SPECIAL REPORT

Progressing towards TB elimination

A follow-up to the Framework Action Plan to Fight Tuberculosis in the European Union

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The plan was developed by the disease-specific programme for TB, following a request from the EuropeanCommission.
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Contents

Abbreviations

AIDS	Acquired immune deficiency syndrome
CISID	Centralized Information System for Infectious Diseases
DOTS	Directly observed therapy, short-course; the internationally recommended strategy for the control of tuberculosis
DST	Drug susceptibility testing
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EQA	External quality assurance
ERLN-TB	European reference laboratories for tuberculosis
EU	European Union
HIV	Human immunodeficiency virus
MDG	Millennium Development Goals
MDR TB	Multidrug-resistant tuberculosis
MTC	*Mycobacterium tuberculosis* complex
TB	Tuberculosis
TESSy	The European Surveillance System
WHO	World Health Organization
XDR TB	Extensively drug-resistant tuberculosis

Executive summary

Introduction

The Framework Action Plan to Fight Tuberculosis in the European Union was launched by the European Centre for Disease Prevention and Control (ECDC) in 2008. On the basis of a request of the EU Health Commissioner to develop a monitoring framework in support of the plan, ECDC has now produced a Follow-up to the Framework Action Plan. The objectives of the Follow-up to the Framework Action Plan are: to provide an overview of the current strategic environment for TB control in the EU and outline how this relates to the global situation; and, to describe an epidemiological and strategic monitoring framework that would allow progress towards elimination of TB in the EU to be assessed.

Strategic environment at European and global levels

The current level of the TB epidemic in the EU calls for a specific monitoring framework that is directly relevant to the European epidemiological context and easily applicable by the Member States. Therefore, the development of a monitoring framework requires a thorough understanding of the epidemiological and strategic environment to be monitored. Thus, this follow-up report provides an overview of the current environment for the EU and globally, recognising the need for a comprehensive TB control strategy in view of the globalised context of the TB epidemic.

Monitoring the Framework Action Plan

This report proposes a number of core epidemiological and operational indicators and targets as an integral part of the monitoring framework. These indicators and targets are compatible with those already monitored as part of existing global and regional collaborations, and can generally be derived from information already collected and reported by countries. The core indicators of the Follow-up are all specifically related to the eight strategic areas of the Framework Action Plan to allow the assessment of progress of each of these areas.

Epidemiological indicators

1 Trends in case notification rate
2 Trends in MDR-case notification rate
3 Trends in ratio of notification rates in children to adults
4 Trends in mean age of TB cases

Operational indicators

1 Availability of a national TB control plan
2 Availability of guidelines for implementing the national TB control plan
3 Percentage of national TB reference laboratories (adhering to ERLN-TB) achieving adequate performance in the external quality assurance scheme
4 Availability of a strategy for introducing and implementing new tools for TB control
5 Percentage of new pulmonary TB cases confirmed by culture and percentage of cases tested by DST for first-line drugs
6 Percentage of Member States reporting treatment success rate
7 Treatment success rate
8 Percentage of TB patients for whom HIV status is known

Introduction

Background

Tuberculosis (TB) is a serious infectious bacterial disease, which most commonly affects the lungs. It is mainly transmitted from person to person via droplet nuclei (aerosols) from the lungs of people with active pulmonary disease. Because there is currently no completely effective vaccine, control of the disease relies heavily on detecting infectious cases[i] and treating them for at least six months with a combination of antibiotics. The aim of treatment is to cure the patient and achieve non-infectiousness, hence interrupting transmission of the disease, while avoiding the emergence of drug resistance.

In the European Union (EU), TB case notification rates are among the lowest in the world. However, the epidemiological pattern varies considerably from country to country, with some countries showing steady progress towards eliminating the disease, while others still face unacceptably high case notification rates. In all countries, control efforts have to deal with the challenges of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, co-infection of TB and human immunodeficiency virus (HIV) infection, and the concentration of cases in vulnerable groups.

The European Framework Action Plan

In February 2008, at the request of the EU Health Commissioner, the European Centre for Disease Prevention and Control (ECDC), in consultation with experts from EU Member States and elsewhere, produced a *Framework action plan to fight tuberculosis in the European Union* (hereafter referred to as the 'Action Plan') [1]. This Action Plan provides a comprehensive framework for efforts to control TB, both in Member States and at European Community level. It is in line with the United Nations Millennium Development Goals (MDGs) [2] and the WHO Stop TB Strategy [3], which form the basis for international efforts to control TB (see Section 1.3).

The long-term goal of the Action Plan is to control and ultimately eliminate TB in the European Union. Specifically, the plan aims to:

- increase political and public awareness of TB as a public health issue in the EU;
- support and strengthen EU Member States' efforts against TB in line with the national epidemiological situation and challenges; and
- contribute to the control of TB in the EU by supporting those countries from which imported cases originate.

The call for a follow-up to the Framework Action Plan

Following the launch of the Action Plan in 2008, the Commission requested that ECDC develop a monitoring framework in support of the plan.

This follow-up document was therefore developed and has benefited from the input of various groups and the support of senior European TB consultants.

The document was drafted taking into consideration the need for the framework to be concise and feasible, and the need to keep the burden of reporting to a minimum. The challenge of tailoring the development and monitoring of the indicators to the peculiar and heterogeneous epidemiological and control setting of the EU Member States had to be carefully balanced against the commitment to adhere to the agreed principles of global TB control and monitoring.

Building on the Action Plan, the present document has two principal objectives:

1 To provide an overview of the current strategic environment for TB control in the EU and outline how this relates to the global situation.
2 To describe an epidemiological and strategic monitoring framework that would facilitate the assessment of progress towards elimination of TB in the EU.

The current level of the TB epidemic in the EU (see Section 1.1) is such that a specific monitoring framework is needed that is directly relevant to the European epidemiological context and acceptable to, and easily applicable by, Member States. As an integral part of the proposed framework, a number of key operational and epidemiological indicators and targets are put forward (Sections 2.2 and 2.3). These indicators and targets are compatible with those already monitored as part of existing global and regional collaborations, such as the Stop TB Partnership, and can generally be derived from information already collected and reported by countries.

[i] Infectious cases produce sputum in which tuberculosis bacilli can be found by microscopy examination (sputum smear-positive).

1 The strategic environment at European and global levels

In order to identify and develop a valid monitoring framework, a thorough understanding of the strategic environment is required. Recognising the need for a comprehensive TB control strategy in the global context of the epidemic, the overview presented in this section extends beyond the EU to consider the global setting.

1.1 The epidemiological situation in the EU

Since 1 January 2008, ECDC and the World Health Organization (WHO) Regional Office for Europe have jointly coordinated the TB surveillance in Europe. The aim is to ensure a high quality of standardised TB data covering the 53 countries of the WHO European Region and Liechtenstein. Designated national surveillance institutions are responsible for reporting the data to a joint database.

The figures given in this section are taken from the second joint report on TB surveillance in Europe, published in 2010 and covering cases reported in 2008 [4].

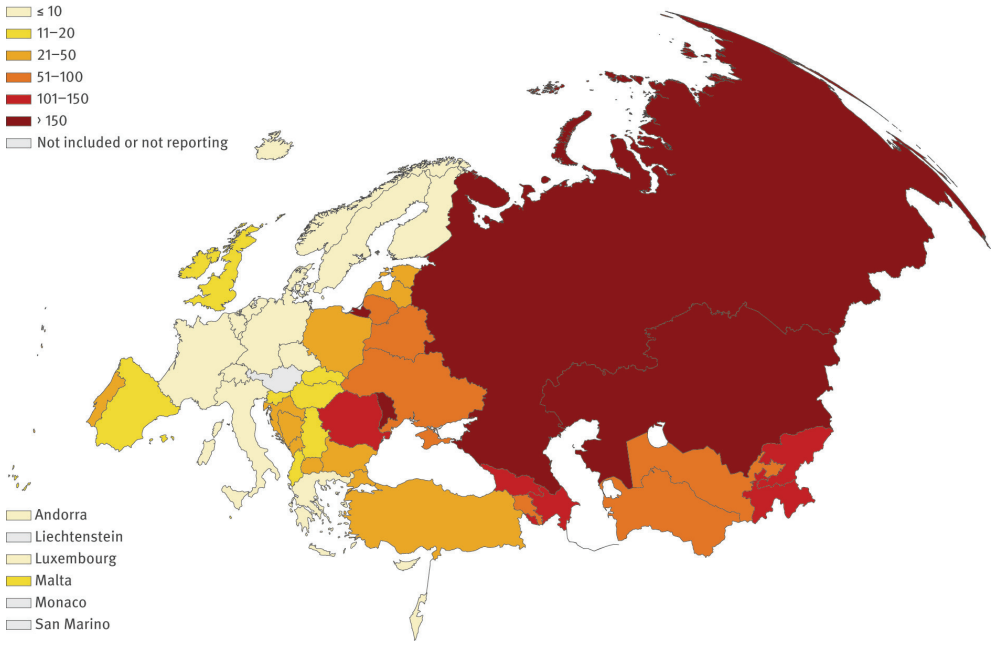
In 2008, 82 611 TB cases were reported by 26 EU countries (all except Austria) and two countries of the EEA (Iceland and Norway), giving an overall notification rate of 16.7 per 100 000 population. The notification rates ranged from 5.5 per 100 000 in Germany to 115.1 per 100 000 in Romania. Notification rates higher than 20 per 100 000 were reported in Romania, Lithuania, Latvia, Bulgaria, Estonia, Portugal and Poland (see Figure 1).

Despite a mean annual decline in notification rates of 3.3 % between 2004 and 2008, the decrease recorded between 2007 and 2008 was the lowest of the previous four years with only a 1.2 % decrease; a mean annual decline similar to that reported for the period 1998–2002 (1.3 %). Of the 28 reporting countries, 18 have experienced a net downward trend in TB notification since 2004.

Notification rates have been used throughout this monitoring framework based on the assumption that notification is a good proxy for incidence in the EU.

Tuberculosis was confirmed by culture in 47 497 of all TB cases (57.5 %) giving an overall culture-confirmed case rate of 9.6 per 100 000 population. However, the level of culture-confirmed cases varies widely across countries (range 34.6–94.4 %) and data were not complete for eight countries. The overall proportion of culture-confirmed cases has remained stable since 2005 except for France, Ireland and Italy. A substantial improvement in culture confirmation has occurred in Cyprus, Poland, Portugal and Slovenia.

Figure 1. Total TB notification rates per 100 000 population, Europe, 2008



Data from Kosovo (in accordance with Security Council Resolution1244 (1999) is not included in the figures reported for Serbia.
Source: Tuberculosis Surveillance in Europe 2008 [4].

Childhood TB

Notification rates of TB in children under 15 years of age are generally declining or stable at a low level and paediatric cases accounted for 4.2 % of all notified cases in 2008. However, Bulgaria, Latvia, Lithuania and Romania have high paediatric TB rates of 15.3–32.2 per 100 000 child population. Increased rates of TB in children were also seen in low-incidence countries and may suggest an increase in transmission rates.

Foreign-origin TB cases

In 2008, 22.4 % of all reported TB cases were in people of foreign origin. This proportion ranged from 21.3 to 88.0 % in 17 countries and the overall proportion was much higher (33.8 %) when excluding data from Bulgaria and Romania. Of the foreign cases, 27.4 % were from Asia, 22.7 % from Africa, 7.9 % from other EU/EEA countries, and 8.5 % non-EU/EEA European countries. Between 2001 and 2008 there was a steady decline in the number of notified cases of national origin in most countries, whilst notifications of cases of foreign origin generally increased. Since 2003, Italy, Malta, Sweden and the United Kingdom have shown a continued increase in the number of cases of TB among individuals of foreign origin[ii].

MDR and XDR TB

The emergence of multidrug-resistant (MDR) TB poses a serious challenge to TB control. MDR TB was reported by 23 of the 30 EU/EEA countries in 2008, with the Baltic States, Spain, Romania, Italy and the United Kingdom reporting 50 or more MDR cases. Further, four of the 27 countries designated by WHO as high-burden MDR TB countries are in the EU (the three Baltic States and Bulgaria). Overall, in the 25 countries that routinely performed culture and drug sensitivity testing, the rate of MDR among all cases increased from 4 to 6.1 % between 2007 and 2008. The overall proportion of cases with MDR TB among previously untreated cases was 2.8 %, ranging from 0 to 25 %. Among previously treated cases the MDR rate was 23.3 %, ranging from 0 to 45.5 %.

Extensively drug resistant (XDR) TB was reported by 13 European countries. In 2008, 90 XDR cases were reported with the proportion of XDR cases increasing from 6.1 % of MDR cases to 7.3 % since 2007. The Baltic countries are reporting the highest numbers and proportions of both MDR and XDR strains.

TB/HIV co-infection

The quality and completeness of country data on the association between HIV infection and TB vary greatly, largely because of differences in testing policies and data collection. Only eight countries reported complete data in 2008, among these countries the mean proportion of TB patients with a positive HIV serostatus was 9.5 % ranging from 0 to 14.6 %. The highest proportions were found in Portugal, Estonia and Malta.

Treatment outcome

Twenty-two countries reported treatment outcome data for culture-confirmed pulmonary TB cases reported in 2007 that were followed up. Treatment outcome monitoring shows a marginal improvement in completeness and number of countries reporting outcomes for the 2007 cohort. However, no significant improvement in the percentage of cases successfully treated can be observed over the past five years.

The overall treatment success among culture-confirmed cases was 73.6 %. Among previously untreated, culture-confirmed, pulmonary TB cases, 79.5 % had a successful outcome but only three countries (Iceland, Portugal and Slovakia) achieved the treatment success rate target of 85 % or higher set by the Stop TB Partnership. Only 51.8 % of previously treated TB cases had a successful outcome and among MDR TB cases the success rate was as low as 30.9 % in the fifteen countries that for the first time reported data on culture-confirmed pulmonary MDR cases after 24 months' follow-up. Success rates of less than 75 % were associated with a high loss-to-follow-up. TB mortality rates have decreased or remained stable in all EU/EEA countries over recent years with 6.6 % among new cases, 11.4 % among retreatment cases and an overall mortality of 7.8 % in 2007.

Conclusions

These data and the relevant analyses demonstrate that the EU remains a highly heterogeneous setting. Three broad groups of countries can be defined for control purposes: (1) low-incidence countries with cases increasingly aggregating among the most vulnerable, including certain groups of foreign-origin population; (2) countries with moderate or relatively high incidence, with low rates of MDR TB; and (3) countries with relatively high incidence and a high proportion of MDR TB cases, but with declining TB rates.

In addition, the data demonstrate that despite the overall EU downward trends in terms of notification there is no room for complacency. In particular, the slowing in the decline of the epidemic, the reversal of notification trends

[ii] Geographical origin of TB cases is classified according to place of birth (born in the country/ foreign-born) or, if unavailable, citizenship (citizen/non-citizen).

in some Member States, as well as the increasing notification of paediatric tuberculosis in a few countries, all indicate the need for renewed action in European and national TB control. In addition, the threat of sustained transmission and emergence of MDR TB remains high, particularly in view of the under-achievement of treatment success targets.

1.2 Global epidemiological setting

Globally in 2008, there were an estimated 8.9–9.9 million incident cases of TB, 9.6–13.3 million prevalent cases of TB, 1.1–1.7 million deaths from TB among HIV-negative people and an additional 0.45–0.62 million TB deaths among HIV-positive people [5].

There were 5.8 million cases notified in 2009, corresponding to 60–67 % of all incident cases, with a best estimate of 63 %. The target for treatment success of 85 % has been achieved among the cohort of patients started on treatment in 2007 and 2008, with 86 % of these being successfully treated. The WHO European Region, however, remains short of reaching this target (66 % for the 2008 cohort) mainly due to its high level of MDR TB (with deaths and failure rates relatively high).

After estimated incidence peaked at 143 cases per 100 000 (range: 136–151) in 2004, the world as a whole is now on track to achieve Millennium Development Goal Target 6.C (see Box 1), as are five of WHO's six Regions (the exception being the South-East Asia Region, where rates are stable).

On current trends, the world as a whole could achieve the target of halving the 1990 mortality rate by 2015, as could five of six WHO Regions (the exception is the African Region). Three Regions are on track to halve prevalence (per 100 000 population) by 2015 compared with 1990 (the Region of the Americas, the Eastern Mediterranean Region and the Western Pacific Region), and this target could also be achieved in Europe. Globally, the target appears unlikely to be met because the African Region is so far from the target following a major upsurge in cases associated with the HIV epidemic in the 1990s.

1.3 The strategic environment

Actions at global level

TB was explicitly recognised as a major global public health problem in the early 1990s, when the World Health Assembly adopted a resolution calling for increased efforts to control the disease. The resolution set two major targets for global action against TB: the detection of 70 % of new smear-positive cases, and cure of 85 % of such cases. In 1994, the internationally recommended control strategy, DOTS, was launched, followed in 1998 by the Stop TB Initiative. In 2000, this became the Stop TB Partnership, a global network of international organisations, countries, donors, non-governmental organisations and other interested parties committed to controlling and eventually eliminating TB. The first Stop TB Partners' Forum, held in Washington in 2001, launched a Global Plan to Stop TB for the period 2001–05. Subsequently, a plan for 2006–15 was launched in January 2006, and more recently an updated version for the period 2011–15 has been developed. These global plans form the overarching framework for the Stop TB Partnership's combined actions.

The Millennium Development Goals and the Stop TB Strategy

The adoption of the Millennium Development Goals by the global community in 2000 provided renewed impetus for TB control efforts. Specifically, MDG6 calls for action to combat HIV/AIDS, malaria and other diseases, including TB. Widespread implementation of the DOTS strategy led to significant progress in control of the disease. For example, by 2007 the treatment success rate among new smear-positive cases had reached 86 %, while in 2008, the global case detection rate was 61 % [6].

However, by 2005, it had become clear that DOTS alone would not be sufficient to achieve global TB elimination. In 2006, therefore, the Stop TB Strategy was launched, designed to meet both the TB-related MDG targets and the Stop TB Partnership targets for 2015 (see Box 1). The Stop TB Strategy underpins the Global Plan to Stop TB 2006–2015 [7].

Box 1. Global goals and targets relevant to TB control

MDG 6: Combat HIV/AIDS, malaria and other diseases

Target 6.C: To have halted by 2015 and begun to reverse the incidence of malaria and other major diseases [including, specifically, TB].

Indicator 6.9: Incidence, prevalence and death rates associated with TB.

Indicator 6.10: Proportion of TB cases detected and cured under DOTS.

Stop TB Partnership targets

- by 2015, reduce TB prevalence and death rates by 50 % relative to 1990;
- by 2050, eliminate TB as a public health problem (incidence < 1 case per million population).

The current European context

The goals and targets outlined in Box 1 have been endorsed by European countries. However, because the MDGs in particular were conceived in a context of promoting development and eradicating poverty, these targets are not necessarily optimally adapted to the European context. For example, many European countries are already seeing a steady decline in TB case notification rates (see Section 1.1), and have in place the infrastructure and personnel needed to implement the necessary TB control activities. The impact of the global targets in promoting and motivating TB control in Europe has therefore been limited.

Nevertheless, it has to be recognised that, with current trends, Europe is unlikely to achieve elimination of the disease by the target date of 2050. Imported cases and drug resistance will continue to pose challenges, even for low-incidence countries, and will require concerted action on a broad front, tailored to the specific situation.

Recognition of the particular challenges to TB control in Europe has led recently to a number of broad-based initiatives, as outlined below.

The Berlin Declaration

In October 2007 in Berlin, Germany, the WHO Regional Office for Europe convened a Ministerial Forum on Tuberculosis, to seek increased commitment from governments to work together to tackle the TB epidemic in the Region. In the resulting Berlin Declaration [8], countries undertook, inter alia, to strengthen their public health and social services systems to respond to the TB situation in the Region, to adopt the Stop TB Strategy, and to seek sustainable funding for TB control efforts. The Declaration effectively reset TB control agendas across the European Region.

The plan for high-priority countries in Europe

Recognising that within the European Region the countries of eastern Europe were hardest hit by TB, the WHO Regional Office in 2007 produced a plan to tackle the disease in those countries [9]. Of the 18 countries targeted in the plan, five – Bulgaria, Estonia, Latvia, Lithuania, and Romania – are members of the EU. The purpose of the plan was to contribute to the achievement of Target 6.C of MDG6, and had six specific targets for 2010:

1 To reach 100 % DOTS population coverage in all eastern European countries.
2 To increase the case detection rate of new infectious (sputum smear-positive) TB cases to at least 73 %.
3 To achieve treatment success in at least 85 % of detected new infectious TB cases.
4 To provide treatment according to internationally recommended guidelines for 100 % of multidrug-resistant TB cases (new and previously treated).
5 To reduce the prevalence of TB (all forms) to 188 cases per 100 000 population.
6 To decrease the mortality rate from TB (all forms) to 16 deaths per 100 000 population.

The Framework Action Plan to Fight TB in the EU

Also in 2007, ECDC began to develop a framework for action to be taken by and within countries, as well as at European Community level, to combat TB [1]. The Action Plan, which is compatible with both the Global Plan to Stop TB and the plan for high-priority countries in Europe, is based on four principles: ensuring prompt and quality care for all; strengthening capacity of health systems; developing new tools; and building partnerships and collaboration with countries and stakeholders. Eight areas for strategic development (Box 2) are organised around these four principles, and recognise the need to consider the heterogeneous epidemiological picture in the EU and the different needs of countries with high or low TB incidence.

Box 2. The eight strategic areas of the Framework Action Plan

Area 1. TB control commitment, TB awareness and capacity of health systems

Area 2. Surveillance

Area 3. Laboratory services

Area 4. Prompt and quality TB care for all

Area 5. MDR- and XDR TB

Area 6. TB/HIV co-infection

Area 7. New tools for TB control

Area 8. Build partnership and collaboration with countries

Recent developments

The launching of the Framework Action Plan had the immediate effect of raising the profile of TB control in the European Union. Soon afterwards, the Council of the European Union made specific reference to particular aspects of TB control in two separate conclusions [10]. The first related to health and migration in the EU, and invited Member States and the Commission to undertake a number of actions to improve the health of migrants, referring specifically to the vulnerability of migrants to certain infectious diseases, including TB. The second [11], dealing with antimicrobial resistance in general, stressed the importance of improving susceptibility testing of TB to anti-TB medicines and called on Member States to 'improve management of patients infected with MDR- or XDR TB, including infection control, isolation precautions, contact tracing, prophylaxis practices and use of anti-TB medicines according to international guidelines, such as WHO Stop TB Strategy'.

Box 3. Recommendations from the EC/ECDC/WHO Europe tuberculosis meeting

1. Monitoring implementation of the Berlin Declaration

In order to ensure that all the 53 countries of the WHO European Region remain committed to the objectives identified in the Berlin Declaration, the WHO Regional Office for Europe should monitor implementation of the Declaration, by:

- producing an initial report by the end of 2009;
- focusing on policy and financial commitment/performance;
- continuing epidemiological and programmatic monitoring under the implementation of the plans.

2. Involvement of civil society

Participants of the TB meeting expressed their deep wish to see the establishment of a platform for civil society, non-governmental organisations and professional organisations involved in TB control across the region. This network could be based on the example of the existing HIV/AIDS Civil Society Forum currently supported by the European Commission.

3. Promote health systems strengthening and multi-sectoral approaches

There was a clear call for convening a high level forum for policy discussions on issues which are recognised as priorities in practise (like rational use of drugs) but need engagement at a political level in order to move forward.

4. Ensure access to different global funding mechanisms

To ensure the access of countries of the WHO European Region to different funding mechanisms, the eligibility criteria for the Global Fund to Fight AIDS, Tuberculosis and Malaria should be revisited (eligibility criteria should be based on the epidemiological burden rather than gross domestic product, while countries not funded by the GF gain access to alternative sources), and possibilities for other sources of funding, such as from the European Commission, made clearer.

5. Maintain TB research as a priority

It should also be ensured that the results of research are used for programmatic improvement; the EU should ensure funding is allocated according to priorities and with special emphasis on operational research.

In 2009, at a meeting organised by the European Commission in Luxembourg, ECDC and the WHO Regional Office for Europe [12], representatives from Ministries of Health, donors, partner organisations and civil society discussed the implementation of the Berlin Declaration, identified the main challenges to be faced in the control of TB, and made a number of recommendations for future action (see Box 3). The participants stressed that TB remains a major public health problem in Europe and recognised both the ECDC Action Plan and the WHO Regional Office plan for 18 High-priority countries as key – and complementary – components of coordinated regional activities.

More recently, the WHO Regional Office for Europe called upon its partners and Members States to build upon the findings of the Beijing Call for Action on M/XDR TB [13]. It calls for the consolidation of plans to reverse the spread of drug-resistant TB by scaling up specific responses in all Member States of the WHO European Region. The resulting Action Plan to fight MDR- and XDR TB in the WHO European Region 2010–2015 is expected to be launched in 2011.

National plans

If TB is to be eliminated in Europe, it is essential that every country organises control activities in line with its own epidemiological situation. A survey by ECDC of the countries of the European Union, Iceland, Liechtenstein and Norway found that only nine countries have an explicit national control plan for TB.

Other Member States have, however, developed detailed technical guidance for TB case management. Nevertheless, the lack of strategic plans and monitoring platforms hampers a consolidated and strategic approach to TB control and does not allow a systematic assessment of the impact of interventions. As EU-wide and Regional TB control ultimately relies on national efforts, the EU Action Plan requires the availability and implementation of national plans to ensure its effectiveness and impact.

Impact of the global TB situation on the EU

As noted in the Introduction, case notification rates for TB in the EU are among the lowest in the world. However, in many low-incidence countries in Europe, TB case notification rates among the immigrant population are considerably higher than the average. Often, cases in this population arise as a result of activation or reactivation of a latent infection acquired in the country of origin. There is as yet no evidence of a high level of transmission between the immigrant and the local populations (see Box 4).

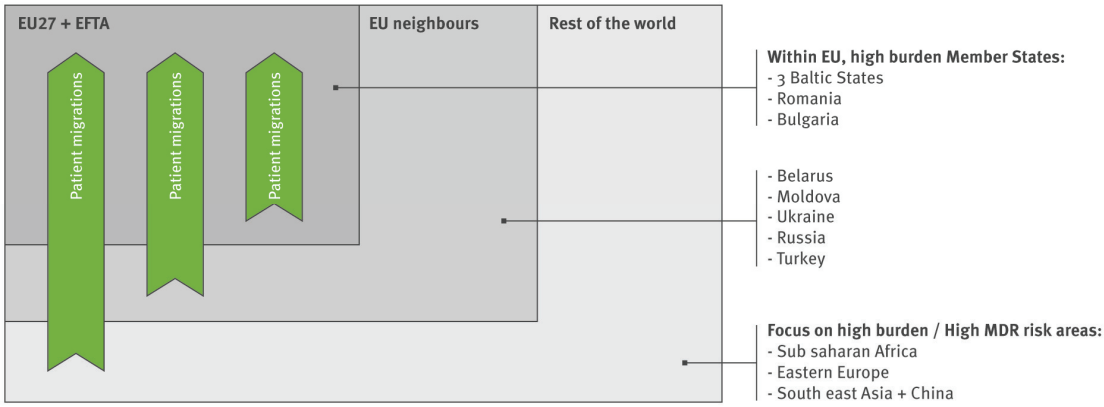
Box 4. Transmission of TB between migrant and local populations

To date, there are several published reports such as the work by Dahle, et al. investigating the extent to which immigration to developed countries has increased the risk of TB among the local population [14]. Eight of these studies were undertaken in the EU and one in the United States. Both molecular fingerprinting and epidemiological studies were used to identify clusters of TB cases. These studies mostly conclude that cross-transmission from foreign-origin cases to the local population remains limited. The epidemiological impact of imported TB thus appears to remain limited to an overall increase of the burden of disease, rather than transmission to the local population.

One of the challenges for TB control in these countries for the near future, therefore, is how to target specific control measures at the immigrant community. This implies also establishing collaborative partnerships with the countries of origin. Within the EU, migration of TB cases can be divided into three categories (see Figure 1):

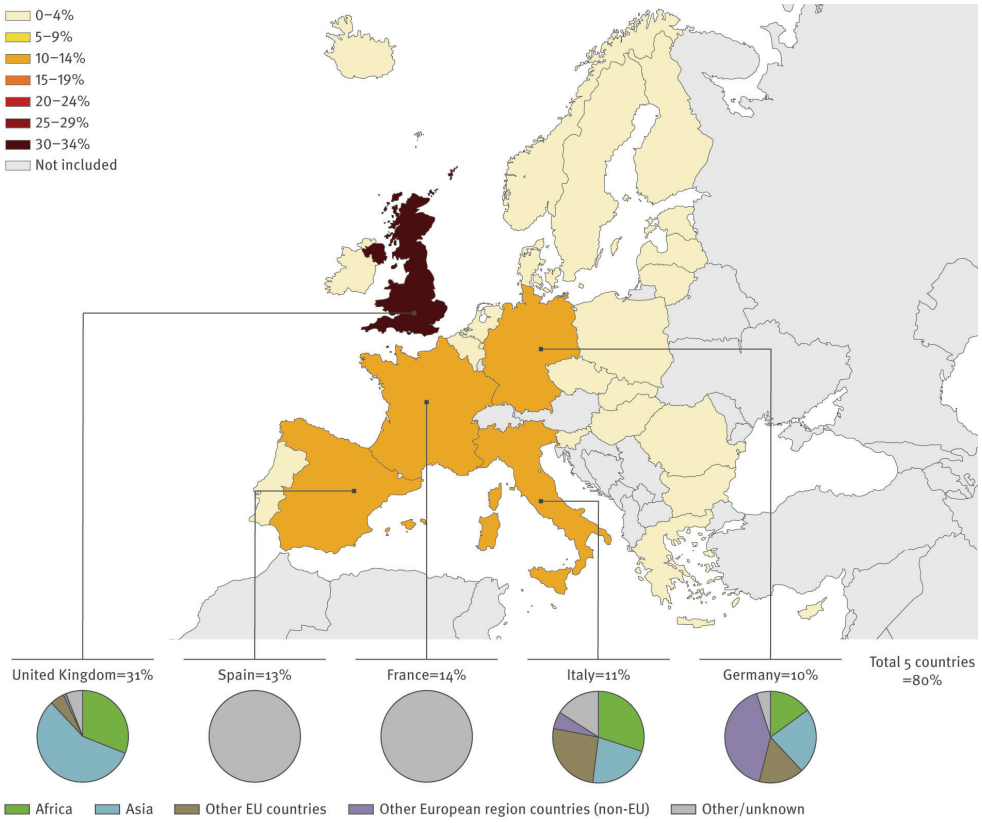
- migration from another country within the Union, and particularly from those Member States with the highest case notification rates (Bulgaria, Estonia, Latvia, Lithuania and Romania);
- migration from neighbouring states to the EU (Belarus, Moldova, Russian Federation, Turkey and Ukraine); and
- migration from the rest of the world.

Figure 1. Migration of TB cases within and into the EU



Five Member States – France, Germany, Italy, Spain and the United Kingdom – notify 80% of all imported cases (Figure 2). In the United Kingdom, most cases originate from Asia, while in Germany they originate from Eastern Europe, and in Italy they come from Africa, Asia and other EU countries. The origin of cases was not available for Spain or France.

Figure 2. Origin of migrant TB cases in five countries of the EU



If TB is to be controlled in these migrating populations, it will be essential – as specified in the principles of the Action Plan – to build partnerships and collaborate with relevant stakeholders. These will include organisations in the countries themselves as well as organisations within Europe that are working beyond their national context.

1.4 Strategic areas of work in the EU

Although TB control and progress towards TB elimination rely on national effort, in the context of a European and global epidemic, concerted efforts are crucial. Within the EU, the European Commission and ECDC support concerted national TB control and coordinate key EU activities. This section summarises the work that is currently being undertaken by either ECDC or the European Commission under each of the eight strategic areas of the Framework Action Plan (see Section 1.3, Box 2).

Area 1. TB control commitment, TB awareness and capacity of health systems

Activities

The Commission has catalysed action in several strategic areas of TB control at EU level since their call for the Action Plan. This initiative reflects the priority given to TB in the EU. Similarly, the Commission has played a key role in supporting the Berlin Declaration with activities such as hosting the joint EC/ECDC/WHO meeting for the follow-up to the Berlin Declaration (Luxembourg 2009).

ECDC is supporting the Commission in its activities by providing scientific evidence and technical assistance. In addition, ECDC is promoting awareness and supporting the capacity of health systems through a number of activities. Most importantly, in collaboration with the WHO Regional Office for Europe, ECDC is working with EU Member States to strengthen TB control at national level. The two organisations are carrying out a series of joint country visits to analyse the current situation in the countries and identify areas for support and intervention.

Area 2. Surveillance

Activities

In 2000, TB was included in the list of priority diseases to be placed under EU-wide surveillance. Through its Public Health Programme, the Commission supported the development of the EURO-TB project (later becoming a WHO Collaborating Centre). The project was transferred to ECDC in 2008 and led to the launch of the ECDC/WHO Regional Office for Europe Joint TB Surveillance System which coordinates the surveillance of TB in the 53 countries of the WHO European Region.

ECDC, together with the WHO Regional Office, is also continuing work to standardise data collection and reporting for TB surveillance, through the establishment of a Coordination Group for TB Surveillance. The aim is to provide a 'one-stop shop' for Member States for reporting and retrieval of data, as well as a consistent and easily available overview of the current situation in the EU.

Several projects are supported and coordinated by ECDC to enhance surveillance and its output:

- Molecular surveillance of EU-wide MDR TB strains.
- Situational analysis and needs assessment on treatment outcome monitoring surveillance in EU/EEA countries.
- Situational analysis for improvement of EU-wide surveillance of TB/HIV co-infection.

Area 3. Laboratory services

Activities

A network of European reference laboratories for tuberculosis (ERLN-TB) has been set up, involving laboratories from all Member States. The network is coordinated by ECDC, and its main goals are to: (1) improve access to, and performance of, laboratories involved in TB control, in order to ensure the provision of reliable and timely diagnostic services; and (2) build capacity and strengthen infrastructure, human resources and competency.

Area 4. Prompt and quality TB care for all

Activities

ECDC is working on:

- an assessment of evidence on TB in migrants, including the impact of interventions;
- an assessment and analysis of social determinants and drivers of the TB epidemic in the EU;
- an assessment of interventions for vulnerable populations (e.g. BCG vaccination).

Area 5. MDR and XDR TB

Activities

In addition to its surveillance and molecular surveillance work on M/XDR TB, ECDC is collecting and analysing scientific evidence towards the development of guidance for:

- management of contacts of M/XDR TB cases;
- management of contact with TB cases on aircraft;
- assessment of the impact of case management practices on TB control.

Area 6. TB/HIV co-infection

Activities

Surveillance activities and situational analyses for the improvement of EU-wide surveillance of TB/HIV co-infection (see also Area 2, above).

Area 7. New tools for TB control

Activities

Through its Research Framework Programme, the Commission also supports the development of new treatments, vaccines, drugs and diagnostic tools against TB. Approximately EUR 68 million was allocated to TB research projects in the 6th Framework Programme (2002 and 2006), and approximately EUR 56 million has been allocated in the first calls of the 7th Framework Programme.

Guidelines are being developed by ECDC for the use of the new blood-based diagnostic tool, the interferon gamma release assay (IGRA). IGRAs are already in use in a number of EU countries, but there is little consistency in how they are used.

Guidelines are also planned on the use of line probe assays for the rapid detection of drug resistance, as well as for other available diagnostic tools.

Area 8. Build partnership and collaboration with countries

Activities

At the international level, the Commission supports developing countries in their TB control programmes, through a variety of actions as agreed in the European Programme for Action to Confront HIV/AIDS, Malaria and Tuberculosis through External Action (2007–2011). In November 2009, the Council of the European Union invited the Commission to prepare a new geographically comprehensive programme for 2012 and beyond [15].

The main channel for financing this support is the Global Fund to fight AIDS, TB and Malaria, to which the Commission has contributed EUR 872.5 million since 2002 with an annual contribution that amounts to EUR 100 million since 2008. This fund had a significant impact on the capacity to control these three diseases and provides more than 60% of international aid to help fight TB.

In addition, clinical trials and capacity building for clinical trials on TB research in sub-Saharan Africa are also financed through the European and Developing Countries Clinical Trials Partnership (EDCTP), an initiative in coordination with European and African countries.

ECDC collaborates closely with key partners in the European Region including the WHO Regional Office for Europe, the KNCV Tuberculosis Foundation and the Wolfheze Initiative, the Stop TB Partnership, TBNET and formally interacts with Member States through its Advisory Forum, the TB Surveillance Contact Points and the ERLN-TB.

2 Monitoring the Framework Action Plan

This section presents the proposed TB monitoring framework for the European Union.

The framework has three components:

1 Definition and interpretation of international targets in the EU context (Section 2.1: epidemiological monitoring).
2 EU epidemiological framework describing indicators, targets and an analytical approach for assessment of epidemiological impact at EU and Member State level (Section 2.2: EU epidemiological framework).
3 Core indicators and relative targets linked to the objectives of the Framework Action Plan to Fight Tuberculosis in the EU. This component identifies eight key input, output and outcome indicators to assess programmatic performance (Section 2.3: core indicators).

The indicators – in particular the eight core indicators – have been developed in view of their measurability and importance in optimising TB control. While realising that several other programmatic aspects could be monitored, this monitoring framework is not intended to replicate already available and extensive monitoring approaches, but rather offer a model of high acceptability that could provide a stimulus to assess and improve TB control in the EU.

2.1 Epidemiological monitoring

Elimination of TB

The ultimate target of the Stop TB Partnership is to eliminate TB as a global health problem by 2050. The definition of elimination has been the subject of considerable discussion in recent years, with a number of different approaches adopted in different circumstances and for different communicable diseases.

Currently, the most widely accepted definition of elimination in general is that put forward at a Dahlem workshop [16] in 1997. This considers elimination of a communicable disease as 'the reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts'. Elimination of infection was defined at the same workshop as 'the reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts'.

These definitions are generally considered inapplicable to TB, because of the high proportion of latent infections with *Mycobacterium tuberculosis*. The Stop TB Partnership, therefore, has adopted a definition of elimination of TB of an incidence of less than one case per million population. Previous European recommendations had suggested an elimination target of less than one smear-positive case per million population [17]. The Stop TB Partnership preferred the definition of less than one case per million because the aim was – and still is – to eliminate all forms of TB, and because they considered that by 2050 diagnosis by smear microscopy might well be obsolete.

The global target – a TB incidence of less than one case per million population – should be maintained as the ultimate target for TB control activities in the EU.

MDG and Stop TB Partnership targets

As mentioned in Section 1.3, a number of targets and indicators have been agreed for TB control efforts at global level (see Box 1).

The MDG target of reversing the incidence of TB by 2015 remains a key target for global efforts. In the EU, most of the low-incidence countries have already met this target, as well as the Stop TB targets for 2005. In these countries, TB case notification rates are declining and control measures are functioning well. Continued vigilance is nevertheless needed to continue to progress towards elimination.

In a few low-incidence countries of the EU, however, TB case notification rates are currently increasing, generally as a result of an increase of imported TB cases (or reactivation of imported latent TB cases) [4]. The MDG target of reversing incidence, as well as the Stop TB Partnership targets of reductions in prevalence and death rates, can usefully be applied to vulnerable groups in these low-incidence countries.

Five countries of the EU – Bulgaria, Estonia, Latvia, Lithuania and Romania – are among the high-priority countries designated by the WHO Regional Office for Europe. Four of these countries have reported on their progress towards the MDG and Stop TB Partnership targets. While the case notification rate is now decreasing in these countries, it is unlikely that they will be able to meet the Stop TB Partnership target for 2015 of halving prevalence and death rates from the level in 1990. This is because of the particular situation in these countries in the 1990s when, as a result of the upheavals following the break-up of the Soviet Union, the number of TB cases increased to

levels considerably higher than the 1990 level. The countries have therefore set revised targets for themselves, which take into account the high levels in 2000, relative to 1990 (see Table 1).

Table 1. Estimated TB incidence for 1990, 1998, 2007, with revised targets, for four countries

Country	Year	WHO estimated incidence: cases per 100 000 population	Targets set by country
Bulgaria	1990	27	Reduce TB incidence to 22 per 100 000 by 2015[a].
	1998	45	
	2007	39	
Latvia	1990	34	Reduce TB incidence to 1990 level[b].
	1998	85	
	2007	53	
Lithuania	1990	40	No national targets set[c].
	1998	82	
	2007	68	
Romania	1990	74	Reduce TB incidence by 30% between 2006 and 2015[d],[e].
	1998	125	
	2007	115	

(a) http://www.undp.bg/uploads/documents/2691_856_en.pdf
(b) http://www.undg.org/archive_docs/6160-Latvia_MDG_Report.pdf
(c) http://www.undg.org/archive_docs/154-Lithuania_MDG_Report__CCA_-_Lithuania_MDG.pdf
(d) http://www.undp.ro/download/files/mdg/Selected%20MDG%20progress%20FEB09%20_2__1.pdf
(e) http://www.undg.org/archive_docs/3654-Romania_MDG_Report_-_English.pdf

EU countries should remain committed to MDG6 target 6.C, which is applicable to all countries. Low-incidence countries should seek to ensure that the target, as well as related Stop TB Partnership targets, are met for vulnerable groups in the population, such as migrants, as well as nationally.

MDG indicators 6.9 and 6.10 are useful for monitoring TB control activities, particularly in high-incidence countries. Targets for these indicators may be adapted in countries that saw a significant increase of TB cases in the 1990s.

Molecular typing for monitoring TB transmission

The introduction of molecular methods for the genetic characterisation of *M. tuberculosis* isolates, so called genotyping, offers the potential to more accurately characterise TB transmission in a population. Isolates with identical genotypes constitute a cluster where the cases are considered to be caused by the same strain, reflecting a common chain of transmission. In contrast, isolates with unique genotypes are considered to result from reactivation of latent infection. Genotyping has permitted a tremendous gain in knowledge on the dynamics of transmission, the population structure, evolution and pathogenesis of *M. tuberculosis*. Genotyping has also been shown to be a powerful tool with relevance for the provision of effective TB prevention and control measures (see Box 5).

Box 5. Common applications of genotyping relevant for TB control

- As a complement to conventional contact tracing and to evaluate its effectiveness.
- To identify unsuspected relationships and transmission chains.
- To identify and assess outbreaks.
- To identify risk groups.
- To identify transmission across jurisdictions.
- To discriminate between cases arising from re-infection and relapsing infection.
- To identify incorrect diagnosis and laboratory cross-contamination.
- To determine the level of strain clustering to assess the rate of recent transmission.

Thus, in addition to being a valuable tool for understanding basic features of *M. tuberculosis* and providing insight into the transmission dynamics of TB, genotyping has the potential, if used properly, to inform and evaluate TB prevention and control efforts. As a number of countries reach the elimination phase of TB, the question of using the rate of recent transmission as a proxy indicator for assessing progress towards elimination has become relevant.

Currently, genotyping is often used on a limited scale mainly for outbreak investigations or in retrospective studies as a tool for describing transmission events. The full potential of these methods is therefore not always used. In the future, genotyping of *M. tuberculosis* isolates may well be a useful way of more systematically monitoring disease transmission. Provided that the genotyping is incorporated into the prospective regular surveillance activities and performed continuously it may have great power as a tool to track progress towards TB elimination. Below, examples of two different studies are briefly described where genotyping has been used to measure ongoing transmission (Box 6) and to assess the use of ongoing transmission as a proxy of TB elimination (Box 7).

However, there are still a number of questions that remain regarding the way molecular epidemiological tools can best be used in TB control programmes.

One of the limitations of the use of molecular epidemiology is the difficulty in matching the molecular typing data with the case-based surveillance data at the local and national levels. Up to now, only a few countries in the EU report molecular typing data linked to the case. To perform further EU-wide epidemiological analysis, it is crucial to link the molecular typing data to the case at national level and to report this to the European level.

Another concern is that there are technical limitations with the different molecular typing methods currently used and a lack of agreement on which methods should be used. None of the available methods are optimal and they have different discriminatory power. Therefore, care is needed in agreeing on the method to be used and defining what constitutes a cluster with the method of choice.

Box 6. Use of genotyping to measure ongoing transmission

Defining recent transmission as cases appearing within two years of each other, van Deutekom, et al. [18] assessed the value of molecular typing for identifying recent transmission in the province of North Holland in the Netherlands. Among the 481 culture-positive cases, 138 fell into a total of 43 clusters. Assuming that one case in each cluster was the index case, the authors showed that 95 cases (20% of the 481 culture-positive cases) of active TB in the region were a result of recent transmission.

The third concern is that there is still no systematic way to analyse and deal with bias introduced in molecular epidemiological studies when determining rates of clustering. Thus, the validity of using the current ways of calculating clustering, and from that draw inferences about the rate of recent transmission, may not always be assured. Therefore, key concepts such as level of strain clustering and recent transmission must be carefully defined. The time-frame used when determining whether isolates are clustered or not will have a major impact on the calculations.

Box 7. Use of ongoing transmission as a proxy for TB elimination

In San Francisco there was an intensification of TB control measures, beginning in 1991, focusing on prevention of transmission and on the use of preventive therapy. To determine whether these measures would reduce the overall incidence and the frequency of recent transmission, Jasmer, et al. [19] genotyped all TB cases during a seven-year period. Between 1992 and 1997, TB incidence decreased from 51.2 to 29.8 per 100 000 persons and the rate of clustered cases decreased over time from 10.4 in 1991 to 3.8 in 1997 per 100 000 persons. They concluded that the rates of TB cases and clustered cases decreased both overall and also among persons in high-risk groups of clustering such as HIV infected individuals.

Despite these limitations, genotyping remains a promising technique for monitoring progress in TB control, particularly in low-incidence countries that need to show a declining ongoing transmission as a proxy for elimination. Several European countries have ongoing genotyping projects on country level. Thus we should draw on their experience and document the best practices identified for development of an EU approach to monitoring TB surveillance.

2.2 EU epidemiological monitoring framework

Many countries in the EU have achieved a low TB notification rate of fewer than 20 cases per 100 000 population. These countries now need to consolidate their efforts to move towards the ultimate goal of eliminating TB.

Countries can be considered to be in a TB elimination phase if the case notification rate of TB is low (< 20 per 100 000) [17] *and* the case notification rate has been decreasing over the previous five years.

As case notification rates fall, it becomes more important to monitor the level of disease transmission taking place in the country. This is difficult to measure directly, since there is currently no reliable test that is easy to use in practice. Thus, surrogate markers of transmission are needed for monitoring purposes. Four parameters are proposed for monitoring purposes, which together reflect not only the disease burden but also levels of transmission:

1 trends in case notification rate;
2 trends in MDR case notification rate;
3 trends in ratio of notification rates in children to adults;
4 trends in mean age of TB cases.

These four indicators can provide a valid picture of progress towards TB elimination provided that the case surveillance and reporting system captures close to 100% of all TB cases and, most importantly, there are no variations in the sensitivity of the surveillance system in capturing cases. The quality and coverage of the surveillance system can be assessed using the framework and associated tools developed by the WHO Global Task Force on TB Impact Measurement [20], (see Box 8). This framework includes techniques such as capture–recapture analysis, cross-linking of databases and analysis of vital registration statistics.

The proposed EU Epidemiological Monitoring Framework relies on the quality and coverage of TB surveillance systems at the national level. In particular, the framework should only be applied when an acceptable degree of non-variability of surveillance coverage (i.e. the ability to capture all TB cases) can be assured for the years to be analysed.

Box 8. Relevance of the Impact Measurement Framework to the EU

A Global Task Force on TB Impact Measurement was established in June 2006 by the World Health Organization with the purpose of assessing epidemiological impact and strengthening capacity in monitoring and evaluation of TB control.

The work of the Task Force has led to a number of WHO policies for how TB incidence, prevalence and mortality should be measured. The policies encompass various measurement approaches including strengthened surveillance through notification systems, TB prevalence surveys and the development of national vital registration systems for recording TB deaths.

Of key relevance to the EU setting, is the policy statement calling for improvement of surveillance systems towards the ultimate goal of measuring TB incidence and mortality directly from TB notifications and vital registration systems, respectively.

The proposed epidemiological monitoring framework for the EU relies on this principle. Thus, the assurance of the quality and coverage of TB surveillance systems is vital to ensure the applicability of the framework.

The Task Force has developed a standard approach to assess reliability of notification and mortality trends which include three distinct components: (1) assessment of data quality; (2) assessment of the extent to which time-series of notification data and vital registration provide a proxy for trends in incidence and mortality; and (3) assessment of the fraction of all incident cases and deaths from TB that are recorded in surveillance data.

This, alongside similar work initiated by ECDC for quality assurance of all communicable disease surveillance systems, should be of assistance to Member States in assessing reliability and interpretability of TB notifications time trends.

The four indicators are described in more detail below. Two real-life case studies, showing how these parameters reflect different epidemiological situations, are given in Annex 1.

It is important to underline that in the presence of high levels of imported TB cases (as is the case for several low-incidence countries) the targets proposed for trends might not be achievable. In these situations, analysis disaggregated by 'foreign-origin' and 'native cases', supported by molecular epidemiology, might be useful in interpreting trends.

Indicator 1. Trends in case notification rate

Definition

The 5-year trend in case notification rate, where the rate is defined as the number of all TB cases reported per year per 100 000 population:

$$\frac{\text{number of all TB cases reported in the one year}}{\text{total population of the country}} \times 100\,000$$

Description

The indicator provides information on the trends over time in the number of all TB cases per 100 000 population. At high levels of case detection – as is the case in most EU countries – the indicator reflects changes in the incidence of TB in the community.

Target

A mean declining trend in case notification rate over the previous five years allowing for annual random variation, in a context where case-finding efforts remained constant or increased.

Level of applicability

Member States and the EU as a whole.

Reference

WHO. Compendium of indicators for monitoring and evaluating national tuberculosis programmes. Geneva: World Health Organization, 2004.

Indicator 2. Trends in MDR case notification rate

Definition

The 5-year trend in MDR case notification rate, where the rate is defined as the number of MDR TB cases reported per year per 100 000 population:

$$\frac{\text{number of MDR TB cases reported in one year}}{\text{total population of the country}} \times 100\,000$$

Data for trends in MDR cases should be disaggregated and analysed separately for new cases and retreatment cases.

Description

Provided that drug susceptibility testing (DST) for isoniazid and rifampicin is complete (i.e. when more than 50% of all cases are culture-confirmed and more than 80% of them have DST for isoniazid and rifampicin performed) [4], the indicator provides information on the trends over time in the number of MDR TB cases per 100 000 population.

Target

A mean declining trend in MDR case notification rate over the previous five years allowing for annual random variation, in a context where MDR case-finding efforts remained constant or increased.

Level of applicability

Member States and the EU as a whole.

Reference

WHO. Compendium of indicators for monitoring and evaluating national tuberculosis programmes. Geneva: World Health Organization, 2004.

Indicator 3. Trends in ratio of notification rates in children to adults

Definition

The 10-year trend in the ratio of the case notification rate in children under 15 years old to that in adults, i.e. change in the ratio:

$$\frac{\text{case notification rate in children } (< 15 \text{ years})}{\text{case notification rate in adults } (\geq 15 \text{ years})}$$

Description

The case notification rate of TB in children, especially infants, is an indirect measure of the level of transmission in the community. Because young children have a much higher rate of primary progression to TB, a lower

transmission rate should be reflected in a decrease in the ratio of the notification rate in children to that in adults. This, in turn, is an indicator of early case-finding and effective treatment.

Target

A mean declining trend in the ratio of the notification rate in children to that in adults over the previous ten years, allowing for annual random variation.

Level of applicability

Member States. This indicator is unlikely to be applicable at EU level (in the form of an average trend for all EU cases) given the high heterogeneity expected among Member States.

References

WHO. Global tuberculosis control: epidemiology, strategy, financing: WHO Report 2009. Geneva, World Health Organization, 2009 (WHO/HTM/TB/2009.411). Available from: www.who.int/tb/publications/global_report/2009/en/index.html

Stop TB Partnership and World Health Organization. Global Plan to Stop TB 2006-2015. Geneva, World Health Organization; 2006.

TB epidemiology and surveillance workshop [internet]. World Health Organization, Geneva. Available from: http://apps.who.int/tb/surveillanceworkshop/trend_analysis/increasing_decreasing_performance_of_tb_control_program_ratio_of_rates_children_adults.htm

Indicator 4. Trends in mean age of TB cases

Definition

The trend in mean age of all TB cases, calculated either as crude mean age or population-standardised mean age.

Crude mean age

To calculate the crude mean age of TB cases, all cases need to be stratified into age groups. The crude mean age is the sum of the products of the number of cases in each age group and the mid-age of the age group (e.g. the mid-age of the age group 0–4 years is 2), divided by the total number of cases:

$$\frac{\sum \text{number of cases in each age group} \times \text{mid-age of the group}}{\text{total number of cases}}$$

Population-standardised mean age

The standardised mean age is the sum of the products of the standardised number of cases in each age group and the mid-age of the age group, divided by the total standardised number of cases:

$$\frac{\sum \text{standardised number of cases in each age group} \times \text{mid-age of the group}}{\text{total standardised number of cases}}$$

The population-standardised mean age can be helpful in adjusting for different trends in the general population. The standardised population can be chosen as the population of one year or as the average population over several years. The TB rate for each age group is then multiplied by the standardised population in the age group to get a standardised number of cases for each age group. Migrant populations may have an impact on the age structure, thus, the analysis may require careful disaggregation by origin.

Description

An effective TB control programme will result in less than one new infectious case for each diagnosed case, i.e. the case notification rate of TB will decline. This decline will be seen mainly in younger people, since there will be no effect on cases arising through endogenous reactivation, which mostly occur among the elderly (and in younger people who are immunocompromised, malnourished, or otherwise particularly vulnerable). Thus the mean age of cases will increase.

A rise in the crude mean age of TB cases may be due to either an ageing population or an ageing epidemic. Conversely, an increasing mean age may be masked if the population is becoming younger. To avoid effects caused by a change in the population structure, the population-standardised mean age can be calculated (see above).

Target

An increasing trend in mean age of TB cases over the previous 10 years.

Level of applicability

Member States. This trend/indicator is unlikely to be applicable at EU level (in the form of an average trend for all EU cases) given the high heterogeneity expected among Member States.

References

WHO. Global tuberculosis control: epidemiology, strategy, financing: WHO Report 2009. World Health Organization, Geneva; 2009 (WHO/HTM/TB/2009.411). Available from: www.who.int/tb/publications/global_report/2009/en/index.html

Stop TB Partnership and World Health Organization. Global Plan to Stop TB 2006-2015. Geneva, World Health Organization; 2006.

TB epidemiology and surveillance workshop [internet]. World Health Organization, Geneva. Available from: http://apps.who.int/tb/surveillanceworkshop/trend_analysis/increasing_decreasing_performance_of_tb_control_program_ratio_of_rates_children_adults.htm

2.3 Core indicators for the Framework Action Plan

This section describes a number of key indicators for monitoring the implementation of the Framework Action Plan to Fight TB in the EU. Through the joint surveillance system of ECDC and the WHO Regional Office for Europe, countries currently report on over 400 variables covering epidemiological, laboratory, programmatic and other areas related to TB control. In setting up the framework described below, it is not the intention to impose an extra burden on countries; rather ECDC will seek to use existing information to inform the monitoring process.

The indicators proposed include both input, output and outcome indicators, specifically related to the Action Plan. All the indicators are compatible with those proposed by WHO for monitoring national TB programmes [21] and for use in the high-priority countries of Europe [9]. The proposed indicators are:

1 Availability of a national TB control plan.
2 Availability of guidelines for implementing the national TB control plan.
3 Percentage of national TB reference laboratories (adhering to ERLN-TB) achieving adequate performance in the external quality assurance scheme.
4 Availability of a strategy for introducing and implementing new tools for TB control.
5 Percentage of new pulmonary TB cases confirmed by culture and percentage of cases tested by DST for first-line drugs.
6 Percentage of Member States reporting treatment success rate.
7 Treatment success rate.
8 Percentage of TB patients for whom HIV status is known.

Indicator 1. Availability of a National TB control plan

Definition

This indicator concerns the availability of a national TB control plan which is in line with the areas and objectives of the Framework Action Plan to Fight TB in the EU and with international standards for TB control. The plan should have been formally adopted by the national government.

This is a yes/no indicator.

Specific link to listed objectives under the Action Plan

Area 1, objectives 1 and 2:

- To increase Member States' political and resource commitment to plans for TB control as part of the overall public health strategies.
- To strengthen the capacity of Member States' health systems to carry out activities for TB control and elimination.

Level of applicability

EU and Member States.

Target

Member State: An up-to-date and endorsed national TB control plan is available.

EU: All Member States (100%) have an up-to-date and endorsed national TB control plan.

Scope

The adoption of a formal plan demonstrates political commitment. This indicator may be helpful for stimulating policy development and for identifying strengths and weaknesses of national TB control policy.

Proposed measurement approach
Analysis of availability of up-to-date TB control plans should be conducted at Member State level. A content analysis of the national TB plan should also be conducted and matched against the areas of the Framework Action Plan, as well as international standards for TB control, as given in the Global Plan to Stop TB [22], the plan for the high-priority countries in Europe [9], and the International Standards for Tuberculosis Care [23].

Possible data sources
Availability of formal national plan from the Ministry of Health; survey; ad hoc collection through the ECDC and WHO Regional Office for Europe joint surveillance system (TESSy and CISID).

Frequency of measurement
Annual, in order to evaluate whether directives have been updated on the basis of the national epidemiological situation and international guidelines.

Strengths and limitations
Evaluation of political commitment requires some subjective assessment; it is difficult to make cross-national comparisons and a trend over time cannot be computed. The existence of an adequate plan does not guarantee that all components are fully implemented, only that the Ministry of Health has articulated political commitment to them.

References
WHO. Compendium of indicators for monitoring and evaluating national tuberculosis programs (WHO/HTM/TB/2004.344). Geneva: World Health Organization; 2004.

Broekmans JF, Migliori GB, Rieder HL, et al; World Health Organization, International Union Against Tuberculosis and Lung Disease, and Royal Netherlands Tuberculosis Association Working Group. European framework for tuberculosis control and elimination in countries with a low incidence. Recommendations of the World Health Organization (WHO), International Union Against Tuberculosis and Lung Disease (IUATLD) and Royal Netherlands Tuberculosis Association (KNCV) Working Group. Eur Respir J, 2002; 19:765-775.

Indicator 2. Availability of guidelines for implementing the national TB control plan

Definition
This indicator concerns the availability of guidelines for the implementation of the TB control plan. Such guidelines should be in line with the areas and objectives of the Action Plan for the EU and with international standards for TB control. The guidelines should have been formally adopted by the national government.

This is a yes/no indicator.

Specific link to listed objectives under the action plan
Area 1, objectives 1 and 2:

- To increase Member States' political and resource commitment to plans for TB control as part of the overall public health strategies.
- To strengthen the capacity of Member States' health systems to carry out activities for TB control and elimination.

Level of applicability
EU and Member States.

Target
Member State: Up-to-date and endorsed TB guidelines are available.

EU: All Member States (100%) have up-to-date and endorsed TB guidelines.

Scope
The existence of an implementation guide shows that the Ministry of Health is committed to institutionalising standard procedures throughout the national health system.

Proposed measurement approach
Analysis of availability of up-to-date TB control guidelines should be conducted at Member State level. A content analysis of the national TB guidelines should also be conducted and matched against the areas of the Framework Action Plan, as well as international standards for TB control, as given in the Global Plan to Stop TB [22], the plan for the high-priority countries in Europe [9], and the International Standards for Tuberculosis Care [23].

Possible data sources
Availability of formal guidelines from the Ministry of Health; survey; ad hoc collection through the ECDC and WHO Regional Office for Europe joint surveillance system (TESSy and CISID).

Frequency of measurement
Annual, in order to evaluate whether directives have been updated on the basis of the national epidemiological situation and international guidelines.

Strengths and limitations
The existence of an implementation guideline does not guarantee that directives are routinely put into practice in all facilities. However, without such guidelines, the implementing authority has no central reference for those who need information on procedures.

References
WHO. Compendium of indicators for monitoring and evaluating national tuberculosis programs (WHO/HTM/TB/2004.344). Geneva: World Health Organization; 2004.

Broekmans JF, Migliori GB, Rieder HL, et al; World Health Organization, International Union Against Tuberculosis and Lung Disease, and Royal Netherlands Tuberculosis Association Working Group. European framework for tuberculosis control and elimination in countries with a low incidence. Recommendations of the World Health Organization (WHO), International Union Against Tuberculosis and Lung Disease (IUATLD) and Royal Netherlands Tuberculosis Association (KNCV) Working Group. Eur Respir J, 2002; 19:765-775.

Indicator 3. Percentage of national TB reference laboratories (adhering to ERLN-TB) achieving adequate performance in the external quality assurance scheme

Definition
The number of national TB reference laboratories (adhering to the European Reference Laboratory Network for TB) achieving a cumulative performance score of 80% or above for quality assurance of smear microscopy, culture and DST for first- and second-line drugs under the ERLN-TB external quality assurance (EQA) scheme.

Specific link to listed objectives under the Action Plan
Area 3, objectives 1 and 2:

- Develop and implement high quality laboratory services which support clinical, public health and research needs in TB.
- Ensure safe, accurate, quality laboratory services and appropriately trained staff to perform the work.

Level of applicability
EU level. The indicator should be used at EU level to measure progress within the European Reference Laboratory Network for TB with results presented in an aggregated format (i.e. without country identifiers).

Target
100% of national TB reference laboratories adhering to the ERLN-TB achieve a level of performance of 80% or above for smear microscopy, culture and DST for first- and second-line drugs.

Scope
This indicator measures the capacity of the TB control programme to accurately diagnose and follow up TB patients at national (reference laboratory) level. To provide reliable TB diagnoses, it is essential to ensure methods are performed optimally, in which EQA schemes play an important role. For this, countries need a TB reference laboratory to coordinate EQA activities. In addition, the quality and reliability of mycobacteriological services ensure the validity and reliability of the surveillance system.

Proposed measurement approach
International EQA systems for TB diagnostics are already available (e.g. WHO Collaborating Centre, INSTAND e.V., the WHO Supranational Reference Laboratory Network (SRLN)) to which TB laboratories can sign up. Furthermore, during 2010 the ERLN-TB has developed EQA-schemes within the network.

National reference laboratories should, through the ERLN-TB EQA schemes, be tested for performance in the following methods: perform sputum smear microscopy, primary isolation and culture, *M. tuberculosis* identification and drug susceptibility testing (to first- and second-line drugs);

The national laboratory designated to coordinate EQA schemes should also:

- be linked to a supranational reference laboratory that coordinates overall EQA schemes;
- provide training and carry out proficiency testing;
- provide positive and negative feedback to participating laboratories.

Possible data sources
ERLN-TB EQA scheme.

Frequency of measurement
Annual.

Strengths and limitations
This indicator only provides assessment of the national TB reference laboratories. The indicator can be further extended, following the first year of measurement, to include sub-national laboratories' overall EQA score in the different diagnostic methods. The national laboratory designated to coordinate the EQA schemes would be responsible for reporting the overall EQA score for the different methods.

References
Drobniewski FA, Nikolayevskyy V, Hoffner S, Pogoryelova O, Manissero D, Ozin AJ. The added value of a European Union tuberculosis reference laboratory network – analysis of the national reference laboratory activities. Euro Surveill. 2008 Mar 18;13(12). pii: 8076.

WHO. Compendium of indicators for monitoring and evaluating national tuberculosis programs (WHO/HTM/TB/2004.344). Geneva: World Health Organization; 2004

Indicator 4. Availability of a strategy for introducing and implementing new tools for TB control

Definition
New tools for TB are defined as new diagnostic methods, drugs and vaccines. This indicator is a yes/no indicator assessing the existence of a strategy within the national TB programme for introducing and implementing new tools for TB as they become available.

As described in the Stop TB Partnership Retooling Taskforce document 'New technologies for TB control' [24], once new tools for TB control become available, it is essential they are rapidly and optimally implemented to assure their longevity and, more importantly, to ensure TB patients receive access to the best TB care as soon as possible.

Specific link to listed objectives under the Action Plan
Area 7, objective 1:

- Set priorities for basic, applied and operational research in the EU.

Level of applicability
Member State.

Target
Member State: A strategy within the national TB programme supporting the introduction and implementation of new tools for TB control is in place.

EU: All Member States (100%) have a strategy within the national TB programmes supporting the introduction and implementation of new tools for TB control.

Scope
Confirming that national TB programmes include a strategy indicates that Member States are prepared to take on new tools for TB control. As discussed in the Stop TB Partnership's 'New technologies for TB control', it is essential to have considered the various areas within a national TB programme that will need to be adjusted to include a new tool. This includes technical and operational considerations, as well as assuring monitoring and evaluation systems for the new tools.

Proposed measurement approach
A content analysis of the national TB plan and guidance should be conducted to determine the inclusion of a strategy for introducing and implementing new tools.

Possible data sources
Availability of formal national plan and guidance from the Ministry of Health.

Frequency of measurement
Annual, in order to evaluate whether strategies have been updated.

Strengths and limitations

This indicator shows a Member State's preparedness for introducing new tools for TB as they become available; with several new diagnostic tools having already become available. However, it does not measure the adequacy of the strategy and/or the level of resources within a country to ensure that the strategy can be fully implemented when a new tool becomes available.

References

Stop TB Partnership/WHO. New Technologies for Tuberculosis Control: A framework for their adoption, introduction and implementation (WHO/HTM/STB/2007.40). World Health Organization, Geneva: 2007.

Indicator 5. Percentage of new pulmonary TB cases confirmed by culture and percentage of new cases tested by DST for first-line drugs

Definition

Percentage of new pulmonary TB cases that are confirmed by culture and identified as the *M. tuberculosis* Complex (MTC) and the percentage of cases for which DST for first-line drugs has been performed.

Specific link to listed objectives under the Action Plan

Area 4, objective 1:

- Promptly diagnose all cases and ensure proper TB treatment and care.

Scope

Culture-confirmation of specimens and identification of MTC is the most accurate method of confirming active tuberculosis and is the case definition of TB in Europe. This indicator assesses the adequacy of culture diagnosis of suspected cases of TB, assessing both diagnostic laboratories' and physicians' ability to correctly diagnose TB. Furthermore, following the changes in the proportion of culture-confirmed pulmonary TB cases over time is indicative of the TB control performance in the defined setting.

Level of applicability

Member States.

Target

Member State: 80% of all new pulmonary TB cases are culture-confirmed. 100% of the culture-confirmed cases should be tested by DST for first-line drugs.

EU: 80% of all new pulmonary TB cases in the EU are culture-confirmed. 100% of the culture-confirmed should be tested by DST for first-line drugs.

Proposed measurement approach

The proportion is obtained by dividing the total number of new culture-confirmed pulmonary TB cases during the defined period (in this case a year), by the total number of notified new pulmonary TB cases during the same period.

$$\frac{\text{number of new culture-confirmed pulmonary TB cases registered during defined time period}}{\text{total number notified new pulmonary TB cases during defined time period}} \times 100$$

Possible data sources

TB Joint Surveillance System of ECDC and WHO Regional Office for Europe (TESSy and CISID).

Frequency of measurement

Annual.

Strengths and weaknesses

This indicator only considers the new *pulmonary* culture-confirmed cases, i.e. it does not indicate the capacity to correctly diagnose extrapulmonary TB cases.

Indicator 6. Percentage of Member States reporting treatment success rate

Definition

Percentage of Member States submitting reports of treatment success rate to the ECDC on an annual basis.

Specific link to listed objectives under the Action Plan
Area 8, objective 4:

- Further develop collaboration and coordination jointly between ECDC, the European Commission, individual countries, WHO and other stakeholders.

Level of applicability
EU.

Target
All Member States (100%) report treatment outcome monitoring to ECDC.

Scope
This indicator measures the completeness and timeliness of submission of reports of treatment success rate, which are essential for efficient programme management.

If the total number of reports submitted falls below the 100% threshold, then an appropriate course of action should be considered to increase the number of complete reports to the required level.

Proposed measurement approach
The numerator is the number of Member States that submitted reports on treatment success rate to ECDC in the previous year. The denominator is the total number of Member States that were required to submit treatment success rate reports to ECDC in that year.

Possible data sources
ECDC and WHO Regional Office for Europe joint surveillance system (TESSy and CISID).

Frequency of measurement
Annual.

Strengths and limitations
The ability of the national system to report on TB control activities depends on the proper balance of logistic support and infrastructure, and the ability of staff at national and subnational level. While this indicator does not measure the quality of reports, it does measure whether the existing reporting and recording systems are functioning.

Reference
WHO. Compendium of indicators for monitoring and evaluating national tuberculosis programs (WHO/HTM/TB/2004.344). Geneva: World Health Organization; 2004.

Indicator 7. Treatment success rate

Definition
The proportion of new pulmonary culture-positive TB cases in a given year that successfully completed treatment, either with bacteriological evidence of success (cured) or without (treatment completed).

The numerator is the number of new pulmonary culture-positive TB cases registered in the year that were cured plus the number of those who completed treatment. The denominator is the total number of new pulmonary culture-positive TB cases registered in the same year.

This indicator should also be calculated for MDR cases, in which case the treatment outcome should be measured after 24 months. Only confirmed MDR TB cases should be included in an MDR cohort.

Specific link to listed objectives under the Action Plan
Area 4, objectives 1 and 4:

- Promptly diagnose all cases and ensure proper TB treatment and care.
- Ensure that individual health needs of all TB patients are met.

Area 5, objectives 2 and 3:

- Specifically improve TB drug-sensitivity testing services within the EU in the context of strengthened TB laboratory services.
- Improve care and management of patients with MDR- or XDR TB.

Level of applicability
Member States and the EU.

Targets

Member State: Treatment success of 85% at 12 months for the complete cohort of new pulmonary culture-positive cases.

EU: Treatment success of 85% at 12 months for the complete cohort of new pulmonary culture-positive cases.

Member State: Treatment success of 70% at 24 months for new pulmonary culture positive pulmonary MDR cases.

EU: Treatment success of 70% at 24 months for new pulmonary culture-positive pulmonary MDR cases.

Scope

This indicator measures a programme's capacity to retain patients through a complete course of chemotherapy with a favourable clinical result.

Proposed measurement approach

The measurement is performed on the basis of cohort analysis principles as described in the ECDC/WHO annual report 'Tuberculosis surveillance in Europe'. A cohort should include all TB cases notified in the calendar year of interest, after exclusion of cases with final diagnosis other than TB or cases found to be reported more than once. Cases are observed until the first outcome is encountered, up to a maximum of 12 months after the start of treatment. For monitoring MDR TB cases observation is extended up to a maximum of 24 months. At the end of the treatment course, one of eight treatment outcomes is recorded for each new pulmonary culture-positive TB case: cured, treatment completed, died, failed, defaulted, still on treatment, transferred out or unknown. The numerator is treatment success, which is the sum of cases registered in a year and recorded with the treatment outcome of either cure or treatment completed at the end of a 12-month observation period. The denominator is the total number of new pulmonary culture-positive TB cases recorded in that year.

For MDR TB cases the observed outcome in a cohort of MDR new pulmonary culture-positive TB cases is recorded at the end of a 24-month observation period.

This indicator can also be measured for different groups of patients, such as retreatment cases or migrants.

Possible data sources

ECDC and WHO Regional Office for Europe joint surveillance system (TESSy and CISID).

Frequency of measurement

Annual.

Strengths and limitations

This outcome indicator may be influenced by several factors. In populations with a high HIV prevalence, or with a high proportion of elderly people, it may be difficult to reach the 85% target, because of a high percentage of deaths (not necessarily related to TB). The same problem can arise if the prevalence of MDR TB is high; this issue can be bypassed by analysing treatment outcome at 24 months following treatment completion.

Even where treatment is of high quality, the reported treatment success rate will only be high if the routine surveillance system is functioning well. The reported rate will be affected if the outcome of treatment is not recorded for all patients. Where the reported treatment success rate is low, the underlying cause can only be identified by determining which of the unfavourable treatment outcomes is most common. The success rate among retreatment cases is generally lower than that among new patients. It is usually reported as two separate rates: that for treatment after failure (where the initial failure was probably due to drug resistance) and that for treatment after default (where the default was probably due to poor adherence and/or drug resistance). Measurement has always been based on 100% of pulmonary culture-positive TB cases.

Calculation of this indicator for vulnerable groups will be especially important in countries with a low overall TB case notification rate and a high case notification rate in specific groups (e.g. migrants, intravenous drug users, alcohol-dependent people and the homeless).

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Indicator 8. Percentage of TB patients for whom HIV status is known

Definition

The proportion of all TB patients for which the HIV status is known.

Specific link to listed objectives under the Action Plan

Area 6, objective 1:

- Decrease the burden of TB/HIV co-infection in the EU by strengthening the collaboration between TB and HIV/AIDS plans or the appropriate services within the health system.

Level of applicability

EU and Member States.

Target

Member State: HIV status is known for 100% of notified TB cases[i].

EU: HIV-status is known for 100% of TB cases.

[i] The target of 100% is in agreement with the Impact Measurement Task Force Global Plan 2011–2015 with a target of 100% of TB patients tested for HIV. There are certain exceptions where HIV testing and thus HIV status will not be relevant, for example when diagnosing TB post mortem.

Scope

This indicator measures the extent to which HIV-positive TB patients are identified and is therefore a measure that Member States have incorporated HIV testing in the national TB programme.

Proposed measurement approach

The numerator is the total number of TB patients for which HIV status is known and the denominator is the total number of TB patients.

Possible data sources

ECDC and WHO Regional Office for Europe Joint surveillance system (TESSy and CISID).

Frequency of measurement

Annual.

Strengths and limitations

This indicator measures the number of TB cases for which HIV status is known and is thus a first indication that national TB programmes have an incorporated TB/HIV plan. However, this is only an indirect measure and does not directly indicate whether systems are in place within the country to provide HIV patients with adequate treatment, management and follow-up.

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Annex 1. Examples of use of the epidemiological indicators

The two real-life case studies described below demonstrate how three of the epidemiological indicators proposed in Section 2.2 reflect different epidemiological situations.

Country A

Country A has a fairly steady TB incidence of around 40 cases per 100 000 population (Figure A1). However, as can be seen from Figure A2, the ratio of the notification rates in children under 15 years old to adults is increasing. This suggests that cases are not being detected early enough to bring down transmission rates, which is confirmed by the fact that the standardised mean age of new TB cases is decreasing in both males and females (Figures A3 and A4).

Figure A1. TB case notification rate, country A

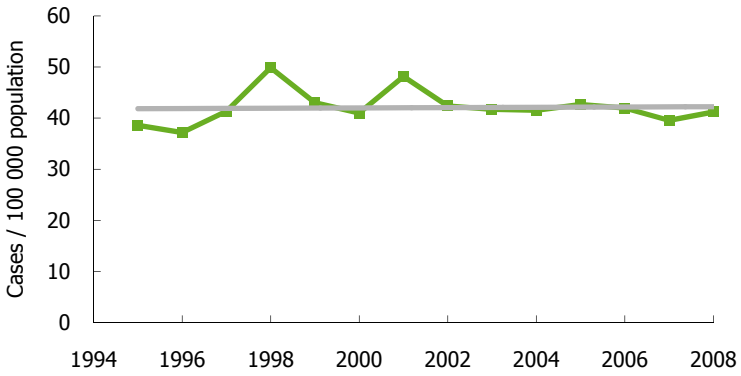


Figure A2. Ratio of case notification rates in children (under 15 years) to adults, country A

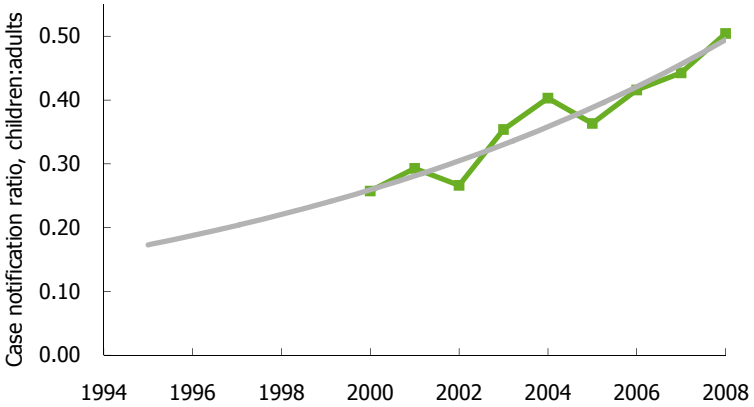


Figure A3. Mean age of new TB cases, males, country A

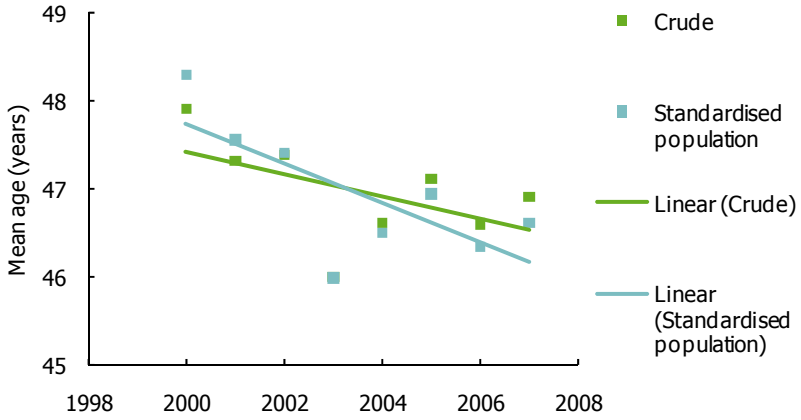
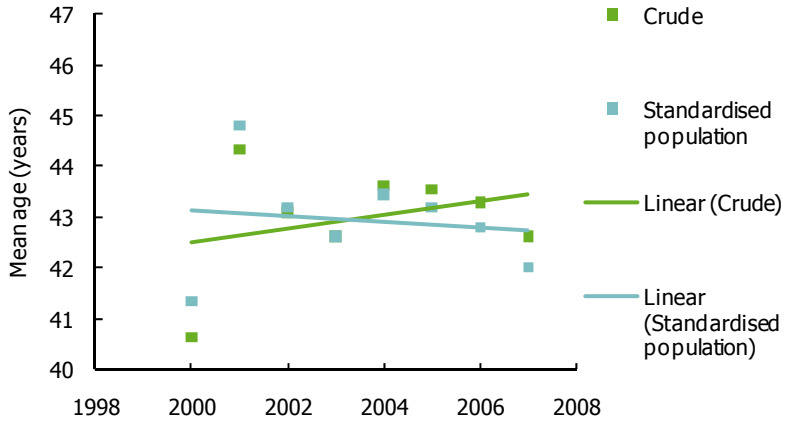


Figure A4. Mean age of new TB cases, females, country A



Country B

In country B, the case notification rate fell from around 55 per 100 000 in 1995 to just under 30 per 100 000 in 2007 (Figure B1). In contrast to country A, the ratio of the notification rate in children under 15 years to the rate for adults also decreased over the same period (Figure B2), although the increase in 2006 and 2007 might serve as a warning that control measures are becoming less effective. The mean age of new TB cases shows a steady increase in both males and females (Figures B3 and B4), suggesting that the control programme is functioning well.

Figure B1. TB case notification rate, country B

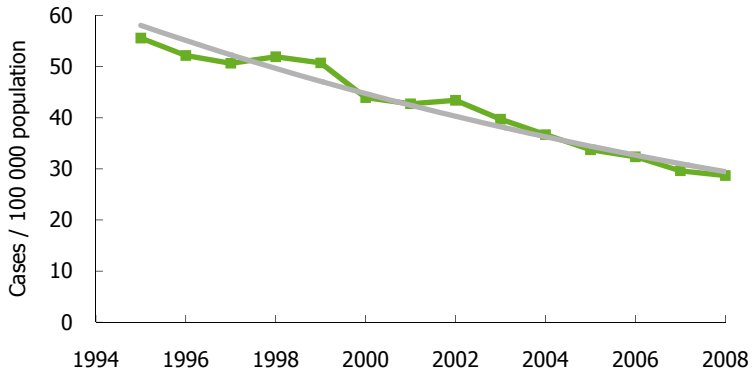


Figure B2. Ratio of case notification rates in children (under 15 years) to adults, country B

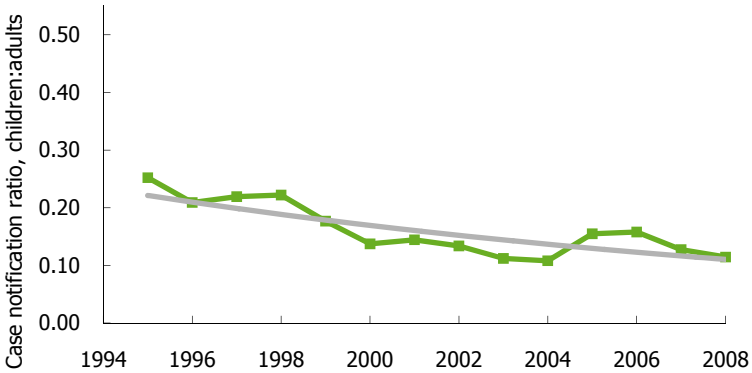


Figure B3. Mean age of new TB cases, males, country B

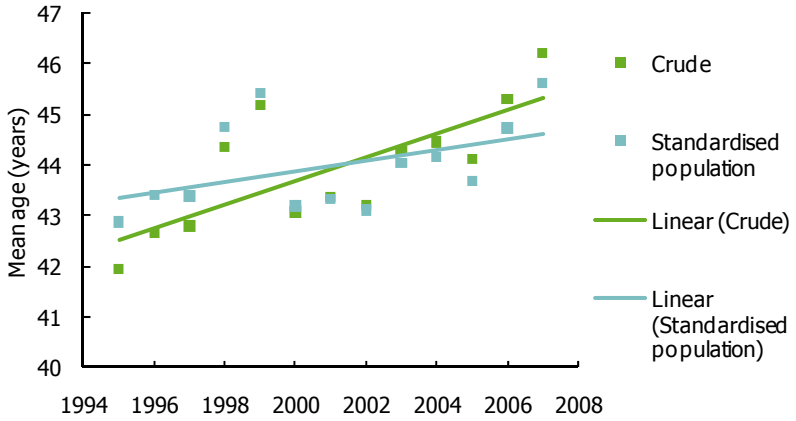


Figure B4. Mean age of new TB cases, females, country B