Early View

Research letter

Global reporting on tuberculosis preventive treatment among contacts

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Global reporting on tuberculosis preventive treatment among contacts

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Body text

Dear Editor - Tuberculosis (TB) remains a major public health challenge and one of the leading infectious killers in the world (1). About 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 or 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 TB preventive treatment depends on the correct identification of people who would benefit from it most, the use of regimens of proven efficacy and maximizing adherence to treatment unto the end. Unless these measures are implemented consistently, treatment may have negative repercussions on TB transmission and health-care 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 TB preventive treatment: TB contacts assessed out of those identified, people started on TB preventive treatment out of those eligible and people completing TB preventive treatment out of those starting it (8). Whereas data for the first two indicators have been collected since 2018, WHO received the first-ever country reports on the completion of TB preventive treatment among TB contacts starting treatment in 2019. This letter discusses the country performance on the indicators and the implications of the latest data for the global scale-up of TB preventive treatment, 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 over 499,000 contacts on TB preventive treatment. The relationship between the number of TB contacts screened and number started on TB preventive treatment differed in each of the WHO regions (**Fig 1, panel a**). In some countries, the numbers reported suggested that more contacts were started on TB preventive treatment than had been screened. In all regions, one or more countries reported equal numbers of contacts screened and started on TB preventive treatment, while in most other countries the latter number was much lower than the former.

Eighty countries reported data for over 230,000 contacts who started TB preventive treatment in 2019 and completed it (**Fig 1, panel b**). These include 19 of the 30 WHO high TB burden countries. Median percentage completion among people starting TB preventive treatment in all countries reporting was 86% (interquartile range [IQR], 71–96%). In the 19 high TB burden countries, this was slightly lower at 83% (IQR, 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; **Fig 1, panel c**).

These findings highlight several important points about the status of TB preventive treatment globally. Firstly, while TB contacts are identified as risk populations in many countries, less than 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 during household outreach. The number of contacts identified as being at risk by programmes may itself be under-detected although it is often used as a starting point of the cascade given difficulties to accurately estimate 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 COVID-19 (1). Secondly, on average, only about one in eight contacts evaluated were started on TB preventive treatment. It is expected that not all contacts identified start TB preventive treatment 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 prioritization of preventive TB care and household contact follow-up by programmes and incomplete reporting of people treated. The observation that more contacts start TB preventive treatment 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 TB preventive treatment 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. About 40% of countries that reported starting contacts on TB preventive treatment 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 TB preventive treatment is equivalent to about 4% of contacts evaluated in 2019. Given that programmes are less accustomed to monitoring outcomes for people on TB preventive treatment 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 health-care services. In one meta-analysis in 2016 only 29% (95% confidence limits 19-40) completed TB preventive treatment among over 48,000 contacts, and completion was nearly three times higher with rifamycin-based regimens than isoniazid monotherapy (9). This study also reported substantive numbers of people eligible for TB preventive treatment dropping out throughout the cascade of care.

In conclusion, global action to find and evaluate contacts of TB patients and support them to take TB preventive treatment remains unsatisfactory. In 2018, heads of state at the United Nations High Level Meeting on TB declared that at least 24 million contacts and at least 6 million people with HIV should be started on TB preventive treatment between 2018 and 2022 (5). By 2020, only about 6% of contacts targeted had been reached, while the target for people with HIV was exceeded by over 1 million. WHO urges governments and other stakeholders to urgently accelerate global coverage of TB preventive treatment (10). The COVID-19 pandemic makes this plea all the more pressing (11),(12),(13). Findings from the analysis in this Letter also 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 TB preventive treatment; 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.

Conflict of Interest statement

The authors declare no conflict of interest. No specific funding was used to write this paper. All authors contributed substantively to the paper and agreed with the version submitted for publication. SDB, DF, TK, AK and MZ are staff members of the World Health Organization (WHO). They alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of WHO. The designations used and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area, or of its authorities, nor concerning the delimitation of its frontiers or boundaries. Graphics were created using *ggplot2* and *whomap* packages in R (15).

Twitter feed

Country reports to the World Health Organization show low TB preventive treatment (TPT) coverage in contacts of people with TB, below global targets. More efforts are needed to find & evaluate TB contacts, help them access better regimens and complete TPT.

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Figure 1, panel a. Tuberculosis contacts screened (x-axis; log 10 scale) versus contacts started on tuberculosis preventive treatment (y-axis; log 10 scale), all countries by 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 more contacts starting treatment than screened (lighter shade); to the right more contacts screened than starting treatment (darker shade))

Figure 1, panel b. Percentage completion of tuberculosis preventive treatment started in 2019 by contacts of people with tuberculosis

Figure 1, panel c. Tuberculosis contacts started on preventive treatment (x-axis; log 10 scale) versus percentage treatment completion (y-axis), high tuberculosis burden countries, 2019 (Each circle represents a country report, coloured according to the WHO Region of the country)