

# RESULTS

## 4.1. Tuberculosis cases notified in 1997

In 1997, 353 871 cases of tuberculosis were notified in 51 countries of the WHO European Region. Countries of the European Union notified 50 907 cases (14% of the total) and countries of the former USSR notified 216 371 cases (61% of the total). Compared with 1996, the number of cases decreased by 2% in the European Union, but increased by 7% in the countries of former USSR and by 4% in the whole WHO European Region.

The notification rate per 100 000 population varied between countries from 0 in Monaco and San Marino to 154 in Georgia with a median of 28 cases (Table 4).

The notification rate was under 20 cases per 100 000 population in 22 countries, mostly situated in the western part of Europe except for Albania, the Czech Republic and Israel. Among these 22 countries, 11 notified less than 10 cases per 100 000. The rate was 20 to 49 cases per 100 000 in 14 countries mostly located in central or eastern Europe except for Andorra and Spain. It was 50 cases or over per 100 000 population in 15 countries, all located in the eastern part of Europe except for Portugal (Map 1).

Tuberculosis notification rates in 1995 (Map 1), 1996 and 1997 (Map 2) were compared. For Andorra and Georgia, rates were compared between 1996 and 1997. An increase in rate was defined as at least 1.5% average increase per year, and a decrease as at least 1.5% average decrease per year, over the two-year period. The rate was defined as stable if not varying by more than 3% over the two years.

Among the 11 countries notifying **less than 10 cases** per 100 000 population in 1997, the rate decreased since 1995 in Greece, Iceland, Monaco, Netherlands, Norway, San Marino, Sweden and remained stable in Israel and Italy. In Luxembourg and Malta, the rate increased between 1995 and 1997, but variations in these two countries are difficult to interpret because of the low number of cases.

Among the 11 countries with a notification rate **between 10 and 19 cases** per 100 000 population in 1997, the rate decreased since 1995 in Albania, Belgium, Finland, France, Germany, Ireland and Switzerland, remained stable in Austria, Czech Republic and United Kingdom and increased in Denmark: this increase may mostly be due to an increase in cases among the foreign-borns (see Section 4.3. on Geographic origin).

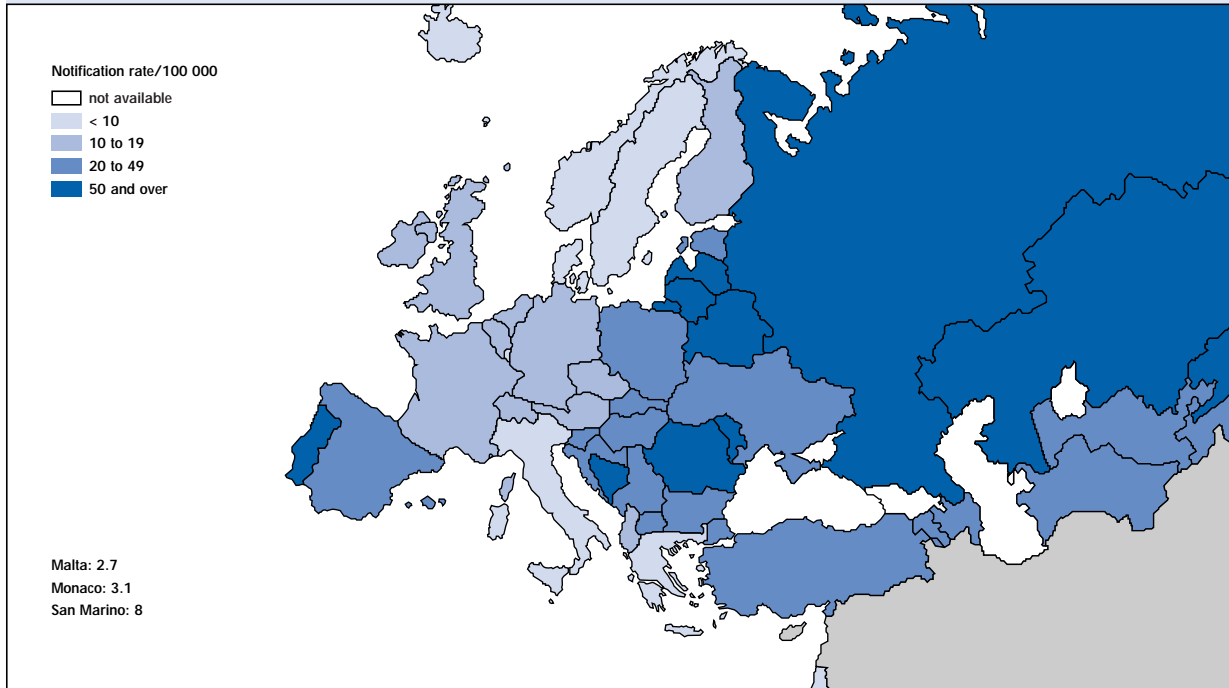
Among the 14 countries with a notification rate **between 20 and 49 cases** per 100 000 population in 1997, the rate decreased or remained stable since 1995 in Croatia, Hungary, Macedonia, Poland, Slovakia, Slovenia, Tajikistan and Yugoslavia. In Tajikistan, the variable trends in notification rate, i.e., a decrease between 1995 and 1996 and an increase between 1996 and 1997, may partly result from variations in reporting due to previous disruption of the health services. The notification rate increased in 6 other countries (Andorra, Armenia, Bulgaria, Estonia, Spain, Turkey). The increase observed in Spain is probably partly due to an extension of the case definition (see Chapter 3 on Country surveillance systems).

Among the 15 countries with a notification rate of **50 cases or over** per 100 000 population in 1997, the rate increased since 1995 in all except Portugal and Georgia where it decreased. The decrease in notification rate in Georgia between 1996 and 1997 may be partly explained by an over-reporting of cases in 1995 and 1996, because of the disruption of the tuberculosis control programme between 1991 and 1995. The notification rate increased by less than 10% per year on average in 3 countries (Belarus, Moldova and Romania) and by 10% per year or more in 10 countries (Azerbaijan, Bosnia-Herzegovina, Kazakstan, Kyrgyzstan, Latvia, Lithuania, Russian Federation, Turkmenistan, Ukraine, Uzbekistan).

Between 1995 and 1997, the tuberculosis notification rate thus decreased or remained stable in most countries notifying less than 20 cases per 100 000 (almost all in western Europe) and in several countries notifying between 20 and 50 cases per 100 000 (almost all situated in central Europe), while increasing in most

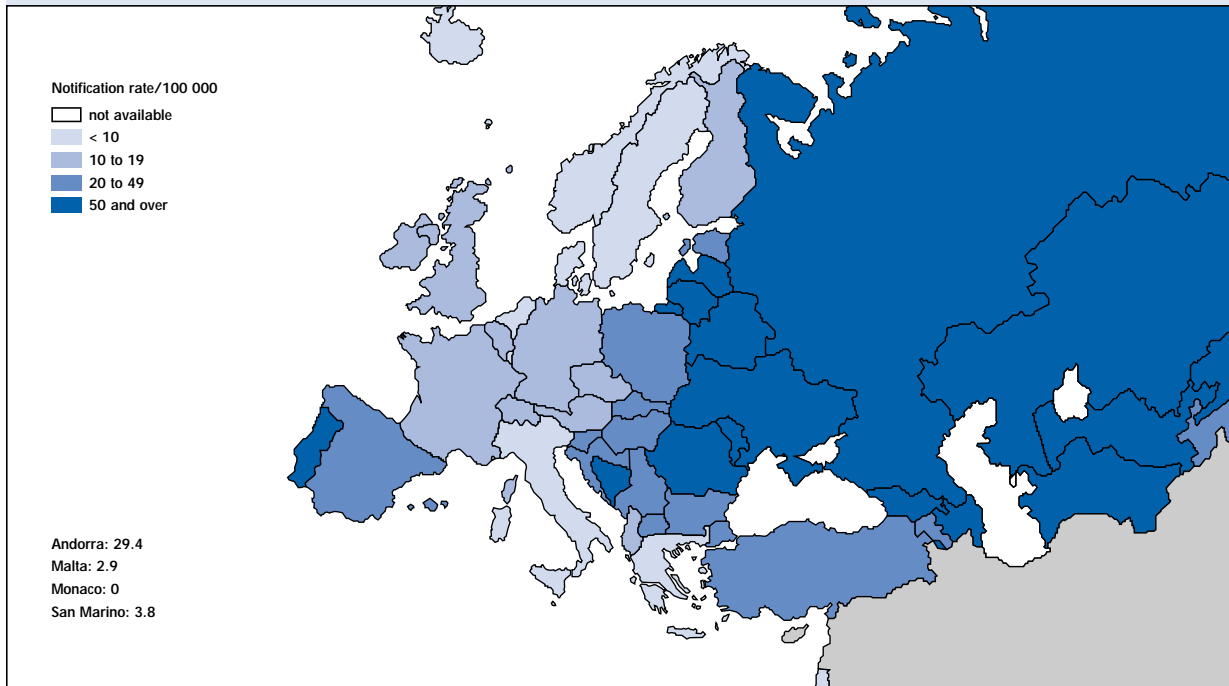
**MAP 1**

**Tuberculosis notification rate 1995, 50 countries, WHO European Region**



**MAP 2**

**Tuberculosis notification rate 1997, 51 countries, WHO European Region**



countries notifying 50 cases and over per 100 000 (almost all situated in eastern Europe). The largest increases were observed in several ex-USSR republics. Changes in the surveillance system in some of these countries are probably too recent to fully explain all observed increases.

In the 38 countries with available information on previous tuberculosis history (Table 5), the median proportion of recurrent cases was 11%. It was:

- 0 to 9% in 15 countries;
- 10 to 14% in 16 countries;
- 15% or over in 7 countries.

Between-country differences in the proportion of recurrent cases should be interpreted with caution, considering the differences in definitions of recurrent case included in the notification (see Chapter 3 on Country surveillance systems). For example, the high proportion of recurrent cases in Norway (18%) and Iceland (60%) may be related to the fact that more than 2/3 of the recurrent cases notified in these countries were cases with untreated previous tuberculosis (mostly elderly patients with a previous episode of tuberculosis diagnosed before 1950).

## 4.2. Age and sex

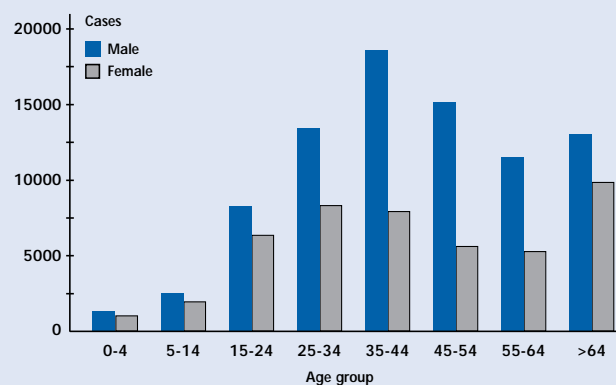
Overall, among the 38 countries with information available on sex, the majority (64%) of the tuberculosis patients reported were male. The median sex ratio (number of males/number of females) was 1.6, ranging from 0.7 in Iceland to 3.4 in Armenia (Table 6). Eleven countries reported at least twice as many cases in males as in females; of these countries, eight notified 20 cases or more per 100 000 population in 1997.

A total of 35 countries provided information on the age and sex distribution of all new and recurrent cases according to recommended age groups (Box 6, Table 7 & 8). Patients under 15 years of age accounted for 5% of the reported cases and children under 5 for 2%. Almost half of the cases (48%) were in the 15-44 year age group, 29% in the 45-64 year age group and 17% in those aged over 64. In all age groups, there were more male than female cases. The sex ratio was 1.4 among patients under 35 years of age, 1.3 among those aged 65 and over and 2.4 among those between 35 and 64 years of age. The overall age distribution was similar in 1996 and in 1997.

The distribution of cases by age and sex as well as the age and sex-specific notification rates varied considerably across countries (country profiles).

Patterns of age distribution differed according to the level of tuberculosis notification rate. In general, the proportions of patients in older age groups increased, and the proportions in younger age groups decreased, with decreasing notification rates. For example, the proportion of patients aged 65 years or more in countries notifying less than 20 cases per 100 000 (28%) was larger than that in countries notifying 20 to 49 cases per 100 000 (13%) and much larger than that in countries notifying 50 or more cases per 100 000 (9%).

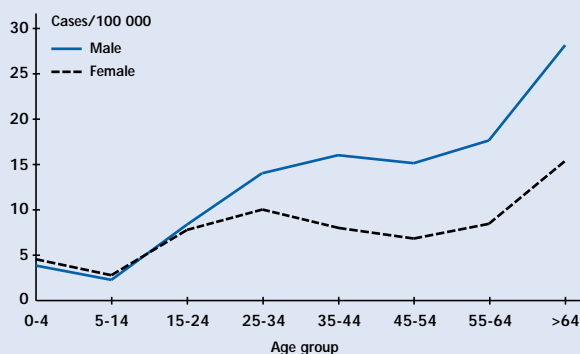
**BOX 6 Tuberculosis cases by age group and sex, 1997, 35 countries\* (N = 130 590)**



\* Andorra, Armenia, Austria, Belgium, Bosnia-Herzegovina, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Hungary, Iceland, Israel, Italy, Kazakstan, Latvia, Lithuania, Luxembourg, Macedonia, Malta, Moldova, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, Switzerland, United Kingdom, Yugoslavia.

In countries with less than 20 cases per 100 000 (Box 7), notification rates in both sexes increased with age after age 14, with a small peak in the 25-34 year age group in females. The sharpest increases were observed in the group aged 65 years or over. In countries notifying 20 to 49 cases per 100 000 (Box 8), rates increased rapidly after age 14 in males but less rapidly in females, resulting in large sex differences, particularly between 35 and 64 years of age. In countries notifying 50 cases per 100 000 or over (Box 9), the rate increased with age only up to the 45-54 age group in males and to the 25-34 age group in females, and decreased thereafter.

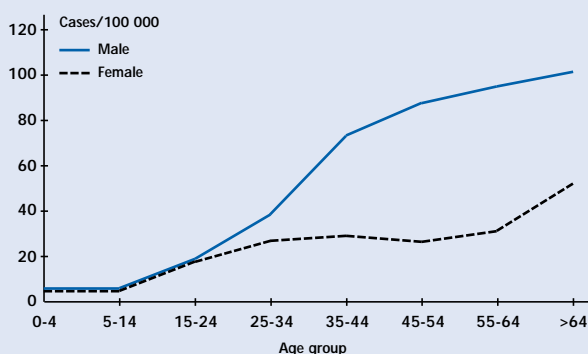
**BOX 7 Tuberculosis notification rate by age group and sex, 1997, 17 countries\* with < 20 cases per 100 000**



\* Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Iceland, Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Sweden, Switzerland, United Kingdom

In all countries, notification rates among children were similar in males and females. In countries with lower notification rates (Box 7), rates were higher in younger (under 5 year-old) than in older (5-14 year-old) children, probably reflecting the fact that young children have a much higher risk of developing tuberculosis after infection than older children [8]. However, in countries with higher notification rates (Box 8 & 9), this was not the case, suggesting a possible under-reporting of cases in children under 5 in some countries.

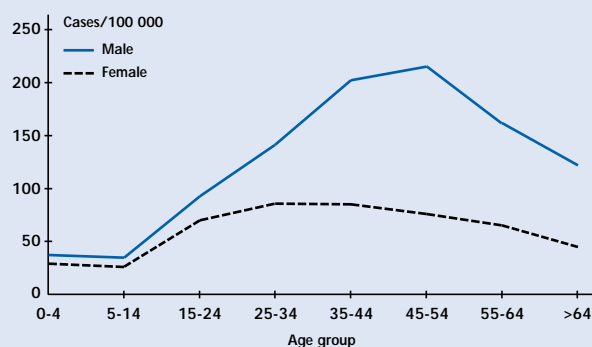
**BOX 8 Tuberculosis notification rate by age group and sex, 1997, 10 countries\* with 20-49 cases per 100 000**



\* Andorra, Armenia, Croatia, Estonia, Hungary, Macedonia, Poland, Slovakia, Slovenia, Yugoslavia

Some of the between-country variations in age distribution and in age-specific notification rates were related to differences in the distribution of cases by geographic origin. In the 26 countries with information available on patients' age group and geographic origin, the proportion aged 15 to 44 years was larger in foreigners than in nationals (69% versus 47%), while the proportion aged over 44 years was lower (25% versus 44%), and differences by sex were more marked in patients of foreign origin (more male patients). These differences are likely to influence age-specific notification rates in countries with larger proportions of cases in foreigners (see Section 4.3. on Geographic origin).

**BOX 9 Tuberculosis notification rate by age group and sex, 1997, 8 countries\* with >49 cases per 100 000**



\* Bosnia-Herzegovina, Georgia, Kazakhstan, Lithuania, Latvia, Moldova, Portugal, Romania.

**4.3. Geographic origin**

Among the 42 countries including patients of foreign origin in their notification in 1997 (Table 1), 29 provided information on origin (Table 9), based on birth place (as recommended) in 19, on citizenship in seven, and on both birth place and citizenship in three (France, Luxembourg and Switzerland).

Data from Croatia were not analysed because information was missing for a high proportion of cases (44%). The proportion of patients of foreign origin in the remaining 28 countries is illustrated in Map 3. For Luxembourg and Switzerland, information on birth place was used. Citizenship was used for France because information on birth place was missing for a high proportion of cases (26%).

The proportion of cases in foreign-born patients was:

- 0% in Armenia, Moldova and Slovakia;
- 1 to 9% in 7 countries (Czech Republic, Estonia, Finland, Hungary, Ireland, Latvia, Lithuania);
- 10 to 49% in 4 countries (Iceland, Luxembourg, Malta, Slovenia);
- 50% or over in 6 countries (Andorra, Denmark, Israel, Norway, Sweden, Switzerland).

In countries providing information based on citizenship, the proportion of cases in foreigners was:

- 0% in Georgia and Romania;
- 10 to 49% in 5 countries (Austria, Belgium, France, Germany, Italy);
- 55% in the Netherlands.

Comparisons of the proportion of patients of foreign origin across countries should however be made with caution, taking into account differences in notification of some population groups (e.g. asylum seekers, illegal immigrants), possible under-notification of patients of

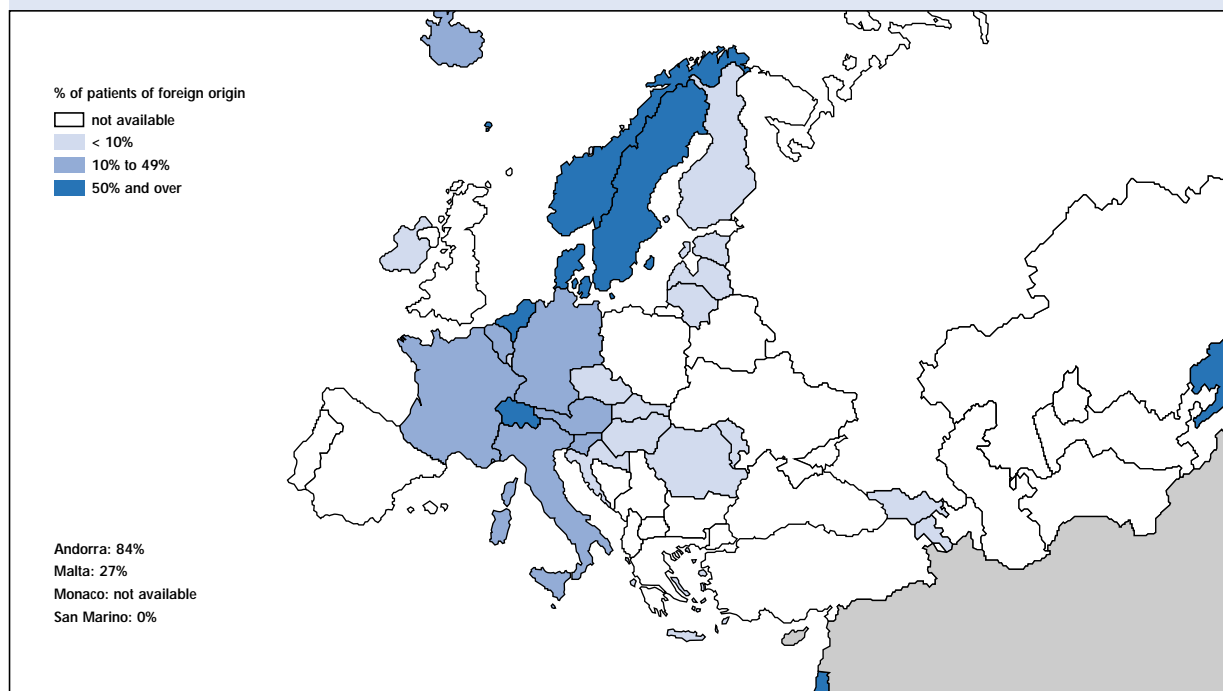
foreign origin, variations in immigration patterns and in policies regarding acquisition of nationality, and potential differences in tuberculosis screening programmes for immigrants.

Among the 22 countries with information available both in 1996 and in 1997, the proportion of patients of foreign origin:

- decreased (by  $\geq 3\%$ ) or remained stable (less than 3% change) in 9 countries (Armenia, Austria, Belgium, France, Hungary, Iceland, Luxembourg, Malta, Slovakia). Interpretation of variations in Iceland, Luxembourg and Malta is however difficult because of the very small number of cases.
- increased (by  $\geq 3\%$ ) in 13 countries (Andorra, Czech Republic, Denmark, Estonia, Finland, Germany, Israel, Italy, Netherlands, Norway, Slovenia, Sweden, Switzerland). Among these countries, 10 notified less than 20 cases per 100 000 population in 1997. The increase was greater than 10% in all countries notifying more than 50% of tuberculosis cases in patients

MAP 3

Proportion of tuberculosis cases among patients of foreign origin, 1997, 28 countries, WHO European Region



of foreign origin in 1997 (Andorra, Denmark, Netherlands, Norway, Sweden, Switzerland), except in Israel where it was 5%.

The notification rate was calculated separately for nationals and for patients of foreign origin in 10 countries (Belgium, Denmark, Finland, France, Germany, Hungary, Netherlands, Norway, Slovenia and Sweden) which could provide corresponding population figures for 1997. Rates were consistently higher in foreigners than in nationals (from 2 times higher in Slovenia to 42 times higher in Denmark), except in Hungary where rates were similar.

All these countries but one (Hungary) provided these figures for 1995 also. Between 1995 and 1997, the notification rate among nationals decreased at a decreasing rate of 3% or more per year on average. Notification rate among patients of foreign origin followed diverging trend, decreasing by 3% or more per year on average in 4 countries (Belgium, France, Slovenia and Sweden), remaining stable (< 3% change per year) in Germany and Norway and increasing by 10% or more per year on average in Denmark, Finland and the Netherlands. However, trends in the foreign population are probably less valid than those in nationals and should be interpreted with particular caution considering the difficulties in obtaining accurate population figures.

Of the 10 countries, all but two (Denmark and Hungary) provided also the age distribution by geographic origin of both the tuberculosis cases and the population. Large differences in age-specific rates by geographic origin were observed in the 8 countries (Box 10). Among the population of foreign origin, the notification rate clearly peaked in the 25-34 year age group, at a higher level in males than in females, then decreased before increasing again in the oldest age group (>64 years). Among nationals, the rate increased regularly with age from 14 years upwards with no peak in young adults, while remaining always at a much lower level than among the foreign population. Differences between males and females were more marked among the foreign population than among nationals.

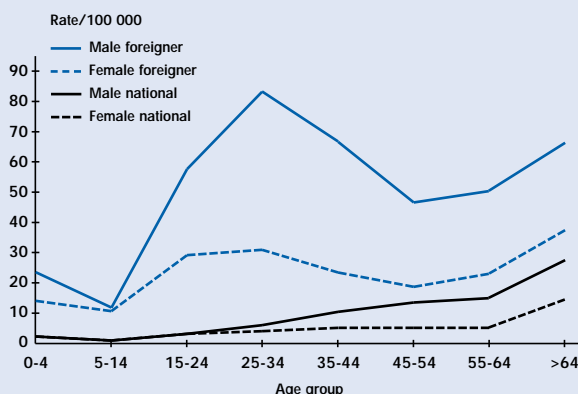
Information on the specific country of origin of patients was provided by 15 countries in 1997 (Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, Iceland, Italy, Luxembourg, Malta, Netherlands, Norway, Slovenia, Sweden and Switzerland). The distribution by continent of origin is presented in Table 10. In the 11 of these 15 countries providing geographic origin based on birth place, 36% of the foreign-born patients were born in Europe, 35% in Africa, and 25% in Asia. In countries providing information based on citizenship, 21% of the foreign patients were citizens of countries within Europe, 44% within Africa and 26% within Asia. Because several countries of the WHO European Region are situated outside the European continent (Armenia, Azerbaijan, Georgia, Israel, Kazakstan, Kyrgyzstan, Tajikistan, Turkey, Turkmenistan and Uzbekistan), the proportion of patients from the WHO European Region was higher than that of patients coming from the European continent only (34% vs 27%). The distribution by continent of origin in 1997 was similar to that in 1996 for countries providing information in both years.

As in 1995 and 1996, foreign or foreign-born patients in 1997 had very diverse origins, but almost half (46%) were born in, or were citizens of, one of the following five countries: Somalia (17%), Morocco (10%), Federal Republic of Yugoslavia (8%), Turkey (6%) and Bosnia-Herzegovina (5%).

#### 4.4. Site of disease

Information on site of disease for all new and recurrent cases was reported by 37 countries (Table 11): 9 countries provided detailed information on major and minor site of disease from which it was possible to classify cases as pul-

**BOX 10 TB rates by age group sex and geographic origin, 1997, 8 countries\***



\* Belgium, Finland, France, Germany, Netherlands, Norway, Slovenia, Sweden.

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monary or extra-pulmonary, 18 provided information based on the pulmonary classification and 10 provided information by classifying cases as respiratory or extra-respiratory. Among the countries providing information based on detailed site or on pulmonary classification, the median proportion of pulmonary cases was 78%, ranging from 55% in Albania to more than 90% in Andorra, Bosnia-Herzegovina, Croatia and Hungary. In the countries providing information based on respiratory classification, the median proportion of respiratory tuberculosis was 91%, ranging from 76% in United Kingdom to 95% or over in Latvia and Poland.

Among the 9 countries (Austria, Belgium, Iceland, Luxembourg, Malta, Norway, Romania, Slovenia and Switzerland) providing detailed information on major and minor site of disease (Box 11), 85% of the patients had pulmonary tuberculosis. Pulmonary tuberculosis

could be reported as a major site only, whereas extra-pulmonary localisations could be reported either as major sites (if not associated with pulmonary tuberculosis) or as minor sites (if associated with another localisation). Pleural tuberculosis was reported in 11% of the patients. All other sites were reported in less than 3% of the patients. A minor site of disease was reported for 1085 patients (4%), of which 1001 also had pulmonary tuberculosis. Among those 1001 patients, 464 (46%) had pleural tuberculosis, 238 (24%) had disseminated tuberculosis and 78 (8%) had intrathoracic lymphatic tuberculosis.

Sites of disease were distributed differently according to age (Box 11). Extra-pulmonary tuberculosis without pulmonary localisation was significantly more frequent among children (less than 15 years of age) than among adults (20% versus 15%,  $p < 0.01$ ).

### BOX 11 Site of disease by age group, 9 countries\* reporting individual data on major and minor site of disease

| Site of disease             | Age group  |        |             |        |                   |        |         |        |
|-----------------------------|------------|--------|-------------|--------|-------------------|--------|---------|--------|
|                             | 0-14 years |        | 15-44 years |        | 45 years and over |        | Total † |        |
|                             | N          | (%)    | N           | (%)    | N                 | (%)    | N       | (%)    |
| Pulmonary                   | 1044       | (80.0) | 13173       | (83.7) | 9513              | (86.7) | 23730   | (84.7) |
| Pleural                     | 157        | (12.0) | 1993        | (12.7) | 858               | (7.8)  | 3008    | (10.7) |
| Intrathoracic lymphatic     | 54         | (4.1)  | 96          | (0.6)  | 45                | (0.4)  | 195     | (0.7)  |
| Extrathoracic lymphatic     | 62         | (4.8)  | 336         | (2.1)  | 248               | (2.3)  | 646     | (2.3)  |
| Spine                       | 11         | (0.8)  | 52          | (0.3)  | 54                | (0.5)  | 117     | (0.4)  |
| Bone/joint other than spine | 16         | (1.2)  | 79          | (0.5)  | 112               | (1.0)  | 207     | (0.7)  |
| Meningitis                  | 52         | (4.0)  | 69          | (0.4)  | 43                | (0.4)  | 164     | (0.6)  |
| CNS ‡ other than meningitis | 3          | (0.2)  | 1           | (0.0)  | 0                 | (0.0)  | 4       | (0.0)  |
| Genito-urinary              | 2          | (0.2)  | 108         | (0.7)  | 242               | (2.2)  | 352     | (1.3)  |
| Peritoneal/digestive        | 9          | (0.7)  | 81          | (0.5)  | 56                | (0.5)  | 146     | (0.5)  |
| Disseminated §              | 34         | (2.6)  | 111         | (0.7)  | 127               | (1.2)  | 272     | (1.0)  |
| Other                       | 8          | (0.6)  | 122         | (0.8)  | 128               | (1.2)  | 258     | (0.9)  |
| Unknown                     | 0          | (0.0)  | 1           | (0.0)  | 6                 | (0.1)  | 7       | (0.0)  |

Note: The total number of patients is 28 027. Data shown are the number of sites; added % exceed 100% because some patients were reported with > 1 site of disease

\* Austria, Belgium, Iceland, Luxembourg, Malta, Norway, Romania, Slovenia, Switzerland

† Including 5 cases with unknown age

‡ CNS = Central Nervous System

§ Disseminated tuberculosis includes:

- miliary tuberculosis
- tuberculosis in which *M. tuberculosis* complex has been isolated from the blood
- tuberculosis of more than two organ systems

Several localisations, associated or not with pulmonary tuberculosis, were reported more frequently in children than in adults:

- intrathoracic lymphatic (4% versus < 1%);
- extrathoracic lymphatic (5% versus 2%);
- meningeal (4% versus < 1%);
- disseminated (3% versus < 1%).

Pleural tuberculosis was rarely reported among children under 5 years of age (4%). The proportion of cases with pleural tuberculosis was the highest among children aged 5 to 14 (18%) and in the 15-24 year age group (20%). Above 24 years of age, the proportion of cases with pleural tuberculosis decreased with age (12% in patients aged 25-34, 9% in patients aged 35-44, 8% in patients aged 45 or more).

The distribution by site of disease also differed by sex: among adults over 15 years of age, women were 1.8 times more likely than men to have extra-pulmonary tuberculosis without pulmonary localisation (22% versus 12%).

The distribution of cases by detailed site of disease and by geographic origin was analysed for 7 countries reporting more than 5% of cases in patients of foreign origin (Austria, Belgium, Iceland, Luxembourg, Norway, Slovenia and Switzerland). The proportion of cases with extra-pulmonary tuberculosis without pulmonary localisation was higher among patients of foreign origin than among nationals (24% vs 20%,  $p < 0.01$ ). This difference was found for children and younger adults (15 - 44 years) among whom patients of foreign origin, both males and females, were 1.5 times more likely than nationals to have extra-pulmonary tuberculosis only, whereas no difference by geographic origin was found among older adults (aged > 44 years).

Among patients aged less than 45 years, intrathoracic and extrathoracic lymphatic tuberculosis, associated or not with pulmonary tuberculosis, were reported more frequently in patients of foreign origin than in nationals (6% vs 3%, and 14% vs 4%, respectively).

Between 1996 and 1997, there was little change in the overall distribution of disease sites among countries providing individual data, except for the pulmonary localisation which was slightly more frequent in 1997 than in 1996 (85% versus 82%), while the intrathora-

tic lymphatic localisation was less frequent (0.7% versus 2.4%). This change was mainly due to the reclassification, in 1997, of the pediatric cases (the majority of which were reported in Romania) which were initially reported with intrathoracic lymphatic localisation only, as cases having pulmonary tuberculosis as major site and intrathoracic lymphatic localisation as minor site, according to the European recommendations [3,4].

## 4.5. Bacteriology

### 4.5.1. Sputum smear results

Information on sputum smear results was available in 32 countries (Table 12). The median proportion of smear positive cases was 48% (range 18% to 71%, excluding Malta with 0%) among the pulmonary cases, and 38% (range 17% to 61%) among the respiratory cases. In 15 countries, the proportion of pulmonary/respiratory cases with negative or unknown smear results was over 60%.

Individual information on sputum smears was provided by 17 countries. The median proportion of pulmonary or respiratory cases for which smear examination was reported as performed was 87%, ranging from 34% to 100%. The median proportion of smear positive cases among pulmonary cases (among respiratory cases in the Czech Republic) was 47% (range 30% to 71%, excluding Malta with 0%). The proportion of pulmonary or respiratory cases with unknown smear results ranged from 0% to 66% (median 13%). Unknown smear results could be due to the smear being reported as performed but results being unknown, to the smear not being performed, or to a complete absence of information.

The proportion of pulmonary/respiratory tuberculosis cases with a positive smear was lower in children under 15 years of age (12%) than in adults (59% in patients aged 15 to 44 years, 54% in patients aged 45 years and over).

### 4.5.2. Bacteriological confirmation

Information on bacteriological confirmation of the cases was available in 33 countries (Table 13): based on positive culture, as recommended, in 12 countries, and based on positive culture or positive sputum smear in 21, including Armenia for which confirmation was based on sputum smear only. The median proportion of bacteriol-



ogically confirmed cases was 71% in the first group of countries (range 40% to 90%) and 51% in the second group (range 14% to 80%). In 12 countries, the proportion of cases without bacteriological confirmation (non-confirmed or unknown) was over 50% regardless of the type of confirmation.

**4.5.3. Culture results**

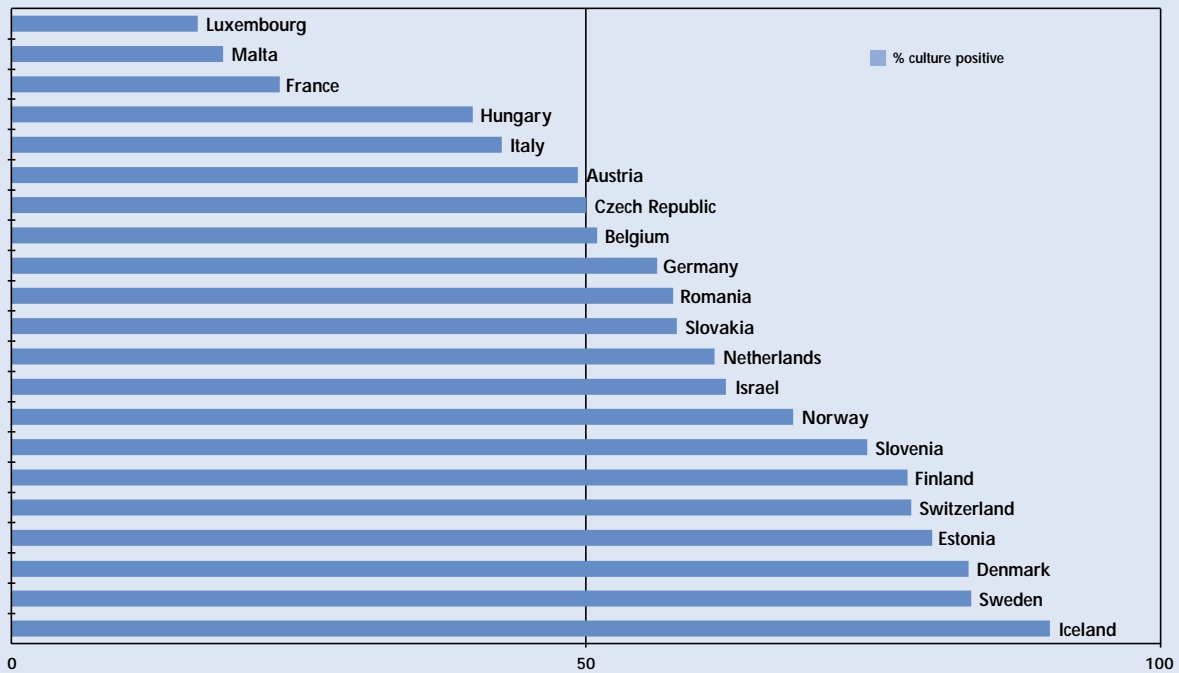
In 1997, information on culture was available in 21 countries. As in 1995 and in 1996, large between country differences in the proportion of cases with a positive culture were observed (Box 12). The proportion ranged from 16% to 90% (median: 58%). Such differences may not reflect real differences in the bacteriological status of the cases, as evidenced by the large between-country variations in the availability of information on culture.

Among the 18 countries providing individual information on culture, it was possible to separate cases for

which culture was done but results were unknown from those with no culture done and those with no information on culture. The proportion of cases for which the culture was reported as performed but with unknown results ranged from 0% (in 10 countries) to 29%. The proportion of cases for which culture was reported as not done ranged from 0% (in 7 countries) to 30%. The proportion of cases with no information on culture ranged from 0 (in 4 countries) to 79%. The differences between countries may be explained by differences in diagnostic practices or in reporting patterns. For example:

- culture examination may not be possible for all suspected tuberculosis cases in the whole country, as in Italy and Romania;
- culture may not always be performed or, if performed and positive, may not necessarily be reported in countries where culture positivity is not required for bacteriological confirmation of the cases. This may

**BOX 12** Proportion (%) of cases with positive culture, 1997, 21 countries



partly explain the high proportion of cases with no culture done (> 10%) in, for example, Austria, Belgium, Italy and Malta, and the high proportion of cases with unknown information on culture (> 20%) in France, Italy and Luxembourg. Indeed, the completeness of information and the proportion of cases with positive culture were higher in countries where culture positivity is required to classify a case as definite, as recommended [3,4];

- results of culture may not be systematically reported, because laboratories do not participate in the notification system. This may partly explain the low proportion of positive culture in some countries (e.g. France);
- only positive culture results may be required to be reported, as is the case in Denmark and Finland. Culture results are then provided as either positive or unknown, resulting in a high proportion of cases with unknown information on culture.

The average proportion of cases with a positive culture was significantly higher in cases with pulmonary/respiratory tuberculosis than in those with extrapulmonary/extra-respiratory tuberculosis (60% versus 18%) and lower among children under 15 (18%) than among adult patients (54%).

Individual information on both culture and sputum smear results was provided by 17 countries in 1997 (Table 14). Among pulmonary tuberculosis cases confirmed by a positive culture, the proportion of cases with positive sputum smear ranged from 35% to 87% (excluding Malta with 0%) with a median of 50%.

Although it would be expected that almost all pulmonary smear positive cases are also culture positive, a small proportion (< 4%) of all cases were smear positive with a negative culture, in 8 countries (Austria, Belgium, France, Italy, Norway, Slovenia, Sweden, Switzerland).

Nine countries reported pulmonary smear positive cases with no culture results. These cases accounted for more than 5% of all cases in 7 countries (Austria, Belgium, Finland, France, Italy, Netherlands and Romania), 5 of which did not require culture positivity for classifying case as definite.

Compared to 1996, the proportion culture-positive among

all cases increased in 1997 (median 58% vs 55%) among the 21 countries with available information.

#### 4.6. Drug resistance

Information on drug susceptibility at start of treatment for tuberculosis cases notified in 1997 was collected from 10 countries providing individual data (Table 15).

Among these 10 countries, 9 (all except Finland) provided information on previous history of tuberculosis, and 7 (all except Finland, Denmark and Estonia) provided information on previous antituberculosis treatment. For the separate calculation of proportions of drug resistance in “patients never treated” and in “patients previously treated” (Box 2):

- patients with no previous treatment (if this information was available) and those with no previous episode of tuberculosis (if information on previous treatment was not available) were included in the first category;
- patients with previous treatment (if this information was available) and those with a previous episode of tuberculosis but no information on previous treatment were included in the second category.

##### 4.6.1. Representativeness

The proportion of culture positive cases which were tested for isoniazid, rifampicin and ethambutol susceptibility varied by country (Table 15):

- 100% in Iceland, the Netherlands and Sweden;
- between 88% and 96% in Denmark, Norway and Slovenia;
- between 63% and 78% in Estonia, Finland and Switzerland;
- 28% in Romania.

Susceptibility to streptomycin was tested systematically in 6 countries. It was not tested in Iceland and Switzerland, and was not systematically tested in Norway and Slovenia (thus results for these countries are not presented).

Cases tested for drug susceptibility did not differ from cases not tested with regard to sex, age group, geographic origin, case status, site of disease and sputum smear results except:

- in Estonia, where the proportion tested was significantly higher in smear negative pulmonary cases or extrapulmonary cases than in smear positive pulmonary cases (78% versus 50%,  $p < 0.01$ );
- in Romania, where the proportion tested was significantly higher in cases previously treated than in cases never treated (31% versus 27%,  $p < 0.01$ ) and significantly higher in smear positive than in other cases (29% versus 25%,  $p < 0.01$ ). Because of these differences and because of the low overall proportion of cases tested, results may not be representative for Romania and should be interpreted with caution;
- in Switzerland, where the proportion tested was significantly higher in men than in women (82% versus 72%,  $p < 0.01$ ) and higher in foreign-born patients than in those born in the country (81% versus 73%,  $p = 0.05$ ).

#### 4.6.2. Results by country

The proportion of drug resistance among all culture positive cases tested for drug susceptibility varied between countries (Table 15). The median proportion was:

- 5.7% for isoniazid (range: 0% to 23.3%);
- 1.0% for rifampicin (range: 0% to 13.8%);
- 0.9% for multi-drug resistance (MDR), i.e. resistance to at least isoniazid and rifampicin (range: 0% to 13.0%);
- 0.4% for ethambutol (range: 0% to 7.4%);
- 8.9% for streptomycin among the six countries where susceptibility to this drug was systematically tested (range: 1.3% to 25.7%).

For all drugs, the proportions were highest in Estonia and lowest in Iceland (however, very few patients were tested in Iceland).

According to levels of drug resistance, two groups of countries could be defined: countries with lower levels of resistance (Denmark, Finland, Iceland, Netherlands, Norway, Slovenia, Sweden and Switzerland) and countries with higher levels of resistance (Estonia and Romania).

#### 4.6.3. Results by patients' geographic origin

The proportions of resistance to all drugs tested were consistently higher among patients of foreign origin than among nationals in all countries except Estonia, Romania and Slovenia where proportions were similar. In Estonia and Romania however, this similarity cannot be meaningfully interpreted since very few patients were of foreign origin (4% in Estonia and <1% in Romania).

In the 8 countries with lower levels of drug resistance (i.e., all except Estonia and Romania), patients of Asian or African origin had a higher proportion of resistance to isoniazid (9.2% and 9.6% respectively) than patients originating from foreign countries in Europe (3.7%) or nationals (2.3%). Similar differences were observed for streptomycin resistance (10.1% and 12.9% respectively, versus 2.8% and 2.0%) and for MDR (1.3% and 1.3%, respectively, versus 0.6% and 0.1%). All differences were found both in patients never treated and in patients previously treated.

These differences may be due to high drug resistance levels in some countries of origin. For example, 465 of the 685 culture positive patients of African origin tested for drug susceptibility (68%) originated from countries of the horn of Africa (Ethiopia, Eritrea or Somalia) where drug resistance levels are probably high due to the disorganisation of antituberculosis treatment caused by civil wars and socio-economic problems. Immigration from these countries is likely to have been relatively recent. Proportions of resistance were high in patients from this region: 11.2% to isoniazid, 1.9% to rifampicin and 12.7% to streptomycin. Patients from these countries are at risk both for having developed drug resistance during treatment (acquired resistance) and for having tuberculosis following an infection by drug resistant bacilli (primary resistance) in their country of origin.

Differences by geographic origin should however be interpreted with caution. Drug resistance may not result only from problems in the country of origin. There may also be specific problems in the case management of immigrants and/or difficult living conditions which expose them to the risk of both acquired primary and drug resistance in the country of diagnosis. In addition, the number of patients originating from each specific country was too small to allow meaningful comparisons. Patterns of migration differ from one country to another, and the time elapsed since arrival of migrants was not known.

4.6.4. Results by case status

Among the 9 countries with information on case status, the proportions of drug resistance were higher among patients previously treated than among patients never treated in most countries and for most drugs (Table 15).

The median proportions of resistance in patients never treated and in patients previously treated were, respectively (Box 13):

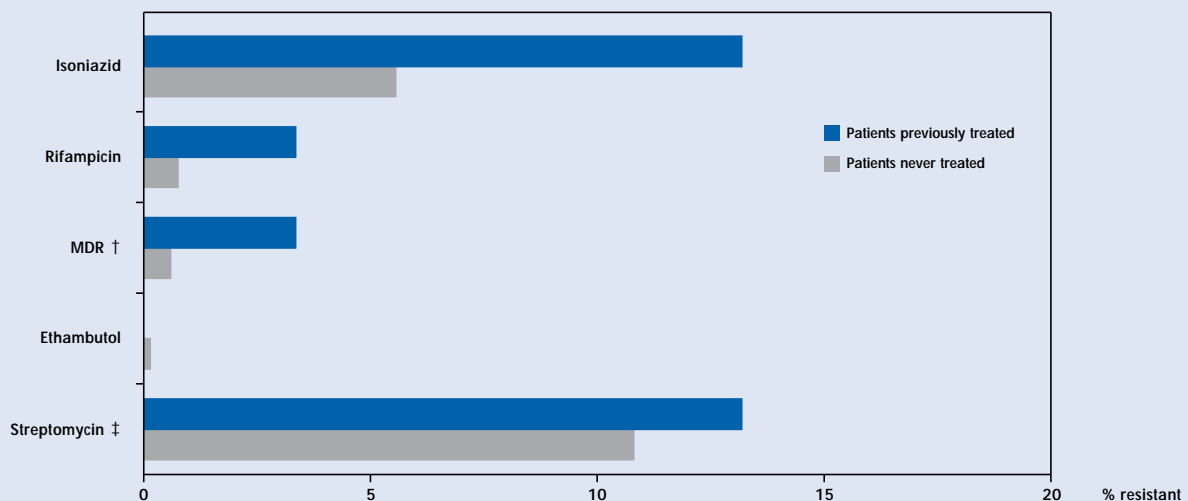
- 5.6% (range: 0% to 22.8%) and 13.1% (range: 0% to 27.3%) for isoniazid;
- 0.7% (range: 0% to 13.8%) and 3.3% (range: 0% to 14,3%) for rifampicin;
- 0.6% (range: 0% to 12.9%) and 3.3% (range: 0% to 13.6%) for MDR;
- 0.1% (range: 0% to 6.3%) and 0% (range: 0% to 15.9%) for ethambutol;

- 10.7% (range: 4.8% to 24.9%) and 13.1% (range: 3.8% to 31.8%) for streptomycin among the five countries where susceptibility to this drug was systematically tested.

These differences by case status were expected since patients previously exposed to antituberculosis drugs may have developed acquired resistance during their previous treatment.

Differences varied by country. For example, the proportion of isoniazid resistance was 7.5 times higher in patients previously treated than in patients never treated in Switzerland, whereas it was only 1.2 times higher in Estonia. These variations may be influenced by differences in criteria for notification of recurrent cases : indeed, only true relapse cases were included in the category of recurrent cases in Estonia, whereas other cases such as patients returning after treatment interruption, who are at higher risk of drug resistance than relapse cases, were included in the notification in Switzerland.

**BOX 13** Median proportions (%) of drug resistance, 1997, 9 countries\*



\* Denmark, Estonia, Iceland, Netherlands, Norway, Romania, Slovenia, Sweden and Switzerland

† multi-drug resistance (resistance to at least isoniazid and rifampicin)

‡ in 5 countries: Denmark, Estonia, Netherlands, Romania and Sweden

In three countries, the proportion of resistance to certain drugs was higher in patients never treated than in patients previously treated:

- in Denmark for all drugs except rifampicin;
- in Sweden for streptomycin;
- in Norway, for isoniazid and rifampicin.

In these countries, the numbers of patients previously treated were small and none of the differences were statistically significant. Nevertheless, the relatively high proportions of drug resistance among patients never treated are likely to be explained by the large proportion of foreign-born patients (70% in Denmark, 68% in Sweden, 53% in Norway), most of whom originated from countries in Africa or in Asia with possibly high levels of drug resistance. These patients may have been infected by drug resistant tubercle bacilli in their country of origin. They may also have acquired drug resistance during a previous treatment but have been misclassified as "never treated" because of language problems during the recording of their previous history.

Drug resistance among **never treated patients** who are **nationals** is an indicator of past or present transmission of drug resistant bacilli within the country. The younger the patients, and the more recent the introduction of the drug in tuberculosis treatments (rifampicin being the most recently introduced), the more likely the transmission is to be recent. The proportion of drug resistance among such patients was examined separately in countries with lower levels of drug resistance (Denmark, Iceland, Netherlands, Norway, Slovenia, Sweden and Switzerland) and in countries with higher levels (Estonia and Romania), according to age, sex, site of disease and smear results.

- In countries with lower levels of resistance, no significant differences were found by sex or by site of disease and smear results (smear positive pulmonary cases compared with other pulmonary cases and extrapulmonary cases). The proportions were lower in younger (<35 years) than in older patients, although not significantly (0.5% versus 2.5% for isoniazid, 0% versus 0.3% for rifampicin). This indicates that there was probably little transmission of drug resistant tubercle bacilli in these countries during recent years.
- Patterns were different in countries with higher levels of resistance. In Estonia, proportions of drug

resistance were higher among patients younger than 35 years than in older patients (25.8% versus 21.6% for isoniazid, 19.1% versus 11.4% for rifampicin,  $p=NS$ ). In Romania, the proportion resistant to rifampicin was similar in the two age groups. The high proportion of drug resistance among younger patients observed in these two countries may indicate a relatively high level of transmission of drug resistant tubercle bacilli during recent years.

The proportion of drug resistance among patients previously treated, together with the proportion of previously treated patients among all patients, reflects to a large extent the quality of antituberculosis treatment.

- In the 7 countries with lower levels of resistance, the proportions of drug resistance among patients previously treated varied considerably between countries. However, they were based on small numbers of patients and differed according to geographic origin: the proportion resistant to isoniazid and to rifampicin was higher in foreign-born patients than in nationals.
- In Estonia and Romania, proportions of drug resistance were high, with no significant differences according to any of the patients' characteristics analysed.

#### 4.6.5. Multi-drug resistance (MDR)

Among 7 140 cases tested for drug susceptibility in the 10 countries, a total of 202 MDR tuberculosis cases were reported.

The majority (180) of these cases were reported in Romania (131 cases) and Estonia (49 cases). In these two countries, 76% of the MDR cases were in patients never treated. Since MDR tuberculosis cases among patients never treated are likely to result from infection by multi-drug resistant bacilli, they may indicate specific problems in infection control policies in hospitals, prisons or other institutions. All but two of the 180 cases were reported in nationals.

In the 8 other countries, 22 MDR cases were reported, among which 10 were reported in patients never treated and 11 in patients previously treated (case status was unknown for one). Most patients (18) were of foreign origin: 5 from Asia, 8 from Africa and 5 from other continents. Only 2 cases were diagnosed in nationals, both previously untreated.