



“Post tuberculosis”: the urgent need for inclusion of lung health outcomes in tuberculosis treatment trials

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To the Editor:

We read with interest the systematic review by IVANOVA *et al.* [1], recently published in the *European Respiratory Review*, highlighting significant long-term lung function impairment experienced by people that survive tuberculosis (TB). Lung function impairment is a well-described characteristic of post-TB lung disease (PTLD), a condition that spans the spectrum of obstructive airway disease, bronchiectasis and fibro-cavitating disease, along with fungal and other respiratory infections [2]. The pathophysiology of PTLT will also be described in detail in the *ERS Monograph* entitled “The Challenge of Tuberculosis in the 21st Century”.

Despite a surge in research interest in PTLT and recently published clinical standards for its management [3], this condition remains largely neglected at a programmatic level, especially in high TB burden countries. TB treatment traditionally assesses outcomes on a set of standardised microbiological parameters, entirely disconnected from a person’s health and wellbeing. In most programmes, TB treatment completion compels exit from care facilities, regardless of residual lung damage, which was estimated by IVANOVA *et al.* [1] to be severe in at least 10–15% of survivors. With an estimated 155 million TB survivors alive in 2020, or 1 in 50 people globally, the burden of post-TB morbidity is potentially enormous [4]. Effective TB treatment remains one of our most important tools in preserving long-term lung health.

Clinical TB trials represent an opportunity to advance the study of post-TB outcomes. Most TB treatment trials, including three published in the past 2 years, have longitudinal follow-up of participants for 6–24 months after treatment completion, combined with clinical resources exceeding those in routine care [5–7]. TB trials should perform longitudinal evaluations described in the recent standards [3] to assess clinical status, quality of life, and lung function in participants. Unfortunately, however, the study designs and microbiologically focused end-points in TB treatment trials to date preclude any direct comparison of lung health outcomes. The absence of such important and clinically relevant end-points would be almost incomprehensible in treatment trials for other disease entities, and leaves TB clinicians and policy-makers entirely uninformed on these outcomes.

Clinical trials could, and should, examine the impact of novel regimens on a broad set of physiological and clinical outcomes, in order to weigh the risk/benefit decisions needed to optimise health outcomes. If shorter, simplified regimens result in similar microbiological success, but worsened pulmonary function, there are important considerations for policy, clinical practice, patient consent and health system planning. Alternatively, if novel regimens result in improved lung health outcomes, they could have a major beneficial impact on both individual and population health. These issues are most pronounced in people with drug-resistant TB, where treatment is often associated with pronounced declines in lung health and quality of life [8]. Although shorter regimens have enormous advantages to patients and health systems, there is no evidence to support differences in post-treatment quality of life or pulmonary function outcomes for participants.

PTLT remains under-diagnosed and under-treated, despite TB annually affecting nearly 11 million children, adolescents and adults worldwide [9]. The 2nd International Post TB Symposium in Stellenbosch, South Africa, which took place 17–19 April 2023 and was attended by expert clinicians,



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New TB treatment regimens are a welcome advancement. However, for the millions of TB survivors with impaired lung function and quality of life, more holistic outcome measures and the inclusion of lung function is essential in future TB treatment trials. <https://bit.ly/3PWT0o2>

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researchers, funders, survivors and policy-makers from over 30 countries, called for greater awareness, advocacy, research and action for this important chronic health condition [10]. The integration of diagnosis and management of the “acute infectious” stage of TB disease with the “post-acute” chronic disease would be consistent with a person-centred approach to TB care endorsed by the World Health Organization. This approach is not only desirable, but crucial in reducing TB-associated chronic disability and the associated catastrophic economic costs, and is endorsed by the EndTB Strategy.

On behalf of the Global Steering Committee of the 2nd International Post TB Symposium, we urge researchers, funders and other stakeholders to include more holistic measurements of health and wellbeing in future TB treatment trials, including, as a minimum, lung function testing and quality of life assessments. We also encourage policy-makers to consider the integration of both acute and chronic care for TB survivors to optimise long-term health long after TB treatment regimens are complete.

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