

## 6. Technical Note

All the 52 countries of the WHO European Region participate in the tuberculosis surveillance activities co-ordinated by EuroTB (see list of national correspondents on back cover). National surveillance institutions are responsible for the quality of data provided. Country participation is on a voluntary basis. The principles, methods and definitions guiding EuroTB activities are those recommended by working groups including European experts, WHO and the International Union against Tuberculosis and Lung Disease (UNION) [1-4].

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

#### TB case surveillance

Since 1996 (reporting year 1995), data on TB notification for the previous calendar year have been collected annually, some months after the end of the year of report, in order to allow for validation at national level. Data are preferably submitted in individual, anonymous format according to standardised definitions and specifications. Since the reporting year 2003, individual data are requested for the last two years to allow for belated updating of certain data, including the treatment outcome information. Countries may otherwise 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, the EuroTB team validates data in collaboration with the respective country. Since 1999, aggregate TB notification and outcome data have been collected and validated in collaboration with the TB staff in WHO European Regional office, using a web-based information system (Computerised Information System for Infectious Diseases or CISID, <http://data.euro.who.int>).

#### TB/HIV surveillance

Information on HIV sero-status of notified TB cases is collected in aggregate form only. Information on TB morbidity at AIDS diagnosis is derived from European AIDS reporting data (European Non Aggregate AIDS Data Set, ENAADS, produced by the EuroHIV project). The ENAADS dataset includes information on initial AIDS-indicative diseases, which include TB [5]. TB episodes occurring in a patient 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) of 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. Information on the organisation of DRS and on laboratory practices for DST is also collected using a standard form. Data from drug resistance surveys published by WHO are also included in this report [6].

#### Treatment outcome monitoring

Since the reporting year 2002, outcome data are collected for all cases in individual format by resubmission of an updated individual data set for the year before the last (thus in 2005, data were collected for TB cases notified in 2003). Alternatively, treatment outcome data are reported separately in tabular format for definite pulmonary cases by prior treatment history (new, re-treated and unknown).

### 6.2 Data analysis and presentation

#### TB case notification

Updates to information presented in this report were accepted until 21 December 2005. Notification data are not adjusted for under-reporting or over-reporting. The incomplete geographic coverage of notification data from certain countries is noted in the report. For calculation of notification rates, country population denominators by age and sex are taken from United Nations estimates in 2004 [7]. The national correspondent of Serbia & Montenegro supplied population data for the period 1998-2004 for that country. Population estimates by geographic origin for 13 countries were forwarded by the respective national correspondents (Figure 7).

#### TB/HIV surveillance

Information on HIV sero-status of TB cases is incomplete in many countries. HIV prevalence is calculated as the percentage of all TB cases reported known to have a positive test, which may thus result in an under-estimated HIV prevalence. 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. Time trends in numbers of AIDS-defining TB cases are presented by year of diagnosis, adjusted for reporting delays [8].

#### 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. The results for ethambutol and streptomycin are only presented if DST results are available for at least 90% of the cases tested for isoniazid and rifampicin. 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 analysed and presented in two groups:

#### **group A:**

- nationwide data matched with TB case notification in countries where culture is routinely used (at least 50% of cases reported as culture positive in 2004) and DST results for INH and RMP are available for the majority of culture positive cases (at least 80% in 2004) or  
- data from national surveys using representative sampling methodology;

#### **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% 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. Time-trends are only shown for countries with representative data and considered statistically

significant if Chi-squared test for linear trend has a P-value under 0.05.

#### Treatment outcome monitoring

Treatment outcome information is collected for all cases in individual data and for definite (culture positive or sputum smear positive) pulmonary cases in aggregate data. 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 data set updated since initial notification (see above). In countries reporting aggregate outcome data, completeness of cohorts is assessed by comparing the total number of cases initially notified with the sum of new cases, retreatment cases or cases with unknown treatment history included in TOM cohorts.

On the basis of available information, TOM data are classified in two groups for data presentation:

- **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.

#### Geographic areas

Based on epidemiological and geo-political considerations, the 52 countries of the WHO European Region have been grouped into three geographic areas (Table 1, map on cover page of Country Profiles):

- the European Union and West (EU & West): the 25 Member States of the EU plus Andorra, Iceland, Israel, Monaco, Norway, San Marino and Switzerland.
- the Centre: Balkan countries (Albania, Bosnia & Herzegovina, Bulgaria, Croatia, the F.Y.R. of Macedonia, Romania, Serbia & Montenegro and Turkey).
- the East: 12 countries of the former Soviet Union (Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan).

The respective total populations of the three areas were 479, 124 and 278 million in 2004.

Data for 2004 notifications from Greenland and Kosovo are noted in Table 1 and in the Country Profiles of Denmark and Serbia & Montenegro respectively, but are not included in the totals of the latter countries or for the WHO European Region. Data for Northern Cyprus, Abkhazia and Southern Ossetia were not available.

The template for maps included in this report were adapted from the map of the WHO European Region located on WHO EURO website ([www.who.dk](http://www.who.dk)), using the Vertical Near-side perspective, central meridian: 45, reference latitude: 35, height of viewpoint: 20000000-.

### 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.

#### Previous anti-TB treatment status

##### *Never treated case*

A case who never received a 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 who was diagnosed with TB and 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 as defined above. Pleural TB and intra-thoracic lymphatic TB without involvement of the lung parenchyma are classified as extra-pulmonary.

#### Note

- The above definitions conform to the European Commission's definitions for tuberculosis surveillance [4]. Laryngeal disease is enumerated with pulmonary for the scopes of surveillance;
- All definite and other-than-definite TB cases notified in the calendar year of interest should be reported to EuroTB and are included in the totals presented in this report. Cases should be notified only once in a given calendar year;
- 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 (cases having bacteriologically positive TB who had previously completed treatment for tuberculosis) are included in notifications in all countries whereas cases retreated after failure or after default or chronic cases are variably included in notifications across countries. In countries where information on previous anti-TB treatment is incomplete or not available, previous treatment status is classified according to whether or not TB had been previously diagnosed;
- 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, larynx or tracheo-bronchial tree are involved, and as extra-pulmonary otherwise. Miliary tuberculosis is thus classified as pulmonary. In individual data, detailed information is collected on the major site and one minor site of disease. The pulmonary localisation when present is always classified as the major site. In countries using the respiratory classification of disease - in contrast to the

recommended pulmonary classification - cases with pleural and intra-thoracic lymphatic TB are classified as 'respiratory' cases, and cases with disease of any other site 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). 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

*Mono-resistance:* resistance to a single first-line anti-TB drug (isoniazid, rifampicin, ethambutol or streptomycin).

*Poly-resistance:* resistance to at least two of the first line anti-TB drugs listed above.

*Multi-drug resistance:* resistance to at least isoniazid and rifampicin.

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

*Resistance among cases previously treated:* it 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 [6].

#### Treatment outcome

##### *Cohort*

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

Note: in countries having individual outcome information, outcome is collected for all TB cases notified.

##### *Period of observation*

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

#### *Outcome categories*

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

##### *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 at 5 months or later during 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 referral 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 (ie. 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.

## **6.4 References**

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## Surveillance of Tuberculosis in Europe (EuroTB): participating correspondents and institutions (2005-2006)

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