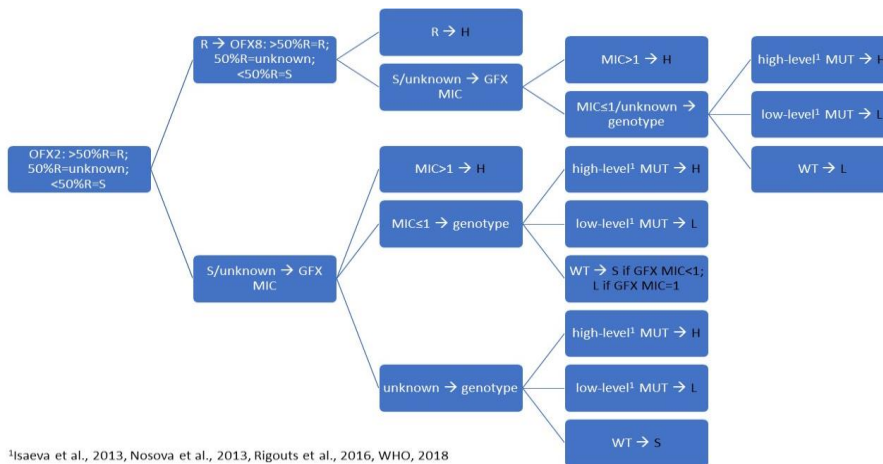


Supplementary Table 1. Classification of drug resistance (level) per drug. R=resistant; S=susceptible; MIC=minimum inhibitory concentration; WT=wild type

Drug	Resistance classification
Fluoroquinolones	See flowchart below.
Clofazimine	Isolates with a clofazimine resistance-associated variant reported by TBProfiler (based on the literature-based TBProfiler library database) were considered resistant, those without were considered susceptible.
Ethambutol	Isolates with an ethambutol resistance-associated variant reported by TBProfiler (based on the literature-based TBProfiler library database) were considered resistant, those without were considered susceptible.
Prothionamide	Isolates with an ethionamide resistance-associated variant reported by TBProfiler (based on the literature-based TBProfiler library database) were considered resistant, those without were considered susceptible. Isolates with an <i>inhA</i> or <i>fabG1</i> variant reported by TBProfiler for isoniazid but not for ethionamide were considered resistant to ethionamide as well.
Isoniazid phenotypic	susceptible: susceptible at 0.2 mg/L - low-level resistant: resistant at 0.2 mg/L but susceptible at 1.0 mg/L or MIC \leq 1.6 mg/L - moderate-level resistant: resistant at 1.0 mg/L but susceptible at 5.0 mg/L or $3.2 \leq$ MIC \leq 6.4 mg/L - high-level resistant: resistant at 5.0 mg/L, or MIC \geq 12.8 mg/L
Isoniazid genotypic	susceptible: no isoniazid resistance-associated variant reported by TBProfiler (based on the literature-based TBProfiler library database) - low-level resistant: <i>inhA</i> or <i>fabG1</i> mutation alone - moderate-level resistant: <i>katG</i> mutation alone; or <i>inhA</i> and <i>fabG1</i> mutation - high-level resistant: <i>katG</i> and <i>inhA</i> mutation; or <i>katG</i> and <i>fabG1</i> mutation; or two <i>katG</i> mutations; or <i>katG</i> insertion, deletion, or introduction of a termination codon
Isoniazid composite	Isoniazid phenotypic and genotypic resistance levels as described above were combined. In case of discordance between phenotypic and genotypic level, the highest level was taken as final.
Kanamycin	Isolates resistant at 6.0 mg/L and/or having a kanamycin resistance-associated variant reported by TBProfiler (based on the literature-based TBProfiler library database) were considered resistant, all others susceptible.
Pyrazinamide	Isolates with a pyrazinamide resistance-associated variant reported by TBProfiler (based on the literature-based TBProfiler library database) were considered resistant, those without were considered susceptible.



¹Isaeva et al., 2013, Nosova et al., 2013, Rigouts et al., 2016, WHO, 2018

Supplementary Figure 1. Flowchart showing classification of fluoroquinolone drug susceptibility test (DST) results into susceptible (S), low-level resistant (L), and high-level resistant (H). For ofloxacin DST, all DST results of a patient were considered. An isolate was considered resistant if >50% of tests from the same patient was R, and susceptible if >50% was S. When the number of resistant tests was equal to the number of susceptible tests, no conclusion was drawn (unknown). OFX=ofloxacin; GFX=gatifloxacin; R=resistant; S=susceptible; MIC=minimum inhibitory concentration; WT=wildtype; MUT=mutant

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