53. MDR- and XDR-TB: epidemiological and public health overview

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Time trends in multidrug-resistant tuberculosis

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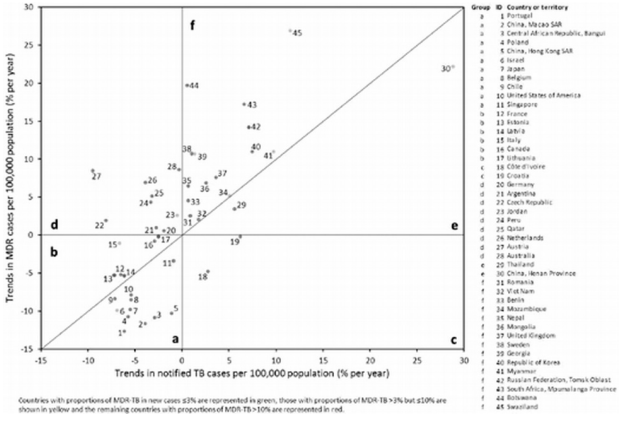
Background: To investigate time trends in multidrug-resistant tuberculosis (MDR-TB) in different geographical settings worldwide we used data collected by the World Health Organization over the period 1994-2010.

Methods: Time trends in MDR-TB rates from 45 countries or territories were calculated by multiplying the new TB case notification rates by the frequency of MDR-TB in new TB cases in the same year. The number of available country-year data points differed between countries. The annual percentage change in MDR-TB rates was plotted against the annual percentage change in TB notification rates, placing all countries or territories in one of six groupings according to whether MDR-TB rates and TB notification rates were increasing or decreasing.

Results: In countries like Japan, Poland, Singapore and the US, the incidence of MDR-TB has been falling quicker than the incidence of TB. Countries with a high proportion of MDR-TB among TB cases (Georgia, Russian Federation: Tomsk Oblast), with a majority of TB cases of foreign origin (Sweden, United Kingdom) and with high HIV prevalence (Botswana, South Africa: Mpumalanga Province, Swaziland) show net increments in both TB and MDR-TB incidence, with the latter increasing faster than the former.



Conclusions: While global trends in MDR-TB may not be inferred directly from

the national data currently available, MDR-TB incidence is increasing in countries with disparate epidemiological and geographical settings.

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Determinants of multidrug-resistant tuberculosis (MDR-TB) in Belarus

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Introduction: A nationwide survey to investigate risk factors for multidrug-resistant tuberculosis (MDR-TB) was conducted in Belarus in 2010-2011. A total of 1,344 TB patients were enrolled.
Results: MDR-TB was found in 32.3% (95% CI: 29.7-35.0) and 75.6% (95% CI: 72.1-78.9) of new and previously treated patients, respectively. History of previous treatment for TB was the strongest independent risk factor for MDR-TB (Odds Ratios [OR] 6.1, 95%CI: 4.8-7.71) followed by HIV infection (OR 2.2, 95%CI: 1.4-3.5). Other independent risk factors were young age (<35 years) (OR 1.4, 95%CI: 1.0-1.8), history of imprisonment (OR 1.5, 95%CI: 1.1-2.0), disability in such a way as to be unable to work (OR 1.9, 95%CI: 1.2-3.0), alcohol abuse (OR 1.3, 95%CI: 1.0-1.8), and smoking (OR 1.5, 95%CI: 1.1-2.0).
Discussion: MDR-TB is a widespread problem in Belarus, with very high levels documented countrywide. The convergence of the MDR-TB and HIV epidemics and association between MDR-TB and numerous risk factors calls for stronger collaboration between TB and HIV control programmes and a more targeted approach to high-risk groups. Adherence to TB treatment could be improved by integrating treatment for alcohol use disorders into TB services and enhancing patient incentives and enablers.

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Survival and risk factors of mortality among defaulters from treatment of pulmonary tuberculosis

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Defaulters from treatment of pulmonary tuberculosis (PTB) convey a significant transmission risk that is particularly dangerous during increasing prevalence of MDR-TB and TB/HIV co-infection.
We estimated 1- and 5-year survival, assessed infectiousness and identified risk factors of mortality of PTB patients after treatment default.
We observed all patients with PTB registered in the Estonian Tuberculosis Registry as defaulters during 2004-2006 (n=160) in a cohort study until 12.12.2011 and used multivariate Cox regression analysis to identify risk factors of mortality.
Median follow-up time was 5.94 (IQR 3.21-6.68) years after default. One-year and 5-year survivals were 90.5% and 68.8%, respectively. Among the 50 patients (31.3%) who died, median survival time was 1.86 (IQR 0.88-3.04) years; 24 deaths (48.0%) occurred due to TB and 26 (52.0%) due to other reasons. At 1 and 5 years after default, 22.8% and 12.2% of surviving patients, respectively, were smear/culture positive.
Smear-positivity (HR 2.86, 95% CI 1.05–7.80), previous TB (HR 2.99 95% CI 1.27–7.04) and ofloxacin resistance (HR 5.77, 95% CI 1.74–19.18) increased risk of TB-related mortality. Disabled (HR 7.97, 95% CI 1.01–62.63), retired (HR 17.10, 95% CI 1.71–171.41), homeless (HR 2.36, 95% CI 1.61–4.78) and imprisoned people (HR 34.01, 95% CI 2.92–398.11) were at increased risk of all-cause mortality, whereas targeted case detection by medical personnel lowered this risk (HR 0.19, 95% CI 0.56–0.61).
Among defaulters, TB-related mortality is not associated with demographic factors, which influence all-cause mortality instead. Infectiousness of defaulters remains high, though decreases with time.
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Is multidrug-resistant TB more common in children? An analysis of surveillance data

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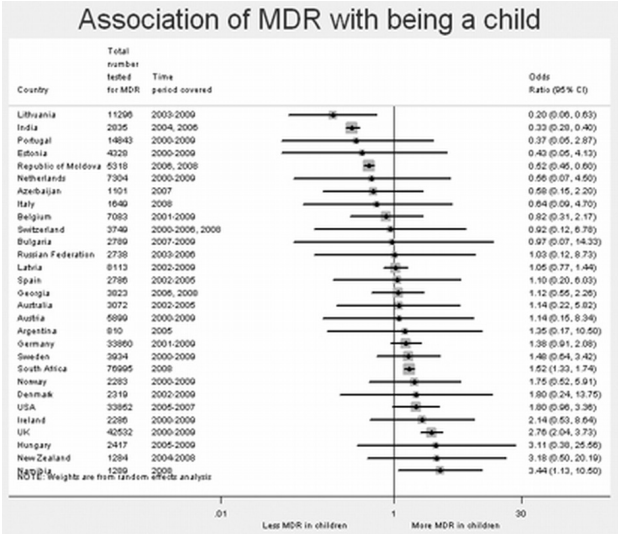
Tuberculosis (TB) caused by strains resistant to isoniazid and rifampicin (multidrug-resistant TB; MDR-TB) can affect persons of any age. Little is known about the global epidemiology of childhood MDR-TB.
We analysed representative drug-resistance surveillance data reported by countries to the World Health Organization to test the association between MDR-TB and age-group (<15 years vs 15+), using odds ratios derived by logistic regression with random effects to account for within-country dependencies.
Of 74 countries with data from surveys or continuous surveillance systems with a high coverage of testing, 29 reported at least one paediatric MDR-TB case. Disaggregated data by age and drug-susceptibility testing for 292,587 TB cases notified in 2000-2009 were used. ORs for MDR-TB in children varied widely between countries from 0.20 (95%CI0.06-0.63) to 3.44 (1.13-10.50). In India, Lithuania, and Rep. of Moldova, MDR-TB was negatively associated with age<15y while, in Namibia, South Africa, and United Kingdom, it was positively associated with age<15y. In all other countries, the association was not statistically significant.



Despite the limited availability of data and the possible bias from selective diagnostic testing, results indicate that MDR-TB in children is no less frequent than in adults in many settings. Of particular concern is the link between children and MDR-TB in southern African countries with high HIV prevalence.

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Multidrug-resistant tuberculosis and HIV infection in Eastern Europe: Two overlapping epidemics

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Background: The number of people living with HIV has increased nearly three times in the former Soviet Union since 2000. Meanwhile, this is one of the world's region most severely affected by multidrug-resistant tuberculosis (MDR-TB), with nearly half of patients with TB having MDR-TB in some settings.
Methods: Available drug resistance surveillance data between 2006 and 2011 were analysed from Belarus, Estonia, Latvia, Republic of Moldova, and Ukraine to explore the association between HIV and MDR-TB.
Results: In all 5 countries a significant positive association between MDR-TB and HIV was documented (range OR: 1.5-2.6, p value<0.05 for all). Overall, combining data from all countries (6,455 TB cases tested for HIV and MDR-TB) the odds of having MDR-TB among HIV-positive patients were 110% higher than among HIV-negative patients (pooled OR: 2.1, 95%CI: 1.2-3.3; OR consistent across countries I^2=19.2%) and the difference was statistically significant.
Conclusions: The association between HIV and MDR-TB epidemics found in these countries is alarming. Patients with dual HIV/MDR-TB infection require complex treatment with anti-retrovirals and toxic, expensive anti-TB drugs. The likelihood of successful outcome is low and transmission of MDR-TB to others is high. Urgent measures should be implemented to strengthen HIV prevention and treatment, contain the spreading of MDR-TB, and improve collaboration between HIV and TB control activities, particularly for individuals at high risk of dual infection such as people who inject drugs and those in congregate settings. Further operational research to identify the determinants and conditions leading to MDR-TB in people living with HIV is needed.

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Rational use of tuberculosis drugs to prevent the development of drug resistance

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The tuberculosis (TB) drug pipeline has finally thickened and several new agents are under clinical development. We assessed risks related to the introduction of new drugs and the development of drug-resistance with the aim to support stakeholders when introducing new drugs and regimens in TB Programs.
Using standardised Cochrane and PRISMA Guidelines systematic reviews were conducted. We assessed; how often TB patients are prescribed inadequate drug regimens; the knowledge of healthcare workers (HCW) on TB regimens; and the risk of developing multi-drug resistant TB (MDR-TB) when an inappropriate regimen was prescribed. A questionnaire was developed by ECDC and ERS to map national Community Acquired Pneumonia (CAP) guidelines and the risk of fluoroquinolone (FQ) resistant TB after treatment for CAP was assessed.
Between 0.4% and 100% of TB patients were prescribed an inadequate regimen. Between 8% and 100% of HCW reported having inappropriate knowledge of TB regimens. The risk for MDR-TB after being prescribed an inappropriate regimen increased by 27-fold (26.7, 95% CI 5.0-141.7). In the EU/EEA, 18 countries had CAP guidelines, of which two recommended FQ as the first drug for CAP treatment. Treatment with FQ before TB diagnosis resulted in a three-fold higher risk of having FQ resistant TB (OR 2.81, 95% CI 1.47-5.39).
These studies provide evidence that TB drugs are prescribed in inadequate regimens and that inadequate regimens, or the use of FQ for CAP, present an increased risk of drug-resistance. There is an urgency to strengthen guidelines and adherence to these to ensure a rational use of TB drugs and prevent the further development of resistant TB.

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ECDC guidance on management of contacts of MDR-TB and XDR-TB patients

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Multidrug resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB) are becoming more prevalent and pose a great public health threat in the EU. There is an urgent need to prevent further cases from developing and to stop the transmission of infection. The management of contacts of MDR-TB and XDR-TB patients is controversial with little scientific evidence to support guideline development. This is evident from a recent review of the management of MDR-TB contacts in EU which revealed a lack of national guidelines in several Member States, and discrepancy between national guidelines among other Member States. European Centre for Disease Prevention and Control (ECDC) therefore identified a need to provide guidance to EU Member States on the subject. The guidance document presents the evidence-based expert panel opinions on how to manage contacts of MDR-TB and XDR-TB patients. The expert panel stated that the current evidence-base does not provide the support to neither reject nor support provision of preventive therapy at this stage with the currently available drugs. It therefore expressed its opinions on the two possible alternatives: i) to provide preventive therapy and ii) to provide information and follow-up with careful clinical observation of the contacts. The central principle in the expert panel's opinions is that a comprehensive evaluation of risk factors for adverse events of preventive therapy should be performed and be part of an overall individual risk assessment of the MDR-TB or XDR-TB contact. The guidance document will be published for World TB Day 2012.