

# Standard Short-Course Chemotherapy for Drug-Resistant Tuberculosis

## Treatment Outcomes in 6 Countries

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**T**HE WORLD HEALTH ORGANIZATION (WHO) tuberculosis (TB) control strategy, directly observed treatment short-course (DOTS), consists of 3 components, including the administration of standardized short-course chemotherapy (SCC) regimens with first-line drugs (isoniazid, rifampicin, pyrazinamide, and streptomycin or ethambutol or both) under direct observation, at least in the intensive treatment phase, regardless of patient drug-susceptibility pattern.<sup>1</sup> This strategy, which is considered by the World Bank as one of the most cost-effective interventions in human health,<sup>2</sup> has now been adopted by 119 countries worldwide.<sup>3</sup>

A recent study revealed that TB cases with multidrug-resistance to isoniazid and rifampicin are a major problem in some countries.<sup>4</sup> Patients carrying multidrug-resistant strains of *Mycobacterium tuberculosis* might be at greater risk of experiencing SCC failure and of dis-

**Context** No large-scale study has investigated the impact of multidrug-resistant tuberculosis (TB) on the outcome of standard short-course chemotherapy under routine countrywide TB control program conditions in the World Health Organization's (WHO) directly observed treatment short-course strategy for TB control.

**Objective** To assess the results of treatment with first-line drugs for patients enrolled in the WHO and the International Union Against Tuberculosis and Lung Disease's global project on drug-resistance surveillance.

**Design and Setting** Retrospective cohort study of patients with TB in the Dominican Republic, Hong Kong Special Administrative Region (People's Republic of China), Italy, Ivanovo Oblast (Russian Federation), the Republic of Korea, and Peru.

**Patients** New and retreatment TB cases who received short-course chemotherapy with isoniazid, rifampicin, pyrazinamide, and either ethambutol or streptomycin between 1994 and 1996.

**Main Outcome Measure** Treatment response according to WHO treatment outcome categories (cured; died; completed; defaulted; or failed treatment; or transferred).

**Results** Of the 6402 culture-positive TB cases evaluated, 5526 (86%) were new cases and 876 (14%) were retreatment cases. A total of 1148 (20.8%) new cases and 390 (44.5%) retreatment cases were drug resistant, including 184 and 169 cases of multidrug-resistant TB, respectively. Of the new cases 4585 (83%) were treated successfully, 138 (2%) died, and 151 (3%) experienced short-course chemotherapy failure. Overall, treatment failure (relative risk [RR], 15.4; 95% confidence interval [CI], 10.6-22.4;  $P < .001$ ) and mortality (RR, 3.73; 95% CI, 2.13-6.53;  $P < .001$ ) were higher among new multidrug-resistant TB cases than among new susceptible cases. Even in settings using 100% direct observation, cases with multidrug resistance had a significantly higher failure rate than those who were susceptible (9/94 [10%] vs 8/1410 [0.7%]; RR, 16.9; 95% CI, 6.6-42.7;  $P < .001$ ). Treatment failure was also higher among patients with any rifampicin resistance ( $n = 115$ ) other than multidrug resistance (RR, 5.48; 95% CI, 3.04-9.87;  $P < .001$ ), any isoniazid resistance ( $n = 457$ ) other than multidrug resistance (RR, 3.06; 95% CI, 1.85-5.05;  $P < .001$ ), and among patients with TB resistant to rifampicin only ( $n = 76$ ) (RR, 5.47; 95% CI, 2.68-11.2;  $P < .001$ ). Of the retreatment cases, 497 (57%) were treated successfully, 51 (6%) died, and 124 (14%) failed short-course chemotherapy treatment. Failure rates among retreatment cases were higher in those with multidrug-resistant TB, with any isoniazid resistance other than multidrug resistance, and in cases with TB resistant to isoniazid only.

**Conclusions** These data suggest that standard short-course chemotherapy, based on first-line drugs, is an inadequate treatment for some patients with drug-resistant TB. Although the directly observed treatment short-course strategy is the basis of good TB control, the strategy should be modified in some settings to identify drug-resistant cases sooner, and to make use of second-line drugs in appropriate treatment regimens.

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# Short Course Chemotherapy For Tuberculosis

**Ying-Ying Zheng**



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