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Therapeutic drug monitoring and fluoroquinolones for multidrug-resistant tuberculosis

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Fluoroquinolones at currently prescribed standard dose are suboptimal for treatment of multidrug-resistant tuberculosis. The dose should be increased with therapeutic drug monitoring to determine the drug exposure and to prevent adverse events. https://bit.ly/3nMip2Z

Cite this article as: Srivastava S, Gumbo T. Therapeutic drug monitoring and fluoroquinolones for multidrug-resistant tuberculosis. *Eur Respir J* 2021; 57: 2004454 [https://doi.org/10.1183/13993003.04454-2020].

To the Editor:

We read the paper by Davies Forsman *et al.* [1] and could not agree more with their findings. The authors report that in the studied geographical area and clinical population, the dose of levofloxacin and moxifloxacin should be increased to achieve the optimal exposure target in order to effectively treat multidrug-resistant tuberculosis, and suggested therapeutic drug monitoring (TDM) to avert any adverse event [1, 2]. The target drug exposure and dose in the study were selected based on the evidence collected using pharmacokinetic/pharmacodynamic studies in both pre-clinical models and in the clinic [3]. Indeed, pre-clinical studies using the *in vitro* hollow fibre system model of tuberculosis (HFS-TB) in tandem with Monte Carlo clinical trial simulations, as well as machine-learning-based analyses of clinical data, have identified that moxifloxacin 800 mg per day could achieve the 24 h area under the concentration–time curve (AUC_{0-24}) to minimum inhibitory concentration (MIC) ratio of 53, and levofloxacin 1500 mg per day for pulmonary tuberculosis and 25 $mg \cdot kg^{-1}$ per day for meningeal tuberculosis to achieve the target AUC_{0-24}/MIC of either 146 (HFS-TB) or 160 (clinical data-based) [4–8]. Therefore, the high dose could be effective against isolates with a broader MIC range of these drugs. While these fluoroquinolones are used to treat multidrug-resistant tuberculosis, there are clinical studies exploring the probability of tuberculosis treatment-shortening regimens [9] in patients with drug-susceptible tuberculosis.