A false economy: we cannot afford to be complacent when it comes to tuberculosis control

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During the 19th century a staggering one in four people died from tuberculosis. Incidence steadily declined with socioeconomic improvements and medical advances such that by the 1980s tuberculosis was considered a disease of the past and control measures were relaxed. This approach was premature: rising incidence led WHO to declare tuberculosis a global emergency in 1993. Control efforts were re-intensified and although incidence has now peaked, world population growth means that absolute numbers remain stable. The costs involved are substantial, with an estimated US$6·9 billion spent on global tuberculosis control in 2017,[1] yet the effectiveness of available interventions across different populations remains poorly understood.

In their study published in *The Lancet Public Health*, Kianoush Dehghani and colleagues[2] analysed factors affecting incidence of tuberculosis in six Indigenous populations in the USA, Canada, and Greenland with exceptionally high incidence of tuberculosis and social deprivation. Tuberculosis incidence fell substantially in all groups from 1960 to 1980, when anti-tuberculosis interventions were discontinued across the region. Incidence then continued to decrease in three (non-recrudescent) populations but substantially increased in the other three (recrudescent) populations. The data impart two important lessons. First, recrudescence was associated with discontinuation of anti-tuberculosis interventions, demonstrating the effectiveness of these interventions. Second, the fact that half the populations studied had recrudescence and half did not implies a fundamental difference between the two groups.

The effective interventions were bacillus Calmette-Guérin (BCG) vaccination of infants and testing and treatment for latent tuberculosis infection (LTBI), but not chest radiographic screening for active disease. Despite variable efficacy in clinical trials,[3,4] a meta-analysis has shown BCG vaccination to be cost-effective, particularly in high-incidence settings.[5] In areas where tuberculosis incidence is declining the International Union Against Tuberculosis and Lung Disease (IUATLD) recommends that BCG vaccination could be discontinued if the average annual smear-positive pulmonary tuberculosis notification rate falls below five per 100 000 population, average annual tuberculosis meningitis notification in children younger than 5 years has been below one per 10 million population for 5 years, or the average annual risk of infection is lower than 0·1%.[6] Dehghani and colleagues found that discontinuation occurred when tuberculosis incidence was "perceived to be low", yet notification rates remained above the recommended threshold in all groups.

The effectiveness of LTBI testing and treatment in this study contrasts with the absence of effect shown in a large-scale trial done in gold mines in South Africa.[7] In their cluster-randomised trial, Churchyard and colleagues randomly assigned miners to receive an intervention (tuberculosis screening followed by either treatment of active cases or 9 months of isoniazid preventive therapy) or control (no intervention). Although tuberculosis incidence fell by 58% among the intervention group during the 9-month treatment period, no overall benefit was observed. The risk of reinfection resulting from exceptionally high occupational and household exposure, compounded by low population coverage due to high default rates, might have entirely negated any effect of the intervention. Mathematical models have shown that isoniazid preventative therapy has the greatest effect in intermediate-incidence settings, becoming less effective in higher-incidence settings where robust measures to interrupt tuberculosis transmission and treat patients with active disease become increasingly necessary.[8]

The persisting effect of the interventions in some populations but not others deserves further scrutiny. In the present study,[2] tuberculosis incidence initially fell substantially in all groups. However, the initial incidence was much greater in recrudescent groups than in non-recrudescent groups (mean 536 cases per 100 000 *vs* 310 cases per 100 000 population, 1960–79), and remained higher even after this initial improvement (mean 90 cases per 100 000 *vs* 62 cases per 100 000 population, 1980–99). Increased deprivation among the recrudescent populations might also have rendered them more vulnerable to resurgence after the interventions were stopped. The rising infant mortality and suicide rates in recrudescent populations indicate

societal stress, suggesting that confounding factors might account for both increasing social marginalisation and rising incidence of tuberculosis. Tuberculosis and poverty are inextricably linked and regional inequalities must be addressed if tuberculosis control is to be achieved.

The findings of this study are applicable to other high-burden populations. However, caution is needed where population characteristics differ. In particular, adequate measures to detect and treat drug-resistant tuberculosis are important when considering population-wide isoniazid administration, since inappropriate use of isoniazid monotherapy could exacerbate resistance. Reassuringly, although a theoretical risk of selective pressure for resistance has been proposed,[9] drug-resistant strains did not emerge despite the large numbers of patients treated.

Policy decisions are rarely based on scientific data alone but are influenced by factors including availability of resources and political will, particularly where evidence is weak. The relative contributions of socioeconomic improvements versus specific interventions to reductions in global tuberculosis incidence are poorly defined. This study shows that interventions can be effective, and that premature discontinuation could lead to resurgence of tuberculosis in vulnerable populations. It also highlights the importance of addressing socioeconomic deprivation and inequality in tuberculosis control efforts. Experience teaches us that we cannot afford to be complacent when it comes to tuberculosis control, and that a cautious approach could be beneficial in the long term.

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