Economic Area found that the broad implementation of LTBI screening and treatment programmes is severely hindered by a multitude of factors, including a high number of migrants with LTBI (a small proportion of whom will develop active tuberculosis), diagnostic tests that poorly predict who will develop active tuberculosis, long LTBI treatment regimens, as well as several patient, provider, and institutional barriers that lead to poor uptake of screening and treatment completion.

Proactive screening and treatment for LTBI in all new migrants is not a key component in the European Centre for Disease Prevention and Control guidance[4] on the programmatic management of LTBI.

During the higher-than-usual influx of refugees into Europe, we suggested that more standardised data collection and analysis are needed to draw conclusions on the usefulness, cost-effectiveness, and epidemiological effect of tuberculosis and LTBI screening of migrants in Europe.[5] Many policies and suggestions depend on assumptions modelling and high levels of uncertainty because of a scarcity of empirical data.

Another unanswered public health question is why would latent infections in migrants be reacitivated,[6] given that it is a rare occurrence in healthy adults living in high-income countries. There is no evidence that the social determinants that cause reactivation (such as poor living conditions, poverty, bad nutritional status, few earning possibilities, limited access to education, and multiple stress factors influencing immunity) would be any different from those experienced by the non-migrant population. By de-racialising and de-medicalising the epidemic and looking at the common social determinants for transmission and reactivation, European countries could be more effective in preventing active cases and thus prevent transmission and decrease treatment costs. By countries improving their migrant health strategies, tuberculosis infection reactivation could be prevented more effectively than through LTBI screening programmes.

I declare no competing interests.

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Author's reply

We have several points in response to Wouter Arrazola de Oñate's claim that only a few countries actively screen for latent tuberculosis infection (LTBI) in migrants.[1]

First, our statement that "all high-income countries now have proactive latent tuberculosis infection screening and treatment programs for all new migrants and refugees"[2] does not imply that all high-income countries have an active operational and functional screening programme. The word proactive implied that the issue of LTBI is being continually addressed, but not necessarily that action is in place. The new WHO EndTB strategy, which aims to end the global tuberculosis epidemic, has placed LTBI firmly on the agenda and should be addressed to achieve the strategies' goal.[3,4]

Second, Arrazola de Oñate refers to a review by Greenaway and colleagues[5] on the cost-effectiveness of screening migrants for LTBI in Europe to support his argument against active screening for tuberculosis in migrants arriving to Europe. However, the study concluded that "despite these limitations, migrant-focused latent tuberculosis screening programmes may be effective and cost-effective if they are highly targeted and well implemented".[5]

Third, Arrazola de Oñate cites his own study,[6] arguing that screening for tuberculosis has a low diagnostic yield and is not cost-effective. However, his study focused on screening for active pulmonary tuberculosis and was written in 2016, which was before the WHO EndTB strategy announcement.

Fourth, although the risk of LTBI reactivation is low, most active cases in migrants in Europe are due to reactivation of an LTBI acquired in their countries of origin. Migrants make up about 11·4% of the EU and European Economic Area (EEA) population, and represented more than a quarter of reported tuberculosis cases in 2015.[3,7] This burden is even greater in European countries with a low tuberculosis incidence, where often more than half of all reported cases occur in migrants.[3]

The estimated lifetime risk of LTBI developing into an active state is 10%, and the estimated remaining lifetime of arriving migrants is 40 years; therefore, the annual risk of developing active tuberculosis in people with LTBI is about 0·25%. With about 45 million people in Europe born outside of the EU and EEA, and an estimated proportion with LTBI of 25% in people from high-endemic countries in Asia and Africa, the annual number of active tuberculosis cases evolving from the latent state is roughly 28 125. In the 31 EU and EEA countries, 55 337 cases were reported in 2017.[8]

Fifth, although we agree that tools for LTBI screening are not ideal, it is

better to use them than not to screen for the infection at all.

Managing LTBI requires further search for tests with a high predictive value for future development of the active state and research to address system bottlenecks in programmes for screening and treating people with LTBI. A 2019 study[9] concluded that "preimmigration interferon-γ release assay screening coupled with postarrival rifampin treatment among migrants from countries with moderate to very high incidence of TB resulted in the lowest cost-effectiveness ratios".[9]

We declare no competing interests.

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Efficacy and effectiveness of ten-valent versus 13-valent pneumococcal conjugate vaccines

We note some mischaracterisations in the Comment by Shabir A Mahdi and David Goldblatt[1] on the Article by Beth Temple and colleagues.[2] As an overarching framework, the data from Temple and colleagues cannot be used for predicting vaccine performance against most clinical outcomes, since the only accepted correlate of protection for pneumococcal conjugate vaccines (PCVs) is against invasive pneumococcal disease 1 month after three primary doses during infancy. For all other outcomes (carriage, mucosal disease), schedules, ages, and doses, no such association exists; thus the interpretation of immunogenicity data remains in doubt. For example, mucosal and circulating memory B cells might be the most important mediator against carriage endpoints.

Mahdi and Goldblatt[1] stated that 13-valent PCV (PCV13) "has no effect on serotype 3 invasive pneumococcal disease", despite substantial evidence to the contrary; PCV13 has been shown to provide direct protection against serotype 3 disease in both children and adults (table).[3,4] Suggestive of even some indirect effects, the European Centers for Disease Control and Prevention (ECDC) have reported that in countries using PCV13 in paediatric immunisation programmes, the incidence of serotype 3 disease decreased by 11% among people aged 65 years and older, compared with an increase of 51% in countries that used ten-valent PCV (PCV10).[5]

With respect to serotype 19A, Mahdi and Goldblatt correctly note that low crossreactive responses to 19A might explain the reported failure of PCV10 to decrease 19A colonisation in children and its inability to provide indirect protection against 19A in unvaccinated individuals. They omit that even among vaccinated age cohorts, PCV10 might provide inadequate protection, as suggested in Belgium, which had an immediate increase in paediatric 19A

	Study type	Age	Vaccine efficacy or effectiveness (95% CI)
Invasive pneumococcal disease[3]	Meta-analysis	≤5 years	63·5% (37·3–89·7)
Clinical community-acquired pneumonia[4]*	Randomised controlled trial	≥65 years	61·5% (17·6–83·4)
Chest radiology-confirmed community-acquired pneumonia[4]†	Randomised controlled trial	≥65 years	60·0% (5·2–84·8)

*At least two of the following symptoms: cough, production of purulent sputum, or a change in the character of sputum; temperature >38°C or <36·1°C; auscultatory findings consistent with pneumonia; leucocytosis (>10 × 10^9 white blood cells per L or >15% bands); C-reactive protein value >3 times the upper limit of normal; or hypoxaemia with a partial oxygen pressure >60 mm Hg while breathing room air, regardless of radiographic findings. Reported vaccine efficacy data are for first episodes of serotype 3 community-acquired pneumonia in the modified-intention-to-treat population. †Based on adjudication by an independent and blinded committee in which two of three members agreed that a radiograph (lateral and posterior-anterior chest radiograph, if the clinical condition permitted, and otherwise an anterior-posterior image) was consistent with community-acquired pneumonia. Reported vaccine efficacy data are for modified-intention-to-treat population.

***Table*: 13-valent pneumococcal conjugate vaccine efficacy or effectiveness against serotype 3 disease**