2. TECHNICAL NOTE

All the 51 countries of the WHO European Region participate in the tuberculosis surveillance activities co-ordinated by EuroTB. National surveillance institutions are appointed for participation in EuroTB activities and 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 WHO and the International Union against Tuberculosis and Lung Disease (IUATLD) and approved by European country representatives **[1-3].**

2.1 Data collection and management

Data are collected once per year. In order to allow for validation and consolidation at national level, data are collected several months after the end of the reporting year of interest and treatment outcome data more than 18 months after the end of the reporting year of interest. Data reported for previous years are not routinely updated.

TB case surveillance

Individual, anonymous data, according to standardised definitions and data file specification are collected yearly on TB cases notified at the national level in the previous calendar year. Individual data are validated by the EuroTB team in collaboration with national correspondents and then collated in a European data set.

When individual data cannot be provided, data on TB cases notified are provided as aggregate data through standard tables including numbers of TB cases by age and sex, geographic origin, previous anti-TB treatment status (never treated / previously treated), site of disease and bacteriological confirmation (culture and sputum smear results). Since 1999, aggregate data are being collected jointly with the WHO Regional Office for Europe, using a common form which includes sections on characteristics of national surveillance and TB control policies and on treatment outcome monitoring. The form may be completed through the Internet, via the Computerised Information System for Infectious Diseases (CISID), an application developed by the WHO Regional Office for Europe, or using electronic or paper versions. Data provided are validated by both WHO and EuroTB teams. After validation, specific aggregate data sets are created (e.g. data by sex and age group) which also include data initially provided in individual form and constitute the basis for the analyses published in this report. Data presented in this report may differ from those published from WHO **[4],** mainly due to the later provision of individual data or to further validation of data.

Drug resistance surveillance (DRS)

Since 1998, data on the results of drug susceptibility testing (DST) at the start of treatment for isoniazid, rifampicin, ethambutol and streptomycin are collected yearly, together with information on the organisation of DRS and on laboratory practices for DST. DST results are provided as "susceptible" or "resistant". If the proportion method is used for DST, resistance is defined as $\geq$ 1% colony growth at the critical concentrations of the drug being tested.

In countries providing individual data on TB cases, DST results are usually provided as part of the individual data set (see below). In countries unable to provide individual data or where DRS is not linked to TB case notification, DST results are provided in aggregate form including total number of cases with DST results and numbers of cases resistant to each drug or drug combination, by previous anti-TB treatment status and by geographic origin.

According to the characteristics of national DRS, data provided to EuroTB may be collected for all culture positive TB cases notified in the country or for TB cases diagnosed in selected laboratories or clinical centres, with variable geographic coverage. In the latter case the representativeness of data collected is frequently unknown. In countries where culture and/or DST are not routinely performed at TB diagnosis, results of DST done for diagnostic purposes may be unrepresentative. The geographic coverage of DRS is partial in some countries. Due to these differences DRS data are analysed and presented in two groups:

group A includes countries in which:

- culture and DST at the start of treatment are routinely performed at TB diagnosis

and

- DST results are collected for all or large national samples of culture positive TB cases notified in the country or included in representative national surveys;

group B includes countries in which:

- culture and/or DST at the start of treatment are not routinely performed at TB diagnosis

or

- DST results are collected on TB cases diagnosed in selected laboratories / clinical centres, not linked to TB notification,

or

- DST data provided have partial geographic coverage.

Data in group A are considered as representative. Data in group B, unless deriving from well-designed surveys or sentinel surveillance systems, should not be considered as representative of the country situation, particularly in countries where culture and DST are not routinely performed for TB diagnosis.

In order to provide an indication of primary and acquired drug resistance, data are analysed by previous anti-TB treatment status. Resistance among cases never treated indicates primary resistance and resistance among cases previously treated indicates acquired drug resistance. In countries providing individual data with missing or incomplete information on previous anti-TB treatment status, DST results are presented by previous TB diagnosis instead of previous anti-TB treatment status.

Proportions of cases resistant to specific drugs are calculated using as a denominator cases with available DST results for at least rifampicin and isoniazid. 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.

Treatment outcome monitoring (TOM)

Treatment outcome information is collected in aggregate form separately for sputum smear positive cases and for pulmonary culture positive cases (regardless of sputum smear status) notified in the calendar year before the last (i.e. in 1999 for data collected in 2001). In each group of cases, outcome information is collected separately for new and retreated cases, for a total of four groups of cases (cohorts). Cases notified but non-eligible for TOM (e.g. reclassified during follow-up because of final diagnosis other than TB, clerical errors, elimination of duplicate reports, etc.) are excluded from analysis. The criteria for non-eligibility for TOM differ across countries. For example, cases diagnosed post mortem, or defaulting before the start of treatment may be excluded in some countries but not in others.

In order to estimate the "completeness of inclusion" of notified cases in TOM cohorts, the sum of new and retreated cases considered for TOM (i.e. eligible and non-eligible) was compared with the total number of smear positive or pulmonary culture positive TB cases notified to EuroTB for the same year (i.e. including those initially reported with unknown anti-TB treatment status). When large differences between those figures were observed, information on inclusion criteria in use was requested from the countries. In countries providing TOM data from selected areas the same comparison was made to estimate TOM coverage.

Outcome categories used for data collection are those internationally recommended **[3, 5]**, with an additional category "other / unknown" to classify cases with no information on outcome. However, outcome definitions in use at country level differ. For example, in some western European countries bacteriological information to distinguish cure from treatment completion is not available or incomplete and cases who are still on treatment at the time of outcome assessment are classified in a category "still on treatment" and reported internationally in the category "other / unknown". These differences limit the use of TOM data for international comparisons. Further harmonization of TOM in Europe is currently being discussed.

Data published may differ from those published from WHO **[4]** due to further validation and to inclusion in the cohorts of cases with no information on outcome.

Surveillance of TB-HIV coinfection

HIV serostatus of TB cases is collected through TB notification in some European countries **[6]** but this information is not routinely reported at the European level. TB is an AIDS indicative disease **[7]** and information on TB as an AIDS indicative disease in Europe, available through the project "Surveillance of HIV/AIDS in Europe" (EuroHIV), provides an indication of TB morbidity at AIDS diagnosis. It should be emphasized that TB diagnosed at the time of AIDS represents an underestimate of HIV-associated TB, as TB diagnosed in HIV infected individuals after AIDS is not reported to AIDS notification systems.

Data from the European Non Aggregate AIDS Data Set (ENAADS), of which a public version is available are presented in Table 16. To be consistent with TB notification data, AIDS data from ENAADS are presented by year of report, which leads to figures different from those published by EuroHIV, which are based on year of diagnosis, adjusted for reporting delays.

2.2 Definitions

Case definition

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* complex.
- 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 case 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

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 previously treated cases, relapses are included in notifications in all countries whereas the notification of other previously treated cases (failures, returns after default and chronic cases) varies across countries **[8]**. In countries where information on previous anti-TB treatment is not available or is incomplete, previous treatment status is classified according to previous TB diagnosis.

Site of disease

Pulmonary case

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

Extrapulmonary case

A case with TB affecting any site other than pulmonary as defined above. Pleural TB and intrathoracic lymphatic TB without involvement of the lung parenchyma are classified as extrapulmonary.

Cases with both pulmonary and extrapulmonary localisation are classified as pulmonary cases. Cases with disseminated TB (i.e. TB involving more than two organ systems, miliary TB or isolate of *M. tuberculosis* complex from blood) are classified as pulmonary if the lung parenchyma or tracheo-bronchial tree are affected and as extrapulmonary 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 can be classified according to the "respiratory" classification, in which pleural and intrathoracic lymphatic TB cases are classified as "respiratory" cases together with pulmonary cases (as defined above), and cases with disease of any other site as extrarespiratory.

Geographic origin

The geographic origin of TB cases is provided according to place of birth (born in the country / foreign born) or, if unavailable, citizenship (citizen / non citizen). The specific country or continent of origin is collected in individual data.

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.

Treatment outcome

Cure: A patient who is culture or sputum smear-negative in the last month of treatment and on at least one previous occasion.

Treatment completion: A patient who has completed treatment, but who does not meet the criteria to be classified as cure or treatment failure.

Success: A patient who was cured or successfully completed treatment.

Treatment failure: A patient who is culture or sputum smear-positive at five months or later during treatment.

Death: A patient who dies for any reason during the course of treatment.

Default: A patient whose treatment was interrupted for two consecutive months or more.

Transfer: A patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known.

Other / unknown: A patient who does not meet the criteria of the outcome categories above or for whom no outcome information is available.

2.3 Data presentation

The numbers of cases are not adjusted for under-notification or for over-notification, on which the most recent country estimates were provided for 1997 **[9]**. For calculation of notification rates, country population denominators by age and sex are taken from United Nations demographic estimates, 2000 update **[10]**, except for Andorra, Monaco and San Marino **[11]** and for Yugoslavia (provided by national correspondent). Population estimates by geographic origin (last updated in 1999) were provided from national correspondents.

Based on epidemiological and geographical considerations, the 51 countries of the WHO European Region have been grouped into three geographic areas:

- West: the 15 European Union countries (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, and United Kingdom) plus Andorra, Iceland, Israel, Malta, Monaco, Norway, San Marino, Switzerland);
- Centre: Albania, Bosnia-Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, the Former Yugoslav Republic of Macedonia, Poland, Romania, Slovakia, Slovenia, Turkey, Yugoslavia.
- East: the 15 Newly Independent States of the former Soviet Union: Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan.

The respective total populations of the three areas were 397, 185 and 291 million in 2000.

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: 20 000 000-.