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Introduction of new drugs for drug-resistant TB in Iraq

Dear Editor,

We read with interest the recent correspondence by Van Deun et al. discouraging the use of all-oral, rifampicin-resistant TB regimens before robust evidence on their safety and efficacy is available.[1] We would like to share the example of Iraq, an Eastern Mediterranean Region country with estimated drug-resistant TB (DR-TB) incidence of 2.9/100,000 population in 2019,[2] which has suffered from decades of conflict, sanctions and civic unrest, which has disrupted its healthcare services, including TB care.[3] In 2020, the Iraqi National Tuberculosis Programme (NTP), with the support of Medecins Sans Frontieres (MSF), introduced an all-oral, long DR-TB treatment regimen based on the new TB drug, bedaquiline (BDQ).[4] This made Iraq one of the first Middle Eastern countries to provide access to better and safer DR-TB treatment. Until recently, DR-TB treatment guidelines in Iraq recommended the older 18–24-month long regimen comprising 6–8 months of injections.[5] Loss to follow-up was at 20%, and irreversible hearing loss due to injectables and challenges in adverse events monitoring were common. In addition, DR-TB regimen design and treatment initiation were centralised in the capital, Baghdad (the main TB hotspot in the country), contributing to delayed treatment initiation, and increased morbidity and transmission. This was exacerbated by common security issues,[6] and the lockdown due to the current COVID-19 pandemic.

In Baghdad, MSF has collaborated with the NTP since 2018 to provide care to DR-TB patients and help improve overall DR-TB programmatic management through 1) laboratory support to increase access to diagnostics methods such as Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) and line-probe assays; 2) technical support to healthcare workers for DR-TB regimen design, management and monitoring; 3) patient and community support by raising awareness, fighting stigma and patient empowerment; and 4) introduction/provision of new drugs, and other repurposed oral regimens, previously unavailable in the country.

In 2020, the Iraqi NTP was able to implement a paradigm shift in changing the DR-TB treatment with the introduction of BDQ as part of an all-oral, long regimen for newly and previously diagnosed and treated patients with complex resistance profiles (Figure).[7] Furthermore, the NTP expanded this access to highly vulnerable groups, including children, pregnant women and patients with comorbidities. With the support of MSF, the NTP enrolled 90 DR-TB patients between 1 January and 30 November 2020, of whom 43 (48%) were placed on the recommended WHO long all-oral regimen. Of the 43, respectively 77% ($n = 33$) and 14% ($n = 6$) received a BDQ-based or a delamanid-based regimen; 12% ($n = 5$) received a combination of BDQ and delamanid. Moving from an injectable-based to an all-oral DR-TB regimen is a huge achievement for the

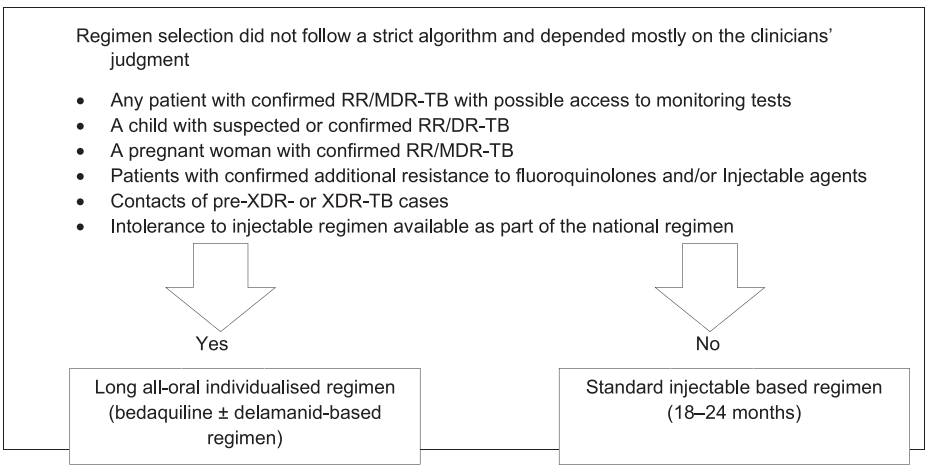

Figure Patient selection criteria supporting the all-oral vs. standard injectable regimen, Iraq, 2020. Adapted from the WHO consolidated guidelines on drug-resistant TB treatment, 2019 (file:///D:/Users/MSFuser/Downloads/9789241550529-eng.pdf). RR/MDR-TB = rifampicin-resistant/multidrug-resistant TB; XDR-TB = extensively drug-resistant TB.

NTP.[8,9] Following this, the DR-TB guidelines for Iraq were updated in 2021 to include all-oral regimens with new drugs as part of its standard national recommendations for DR-TB patients, including children and special populations. Next actions for the country will be 1) moving toward oral regimens for all patients, and 2) implementing patient-centred approaches through decentralised models of care with the first decentralised DR-TB treatment initiating centre outside the capital, already designated by the NTP.

The introduction of longer all-oral DR-TB treatment with new drugs – despite the overstretched healthcare system due to the national political unrest and the COVID-19 pandemic – is an achievement for the NTP and the country.[10] Iraq is an example in the region of the feasibility of implementing new treatments despite the challenges caused by conflict and violence. It should serve as a model that neighbouring conflict-affected countries can learn from and replicate to win the fight in ending TB globally.

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Pulmonary TB and chronic pulmonary aspergillosis

Dear Editor,

We are in agreement with Baluku et al.[1] regarding their response to our comments[2] on the importance of ruling out chronic pulmonary aspergillosis (CPA) in cases of persistent cough after treating TB, and the need for further studies on concomitant treatment with azoles and rifampicin-based anti-TB therapy regimen. However, the authors' comments that "resolution of cough is expected with anti-TB treatment" merits further discussion. Respiratory symptoms, most commonly cough and/or breathlessness, may not resolve in up to 40% of cases of pulmonary TB at the end of treatment.[3,4] It is not surprising that studies conducted in TB-endemic areas such as South Africa report a history of TB as one of the strongest predictors of chronic bronchitis, which also manifests as chronic productive cough.[5] Resolution of cough, thus, may be elusive even after successful anti-TB treatment. In case of persistent cough, one needs to keep in mind a long list of possible causes in addition to CPA, including residual parenchymal damage, obstructive lung disease, bronchiectasis, non-TB mycobacterium, etc. As the literature is evolving on post-TB disease, our focus should not only be on treatment completion, but also