suggests ZIKV as the primary flavivirus infection. The limited antibody response in Patient 2 was presumably due to her ongoing immunosuppressive therapy. Although neither patient reported symptoms associated with ZIKV infection during the investigation, these data show evidence for ZIKV transmission by means of platelet transfusion.

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Treatment Outcomes in Multidrug-Resistant Tuberculosis

TO THE EDITOR: Despite lengthy treatment with costly second-line drug regimens, curing multidrug-resistant (MDR) tuberculosis (bacillary resistance to at least isoniazid and rifampin) remains a challenge.[1] The World Health Organization (WHO) defines "cure" as "treatment completion" with at least three negative cultures after the intensive phase of therapy in the absence of "treatment failure." The definition of "treatment failure" requires early termination of treatment or the need for permanent regimen change of at least two antituberculosis drugs. "Treatment success" is defined as the sum of cure and treatment completion.[2]

We evaluated treatment outcomes according to WHO definitions in the TBNET cohort of 380 patients with MDR tuberculosis at 23 European centers, including 89 patients with pre–extensively drug-resistant (XDR) tuberculosis and 33 patients with XDR tuberculosis,[3,4] and compared them with simplified definitions of MDR tuberculosis treatment outcomes (see the Supplementary Appendix, available with the full text of this letter at NEJM.org). Cure was defined as a negative culture status 6 months after treatment initiation, no positive culture thereafter, and no relapses within 1 year after treatment completion. Treatment failure was defined as a positive culture status 6 months after treatment initiation or thereafter or a relapse within 1 year after treatment completion. An undeclared outcome was defined as an outcome that was not assessed (owing to transferral out of the cohort, no culture status at 6 months while the patient was receiving care, or no post-treatment assessment). Death was defined as death during observation. Loss to follow-up was defined as nonreceipt of care 6 months after treatment initiation.

Fifty of 88 patients with treatment failure (57%) were not identified by the WHO definition. Assessment of WHO-defined cure was possible for only 13% of the patients in countries with a low incidence of tuberculosis (with a notification rate <20 per 100,000 population), 58% of the patients in countries with an intermediate incidence (with a notification rate of 20 to 100 per 100,000 population), and 52% of the patients in countries with a high incidence (with a notification rate >100 per 100,000 population), owing to a lack of sputum cultures obtained after the intensive-treatment phase. This could reflect the limited access to health care of mostly foreign-born patients or the inability of patients to produce sputum in the latter stages of therapy.

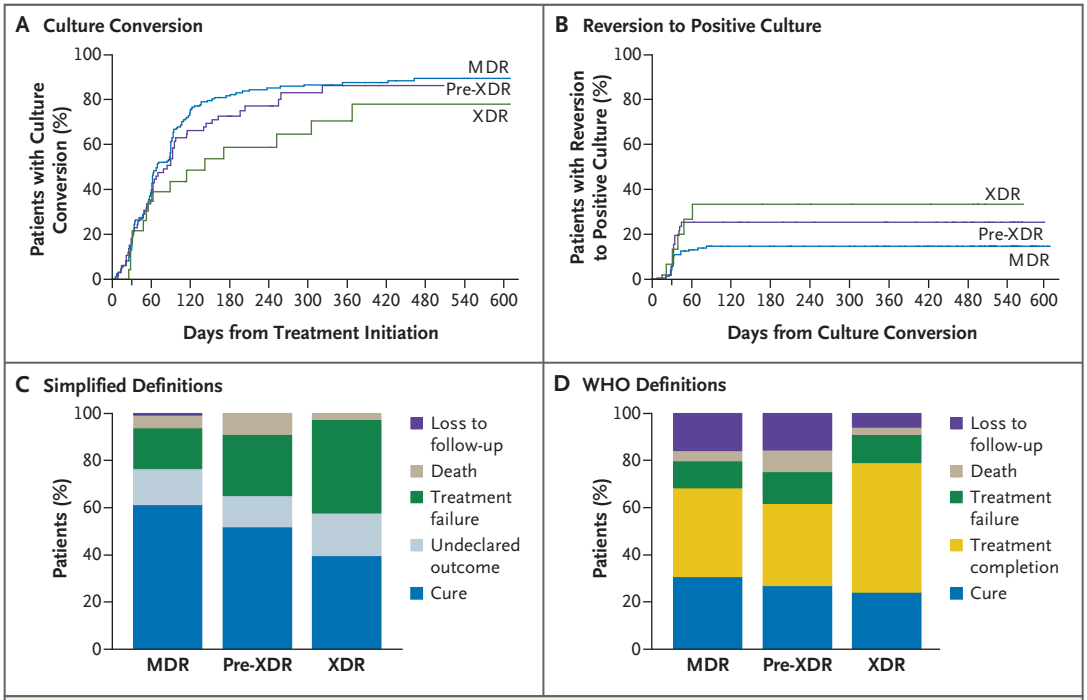

Figure 1. Culture Conversion, Subsequent Reversion, and Outcomes of Tuberculosis Treatment According to Simplified and WHO Definitions.

Panel A shows culture conversion to negative cultures in all patients with a positive culture at the start of second-line treatment for tuberculosis. Panel B shows reversion to positive cultures in patients in whom culture conversion occurred during the study. Panel C shows final outcome according to proposed simplified definitions. Panel D shows final outcome according to World Health Organization (WHO) definitions. Multidrug-resistant (MDR) tuberculosis was defined as bacillary resistance to at least isoniazid and rifampin but excluding pre–extensively drug-resistant (XDR) tuberculosis and XDR tuberculosis. Pre-XDR tuberculosis was defined as bacillary resistance to isoniazid and rifampin and either any fluoroquinolone or any second-line injectable drug. XDR tuberculosis was defined as bacillary resistance to isoniazid and rifampin, any fluoroquinolone, and any second-line injectable drug (amikacin, capreomycin, or kanamycin).

WHO-defined treatment success in MDR tuberculosis is predominantly driven by completing treatment rather than by a biologic end point and fails to address relapse-free survival as a clinically more relevant assessment of treatment efficacy.

Relapse-free cure was achieved in 61% of the patients with MDR tuberculosis, 52% of the patients with pre-XDR tuberculosis, and 39% of the patients with XDR tuberculosis when simplified definitions were used, in contrast to WHO-defined cure in 31%, 27%, and 24% of patients, respectively (Fig. 1).

Of the 318 patients with a negative culture status at 6 months, 35 (11%) reverted in the continuation phase, and 9 (3%) had a post-treatment relapse, findings that suggest that culture status at 6 months may be a reliable predictor of relapse-free cure in patients with MDR tuberculosis.[5]

In conclusion, current WHO definitions may underestimate cure in patients with MDR tuberculosis. These definitions could be simplified while incorporating the assessment of post-treatment relapse.

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