

# Latent tuberculosis infection

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Updated and consolidated guidelines for programmatic management

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## ANNEX 3

Values and preferences for the management of latent tuberculosis infection: survey of populations affected by the recommendations

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Annex 3. Values and preferences for the  
management of latent tuberculosis infection: survey of  
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## Background

Management of latent tuberculosis infection (LTBI) is critical to end the global tuberculosis (TB) epidemic, as stated in the WHO End TB strategy. WHO currently recommends two approaches for the management of LTBI, based on TB incidence and on income (1). The recent WHO guidelines recommend several LTBI treatment options for a wide range of risk groups in countries with a low burden of TB, defined as high- or upper-middle-income countries with an estimated TB incidence rate of < 100 per 100 000 population (1). For countries with a high TB burden, WHO recommends isoniazid as preventive therapy for people living with HIV and for children aged < 5 years who are household contacts of TB cases (2,3). At the request of Member States, WHO is preparing a unique, comprehensive document to guide policy for the management of LTBI in countries with high and low TB burdens.

Understanding the values and preferences of populations affected by the recommendations is essential for determining the strength of the recommendations (4). Values and preferences are particularly important in the management of LTBI, as treatment is given to asymptomatic individuals with no immediate harm due to TB infection in order to reduce their risk for active TB (5). We therefore conducted an online survey of the values and preferences for LTBI management of populations affected by the recommendations.

## Methods

We developed an online survey to solicit values and preferences for the management of LTBI on Survey Monkey (Palo Alto, CA, USA; www.surveymonkey.com). The survey contained two types of question: preferences for receiving LTBI treatment and features of the treatment. Background information was provided, including the concept of LTBI and the benefits and harm associated with its treatment. Three groups of respondents were asked about their preferences for LTBI treatment: people living with HIV, household contacts of a person with active TB disease and household contacts of a person with active MDR-TB disease. People with children were also asked about their preferences for LTBI treatment for their children.

The survey was in English and was disseminated through the WHO ENGAGE-TB listserv, which has members working on TB within nongovernmental and civil society organizations. It was also disseminated through networks of members of the Guideline Development Group who represent civil society organizations. Participation in the survey was voluntary and anonymous. The survey was open, and data were collected for 2 weeks in February 2017.

Data were exported into Excel spreadsheets, and descriptive analyses were performed with STATA, version 13.1.

## Results

Of the 174 participants, 142 completed at least one question about their preferences and were included in the analysis. Their characteristics are shown in Table 1. The median age was 46 years (interquartile range [IQR]: 37–54 years). Participants in the African Region accounted for 35.9% of respondents. Only 12 (7.0%) respondents reported that they were HIV-positive.

### People with HIV

Of the 12 respondents with HIV, 8 reported they would strongly or somewhat prefer to receive preventive treatment (Table 2). One respondent stated he/she would “somewhat not prefer” because of “additional pill burden and toxicity with reduced efficacy”. All the features of preventive treatment were considered very important or important by 80–100% of the respondents (Table 3).

### Household contacts of a person with active TB disease

More than 80% (n = 113) of the respondents said that they would strongly or somewhat prefer to receive TB preventive treatment if they had contact with a person with active TB in their household (Table 2). Similarly, of

59 respondents with children, more than 80% would strongly or somewhat prefer to give preventive treatment to their children, regardless of their age. The reasons for not preferring preventive treatment included: concern about side-effects and drug-resistant TB, insufficient efficacy, low risk for active TB, duration of treatment and belief that treatment is unnecessary for healthy individuals or those without active disease.

More than 90% of the respondents considered that the following features of preventive treatment are very important or important: shorter duration, fewer side-effects, fewer visits to a clinic and fewer pills (Table 4). Fewer respondents rated “less frequent intake” and “no need for directly observed therapy (DOT)” as very important or important (77.3% and 74.4%, respectively). Similarly, 90-100% of the respondents rated all the features as very important or important for their children, except for “no need for DOT” (Table 5).

### Household contacts of a person with MDR-TB disease

More than 80% of respondents would strongly or somewhat prefer to receive preventive treatment or give it to their children if they were exposed to someone with MDR-TB disease in their household. The reasons for not preferring preventive treatment included: limited evidence of the efficacy of preventive treatment for MDR-TB and concern about side-effects and the development of drug resistance.

## Discussion

The survey consistently showed a strong preference for TB preventive treatment, even against MDR-TB, despite the limited evidence. The strong preferences should be taken into account in making recommendations. As expected, shorter duration and fewer side-effects were considered important attributes of preventive treatment, as they may result in shorter regimens, such as 3 months' weekly rifapentine plus isoniazid, which also has fewer side-effects than isoniazid monotherapy. No requirement for DOT was considered another important attribute, to a similar extent as shorter duration and fewer side-effects. The 2015 WHO LTBI guidelines state that “The (Guideline) Panel noted that the 3-month weekly rifapentine plus isoniazid regimen should be given under direct observation as the evidence available so far is based on this circumstance” (1). A need for DOT could be a barrier to the scale-up of the weekly regimen.

The survey had several limitations. First, self-selection bias might have resulted in an overestimate of the preference for preventive treatment. It is possible that individuals who supported provision of preventive treatment were more likely to participate in the survey. Secondly, the results may be of limited generalizability, as the survey was conducted in English, and only people with access to the Internet could participate. Thirdly, a history of TB and treatment for TB might have affected the preference of respondents for preventive treatment, and we did not collect data on history of TB. Fourthly, there were few participants with HIV infection.

In conclusion, preventive treatment was strongly preferred by the participants in the survey. This should be taken into account in determining the strength of the recommendations.

## References

1. Guidelines on the management of latent tuberculosis infection. Geneva: World Health Organization; 2015.
2. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva: World Health Organization; 2011.
3. Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries. Geneva: World Health Organization; 2012.
4. WHO handbook for guideline development. 2nd edition. Geneva: World Health Organization; 2014.
5. Denholm JT, Matteelli A, Reis A. Latent tuberculous infection: ethical considerations in formulating public health policy. *Int J Tuberc Lung Dis*. 2015;19:137-40.
6. Belknap R, Borisov A, Holland D, Feng PJ, Millet JP, Martinson N et al. Adherence to once-weekly self-administered isoniazid and rifapentine for latent TB infection: iAdhere. In: Conference on Retroviruses and Opportunistic Infections; Boston (MA); 2016:Abstract 827LB ([www.croiconference.org/sessions/adherence-once-weekly-self-administered-inh-and-rifapentine-latent-tb-iadhere](http://www.croiconference.org/sessions/adherence-once-weekly-self-administered-inh-and-rifapentine-latent-tb-iadhere), accessed 27 December 2017).

**Table 1. Characteristics of respondents (n = 142)**

Age (years), median (IQR)	46 (37-54)
Gender, n (%)	
Female	64 (45.1)
Male	77 (54.2)
Prefer not to indicate	1 (0.7)
WHO region, n (%)	
African	51 (35.9)
Americas	25 (17.6)
Eastern Mediterranean	7 (4.9)
European	28 (19.7)
South-East Asian	26 (18.3)
Western Pacific	5 (3.5)
HIV status, n (%)	
Positive	10 (7.0)
Negative	127 (89.4)
Prefer not to indicate	5 (3.5)
Living with children, <sup>a</sup> n (%)	
Yes	62 (44.6)
No	77 (55.4)

IQR, interquartile range

<sup>a</sup> Data were missing for three participants.

**Table 2. Preferences for TB preventive treatment**

	Strongly prefer, n (%)	Somewhat prefer, n (%)	Neither prefer nor not prefer, n (%)	Somewhat not prefer, n (%)	Strongly not prefer, n (%)
<b>People living with HIV</b>					
Would prefer to receive (n=10)	7 (70.0)	1 (10.0)	1 (10.0)	1 (10.0)	0 (0.0)
<b>Household contact of a person with active TB disease</b>					
Would prefer to receive (n=141)	83 (58.9)	30 (21.3)	8 (5.7)	15 (10.6)	5 (3.6)
Would prefer to give to your children					
0-4 years (n=59)	38 (64.4)	11 (18.6)	1 (1.7)	5 (8.5)	4 (6.8)
5-9 years (n=59)	33 (55.9)	15 (25.4)	2 (3.4)	6 (10.2)	3 (5.1)
10-14 years (n=59)	31 (52.5)	16 (27.1)	2 (3.4)	6 (10.2)	4 (6.8)
<b>Household contact of a person with MDR-TB disease</b>					
Would prefer to receive (n=129)	75 (58.1)	29 (22.5)	13 (10.1)	6 (4.7)	6 (4.7)
Would prefer to give to your children					
0-4 years (n=59)	31 (57.4)	13 (24.1)	3 (5.6)	3 (5.6)	4 (7.4)
5-9 years (n=59)	30 (55.6)	14 (25.9)	3 (5.6)	4 (7.4)	3 (5.6)
10-14 years (n=59)	33 (61.1)	12 (22.2)	2 (3.7)	3 (5.6)	4 (7.4)

**Table 3. Important features of preventive treatment for people living with HIV**

	Median score <sup>a</sup> (IQR)	Very important, n (%)	Important, n (%)	Somewhat important, n (%)	Less important, n (%)	Not important, n (%)
Shorter duration	5 (4-5)	6 (60.0)	4 (40.0)	0	0	0
Less frequent intake	4.5 (4-5)	5 (50.0)	3 (30.0)	0	0	2 (20.0)
Fewer side-effects	5 (4-5)	7 (70.0)	3 (30.0)	0	0	0
Fewer visits to the clinic	5 (5-5)	8 (80.0)	1 (10.0)	1 (10.0)	0	0
Fewer pills	5 (4-5)	5 (50.0)	4 (40.0)	1 (10.0)	0	0
No need for DOT	5 (4-5)	7 (70.0)	3 (30.0)	0	0	0
No need to change dosage of anti-HIV drugs	4.5 (4-5)	5 (50.0)	3 (30.0)	1 (10.0)	0	1 (10.0)

HIV: human immunodeficiency virus; IQR: interquartile range; DOT: directly observed therapy

<sup>a</sup> 5-point rating scale where 5 is "very important" and 1 is "not important".

**Table 4. Important features of preventive treatment for adult household contacts**

	Median score <sup>a</sup> (IQR)	Very important, n (%)	Important, n (%)	Somewhat important, n (%)	Less important, n (%)	Not important, n (%)
Shorter duration	5 (5-5)	116 (82.3)	23 (16.3)	2 (1.4)	0	0
Less frequent intake	4 (4-5)	68 (48.2)	41 (29.1)	14 (9.9)	12 (8.5)	6 (4.3)
Fewer side-effects	5 (5-5)	119 (84.4)	20 (14.2)	2 (1.4)	0	0
Fewer visits to the clinic	5 (4-5)	89 (63.1)	44 (31.2)	5 (3.6)	2 (1.4)	1 (0.7)
Fewer pills	5 (4-5)	90 (63.8)	38 (27.0)	10 (7.1)	3 (2.1)	0
No need for DOT	5 (3-5)	85 (56.7)	25 (17.7)	23 (16.3)	4 (2.8)	9 (6.4)

IQR: interquartile range; DOT: directly observed therapy

<sup>a</sup> 5-point rating scale where 5 is "very important" and 1 is "not important".

**Table 5. Important features of preventive treatment for child household contacts**

	Median score <sup>a</sup> (IQR)	Very important, n (%)	Important, n (%)	Somewhat important, n (%)	Less important, n (%)	Not important, n (%)
Shorter duration	5 (5-5)	50 (84.8)	9 (15.3)	0	0	0
Less frequent intake	5 (4-5)	41 (69.5)	14 (23.7)	3 (5.1)	0	1 (1.7)
Fewer side-effects	5 (5-5)	54 (91.5)	5 (8.5)	0	0	0
Fewer visits to the clinic	5 (4-5)	41 (69.5)	14 (23.7)	2 (3.4)	2 (3.4)	0
Easy to swallow (e.g. water-dispersible)	5 (4-5)	52 (88.1)	7 (11.9)	0	0	0
No need for DOT	5 (4-5)	37 (62.7)	9 (15.3)	6 (10.2)	3 (5.1)	4 (6.8)

IQR: interquartile range; DOT: directly observed therapy

<sup>a</sup> 5-point rating scale where 5 is "very important" and 1 is "not important".



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