

6. Technical Note

All 53 countries of the WHO European Region are included in tuberculosis surveillance activities coordinated by EuroTB (list of national Contact Points after title page; map on cover page of Country Profiles). National surveillance institutions are responsible for the quality of data provided. The procedures, methods and definitions guiding EuroTB activities are those recommended by European experts, WHO and the International Union against Tuberculosis and Lung Disease (UNION) [1-4].

6.1 Reporting of tuberculosis cases, mortality, drug resistance and treatment outcome

TB case reporting and mortality

Since 1996 (reporting year 1995), data on TB notification for the previous calendar year have been collected annually. Reporting of case-based, anonymous data, in accordance with standardised specifications (see www.eurotb.org), is preferred over aggregate reporting.¹ Individual data are now requested for the latest two years to allow for belated exclusion of cases included more than once or found not to have TB, as well as for updates of certain data including culture and treatment outcome. This may explain differences in data presented in the current report and those shown in previous years or in other publications.

Countries not reporting case-based records report notifications in standard, aggregate tables by age-group, sex, geographic origin, previous history of anti-TB treatment, site of disease, culture and sputum smear results. Following reception, EuroTB staff control data in liaison with the respective country. Since 1999, aggregate TB notification and outcome data have been collected and validated in collaboration with WHO personnel.

Data on tuberculosis as underlying cause of death were retrieved from the WHO Statistical Information System (WHOSIS) Mortality Database, available on Internet [5]. These data are coded and reported by national vital registration authorities. Population data for calculation of mortality rates alone were downloaded from the same source.

TB/HIV surveillance

Information on HIV sero-status of notified TB cases is collected by EuroTB in aggregate format only. Information on TB morbidity at AIDS diagnosis is

obtained from case-based information on initial AIDS-indicative diseases reported to EuroHIV (accessed in September 2007) [6]. The number of cases with HIV-associated TB obtained from both TB and AIDS notification is an underestimate. Testing and reporting of HIV sero-status of TB cases is incomplete. Moreover, TB episodes occurring after initial AIDS diagnosis are not reported to AIDS notification systems.

Drug resistance surveillance (DRS)

Since the reporting year 1998, the results of drug susceptibility testing (DST) from initial isolates of *M. tuberculosis* have been collected for isoniazid, rifampicin, ethambutol and streptomycin. In countries where DST results are matched with TB case notifications, DST information is collected as part of the individual data. When this is not possible, or when DRS data are not matched with TB case notifications (e.g. surveys), data are collected as aggregate tables by previous history of anti-TB treatment and by geographic origin (see www.eurotb.org). Information on the organisation of DRS and on laboratory practices for DST is also collected using a standard form. Data from drug resistance surveys reported separately to WHO are also included in this report [7, 8].

Treatment outcome monitoring

Since the reporting year 2002, outcome data are collected for all cases in individual format by resubmission of an updated individual dataset for the year before the last (thus in 2007, outcome data were collected for TB cases notified in 2005). Alternatively, treatment outcome data are reported separately in tabular format (see www.eurotb.org).

6.2 Data analysis and presentation

TB case reporting and mortality

While most countries reported data by November 2007, changes to the national totals of TB notifications shown in this report were allowed until end January 2008. Notification data were not adjusted for under- or over-reporting. Where relevant, particularly for countries in the EU & West, tables have been stratified by origin (national/foreign). Rates of sputum smear TB and TB meningitis in children shown are aligned to the standard recommendations for use of BCG in low prevalence countries [9]. The incomplete geographic coverage of notification data from certain countries has been noted in the report (Table 1). For calculation of notification rates, country population denominators by age-group and sex were derived from United Nations statistics [10]. Population data for Serbia (since 1998) were supplied by the respective national Contact Point. Mortality data collected from WHOSIS were analyzed and interpreted at EuroTB. Only deaths

¹ By 2007, all countries of the EU & West and Balkans except Bulgaria, Israel, Monaco, Montenegro, San Marino and Spain were reporting individual demographic and clinical data on TB cases to EuroTB (Table 1). Of these, 31 countries included data on anti-TB drug-susceptibility testing and 29 on outcome for 2005 (Map 8). In contrast, only one country in the East reported individual data, starting in 2007.

coded as ICD-9 010-018 (BTL 020-025,029) or ICD-10 A15-19 were considered for inter-country comparison. Deaths attributed to late effects of TB or pneumoconiosis associated with TB – ICD-9 137 (BTL 077) and ICD-10 B90, J65, P37.0 - are not included in totals but are shown in [Table 33](#)). Data for countries in which reporting completeness or estimated coverage was <80% in the latest available year (as reported by WHOSIS) are not included in [Map 3](#) but they are shown in the Tables (identified in italics) and in the Country Profiles.

TB/HIV surveillance

Information on HIV sero-status of TB cases is expressed as the percentage of all TB cases reported known to have a positive test, and may thus underestimate HIV prevalence in TB patients. AIDS data for the latest year are presented by year of report. The number of AIDS cases with TB as initial AIDS indicative disease, expressed as a proportion of total TB cases notified in the same year, is used to give a conservative estimate of HIV-associated TB. The trend in AIDS-defining TB cases over time is presented by year of diagnosis adjusted for reporting delays [\[11\]](#).

Drug resistance surveillance

Data on the result of DST for isoniazid, rifampicin, ethambutol and streptomycin at the start of treatment are reported as "susceptible" or "resistant". Proportions of drug-resistant cases are calculated using as a denominator cases with available DST results for at least isoniazid and rifampicin. If 90% of these cases or more had results for ethambutol and streptomycin, DST results for the latter antibiotics are also shown. DRS methodology varies across countries. Initial DST results may be collected routinely for all culture positive TB cases notified, or for cases included in specific surveys or diagnosed in / referred to selected laboratories. Geographic coverage of DRS is partial in some countries. The representativeness of diagnostic DST data depends on the routine use of culture and DST at TB diagnosis. On the basis of differences in geographic coverage and on underlying laboratory practices, DRS data are analyzed and presented in two groups:

Group A:

- nationwide data matched to TB case notification in countries using culture routinely (50%+ of cases reported as culture positive in 2006) and DST results for isoniazid and rifampicin are available for the majority of culture positive cases (80%+ in 2006)

or

- data from laboratory networks or surveys using sampling methods considered nationally representative;

Group B:

- data with incomplete or undefined geographic coverage;
- diagnostic DST data from countries where:
 - culture and DST are routinely used but conditions for being in group A above are not met (<50% culture confirmation or <80% culture positive cases with DST results)

or

- diagnostic DST results are provided from selected laboratories or areas.

Data in Group A are considered representative of the national situation and comparable across countries, whereas data in Group B are not considered representative.

Trends of MDR over the years are considered statistically significant if Chi-squared test for linear trend has a P value <0.05.

Treatment outcome monitoring

Cases eligible for outcome analysis (cohorts) are expected to include all definite pulmonary TB cases notified in the calendar year of interest, after exclusion of cases with final diagnosis other than TB as well as cases found to have been reported more than once. In countries reporting individual data, the cohort is defined on the basis of the new dataset updated following initial notification (see above). In countries reporting aggregate outcome data, completeness of cohorts is assessed by comparing the total number of cases included in TOM cohorts with those initially notified as pulmonary culture or smear positive depending on the type of cohort.

On the basis of available information, TOM data are presented in two groups:

- **Group A**, cohorts including at least 90% of definite pulmonary TB cases notified, considered as country-representative and complete
- **Group B**, cohorts including less than 90% of TB cases initially notified, or from selected areas, or for which data for assessing completeness of TOM cohorts were not available. If the total of Defaulted, Transferred and Unknown exceeds 35% of cases included in the cohort, data are included under Group B.

'DOTS areas' as used in this report refer to units within the country adopting the WHO-recommended strategy of TB control.

Geographic areas

The 53 countries of the WHO European Region have been grouped into geographic areas, based on epidemiological and geo-political features (map on first page):

- the European Union and West (EU & West): the 27 Member States of the EU in 2008 plus Andorra, Iceland, Israel, Monaco, Norway, San Marino and Switzerland.
- the Balkans: Albania, Bosnia & Herzegovina, Croatia, the Former Yugoslav Republic of Macedonia, Montenegro, Serbia and Turkey.
- the East: 12 countries of the former Soviet Union² - Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova Rep. of, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan.

The respective total populations of the three areas in 2006 were 513, 96 and 278 million.

TB notifications from Greenland and Kosovo in 2006 are footnoted in [Table 2](#), but are not included in the totals of the WHO European Region. Data for the part of Cyprus outside the government-controlled area, for Abkhazia and for Southern Ossetia were not available. The template used for maps in this report was adapted from the map of the WHO European Region located at the WHO/EURO website (www.euro.who.int).

6.3 Definitions

TB case definition for surveillance

Definite TB case

- in countries where laboratories able to perform culture and identification of *M. tuberculosis* complex are routinely available, a definite case is a patient with culture-confirmed disease due to *M. tuberculosis*, *M. africanum* or *M. bovis* (excluding *M. bovis* BCG);
- in countries where routine culturing of specimens is not feasible, patients with sputum smear positive for acid-fast bacilli (AFB) are also considered as definite cases.

Other-than-definite TB case

A patient meeting the two following conditions:

- a clinician's judgement that the patient's clinical and/or radiological signs and/or symptoms are compatible with tuberculosis,
- and
- a clinician's decision to treat the patient with a full course of anti-tuberculosis treatment.

In the 2007 round of data collection, information was collected to allow classification of cases according to the **revised European case-definition**, expected to be applied from 2008 (see [Table 16](#)). By the new definition, cases will be divided into *possible* (based on clinical criteria alone), *probable* (having in addition positive AFB or detection of *M. tuberculosis* nucleic acid or granulomata on histology) and *confirmed* (by culture or by detection of both positive AFB and *M. tuberculosis* nucleic acid). A case discovered post-

mortem with gross pathological findings of active TB that would have indicated anti-TB treatment had the patient been diagnosed before dying would fit the clinical criteria.

Previous anti-TB treatment status

Never treated case

A case who never received drug treatment for active TB in the past, or who received anti-TB drugs for less than one month.

Previously treated case (retreated case)

A case diagnosed with TB in the past and who received treatment with anti-TB drugs (excluding preventive therapy) for at least one month.

Site of disease

Pulmonary case

A case with TB affecting the lung parenchyma, the tracheo-bronchial tree or the larynx.

Extra-pulmonary case

A case with TB affecting any site other than pulmonary (see above). Pleural TB and intra-thoracic lymphatic TB by themselves are considered as extra-pulmonary.

Notes

- The above definitions conform to the European Commission's definitions for tuberculosis surveillance [4]. Cases with laryngeal TB are included with pulmonary for surveillance purposes;
- All definite and other-than-definite TB cases detected in the calendar year of interest are reported to European surveillance and are included in the totals presented in this report. Under the revised European case definition, if no clinical information is available, laboratory confirmed cases should also be reported. Cases are to be notified only once in a given 12-month period. A case, however, should be reported again if the diagnosis of confirmed tuberculosis is made following completion of anti-tuberculosis treatment (relapse case) even if this occurs within the 12 months since reporting of the initial episode of disease;
- Never treated cases are commonly referred to as new cases although this term should not be considered to indicate incidence in the strict epidemiological sense. Among retreated cases, relapses are included in notifications in all countries whereas cases retreated after failure or after default or chronic cases are variably included. In countries where information on previous anti-TB treatment is incomplete or not available, information on whether or not TB had been previously diagnosed is used as a proxy (as in [Table 13](#));
- Cases with disseminated tuberculosis (i.e. tuberculosis involving more than two organ systems or the isolation of *M. tuberculosis* complex from blood) are classified as pulmonary if the lung parenchyma, the tracheo-bronchial tree or the larynx

² The Baltic States (Estonia, Latvia and Lithuania) are included with EU & West since 2004.

are involved, and as extra-pulmonary otherwise. Miliary tuberculosis is included under pulmonary (shown separately from respiratory in analysis of mortality, see [Table 33](#)). In individual data, detailed information is collected on the major site and one minor site of disease. A pulmonary localization when present is always classified as the major site. In contrast to the recommended pulmonary classification, under the respiratory classification pulmonary cases as well as cases with pleural and intra-thoracic lymphatic TB, are classified as 'respiratory' cases, and cases with another localisation as 'extra-respiratory'.

Geographic origin

The geographic origin of TB cases is classified according to place of birth (born in the country / foreign born) or, if unavailable, citizenship (citizen / non citizen). In Denmark, the place of birth of the parents is also used in classifying origin (similarly in the Netherlands for time-trend data shown in [Table 7](#) and in the Country Profile). The country or continent of origin is included in individual data. The term "national" as used in this report refers to cases born in, or having citizenship of, the country of report.

Drug resistance

Resistance among cases never treated: indicates primary drug resistance due to infection with resistant bacilli.

Resistance among cases previously treated: usually indicates acquired drug resistance emerging during treatment as a consequence of selection of drug-resistant mutant bacilli. It can also result from exogenous re-infection with resistant bacilli.

Combined resistance: overall resistance in the population regardless of prior treatment.

Multi-drug resistance (MDR): resistance to at least isoniazid and rifampicin.

Extensive drug resistance (XDR): resistance to (1) at least isoniazid and rifampicin (i.e. MDR) and (2) resistance to a fluoroquinolone and (3) resistance to one or more of the following injectable drugs: amikacin, capreomycin, or kanamycin [[12](#)].

Treatment outcome

Cohort

TB cases notified in the calendar year of interest, after exclusion of cases with final diagnosis other than TB or cases found to have been reported more than once.

Notes:

1) since 2002 cohorts, individual outcome data have been collected for all TB cases;
2) until 2003 cohorts, aggregate outcome data were only collected for definite pulmonary cases. Since 2004 cohorts, aggregate data collection has been

extended to all pulmonary cases as well as new extra-pulmonary cases.

Period of observation

Cases are observed until meeting the first outcome, for a maximum of 12 months after the start of treatment.³

Outcome categories

Since 2001 cohorts, outcome categories are those internationally recommended - with two additional categories "still on treatment at 12 months", and "unknown" [[3](#), [13](#)]

Cured: Treatment completion and:

- culture becoming negative on samples taken at the end of treatment and on at least one previous occasion
- or
- in countries where sputum smear positive cases are classified as definite cases sputum microscopy becoming negative for AFB at the end of treatment and on at least one previous occasion.

Completed: Treatment completion and does not meet the criteria to be classified as cure or treatment failure

Failed: Culture or sputum smear remaining positive or becoming positive again 5 months or later into the course of treatment.

Died: Death before cure or treatment completion, irrespective of cause.

Defaulted: Treatment interrupted for 2 months or more, not resulting from a decision of the care provider or patient lost to follow-up for 2 months or more before the end of treatment, except transferred.

Transferred: Patient referred to another clinical unit for treatment and information on outcome not available.

Still on treatment: Patient still on treatment at 12 months and who did not meet any other outcome during treatment. It includes patients with:

- initial treatment changed due to polyresistance (i.e. resistance to at least two first line drugs) on the isolate taken at the start of treatment;
- treatment prolonged because of side effects / complications;
- initial regimen planned for > 12 months;
- information on the reasons for being still on treatment not available

Unknown: Information on outcome not available, for cases not known to have been transferred.

In this report:

- "Success" refers to the combined ratios of cured and completed;
- "Loss to follow up" is the combination of defaulted, transferred and unknown.

³ The degree of adherence by countries to the 12 month limit is unknown and a number are known to exceed it.

6.4 References

1. Rieder H, Watson J, Raviglione M, et al. Surveillance of tuberculosis in Europe. Recommendations of a Working Group of the World Health Organization (WHO) and the European Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) for uniform reporting on tuberculosis cases. *Eur Respir J* 1996; 9:1097-1104.
2. Schwoebel V, Lambregts-van Weezenbeeck CSB, Moro ML, et al. Standardisation of antituberculosis drug resistance surveillance in Europe. Recommendations of a World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD) Working Group. *Eur Respir J* 2000; 16: 364-371.
3. Veen J, Raviglione M, Rieder HL, et al. Standardised tuberculosis treatment outcome in Europe. *Eur Respir J* 1998; 12: 505-510.
4. 2002/253/EC. COMMISSION DECISION (19 March 2002) laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council.
5. WHO Statistical Information System (WHOSIS). WHO Mortality Database. Update 15 October 2007 (www3.who.int/whosis/) (accessed 18 Dec 2007).
6. EuroHIV and the national coordinators for tuberculosis surveillance in the WHO European Region. European Non-Aggregate AIDS Data Set (ENAADS). EuroHIV, Institut de veille sanitaire, Saint-Maurice, France. Updated in December 2006.
7. World Health Organization. Anti-tuberculosis Drug Resistance in the World. 3rd global report. WHO, Geneva, Switzerland 2004. WHO/HTM/TB/2004.343.
8. World Health Organization. Anti-tuberculosis Drug Resistance in the World. 4th global report. WHO, Geneva, Switzerland 2008. WHO/HTM/TB/2008.394.
9. Criteria for discontinuation of vaccination programmes using Bacille Calmette-Guerin (BCG) in countries with a low prevalence of tuberculosis. A statement of the International Union Against Tuberculosis and Lung Disease. *Tuber Lung Dis.* 1994;75(3):179-80.
10. United Nations Population Division. Annual Populations 1950-2050 (The 2006 Revision), United Nations, New York, 2007.
11. EuroHIV. HIV/AIDS Surveillance in Europe. End-year report 2006. Saint-Maurice, France: Institut de veille sanitaire, 2007. No 75.
12. World Health Organization. Case definition for extensively drug-resistant tuberculosis. *Weekly Epidemiol Rec* 2006 Oct 20;81(42):408. (www.who.int/wer/2006/wer8142.pdf).
13. Falzon D, Scholten J, Infuso A. Tuberculosis outcome monitoring - is it time to update European recommendations? *Euro Surveill* 2006; 11 (3):20-5.