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Dose optimisation of first-line tuberculosis drugs using therapeutic drug monitoring in saliva: feasible for rifampicin, not for isoniazid

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To the Editor:

The persisting worldwide burden of tuberculosis (TB) is worrisome. In 2018, an estimated 10 million individuals developed TB and 1.45 million infected individuals died [1]. The increase in drug resistance is an important point of concern. Resistance can be acquired by inappropriate drug management, noncompliance and insufficient drug exposure [2, 3]. The last is frequently described for the first-line TB drugs rifampicin and isoniazid due to large interindividual pharmacokinetic variability [3]. Therapeutic drug monitoring (TDM) can be used to verify drug exposure and adjust individual drug dosages if needed [4]. The efficacy of rifampicin and isoniazid is associated with the ratio of the steady-state area under the concentration–time curve from 0 to 24 h (AUC_{0-24}) to minimal inhibitory concentration with a target value of >271 for rifampicin and >567 for isoniazid [5, 6]. Traditional TDM uses plasma or serum samples, whereas other matrices such as dried blood spot and saliva have been recommended as alternatives suitable for programmatic use [4, 7]. Collecting saliva samples is noninvasive and simple with the perspective of home-based self-sampling [8]. Salivary concentrations of rifampicin and isoniazid have been studied before, but highly variable saliva/serum concentration ratios across studies were observed [8]. Moreover, none of these studies assessed the feasibility of TDM using saliva samples.