

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 correspondants on the inside cover). Country participation is on a voluntary basis. National surveillance institutions are responsible for the quality of data provided. 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

Data on TB notification for the previous calendar year are collected annually since the reporting year 1995, some months after the end of the year of report, in order to allow for validation and consolidation at national level. Data are collected preferentially as individual, anonymous data, according to standardised definitions and specifications. Since the reporting year 2003, individual data are collected for the two last years to allow for collection of treatment outcome information (see below). Countries which do not provide individual data, 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 are 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)

Results of drug susceptibility testing (DST) for initial isolates of *M. tuberculosis* are collected since the reporting year 1998 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 [6] are also included in this report.

Treatment outcome monitoring

Since the reporting year 2002, outcome data are collected for all cases in individual form by resubmission of an updated individual data set for the year before the last. Alternatively, aggregate treatment outcome data are reported by history of previous anti-TB treatment, for definite cases notified in the calendar year before the last (i.e. in 2002 for data collected in 2004).

6.2 Data analysis and presentation

TB case notification

Updates to information presented in this report were accepted until 15 June 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 2002 [7], except for Andorra and San Marino [8,9] and Monaco (2000, provided by the national correspondent). Population estimates by geographic origin are provided by national correspondents and were last updated in in 2002-2003. Differences between data published in EuroTB and

WHO reports [10] are mainly due to continuing data validation by EuroTB after the deadline for publication of WHO report.

TB/HIV surveillance

Information on HIV sero-status of TB cases is incomplete in many countries. HIV prevalence is calculated on the total number of TB cases reported, including those with unknown HIV serostatus, which may result in under-estimated HIV prevalence among TB cases. AIDS data for the latest year are presented by year of report. To provide a conservative estimate of the proportion of HIV-associated TB, numbers of AIDS cases with TB as initial AIDS indicative disease are divided by total TB cases notified in the same year. Time trends in numbers of AIDS-defining TB cases are presented by year of diagnosis, adjusted for reporting delays [11].

Drug resistance surveillance

Data on the results of DST at the start of treatment for isoniazid, rifampicin, ethambutol and streptomycin 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 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 2003) and DST results for INH and RMP are available for the majority of culture positive cases (at least 80% in 2003) or
- data from national surveys with a defined sampling frame;

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 tested using Chi-squared test for linear trend and considered statistically significant if P-value is less than 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) should include 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. In countries providing 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 98% of definite pulmonary TB cases notified, considered as country-representative and complete
- **group B**, cohorts including less than 98% of TB cases initially notified, or from selected areas, or for which data for assessing completeness of TOM cohorts were not available.

Outcome data may also differ due to presentation of culture positive cohorts and pooling of national data from DOTS and non-DOTS areas in EuroTB reports.

Geographic areas

Based on epidemiological and geographical considerations, the 52 countries of the WHO European Region have been grouped into three geographic

areas (see map):

- 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: 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 Federa-

tion, Tajikistan, Turkmenistan, Ukraine and Uzbekistan).

The respective total populations of the three areas were 475, 126 and 280 million in 2003.

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), 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.

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.

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.

Note: 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 (retreated cases having bacteriologically positive TB previously declared cured or completing treatment) 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.

Site of disease*Pulmonary case*

A case with TB affecting the lung parenchyma and/or the tracheo-bronchial tree

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: Cases with both pulmonary and extra-pulmonary localisation are classified as pulmonary cases. Cases with disseminated TB (i.e. TB involving more than two organ systems, miliary TB or isolation of *M. tuberculosis* complex from blood) are classified as pulmonary if the lung parenchyma or tracheo-bronchial tree are affected and as extra-pulmonary otherwise. In individual data, detailed information is collected on the major site and one minor site of disease. The pulmonary localisation is always classified as the major site.

As an alternative to the recommended "pulmonary" classification above, cases are classified according

to the "respiratory" classification, in which pleural and intra-thoracic lymphatic TB cases are classified as respiratory cases together with pulmonary 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 providing individual outcome information, outcome is collected for all TB cases notified (not shown in the report).

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 [3,4], 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

6.4 References

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