Reconsidering global targets for tuberculosis control

A recent paper by Dowdy & Chaisson[1] used mathematical modelling to investigate whether annual declines in tuberculosis (TB) incidence can be sustained by maintaining adequate case detection rates (CDRs). In their model, once CDRs stabilized at any constant level below 80%, the projected TB incidence also stabilized. They concluded that TB control programmes should vigorously pursue improvements in case detection, regardless of the CDRs achieved.

Performance targets for global TB control were first formulated in 1991 at the 44th World Health Assembly. National TB control programmes were encouraged to achieve CDRs of at least 70% and cure rates in excess of 85%.[2] The underlying rationale was based on epidemiological estimates that TB prevalence, and later TB incidence, should decline by about 5–10% per year if these targets could be met and sustained. Epidemiological estimates were derived from empiric observations in European countries following the introduction of chemotherapy in the 1950s.[3] However, even in situations where both targets were reached and achievements sustained, incidence rates failed to decline as predicted. On critical review it is evident that, even if these targets are met, only 60% ($0.7 \times 0.85 = 0.595$) of TB cases will be "cured" by the programme. In addition, these targets only apply to new sputum smear-positive cases, while a huge percentage of patients in endemic areas are either retreatment cases or sputum smear-negative (particularly in HIV-affected areas).

Only two public health intervention avenues exist to gain control of the global TB epidemic.[4] First, every effort should be made to reduce host vulnerability at the population level. Host vulnerability is influenced by multiple factors and creative efforts are urgently required to address issues like poverty, malnutrition and HIV infection. Second, effective measures should be implemented to limit *Mycobacterium tuberculosis* transmission within communities. This relates directly to the appropriateness of current WHO-defined performance targets, which is the focus of this letter. We introduce two novel concepts that have not been considered in previous models but seem crucial to help advance the discussion.

Case density

The vast differences that exist between endemic and non-endemic areas and

[a] Department of Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India.
Correspondence to MB Soudarssanane (e-mail: drmybase@gmail.com).

the impact this has on transmission dynamics within communities are rarely appreciated. The intensity of the infection pressure that exists in some endemic areas is evidenced by the frequency of disease caused by re-infection and/or multiple strain infection.[5,6] Case density is a variable that describes the proximity of cases in space and time. From a transmission perspective, case density provides a measure of transmission overlap. Mathematical models using hypothetical scenarios assign a fixed number of secondary infections to each source case. By diagnosing and treating the source case it is assumed that a fixed number of secondary infections will be prevented. However, in endemic areas with high case densities the elimination of a single source case has limited impact on secondary infections among close contacts due to significant transmission overlap. Therefore, if we hope to develop mathematical models that are more robust and predictive of the situation in endemic areas, it seems relevant to adjust for case density. It should also be noted that, with transmission overlap, contacts are at risk of being infected multiple times by different source cases. The effect of repeated infections remains poorly understood, but multiple infectious challenges may “overwhelm” host immunity and predispose to the development of active disease.

Transmission saturation

Most source cases have fairly fixed circles of social interaction. This implies that once the majority of close contacts have been infected, the risk of infecting new people may decline even though the source case remains highly infectious. This phenomenon is referred to as transmission saturation. Transmission saturation illustrates the importance of early diagnosis and immediate institution of effective treatment. In this respect, the traditional focus on the most infectious sputum smear-positive cases, although clearly warranted, may not be the optimal strategy to limit the spread of disease within communities if it implies diagnostic delay beyond the point of transmission saturation. With delayed diagnosis, the transmission impact of ultimate treatment is greatly reduced. Current targets do not reflect the importance of limiting diagnostic delay and more sensitive diagnostic tools are required to achieve this.

There is a need to reconsider the accuracy and applicability of current mathematical models and to identify pragmatic ways of quantifying additional factors that may be at play in endemic areas. The incorporation of case density and transmission saturation in future mathematical models may assist the identification of more stringent, albeit more realistic, performance targets for global TB control. ■

Competing interests: None declared.

BJ Marais[a] **& PD van Helden**[b]

References

1. Dowdy DW, Chaisson RE. The persistence of tuberculosis in the age of DOTS: reassessing the effect of case detection. *Bull World Health Organ* 2009;87:296-304. PMID:19551238 doi:10.2471/BLT.08.054510
2. Resolution WHA 44.8. In: *Forty-fourth World Health Assembly, Geneva, 6-16 May, 1991. Resolutions and Decisions*. Geneva: World Health Organization;1991 (WHA44/1991/REC/1).
3. Styblo K, Bumgarner JR. *Tuberculosis can be controlled with existing technologies: evidence*. The Hague: Tuberculosis Surveillance Research Unit; 1991.
4. Marais BJ, Obihara CC, Warren RW, Schaaf HS, Gie RP, Donald PR. The burden of childhood tuberculosis: a public health perspective. *Int J Tuberc Lung Dis* 2005;9:1305-13. PMID:16466051
5. Van Rie A, Warren R, Richardson M, Victor TC, Gie RP, Enarson DA, et al. Exogenous reinfection as a cause of recurrent tuberculosis after curative treatment. *N Engl J Med* 1999; 341:1174-9. PMID:10519895 doi:10.1056/NEJM199910143411602
6. Warren RM, Victor TC, Streicher EM, Richardson M, Beyers N, van Pittius NC, et al. Patients with active tuberculosis often have different strains in the same sputum specimen. *Am J Respir Crit Care Med* 2004;169:610-4. PMID:14701710 doi:10.1164/rccm.200305-714OC