3. TUBERCULOSIS CASES NOTIFIED IN 2000

3.1 Completeness of TB notification

Geographic coverage

All countries provided data on TB cases notified in the whole country, except Yugoslavia where cases in Kosovo were not included and Denmark, where cases from Greenland and the Faeroe islands were not included.

Previously treated cases

In all countries, both new and previously treated TB cases were notified. However, the criteria for notification of previously treated cases differ across countries **[8]**, which can affect the comparison of notification data for recurrent cases. Completeness of reporting improved in 2000 in the East, with only five countries providing parts of their data on new cases alone, down from 10 in 1999.

Site of disease

Countries notified TB cases with any disease localisation, except for Spain, where notification of extrarespiratory cases was limited to meningeal TB, and where total notification rates are therefore not comparable with those of other countries.

Inclusion of specific population groups

In 2000, 32 countries included in their TB notifications cases diagnosed in specific population groups (Table 1), i.e. foreigners, prisoners, military personnel, homeless, persons with HIV infection or AIDS and institutionalised persons. In the other countries one or more of the groups listed above were not included in TB notification, which directly affects completeness of reporting.

Sources of reporting

In 25 countries (14 in the West, 7 in the Centre and 4 in the East), both clinicians and laboratories notified TB cases whereas in the other countries only clinicians notified TB cases. Laboratory reporting is recommended **[2]** and may result in higher completeness of reporting for definite cases.

3.2 Information provided

All the 51 countries in the WHO European Region provided data on national notification systems and on TB cases notified in 2000 (Tables 1-3). No TB cases were notified in Monaco. Individual data on TB cases were provided from 24 countries (16 in the West, seven in the Centre and Estonia).

A breakdown of cases by sex was provided from all countries except Turkey (Table 4). The number of cases by age group was provided from all countries except Azerbaijan, Belarus, Kyrgyzstan and Turkey (Table 5). Paediatric age groups provided from the Russian Federation (0-6 and 7-14 years) were different from those requested (0-4 and 5-14 years). The distribution of cases by both age group and sex was also available for most countries (Country profiles). The distribution of cases by site of disease and sputum smear result was available for most countries, whereas information on previous anti-TB treatment status (43/51), geographic origin (34/51) and culture result (42/51) was less complete.

Geographic origin of cases was provided from 34 of the 42 countries that include cases of foreign origin in TB notifications (all 23 countries in the West, seven countries in the Centre and four countries in the East, Table 6). Cases were classified by country of birth, as recommended, in 25 countries, by citizenship in 8 countries and variably in the two parts of Bosnia-Herzegovina. In addition to the 43 countries providing case classification by previous anti-TB treatment status, three others provided only information by previous TB history (Table 9).

All countries notified cases with any anatomic localisation, except for Spain, which notified only respiratory and meningeal TB cases. Numbers of cases by site of disease were available for all countries except Turkmenistan and Uzbekistan (Table 10). The recommended pulmonary classification (see technical note) was used in 34 countries and the respiratory classification in 16 countries. In 2000, three countries in the East moved from respiratory to pulmonary classification. Information on the major site and one minor site of disease (see technical note)

was available for 15 countries, representing 63% of individual records reported (Table 11).

In 2000, culture for *Mycobacteria* was considered to be routinely performed for diagnosis of pulmonary TB in the whole country in 37 countries and in some areas in 11 countries. In Albania and Moldova culture was not routinely performed, while no information was provided from Turkey (Table 12). In countries providing individual data, information on culture was quite incomplete: 79% of pulmonary cases in the Centre and 61% in the West, and 42% of extrapulmonary cases in each area. Sputum smear was considered to be routinely used for TB diagnosis in the whole country in 43 countries (Table 15).

3.3 General figures and trends

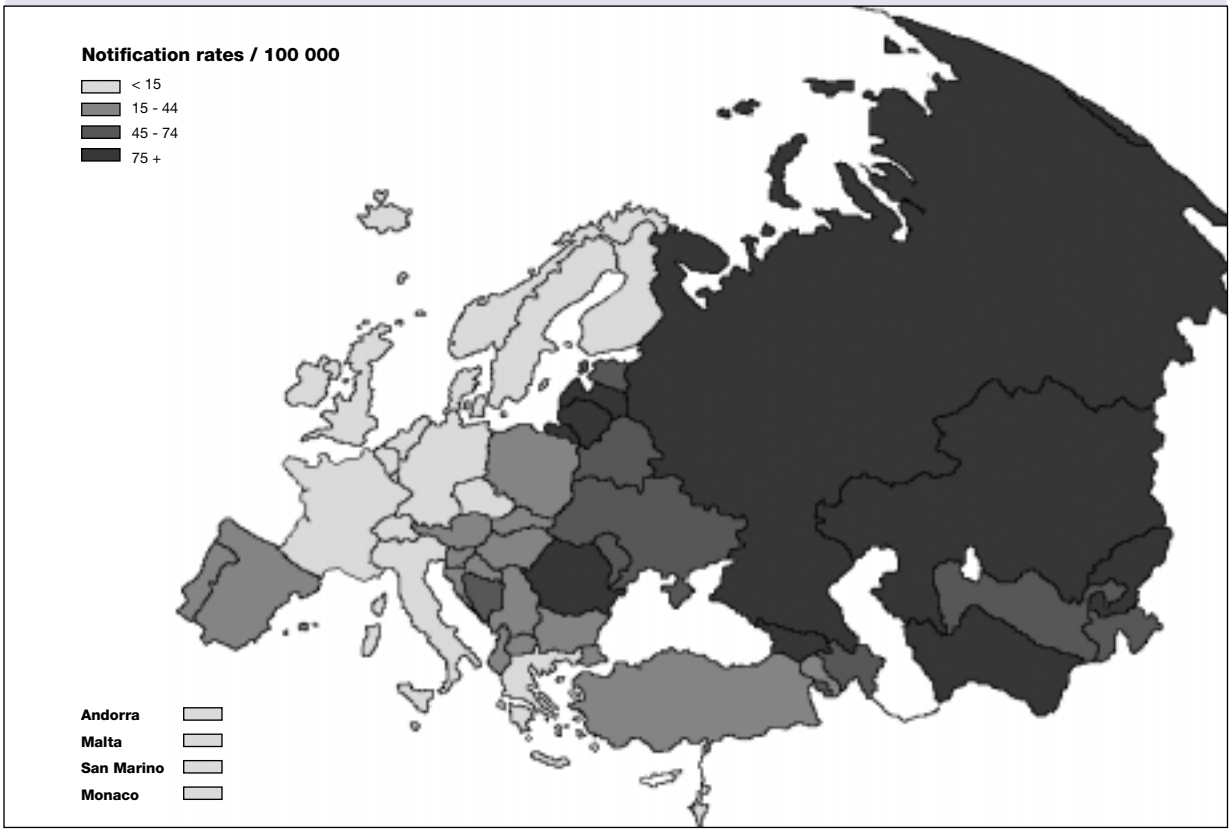
In 2000, 385 810 TB cases were notified by the 51 countries of the WHO European Region, representing 10.5% of notifications made to WHO worldwide in the same year **[4].** In the European Region, 68% of notifications derived from the East, 20% from the Centre and 13% from the West (Table 3). In the East, 55% of the cases were notified by the Russian Federation. In the Centre, 37% of the cases were from Romania and 24% from Turkey.

The overall notification rate was 44 per 100 000 population, with important geographic variations between areas and countries (Table 3, Map 1). TB notification rates in 2000 were:

- 12 per 100 000 population in the West, where rates were 15 or less in 21 countries, and were higher in Portugal (45) and in Spain (21);
- 41 per 100 000 population in the Centre, ranging between 20 and 44 in nine countries, lower in the Czech Republic (14) and Slovenia (19) and higher in Romania (124) and in Bosnia-Herzegovina (66);
- 90 per 100 000 population in the East, where rates were 45 or more in all countries except Armenia (36), and were highest in Kazakhstan (175), Kyrgyzstan (130) and Georgia (122).

Trends in notification rates between 1995 and 2000 varied widely across areas and countries (Table 3, Figures 1-3 and Country profiles). In the West, the overall notification rate was 14% lower in 2000 than in 1995, with an average annual decrease of 3.1%. This rate of decline was sharper than that observed between 1990 and 1995 (1.0%), when a net increase in notification rates was actually observed between

Map 1. Tuberculosis notification rates per 100 000 population, 2000



1991 and 1993, reflecting a tendency in six of the 19 countries depicted in Figure 3. However, the downward trend in mean annual rates between 1995 and 2000 was lower than that observed between 1985-1990 (4.5%), and from 1974 to 1985 (4.9%, 14 countries **[12]**). In countries reporting more than 20 cases in 2000, between 1995 and 2000, rates decreased by an annual average of 2% to 6% in 10 countries with stable surveillance by systems. Rates decreased by less than 2% yearly in Belgium and Italy, increased by less than 2% yearly in Norway and in the United Kingdom, and increased by more than 2% yearly in Denmark, and Luxembourg (Figure 2). In 10 countries with available data, average annual decreases in

Figure 1. Tuberculosis notification rates by geographic area, 1995-2000

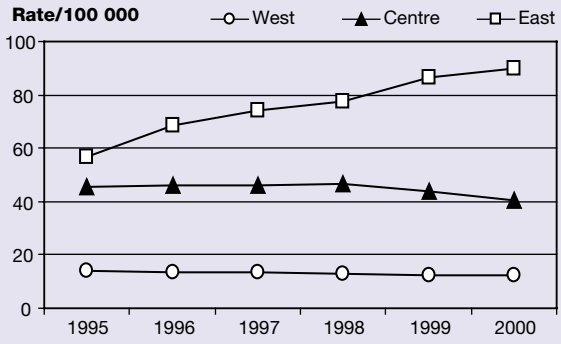
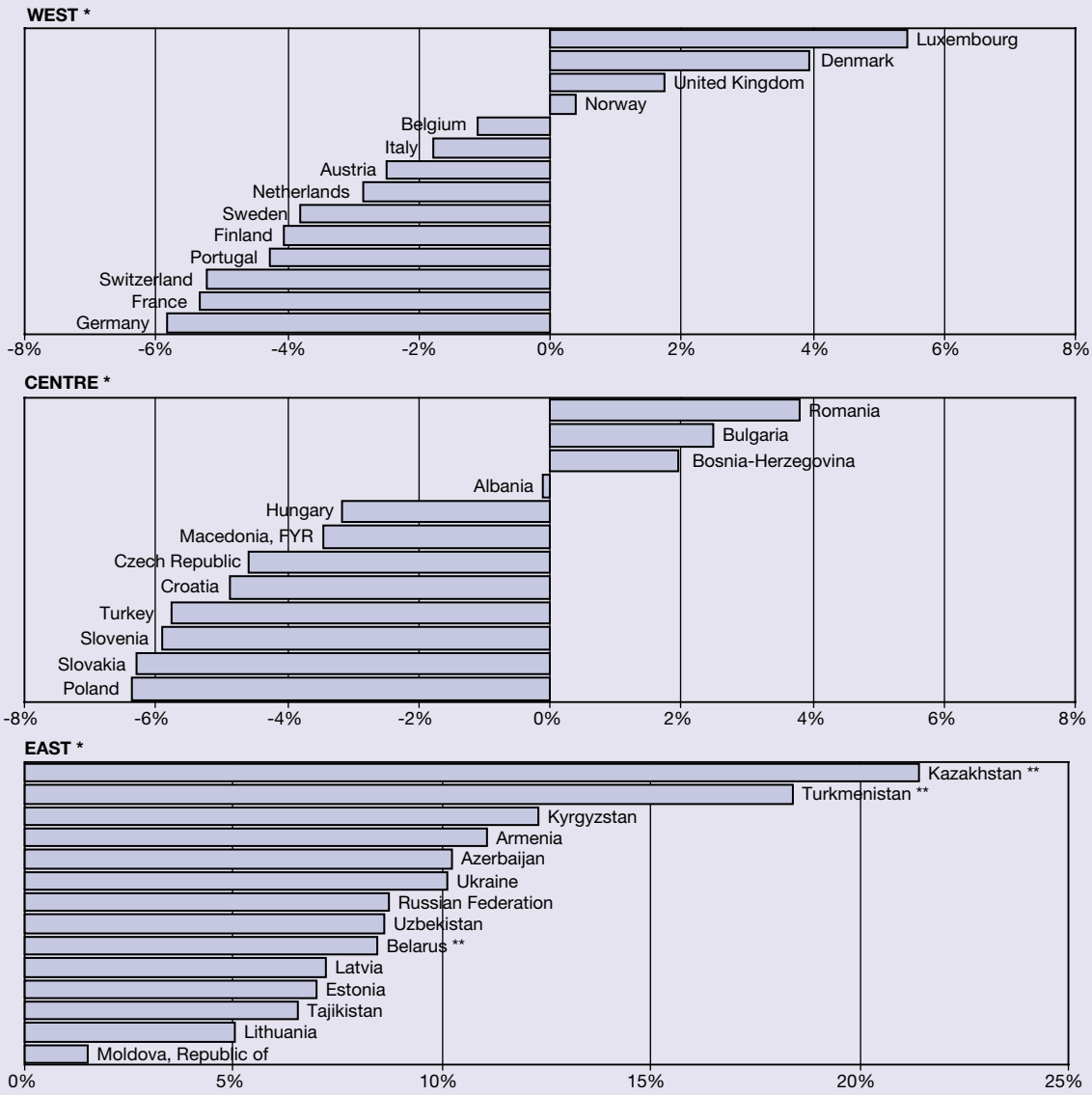
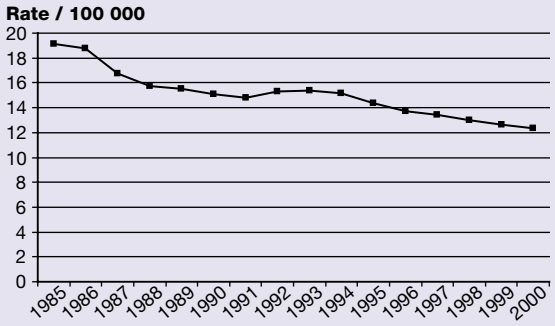


Figure 2. Mean annual percentage change in TB notification rates, 1995-2000



* Countries with > 20 cases notified in 2000 and stable TB notification system
** Calculated on selected years with comparable data.

Figure 3. Trends in TB notification rates, Western Europe *, 1985-2000 **



* Excluding Andorra, Greece, Monaco and San Marino (missing data points).
** Main source of data for 1985-1994: WHO (see ref. 5)

the numbers of notified cases between 1995 and 2000 were more marked among nationals (-7%) than among persons of foreign origin (-1.5%) (See Figure 6 and Section 3.5 below).

In the Centre, overall notification rates were 12% lower in 2000 than in 1995, with notification rates decreasing on average by 3 to 7% yearly in nine countries, stable in Albania and increasing by 2-4% yearly in Bosnia-Herzegovina, Bulgaria and Romania. Wide yearly fluctuations in rates in some countries may point to unstable notification systems, on which detailed information is not available. Stable or increasing rates, may indicate sub-optimal performance of TB control in Albania, Bulgaria and Romania, and the effects of the war in Bosnia-Herzegovina, where rates peaked in 1998-1999. The extremely high and increasing notification rates in all age groups in Romania indicate a persisting high level of TB transmission, making it distinct from other countries in the Centre.

In the East notification rates were 57% higher in 2000 than in 1995 (excluding Georgia where no data were available for 1995), with mean annual increases of 5-12% in most countries. In Kazakhstan, the yearly increase since 1997 averaged 21%. Between 1999 and 2000, the increase of notification rates was higher than 5% in six countries, down from 12% between 1995 and 1996). In several of these countries, recent trends in notifications may have been variably affected by global changes in health and surveillance systems, including the increasing notification of cases diagnosed in specific population groups such as prisoners and foreigners, not previously included in statistics (see Section 3.1), and by increasing case detection in the context of expanding DOTS implementation.

In several countries in the East increasing incidence is coupled with high levels of multi-drug resistance (see Section 5 and **[13]**) and with the spread of HIV epidemics, starting in 1995 **[14].** HIV co-infection is expected to increase TB caseload in the coming years. In some countries in the East, TB represented a major cause of morbidity among AIDS cases reported in 2000 (see Section 4). These elements depict a serious situation, which deserves urgent large-scale public health interventions.

3.4 Sex and age

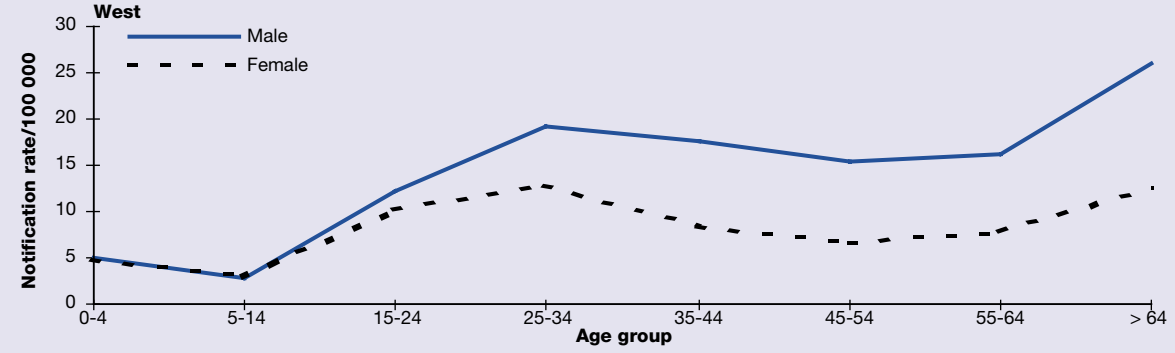
Sixty-nine percent of all TB cases notified in 2000 were males (Table 4). As in 1999, the proportion of male cases notified increased from West (62%) to Centre (66%) to East (71%). Twenty countries, of which 10 in the East, reported two times or more cases in males as in females. While this suggests regional differences in frequency of disease by sex, it may also be a result of differential notification practices and access to care.

Paediatric cases (0-14 years) accounted for 5% of cases overall (Table 5), with less than one third of these under 5 years. Notifications in the age-group 0-14 years represented more than 10% of cases notified in Israel, the FYR of Macedonia, Malta, Tajikistan, Turkmenistan and Uzbekistan, suggesting over-notification of paediatric TB cases in some of these countries. In the West, rates were higher in children under 5 than in children aged 5-14 (Figure 4), reflecting higher risk of developing TB after infection in younger children than in older children **[15]**. Rates were comparable in the two paediatric age groups in the Centre and the East, suggesting that over-reporting of paediatric cases, where occurring, concentrates in the age group 5-14 years.

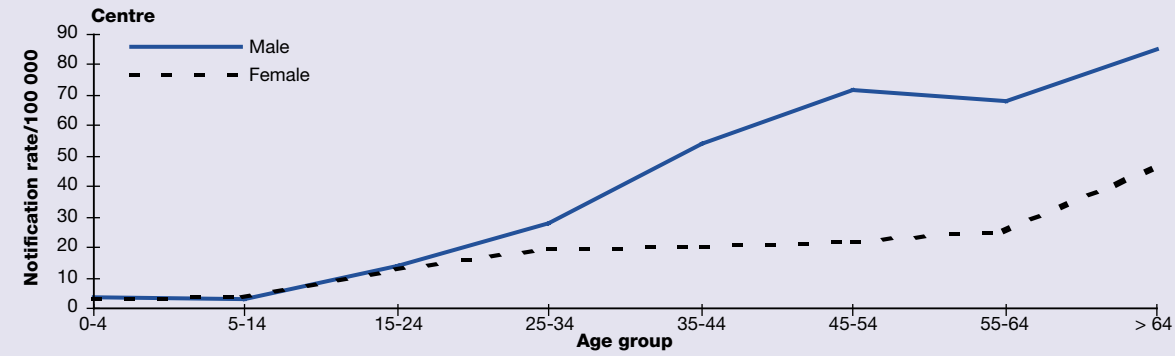
Among adults, the age group 15-44 years accounted for 48% of the cases notified in the West, 44% in the Centre and 63% in the East. Conversely, the age group over 64 years represented 24% of the cases in the West, 18% in the Centre and 6% in the East.

The ratio of males to females was found to vary by age. While it was 1.1 among those under 15 years, the ratio increased to 3.0 in the age group 45-54 years, decreasing to 1.4 amongst those over 64 years. The high sex ratio in the 45-54 age group was observed in all the three areas, but was more pronounced in the Centre and in the East (Figure 2) than in the West. While this trend was observed amongst

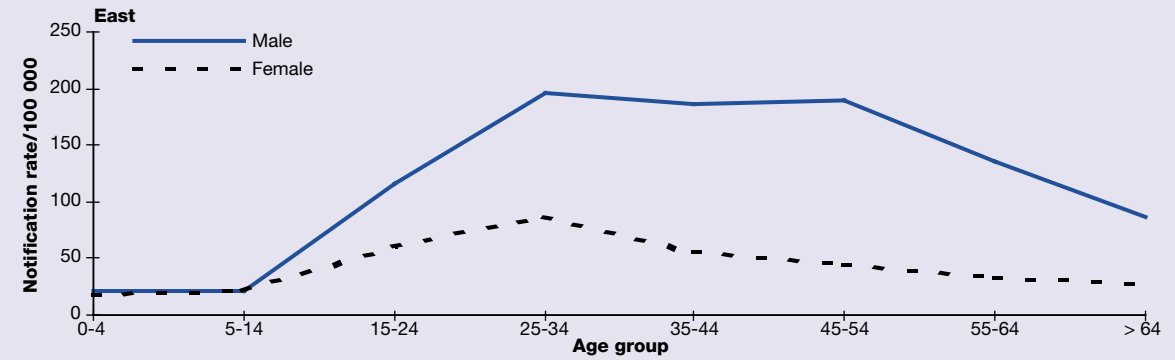
Figure 4. Notification rates by age group and sex, 2000



Excluding Andorra and San Marino



Excluding Romania and Turkey



Excluding Azerbaijan, Belarus and Kyrgyzstan
For Kazakstan, Russian Federation and Ukraine, new cases only
Paediatric age groups for the Russian Federation: 0-6 and 7-14 years

national cases, foreigners tended to have lower sex ratios at nearly all ages when compared to nationals, except in young adulthood (Figure 5 and Country profiles).

In the West, age specific notification rates among men were relatively stable across the age groups 25-34 years to 55-64 years and were highest among the elderly (over 64 years). In women, rates were highest in the age groups 25-34 years and among the elderly. In the Centre, rates increased markedly after age 14 in men but less so in women, resulting in large sex differences in the age groups 35-44 years and older. In the East, rates were highest in the age group 25-34 years in both sexes and decreased steadily from the age group 35-44 years in women. Among men rates remained high until the age group 45-54 years and decreased markedly in the older ages.

The higher TB notification rates in adult men compared to women observed in all countries result from higher prevalence of infection in men **[16]**. The larg-

er difference in notification rates by sex observed in the Centre and in the East could also be partly explained by under-reporting of female cases due to differences in the access to health services in some countries **[17]**.

The higher notification rate in the older age group in the West mainly reflects reactivation of old *M. tuberculosis* infection. Higher notification rates in young adults in the East indicate high levels of transmission in recent years in this area. However, it should be pointed out that a large proportion of cases from the East were new cases (82% of cases included in Figure 4), which have a median age 5 years lower than cases with previous TB episodes (based on individual data, not shown).

In the 32 countries providing the age distribution of TB cases by geographic origin, the proportion of cases aged 15 to 34 years was much higher in foreigners (46%) than in nationals (26%) (see Section 3.5 and Country profiles).

In the 15 countries in the West and Centre with decreasing total notification rates between 1995 and 2000, and with available data (Figure 2), the age specific rates decreased in the under-45 population, except in Austria, Macedonia and Slovenia (0-14) and Belgium (15-44) (Country profiles). This suggests decreasing transmission in the West and Centre. In the East, in contrast, age specific TB notification rates increased in the under-45 population in five countries with available data (Armenia, Estonia, Latvia, Lithuania and Rep. of Moldova), although decreasing in the 0-14 age group in Armenia. Trends in the East have to be interpreted with caution, considering the recent inclusion of cases from specific population groups (e.g. prisoners in the Rep. of Moldova), which may have variably affected the age distribution of cases over this time period.

3.5 Geographic origin

In the West, cases of foreign origin represented 30% of notified cases overall and more than 40% in nine countries (Table 6, Map 2). In the Centre and in the East, countries reporting the highest proportions of foreign-born cases were Slovenia (25%), Estonia (23%) and Croatia (11%).

Map 2. Proportion of tuberculosis cases of foreign origin, 2000

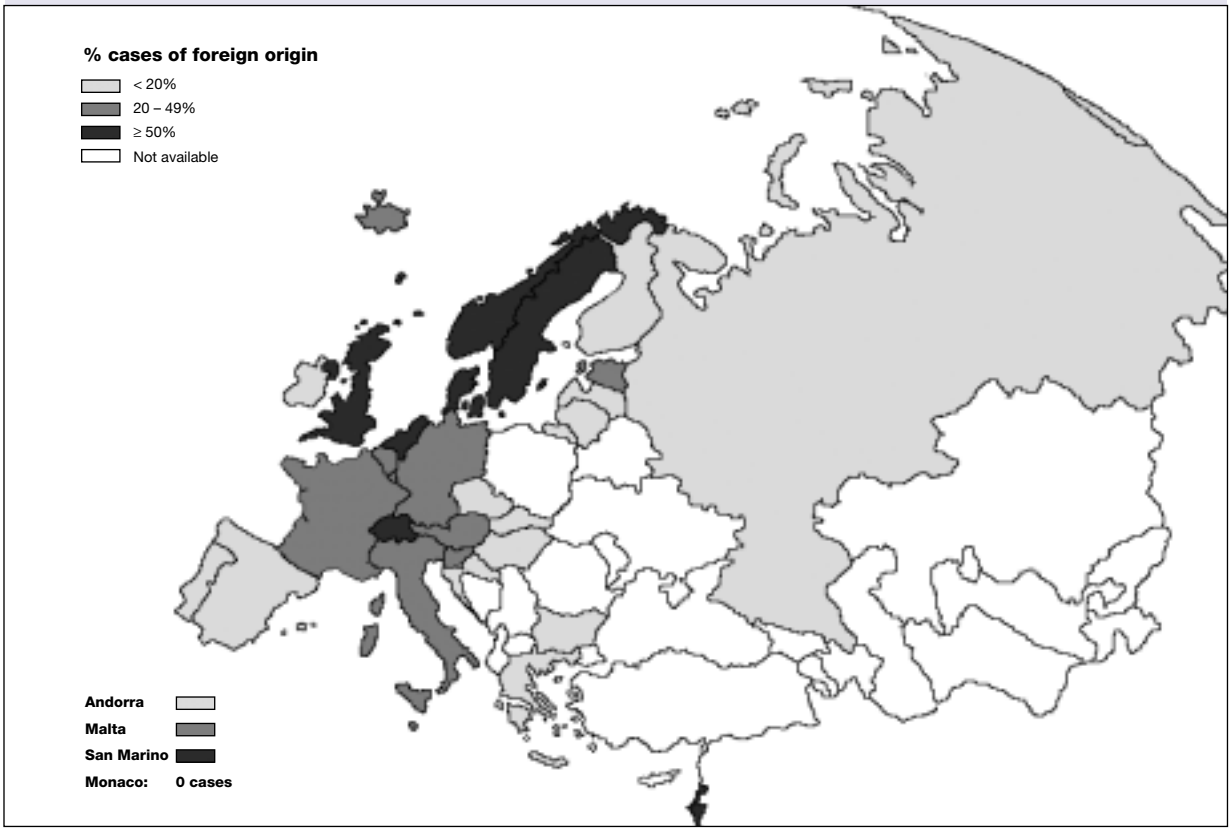
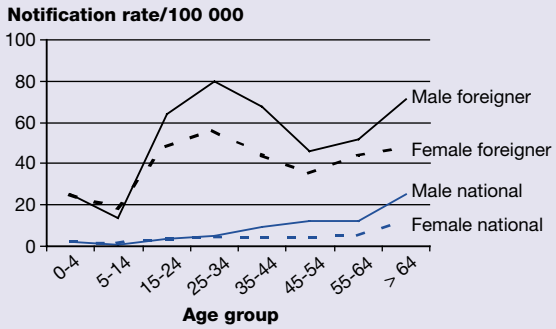
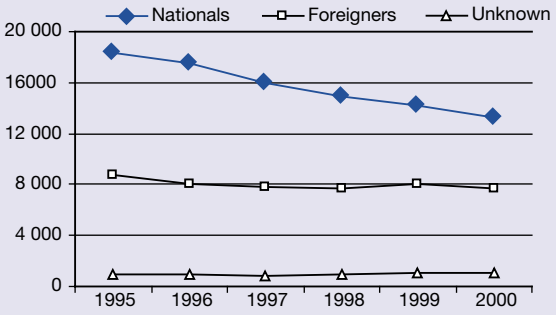


Figure 5. TB notification rates by age group, sex and geographic origin, 11 countries *, 2000



* Austria, Belgium, Denmark, Finland, France, Germany, Iceland, Netherlands, Norway, Slovenia, Sweden

Figure 6. Tuberculosis cases by geographic origin, Western Europe *, 1995-2000



* Austria, Belgium, Denmark, Finland, France, Germany, Netherlands, Norway, Sweden, Switzerland

In 11 countries providing denominator population statistics (Austria, Belgium, Denmark, Finland, France, Germany, Iceland, The Netherlands, Norway, Slovenia, Sweden), notification rates were overall seven times higher in foreigners (49.7 per 100 000) than in nationals (7.2), with rate ratios ranging from 2.8 in Slovenia to 37 in The Netherlands and in Norway. In the population of foreign origin, age specific notification rates were higher in men than in women, and peaked in the age groups 25-34 and over 64 years (Figure 5). Among nationals, adult rates increased regularly with age and were highest in the age group over 64 years. Rates in nationals were much lower at all ages than those in the foreign population. These differences in rates by geographic origin depend on migration patterns, which vary widely across western Europe and should be interpreted with caution considering the difficulties in obtaining accurate denominators for the population of foreign origin.

Notifications in nationals in the West decreased progressively from 1995 to 2000 (Table 7 and Country profiles). The downward trend in total notifications in the West from 1995-2000 (Figure 6) was steeper in cases amongst nationals (28%) than amongst foreigners (12%), resulting in an increase in the proportion of TB notifications in persons of foreign origin from 31% in 1995 to 35% in 2000. TB among nationals decreased in five countries of the Centre over the period 1997-2000 and increased significantly in Romania. (Table 7)

In 22 countries providing information on country of origin (Table 8), 37% of cases of foreign origin were from Africa (10% from Somalia and 5% from Morocco), and 32% from Asia (20% from the Indian subcontinent). Twenty three percent were from a country of the WHO European Region other than the country of notification: 14% from the Centre (the majority from the countries of the former Yugoslavia), 5% from the West and 3% from the East.

3.6 Previous anti-tuberculosis treatment

Overall, 88% of TB cases notified in 2000 had never been treated for TB, 10% had been previously treated for TB and 2% had no information on previous anti-TB treatment (Table 9). Cases with missing information on previous anti-TB treatment were concentrated in the West, where they represented 18% of cases. A minority of these cases had been previously diagnosed with TB.

No clear West – East trend could be observed in the proportion of cases with a history of anti-TB treatment. Previously treated cases represented 7% of the cases in the West (range 0-14%), 12% in the Centre (6-17%) and 10% in the East (1-32%). Some of these variations may reflect differences in definitions used (e.g. previous TB history being used as a proxy for past treatment), as well as in completeness of notification of previously treated cases (see Section 3.1). Therefore, these data cannot be interpreted as an indicator of the effectiveness of previous anti-TB treatments.

3.7 Site of disease

In the 20 countries in the West using the pulmonary classification, the proportion of pulmonary cases was 70% (range 58-99%, Table 10). Pulmonary cases represented 86% (range 62-93%) of cases in the countries in the Centre and 82% (range 73-95%)

in the countries in the East using the pulmonary classification. Respiratory cases represented 94% of cases in the countries in the Centre (range 77-99%) and 95% in the countries in the East (range 85-96%) using the respiratory classification.

In the West in 2000, extra-pulmonary TB was much more frequent in cases of foreign origin than in nationals (37% versus 25%). This partly explains the higher frequency of extra-pulmonary cases in the West compared to the Centre and East, although there may also be differences in completeness of notification of extra-pulmonary cases within the Region.

In the countries providing individual data, the site of disease was analysed by age, sex and geographic origin. Cases with exclusive extra-pulmonary disease tended to be younger than those with pulmonary disease (40 years versus 45 years). Extra-pulmonary TB was also more frequent among children than among adults (27% versus 18%). Among adults, female cases were much more likely than male cases to have extra-pulmonary TB (24% versus 14%).

In 15 countries providing major and minor sites of disease (Table 11), 80.3% of all cases were classified as pulmonary, 19.5% as extra-pulmonary, and 0.2% as unknown. One or more extra-pulmonary localisations (as major and/or minor site of disease) were reported in 25% of the cases. The commonest extra-pulmonary localisations were the pleura (6.6% of cases), extra thoracic lymph nodes (3.8%) and the genito-urinary system (2.6%). Intra-thoracic lymphatic TB and meningeal TB were more frequently reported among children than among adults (respectively 16.7% versus 1.3% and 1.7% versus 0.5%).

3.8 Bacteriology results

3.8.1 Culture

In some countries in the Centre and in the East (e.g. Russian Federation, Ukraine), "bacteriological confirmation" of diagnosis is reported, without distinguishing between culture or sputum smear results. This information is not presented in the Tables.

While nearly half of all notified cases were culture positive in the West and in the Centre, only 21% were culture positive in the East, where data were available from only eight countries (Table 12). Proportions of culture positive cases were:

- 60% or higher in 12 countries in the West and in six countries in the Centre (Bosnia-Herzegovina, Czech Republic, Estonia, Latvia, Slovenia and Yugoslavia).
- 40% or lower in Italy and France in the West, in Albania and Hungary in the Centre and in Azerbaijan, Kazakhstan, Rep. of Moldova and Turkmenistan in the East.

Low proportions of cases with positive culture may be due to:

- difficult access to laboratories, as in several countries in the East,
- diagnostic practices such as request of culture in selected cases (e.g. Hungary), preferential use of radiology (as in some NIS) or of direct microscopy (as in NIS countries implementing DOTS);
- characteristics of surveillance, such as missing laboratory reporting leading to incomplete information on culture (e. g. France) (Table 12).

Culture results were further analysed by site of disease in countries providing individual data (Table 13). In countries using the pulmonary classification, culture results were available in a higher proportion of pulmonary cases in the Centre than in the West and positive culture results were commoner in the West (55%) than in the Centre (48%). This was also the case for extra-pulmonary cases (34% versus 12%). High proportions of "negative" culture results in some countries suggest that coding of culture results needs further validation.

3.8.2 Species identification

Species identification for culture positive TB cases notified was available for 20 countries providing individual data (Table 14). Excluding Romania, in which a large proportion of cases had no species identified, 91% of culture positive cases were due to *M. tuberculosis* and 8.7% had no information on species. In the West, *M. bovis* represented 0.5% of the cases and *M. africanum* 0.6%. The Netherlands reported the highest proportion of cases with non-*M. tuberculosis* strains, with 1.2% *M. bovis* and 2.3% *M. africanum*. In the Centre and East, all cases were due to *M. tuberculosis* apart from five cases due to *M. bovis* in the Czech Republic.

3.8.3 Sputum smear

The results of sputum smear microscopy were provided from 46 countries (Table 15). In the countries using the pulmonary classification, the proportion of pulmonary cases with sputum smear positive for

acid-fast bacilli was 50% in the Centre and 45% in the West. In the East, 34% of pulmonary cases were sputum smear positive (seven countries), compared to 30% of respiratory cases for the five countries submitting data using this classification. This lower proportion is to be expected since the respiratory classification includes forms of disease without lung involvement (pleural and intra-thoracic lymphatic cases). Low proportions of smear positive cases could also be due to:

- earlier diagnosis, with cases having lower bacillary loads at detection
- differences in the availability or in the quality of sputum microscopy
- use of microscopy of bronco-alveolar lavage specimens rather than sputum for diagnosis: results from such specimens are excluded under current definitions used in surveillance, since they would not be comparable in terms of test sensitivity and specificity with smear microscopy of spontaneous sputum
- non-inclusion of results of smear microscopy using auramine stain instead of Ziehl-Nielsen stain.

Differences in diagnostic practices and in the quality of the information on culture and on sputum smear available through TB notifications limit the use of these data for international comparisons. More complete and accurate information on laboratory confirmation of diagnosis could be obtained through laboratory reporting of TB cases, recommended in Europe **[1]** but still not implemented in several countries (Table 1) and possibly by the collection of complementary laboratory evidence of diagnosis (e.g. DNA-based tests).

4. HIV-ASSOCIATED TUBERCULOSIS IN 2000

Data on HIV prevalence among TB cases are not routinely collected at European level. Data on tuberculosis as AIDS indicative disease in Europe are available through AIDS case reporting data collected by EuroHIV (see technical note). AIDS indicative diseases are provided from all 51 countries except Romania. Excluding Romania, in 2000, a total of 12 008 AIDS cases were notified in the other countries of the WHO European Region (Table 16), with AIDS notification rates of 2.8 per 100 000 population in the West (range 0-11.9), 0.2 in the Centre (0.05-0.6) and 0.3 (range 0-1.3) in the East. No AIDS cases were notified in six countries (Andorra, Belarus, Kazakhstan, Monaco, Tajikistan and Turkmenistan). Information on AIDS indicative diseases was available for over 99% of the 12 008 cases, of which 3 067 (26%) had TB at the time of AIDS diagnosis.

Tuberculosis was the single most common AIDS indicative disease overall and its frequency varied widely across geographic areas and countries. The average proportions of AIDS cases with TB were:

- 22% in the West (range 0-55%; median: 16%, excluding countries reporting zero AIDS cases), with highest proportions in Portugal (55%), Israel (38%) and Spain (34%);
- 17% in the Centre (range: 0-56%; median: 9%), with highest proportions in Bulgaria (56 %);
- 73% in the East (range 0-100%; median 33%), with highest proportions in Kyrgyzstan (100%; 1 case), Ukraine (82%), Georgia (50%), Azerbaijan and Lithuania (42%).

These data indicate that TB significantly contributes to HIV-related morbidity in Europe, and more so in the East. High proportions of AIDS cases with TB at AIDS diagnosis reflect high prevalence of TB infection in the HIV infected population, the earlier appearance of TB compared to other AIDS defining conditions in countries where HIV epidemics are recent and possibly also better diagnosis of TB compared to other AIDS defining diseases in some countries. In some western European countries, high proportions of AIDS cases with TB may be also due to high proportions of HIV/AIDS cases among migrants from high incidence countries, among whom TB co-infection is frequent.

The contribution of HIV to total TB incidence is higher than that inferable from cases of TB reported as an AIDS indicative disease. Persons with AIDS can develop TB after initial AIDS diagnosis and yet this event will not be reported to AIDS surveillance. However, in the attempt to estimate a "minimum" proportion of HIV-associated TB, numbers of AIDS cases with TB were compared with total TB cases notified in 2000 (shown in Table 3). This comparison was not done for Spain where only respiratory and meningeal TB cases are notified whereas all TB sites are reported as AIDS indicative disease. In the other countries, AIDS cases with TB as AIDS indicative disease represented 15% of total TB cases in Portugal, 2-5% in nine countries in the West, 1-1.9% in three countries in the West and in Ukraine, and less than 1% in the other countries. These minimum estimates may be affected by different completeness of TB and AIDS case detection and notification at country level. AIDS notification may be particularly incomplete in some countries of the East where numbers of AIDS cases remain very low in spite of high numbers of HIV cases reported in recent years **[14].**

In order to improve coordination of TB and HIV prevention and care, surveillance of HIV-TB co-infection should be strengthened through an improved use of surveillance information already available at both national and international level and the implementation of specific HIV prevalence surveys, particularly in countries where both infections are prevalent.

5. DRUG RESISTANCE SURVEILLANCE IN 2000

5.1 Laboratory practices

Data on laboratory practices for drug susceptibility testing (DST) were provided from 43 countries (Table 17). DST was performed by a single laboratory in 11 countries (located abroad in two of these), 2-10 laboratories in 14 countries, 11-20 laboratories in nine countries and 20-300 laboratories in eight countries. A national DST proficiency-testing scheme existed in 18 of the 31 countries where more than one laboratory performed DST.

Twenty-nine countries participated in an international proficiency-testing scheme between 1999 and 2001. The concordance of DST results for isoniazid (INH) and rifampicin (RMP) between the national reference laboratory (NRL) and the supranational reference laboratory was not provided from Austria and Bosnia-Herzegovina, was 90% or over for both drugs in 26 countries, and was 90% for INH and 80% for RMP in the Russian Federation.

In 25 countries more than one DST method was used. Non-radiometric proportion was used in a total of 28 countries, radiometric proportion in 24 countries, absolute concentration in 14 countries and resistance ratio in four countries. Other methods were used in eight countries, including the Mycobacteria Growth Indicator Tube (MGIT®), a modified non-radiometric proportion method, in six countries.

5.2 Type of data provided

DST results at the start of treatment were provided from 39 of the 43 countries providing information on laboratory practices (Table 18). DST results from Luxembourg and Georgia were included in the analysis, although they may also refer to isolates taken during treatment.

In 30 countries DST data were linked to TB case notification, i.e. were provided on the initial isolate of TB cases notified countrywide (24 countries) or in selected areas (6 countries). In nine countries DST results were not linked to TB notifications and data were provided on cases diagnosed at the NRL (6 countries) or in other laboratories (3 countries) (Table 18). INH, RMP and ethambutol (EMB) were systematically tested in all countries while streptomycin (SM) was tested for less than 90% of the cases tested for INH and RMP in seven countries from the West (data not shown in the Tables). Data were provided for each combination of resistance from all countries except Belarus where only total numbers of mono-resistant, multi-drug resistant (MDR) and other poly-resistant cases were available.

Data by previous anti-TB treatment status were provided from all countries except Albania and Azerbaijan (Table 20-21). For Belarus and Spain data were provided only for never treated cases. When the information on previous treatment was not available or incomplete, DST data were presented and analysed according to previous TB diagnosis (see technical note). Therefore the terms “never treated” or “previously treated” should be taken to mean “never treated or diagnosed” and “previously treated or diagnosed” respectively. Data by geographic origin were provided from 33 countries (Tables 22-23).

Countries were classified in two groups, according to the TB case population included in DRS and the completeness of DST results provided (Tables 18-23). Group A includes countries in which culture and DST are routinely performed for TB diagnosis and in which DST results were provided for all or a large national sample of notified culture positive cases; group B includes countries in which data provided did not meet the conditions above and were not considered representative of the national situation (see also technical note).

5.3 DST results in countries providing representative national data (group A)

Of the 39 countries providing DRS data, 24 were included in this group: 16 in the West, five in the Centre and three in the East (the Baltic states) (Table 18). DST results were provided for all culture

positive cases notified at national level in 23 of these countries. In Germany DST results were provided for TB cases notified in two thirds of local health units accounting for 56% of cases notified nationwide. In 17 countries, DST data were provided as a part of the individual TB data set. Overall, in the countries of group A culture positive cases represented 61% of the TB cases notified (range: 45-100%). DST results for INH and RMP were available for 17 049 of the 19 815 culture positive cases (86%). The proportion of culture positive cases with missing DST results was highest in Lithuania (41%), Andorra (40%), Czech Republic (27%), Bosnia-Herzegovina (26%; incomplete information from Rep. Srpska), Belgium (25%) and Germany (19%).

Global proportions of resistant and MDR cases were much higher in the Baltic states and in Israel compared to the other countries in the West and the Centre (Table 19). Global proportions of resistance are not commented further, as priority is given to analysis of data according to history of previous anti-TB treatment, indicating respectively primary resistance among cases never treated and acquired resistance among cases previously treated.

5.3.1 Resistance by previous anti-TB treatment status

Data were analysed by previous treatment history in 14 countries and by previous TB diagnosis in 10 countries (Tables 20-21). Overall, of the 17 049 cases with DST results 78% were never treated, 12% had a history of previous anti-TB treatment and 11% were reported with no information on previous TB or anti-TB treatment history.

Proportions of resistant cases were generally higher among previously treated cases than among never treated cases. In both groups of cases, resistance to individual drugs and multi-drug resistance where much higher in the Baltic states and Israel than in the other countries in the West and in the Centre. The proportions of MDR cases among never treated cases were 9.7% (9-12%) in the Baltic states, 14.2% in Israel, 0.8% (0-2%) in the other countries in the West and 0.4% (0-1.1%) in the Centre (Table A, Figure 7).

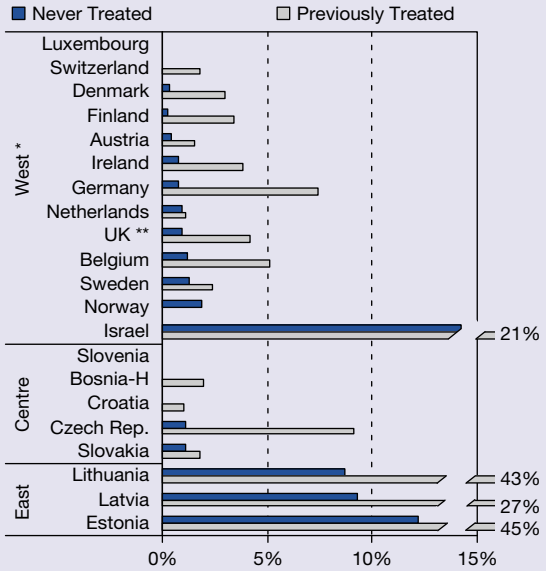
High proportions of both primary and acquired resistance in the Baltic states indicate a poor performance of treatment programmes in previous years. Between 1998 and 2000, proportions of primary and acquired MDR cases were relatively stable in Estonia and Latvia and increased markedly in Lithuania. The observed trend in Lithuania is possibly due to decreasing completeness of information on DST results (from 100% in 1998 to 59% in 2000) resulting in the increasing selection of cases with higher risk of resistance.

Table A. Anti-TB drug resistance by previous anti-TB treatment status, 2000, group A

Drug	Country / country group	Previous anti-TB treatment status: Never treated	Previously treated
INH	Baltic States	25.2%	47.1%
	Israel	25.7%	37.5%
	West, other	5.3%	11.3%
	Centre	1.8%	6.2%
RMP	Baltic States	10.0%	37.5%
	Israel	14.6%	20.8%
	West, other	1.0%	5.0%
	Centre	0.7%	4.0%
INH and RMP (MDR)	Baltic States	9.7%	36.8%
	Israel	14.2%	20.8%
	West, other	0.8%	4.3%
	Centre	0.4%	1.9%
EMB	Baltic States	7.1%	22.1%
	Israel	9.9%	8.3%
	West, other	0.7%	2.8%
	Centre	0.5%	3.3%
SM	Baltic States	22.3%	42.5%
	Israel	22.1%	29.2%
	West, other *	2.5%	5.7%
	Centre	1.1%	4.3%

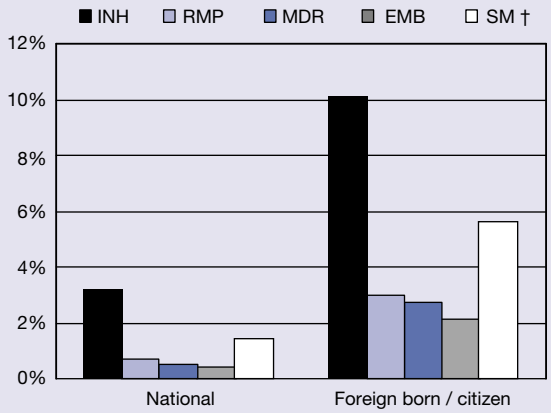
* Nine countries where SM was tested for at least 90% of cases tested for INH and RMP (see Tables 20-21)

Figure 7. Proportion of MDR-TB cases by previous anti-TB treatment status, 2000, group A



* Andorra, Iceland and Malta: ≤ 10 cases with DST results, all susceptible
** without Scotland

Figure 8. Anti-TB drug resistance by geographic origin, Western Europe *, 2000



* 16 countries
† 9 countries with DST results for >90% of the cases tested for INH & RMP

The high levels of resistance in Israel are likely to reflect prevalence of resistance in the countries of origin of recent immigrants, many of whom derive from the NIS **[18]**. In the other countries in the West and in the Centre the levels of resistance and MDR remained low and were associated with previous TB history and, in the West, with foreign origin (see below). The analysis of data for the period 1998-2000, available from 11 countries did not show any clear trend in the levels of drug resistance. A longer observation will be needed to get more conclusive indications on drug resistance trends.

5.3.2 Resistance by geographic origin

DST results by geographic origin were provided from all 24 countries in group A (Tables 22-23). Geographic origin was defined according to country of birth in 21 countries and to nationality in Austria, Belgium and the Netherlands.

In the West, among the 10 892 cases with DST results 46% were of foreign origin, 47% were nationals and 8% were notified without information on geographic origin. Proportions of resistant cases were overall higher among the cases of foreign origin (Figure 8). The proportion of MDR among cases of foreign origin was 2.7% compared to 0.5% among nationals. Cases of foreign origin represented overall 85% of MDR cases notified (136/160) in the West. In the five countries of the Centre and in the three Baltic states, 8% of cases with DST results were born abroad and proportions of resistant cases did not differ markedly when analysed by geographic origin.

5.4 DST results in countries providing data for selected cases (group B)

In the 15 countries classified in group B, data were considered as less representative than data from countries in group A. International comparisons based on these data should be made with caution.

- In France, data were collected through a stable sentinel network of university hospital laboratories covering 15 of the 23 regions (including Paris), not linked to case notification. Although the representativeness of this network has not been formally assessed, data collected show consistently low and stable levels of resistance over time **[19].**
- In Italy data were collected through a convenience sample of 20 laboratories located in 10 of the 20 regions, for which representativeness has not been assessed **[20]**. The denominator of culture positive cases diagnosed in these laboratories was not available to assess completeness of case inclusion.
- In six countries data were provided on TB cases notified but were not considered representative because of incomplete geographic coverage (Yugoslavia), or because of selective use of culture (Belarus and Republic of Moldova), DST (Portugal) or both (Romania and Hungary), leading to a selection of cases for which DST results were available. This can possibly affect the observed levels of resistance.
- In Albania, Armenia, Azerbaijan, Georgia, Kyrgyzstan and Spain, DST data were provided for cases diagnosed at the National Reference Laboratory, likely to be unrepresentative of TB cases both in regards of the geographic coverage and of the characteristics of patients included.
- In Kazakhstan data were provided from all laboratories performing DST but were not linked to case notifications and included all patients diagnosed, resulting in an over-representation of previously treated cases.

Among countries in group B, data from countries in the East showed very high levels of resistance, with primary multi-drug resistance reported in 5% of the cases or more. Although these data cannot be taken as representative of national situations they should further stimulate the implementation of representative anti-TB drug resistance surveys, a high priority for the orientation and monitoring of control measures **[21]**.

6. TREATMENT OUTCOME MONITORING IN 1999

6.1 Type of data provided

Thirty countries provided treatment outcome data on at least one cohort of cases notified in 1999: 11 countries in the West, seven in the Centre and 12 in the East (Table 23). Data were provided only for sputum smear positive cases in 10 countries, for both sputum smear positive and pulmonary culture positive cases in 18 countries, and only for pulmonary culture positive cases in Israel.

The Russian Federation provided data from selected DOTS areas for smear positive cases and nationwide data for culture positive cases notified to the Ministry of Health. Among the other countries, 24 provided outcome data for TB cases notified in the whole country and five countries provided data with incomplete geographic coverage, including cases notified in selected areas implementing DOTS (Armenia, Poland, Romania and Uzbekistan) or diagnosed in a network of clinical Centres (Italy).

Outcome categories used differed across countries. In several countries of the West:

- the category "cured" was not reported because information on sputum smear or culture result at the end of treatment is not routinely collected or incomplete. In these countries cases with favourable outcome were all reported in the category "treatment completed". For comparison of favourable outcomes, in Tables 25-28 a subtotal of cured and completed outcome (success) is presented.
- the category "failure" was not used. Failing cases still continuing treatment at the time of outcome assessment were rather classified at national level in a specific outcome category "still on treatment", reported here in the category "other / unknown".

In the Russian Federation, in the culture positive cohort all favourable outcomes were reported as cured. Different outcome definitions were reported from the Republic of Moldova where only cases "cured" (based on radiological improvement) were reported, while for the rest of the cases outcome information was not available and cases were all classified as "others" (not included in the analysis below).

6.2 Completeness of TOM cohorts

In order to assess the completeness of inclusion in TOM cohorts, total cases considered for TOM were compared with smear positive or pulmonary culture positive cases notified to EuroTB in 1999 (Table 24, see also technical note). In 13/22 countries providing nationwide data, the sum of new and retreated smear positive cases considered for TOM (including those non-eligible) was identical to the total number of smear positive cases notified to EuroTB. In seven countries, smear positive TOM cohorts were smaller compared to 1999 notifications (87-99% of notified cases), due to exclusion of cases for:

- administrative reasons (e.g. records lost, identification as duplicate report, erroneous initial report of positive laboratory results);
- missing information on anti-TB treatment history, as cases could not be entered in either the new or the retreated cohorts
- other case characteristics, e.g. death or default before starting treatment.

In two countries, numbers of smear positive TOM cohorts were slightly larger than those of notified cases (102% in Azerbaijan and Ireland), possibly due to reclassification of smear status after notification or to double inclusion of some cases in the new and retreated cohorts. For pulmonary culture positive cases, the comparison of the sizes of TOM cohorts and notifications showed identical numbers in six countries. TOM cohorts were smaller than notifications in four countries (82-99%) and larger in four countries (107-145%).

In the majority of countries providing national data the numbers of cases considered for TOM are comparable to those of notified cases, which should ensure completeness and representativeness of the outcome data provided. However the large differ-

ences observed in some countries limit the use of TOM data for international comparisons. Further harmonization of TOM in Europe is needed and is currently being discussed.

In countries providing data with incomplete geographic coverage, numbers of cases notified in the areas included in TOM were not available. In these countries the comparison of the size of TOM cohorts with nationwide notifications provided an estimate of TOM coverage.

6.3 Outcome in countries providing nationwide data

6.3.1 Sputum smear positive cohorts

Nationwide outcome data for new smear positive cases were available for 22 countries (Table B and Table 25). The proportion of cases with unknown outcome was 0 in 11 countries and higher than 10% in Ireland (44%), Belgium (24%) and FYR of Macedonia (11%). Potentially unfavourable outcomes (default or transfer) were more frequently reported in the East (median: 13%) than in the West (3%) or in the Centre (4%). Death was reported in a comparable median proportion of cases in the three areas (7-8%). Failure was almost not reported in the West, and represented a median of 1% of cases in the Centre and 5% in the East. The median proportion of favourable outcomes (cure or completion) was 84% in the Centre, 77% in the West and 73% in the East.

Table B. Treatment outcome of new smear positive TB cases, 1999, countries providing nationwide data

outcome	West (9 countries)		Centre (5 countries)		East (8 countries) *	
	median %	range % **	median %	range %	median %	range %
cure	0	(0-45)	68	(26-81)	67	(47-83)
completion	67	(32-77)	14	(3-60)	6	(0-15)
success (cure + completion)	77	(48-85)	84	(74-90)	73	(61-83)
death	7	(6-13)	8	(2-16)	7	(2-15)
failure	0	(0)	1	(0-2)	5	(1-21)
default	3	(3-16)	2	(1-9)	5	(3-22)
transfer	0	(0-3)	1	(0-2)	2	(0-10)
other / unknown	0	(0-44)	4	(0-11)	0	(0-8)

* Rep. of Moldova excluded

** Does not include countries reporting < 10 cases (Andorra, Iceland and Malta)

Eighteen of the 22 countries providing outcome for the new sputum smear positive cohort also provided data on the corresponding cohort of retreated cases (Table 26). Among retreated cases the median proportions of successful outcomes were lower compared to new cases (73% in the Centre, 61% in the West and 62% in the East). Deaths represented a median of 15% of outcomes in the West, 14% in the Centre and 9% in the East. Proportions of potentially unfavourable outcomes were comparable to those of the cohort of new cases. Failure was more frequently reported among retreated cases than among new cases in the Centre (median 3% and 1% respectively) and in the East (10% and 5% respectively).

6.3.2 Pulmonary culture positive cohorts

Nationwide outcome data on new culture positive pulmonary cases were available for Israel, the Russian Federation and 15 countries providing also nationwide data on the new smear positive cohort (Tables 27-28 and Country profiles). In most of these countries culture is used routinely for TB diagnosis and cohorts of new culture positive pulmonary cases were larger than those of smear positive cases (Table 24), as they include most smear positive cases. Outcomes of culture positive cohorts provide a more complete picture of treatment outcome of all potentially infectious TB cases, and were roughly comparable to those of smear positive cohorts in most countries.

6.4 Outcome in countries providing data from selected areas

Outcome data with partial geographic coverage were provided from six countries for the smear positive cohorts and two countries for the culture positive cohorts. These data cannot be considered as representative of country situations. However, in countries with partial DOTS coverage, outcome data from DOTS areas provide an indication of the effectiveness of this strategy.

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