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:: Home > Archives : Eurosurveillance edition 2008 > Volume 13 / Issue 12 [previous page]

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Demographic features and trends in tuberculosis cases in the European Region, 1995-2005

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Demographic features and trends in tuberculosis cases in the European Region, 1995-2005

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In 2005, 426,457 tuberculosis (TB) cases were notified in the World Health Organization (WHO) European Region, with a wide variation and an incremental west-to-east gradient in notification rates also reflected in TB mortality rates. In the enlarged European Union ('EU-27') and other western countries - where 19% of cases were of foreign origin in 2005 (>50% in 13 countries) - overall TB notification rates decreased by 2.4% yearly between 2000 and 2005, compared to 1.6% in 1995-2000, reflecting a declining incidence in all age groups and in most countries. Half the cases notified by the 12 ex-republics of the former Soviet Union in the East in 2005 were reported by the Russian Federation. In the East, the mean annual increase in 1995-2000 (10.0%) was higher than in 2000-2005 (3.9%), and in recent years the number of new cases stabilised while previously treated cases have increased. Efforts are still needed to improve and standardise TB surveillance across the Region. The collection of additional data on risk factors of TB may be useful for surveillance and control.

Introduction

The last years of the 20th century saw the resurgence of TB incidence in different parts of the world. In western countries of the World Health Organization (WHO) European Region where rates had been falling steadily for many years, the rate of decline decreased and, in some countries, a perceptible increase was observed [1]. At that time, countries in the central and eastern part of the Region were experiencing profound economic upheavals which impacted negatively upon their public health [2]. TB notification rates started increasing in the Baltic States (Estonia, Latvia and Lithuania) and in certain central Asian states after the end of the 1980s [3]. This heralded an upturn in TB rates in other former Soviet Union republics, which was sharper and more protracted than that seen further west. The true extent of the epidemic was difficult to assess since case definitions and completeness of reporting differed. In the wake of these developments, a TB surveillance network – EuroTB (http://www.eurotb.org) – was established in 1996 through funding by the European Commission to support TB surveillance across the WHO European Region. This article uses data from this network and from the WHO to describe the main demographic features and trends in TB between 1995 and 2005 in the Region.

Methods

Until 2007, the coordinating hub of EuroTB, located at the Institut de veille sanitaire in France, collected TB data from European national surveillance authorities in coordination with the WHO. In this article the 53 countries of the WHO European Region have been grouped into three geographic areas, based on epidemiological and geographic features (Table 1)

- the European Union and West (EU and West), composed of the 27 current Member States of the EU as well as other industrialized countries of Western Europe (Andorra, Iceland, Israel, Monaco, Norway, San Marino, Switzerland);
- the Balkans (Albania, Bosnia and Herzegovina, Croatia, Former Yugoslav Republic of Macedonia, Montenegro, Serbia, Turkey); and

- the East, made up of 12 republics of the former Soviet Union (Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, Uzbekistan).

Data used were updated until 31 December 2007. Population estimates used for calculating TB notification rates were obtained from the United Nations Population Division,4 with the exception of Serbia, which provided its own estimates for 1998-2005. Updates in notification and population data may account for slight differences in values compared to those published earlier. Data about TB deaths were obtained from the WHO Mortality Database website [5].

The definitions and methodology recommended for use in TB surveillance have been described elsewhere [6,7]. TB cases enumerated in this article include both those which were laboratory confirmed as well as others diagnosed only on clinical/ radiological grounds. In 2005, 58% of TB cases in the EU and West (country range: 28-100%) were culture positive, as opposed to 34% in the Balkans (24-57%) and 20% in six countries in the East (4-36%). The geographic origin of TB cases was assigned as ‘national’ or ‘foreign’ in relation to the country of report on the basis of patients’ place of birth or citizenship. Previously treated cases were those who received curative, combination anti-TB chemotherapy for one month or more prior to the current episode.

Rates of notification and mortality are expressed per 100,000 total population and stratified by age group and sex where indicated. No adjustment for reporting completeness was made. In 2006, countries reported completeness of TB notification to be 70-100% in the EU and West (23/34 countries), 90-98% in the Balkans (2/7 countries) and 48-100% in the East (8/12 countries). Methods used to derive estimates of completeness differed between countries and were sometimes not described. The time trend in notification rates was expressed as the mean of the percentage difference in rates (un-rounded) from one year to the next, and was not shown for Montenegro (data first reported separately for 2005) and for individual countries reporting less than 60 cases in 2005.

The contribution of HIV to TB morbidity was expressed as the proportion of all notified TB cases known to be positive for HIV. The availability of HIV-testing results among TB patients depends on testing policies and the methodology used to collect the test results, which differed between countries. Only deaths coded ICD-9 010-018 (BTL 020-025, 029) or ICD-10 A15-19 were considered in the calculation of TB mortality. Indicators on other clinical characteristics of TB cases, on laboratory confirmation, on anti-TB drug resistance, and on treatment outcome were beyond the focus of this report.

Results

Of all the 426,457 TB cases reported in the WHO European Region in 2005, 72% were from the East, 12% from 12 countries joining the EU since 2004, 10% from countries in the original ‘EU-15’ and West, and 6% from the Balkans including Turkey (Table 1). The overall TB notification rate in 2005 was 47/100,000 population, with an incremental gradient when moving from west to east (country range: 4-205/100,000), which was also reflected in TB mortality (0-25/100,000; Table 2).

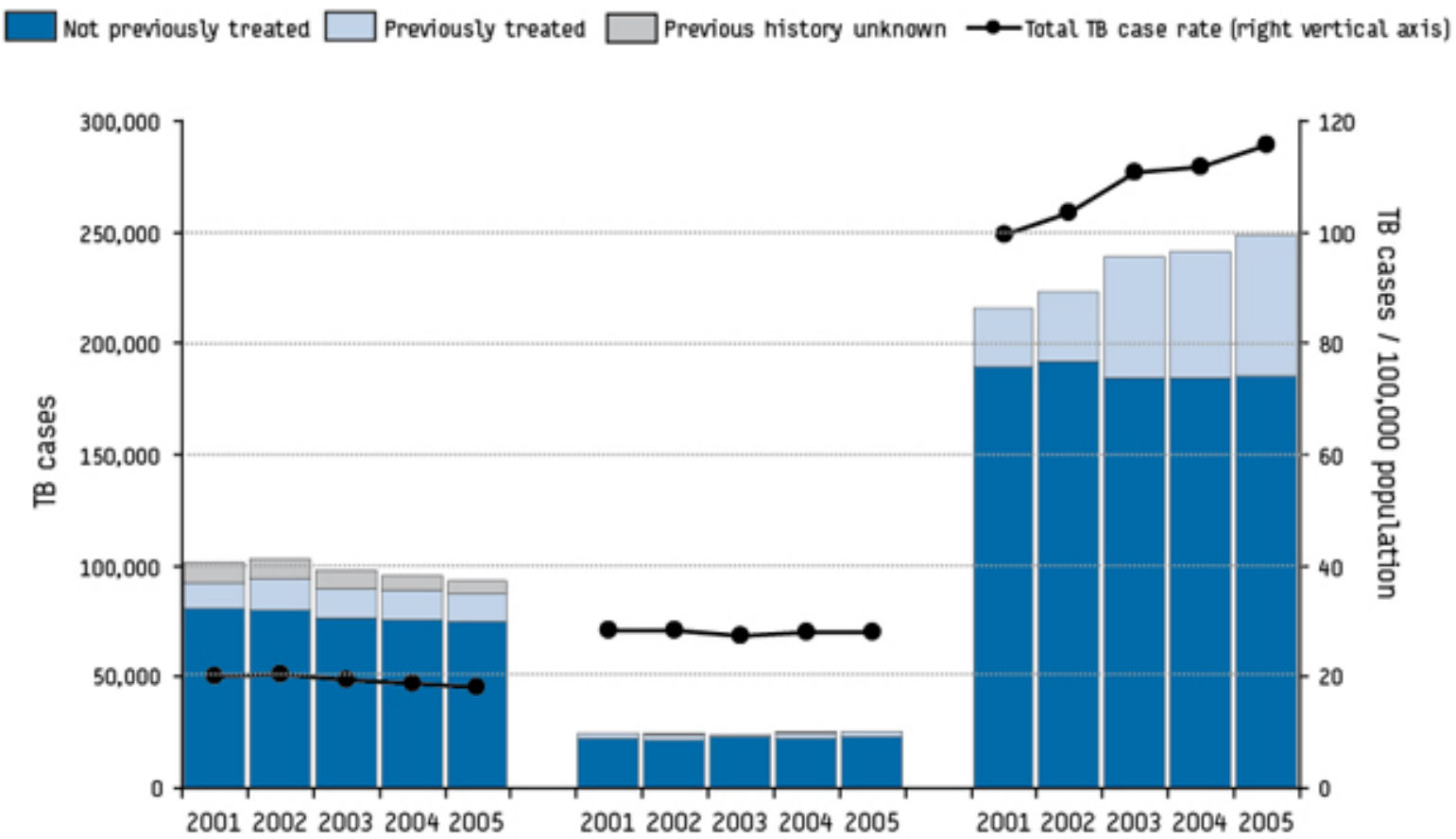
Table 1. Total tuberculosis notifications and notification rates, WHO European Region, 1995-2005

Table 2. Tuberculosis notification and mortality, WHO European Region: selected indicators

Overall the number of TB cases reported yearly in the Region has increased markedly since 1995. This increase however was not uniformly distributed over the years or between the countries. Total notification rates have continued to diverge between the EU and West and the East in recent years (Figure 1).

FIGURE 1

Tuberculosis (TB) notification rates by area and treatment history, WHO European region*, 2001–2005



EU and West Balkans East

* excluding countries with missing data for any year: Cyprus, Monaco, San Marino (**EU and West**); Bosnia and Herzegovina (**Balkans**); Belarus, Tajikistan, Ukraine (**East**)

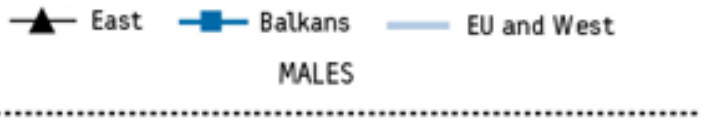
EU and West

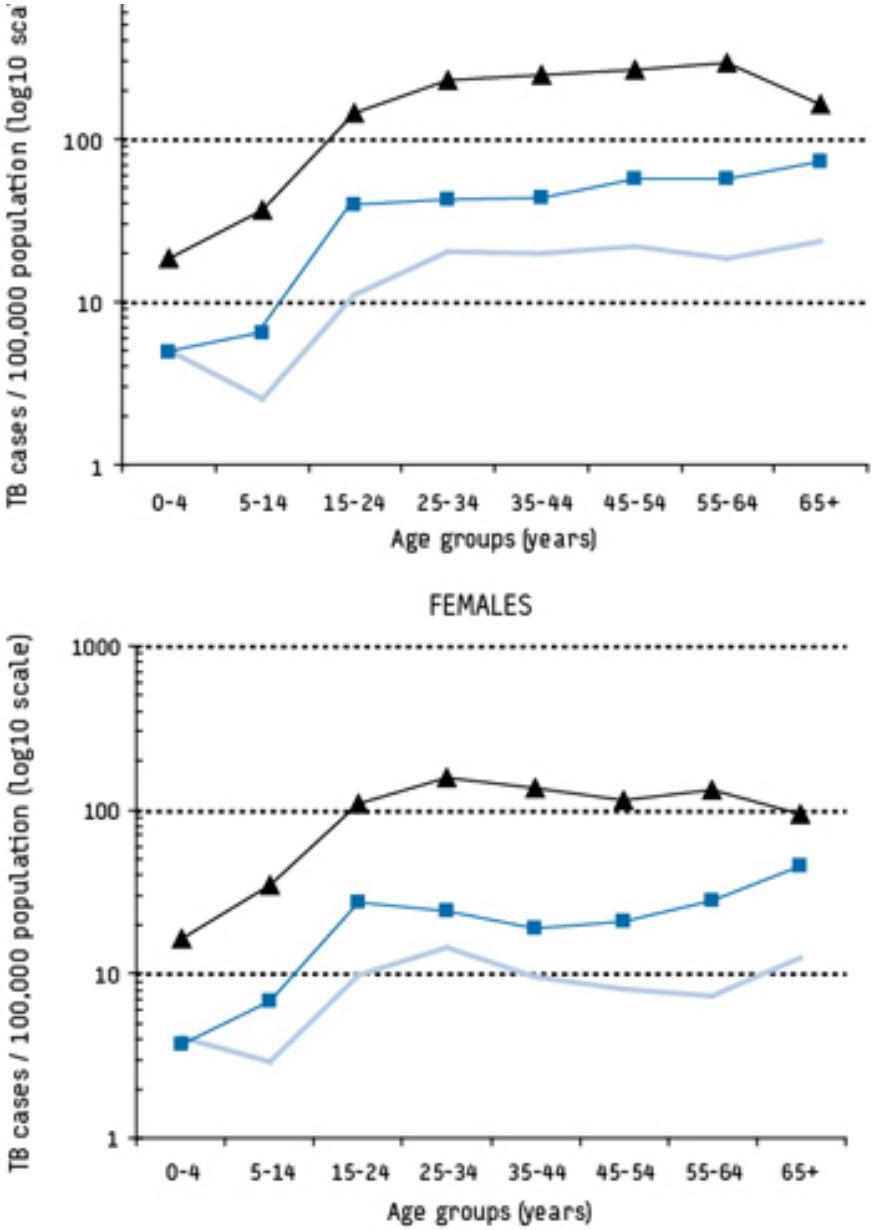
In 2005, the overall notification rate in the EU and West was 18/100,000, with a rate of 10/100,000 or lower in 15 countries and higher than 30/100,000 in Romania (135), the Baltic States (39-75), Bulgaria (43), and Portugal (34). Scandinavian countries and countries on the Mediterranean littoral had some of the lowest notification rates in the area. The overall rate in the 12 countries joining the EU since 2004 was over four times that in the original 15 Member States. Despite the inclusion of countries with a higher TB incidence, the overall notification rate in the EU and West in 2005 was 10% lower than it was in 2001, reflecting a downward trend in 20 countries. Overall rates in the 'EU15' and West decreased by a similar gradient in 1995-2000 and in 2000-2005. Greece, Ireland and Sweden had a net increase in 2000-2005 after a decline in 1995-2000 The United Kingdom had an increase throughout 1995-2005, particularly between 2003 and 2005. In the Baltic States, rates decreased in 2000-2005 following an increase in 1995-2000, while in the Czech Republic, Hungary and Slovakia the decline was faster in the latter period than in earlier years. Bulgaria and Romania had smaller increases in rates in 2000-2005 than in 1995-2000.

In 2005, two thirds of notifications were among males, and rates among them increased after childhood, reaching a plateau in adulthood with a subsequent slight increase in old age (Figure 2). In females, rates were lower than in males after childhood, with a bi-modal pattern peaking in early adulthood and in old age. Rates decreased progressively in all age groups over time (Figure 3). This largely reflected the trend in many countries, including France, Germany, the Netherlands and Portugal. However, while rates in cases aged 55 or older decreased sharply in all countries, differences were noted in the progression of rates in children and young adults between countries (data not shown). In Romania (not included in Figure 3), rates increased in all age groups until 2002, after which they declined. In this country, the proportion of previously treated cases increased progressively in 1995-2005 to reach 24% in 2005, by far the highest in all the EU and West.

FIGURE 2

Age-group- and sex-specific tuberculosis (TB) notification rates, WHO European region*, 2005

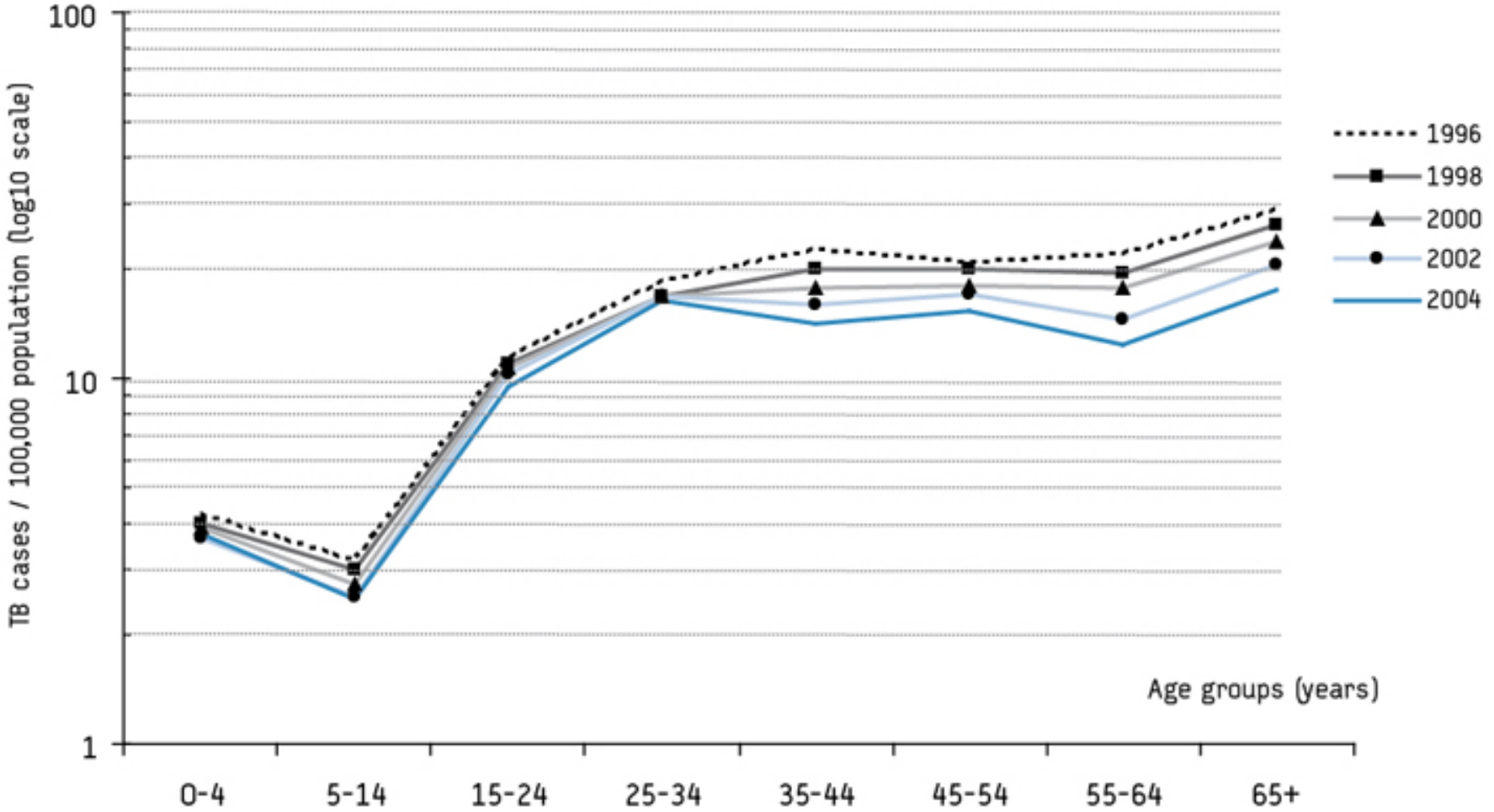




* N=170,795; excluding cases without information on age or sex (407) and cases from countries without age-group distribution of TB cases or population: Andorra, Monaco, San Marino (**EU and West**); Belarus, Kyrgyzstan, Moldova, Russian Federation, Tajikistan, Ukraine (**East**). Romania excluded as the age-specific rates are very different from the rest of the **EU and West**.

FIGURE 3

Age-group-specific tuberculosis (TB) notification rates, EU and West*, 1996–2004



* excluding cases without information on age (769) and cases from countries without full age distribution for one or more years: Andorra, Bulgaria, Cyprus, Greece, Ireland, Monaco, San Marino, Spain. Romania excluded as the age-specific rates are very different from the rest of the EU and West.

The Baltic States experienced a substantial rise in notification rates in the 1990s after their independence from the Soviet Union, which has only abated in recent years. In Latvia and Lithuania, which accounted for most cases from the Baltic States, TB notification rates increased in under-5 year olds, but decreased in adults in recent years. In the United Kingdom, rates

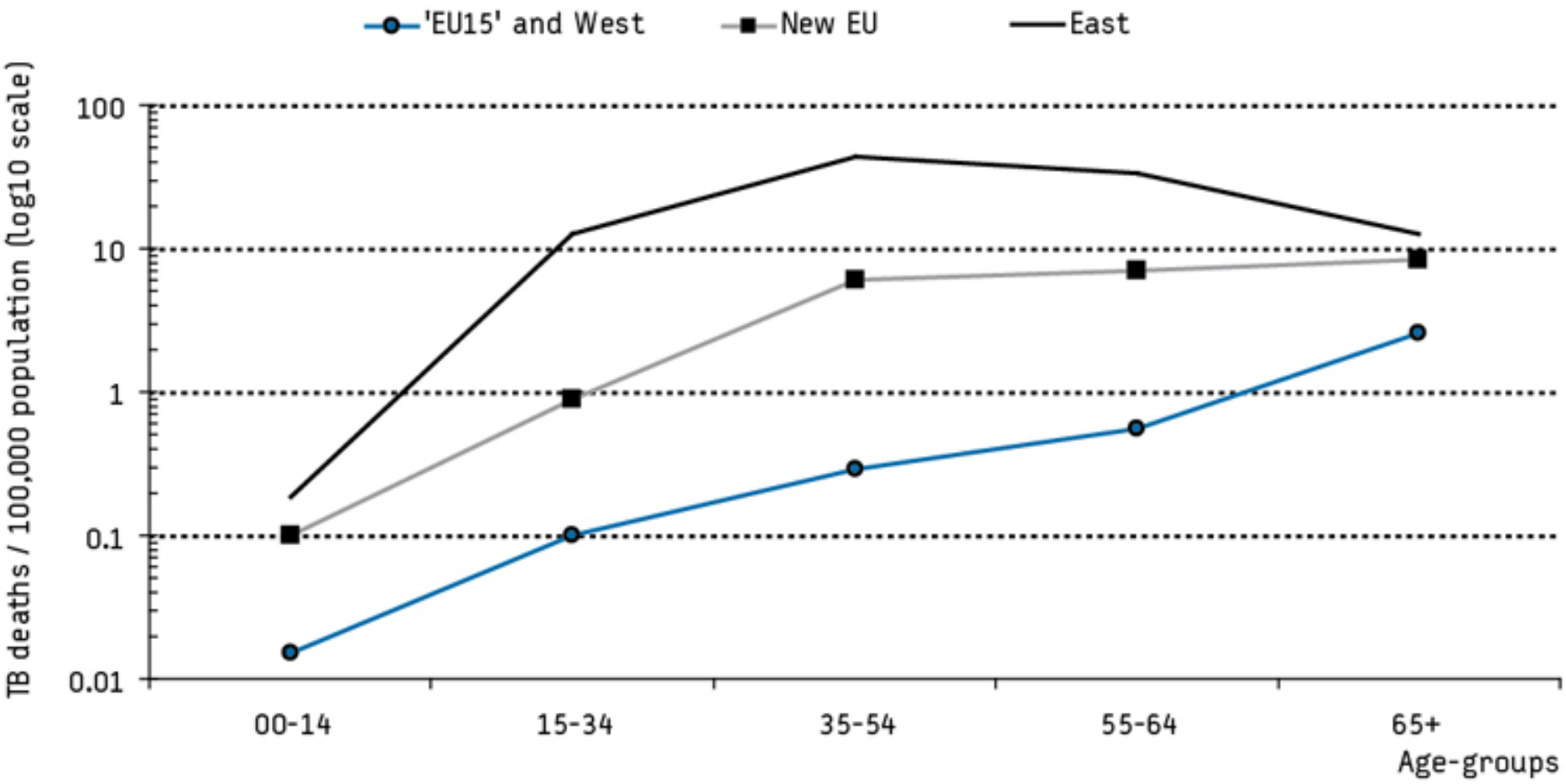
remained stable at low levels in children but increased progressively in all age groups between 15 and 54, with a doubling in rates in the 25-34 year olds over the period, during which time the proportion of foreign TB cases increased steadily to 79% in 2005. The contribution of TB in immigrants to overall notification varied greatly between countries. While only 1% of cases reported by the central European countries in 2005 were not autochthonous (new EU countries excluding Cyprus and Malta; country range: 0-17%), in the other countries 42% of TB cases were of foreign origin (range: 12-82%). In 27 countries with data for 2005, two thirds of cases of foreign origin were equally distributed between Asia and Africa, 19% were from another country of the EU and West or the Balkans, and 9% from a former Soviet Union republic outside the EU. Half the foreign cases originated from only 11 countries, which included high-burden countries from the Indian Sub-continent and Sub-Saharan Africa as well as other populous countries within the WHO European Region itself.

Aggregated data on HIV sero-status of TB cases reported in 2003 to 2005 were available for 21 countries. The highest HIV prevalence among TB cases was reported by Portugal (15%) and Iceland (9%, 1 case), and was 2-8% in 8 countries and 0-1% in 11 countries. HIV prevalence among TB cases was reportedly stable in 2000-2005 in most countries, but increased markedly in Estonia (from 0.1% to 6.4%) and Latvia (from 0.7% to 3.5%).

Total TB mortality rate was 1/100,000 population or less in most countries, but was higher in Bulgaria, Hungary, Poland, and Portugal (2-3), and even higher in the Baltic States and Romania (4-10). In the ‘EU15’ and West, mortality increased progressively by age, being more than four times higher in persons over 64 years when compared to those aged 55 to 64 years (Figure 4). In contrast, in the central European Member States, rates increased sharply from childhood to early middle-age but then more smoothly into old age.

FIGURE 4

Tuberculosis (TB) mortality rates by age group — EU and West, and East*, latest available data



* excluding 438 TB deaths with age unknown and including latest data (2003-2005) for countries using ICD-10 coding: **'EU15' and West** (N=1,895): Austria, Finland, France, Germany, Israel, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom; **New EU** (N=3,739): Czech Rep, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Slovenia; **East** (N=52,252): Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russian Federation, Ukraine, Uzbekistan (Source: WHO Mortality Database, WHOSIS, update October 2007)

The Balkans

In 2005, 27,582 TB cases were reported by the seven Balkan countries, 74% of these cases by Turkey alone. The overall TB notification rate in the countries was 29/100,000, with rates higher in Bosnia and Herzegovina (55) than in the other countries (17-32). Between 2000 and 2005, rates decreased by 0.5-6.9% yearly in all countries, except for Turkey where they increased by 1.3%. A decline was observed in Bosnia and Herzegovina following an increase in the late 1990s.

Males predominated (range: 54-67%) among notifications. Children represented 5% of reported cases in 2005 but reached 14% in the Former Yugoslav Republic of Macedonia (overall rate 32/100,000). Notification rates in males increased sharply from childhood to early adulthood, and then increased slowly into old age. In females, rates were lower than in males in adults and decreased after early adulthood to rise again smoothly in the elderly.

As for central EU Member States, only 1% of cases overall were of foreign origin (9% in Croatia) and two thirds of these were from another Balkan country. HIV sero-prevalence among TB cases was reported by four countries and was low (range: 0.0-0.3%).

TB mortality rates were moderate in Croatia and the Former Yugoslav Republic of Macedonia (2.5 and 3.8/100,000 population respectively).

East

In 2005, the overall TB notification rate in the 12 former Soviet Union republics in the East reached 110/100,000 population. Rates were higher than average in Kazakhstan (205), Moldova (162), Georgia (144) and Kyrgyzstan (130). Over half of the 306,015 cases reported in this area were from the Russian Federation. Notification rates in the East increased on average by 3.9% yearly between 2000 and 2005, but this ranged widely between countries (-3.9% to +19.9%). Much of the overall increase is attributable to increasing inclusion of previously treated cases, the proportion of which increased from 12% to 25% over this period as the number of new cases remained stable (Figure 1). However, the mean annual increase in rates was 2.5 times lower in 2000-2005 than that observed between 1995 and 2000.

While there was a male predominance among notified cases this is lower in the central Asian republics than in the other countries (57% vs. 72% respectively). Children accounted for 4% of the cases overall, but reached 13% in Kyrgyzstan among previously untreated cases. Most cases aggregated in the ages 15-44 years with only 7% of cases being over 64 years. Rates in males increased from childhood to middle age by a factor of 10 and then decreased sharply in the older ages. Notification rates in childhood were similar between the sexes but much higher in adult males than in females, in whom they peaked in young adulthood and in middle-age.

Most Eastern countries do not report TB in foreign citizens. In Moldova and the Russian Federation, foreign citizens represented 1% of notified cases. Information on TB-HIV comorbidity was sparse. Six countries reported results of HIV testing in TB patients, in which 0.2-2.0% of notified TB cases were HIV positive in recent years.

Mortality data for TB were available for nine countries, of which four had low coverage or completeness. Total TB mortality rates in the other five countries varied between 10.4 and 25.4/100,000 in the latest available year. Mortality rates increased rapidly from childhood to peak at age group 35-54 years, and then decreased at old ages.

Discussion

The reversal in the decline in TB notification rates observed in the early 1990s in western countries of the WHO European Region persisted for some years but, with some notable exceptions, most countries have experienced a steady decrease in newly-diagnosed TB cases in recent years. As notifications among nationals decreased or remained stable in nearly all countries, cases of foreign origin came to represent a larger proportion of all TB cases reported. Immigration from countries with high TB prevalence has been one of the most important recent developments concerning TB in much of the industrialised EU. Thus, the recent increase in total TB cases observed in Sweden and the United Kingdom reflect the incremental trend in foreign-born cases as rates largely stabilised among the indigenous population. Populations of foreign origin generally experience higher TB notification rates than nationals [8]. The bi-modal pattern in age-specific notification rates in the western countries reflects the superimposition of patterns from foreign (largely young adult) and autochthonous (mostly elderly) populations. These changes in the profile of TB patients in the western countries are likely to impact negatively on treatment outcome. Foreign patients are more likely to have drug resistance [9]. Treatment interruption is more common in immigrants [10]. Furthermore, the increasing age of TB patients has a negative impact on likelihood of treatment success [11]. In Finland, deaths among TB cases - half of whom are nowadays elderly - are higher than elsewhere [12].

TB surveillance data and trends in the East have to be interpreted carefully, as in several countries TB notification has been influenced differently by changes in TB control systems since the early 1990s. Stabilisation or increase in notification rates may thus reflect improved case detection or changes in case definitions rather than actual incidence. The wide range in the proportion of notified cases having had TB in the past reflects differences in patient recruitment and in the definition of a notifiable case. Much of the increment in case reports in the East in recent years was due to the increased inclusion of previously treated cases while the number of newly diagnosed cases levelled off. This explains the spike in the Russian Federation in 2003, which influenced overall rates in the East given the large share of cases coming from this country alone (Figure 1). Similarly, the Baltic States started including forms of previously treated cases in addition to relapses midway in the period under study partly explaining a peaking of total notification rates around this time. Despite these artifacts, the high notification rates in young adults in the East still indicate intense transmission in recent years.

Testing for HIV among TB patients and for TB among HIV-positive individuals is problematic and comment on trends of TB/HIV comorbidity are impeded by incomplete information. In most countries the HIV status is known for only a small proportion of TB cases. The proportion of TB cases infected with HIV when calculated by including all notified TB cases in the denominator gives a conservative estimate in countries where HIV testing is offered only to a selection of patients based on

risk. Retrieval of testing results is also incomplete. Notwithstanding, a number of observations can be made. In Balkan countries, the low prevalence of HIV among TB cases is associated with a low HIV prevalence in the general population of these countries up to now [13,14]. The increase in HIV prevalence among TB cases observed elsewhere reflects separate processes of particular concern. In the United Kingdom, there has been increasing immigration from countries with high prevalence for both TB and HIV in recent years [15]. In western countries injecting drug users (IDUs) usually predominate among HIV cases with TB, suggesting a higher risk for developing TB among this HIV transmission group [16]. The same appears to be the case in the former Soviet Union republics where a dramatic increase in newly diagnosed HIV infections has occurred since the mid-1990s, mostly among IDUs [17]. Being an IDU was a strong predictor of HIV infection in younger adults with TB in Kiev city (Ukraine) in 2004-2005, and TB/HIV comorbidity among IDUs has reportedly increased since 2002 [18]. In 2002-2003, 92% of 49 TB/HIV cases detected in a cross-sectional survey of St Petersburg (Russian Federation) had injected drugs [19]. In Estonia, which has endured a sharp HIV-epidemic in the early years of this decade mostly in IDUs, [20] the steady rise in TB/HIV comorbidity is likely to represent an overlap of the HIV and TB epidemics in the indigenous population. And in Latvia, where cases having TB and HIV increased, 31 of 51 TB/HIV cases detected in 1998-2001 were in IDUs [21].

TB mortality rates follow roughly the same geographic gradient as TB morbidity. All former Soviet Union republics had high TB death-to-notification ratios. In contrast to countries further west mortality rates and death-to-notification ratios peaked before old age. This may reflect a higher lethality due to drug-resistant disease, the prevalence of which is high in countries like Kazakhstan [22]. In Ukraine, a country which has been particularly affected by the HIV epidemic for a number of years [13], this may be the effect of comorbidity. Despite these observations, some limitations are noted when comparing data between countries. The practice of coding the cause of death varies between vital registration systems in different countries. For instance Lithuania attributes much more TB deaths to miliary disease than neighbouring Estonia and Latvia. Most countries in the East never use codes for death from the late effects of TB (i.e. ICD-9 137 or ICD-10 B90), in contrast to many Western countries, some of which - like Norway and Sweden - register more deaths in these categories than under the standard tuberculosis codes used in this article [5].

Conclusion

Countries in the East, with their high TB morbidity and mortality, remain a priority for TB surveillance in the WHO European Region. Surveillance systems need to be reinforced and modernized, and data collection increasingly automated. Access of TB patients to health care facilities with reliable laboratory facilities to perform culture examination and HIV testing, and the reporting of these test results should become more widespread. Cases of foreign origin should be more widely reported. The male predominance among adult TB cases, albeit more or less ubiquitous in the world [23], should serve as an alert to investigate possible barriers to access to care for women, especially when sex-ratios differ markedly between neighbouring countries with similar epidemiological patterns.

Today’s EU presents a wide spectrum of TB patterns. Notification rates in the Baltic States remain high even if in decline, and

these countries are particularly concerned by TB/HIV comorbidity and drug resistance. Central European countries, several bordering the former Soviet Union, need to be vigilant regarding a possible re-emergence of TB. The low TB incidence in much of the EU and West are no reason for complacency. The elimination of TB (<1 TB case/1,000,000 population) is still a distant prospect for all countries. The measurement of progress towards elimination will necessitate sensitive indices of disease activity in sub-populations at increased risk of TB infection. These groups need to be better profiled at the supranational level. Similar to the way geographical origin has been built into international reporting, the collection of additional variables that are amenable to adequate standardisation can be useful for targeting public health action. These could include indices of social deprivation, history of imprisonment, use of tobacco, use of alcohol, injecting drug use, contact with active TB and area of residence within the country.

Despite efforts throughout the lifetime of EuroTB to standardise the European case definition for TB case reporting, more work is required. The Regional network of national TB surveillance authorities has provided a useful forum for discussion and exchange of experiences in the past, including the revision of the European case definition in 2006. This resource should be developed in future to enhance the process of routine data collection, conduction of surveys and standardisation of methodology.

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