Treatment effectiveness and predictors of poor outcome in MDR-TB and XDR-TB

Extensively drug-resistant (XDR) tuberculosis (TB) has recently emerged as a global health threat especially when combined with HIV. Annually, ~40,000 new cases of XDR-TB occur worldwide. Estonia has one of the highest rates of MDR-TB and XDR-TB.

Methods
All patients with culture-confirmed pulmonary TB who started TB treatment in Estonia from Jan 2003 to Dec 2005 were included in a retrospective case-control study. All cultures were carried out with Löwenstein-Jensen solid media and in BACTEC broth media. Drug susceptibility testing (DST) was performed with rifampicin, isoniazid, streptomycin, ethambutol, pyrazinamide, capreomycin, amikacin, kanamycin, ethionamide and ofloxacin. If resistance was identified to isoniazid or rifampicin, the respective isolate was tested against second-line drugs. Regimens were individually tailored on the basis of DST results and contained at least four oral drugs used daily for the full course of treatment and an injectable drug until the Mycobacterium tuberculosis culture was negative. After culture conversion, the injectable drug was continued three to five times weekly for an additional 2–3 months. Treatment continued for 12–18 months after culture conversion. Treatment outcome was regarded as successful for cases considered cured or completed, while death, default and failure were considered as poor outcome.

Results
Anti-TB treatment outcomes were assessed for 235 MDR-TB patients. The proportion of XDR-TB among MDR-TB patients was 23%. At the start of treatment, 79.1% of all MDR-TB cases had resistance to all first-line anti-TB drugs. MDR- and XDR-TB patients had a median resistance to five and seven drugs, respectively. In cases with MDR-TB successful treatment outcome was 60.4%. There was a significantly higher proportion of successful treatment, lower proportion of treatment failures and lower mortality in patients not previously treated for TB. In XDR-TB cases, successful treatment outcome was 42.6%. In new XDR-TB cases, the proportion of defaults was nonsignificantly higher than in the previously treated cases, but mortality was slightly lower. Compared with MDR-TB patients, those with XDR-TB had higher successful treatment outcome. In MDR-TB cases, HIV infection increased the risk of poor treatment outcome 10-fold and previous TB treatment increased the risk by almost 3-fold. Resistance to ofloxacin and positive AFB smear at the start of the treatment were independent risk factors of poor treatment outcome. XDR-TB cases living in an urban area and cases with positive AFB smear results at the start of treatment were more likely to have a poor treatment outcome.

Editorial comment
Although the highest rates of XDR-TB are in the countries of the former Soviet Union and China, XDR-TB has also emerged in countries where TB control has functioned effectively for many years. It is clear that rapid diagnostic tools to shorten the time to effective treatment initiation for drug-resistant disease and new drugs to meet the challenge of XDR-TB are essential to improve outcomes. Regrettably, a new anti-TB drug has not been licensed in decades. Moxifloxacin and linezolid are promising under some circumstances. Other studies suggest that aggressive treatment and case management may be the best hope for patients with XDR-TB [1]. For the time being there is a fear that having XDR-TB can mean a death sentence to the patient since it is still not clear which approach to treatment might give the best results [2]. And the most troubling question of all, regarding XDR-TB is: are we going back to the time before there were anti-TB drugs at all? [3]. This country-wide study from Estonia provides evidence that to improve treatment outcome in MDR-TB and XDR-TB, special care should be taken to treat HIV-infected patients and urban residents, as well as to make efforts to diminish re-treatment cases [4].

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References

Message
Risk factors for poor treatment outcome in MDR-TB are HIV infection, previous TB treatment, resistance to ofloxacin and positive acid-fast bacilli (AFB) smear at the start of treatment. Predictors of poor treatment outcome in XDR-TB are urban residence and positive AFB smear.

Competing interests
None declared.