

UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA

**DOCTORAL THESIS ABSTRACT**

**“Epidemiological aspects of tuberculosis disease in disadvantaged population groups in Dolj county in the period 2006-2011”**

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## Introduction

Although since 2002 the trend has been continuous decline in the incidence of tuberculosis, Romania has constantly occupied the first place among the countries EU / EEA and leading places among the countries of the European region, indicators of endemic tuberculosis epidemiometric lift positioning Romania in the group of 18 high-priority countries (HPC) in Europe: five EU countries (Bulgaria, Estonia, Latvia, Lithuania, Romania), 13 non-EU countries (Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkey, Turkmenistan, Ukraine and Uzbekistan).

The 2015 Millennium Development Goal (MDG), the main component of the Millennium Declaration, adopted in September 2000 at the Millennium Summit, 191 countries, including Romania from 2015 to halt the spread of TB and initiate the downward trend incidence, the overall prevalence of tuberculosis and tuberculosis related deaths by 50% (compared to 1990) [4] was partially realized in 2011 with a falling incidence of TB in the region, at a rate of about 5% per year between 2000 and 2011. . Nevertheless, the prevalence of TB was estimated at 56 cases per 100 000 population (about 500 000 prevalent cases) in the Region and TB mortality was 4.9 deaths per 100 000 population (around 44 000 in total). It will therefore not be possible to reach the target of 50% reduction by 2015.

The incidence of TB in the European Region varies among and within the countries, from a range of less than one TB case per 100 000 population to above 200 TB cases per 100 000 in others. The 53 countries of the WHO European Region account for around 4.4% of the world's cases, representing an estimated 380 000 individuals with a new episode of TB (or relapse), or 42 cases per 100 000 population.[1]

**Material / Methods:** were analysed data presented in the Tuberculosis surveillance and monitoring in Europe 2013 Report of ECDC-WHO/Europe and statistical data provided by the National Center for Communicable Diseases of the Institute of Public Health and the National Institute for Lung Diseases "Prof. Dr. Marius Nasta", the competent body for monitoring tuberculosis in Romania.

The objective was to analyze, using epidemiometric indicators, the situation of tuberculosis in Dolj county in 2006-2011

## Results and discussion

The Report on Surveillance and monitoring of tuberculosis in Europe in 2013 is fifth report launched jointly by the European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe (WHO/Europe) following on from reports under the EuroTB project, established in 1996[1].

By Decision 2119/98/EC of the European Parliament and of the Council of Europe was established in the European Community, a network that promotes cooperation and coordination between Member States in order to improve prevention and control of communicable diseases. One of the working tools used for this purpose is TESSy (The European Surveillance System). [2]

Between 1996 and 2007 TB surveillance data from the European Region were collected and analyzed annually in the "EUROTb" project [1]

Since 1 January 2008, ECDC and the WHO Regional Office for Europe (WHO / Europe) jointly coordinated action for the collection and analysis of TB surveillance data in Europe, aiming to ensure data standardization and high quality across countries of the WHO European Region (except Liechtenstein, Monaco and San Marino). Basic standards and definitions were agreed by leading European experts [3]

Quality and comparability of reported data have improved considerably in recent years.

A total of 29 EU / EEA Member States, including Romania, have reported cases in the database. Updates were provided for the years 2008, 2009 and 2010 to allow the exclusion of duplicate cases or those laterfound not to have TB as well as updates of the variables, the treatment. The remaining countries of the European Region reported aggregate data [1]

Total European Region (TER) comprises the 53 countries of the WHO European Region and Liechtenstein.

To calculate rates of notification denominators population of age group and sex were obtained from Eurostat. The overall rates of notification were directly age-standardized using the 2000-2010 EU / EEA average as the average population standard [1].

Since 2005, TB notifications fell by almost a quarter, 41-33 cases per 100 000 population[1].

### Notification of cases of TB in 2011

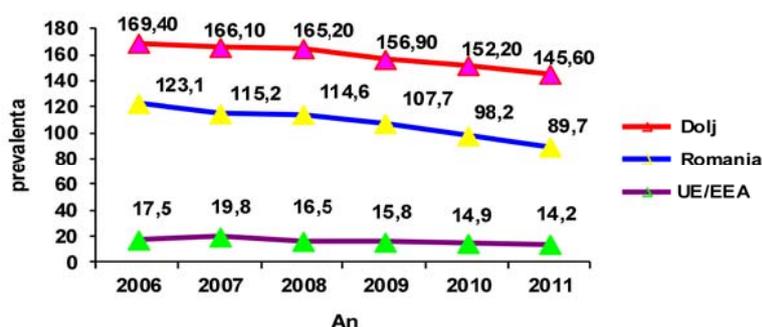
- Total European Region (TER) : 380 366 cases notified to WHO, rate 42.2 per 100000 population, mean annual% changein rate -5.7%
- EU/EEA : 72 334 cases, rate 14.2 per 100000 population, mean annual% changein rate - 4%
- Non-EU/EEA: 308 032 cases, rate 78.1 per 100000 population, mean annual% -5,9%
- 18 High-Priority Country (HPC): 326 656 cases, rate 84 per 100000 population, mean annual% changein rate -5.9%
- **Romania**: 19 212 cases notified, rate 89. per 100000 population, mean annual% -6%.

With these values Romania ranks first among nations in the EU / EEA (followed by Lithuania, Latvia, Bulgaria, Estonia) and ranks 9th among the 18 HPC (after Kazakhstan, Moldova, Georgia, Kyrgyzstan, Russia, Tajikistan, Azerbaijan, Ukraine). Also, from 2006-2011 Romania constantly had the highest rate incidence between EU / EEA countries.

In 2011, 10 of the 29 countries EU / EEA have rates higher than average raw total EU / EEA

Dolj County with a total of 1016 TB cases notified in 2011 was the county with the highest prevalence rate in Romania (145.6 per 100000).

Fig. 1 Comparative prevalence UE/EEA, Romania, Dolj, 2006-2011

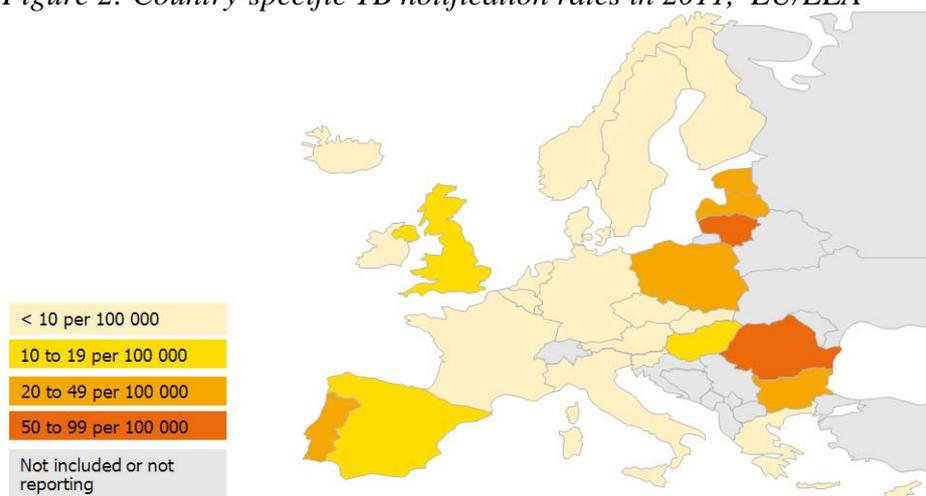


### New cases and relapses in 2011

- Total European Region (TER): 295 968 cases, rate 32,8 / 100000
- EU/EEA: 61273 cases, rate 12,1 / 100000
- Non EU / EEA: 234 695 cases, rate 58,3 / 100000
- 18 High-Priority Country: 250 960 cases, rate 64,3 / 100000
- Romania**: 16992 cases, rate 79.4 / 100000

Romania is well above the national average EU / EEA (12.1/100000 rate) of the European region (32.8/100 000), or those 18HPC (64.3/100,000), occupying first place between EU/ EEA countries and 6th in the European region (after Moldova, Kazakhstan, Georgia, Kyrgyzstan, Tajikistan).

Figure 2: Country-specific TB notification rates in 2011, EU/EEA



[http://www.ecdc.europa.eu/en/healthtopics/Tuberculosis/epidemiological\\_data](http://www.ecdc.europa.eu/en/healthtopics/Tuberculosis/epidemiological_data)

### Cases of tuberculosis treatment in history

Regarding the treatment of tuberculosis cases in history in 2011 of the 19212 of tuberculosis notified in Romania, **14543** cases (75.7% of all TB cases) were **new** cases, no treatment history (TER-71,3%, EU/EEA-79,7%, non-EU/EEA-69.4%, 18HPC- 69.6%), and **4669** (24.3%), previously treated [1,2], (TER-26,7%, EU/EEA-12,3%, non-EU/EEA- 30.1% 18HPC-29.9%) [1]. In terms of completed treatment 3139 cases (67.2%) had completed treatment, 801 cases (17.2%) were failures, and 729 cases (15.6%) were abandoned [1,2 ]. There has been no case with other historical re-treatments or therapeutic unknown [1].

### Notification by site of disease

Romania has notified in 2011year, **16431 cases of pulmonary TB -85, 5%** of all cases of TB (TER-81,4%, EU/EEA-77,3%, non-EU/EEA-82,4%, 18HPC- 82.8%) and **2781 cases(14,5%)** only of **extrapulmonary** location (TER-13,2%, EU/EEA-22, 3%, non-EU/EEA-11.1% , 18HPC-11.3%). Romania is ranked 9th place by pulmonary locating and 20<sup>th</sup> place by extrapulmonary location among the countries EU / EEA. There were no recorded cases without a localization of tuberculosis.

### Notification by laboratory confirmation

In 2011 in Romania laboratory confirmation of a new pulmonary TB cases were in proportion of 78.0%.

There were 72.9% positive culture (56.9% smear positive). These indicators were superior both European Region (55% with laboratory confirmation, 45.9% positive cultures) and EU / EEA (74.6% with laboratory confirmation, 69.2% positive cultures).

There were 16% new pulmonary TB cases with smear negative and positive culture (TER-13,8%, EU/EEA-20, 4%).

In 2011 in Romania were 64.8% of all tuberculosis cases laboratory confirmed.

In 2011 in Romania were 113 BK microscopy laboratories, 70 laboratories for culture and DST laboratories 43, 2 laboratories international accredited with external quality assurance for DST. Romania is among the 19 countries in the EU / EEA and seven non-EU countries whose laboratory data based on defined criteria (national coverage of 100% or culture results available for 90% of all cases; 50% of all cases culture-positive, with DST results for 80% of culture-positive cases and EQA results matching for 95% or higher) [1]

## Classification according to the EU case definition

According to EU case definition of tuberculosis approved by Commission Decision of 08/08/2012 amending Decision 2002/253/EC on case definitions of diseases under surveillance in the community laboratory confirmed case criterion refers to the least one of the following two situations:

- isolation of Mycobacterium tuberculosis complex (excluding Mycobacterium bovis-BCG) from a clinical specimen;
- detection of nucleic acid M. tuberculosis complex in a clinical specimen positive microscopy.

Laboratory criteria for probable case refers to at least one of the following three situations:

- smear positive;
- detection of M. tuberculosis complex nucleic acid in a clinical specimen;
- positive results histopathology.

In 2011, in Romania the 19 212 notified cases were classified as follows: **12446 (64.8%) cases confirmed** , **1535 (8%) probable** cases and **5231 (27.2%) possible** cases [1,2]  
Of these 99.7 were diagnosed antemortem and postmortem 0.3% [2]

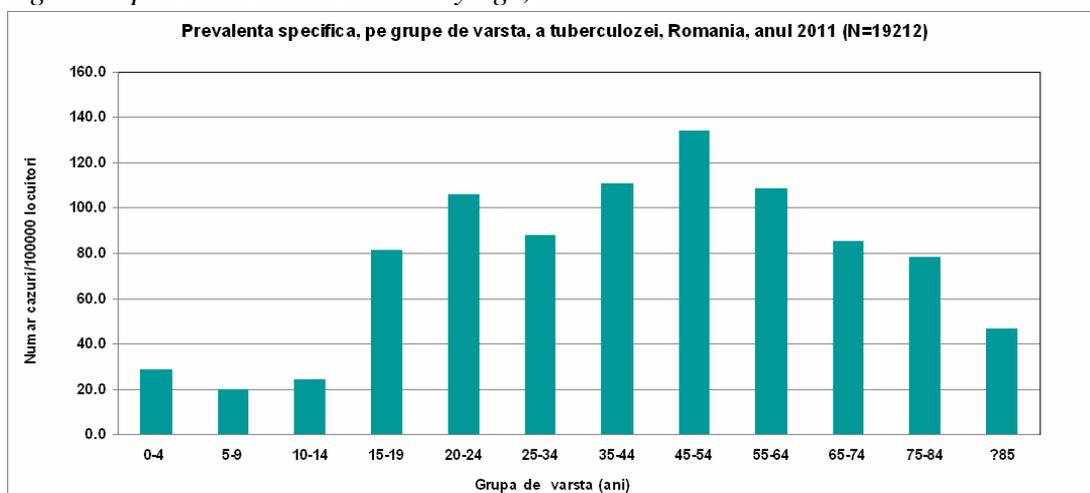
## Notification by gender and age

In 2011, in Romania sex ratio M / F = 2.2 was higher than sex ratio of TER (1.9). In the European region gender distribution of TB cases presenting variations from Norway (1.2:1), about three times higher in Armenia and Georgia (2.9:1 each). If this region countries where TB gender difference likely reflects the over-representation of men in varying risk groups for TB, especially the homeless, prisoners, migrant seasonal workers and people living with HIV among men who have sex with men (MSM) and people who inject drugs (PWID) [1], the gender distribution in Romania this can be attributed to alcohol, tobacco and maybe disorganized life of men towards women.

Most (41%) of TB cases detected in the European Region in 2011 were in the age group 25-44 years. This was also the age group most affected both the EU / EEA and non EU countries, representing 35.4% and 39.9% of new TB notifications, respectively [1]

In 2011 in Romania remains the same trend as it been in years, the analysis of specific age groups prevalence revealing peaks in the age group 45-54 years.

Fig 3. TB prevalence in Romania by age, 2011



Source: CNSCBT Bucuresti

Regarding specific prevalences by age and sex there was an increase in the number of diseases in young women, the maximum being recorded in females 20-24 years age group, for males to remain elevated in group The vast 45-54 [2]

The average age of new cases of TB, Romans: 42.0 years

The average age of new cases of TB, foreign: 37.4 years

### **Tuberculosis in children**

The proportion of cases registered in children (0-14) years is 4% of the total number of cases but with an incidence rate of 23.9 / 100,000, placing Romania in first place in EU / EEA and 3rd respectively in European region after Georgia and Moldova.

The number of cases in children (0-14 years) notified in 2011 in Romania was **776 cases**, of which **303 cases 0-4 years**, **473cazuri the 5-14** age group.

In 2007-2011, the overall trends regionally notifying TB in children (age group 0-14 years) decreased by 23% , in the 8.7 to 6.7 cases per 100 000 inhabitants.

In Romania in 2007-2011, the general trend of TB notification in children (age group 0-14 years) decreased by 21.12%, from 30.3 to 23.9 cases per 100 000 population, contributing to achieve a 23% reduction in TB notification among children seen in HPC 18 (15.1 - 11.6 cases per 100 000 inhabitants). However, the average percentage of patients in this age group, in the region remained stable at around 6% .

### **Tuberculosis and HIV co-infection**

In 2011 in Romania in the 19 212 notified cases of tuberculosis 9383 (48.8%) TB cases were tested for HIV, and 243 (2.6%) cases were HIV-positive TB cases , percents smaller than those recorded in the EU / EEA (53.6% of TB cases tested for HIV, 4.7% diagnosed HIV positive), and, respectively, the European Region( 59.6% known HIV status among tuberculosis patients, 6.2% of them HIV positive).

In the European region estimated HIV prevalence among TB patients was 6%.

### **Notification by history of imprisonment**

There are still too few countries reporting complete quality data on TB detection in prisons, so is difficult to calculate the extent to which prisons contribute to regional TB burden. Countries with high rates of TB incidence such as Kazakhstan, Russia and Turkmenistan have not done any reporting. However, in some countries in Eastern Europe in prisons TB cases exceeded 10% of the national total new cases of TB: Georgia (20.8%), Slovakia (18.9%) and Israel (11%) . The highest TB noti- fication rates in prisons were in Azerbaijan (1984 cases to 100 000 prisoners), Lithuania (948 prisoners per 100 000), Tajikistan (886 prisoners per 100 000) and Slovakia (856-100 000 prisoners). The highest relative risk of TB in prisons is calculated for Slovakia (1445 RR) and Israel (57 RR).

In Romania to an 27 559 incarcerated population were detected 122 cases of tuberculosis (all forms), with a rate of 442.7, the proportion of new cases of TB in the country's prison outside country's total was 0.8%, with a relative risk of 6.5.

With a total of 631 229 prisoners in the European region were 2798 new cases of TB detected with a rate of 560.8, and a relative risk of 12.5.

## Notification by patient origin

In Romania 50 (0.3%) cases detected in 2011 were of foreign origin. This was the lowest percentage in EU / EEA where of the 72 334 TB cases notified in 2011, 51 191 (72%) were EU / EEA inhabitants, 18 646 (26%) were of foreign origin and 1497 (2%) were of unknown origin. country-specific proportions of foreign-origin TB cases ranged from 0.3% in Romania to 89% in Sweden and were inversely correlated with countries' TB notification rates.

## Multidrug-resistant (MDR) tuberculosis and XDR-TB notification

In 2011:

- Total European Region (TER) 29473 cases MDR, XDR 381cazuri
- EU/EEA: 1522 cases MDR, XDR 136 cases,
- Non EU / EEA: 27951 cases MDR, XDR 245cazuri,
- 18 High-Priority Country: 28 963 cases MDR, XDR 352cazuri,
- Romania: 530 MDR cases (117 new cases and 413 cases relapsed), 30 cases of XDR**

For Romania, **drug resistance** was as follows:

**867 isoniazid resistant cases (14.4%)**

**597 rifampin-resistant cases (9.9%)**

**Cases resistant to ethambutol 218 (3.6%)**

**Streptomycin resistant 300 cases (5.0%)**

Close aboard the Baltic countries, Romania ranks among the countries EU / EEA with high proportion MDR, even if the overall trend is slightly decreasing.

Between 2007 and 2011, notification rates for multidrug-resistant TB (MDR TB) have remained stable at around 0.3 per 100 000. Overall, the Proportion of TB Cases with multi drug resistance in the 29 countries was 4.5%, a 0.2 Percentage Point Decrease from 2010. The Proportion Remains High in the Baltic States and Romania (combined MDR TB: 14.8% -29.8% and 8.8%, respectively)[1].

The overall Proportion of Cases with previously untreated MDR TB was 2.4% (range 0% -23.3%) in the EU / EEA and the Proportion of multi drug resistance among previously treated Cases was 16.8% (range 0% -57.7%)[1].

Twelve EU / EEA countries Reported at Least One Extensively drug-resistant (XDR) TB case in 2011. In total there were 136 XDR TB Cases Reported and the Proportion of XDR TB among MDR TB Cases Cases Increased a little compared to 2010 (from 12.6% to 13.4%)[1].

## Treatment outcome

In the 2010 cohort, therapeutic success rate among new pulmonary TB cases detected in the European region was 67.2%.

The success rate was higher in EU / EEA countries than in non-EU countries (76.8% vs 63.4%).

Only eleven countries have achieved the treatment success of 85%. Six other countries, including **Romania (success rate 83.8%)** were close to the target, with success rates between 80 and 85.

Success rate is decreasing probably due to increased incidence of MDR or deficiencies in country's health programs .

In Romania in the cohort of 2010 there were 441 deaths (4.7%), 379 (4%) failures, 538 (5.7%) drop and 171 (1.8%) still in treatment. Returning customer has not been lost in the crowd.

## Conclusions

In the period 2006-2011 Romania was ranked among the countries with the highest TB incidence rate of disease in the European, constantly occupying first place between the EU / EEA. Although the trend in this period was the continuing decline in the incidence of tuberculosis (from 123.1 / 100 000 inhabitants in 2006 to 89.7 / 100,000 population in 2011), however, Romania has an incidence of tuberculosis disease by far superior European average (17.7 / 100 000 inhabitants in 2006 -14.2 / 100 000 inhabitants in 2011).

Romania is part of the 18 high priority countries (HPC).

Collection, storage, analysis, interpretation and use of public health and epidemiological data typing will add a new important dimension of support in response to the European TB surveillance, allowing early detection and monitoring of outbreaks and contain-ment could go international otherwise unnoticed. [1]

It must follow the strict framework of the Plan of Action to combat tuberculosis , both political and financial support from all states to eliminate tuberculosis.

In response to the alarming problem of MDR-TB, all 53 Member States have fully endorsed the Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis in the WHO European Region 2011–2015 and its accompanying Resolution EUR/RC61/R7 from the sixty-first session of the WHO Regional Committee for Europe in 2011. The Action Plan includes a set of activities for countries, WHO and partners in order to achieve universal access to prevention and treatment of M/XDR-TB[1].

## References

1. Tuberculosis surveillance and monitoring in Europe 2013 SURVEILLANCE REPORT
2. [http://www.insp.gov.ro/cnscbt/index.php?option=com\\_docman&task=cat\\_view&gid=68&Itemid=14](http://www.insp.gov.ro/cnscbt/index.php?option=com_docman&task=cat_view&gid=68&Itemid=14)
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