

Groningen, University Medical Centre Groningen/Beatrix Children's Hospital, Groningen, Netherlands (FV)

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See Online for appendix

Low prevalence of antibodies against pertussis in pregnant women in Italy

We read with great interest the Article by Daan Braug and colleagues¹ on the results of the maternal pertussis vaccination trial and its effects on the immune response of infants in the Netherlands.

Since 2016, recommendations for maternal immunisation against pertussis have been introduced in Italy, within the National Vaccination Plan 2016–18 and 2017–19,² with a dose of tetanus, diphtheria, and acellular pertussis (Tdap) vaccine given during the third trimester of pregnancy, ideally during the 28th week. To date, no data on coverage of pertussis vaccination in pregnant women have been published by the Italian Ministry of Health.

To generate data on the level of immunity against pertussis in pregnant women, we did a serological study to determine the prevalence of

antibodies against *Bordetella pertussis* among pregnant women in Apulia, a large Italian region.

195 serum samples were anonymously collected in compliance with Italian ethical law from pregnant women aged 20–46 years (mean 33.6 years [SD 4.6]) in the province of Bari between 2016 and 2017 as part of routine pregnancy medical checks. Samples were tested for IgG against *B pertussis* by use of SERION ELISA classic *Bordetella pertussis* IgG commercial kit (Virion\Serion, Würzburg, Germany). Results below the limit of quantification (10–1000 IU/mL) were considered with an arbitrary value of half the lower limit (5 IU/mL). IgG pertussis titers of 50 IU/mL or higher were regarded as positive by the manufacturer. 77.4% (95% CI 71.0–82.8) of samples had antibody concentrations below 50 IU/mL, and 26.7% (20.9–33.3) had antibody concentrations below the limit of quantification. No significant differences were noted between age groups (appendix).

These findings are consistent with studies done in Italy among pregnant and postpartum women in 2015–18, with very few or no women who had received Tdap during pregnancy,^{3,4} and only a third were willing to be vaccinated if recommended by their health-care provider.³ Adherence to the recommendation seems to be hampered by concerns regarding immunisation safety, poor information, and lack of professional engagement by physicians and health-care providers,^{3,4} highlighting the need for vast information and education interventions on the benefits and safety of pertussis vaccination during pregnancy. Because, in Italy, children are given their primary vaccination with the Tdap vaccine at ages 3, 5, and 11 months, a minimal effect on immune response to pertussis vaccination in infants whose mothers have been vaccinated during pregnancy should occur, according to the results of Barug and colleagues.¹

We declare no competing interests.

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High-income countries and latent tuberculosis infection screening for migrants

I would like to correct a claim in the Comment by Eskild Petersen and colleagues¹ on latent tuberculosis infection (LTBI) strategies. The authors state that “all high-income countries now have proactive latent tuberculosis infection screening and treatment programs for all new migrants and refugees”.¹ However, the literature shows that this claim is incorrect.

A review by Kunst and colleagues² illustrated that policies on the screening of refugees and migrants in Europe (a continent with many high-income countries) are diverse, and screening for LTBI is rarely done.

Another review³ on effectiveness and cost-effectiveness of LTBI screening programmes for migrants living in the European Union/European

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For Italian Ministry of Health vaccination website see www.salute.gov.it/portale/vaccinazioni/homeVaccinazioni.jsp

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 guidance⁴ 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 reactivated,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 deracialising 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 colleagues⁵ 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