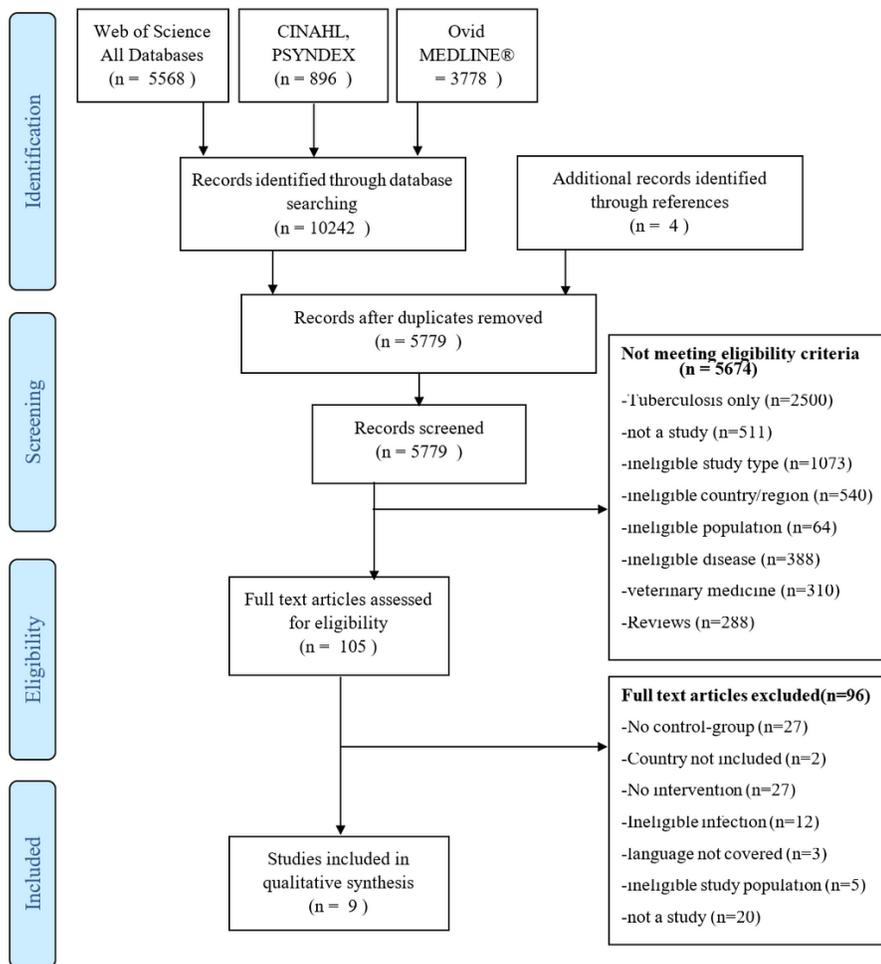


Figure 1

Prisma Flow-Chart

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