More than 550,000 new cases of rifampicin-resistant tuberculosis (RR-TB) or multidrug-resistant TB (MDR-TB), which is RR-TB with additional resistance to isoniazid, emerge each year globally. Bangladesh is one of the world’s high MDR-TB burden countries and, according to the World Health Organization (WHO) Global TB report 2018, the MDR-TB burden is 1.6% among new cases and 29% among retreatment cases. RR- and MDR-TB cannot be treated with the recommended six-month standard course of medication. Patients with MDR-TB are typically treated with more medicines for a much longer period (conventionally 20 months or more). Despite this, many of these regimens are not as effective as standard first-line regimens for drug-susceptible TB.

The longer duration of the MDR-TB treatment regimens and the toxicity of certain agents discourage many patients from completing treatment. In addition, the high cost associated with the regimens poses a significant challenge to health systems. Attempts to reduce the length of treatment and use a more tolerable, more effective, and less expensive combination of medicines have been ongoing for several years. More recently, a fairly standardized treatment regimen (known as Bangladesh regimen) lasting between 9 and 12 months has been reported to give relapse-free cure in more than 85% of selected MDR-TB patients, with adverse reactions typical of those expected with these second-line TB medicines. The regimen recommended by WHO in 2016 has been used more recently in different geographical sites and in the STREAM trial. The regimen contains kanamycin (an injectable agent), moxifloxacin, prothionamide, clofazimine, isoniazid, pyrazinamide and ethambutol given together in an initial phase of 4 months (with the possibility to extend to six months if they remain sputum smear positive at the end of month 4), and followed by 5 months of treatment with four of the medicines (moxifloxacin, clofazimine, pyrazinamide, and ethambutol).
Bangladesh is a pioneer in the use of the shorter treatment regimen (STR) for MDR-TB. With support from the Damien Foundation and in collaboration with the National TB Program (NTP), the STR was introduced in 2005. In 2014, the NTP planned to conduct operational research for wider implementation of the STR, and a protocol was drafted for Bangladesh. However, in May 2016, WHO recommended the STR be implemented at the country level under routine DR-TB programs as more data had become available on its cost effectiveness and improve compliance and cure rates. In response, technical assistance from the USAID-funded Challenge TB (CTB) project was requested to revise and finalize the draft standard operating procedure (SOP) for STR programmatic implementation, incorporating active drug safety monitoring and management (aDSM) and adapting current recording and reporting (R&R) forms to accommodate STR data. This revised SOP enabled the NTP to integrate the STR into national program procedures, which is in line with the recommendations made by the Joint Monitoring Mission in 2016 to have full coverage of the STR and scale up by the end of 2017.

CTB helped finalize the SOP; update existing R&R formats; develop formats for aDSM; and develop the training curriculum, including training materials on the STR. CTB also provided extended support to the NTP for capacity building of clinical experts and health care providers at the National Institute of Diseases of Chest and Hospital (NIDCH) and NTRL (National TB Reference Laboratory) using NTP approved SOP and training materials. The project initiated training in March 2017.

After the initial training and support from CTB, the NTP was able to initiate STR resulting in the enrollment of the first patients in April 2017. CTB provided additional capacity building support to 20 district outpatient DR-TB team, which was completed in September 2017. After completing training and orientation and ensuring the necessary drugs and logistics, the STR was expanded to other regional DR-TB treatment initiation centers in Bangladesh. To date, all five Government hospitals and three Damien Foundation hospitals are implementing the STR. STR data that follow the new R&R format have been collected at the national level by the NTP each quarter. CTB also supported the NTP in intensive central and field-level monitoring and supervision for quality STR implementation.

### ACHIEVEMENTS

Outcome data are not yet available for patients enrolled in the 2017 cohort. However, countrywide enrollment status of patients under the STR versus the standard longer regimen is included. Table 1 shows STR enrollment from April 2017 to December 2018 from all sites in the country.

<table>
<thead>
<tr>
<th>QUARTER</th>
<th>NUMBER OF PATIENTS ENROLLED IN STANDARD TREATMENT REGIMEN</th>
<th>NUMBER OF PATIENTS ENROLLED IN STR</th>
<th>TOTAL DR-TB ENROLLMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apr–Jun 2017</td>
<td>82 (49.4%)</td>
<td>84 (50.6%)</td>
<td>166</td>
</tr>
<tr>
<td>Jul–Sep 2017</td>
<td>90 (45.5%)</td>
<td>108 (54.5%)</td>
<td>198</td>
</tr>
<tr>
<td>Oct–Dec 2017</td>
<td>90 (49.7%)</td>
<td>91 (50.3%)</td>
<td>181</td>
</tr>
<tr>
<td>Jan–Mar 2018</td>
<td>50 (19.5%)</td>
<td>207 (80.5%)</td>
<td>257</td>
</tr>
<tr>
<td>Apr–Jun 2018</td>
<td>44 (15%)</td>
<td>250 (85%)</td>
<td>294</td>
</tr>
<tr>
<td>Jul–Sep 2018</td>
<td>40 (12.2%)</td>
<td>289 (87.8%)</td>
<td>329</td>
</tr>
<tr>
<td>Oct–Dec 2018</td>
<td>54 (20.2%)</td>
<td>213 (79.8%)</td>
<td>267</td>
</tr>
</tbody>
</table>
Acknowledgments

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Authors

This publication was written by Dr. Manzur-ul-Alam, Dr. Mahamudul Hasan Khan, and Dr. Nazis Arefin Saki (NTP) with contributions from Abu Jamil Faisel, Md Mahabub Ul Anwar, and Oscar Cordon.

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WAY FORWARD

According to WHO, a shorter and more cost-effective MDR-TB regimen is likely to increase the number of patients treated and improve treatment adherence. However, patients will need social support to help them overcome the hardships associated with TB and its treatment, including daily adherence, adverse drug reactions, indirect costs, stigma, and discrimination.

Important work remains to make the STR more acceptable to routine DR-TB programs. This includes strengthening laboratory services to expand rapid diagnostics, establish patients centered care under routine programmatic management of DR-TB and incorporation of pharmaco-vigilance within NTP process and guidelines. Cure rates for DR-TB could be further increased by facilitating patient access to an oral regimen of newer, more effective, and less toxic medicines within the STR domain. WHO continues to update recommendations based on new and emerging evidence. More operational and implementation research is needed on new innovations such as injectable-free, shorter MDR-TB treatment regimen.

References