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## Review

# Multidrug-resistant tuberculosis in Lithuania – Still a long way ahead

Greta Musteikienė<sup>a,\*</sup>, Skaidrius Miliauskas<sup>a</sup>, Raimundas Sakalauskas<sup>a</sup>,  
Astra Vitkauskienė<sup>b</sup>, Marius Žemaitis<sup>a</sup>

<sup>a</sup>Department of Pulmonology and Immunology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>b</sup>Department of Laboratory Medicine, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

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## ABSTRACT

Despite the recent advances in the diagnosis of tuberculosis, treatment of the disease, for the most part, remains the same as it was half a century ago. In recent years only two new anti-tuberculosis drugs have been approved by the European Medicines Agency and Food and Drug Administration. Though the prevalence of this disease is slowly decreasing all over Europe, new challenges appear. One of them is multidrug-resistant tuberculosis (MDR-TB). This problem is especially prominent in Lithuania, which is one of the 27 high MDR-TB burden countries in the world and falls behind neighboring countries in terms of the prevalence of the disease. The objective of this paper was to review the situation of tuberculosis and MDR-TB in Lithuania, and current available methods of treatment, control and diagnosis of this disease.

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## 1. Introduction

Regardless of the presence of a global strategy for tuberculosis (TB) this disease remains one of the leading causes of mortality among treatable infections [1]. *Stop TB Partnership* aims to

eliminate TB by 2050, but it can be seen that this will be challenging to achieve with this pace of TB prevalence decline [2,3].

Since 2001 TB incidence in the European Region has been dropping at about 4.5% per year [4]. Nevertheless, to reach the milestones, indicated in the TB Regional Action Plan

\* Corresponding author at: Department of Pulmonology and Immunology, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50161 Kaunas, Lithuania. Tel.: +370 631 73730.

E-mail addresses: [greta.musteikiene@gmail.com](mailto:greta.musteikiene@gmail.com) (G. Musteikienė), [skaidrius.miliauskas@kaunoklinikos.lt](mailto:skaidrius.miliauskas@kaunoklinikos.lt) (S. Miliauskas), [raimundas.sakalauskas@kaunoklinikos.lt](mailto:raimundas.sakalauskas@kaunoklinikos.lt) (R. Sakalauskas).

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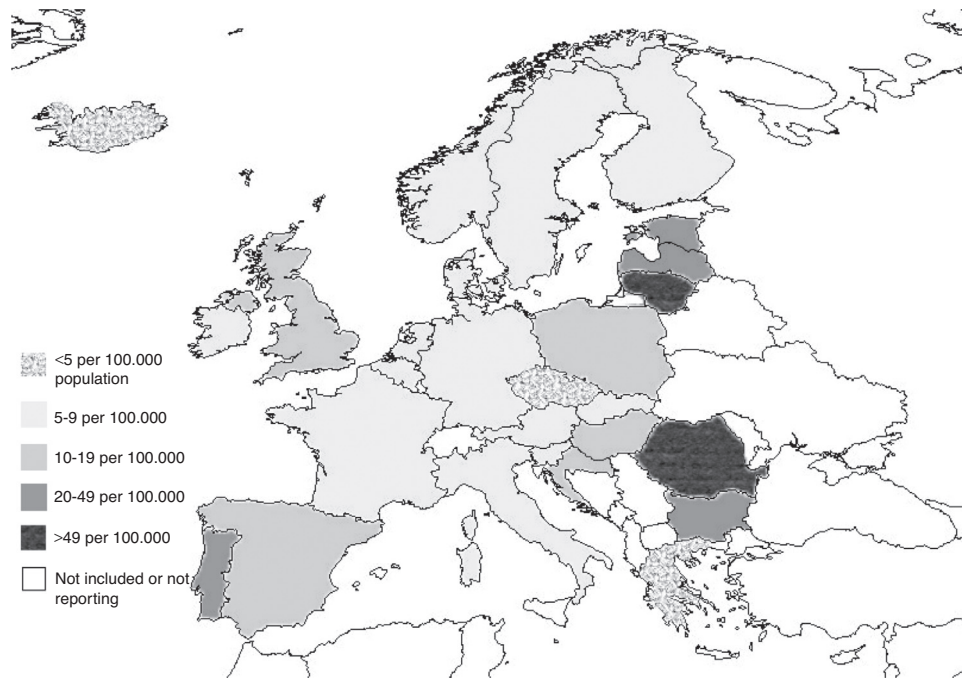


Fig. 1 – Tuberculosis notifications per 100,000 population, by country in European Union, 2013 [13].

2016–2020, we need to ensure the acceleration of this reduction [5].

A total of 18 high-priority countries in European Region (Azerbaijan, Armenia, Bulgaria, Belarus, Estonia, Georgia, Kyrgyzstan, Kazakhstan, Latvia, Lithuania, Moldova, Russia, Romania, Tajikistan, Turkmenistan, Turkey, Uzbekistan, and Ukraine) account for the most of the burden of TB (85% of incidence, 86% of prevalence, 90% of the mortality caused by TB, 90% of TB/human immunodeficiency virus (HIV) co-infections). This means that the key efforts to combat TB need to be focused here [5].

Multidrug-resistant TB (MDR-TB) is also an emerging issue in the European region. The mentioned 18 countries also account for the majority (99.5%) of MDR-TB in the region [5]. MDR-TB is caused by *Mycobacterium tuberculosis* strains resistant to, at minimum, rifampicin (R) and isoniazid (H) [6,7]. The cause of resistance can be multifactorial: improper treatment, transmission of bacteria in public, poor management of drug quality and supply and others [8].

Two paths leading to TB drug resistance are the following: (1) acquired drug resistance is an outcome of inadequate treatment, which allows selection of resistant mutant strains, and (2) primary drug resistance is a consequence of infection with a drug-resistant TB strain that developed resistance, when mutations occurred in genes, encoding drug targets or drug metabolism mechanisms [9].

In 2006, TB with further resistance to second-line drugs was defined as extensively drug resistant TB (XDR-TB). XDR-TB is caused by *M. tuberculosis* resistant to H, R, any fluoroquinolone (FQ), and at least one of three injectable drug: capreomycin (Cm), amikacin (Am) or kanamycin (Km) [7,10]. This makes even fewer options available for the treatment of this disease [8]. By the end of 2013, XDR-TB had been reported in 100 countries (including Lithuania) [5]. Appearance of XDR-TB is a

direct result of mismanagement of MDR-TB cases, and treatment of XDR-TB depends on drugs that are even more toxic and less effective than the ones used for MDR-TB [11].

## 2. Rates of MDR-TB in Lithuania

The highest rates of TB in the European Union (EU) in 2012 were reported by Romania (85.2 per 100,000 population), Lithuania (59.2), Latvia (48.6), Bulgaria (31.1), Portugal (25.2) and Estonia (21.6) [12]. All three Baltic countries belong to the high-incidence countries for TB (Fig. 1), though the rates of TB vary considerably among them (Fig. 2).

While MDR-TB prevalence among new cases in all EU countries was 4% or lower, in the Baltic States it varied from 8.8% in Latvia, to 17.3% in Estonia, Lithuania being in the middle [5]. The World Health Organization (WHO) placed Lithuania among the high TB burden countries in 2007 and since 2008 among high MDR-TB burden countries [14].

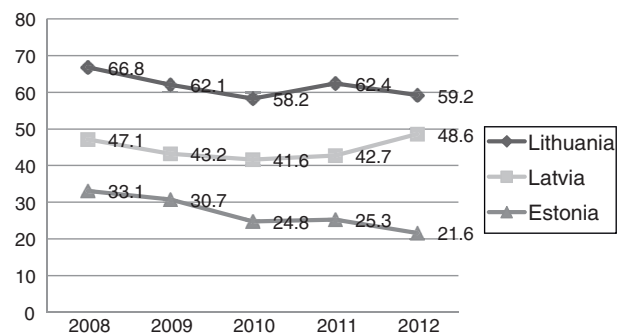


Fig. 2 – Prevalence of tuberculosis in Baltic countries, 2008–2012 (per 100,000 population) [12].

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