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Socio-political prescriptions for latent tuberculosis infection are required to prevent reactivation of tuberculosis

In their review article, Fox et al. detail how the screening and treatment of latent tuberculosis infection (LTBI), an asymptomatic condition, can be coupled with the treatment of active tuberculosis to reduce the global burden of tuberculosis (TB). They differentially sort risk factors associated with disease progression from LTBI to TB based on exposures and comorbidities, outline rationale for different preventive therapy regimens to prevent drug-susceptible and drug-resistant TB, and reflect upon ethical considerations of the widespread scale-up of LTBI treatment. Their clinical and epidemiological considerations are robust, and they recognize that the treatment of active TB alone will be in sufficient to achieve the steep annual reductions in incidence necessary to reach the End TB Strategy targets. However, they do not acknowledge the undeniable impact that improvements in living and social conditions has on reducing TB incidence.

We believe that the politics and ethics of LTBI treatment need to be taken one step further. Given the contextual factors that foster the reactivation of TB in the absence of evident comorbidities, the blanket screening for LTBI using non-specific diagnostic technology with limited predictive value for the risk of TB progression, with the goal of treating LTBI suspects with 3–9 months of multi-drug regimens, outsourcing social, economic, and political issues and frames them as biomedical problems. Administering population-wide LTBI treatment, it follows, is political. Should global health initiatives buttress the impoverished social conditions that foster TB reactivation in this manner?

Fox et al. argue that the risk of drug toxicity and benefits of treatment must be carefully balanced for each individual. Risks and benefits are reconfigured from a public health perspective. Given that only in the instance of high transmission risk and the presence of known TB risk factors can a greater risk of TB development be predicted following a positive LTBI test, blanket TB preventive therapy, which only targets a current infection, is questionable. Is it not overtreatment to administer TB prophylaxis based on the results of an immunological test that only measures prior exposure, gives no indication of current infection status, is poorly predictive of the risk of TB development (those that revert to negative following recent positive conversion are at greater risk of TB than those who remain positive), and is less sensitive in those at greatest risk of disease (i.e., those who are HIV-infected)? In the face of recurrent exposure in high-burden settings, is treatment of LTBI the most economic choice for long-term disease prevention?

TB risk factors are both biomedical and socio-economic and cannot be viewed in isolation: socio-economic status impacts immune competence and vice versa. Would correcting the immunological and socio-structural drivers of disease progression not be more cost-effective for long-term health benefits, with the further societal benefits beyond purely TB elimination?

Treating LTBI in children under 5 years of age, as well as patients with comorbidities, is advisable due to their greater risk of progression to disease. A randomized controlled trial of isoniazid preventive therapy (IPT) in HIV-infected individuals concurrently receiving antiretroviral therapy, showed those negative for LTBI to have a greater benefit from IPT than those positive by LTBI tests, demonstrating that tests for LTBI are not always reliable in predicting those who will benefit from preventive therapy. Fox et al. make sound epidemiological arguments about treating LTBI among the contacts of drug-resistant TB patients, which will arguably be an important measure to prevent strain replacement of drug-susceptible TB by drug-resistant TB (once effective regimens are found through the V-QUIN, TB CHAMP, and PHOENix trials). In high burden settings where TB transmission often occurs outside of the home, the effectiveness of household contact tracing would need to be compared to community-wide prophylaxis programmes, but the question of socio-structural prevention remains. The problem is that the current politics of evidence in science favour the championing of antimicrobial treatments with a direct causal relationship to outcomes over the more distant relationships between social determinants and health.

If we contemplate the blanket treatment of LTBI patients in high-income countries, the situation becomes more ethically questionable. Will widespread treatment of LTBI in a high-income country have a significant effect on global disease burden? In efforts to lower TB disease burden, it can be cost-effective for a low-burden high-income country to help bolster TB care and prevention for active cases in neighbouring high-burden countries. Lowering the TB burden in one country has positive spillover effects in other countries. To emphasize the argument by Fox et al. to lower TB prevalence in high-burden countries, spending money to treat active cases in low-burden settings is a more equitable use of resources than treating LTBI cases in a high-burden setting.

In countries like Australia, a high-income country with a low burden of TB, the bulk of TB occurs among immigrants and other recent arrivals from high-incidence countries, who probably acquired Mycobacterium tuberculosis infection abroad. However, depicting TB as a migrant problem is an artefact of geopolitical history that brushes aside the fact that cross-border mobility is a given in a globalized world, and overlooks the conditions of settlement that foster the disease. The exposure of recent migrants to different climatic conditions and poor living, working, and socio-economic conditions can be considered an effect-

http://dx.doi.org/10.1016/j.ijid.2017.01.033
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modifying variable, detrimentally influencing the association between recent TB exposure and reactivation. Ironically, those who travel abroad are likely the wealthier who can afford to migrate, suggesting they would be less likely to develop TB if they had stayed in their home country. In addition to the recommendations cited by Fox et al. for recently arrived migrants to be given preventive therapy, we would suggest a public health approach that considers and intervenes to mitigate the adverse environmental and social exposures associated with reactivation in recent migrants, which would have positive run-on effects for other health conditions.

Reactivation of TB is socio-political. Thus it follows that mass treatment of LTBI is not just clinical, but manifestly political. Treating LTBI in anticipation of the future likelihood of developing the disease in the absence of comorbidities such as type II diabetes or HIV infection offloads socio-structural issues as biomedical problems. If we were to address the social conditions that foster TB reactivation then there would be little need to mass-produce and distribute community-wide preventive therapy. The cascade of care described by Fox et al. addresses the individual-level factors. In complement, more holistic, largely political interventions are required (Figure 1) to prevent TB reactivation of these population groups who are not inherently vulnerable but are chronically exposed to adverse conditions that place them in an at-risk category.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Levels of biopsychosocial and political therapies required for LTBI management. By focusing solely on the pharmacological treatment of LTBI, healthcare workers who treat TB are inadvertently accepting as given the conditions that foster reactivation, conditions that no clinician with an interest in global health should accept. Clinicians and and scientists have a strong role to play as advocates and in the writing of socio-political prescriptions that are required to dramatically reduce the incidence of TB globally.}
\end{figure}

**Conflict of interest/funding**

None.

**References**

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Received 9 January 2017