Methods to estimate number of child household contacts less than 5 years old eligible for latent tuberculosis treatment

Background

Coverage of latent TB infection (LTBI) treatment among child household contacts less than 5 years old is one of top-10 indicators for monitoring implementation of the End TB Strategy. However, monitoring and evaluation of LTBI management is often challenging due to lack of standard indicators and reporting and reporting systems, involvement of multiple service providers, and difficulty in collecting denominators (i.e. number eligible for preventive treatment). In order to facilitate implementation of LTBI treatment and measuring progress both at the national and global levels, we estimated the number of child household contacts less than 5 years old eligible for LTBI treatment by country. The estimates were discussed and endorsed by the WHO LTBI Task Force.

Methods

Definitions

Low TB burden countries (LBC) are defined as 113 high-income or upper middle-income countries with an estimated incident rate of less than 100 per 100 000 population. The rest of the countries are defined as high TB burden countries (HBC).

In low TB burden countries, the number of child household contacts eligible for LTBI treatment is defined as the number of children under 5 years of age who are household contacts of bacteriologically confirmed pulmonary TB cases and have LTBI; defined as a positive result to a standard tuberculin test or an IGRA test. In high TB burden countries, the number eligible is defined as the number of child household contacts without active TB, based on the current WHO recommendations that do not require LTBI testing among child household contacts < 5 years prior to the provision of preventive treatment in these countries.[1,2] We did not provide estimates for countries or territories with populations < 300 000.

Model and Data inputs

The estimates of number of child household contacts eligible for LTBI treatment were calculated as follows:

for high TB burden countries $N = \frac{n}{c} Hp(1 - t)$; and

for low TB burden countries $N = \frac{n}{c} HpL(1 - t)$

where N is the number of child household contact aged < 5 years eligible for LTBI treatment, n is the number of notified bacteriologically confirmed pulmonary TB, c is the average number of TB cases per household, H is the average household size, p is national proportion of children < 5 years, t is proportion of child household contacts with active TB, and L is prevalence of LTBI among child household contacts < 5 years old.

The following sources of uncertainty were accounted for: prevalence of LTBI, variance in the count of TB cases per household, and in the proportion of child household contacts with active TB.

Uncertainty about United Nations Population Division (UNPD) population size estimates was ignored. Errors were propagated using 2nd order Taylor series expansion[3,4] We used fixed population estimates from the United Nations Population Division and uncertainty in the values was not incorporated. Ninety-five percent confidence intervals of the estimates were calculated assuming normal distribution.

Table 1 shows parameters used in the estimates. County specific values were used for the following parameters: number of notified bacteriologically confirmed pulmonary TB cases; national proportion of children <5 years of age; and national average household size. The other parameters were assumed to be constant across countries due to lack of country level data. Prevalence of LTBI among child household contacts< 5 years of age and average size of TB cluster per household were estimated by conducting systematic review of literature and meta-analyses. The proportion of children with active TB among those who had a household contact with TB cases was calculated using number of children sharing household with an individual with TB and number of children developing active TB disease estimated in a previous modelling study.[5]

Table 1. Parameters and sources

Parameters	Values	Sources
Number of notified bacteriologically confirmed pulmonary TB in 2015	Differ by country	WHO global TB database
National proportion of children <5 years of age in 2015	Differ by country	2015 Revision of World Population, United Nations Population Division (https://esa.un.org/unpd/wpp/)
National average household size	Differ by country	National censuses, DHS statistical year books, or official websites of the national statistical authorities
Prevalence of LTBI among child household contacts <5years old in LBC	Constant across countries = 27.6% (19.2%-38.0%)	Systematic review of literature from LBC up to Dec 2015 (unpublished)
Average cluster size of active TB per household	Constant across countries =1.06 (95%CI 1.04-1.08)	Systematic review of literature between Jan 2005 and Dec 2015 (unpublished)
Proportion of children < 5 years old with active TB among those who had a household contact with TB cases	Constant across countries =6.1% (95%CI 1.0%-16.3%)	Source: Dodd et al, Lancet Glob Health. 2014[5]

1.   World Health Organization Recommendations for Investigating Contacts of Persons with Infectious TuberculosisGeneva, Switzerland: WHO, 2012.
2.   World Health Organization. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva, Switzerland: WHO, 2011.
3.   Ku HH. Notes on the use of propagation of error formulas. *Journal of Research of the National Bureau of Standards* 1966; **70**(4).
4.   Arras KO. An introduction to error propagation: derivation, meaning and examples of equation CY= FX CX FXT: ETH Zurich, 1998.
5.   Dodd PJ, Gardiner E, Coghlan R, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Health* 2014; **2**(8): e453-9.