

## REPORT

# Tuberculosis in the Czech Republic in 2004

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## SUMMARY

In 2004 the number of newly notified cases of tuberculosis, pulmonary TB, definite TB and microscopically positive TB continued to decline in the Czech Republic. The most significant reductions were achieved in the number of definite and microscopically positive pulmonary TB (by 11.5% and 11.3% respectively). The total number of cases of pulmonary TB was 10.3 per 100,000 inhabitants and the number of definite pulmonary TB cases less than 5.7 per 100,000 inhabitants. The declining trend in the number of notified cases of tuberculosis, which started in 1998, was confirmed in 2004. Effective antitubercular therapy contributed to the liquidation of known sources of tuberculosis infection. Mycobacterial resistance to antituberculars was lower than 6% and multiple drug resistance lower than 2%, which is proof of the good quality of TB treatment provided by specialized TB and respiratory diseases medical facilities. Future TB control measures should focus on active search for TB cases among high-risk groups.

**Key words:** tuberculosis, epidemiology, treatment, resistance, high-risk groups.

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In spite of the large amounts of funds spent globally each year on tuberculosis control, it has not yet been possible to curb the disease entirely (1). In Europe alone, the number of notified TB cases increased by one third over the last seven years; in 2002 there were 404,628 notifications of new TB cases in Europe as a whole (2). This rise is due mainly to cases from the countries of the former U. S. S. R. and Romania, while in EU member states, with small exceptions, there has been a decline in the number of notified TB cases (3).

On its accession to the EU, the Czech Republic (CR) joined the ranks of developed countries where the TB situation was satisfactory and the disease under effective control. In the last year, which was assessed according to international criteria, the relative number of notifications of TB cases in CR was almost 20% lower than the EU average, and in the 1998 to 2002 period CR recorded the second largest reduction of TB morbidity of all current EU member states (2). This is the result of the work of all TB and respiratory diseases specialists concerned with TB diagnosis and therapy.

Modern TB control, as recommended by the World Health Organization (WHO) and the EuroTB group, is based on monitoring the TB situation, monitoring the efficacy of antitubercular treatment, and monitoring mycobacterial resistance to antituberculars (2, 4). These three components comprise an integrated picture of the TB situation, including the success achieved in controlling it.

We therefore analyzed the TB situation in 2004 on the basis of the number of cases notified in that year, of the success in controlling TB according to treatment outcome in patients notified in 2003 and of the incidence of the disease caused by TB bacillus strains resistant to antituberculars in newly diagnosed patients notified in 2004. Our data comply with WHO definitions (pulmonary TB, non-pulmonary TB) (4, 5).

## DATA FILE AND APPLIED METHODOLOGY

TB data for 2004 were processed using reports from the TB Patients Register administered by the Institute of Health Care Information and Statistics (ÚZIS). The doctors tending the patient notify the register of newly diagnosed TB cases via the *Mandatory Notification of TB and Other Mycobacterioses form*.

The data are checked and supplemented by the investigation results (including sensitivity results) of mycobacteria acquired by bacteriological laboratories according to the bacteriological register of isolated strains of mycobacteria (ISBT), which is administered by the State Health Institute (SZÚ).

The effectiveness of antitubercular (AT) treatment was assessed on the basis of follow-up reports of patients with definite TB diagnosed in 2003 and evaluated 12 months later.

Statistical evaluation was performed using the  $\chi^2$  test; Yates' correction was applied in the case of small numbers, and the method of smallest squares was applied for the evaluation of long-term trends. A level of 99% or higher reliability was considered statistically significant ( $p \leq 0.01$ ).

## RESULTS

*Assessment of the situation and development of TB*

In 2004 there were 1,057 new cases of TB (Tab.1), out of which 861 were cases of pulmonary TB and 196 were non-pulmonary infections. In 584 pulmonary TB cases cultivation confirmed the causative agent - tubercular bacillus (definite pulmonary TB), including 315 microscopically positive, i. e. the most dangerous sources of infection. The proportion of bacteriologically confirmed pulmonary TB cases reached 67.8%, which is less than in the pre-

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ceding year, but compared to the last seven-year period it represents the second highest bacteriological confirmation rate.

Expressed in relative numbers per 100,000 inhabitants, 10.3 cases of TB cases were notified overall: 8.4 pulmonary TB cases and 5.7 definite cases of pulmonary TB, of this number 3.1 were microscopically positive.

Compared to 2003, there has been a decline in all monitored data. The number of all notified TB cases dropped by 9.0% and reached the limit of statistical significance ( $p=0.027$ ), the number of pulmonary TB cases dropped by 8.6% and was also on the border of statistical significance ( $p=0.06$ ); similarly, the decline in the number of definite pulmonary TB cases reached 11.5% and was on the border of statistical significance ( $p=0.03$ ). The number of microscopically positive cases dropped by 11.3% and of non-pulmonary TB by 11.1%, but the latter two figures did not reach statistical significance. Of crucial importance is the statistically significant declining trend over the last seven years in all monitored categories, with the exception of non-pulmonary TB (Fig. 1). The declining trend confirmed the effectiveness of the control measures adopted.

Of the total number of 1,057 notified cases, 663 were men (62.7%) and 394 women (37.3%). The male to female ratio has not changed significantly compared to previous year. Of the total number of 1,057 notified TB cases, 102 people have been treated for TB in the past, which is 9.6%, of this number 30 (2.8% of all TB cases) in the last 3 years ("relapse" as defined by current Czech legislation). The age composition of pulmonary TB cases in 2004 is shown in Figure 2. Data are compared with 2001 to allow the assessment of the change in the age composition of TB patients over a longer period of time. As in previous years, TB was encountered mainly in older people. Due to the significantly improving TB situation over the last 40 years and the concurrent reduction in the risk of infection, the number of TB patients is declining even in the oldest age groups.

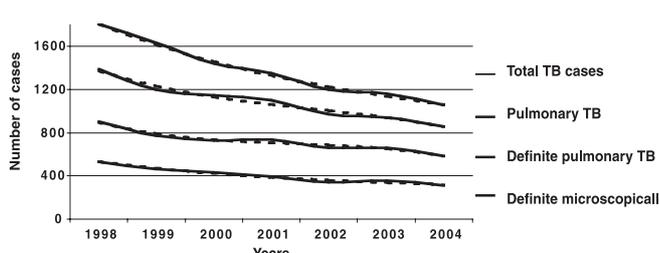


Fig. 1. Trends in the numbers of notified TB cases (new cases and relapses) in CR in 1998-2004

While the age composition curve in women has not changed – with the exception of reduced TB morbidity rates in the oldest age groups - there has been a marked decline in men, with the exception of the 45–60 age group. In the latter age group, 42% of TB morbidity is due to patients from high-risk groups – the homeless, drug addicts, prison inmates, foreigners. The number of new TB cases among individuals below the age of 20 was negligible in CR in 2004. The distribution of notified TB cases in the regions of CR is shown in Tab. 2. The highest number of patients was notified from the Karlovy Vary, Ústí upon Elbe and Prague regions. In these three regions the main factor contributing to TB morbidity were high-risk groups: homeless people (Prague) and foreigners (Karlovy Vary). Of the total number of 1,057 TB cases, 149 individuals were not born in CR (14.1% foreigners). This number does not significantly differ from previous years. In 45 cases the notified country of origin was Ukraine, in 27 cases Vietnam and in 20 cases Slovakia; the vast majority (70%) were men younger than 60 years. This group contributed significantly to the morbidity of men in the productive age of 20-60 years. This corresponds with the assumption that these individuals are economic migrants seeking employment in CR.

In 2004 there were 137 deaths of patients notified as TB cases: in 45 the recorded cause of death was TB, while 92 died of other diseases. TB mortality is 0.44 per 100,000 inhabitants. Of the cases of notified TB, 75% of the deaths were of people over 60 years of age with severe concurrent diseases who were from high-risk groups. The youngest patient who died was a 36-year-old man who died of generalized malignant neoplastic disease and whose TB diagnosis was defined as a concurrent disease only on autopsy.

The productivity of the different methods of detection of TB was similar in 2004 to that in the previous years (Tab. 3). 69.2% of pulmonary TB patients approached their doctor because of health problems (passive method of detection), 16% of pulmonary TB cases were detected by active screening (investigation of contacts and of high-risk groups). In 56 patients TB was not diagnosed until autopsy, usually as a secondary finding during the investigation of a different primary disease that was the cause of death. These results correspond with WHO recommendations to focus active TB screening on population groups that represent a high-risk of contracting TB.

#### Evaluation of the incidence of tubercular bacilli resistance to antituberculous

Of 584 patients with definite pulmonary TB notified to the TB Register, the results of sensitivity to isoniazid, rifampicin, ethambutol and streptomycin according to the Register of Isolated Strains of

Tab. 1. Number of notified TB cases in CR in 1998-2004

a) ABSOLUTE FIGURES	1998	1999	2000	2001	2002	2003	2004
TB cases	1805	1631	1442	1350	1200	1162	1057
<b>Pulmonary TB</b>	1389	1197	1144	1102	972	942	861
Of this number:							
Definite TB	903	778	732	740	658	660	584
Microscopically positive	535	461	436	395	338	355	315
<b>Non-pulmonary TB</b>	270	262	198	165	163	220	196
b) RELATIVE FIGURES (Per 100,000 inhabitants)	1998	1999	2000	2001	2002	2003	2004
TB cases	17.5	15.7	14.1	13.1	11.8	11.4	10.3
<b>Pulmonary TB</b>	13.5	11.6	11.1	10.7	9.6	9.2	8.4
<b>Definite pulmonary TB</b>	8.8	7.6	7.1	7.2	6.4	6.5	5.7
Of this number:							
microscopically positive	5.2	4.5	4.2	3.9	3.2	3.5	3.1

Mycobacteria were acquired in 491 cases. In 2004, as in the previous years, no significant increase of resistance to antituberculous was noted (Tab. 4). A favorable development was the flattening of the growing resistance curve, especially of multiple drug resistance (MDR TB – resistance at least to isoniazid and rifampicin). Of the 6 MDR TB patients four were foreigners, two from Ukraine and two from Georgia. The two Ukrainians and one of the Georgians came to CR in 2004. The latter Georgian came in December 2003 and his TB was diagnosed in April 2004. Of the MDR patients born in CR, one had been treated for TB in the past.

The most common monoresistance was to streptomycin (12 patients), followed by isoniazid (6 patients). Mycobacterial strains resistant to rifampicin alone were found in 2 patients, and there were no cases of resistance to ethambutol.

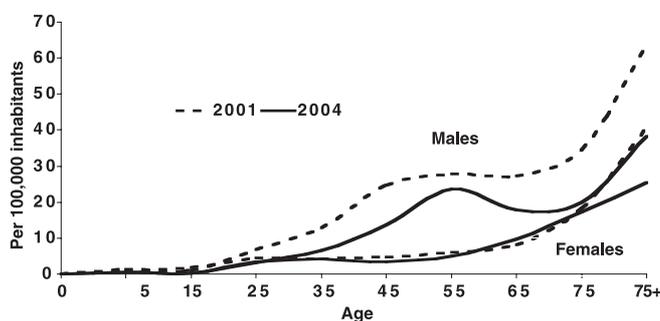


Fig. 2. Newly notified pulmonary TB cases (new cases and relapses) in CR in 2001-2004 according to sex and age

Tab. 2. Notified TB cases in CR according to region in 2002-2004

Region	2002		2003		2004	
	Absol.	Relat. *	Absol.	Relat. *	Absol.	Relat. *
Prague	187	16.1	194	16.7	152	13.0
Central Bohemia	117	10.4	116	10.3	116	10.2
South Bohemia	49	7.9	41	6.6	44	7.1
Pilsen	80	13.9	68	12.4	49	8.9
Karlovy Vary	42	12.1	50	16.4	43	14.1
Ústí upon Elbe	122	14.9	100	12.2	107	14.0
Liberec	47	11.0	42	9.8	30	7.0
Hradec Králové	54	9.8	56	10.2	53	9.7
Pardubice	52	10.3	48	9.5	51	10.1
Vysočina	40	7.8	40	7.7	36	6.9
South Moravia	127	11.3	124	11.1	127	11.3
Olomouc	51	8.0	50	7.9	44	6.9
Zlín	41	6.9	65	11.0	64	10.8
Moravian Silesia	191	15.1	168	13.3	141	11.2
CR (total)	1200	11.8	1162	11.4	1057	10.3

\* Per 100,000 inhabitants

Of the 27 cases with confirmed resistance to one or more antituberculous, 8 had been treated for TB in the past, of this number 2 during the last 3 years.

**Evaluation of the outcome of treatment in hitherto untreated adults with definite pulmonary TB diagnosed in 2003**

Treatment outcomes are evaluated in pulmonary TB cases notified in the preceding year. In 2003 the treatment of 557 adult patients with definite, first diagnosed, earlier untreated pulmonary TB was evaluated (Tab. 5). The treatment was successful in more than 75% of the cases. The WHO recommended percentage (over 85%) had not been achieved; the main obstacle was the high number of deaths either before or during the course of AT therapy, usually of other than tubercular disease. Therapy failed only in isolated cases. The improvement compared to 2002 was achieved by a decrease in the number of deaths due to other reasons.

**DISCUSSION**

Our report on the development of the TB epidemiological situation contains all three basic components (2, 4):

- 1) Evaluation of the number of notified TB cases and trends in its development,
- 2) Evaluation of treatment outcome, and
- 3) Evaluation of incidence of AT resistance.

The EuroTB group together with the WHO and International Union Against TB and Lung Diseases (IUATLD) are currently mounting an enormous effort to standardize TB control measures specified by national programs and to make TB control results comparable (2, 5-7). That is why this report, too, uses WHO recommended definitions.

TB, however, is not only a medical but also a public health issue (8). Patients need to be not only diagnosed and treated but also subjected to early screening, thus preventing transmission of infection. In 2004, compared to the preceding year (9), a marked drop in the number of notified TB cases by more than 11% was recorded. Due to the small numbers, the decline was on the border of statistical significance, but the long-term declining trend, since 1999, is unequivocal and significant and reflects the gradual reduction of sources of TB. The relative number of definite new TB cases was again significantly lower than 10 cases per 100,000 inhabitants annually, which is generally considered a sign of a favorable TB situation in a given location (10).

Unsurprisingly, men and women over 65 prevailed, with most of them having contracted TB many years ago. This age composition is typical for countries with a favorable TB situation and favorable development of the disease (11). Due to the decreasing risk of infection, TB mortality, however, is decreasing even in the highest age groups. The small number of TB cases among the young and middle-aged group is proof of the declining number of new TB infections. In men between the ages of 45-60 years a significant propor-

Tab. 3. Method of detection of new, hitherto untreated cases of pulmonary TB

Method of detection	2001		2002		2003		2004	
	Number	%	Number	%	Number	%	Number	%
Passive	705	67.1	705	67.1	702	73.0	629	69.2
Active	200	19.0	200	19.0	147	15.3	145	16.0
Autopsy	62	5.9	62	5.9	58	6.0	56	6.2
Other	84	8.0	84	8.0	54	5.6	79	8.7
Total	1051	100.0	1051	100.0	961	100.0	909	100.0

Tab. 4. Resistance of tubercular bacilli to antituberculotics

	2002		2003		2004	
	Number	%	Number	%	Number	%
Patients with confirmed sensitivity	509	100.0	556	100.0	491	100.0
<b>Sensitivity results:</b>						
Sensitive to all antituberculotics	476	93.5	529	95.1	464	94.5
Resistant to one or more AT	33	6.5	27	4.9	27	5.5
<b>Mono-resistance to:</b>						
Isoniazid	7	1.4	10	1.8	6	1.2
Rifampicin	2	0.4	0	0	2	0.4
Ethambutol	1	0.2	1	0.2	0	0
Streptomycin	3	0.6	2	0.4	12	2.4
Total mono-resistance	13	2.6	13	2.3	20	4.1
<b>Poly-resistance:</b>						
Multiresistance (MDR)	10	2.0	2	0.4	6	2.0
Other poly-resistance	10	2.0	12	2.2	1	0.2

Tab. 5. Comparison of antituberculous therapy outcome in adult patients with newly diagnosed, hitherto untreated pulmonary TB detected in 2002 and 2003 and evaluated the year after notification

Therapy outcome	Year in which therapy outcome was evaluated			
	2002		2003	
	Number	%	Number	%
Evaluated	653	100	557	100
Successfully concluded therapy	463	70.9	427	76.7
Failure	3	0.5	2	0.4
Interrupted	11	1.7	9	1.6
Died of TB	31	4.7	21	3.8
Died of other disease	79	12.1	43	7.7
Moved	24	3.7	16	2.9
Absent data	42	6.4	39	7.0

tion of pulmonary TB cases are individuals belonging to high-risk groups of homeless and drug-addicted persons and of persons born abroad. TB surveillance and control measures should be targeted on these groups, both in the form of screening and of protection of persons coming into contact with these groups, and of objective quantification of the annual risk of infection (12).

Passive search for new TB cases has predominated in the recent years. About 70% of new TB cases are found in this way. The remaining number is detected by active screening of persons who have had contact with a TB patient. The identification of TB cases that present because of difficulties is currently the most economical method of detection of unknown cases of TB in the general population (4, 5). In 2004 the TB epidemiological situation in CR continued to improve. This trend started in 1998, when stagnation

changed into a declining trend. This decline can be related to improved therapy and its consistent analysis, which has been taking place since 1998. Effective AT treatment is the most efficient method of TB control capable of cutting the chain of transmission of tubercular bacilli (4). The assessment of treatment outcome using the method of quarterly cohort analyses, introduced in the CR in 1998, led to an increase in the intensity of surveillance of the standard of treatment (4, 6, 13). In 2004 the treatment of patients notified in 2003 was assessed. A successful outcome of treatment was achieved in 76% of the cases, less than 1% of the treatments failed and treatment was interrupted in less than 2%. The WHO recommended success rate of 85% in hitherto untreated definite cases of pulmonary TB (6, 14) was not achieved, but this was due to the advanced age and concomitant diseases in a part of the patients who

died of other causes than TB, where the mortality could not be affected by antituberculous therapy. The deaths are stratified according to age to allow a more accurate determination of the effect of age on treatment outcome. Similar results were also achieved in the U.S. (1, 11) and Switzerland (15). In view of the number of patients whose data are missing it will be necessary to focus on tracing these data, especially in the case of foreign-born asylum seekers. These patients are expected to be returned to the states from which they came – the timing depends on EU cooperation.

The efficacy of AT therapy is documented by the low percentage of resistant mycobacteria in 2004. Infection caused by mycobacteria resistant to one or more antitubercotics accounted for only 5.5% of the AT sensitivity investigated cases, which corresponds with data from targeted studies (10,15). The number of MDR cases is affected by the fluctuation of small numbers. Nonetheless, it is evident that foreigners from countries with inadequate standards of TB control represent a significant proportion of MDR resistance in CR. The favorable development of the TB situation observed in CR since 1998 has confirmed that data on the number of notified TB cases in all probability reflect the true TB situation and the low probability of notification errors. Comparison of the monitored data with similar indicators from previous years shows there has been no evident lapse in TB notification. The validity of the data was also enhanced by a comparison of the clinical and bacteriological TB registers. Crucially, the fact that the TB situation has been improving has been acknowledged by the WHO, which moved the Czech Republic from the group of Central European countries to the group including the European countries with the most favorable TB situation, including the Netherlands, the United Kingdom, Germany, Sweden and Denmark (10). Since 1995 the Czech Republic has been included among countries where the actual number of notified TB cases does not differ from the estimate of this number made by the WHO on the basis of a statistical and epidemiological analysis (10).

### CONCLUSION

In 2004, as in the preceding four years, a decline in all notified cases of TB, including pulmonary TB, was recorded. The greatest decrease was achieved in definite microscopically positive pulmonary TB (by 11.3%) and definite pulmonary TB (by 11.5%). The total number of pulmonary TB cases was less than 10 per 100,000 inhabitants, and of definite pulmonary TB less than 6 per 100,000 inhabitants. It has been confirmed that data notified to the register are valid. Effective antituberculous therapy contributed to the liquidation of known sources of TB infection. Resistance to antitubercotics is low, which is proof of adequately provided therapy to TB patients.

#### Abbreviations

AT	- antituberculous
EU	- European Union
ISBT	- register of isolated strains of mycobacteria
MDR	- multiple drug resistance (MDR TB – resistance at least to isoniazid and rifampicin)
SZÚ	- State Health Institute (Prague)

TB	- tuberculosis
ÚZIS	- Institute of Health Care Information and Statistics (Prague)
WHO	- World Health Organization

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