Analysis of tuberculosis treatment outcomes in the European Union and European Economic Area: efforts needed towards optimal case management and control

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An analysis of surveillance data was performed to assess treatment outcomes of patients belonging to selected calendar year cohorts. Twenty-two countries in the European Union (EU) and European Economic Area (EEA) reported treatment outcome monitoring data for culture-confirmed pulmonary tuberculosis (TB) cases reported in 2007. The overall treatment success rate was 73.8% for all culture-confirmed pulmonary cases and 79.5% for new culture-confirmed pulmonary cases. For the cohort of new culture-confirmed TB cases, only three countries achieved the target of 85% success rate. This underachievement appears to be a result of relative high defaulting and unknown outcome information. Case fatality remains high particularly among cases of national origin. This factor appears attributable to advanced age of the national cohort. Treatment outcomes for multidrug-resistant tuberculosis were reported by 15 countries, with a range of 19.8% to 100% treatment success at 24 months. The data underline the urgent need for strengthening treatment outcome monitoring in the EU and EEA in order to ensure an effective programme implementation and case management that will ultimately contribute to TB elimination.

Background

Tuberculosis (TB) remains a global emergency with estimates of 1.8 millions deaths worldwide in 2008 and over nine million cases. In 2008, the estimated global incidence rate fell to 139 cases per 100,000 population after reaching its peak in 2004 at 143 per 100,000. However, this decline was not homogeneous throughout the World Health Organization (WHO) regions, with Europe failing to record a substantial decline, but rather appearing to have reached a stabilisation of rates [1].

The 30 Member States of the European Union (EU) and European Economic Area (EEA) present a peculiar and highly heterogeneous situation in terms of TB epidemiology and control. Three broad epidemiological areas are distinguished within the borders of the EU/EEA: low incidence countries (below 20 notified cases per 100,000 population) with cases aggregating in vulnerable populations and only occasional increased notification rates; countries with moderate-to-high, but declining notification rates and with a low proportion of multidrug-resistant (MDR) TB; and finally, countries with relatively high notification rates (over 100 notified cases per 100,000) and high levels of MDR TB, but again with declining overall TB rates [2-4].

Attention to TB control in the EU and EEA has been raised in recent years through a number of initiatives, including the launching of a Framework Action Plan to Fight Tuberculosis in the EU [5]. Among the key issues underlined in the Action Plan is the need to achieve and sustain acceptable levels of treatment success among all TB patients.

Treatment success measured by a standardised process of treatment outcome monitoring (TOM) is one of the pillars of TB control and, along with case detection, is recognised as a key programmatic output. It is against this rationale that a World Health Assembly (WHA) resolution was passed in 1991, adopting two targets for global TB control: to detect at least 70% of new infectious cases and to cure at least 85% of those detected. These targets were linked to the Millennium Development Goals, and the Stop TB Partnership set the year 2005 as the deadline for achievement [6-8].

Globally, the treatment success rate has exceeded the 85% target for the first time in 2008 since the target was set in 1991, with a percentage of 87% for patients starting treatment in 2007. Furthermore, treatment success rates were maintained or improved between 2006 and 2007 in all WHO regions with the exception of the European Region which recorded the lowest success rate globally at 67% [1].

The importance of strengthening treatment outcome monitoring in Europe has long been recognised. A statement put forward by the WHO and the International Union against Tuberculosis and Lung

Disease underlined in 1998 the need for standardisation and evaluation of treatment results for TB patients in the WHO European region, including those in low and intermediate incidence countries [9].

In this study we aimed to analyse treatment outcomes and progress towards the targets specifically for the EU/EEA region as a whole and its Member States separately.

Since 1 January 2008, the European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe have jointly coordinated the TB surveillance in Europe. Designated national surveillance institutions or individuals are responsible for providing the data, which is reported to a central joint database. Furthermore, historical data are available from the former EuroTB project for TB surveillance activities in Europe from 1996 to 2007. These data represent a valuable source for an in-depth analysis of treatment outcome monitoring and were used in our study.

Methods

A descriptive analysis of surveillance data was performed to assess treatment outcomes of patients belonging to selected calendar year treatment cohorts.

Data were extracted from The European Surveillance System (TESSy) and from the former EuroTB historical database for the 30 EU and EEA countries reporting data to the ECDC. Since the reporting year 2002, outcome data are collected for all individual cases by submission of an individual dataset for the 12 months before the year for which notification data are reported to TESSy, and since 2008 also for MDR treatment outcome for cases reported 24 months before the year for which notification data are reported to TESSy. The cases eligible for outcome analysis (cohorts) include all the culture-confirmed pulmonary TB cases notified in the calendar year of interest, after exclusion of cases with final diagnosis other than TB.

Country-specific data were extracted for 2007 for both new and retreatment laboratory-confirmed pulmonary TB cases for the analysis of 12 months of treatment outcome data. For 2006, country-specific data were extracted for laboratory-confirmed MDR TB cases (combined new and retreatment) for the analysis of 24 months of treatment outcome data. Aggregated EU/EEA data were extracted for the period 2003 to 2007 for trend analysis of treatment outcome for new, retreatment and combined laboratory-confirmed pulmonary

FIGURE 1

Treatment outcome of laboratory-confirmed pulmonary cases, EU/EEA countries[1] 2003-2007
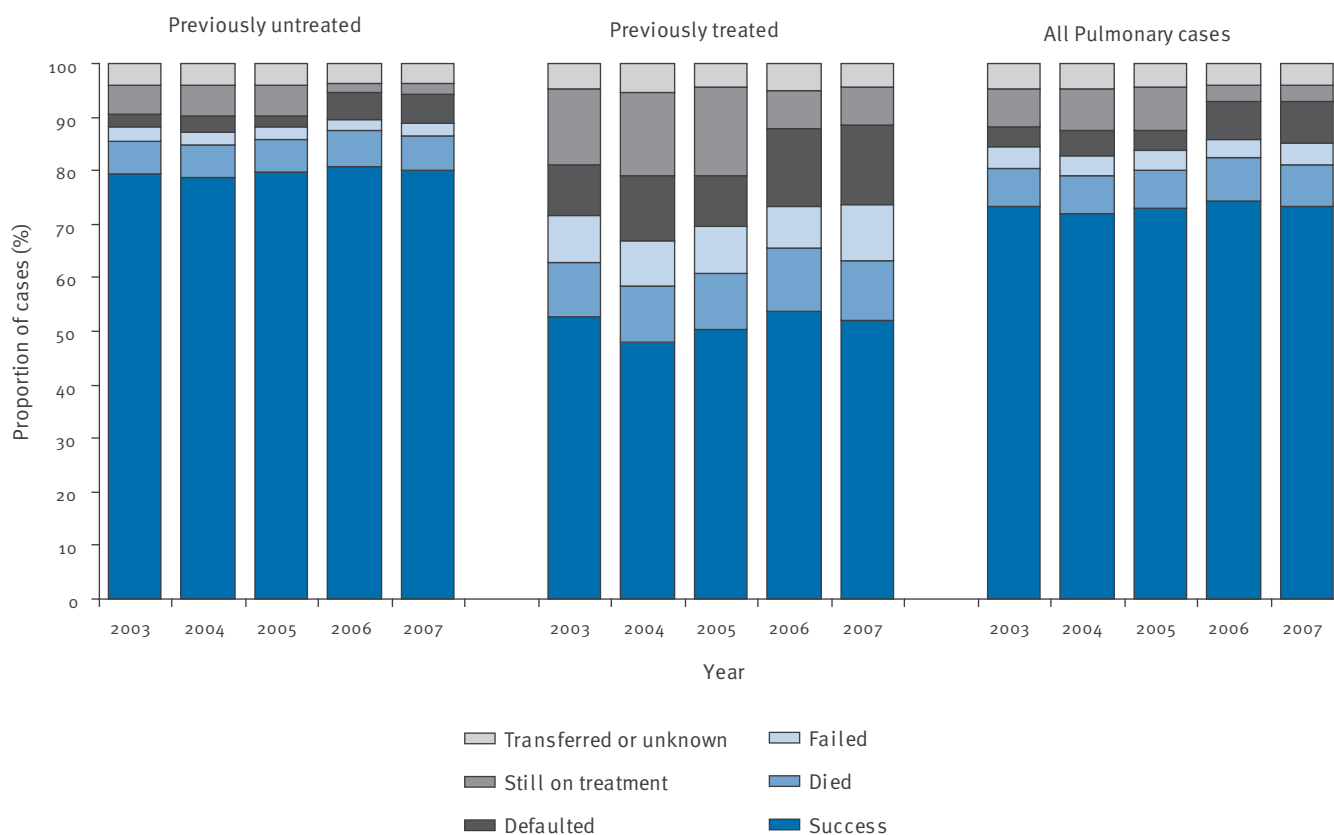
EEA: European Economic Area; EU: European Union.

[1] Excluding countries that did not or not in all years report cases: Austria, Bulgaria, Finland, France, Greece, Liechtenstein, Luxembourg, and Spain.

Table 1

Treatment outcome in new and retreatment culture-confirmed pulmonary tuberculosis cases, by country, EU/EEA countries, 2007 (n=36,377)

Country	Cases notified in 2007	Success		Died		Failed		Defaulted		Still on treatment		Transferred or unknown	
	N	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
New cases													
Austria	-	-	-	-	-	-	-	-	-	-	-	-	-
Belgium[1]	499	342	(68.5)	42	(8.4)	0	(0.0)	44	(8.8)	12	(2.4)	59	(11.8)
Bulgaria	1,233	972	(78.8)	85	(6.9)	4	(0.3)	96	(7.8)	41	(3.3)	35	(2.8)
Cyprus	-	-	-	-	-	-	-	-	-	-	-	-	-
Czech Republic	459	331	(72.1)	86	(18.7)	4	(0.9)	32	(7.0)	4	(0.9)	2	(0.4)
Denmark[1]	213	169	(79.3)	11	(5.2)	2	(0.9)	3	(1.4)	11	(5.2)	17	(8.0)
Estonia	302	185	(61.3)	41	(13.6)	2	(0.7)	29	(9.6)	45	(14.9)	0	(0.0)
Finland	181	126	(69.6)	35	(19.3)	1	(0.6)	2	(1.1)	7	(3.9)	10	(5.5)
France	-	-	-	-	-	-	-	-	-	-	-	-	-
Germany	2,421	1,863	(77.0)	277	(11.4)	3	(0.1)	36	(1.5)	69	(2.9)	173	(7.1)
Greece	-	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	612	311	(50.8)	74	(12.1)	86	(14.1)	34	(5.6)	84	(13.7)	23	(3.8)
Iceland	7	6	(85.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Ireland[1]	181	127	(70.2)	10	(5.5)	0	(0.0)	3	(1.7)	8	(4.4)	33	(18.2)
Italy	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia	772	634	(82.1)	54	(7.0)	1	(0.1)	32	(4.1)	51	(6.6)	0	(0.0)
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-
Lithuania	1,209	860	(71.1)	144	(11.9)	18	(1.5)	89	(7.4)	94	(7.8)	4	(0.3)
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-	-
Malta	12	9	(75.0)	0	(0.0)	0	(0.0)	1	(8.3)	1	(8.3)	1	(8.3)
Netherlands[1]	397	314	(79.1)	18	(4.5)	0	(0.0)	8	(2.0)	0	(0.0)	57	(14.4)
Norway[1]	114	89	(78.1)	2	(1.8)	0	(0.0)	0	(0.0)	4	(3.5)	19	(16.7)
Poland	4,502	3,444	(76.5)	269	(6.0)	12	(0.3)	448	(10.0)	16	(0.4)	313	(7.0)
Portugal	1,694	1,467	(86.6)	90	(5.3)	5	(0.3)	52	(3.1)	56	(3.3)	24	(1.4)
Romania	11,245	9,508	(84.6)	453	(4.0)	442	(3.9)	533	(4.7)	95	(0.8)	214	(1.9)
Slovakia	304	260	(85.5)	36	(11.8)	1	(0.3)	5	(1.6)	1	(0.3)	1	(0.3)
Slovenia	150	123	(82.0)	16	(10.7)	0	(0.0)	4	(2.7)	0	(0.0)	7	(4.7)
Spain	-	-	-	-	-	-	-	-	-	-	-	-	-
Sweden[1]	237	157	(66.2)	17	(7.2)	0	(0.0)	2	(0.8)	8	(3.4)	53	(22.4)
United Kingdom[1]	2,241	1,733	(77.3)	145	(6.5)	0	(0.0)	15	(0.7)	128	(5.7)	220	(9.8)
Total New cases	**28,985**	**23,030**	**(79.5)**	**1,905**	**(6.6)**	**581**	**(2.0)**	**1,468**	**(5.1)**	**735**	**(2.5)**	**1,266**	**(4.4)**
Retreatment cases													
Austria	-	-	-	-	-	-	-	-	-	-	-	-	-
Belgium[2]	49	27	(55.1)	6	(12.2)	0	(0.0)	4	(8.2)	8	(16.3)	4	(8.2)
Bulgaria	146	52	(35.6)	38	(26.0)	2	(1.4)	23	(15.8)	27	(18.5)	4	(2.7)
Cyprus	-	-	-	-	-	-	-	-	-	-	-	-	-
Czech Republic	44	30	(68.2)	7	(15.9)	0	(0.0)	4	(9.1)	2	(4.5)	1	(2.3)
Denmark[2]	18	8	(44.4)	3	(16.7)	0	(0.0)	1	(5.6)	1	(5.6)	5	(27.8)
Estonia	66	31	(47.0)	5	(7.6)	3	(4.5)	13	(19.7)	14	(21.2)	0	(0.0)
Finland	7	7	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
France	-	-	-	-	-	-	-	-	-	-	-	-	-
Germany	178	114	(64.0)	25	(14.0)	3	(1.7)	8	(4.5)	13	(7.3)	15	(8.4)
Greece	-	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	130	51	(39.2)	26	(20.0)	26	(20.0)	12	(9.2)	13	(10.0)	2	(1.5)
Iceland	1	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)
Ireland[2]	28	16	(57.1)	4	(14.3)	0	(0.0)	0	(0.0)	3	(10.7)	5	(17.9)
Italy	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia	167	96	(57.5)	14	(8.4)	2	(1.2)	17	(10.2)	36	(21.6)	2	(1.2)
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-
Lithuania	423	130	(30.7)	119	(28.1)	21	(5.0)	89	(21.0)	63	(14.9)	1	(0.2)

Country	Cases N	Success N	(%)	Died N	(%)	Failed N	(%)	Defaulted N	(%)	Still on treatment N	(%)	Transferred or unknown N	(%)
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-	-
Malta	1	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)
Netherlands[2]	40	27	(67.5)	3	(7.5)	0	(0.0)	1	(2.5)	0	(0.0)	9	(22.5)
Norway[2]	17	13	(76.5)	1	(5.9)	0	(0.0)	0	(0.0)	1	(5.9)	2	(11.8)
Poland	698	429	(61.5)	69	(9.9)	4	(0.6)	141	(20.2)	8	(1.1)	47	(6.7)
Portugal	182	140	(76.9)	13	(7.1)	0	(0.0)	11	(6.0)	12	(6.6)	6	(3.3)
Romania	4,933	2,462	(49.9)	479	(9.7)	683	(13.8)	767	(15.5)	325	(6.6)	217	(4.4)
Slovakia	42	35	(83.3)	1	(2.4)	1	(2.4)	1	(2.4)	4	(9.5)	0	(0.0)
Slovenia	13	10	(76.9)	3	(23.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Spain	-	-	-	-	-	-	-	-	-	-	-	-	-
Sweden[2]	13	7	(53.8)	2	(15.4)	0	(0.0)	1	(7.7)	1	(7.7)	2	(15.4)
United Kingdom[2]	196	141	(71.9)	22	(11.2)	0	(0.0)	0	(0.0)	14	(7.1)	19	(9.7)
Total retreatment	**7,392**	**3,826**	**(51.8)**	**840**	**(11.4)**	**745**	**(10.1)**	**1,093**	**(14.8)**	**545**	**(7.4)**	**343**	**(4.6)**
Total for all	**36,377**	**26,856**	**(73.8)**	**2,745**	**(7.5)**	**1,326**	**(3.6)**	**2,561**	**(7.0)**	**1,280**	**(3.5)**	**1,609**	**(4.4)**

EEA: European Economic Area; EU: European Union.

[1] Not previously diagnosed cases.

[2] Previously diagnosed cases.

TABLE 2

Treatment outcome in culture-confirmed pulmonary TB cases by geographic origin and by country, EU/EEA countries, 2007 (n=37,160)

	Cases	Success		Died		Failed		Defaulted		Still on treatment		Transferred or unknown	
Country	N	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
National origin													
Austria	-	-	-	-	-	-	-	-	-	-	-	-	-
Belgium	327	224	(68.5)	42	(12.8)	0	(0.0)	14	(4.3)	8	(2.4)	39	(11.9)
Bulgaria	1,379	1,024	(74.2)	123	(8.9)	6	(0.4)	119	(8.6)	68	(4.9)	39	(2.8)
Cyprus	-	-	-	-	-	-	-	-	-	-	-	-	-
Czech Republic	407	306	(75.2)	84	(20.6)	3	(0.7)	9	(2.2)	5	(1.2)	0	(0.0)
Denmark[1]	113	89	(78.8)	10	(8.8)	1	(0.9)	1	(0.9)	4	(3.5)	8	(7.1)
Estonia	312	184	(59.0)	38	(12.2)	3	(1.0)	36	(11.5)	51	(16.3)	0	(0.0)
Finland	146	99	(67.8)	35	(24.0)	1	(0.7)	1	(0.7)	5	(3.4)	5	(3.4)
France	-	-	-	-	-	-	-	-	-	-	-	-	-
Germany	1,680	1,214	(72.3)	292	(17.4)	6	(0.4)	28	(1.7)	47	(2.8)	93	(5.5)
Greece	-	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	719	345	(48.0)	100	(13.9)	113	(15.7)	43	(6.0)	94	(13.1)	24	(3.3)
Iceland	1	1	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Ireland	149	103	(69.1)	14	(9.4)	0	(0.0)	3	(2.0)	2	(1.3)	27	(18.1)
Italy	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia	887	691	(77.9)	66	(7.4)	3	(0.3)	44	(5.0)	82	(9.2)	1	(0.1)
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-
Lithuania	1,593	971	(61.0)	258	(16.2)	36	(2.3)	172	(10.8)	151	(9.5)	5	(0.3)
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-	-
Malta	5	4	(80.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Netherlands	198	148	(74.7)	19	(9.6)	0	(0.0)	6	(3.0)	0	(0.0)	25	(12.6)
Norway	26	21	(80.8)	3	(11.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.7)
Poland	5,178	3,863	(74.6)	338	(6.5)	16	(0.3)	586	(11.3)	24	(0.5)	351	(6.8)
Portugal	1,622	1,397	(86.1)	93	(5.7)	5	(0.3)	48	(3.0)	56	(3.5)	23	(1.4)
Romania	16,178	11,970	(74.0)	932	(5.8)	1,125	(7.0)	1,300	(8.0)	420	(2.6)	431	(2.7)
Slovakia	346	296	(85.5)	38	(11.0)	2	(0.6)	6	(1.7)	4	(1.2)	0	(0.0)
Slovenia	128	106	(82.8)	17	(13.3)	0	(0.0)	4	(3.1)	0	(0.0)	1	(0.8)
Spain	-	-	-	-	-	-	-	-	-	-	-	-	-
Sweden	66	37	(56.1)	12	(18.2)	0	(0.0)	1	(1.5)	1	(1.5)	15	(22.7)
United Kingdom	915	673	(73.6)	113	(12.3)	0	(0.0)	7	(0.8)	44	(4.8)	78	(8.5)

|	Total Nationals	32,380	23,765	(73.4)	2,628	(8.1)	1,320	(4.1)	2,428	(7.5)	1,066	(3.3)	1,173	(3.6)
Foreign origin														
Austria	-	-	-	-	-	-	-	-	-	-	-	-	-
Belgium	288	190	(66.0)	17	(5.9)	0	(0.0)	39	(13.5)	13	(4.5)	29	(10.1)
Bulgaria	1	1	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Cyprus	-	-	-	-	-	-	-	-	-	-	-	-	-
Czech Republic	96	55	(57.3)	9	(9.4)	1	(1.0)	27	(28.1)	1	(1.0)	3	(3.1)
Denmark[2]	118	88	(74.6)	4	(3.4)	1	(0.8)	3	(2.5)	8	(6.8)	14	(11.9)
Estonia	56	32	(57.1)	8	(14.3)	2	(3.6)	6	(10.7)	8	(14.3)	0	(0.0)
Finland	42	34	(81.0)	0	(0.0)	0	(0.0)	1	(2.4)	2	(4.8)	5	(11.9)
France	-	-	-	-	-	-	-	-	-	-	-	-	-
Germany	1,157	914	(79.0)	66	(5.7)	1	(0.1)	24	(2.1)	37	(3.2)	115	(9.9)
Greece	-	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	24	14	(58.3)	0	(0.0)	3	(12.5)	4	(16.7)	3	(12.5)	0	(0.0)
Iceland	7	5	(71.4)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(28.6)
Ireland	95	62	(65.3)	3	(3.2)	0	(0.0)	0	(0.0)	9	(9.5)	21	(22.1)
Italy	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia	52	39	(75.0)	2	(3.8)	0	(0.0)	5	(9.6)	5	(9.6)	1	(1.9)
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-
Lithuania	43	21	(48.8)	7	(16.3)	3	(7.0)	6	(14.0)	6	(14.0)	0	(0.0)
Luxembourg	18	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	18	(100.0)
Malta	9	5	(55.6)	0	(0.0)	0	(0.0)	1	(11.1)	1	(11.1)	2	(22.2)
Netherlands	285	216	(75.8)	10	(3.5)	0	(0.0)	4	(1.4)	0	(0.0)	55	(19.3)
Norway	121	90	(74.4)	2	(1.7)	0	(0.0)	0	(0.0)	5	(4.1)	24	(19.8)
Poland	22	10	(45.5)	0	(0.0)	0	(0.0)	3	(13.6)	0	(0.0)	9	(40.9)
Portugal	249	208	(83.5)	8	(3.2)	0	(0.0)	15	(6.0)	12	(4.8)	6	(2.4)
Romania	0	0	-	0	-	0	-	0	-	0	-	0	-
Slovakia	4	2	(50.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(25.0)	1	(25.0)
Slovenia	35	27	(77.1)	2	(5.7)	0	(0.0)	0	(0.0)	0	(0.0)	6	(17.1)
Spain	-	-	-	-	-	-	-	-	-	-	-	-	-
Sweden	184	127	(69.0)	7	(3.8)	0	(0.0)	2	(1.1)	8	(4.3)	40	(21.7)
United Kingdom	1,874	1,467	(78.3)	82	(4.4)	0	(0.0)	11	(0.6)	106	(5.7)	208	(11.1)
Total Foreigners	**4,780**	**3,607**	**(75.5)**	**227**	**(4.7)**	**11**	**(0.2)**	**151**	**(3.2)**	**225**	**(4.7)**	**559**	**(11.7)**

EEA: European Economic Area; EU: European Union.

[1] Excluding native cases < 26 years old whose parents were born outside Denmark

[2] Including native cases < 26 years old whose parents were born outside Denmark

FIGURE 2

Proportion of tuberculosis deaths by geographic origin, EU/EEA countries[1], 2007 (of n=37,160 cases)
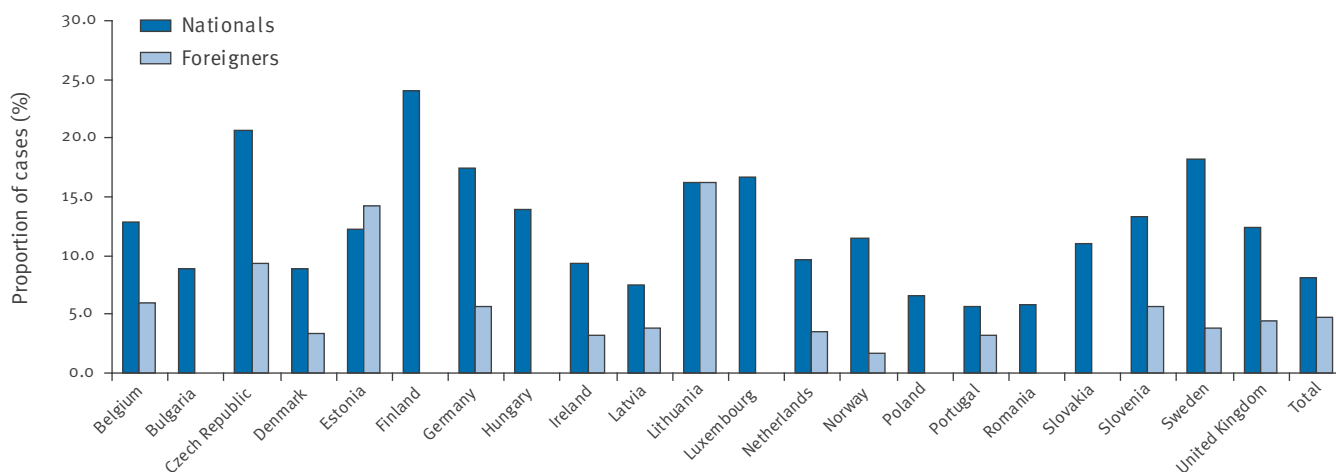
EEA: European Economic Area; EU: European Union.

[1] Excluding countries that did not or not in all years report cases.

TB cases. The following case classification was used for the purpose of the analysis:

- A *laboratory-confirmed TB case* was a patient with culture-confirmed disease due to *Mycobacterium tuberculosis* complex.
- A *new case* was any case who had not received drug treatment for active TB in the past, or who received anti-TB drugs for less than one month.
- A *retreatment case* was a case diagnosed with TB in the past and who received treatment with anti-TB drugs (excluding preventive therapy) for at least one month.
- A *pulmonary case* was any case with TB affecting the lung parenchyma, the tracheo-bronchial tree or the larynx.
- *Multi-drug resistance* was defined as resistance to at least isoniazid and rifampicin.
- *Foreign/national origin* for comparison of treatment outcome by geographical origin of TB cases was classified according to place of birth: born in the country (national origin) or born outside the country (foreign origin). For countries reporting citizenship rather than place of birth, the former was used as a proxy of national/foreign origin. In Denmark, the place of birth of parents was also used to classify geographical origin.

For the purpose of this analysis, internationally recommended outcome categories where used with two additional categories [9]: 'still on treatment' after 12 months of treatment, and 'unknown'. Adopted definitions in our study were:

- *Cured:* The treatment has been completed and culture has become negative on samples taken at the end of treatment and on at least one previous occasion.
- *Completed:* The treatment has been completed but the case does not meet the criteria for cure or treatment failure.
- *Failed:* Culture or sputum smear remain positive or become positive again five months or later into the course of treatment.
- *Died:* Death, irrespective of cause, occurred before the patient was cured or treatment was completed.
- *Defaulted:* The treatment was interrupted for two months or more, not resulting from a decision of the care provider; or the patient was lost to follow-up for two months or more before the end of treatment, except if transferred.
- *Transferred:* The patient was referred to another clinical unit for treatment, and information on outcome is not available.
- *Still on treatment:* The patient is still on treatment at 12 (24 when applicable) months after the start of treatment and did not meet any other outcome during treatment. This category includes patients whose initial treatment was changed due to poly-resistance (i.e. resistance to at least two first-line drugs) of the isolate taken at the start of treatment,

whose treatment was prolonged because of side effects/complications, whose initial regimen had been planned for more than 12 months, or patients for whom information on the reasons for being still on treatment was not available.

- *Unknown:* Information on outcome is not available, for cases not known to have been transferred.
- *Success:* This refers to the combined number of patients belonging to the treatment categories 'cured' and 'completed'. The *success rate target* (established by the WHA as 85% of new smear-positive cases) has been adapted to the EU/EEA setting where bacteriological confirmation of cases is done by culture. Thus for the purposes of this study, a success rate target of 85% applies to new laboratory-confirmed cases.
- *Cohort:* This includes all cases eligible for outcome analysis (cohorts); i.e. all the culture-confirmed pulmonary TB cases notified in the calendar year of interest, after exclusion of cases with final diagnosis other than TB.
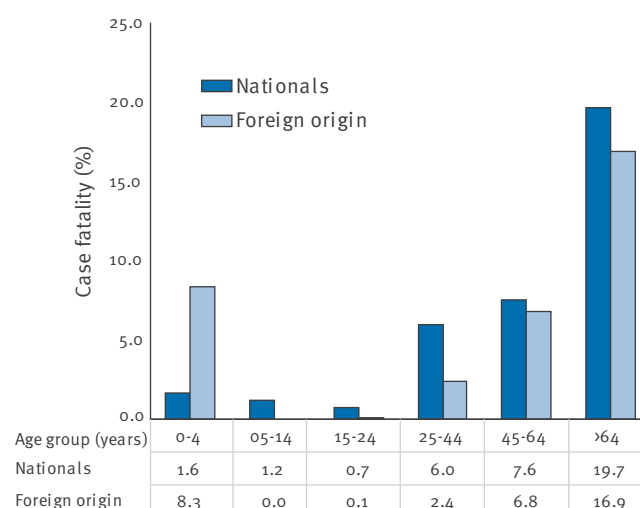
For the purpose of calculating the outcome variables, culture-confirmed pulmonary TB cases notified in the calendar year of interest were used as denominators. Data for one country were considered to be complete if the cohorts used as denominators included all culture-confirmed pulmonary TB cases notified in the year selected for analysis and if the combined total of 'defaulted, transferred and unknown' cases did not exceed 35% of cases notified in that year.

Proportions of deaths by geographic origin were stratified by age to allow comparability.
Adjustments to account for how countries with high numbers of cases influence the EU/EEA average were not performed as the study aimed at presenting overall figures for EU/EEA patients.

Age group (years)	0-4	05-14	15-24	25-44	45-64	>64
Nationals	1.6	1.2	0.7	6.0	7.6	19.7
Foreign origin	8.3	0.0	0.1	2.4	6.8	16.9

EEA: European Economic Area; EU: European Union.

Results

Twenty-two countries reported TOM data at 12 months for culture-confirmed pulmonary TB cases reported in 2007. Data were considered to be complete as per study definition in all reporting countries. The overall treatment success rate for all laboratory-confirmed pulmonary cases was 73.8%. Of these patients, 7.5% died while being treated for TB, 3.6% failed treatment, 7.0% defaulted, 3.5% were still on treatment at the end of the 12-month observation period and 4.4% had an outcome recorded as unknown or transferred (Figure 1, Table 1).

Among new laboratory-confirmed pulmonary cases, 79.5% had a successful outcome, 6.6% died, 2% failed, 2.5% were still on treatment, and 4.4% were transferred or had an unknown outcome (Table 1). Among countries with more than 20 new culture-confirmed pulmonary cases, success rates varied widely from 50.8% in Hungary to 86.6% and 85.5% in Portugal and Slovakia respectively. Three countries achieved treatment success in 85% or more of this category of cases: Iceland, 85.7%, Portugal, 86.6% and Slovakia, 85.5%. The percentage of cases that died while undergoing TB treatment ranged from 1.8% in Norway to 18.7% in the Czech Republic. Overall treatment success rates below 75% were associated with a high loss to follow-up (defaulted and transferred or unknown) ranging from 6.6% to 25.7%.

Treatment outcomes for retreatment culture-confirmed pulmonary TB cases were reported from 22 EU/EEA Member States (Table 1). For seven countries, information about previous treatment was not distinguished and reported as previously diagnosed cases (Belgium, Denmark, Ireland, the Netherlands, Norway, Sweden and United Kingdom). Among these retreatment cases the overall success rate was lower (51.8%; range: 0%–100%) than among new cases. Death (11.4%), treatment failure (10.1%), default (14.8%) and still on treatment (7.4%) were more frequently reported in this group than among new cases. Only six countries achieved a treatment success of at least 70% among retreatment cases (Table 1).

Analysis of data by geographic origin revealed similar proportions of successfully treated cases of national origin (73.4%) and those of foreign origin (75.5%). However, marked differences were observed in the proportion of deaths, with higher percentages among cases of national origin (8.1%) compared with those of foreign origin (4.7%). Similarly, differences were found in the percentages of failed cases (4.1% in nationals versus 0.2% in cases of foreign origin) and transferred/ unknown (3.6% in nationals versus 11.7% in cases of foreign origin) (Table 2, Figure 2).

With regards to the differences in proportion of deaths between foreign origin and national cases, the stratification of case fatality by age group (Figure 3) reveals that age acts as an effect modifier, where the proportion of deaths increased with increasing age. The highest case fatality was in the age group of over 64-year-olds, regardless of geographical origin. The high case fatality in 0-4-year-old children in the group of foreign origin is a doubtful interpretation as there was only one death in this group.

Fifteen countries (12 of which provided complete data as per study definition) reported the treatment outcome at 24 months for culture-confirmed MDR TB cases (new and retreatment). The overall treatment success in the 15 countries ranged from 19.8% to 100%. Of the entire cohort, 16.6% died while on treatment, 17.0% failed treatment and 13.2% defaulted. 17.0% of registered cases were still on treatment at the end of the 24 months observation period and 5.3% had been transferred or had an unknown outcome (Table 3).

Analysis of trends for the cohorts 2003 to 2007 did not reveal any significant difference in the proportions of cases belonging to any of the treatment outcome categories. Treatment success remained in the range of 78% to 80% in the new laboratory-confirmed pulmonary cases. Minimal improvement from 48% to 52.2% was recorded between the 2006 and 2007 cohorts of retreatment culture-confirmed pulmonary cases (Figure 1).

Discussion and conclusions

This analysis of treatment outcome monitoring within the EU and EEA Member States revealed significant findings concerning TB control in the region. Firstly, it is a matter of concern that there has been only a marginal improvement in the number of countries reporting treatment outcomes to the EU-wide database, which increased by only one Member State compared with the 2006 cohort reporting (22 versus 21 countries). Similarly, the number of cases with an unknown treatment outcome because of transfer or 'outcome unknown', remained high with an average of 4.4% of all pulmonary culture-confirmed cases belonging to this category and with six of 22 countries reporting more than 10% of unknown outcomes. This represents a programmatic weakness in one of the pillars of TB control and highlights the importance of the monitoring and evaluation process [2,3,10].

More disturbing is the fact that there has been no significant improvement in the percentage of cases successfully treated over the past five years, with 79.5% of new laboratory-confirmed pulmonary cases successfully treated and 51.8% in retreatment cases. This is reflected at the level of the individual Member States: only three countries achieved the target of 85% success rate in 2007 compared with seven countries for the 2006 cohort.

The authors would have wished to extend the analysis of completeness of treatment to all notified cases to gain further insight in the distribution and quality of outcomes; however data proved insufficient to pro-

ceed with this approach since only few countries report treatment completion for all cases.

Achieving high success rates becomes particularly important in a setting like the EU and EEA where the decline in incidence that was typical of the past few decades is becoming slower in most countries [2]. This trend is certainly influenced by many factors including importation of cases from high-burden countries, outbreaks among vulnerable populations, persisting MDR TB, and in some cases a lack of adequate TB control measures. In this setting it is essential to achieve optimal treatment success in all TB patients.

The need for reaching the success rate target is justified by its potential epidemiological impact. Several epidemiological models have shown [11-14] that achieving the 85% success target coupled with a case detection of at least 70% would cause a decline in the annual TB incidence rate of 5-10% in the absence of co-infection with human immunodeficiency virus (HIV). These theoretical assumptions are further corroborated by empirical findings, particularly in the European context. In fact, the TB incidence has been declining rapidly all over Europe over the past century, but the decline has more than doubled following the introduction of effective treatment.

The analysis of the data by geographical origin (national versus foreign) revealed a similarity in the two groups in terms of overall success rate. Differences exist in the distribution of negative outcomes with regard to geographic origin. However, stratifying case fatality by age showed that the excess proportion of deaths

Table 3

Treatment outcome of multidrug-resistant tuberculosis cases after 24 months of treatment, EU/EEA countries, 2006 cohort (n=1,190)

| Country | Total number of MDR cases | TOM after 24 months | | | | | | | | | | | |
| | | Success | | Died | | Failed | | Defaulted | | Still on treatment | | Transferred or unknown | |
		N	%	N	%	N	%	N	%	N	%	N	%
Austria	-	-	-	-	-	-	-	-	-	-	-	-	-
Belgium	18	10	(55.6)	1	(5.6)	0	(0.0)	0	(0.0)	3	(16.7)	4	(22.2)
Bulgaria	-	-	-	-	-	-	-	-	-	-	-	-	-
Cyprus	0	-	-	-	-	-	-	-	-	-	-	-	-
Czech Republic	12	3	(25.0)	4	(33.3)	0	(0.0)	3	(25.0)	2	(16.7)	0	(0.0)
Denmark	3	2	(66.7)	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)
Estonia	53	24	(45.3)	12	(22.6)	2	(3.8)	14	(26.4)	1	(1.9)	0	(0.0)
Finland	-	-	-	-	-	-	-	-	-	-	-	-	-
France	-	-	-	-	-	-	-	-	-	-	-	-	-
Germany	83	42	(50.6)	4	(4.8)	1	(1.2)	10	(12.0)	14	(16.9)	12	(14.5)
Greece	-	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	17	9	(52.9)	1	(5.9)	5	(29.4)	1	(5.9)	1	(5.9)	0	(0.0)
Iceland	0	-	-	-	-	-	-	-	-	-	-	-	-
Ireland	4	1	(25.0)	0	(0.0)	0	(0.0)	1	(25.0)	0	(0.0)	2	(50.0)
Italy	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia	142	87	(61.3)	34	(23.9)	6	(4.2)	15	(10.6)	0	(0.0)	0	(0.0)
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-
Lithuania	-	-	-	-	-	-	-	-	-	-	-	-	-
Luxembourg	0	-	-	-	-	-	-	-	-	-	-	-	-
Malta	2	2	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Netherlands	-	-	-	-	-	-	-	-	-	-	-	-	-
Norway	3	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(66.7)
Poland	32	11	(34.4)	4	(12.5)	3	(9.4)	4	(12.5)	0	(0.0)	10	(31.3)
Portugal	25	16	(64.0)	6	(24.0)	1	(4.0)	2	(8.0)	0	(0.0)	0	(0.0)
Romania	788	156	(19.8)	130	(16.5)	184	(23.4)	107	(13.6)	178	(22.6)	33	(4.2)
Slovakia	7	3	(42.9)	2	(28.6)	0	(0.0)	0	(0.0)	2	(28.6)	0	(0.0)
Slovenia	1	1	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Spain	-	-	-	-	-	-	-	-	-	-	-	-	-
Sweden	-	-	-	-	-	-	-	-	-	-	-	-	-
United Kingdom	-	-	-	-	-	-	-	-	-	-	-	-	-
Subtotal EU/EEA	**1,190**	**368**	**(30.9)**	**198**	**(16.6)**	**202**	**(17.0)**	**157**	**(13.2)**	**202**	**(17.0)**	**63**	**(5.3)**

EEA: European Economic Area; EU: European Union; MDR: multidrug-resistant; TOM: treatment outcome monitoring.

among nationals was attributed to older age. These findings are not unexpected, and the similarities in terms of success rate, evident also at country level, seem to suggest that foreign-born patients are not at a higher risk of unfavourable outcome.

The analysis also revealed a potential for worsening of the M/XDR TB epidemic in the EU and EEA, resulting from the high default rates recorded among retreatment and MDR TB cases (14.8% and 13.2%, respectively). Despite the data limitations with respect to the MDR TB analysis (with regards to data representativeness completeness and quality assurance of laboratory methods) a clear need for strengthening case holding and treatment monitoring among these two populations (retreatment and MDR TB) emerges. As widely shown in the literature, defaulting and previous unsuccessful treatment represent the biggest risk factor for the emergence of drug resistance, in particular M/XDR TB [15-18].

The role that surveillance of TB treatment outcomes can and ought to play in strengthening TB control needs to be highlighted. Reporting of outcomes allows close monitoring of the ability of TB programmes to support and ensure completion of patients' treatment. It also allows tailoring control activities to high-risk groups defined in terms of their inability to comply with treatment and achieve successful outcomes.

The claim that an unknown or unreported treatment outcome does not necessarily represent a negative one should be balanced against the argument that lack of knowledge about treatment outcomes deprives the programme of essential information to guide TB control.

Finally it should be noted that the importance of achieving the highest possible treatment success rate goes beyond its programmatic and epidemiological impact. Achieving universal success in treating individual patients remains a fundamental point in case management and patient care.

The importance of treatment outcome monitoring needs to be further stressed and mechanisms explored to maximise progress towards achievement of the targets. Clinicians, public health experts and policy makers must be convinced of the importance of a standardised approach to monitoring of treatment including a proper evaluation of its implementation. Only by recognising the key position that treatment outcome monitoring holds in TB control can progress towards elimination be pursued.

Acknowledgements

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