Global reporting on tuberculosis preventive treatment among contacts

To the Editor:

Tuberculosis (TB) remains a major public health challenge and one of the leading infectious killers in the world [1]. Approximately one-fourth of the world's population is estimated to be infected with TB bacilli, creating a large pool of individuals who can develop TB and die from it in the coming years [2, 3]. In the absence of an effective vaccine, measures to diagnose and treat both TB disease and TB infection remain pivotal to reduce global TB incidence to levels envisaged by the End TB Strategy of the World Health Organization (WHO) and other international commitments [4, 5]. Giving medication to treat TB infection, known as TB preventive treatment (TPT), is an established part of care for people living with HIV, contacts of TB patients, people on immunotherapy and others at risk of developing TB [6]. The effectiveness of TPT depends on the correct identification of people who would most benefit from it, the use of regimens of proven efficacy and maximising adherence to treatment to the end. Unless these measures are implemented consistently, treatment may have negative repercussions on TB transmission and healthcare costs [7].

WHO collects, analyses and reports on data from national TB authorities each year to assess country progress towards global targets [1]. Three indicators relate to TPT: TB contacts assessed out of those identified; people started on TPT out of those eligible; and people completing TPT out of those starting it [8]. Whereas data for the first two indicators have been collected since 2018, WHO first requested countries to report on the completion of TPT among TB contacts in 2021, for individuals starting TPT in 2019. This letter discusses the country performance on the indicators and the implications of the latest data for the global scale-up of TPT, for all countries in the six WHO regions and for the high TB burden countries, which concentrate most of the TB incidence worldwide.

In 2020, 7 million contacts of bacteriologically confirmed pulmonary TB patients were identified and reported to WHO by 126 countries [1]. Of these, 3.9 million (55%) in 118 countries were reported as evaluated for both TB infection and disease. These numbers were lower than those reported in 2019, by 29% and 31%, respectively. In 2020, 129 countries reported starting >499 000 contacts on TPT. The relationship between the number of TB contacts screened and the number started on TPT differed in each of the WHO regions (figure 1a). In some countries, the numbers reported suggested that more contacts were started on TPT than had been screened. In all regions, one or more countries reported equal numbers of contacts screened and started on TPT, while in most other countries the latter number was much lower than the former.

80 countries reported data for >230 000 contacts who started TPT in 2019 and completed it (figure 1b). These include 19 of the 30 WHO high TB burden countries. Median percentage (interquartile range (IQR)) completion among people starting TPT in all countries reporting was 86% (71–96%). In the 19 high TB burden countries, this was slightly lower at 83% (61–94%), with completion being lowest in the countries with the biggest number of TB contacts on treatment in each of the four WHO regions to which these countries belong (*i.e.* African, Americas, South-East Asian and Western Pacific; figure 1c).

These findings highlight several important points about the status of TPT globally. Firstly, while TB contacts are identified as risk populations in many countries, <60% of the 7 million identified were reported as having been assessed for TB infection and disease in the latest year. Part of the discrepancy between contacts identified and contacts evaluated may be due to under-reporting of contacts assessed

Shareable abstract (@ERSpublications)
Country reports to WHO show low TB preventive treatment (TPT) coverage in contacts of people with TB, below global targets. More efforts are needed to find and evaluate TB contacts, help them access better regimens and complete TPT. https://bit.ly/3sp0FA3

a) TB contacts starting TPT in 2020 (log₁₀ scale) vs TB contacts screened in 2020 (log₁₀ scale), by WHO region (African, Americas, Eastern Mediterranean, European, South-East Asian, Western Pacific).

b) World map showing contacts completing TPT: <50%, 50–70%, 70–94%, >95%, Not applicable.

c) Contacts completing TPT % vs Contacts starting TPT in 2019 (log₁₀ scale), by WHO region (African, Americas, South-East Asian, Western Pacific).
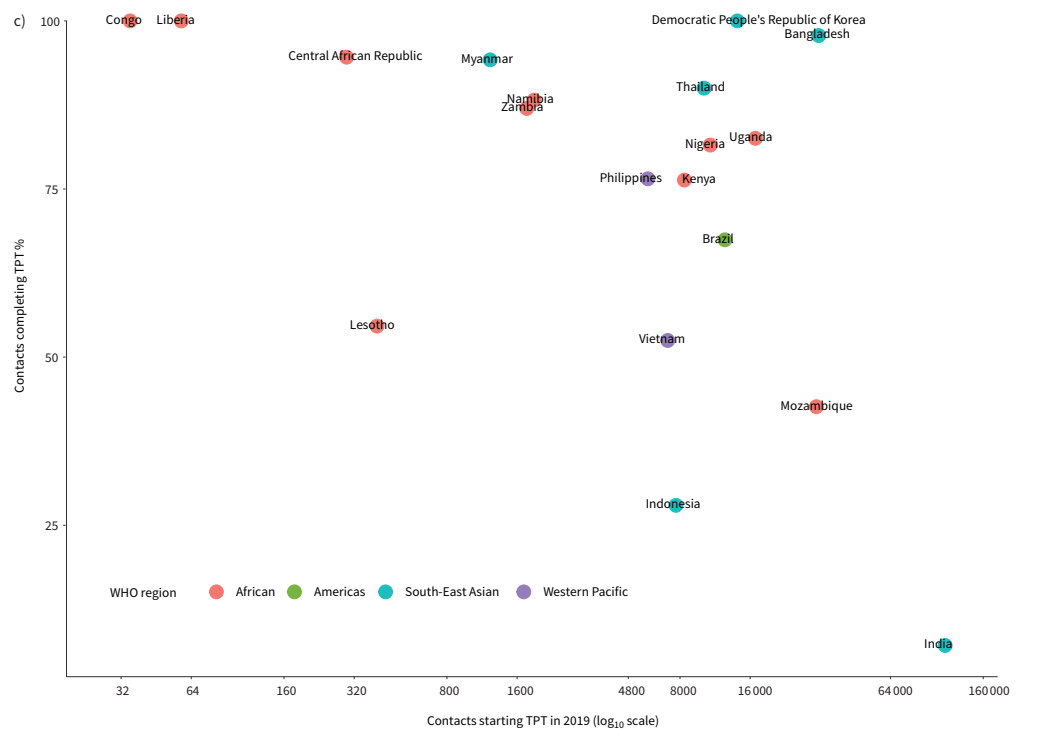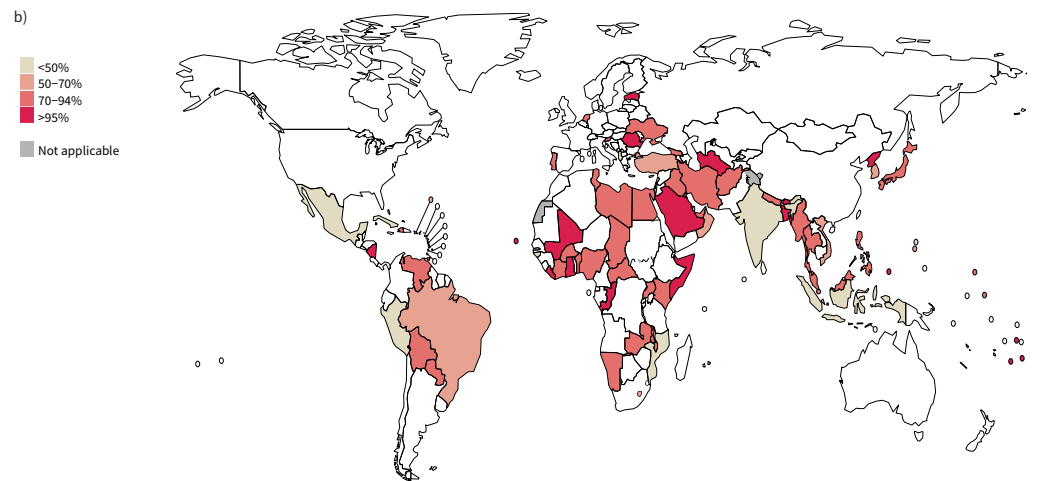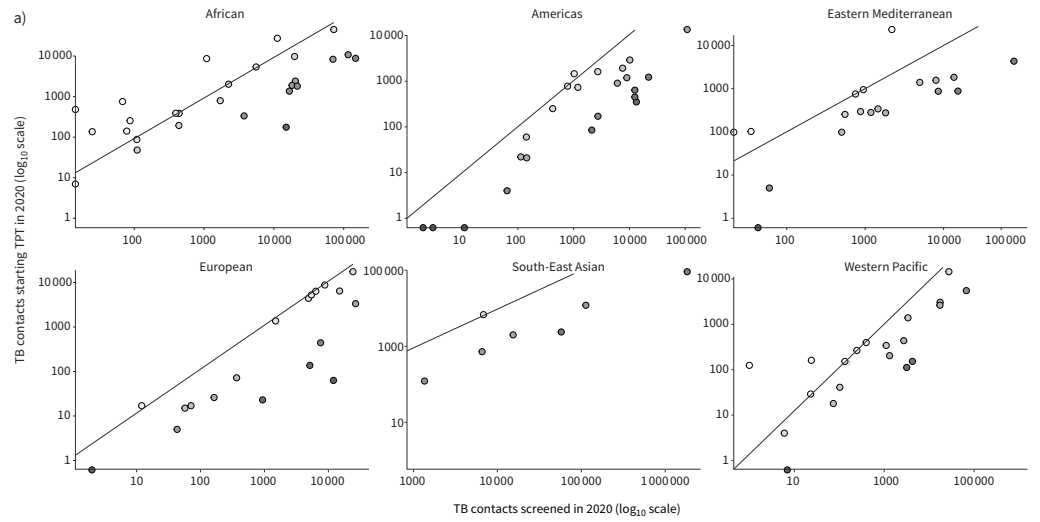
FIGURE 1 a) Tuberculosis (TB) contacts screened *versus* contacts started on TB preventive treatment (TPT), all countries by World Health Organization (WHO) region, 2020. Each circle represents a country report. Countries on the diagonal reported equal numbers of contacts screened and starting treatment; those to the left of the diagonal reported more contacts starting treatment than screened (lighter shade); and those to the right of the diagonal reported more contacts screened than starting treatment (darker shade). b) Percentage completion of TPT started in 2019 by contacts of people with TB. c) TB contacts started on TPT *versus* percentage treatment completion, high TB burden countries, 2019. Each circle represents a country report, coloured according to the WHO region of the country. Graphics were created using ggplot2 and whomap packages in R (www.R-project.org/).

during household outreach. The contacts identified as being at risk by each programme is likely to be less than the true number of eligible persons. Nonetheless, the number of contacts identified is often used as a starting point of the cascade, given the difficulties of accurately estimating the actual number of contacts of all ages who were exposed. As seen in other aspects of TB care, contact evaluation coverage decreased in 2020 compared with 2019 as a result of programmatic disruptions caused by coronavirus disease 2019 (COVID-19) [1]. Secondly, on average, only approximately one in eight contacts evaluated were started on TPT. It is expected that not all contacts identified start TPT because some have TB disease and need curative treatment; others may have a negative test of TB infection; and some may have a contraindication to medication or opt out of treatment. Nonetheless, these reasons are unlikely to explain such a large gap. More likely reasons include suboptimal access to drugs, low prioritisation of preventive TB care and household contact follow-up by programmes and incomplete reporting of people treated. The observation that more contacts start TPT than are reported as screened in some countries suggests unlinked data systems, but it could also point to treatment without a full investigation for disease. Thirdly, not all contacts who start TPT are monitored for completion. While it is encouraging that so many countries reported treatment completion data following a first request, and that the percentage completion tended to be high, there are reservations. ~40% of countries that reported starting contacts on TPT in 2019 did not report completion data. In some countries the reporting was very incomplete, possibly reflecting only data from some geographical areas or subgroups. The number of contacts reported as completing TPT is equivalent to ~4% of contacts evaluated in 2019. Given that programmes are less accustomed to monitoring outcomes for people on TPT than for those on curative TB treatment, completion may be over-reported, including people who did not finish their treatment and were lost to follow-up by the healthcare services. In one meta-analysis in 2016 only 29% (95% CI 19–40%) completed TPT among >48 000 contacts [9]. In this study, completion was nearly three times higher with rifamycin-based regimens than isoniazid monotherapy and substantive numbers of people eligible for TPT were reported dropping out throughout the cascade of care.

In conclusion, global action to find and evaluate contacts of TB patients and support them to take TPT remains unsatisfactory. In 2018, heads of state at the United Nations High Level Meeting on TB declared that ⩾24 million contacts and ⩾6 million people with HIV should be started on TPT between 2018 and 2022 [5]. By 2020, only ~6% of contacts targeted had been reached, while the target for people with HIV was exceeded by >1 million. WHO urges governments and other stakeholders to urgently accelerate global coverage of TPT [10]. The COVID-19 pandemic makes this plea all the more pressing [11–13]. In addition, findings from the analysis in this letter make the case for countries to improve monitoring and reporting of key indicators at critical junctures of the cascade of preventive care and to make good use of digital technologies for this purpose and for other programmatic functions, including adherence support [14]. Monitoring and treatment support should reach all populations who need TB prevention treatment, through linkages with HIV clinics, hospital departments and occupational health services, among others. Clinicians have a central role to play in identifying contacts eligible for TPT; making sure that they are adequately evaluated for TB disease and infection using chest radiography and tests of TB infection as needed; prescribing shorter, better-tolerated regimens; counselling and supporting adherence throughout treatment; and taking measures to prevent, monitor and manage drug toxicity and drug–drug interactions.

Dennis Falzon[1], Saskia den Boon[1], Avinash Kanchar[1], Matteo Zignol[1], Giovanni Battista Migliori ⓞ**[2] and Tereza Kasaeva[1]**

[1]Global Tuberculosis Programme, World Health Organization, Geneva, Switzerland. [2]Istituti Clinici Scientifici Maugeri, IRCCS, Tradate, Italy.

Corresponding author: Dennis Falzon (falzond@who.int)

References

1   World Health Organization (WHO). Global Tuberculosis Report 2021. Geneva, WHO, 2021. www.who.int/tb/publications/global_report/en/

2   Houben RMGJ, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. *PLoS Med* 2016; 13: e1002152.

3   Cohen A, Mathiasen VD, Schön T, *et al.* The global prevalence of latent tuberculosis: a systematic review and meta-analysis. *Eur Respir J* 2019; 54: 1900655.

4   World Health Organization (WHO). Implementing the End TB Strategy: the Essentials. Geneva, WHO, 2015. www.who.int/tb/publications/2015/end_tb_essential.pdf

5   United Nations General Assembly. Resolution A/RES/73.3. Political Declaration of the High-level Meeting of the General Assembly on the Fight Against Tuberculosis. 2018. www.un.org/en/ga/search/view_doc.asp?symbol=A/RES/73/3

6   World Health Organization (WHO). WHO Consolidated Guidelines on Tuberculosis. Module 1: Prevention – Tuberculosis Preventive Treatment. Geneva, WHO, 2020. www.who.int/publications/i/item/who-consolidated-guidelines-on-tuberculosis-module-1-prevention-tuberculosis-preventive-treatment

7   Patel AR, Campbell JR, Sadatsafavi M, *et al.* Burden of non-adherence to latent tuberculosis infection drug therapy and the potential cost-effectiveness of adherence interventions in Canada: a simulation study. *BMJ Open* 2017; 7: e015108.

8   World Health Organization (WHO). WHO operational Handbook on Tuberculosis. Module 1: Prevention – Tuberculosis Preventive Treatment. Geneva, WHO, 2020. www.who.int/publications/i/item/9789240002906

9   Alsdurf H, Hill PC, Matteelli A, *et al.* The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2016; 16: 1269–1278.

10   Kasaeva T, Kanchar, Avinash, *et al.* Call to action for an invigorated drive to scale up TB prevention. *Int J Tuberc Lung Dis*. 2021; 25: 693–695.

11   World Health Organization (WHO). Impact of the COVID-19 Pandemic on TB Detection and Mortality in 2020. Geneva, WHO, 2021. https://cdn.who.int/media/docs/default-source/hq-tuberculosis/impact-of-the-covid-19-pandemic-on-tb-detection-and-mortality-in-2020.pdf

12   Migliori GB, Thong PM, Alffenaar J-W, *et al.* Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study. *Eur Respir J* 2021; 58: 2101786.

13   TB/COVID-19 Global Study Group. Tuberculosis and COVID-19 co-infection: description of the global cohort. *Eur Respir J* 2021; 59: 2102538.

14   World Health Organization (WHO), European Respiratory Society. Digital Health for the End TB Strategy: an Agenda for Action. (WHO/HTM/TB/2015.21). Geneva, WHO, 2015. http://apps.who.int/iris/bitstream/10665/205222/1/WHO_HTM_TB_2015.21_eng.pdf