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*Published in:*  
International Journal of Tuberculosis and Lung Disease

*DOI:*  
[10.5588/ijtld.20.0591](https://doi.org/10.5588/ijtld.20.0591)

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*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2020

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*  
Akkerman, O. W., & Tiberi, S. (2020). The importance of knowing why TB patients stop anti-TB treatment. *International Journal of Tuberculosis and Lung Disease*, 24(10), 989-990.  
<https://doi.org/10.5588/ijtld.20.0591>

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## The importance of knowing why TB patients stop anti-TB treatment

IN MAY 2014, THE WHO LAUNCHED its End TB Strategy with the ultimate goal of a world free of TB. The WHO aimed to reach a target of 90% reduction in incidence and absolute numbers by 2035, leading to a global incidence of <10 per 100 000 population.<sup>1</sup> To reach this target several milestones, need to be achieved. The first milestone is set for 2020, with a reduction of 20%, leading to an incidence of <85/100 000. However, in 2018 the cumulative reduction in global incidence was only 6.3%.<sup>2</sup> Therefore, even without taking into account the impact of COVID-19, it is easy to conclude that massive efforts are required to reach these goals.

In their strategy, the WHO mentioned key actions or pillars to reach the goals. Part of Pillar one is treatment of all people with TB, including drug-resistant TB (DR-TB), and patient support. In the 2019 WHO report, the global treatment success rates improved from 82% to 85%. This success was mostly due to a reduction in the absolute numbers of cases lost to follow up (LTFU) in India's private sector. Among DR-TB cases, 15% of the multidrug-resistant TB (MDR-TB) patients and 18% of the extensively drug-resistant TB patients were LTFU in 2018. It is safe to conclude that the LTFU group makes a significant contribution to reducing success rates.

Therefore, the paper by Kim et al. in this issue of the *Journal* is relevant and timely.<sup>3</sup> The study describes the reasons for LTFU in 94,872 patients treated in public-private mix (PPM) hospitals in South Korea, where 2957 or 3.1% were LTFU. Out of the surveyed and selected LTFU patients, three major groups emerged based on the reason for abandoning treatment. The largest (387/780) consisted of those who were LTFU due to the adverse effects of anti-TB medication. Those who refused treatment constituted the second largest LTFU group; this was the result of a lack of knowledge or lack of microbiologically confirmed diagnosis. The third group comprised the marginalised, where homelessness, alcoholism and social deprivation were major causative factors.

Kim et al. reports that one third of the LTFU group was over 65 years of age and linked with adverse events, whereas the younger LTFU patients were more likely to have treatment experience and/or prior negative outcomes.<sup>3</sup> A large global study on adverse events in the treatment of MDR-TB showed that 75%

of the patients experiencing side effects had a median age below 53.<sup>4</sup> This indicates that education about TB treatment and prevention of side effects needs to be prioritised, and measures for their management implemented. Individualised treatment using therapeutic drug monitoring (TDM) can help in certain situations.<sup>5</sup> TDM can be used to optimise the therapeutic range, increasing the efficacy of some drugs, but also lower side effects by lowering the dose while maintaining efficacy.<sup>6</sup> A recent report showed no severe adverse events in a selected population when the linezolid dose was lowered below 300 mg daily, whereas linezolid is often associated with side effects.<sup>7</sup>

Reducing LTFU rates need much more work, regardless of which patients are treated. As mentioned by the WHO in their End TB Strategy, patient-centred care that addresses the psychosocial and socio-economic needs of individuals are urgently needed.<sup>8</sup> A less paternalistic approach is appreciated by patients and can help understanding of the disease and perhaps, encourage discussions about possible adverse effects at an earlier stage of treatment.<sup>9</sup> Furthermore, new options for monitoring treatment adherence that take into account patients' self-esteem need to be explored. The recent introduction of video-observed therapy can be of help for both treatment adherence and the identification of side effects.<sup>10</sup>

Overall, PPM in South Korea has improved outcomes; Kim et al. highlight where more effort is required to reduce LTFU.<sup>3</sup> In particular, we need to prevent side effects as much as possible, and encourage the development of an equal partnership between patients and health care workers, so that optimal outcomes can be achieved.

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*Conflicts of interest:* none declared.

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