## Launch of the IJTLD Clinical Standards for Lung Health

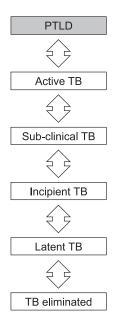
This issue of the *IJTLD* presents the first in a series of Clinical Standards for Lung Health, with a focus on specific clinical standards for the assessment, management and rehabilitation of post-TB lung disease.<sup>1</sup> Future articles in the series will include clinical standards for pulmonary TB, management of adverse events of anti-TB drugs and management of latent TB infection. With support from the Oskar-Helene-Heim Foundation (OHH; Berlin, Germany), the first four of these articles will be made Open Access and freely available to the global community. The first two articles will also be the subject of a presentation at the Union's World Conference on Lung Health in October 2021. The IJTLD Clinical Standards for Lung Health aim to guide clinicians and health care workers with concise recommendations and succinct summaries. Furthermore, they will support decision making and encourage the addition of new strategies in TB programmes with a consensus of experts, where confirmed evidence is still limited. They are intended to complement national and international guidelines, not replace these.

## TIME TO INCLUDE POST-TB LUNG DISEASE IN THE TB SPECTRUM

In the pre-antibiotic era, only approximately one third of patients survived even after treatment for TB in sanatoria.<sup>2</sup> Mortality statistics have shown that half of the patients still alive 5 years after TB diagnosis died within the next 5-year period.<sup>3</sup> The need to follow-up on TB survivors was discussed as an important medical issue, and some sanatoria had an after-care committee to council patients about how to reintegrate into society according to their capabilities. Recommendations were made to improve living conditions and nutrition to avoid relapse.<sup>4</sup> After the introduction of an effective drug treatment, leading to 'cure' in most TB cases, medical attention shifted away from these important aspects of follow-up. Nevertheless, how much 'cure' can we expect after adequate drug treatment even today? Because most treatment outcome definitions do not include post-treatment surveillance or sequelae,5 data on long-term outcomes in programmatic settings are limited to retrospective analyses of health administrative data, such as TB registries.6 A recent proposal for the new WHO outcome definitions includes the documentation of sustained treatment success.7 However, this posttreatment follow-up is only recommended for operational research settings, as long-term surveillance by most healthcare systems is challenging.<sup>8</sup> Nevertheless, a recent symposium has helped to draw attention to the field and provided a better understanding of post-TB lung disease (PTLD).<sup>9</sup>

To develop these clinical standards for PTLD, a panel of 62 global experts with a relevant interdisciplinary background were assembled, and using a Delphi process, they achieved consensus on six recommendations. Especially in an area such as PTLD, where evidence is too weak to make strong recommendations, consensus is needed to accelerate the application of existing knowledge. Careful monitoring and evaluation will be necessary to answer open questions and contribute to the growing literature. Research priorities were listed, and the authors also acknowledge that updates to these standards for PTLD will occur when evidence is growing or changing. The clinical standards for PTLD start with a guide to patient care after drug treatment. There are still no guidelines covering this vulnerable period, but we have enough evidence to suggest that, in many cases, the disease is not 'cured' with the last tablet swallowed. It was estimated in a modelling study that 155 million people were alive in 2020 with a former TB diagnosis. 10 The COVID-19 pandemic has resulted in delays for TB diagnosis and treatment, thus aggravating the severity of TB cases, with unknown impact on treatment outcomes and PTLD.<sup>11,12</sup> More data about PTLD in countries with different healthcare resources and different TB prevalence will be necessary to get a clearer picture.

A considerable number of TB survivors suffer from residual symptoms, making it difficult to manage everyday life and work activities.<sup>13</sup> A variety of psychosocial problems can affect their quality of life after treatment, 9,14 and long-term mortality in this population seems to be higher than in the general population.<sup>15–17</sup> Diverse patterns of lung damage can be found with or without symptoms. This heterogeneity makes it difficult to correctly diagnose a case of PTLD and measure outcomes.8 Measurement of lung functional parameters alone is insufficient to assess the need for rehabilitation. 18 The lessons learnt from long- and post-Covid research have to be adapted for PTLD.<sup>19,20</sup> Symptom scores and validated questionnaires can help to screen for respiratory symptoms and frequent comorbidities such as depression. A validated questionnaire, specific for PTLD is not available, but would be helpful to complement the



**Figure** PTLD added to TB categories, as described by Drain et al.<sup>23</sup> PTLD = post-TB lung disease.

diagnostics suggested in Clinical Standard 1.1 Only with the help of former TB patients and advocacy groups will it be possible to develop patient-centred TB diagnostic, rehabilitation and support programmes addressing PTLD (as recommended in Clinical Standards 2 and 3).<sup>1,21</sup> In low- and middleincome countries, where basic care for lung disease is insufficient,<sup>22</sup> it will be a challenge to establish a rehabilitation programme for TB survivors. The political and financial support for PTLD will have to compete with case-finding and treatment programmes for TB or other diseases of public health importance. Data on cost effectiveness will have to provide proof of benefit to convince decision makers in different settings. Nevertheless, it is likely that we will continue to acquire evidence that TB 'cure' still means suffering for many TB survivors, and it will be increasingly difficult to think about patient-centred TB care without including the post-treatment period (see Figure).<sup>23</sup>

There is an urgent need to integrate PTLD into TB guidelines, but evidence-based recommendations will be difficult in the near future due to the limited data. These *IJTLD* Clinical Standards for PTLD are a necessary step in paving the way for more global activities towards awareness, funding and research in this neglected field. In line with the WHO End TB Strategy,<sup>24</sup> intensified research and innovation (Pillar 3) should lead to an integrated, patient-centred TB care (Pillar 1) and include all TB survivors on the spectrum of TB (Figure).

R. Otto-Knapp B. Häcker T. T. Bauer The German Central Committee against Tuberculosis (DZK), Berlin, Germany.

Correspondence to: Ralf Otto-Knapp, Deutsches Zentralkomitee zur Bekämpfung der Tuberkulose, Walterhöferstr. 11, Haus Q, 14165 Berlin. e-mail: info@dzk-tuberkulose.de

## References

- 1 Migliori GB, et al. Clinical standards for the assessment, management, and rehabilitation of post-TB lung disease. Int J Tuberc Lung Dis 2021; 25: 797–813.
- 2 Crane BT. Is after-care of tuberculosis a medical problem? Trans Am Clin Climatol Assoc 1933; 49: 54–269.
- 3 Thompson BC. Survival rates in pulmonary tuberculosis. Br Med J 1943; 2(4326): 721.
- 4 Knight FI. Importance of supervision of patients leaving sanatoria apparently cured of tuberculosis. Trans Am Climatol Assoc 1907; 23: 180–182.
- 5 Günther G. et al. Defining outcomes of tuberculosis (treatment): from the past to the future. Respiration 2021; 1–10.
- 6 Basham CA. Post-TB outcome science: a sub-discipline for TB survivorship studies? Int J Tuberc Lung Dis 2021; 25(6): 498–501
- 7 World Health Organization. Meeting report of the WHO expert consultation on the definition of extensively drug-resistant tuberculosis, 27–29 October 2020. Geneva, Switzerland: WHO, 2021.
- 8 Avaliani Z, et al. What is behind programmatic treatment outcome definitions for tuberculosis? Eur Respir J 2020; 56(1): 2001751.
- 9 Allwood BW, et al. Post-tuberculosis lung health: perspectives from the First International Symposium. Int J Tuberc Lung Dis 2020; 24(8): 820–828.
- 10 Dodd PJ, et al. Quantifying the global number of tuberculosis survivors: a modelling study. Lancet Infect Dis 2021; 21(7): 984–992.
- 11 McQuaid CF, et al. The impact of COVID-19 on TB: a review of the data. Int J Tuberc Lung Dis 2021; 25(6): 436–446.
- 12 Di Gennaro F, et al. Increase in tuberculosis diagnostic delay during first wave of the COVID-19 pandemic: data from an Italian infectious disease referral hospital. Antibiotics (Basel) 2021; 10(3):272.
- 13 Muñoz-Torrico M, et al. Functional impact of sequelae in drugsusceptible and multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2020; 24(7): 700–705.
- 14 Datta S, Evans CA. Healthy survival after tuberculosis. Lancet Infect Dis 2019; 19(10): 1045–1047.
- 15 Ranzani OT, et al. Long-term survival and cause-specific mortality of patients newly diagnosed with tuberculosis in São Paulo state, Brazil, 2010–15: a population-based, longitudinal study. Lancet Infect Dis 2020; 20(1): 123–132.
- 16 Romanowski K, et al. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. Lancet Infect Dis 2019; 19(10): 1129–1137.
- 17 Basham CA, et al. Cardiovascular morbidity and mortality among persons diagnosed with tuberculosis: a systematic review and meta-analysis. PLoS One 2020; 15(7): e0235821.
- 18 Allwood BW, et al. Persistent chronic respiratory symptoms despite TB cure is poorly correlated with lung function. Int J Tuberc Lung Dis 2021; 25(4): 262–270.
- 19 Spruit MA, et al. COVID-19: interim guidance on rehabilitation in the hospital and post-hospital phase from a European Respiratory Society and American Thoracic Society-coordinated International Task Force. Eur Respir J 2020; 56(6):2002197.
- 20 Koczulla A, et al. AWMF S1-guideline Post-COVID/Long-COVID. https://www.awmf.org/leitlinien/detail/ll/020-027.html. (Accessed August 2021).

- 21 Schoeman I, Sifumba Z. Tuberculosis care does not end at treatment completion- a perspective from tuberculosis survivors. Lancet Infect Dis 2021: 21(7): 896–897.
- 22 Günther G, and Ithete S. Clinical care for patients with post-TB lung disease. Int J Tuberc Lung Dis 2021; 25(3): 252–253.
- 23 Drain PK, et al. Incipient and subclinical tuberculosis: a clinical review of early stages and progression of infection. Clin Microbiol Rev 2018; 31(4): e00021-18.
- 24 World Health Organization. Global tuberculosis report, 2020. Geneva, Switzerland: WHO, 2020.