



SHAREABLE PDF

# Standardised shorter regimens *versus* individualised longer regimens for rifampin- or multidrug-resistant tuberculosis

Syed Abidi<sup>1,2</sup>, Jay Achar<sup>3</sup>, Mourtala Mohamed Assao Neino<sup>4</sup>, Didi Bang<sup>5</sup>, Andrea Benedetti<sup>1,2,6</sup>, Sarah Brode<sup>7</sup>, Jonathon R. Campbell<sup>1,2</sup>, Esther C. Casas<sup>8</sup>, Francesca Conradie<sup>9</sup>, Gunta Dravniece<sup>10</sup>, Philipp du Cros<sup>3,11</sup>, Dennis Falzon<sup>12</sup>, Ernesto Jaramillo<sup>12</sup>, Christopher Kuaban<sup>13</sup>, Zhiyi Lan<sup>1,2</sup>, Christoph Lange<sup>14,15,16,17</sup>, Pei Zhi Li<sup>2</sup>, Mavluda Makhmudova<sup>18</sup>, Aung Kya Jai Maug<sup>19</sup>, Dick Menzies<sup>1,2</sup>, Giovanni Battista Migliori<sup>20</sup>, Ann Miller<sup>21</sup>, Bakyt Myrzaliev<sup>22</sup>, Norbert Ndjeka<sup>23</sup>, Jürgen Noeske<sup>24</sup>, Nargiza Parpieva<sup>25</sup>, Alberto Piubello<sup>19,26</sup>, Valérie Schwoebel<sup>26</sup>, Welile Sikhondze<sup>27</sup>, Rupak Singla<sup>28</sup>, Mahamadou Bassirou Souleymane<sup>19</sup>, Arnaud Trébucq<sup>26</sup>, Armand Van Deun<sup>29</sup>, Kerri Viney<sup>30,31,32</sup>, Karin Weyer<sup>12</sup>, Betty Jingxuan Zhang<sup>1,2</sup> and Faiz Ahmad Khan<sup>1,2</sup>

**Affiliations:** <sup>1</sup>McGill International TB Centre, Montreal, QC, Canada. <sup>2</sup>Respiratory Epidemiology and Clinical Research Unit, Centre for Outcomes Research and Evaluation, McGill University and Research Institute of the McGill University Health Centre, Montreal, QC, Canada. <sup>3</sup>Médecins Sans Frontières/Doctors without Borders, London, UK. <sup>4</sup>National Tuberculosis Program, Niamey, Niger. <sup>5</sup>International Reference Laboratory of Mycobacteriology, National Centre for Antimicrobials and Infection Control, Statens Serum Institut, Copenhagen, Denmark. <sup>6</sup>Dept of Epidemiology, Biostatistics and Occupational Health, Faculty of Medicine, McGill University, Montreal, QC, Canada. <sup>7</sup>West Park Healthcare Centre, University Health Network and University of Toronto, Toronto, ON, Canada. <sup>8</sup>Médecins Sans Frontières/Doctors without Borders, Amsterdam, The Netherlands. <sup>9</sup>Dept of Medicine, University of Witwatersrand, Johannesburg, South Africa. <sup>10</sup>KNCV TB Foundation, The Hague, The Netherlands. <sup>11</sup>Burnet Institute, Melbourne, Australia. <sup>12</sup>World Health Organization, Geneva, Switzerland. <sup>13</sup>Faculty of Health Sciences, The University of Bamenda, Bamili, Cameroon. <sup>14</sup>Research Center Borstel, Leibniz Lung Center, Borstel, Germany. <sup>15</sup>German Center for Infection Research Clinical TB Unit, Borstel, Germany. <sup>16</sup>Respiratory Medicine and International Health, University of Lübeck, Lübeck, Germany. <sup>17</sup>Dept of Medicine, Karolinska Institute, Stockholm, Sweden. <sup>18</sup>KNCV Tajikistan, Dushanbe, Tajikistan. <sup>19</sup>Damen Foundation, Brussels, Belgium. <sup>20</sup>WHO Collaborating Centre for Tuberculosis and Lung Diseases, Istituti Clinici Scientifici Maugeri IRCCS, Tradate, Italy. <sup>21</sup>Dept of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA. <sup>22</sup>KNCV TB Foundation, Branch Office KNCV in Kyrgyzstan, Bishkek, Kyrgyzstan. <sup>23</sup>National TB Programme, Republic of South Africa, Pretoria, South Africa. <sup>24</sup>National Tuberculosis Programme, Yaounde, Cameroon. <sup>25</sup>National TB Institute, Tashkent, Uzbekistan. <sup>26</sup>International Union Against Tuberculosis and Lung Disease, Paris, France. <sup>27</sup>National TB Control Program, Eswatini Ministry of Health, Mbabane, Swaziland. <sup>28</sup>National Institute of Tuberculosis and Respiratory Diseases, Delhi, India. <sup>29</sup>Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium. <sup>30</sup>The University of Sydney, Sydney, Australia. <sup>31</sup>Karolinska Institutet, Stockholm, Sweden. <sup>32</sup>Australian National University, Canberra, Australia.

**Correspondence:** Faiz Ahmad Khan, 3D.60, 5252 Boulevard de Maisonneuve Ouest, Montreal, QC H4A 3S5, Canada. E-mail: faiz.ahmadkhan@mcgill.ca



@ERSpublications

**Standardised shorter regimens for RR/MDR-TB had substantially lower risk of loss to follow-up than individualised longer regimens, but also higher risk of failure or relapse if there was resistance to component drugs** <http://bit.ly/2RQgXzq>

**Cite this article as:** Abidi S, Achar J, Assao Neino MM, *et al.* Standardised shorter regimens *versus* individualised longer regimens for rifampin- or multidrug-resistant tuberculosis. *Eur Respir J* 2020; 55: 1901467 [https://doi.org/10.1183/13993003.01467-2019].

This single-page version can be shared freely online.

**ABSTRACT** We sought to compare the effectiveness of two World Health Organization (WHO)-recommended regimens for the treatment of rifampin- or multidrug-resistant (RR/MDR) tuberculosis (TB): a standardised regimen of 9–12 months (the “shorter regimen”) and individualised regimens of  $\geq 20$  months (“longer regimens”).

We collected individual patient data from observational studies identified through systematic reviews and a public call for data. We included patients meeting WHO eligibility criteria for the shorter regimen: not previously treated with second-line drugs, and with fluoroquinolone- and second-line injectable agent-susceptible RR/MDR-TB. We used propensity score matched, mixed effects meta-regression to calculate adjusted odds ratios and adjusted risk differences (aRDs) for failure or relapse, death within 12 months of treatment initiation and loss to follow-up.

We included 2625 out of 3378 (77.7%) individuals from nine studies of shorter regimens and 2717 out of 13 104 (20.7%) individuals from 53 studies of longer regimens. Treatment success was higher with the shorter regimen than with longer regimens (pooled proportions 80.0% *versus* 75.3%), due to less loss to follow-up with the former (aRD  $-0.15$ , 95% CI  $-0.17$ – $-0.12$ ). The risk difference for failure or relapse was slightly higher with the shorter regimen overall (aRD  $0.02$ , 95% CI  $0$ – $0.05$ ) and greater in magnitude with baseline resistance to pyrazinamide (aRD  $0.12$ , 95% CI  $0.07$ – $0.16$ ), prothionamide/ethionamide (aRD  $0.07$ , 95% CI  $-0.01$ – $0.16$ ) or ethambutol (aRD  $0.09$ , 95% CI  $0.04$ – $0.13$ ).

In patients meeting WHO criteria for its use, the standardised shorter regimen was associated with substantially less loss to follow-up during treatment compared with individualised longer regimens and with more failure or relapse in the presence of resistance to component medications. Our findings support the need to improve access to reliable drug susceptibility testing.