Tuberculosis treatment outcome monitoring in European Union countries: systematic review

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ABSTRACT:

Treatment success measured by treatment outcome monitoring (TOM) is a key programmatic output of tuberculosis (TB) control programmes. We performed a systematic literature review on national level TOM in the 30 European Union/European Economic Areas (EU/EEA) countries to summarise methods used to collect and report data on TOM.

Online reference bibliographic databases PubMed/MEDLINE and EMBASE were searched to identify relevant indexed and non-indexed literature published between January 2000 and August 2010.

The search strategy resulted in 615 potentially relevant indexed citations, of which 27 full text national studies (79 data sets) were included for final analysis. The selected studies were performed in 10 EU/EEA countries and gave a fragmented impression of TOM in the EU/EEA. Publication year, study period, sample size, databases, definitions, variables, patient and outcome categories and population subgroups varied widely, portraying a very heterogeneous picture.

This review confirmed previous reports of considerable heterogeneity in publications of TOM results across EU/EEA countries. PubMed/MEDLINE and EMBASE indexed studies are not a suitable instrument to measure representative TOM results for the 30 EU/EEA countries. Uniform and complete reporting to the centralised European Surveillance System will produce the most timely and reliable results of TB treatment outcomes in the EU/EEA.

KEY WORDS: cohort analysis, death, failure, treatment success, surveillance, tuberculosis control

BACKGROUND

Attention to tuberculosis (TB) control in the European Union (EU) and European Economic Areas (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 [1-3]. 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 a key programmatic output of any TB control programme [3]. In 1998, a World Health Organization (WHO) and European region of the International Union against Tuberculosis and Lung Disease (IUALDT) working group published a consensus statement on standardised TOM in Europe [4]. For clinicians it is relevant to know treatment success is in each individual patient, for countries TOM is essential to systematically evaluate the effectiveness of the national TB programme. In the WHO/IUATLD recommendations emphasis was placed on cohort analysis of definite, i.e. culture-confirmed, cases of pulmonary TB. The initial purpose of TOM was to find out how many of the potential infectious TB patients notified were declared "cured" at the end of treatment [4]. More recent, treatment "success" is measured, combining the number of patients being "cured" and having their "treatment completed" [5].

Since 1 January 2008, the European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe jointly coordinate TB surveillance in Europe. Designated national surveillance institutions or individuals in each EU/EEA Member State are responsible for providing the data, which are reported to The European Surveillance System (TESSy). Since 2002, TOM data are collected for the year cohort of individual cases 12 months after reporting to TESSy, and since 2008 also for Multidrug-Resistant TB (MDR-TB) treatment outcome for cases in the year cohort 24 months after reporting to TESSy. However, the definitions applied for TOM seem to vary between countries as do data collection

methods. A recently published analysis of TOM within the EU/EEA expressed concern about only marginal improvement in the number of reporting countries and concluded that the importance of TOM needs to be further stressed and mechanisms should be explored to maximise progress. [3].

We performed a systematic literature review on TOM at the national level in the 30 EU/EEA member states to: 1) summarise the methods used to collect and report data on TOM, 2) examine reports on TOM proportions calculated for the general population, vulnerable populations, MDR-TB / Extensively Drug-Resistant (XDR) TB sub-cohorts and other identifiable sub-groups and 3) find additional TOM information not available in TESSy.

METHODS

Literature search strategy

Online reference bibliographic databases PubMed/MEDLINE and EMBASE were searched to identify relevant indexed studies published since January 2000 to August 2010. The search strategy consisted of a search only including MeSH terms ("treatment outcome" AND "tuberculosis" AND any of the 30 EU/EEA countries (Austria, Belgium, Bulgaria, Cyprus Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom) combined with (OR) a search including the same terms as free text terms. Exploration of the search strategy revealed that when including a MeSH term relating to study design (e.g. cohort studies, follow-up studies, longitudinal studies) some relevant articles were excluded, and, to ensure maximum sensitivity of the search strategy, this study design MeSH term was not included. The electronic search was supplemented by hand searching reference lists of identified eligible studies and relevant review articles. Furthermore, national focal persons in

the 30 EU/EEA member states were asked to provide recent reports including actual nationwide TOM data or other relevant non-indexed publications regarding TOM. The search strategy was limited to indexed and non-indexed literature published since 2000, being 2 years after publication of the recommendations of the WHO/IUATLD working group for uniform reporting by cohort analysis of treatment outcomes in TB patients [4] and literature published in English, German, Dutch, Swedish, French and Spanish (or translation into one of these languages by the national focal persons)

Inclusion criteria and study selection

Inclusion criteria for systematic review were: 1) retrospective and prospective cohort studies conducted in EU/EEA member states, 2) reporting TB TOM data (expressed as a percentage of the total number of notified cases starting TB treatment) in at least two of the initial six categories (cured; treatment completed; treatment failure; death; treatment interrupted (default) and transferred out) as recommended by WHO/IUATLD [4], 3) at national level and 4) on TB patients meeting either the WHO recommended definitions for 'definite cases' or 'other than definite cases' [4,6] or TB patients meeting the 'possible', 'probable' or 'confirmed' case definition as published by the European Commission in 2008 [7]. Articles categorised as editorials, comments, reviews, case studies and/or drug efficacy tested *in vitro* or through clinical trial were excluded from systematic review. Citations identified by the search strategy were reviewed for possible eligibility by one author (MS) based on title and abstract, according to the inclusion criteria. When identified as such, attempts were made to obtain the full text of the article and subsequently reviewed for eligibility by one of the researchers (MS).

Data extraction

Two researchers (MS and RvH) extracted the data from the included studies and entered them into MS Excel. No attempts were made to obtain missing data from the researchers of eligible

studies. Quality assessment of the included studies was not performed because existing tools were not considered relevant for the articles and reports identified by this systematic review or would result in large variability [8].

The treatment outcome categories were formulated according to international recommendations (cured, treatment completed, treatment failure, death, treatment interrupted (default) and transferred out) [4], with addition of three categories 'still on treatment', 'unknown' and 'successful' [3,7]. The adapted definitions have been used in previous analyses of TB treatment outcomes in the EU and EEA [3,9]. Categories not in these definitions were separately mentioned. For MDR-TB/XDR-TB patients, the outcomes were measured reflecting the definitions proposed by Laserson *et al* [10] and published in WHO guidelines [11], which are similar to the approach in a previous systematic review on treatment outcome of MDR-TB [12]. An overview of all data and outcome categories extracted is available from the authors.

RESULTS

Study selection process

In the systematic literature search, initially 615 potentially relevant indexed citations were retrieved from electronic databases and other sources. After inspection of the titles and abstracts, 530 articles were excluded. Of the 85 articles remaining for full text screening on eligibility criteria, 12 articles could not be retrieved, despite requests to national focal persons. Of the 73 remaining articles, 19 articles were further excluded after more in-depth scrutiny. Of the 54 remaining full text articles, 27 (79 data sets) were national studies and included for further analysis. One article could content more than one data (sub)set, i.e. presenting

treatment outcomes for more types of TB or for more subgroups of the population. The study selection process is shown in detail in Figure 1.

Characteristics of selected studies

An overview of the 27 selected national studies on TOM in EU/EEA countries is presented in Table 1 [3,13-38]. The articles were from 10 EU/EEA countries (United Kingdom (UK) 6 (21%), Latvia 5 (18%), Estonia 4 (14%), the Netherlands 3 (11%), Denmark 2 (7%) and one study each (4%) from the Czech Republic, Finland, Norway, Romania and Sweden). Three studies presented EU/EEA-wide data. One article described data from two EU/EEA countries. The types of TB, publication year and study period, as well as sample size and TOM categories with patients reported varied widely.

Cohort analysis and data sources of selected studies

Retrospective cohort analysis was performed by 25 studies (93%) and 2 articles (7%) described a prospective cohort analysis. Electronic TB databases were used by 21 studies (84%), electronic mycobacterial laboratory databases by 12 studies (44%), hospital records by 7 studies (26%), civil registration sources, such as death registries, by 6 studies (22%), clinicians were contacted in 3 studies (11%), and an AIDS registry and patient interviews were used by one study (4%) respectively. Multiple data sources for the TOM reports were used by 13 studies. Two studies did not report the data sources used. Five described TOM data (partly) ≥10 years old, 17 studies described TOM data (partly) 5-10 years old and 3 studies described data < 5 years old.

TOM definition of selected studies

Three studies (11%) used a WHO or EU TB case definition with reference, 2 studies (7%) used a WHO TB case definition but gave no reference, 4 studies (15%) seemed to use a WHO or EU case-definition with an indirect reference and 18 studies (67%) implicitly used a WHO

or EU TB case definition (but without a reference) because they described culture-positive TB cases.

Completeness of demographic and TOM interval variables and heterogeneity

Fourteen studies (52%) mentioned the proportion of males in the study population and 7 studies (26%) reported the average age of the patient population. Fourteen studies (52%) reported the time interval of TOM reporting after diagnosis or notification. The 79 datasets extracted described very heterogeneous patient populations, subdivided in 41 categories of type of TB (overview of categories available from the authors).

TOM categories in the selected studies

TOM results were reported in 12 categories, of which 9 were in the list of definitions used (Table 1). The number of data sets reporting at least one patient to one of the nine defined categories varied between 15 (unknown) and 69 (died) (Table 2). The range of the minimum and maximum proportion of patients reported in each category varied widely between the various data sets.

TOM among subgroups in the selected studies

TOM results were presented for various subgroups of the population but varied between the selected national studies. Nine studies (33%) presented TOM results by age groups, 8 studies (30%) by gender and 8 studies (30%) by nationality or country of birth. Fifteen studies (56%) presented TOM results for pulmonary TB and 6 studies (22%) for extrapulmonary TB. Fourteen studies (52%) presented TOM results for new TB cases and 8 studies (30%) for retreatment TB cases. Fourteen studies (52%) presented TOM results for MDR-TB cases and 3 studies (11%) for XDR-TB cases.

TOM among vulnerable subgroups in the selected studies

For certain marginalised risk groups TOM results, often a single outcome, i.e. death or default, were presented for HIV seropositive TB cases by 4 studies (15%), for homeless TB

cases by 3 studies (11%), for TB in prisoners by 2 studies (7%) and none of the studies mentioned TOM results for intravenous drug users specifically. Incidentally, TOM results were presented for various other subgroups such as asylum seekers, travellers, alcoholics, illicit drug users or persons using immunosuppressive medication.

TOM for MDR-TB and XDR-TB in the selected studies

MDR-TB data were reported in 14 studies (one study reported for 2 countries) from 6 member states: Estonia (4), Latvia (4), UK (4), and Denmark, the Netherlands and Sweden (1 each). Three of these countries reported 2006 cohort MDR-TB TOM outcomes to TESSy [3]. The number of patients per study could be limited or the data relatively old, e.g. the 4 studies from the UK reported 8 XDR-TB cases, 11 MDR-TB cases, 18 MDR-TB cases and 41 MDR-TB cases respectively, partially overlapping and the studies from the Netherlands and Sweden reported 44 MDR-TB cases (1985-1999) and 3 MDR-TB cases (1995) respectively.

Extracted datasets of selected studies

Of the 79 datasets, 13 were (partly) extracted from the WHO European region, i.e. countries outside the EU/EEA, or EuroTB or ECDC TOM overview articles using TESSy data, i.e. not from individual EU/EEA countries [3,22,38]. Of the remaining 66 datasets 28 (42%) came from 8 studies reporting TOM outcomes for Latvia and Estonia for 1,2 or 3-years periods. The other 38 datasets showed TOM results for various types of TB in 8 member states. A total of 33 of the 79 datasets (42%) reported data on MDR-TB cases. Tables 3 and 4 show that of the 79 datasets extracted relatively few (8 for (new) culture-positive pulmonary TB and 7 for MDR-TB) could potentially be compared to similar TOM outcomes in one of the 3 EuroTB or ECDC overview articles using TESSy data [3,22,38]. Many of the published data are relatively old, especially for MDR-TB. For Estonia the articles on culture-positive and MDR-TB reported considerably higher success rates compared to the latest EU/EEA data from TESSy.

Reports and "grey" literature

A request to 30 national focal persons of the EU/EEA member states to provide one or two most relevant non-indexed reports met 9 reactions. Three national focal persons referred to their web-site for more information. Six articles were received but these referred to local or regional reports, were published after our literature search period, or did not contain TOM data. Three countries reported higher success rates compared to TESSy or earlier reports [3, 38] and 2 countries reported similar results.

DISCUSSION

Main results

TB treatment success in the EU/EEA, measured by a standardised process of TOM is a key programmatic output. Systematic review of published TOM studies from EU/EEA member states reveals that: 1) only 27 eligible publications over a ten year period could be identified from 10 countries, widely varying in publication year, study period and sample size, 2) there is heterogeneity related to TOM methods, processes, policies and practices, e.g. regarding TOM databases, definitions, variables included, patient categories and outcome categories used, as well as population subgroups described, e.g. drug-resistance or vulnerable groups in society, 3) a fragmented presentation exists related to TOM results, with different numbers and types of outcome categories presented for different groups of TB patients, also portraying a heterogeneous picture, prohibiting a useful meta-analysis of the results for the general population and population subgroups, 4) additional TOM information not available in TESSy is available in some member states but only sporadically published in the literature and in a fragmented and heterogeneous way, 5) for the general population EuroTB and ECDC overviews are considerably more complete and 6) TOM data on MDR-TB/XDR-TB are

available for 6 countries but again EuroTB and ECDC overviews are considerably more complete.

Limitations

Apart from the 3 EuroTB and ECDC overviews, only 24 studies from 10 EU/EEA countries were identified, unlikely to be representative for the study area and period. Because of the practices observed in routine TOM data collection and reporting, selection and publication bias cannot be excluded, e.g. because of design, funding and staffing of the studies. Twelve potential eligible studies could not be obtained full text but inspection of the title and abstract revealed that the majority were regional or local studies or comments. Three of the articles were published at least 7 years ago. We consider it unlikely that availability of these articles in full text would have influenced the outcomes of this review substantially. Another limitation is that in some countries, since the publication of older TOM results, over the past decade changes may have occurred in TB epidemiology, diagnosis (e.g. molecular techniques), treatment (e.g. individualised, better second-line drugs), supervision (i.e. admission, incentives) and surveillance, monitoring and reporting (e.g. electronic).

Comparison with previous TOM reviews in the EU/EEA

A previous systematic review in 2005 [39] of TOM in published articles from the WHO European region also showed availability of national estimates for only a limited number of countries, considerable heterogeneity and possible different interpretation given to WHO definitions, especially for unsuccessful outcomes. That review concluded that enhancement of national TB programmes is desirable, treatment characteristics should be more consistently reported and uniform interpretation of definitions should be promoted. According to a recent overview [3], the 30 EU/EEA member states present a highly heterogeneous situation in terms of TB epidemiology and control, distinguishing three broad epidemiological areas [38,40]. Our review also reflects a highly heterogeneous picture of TOM outcomes in the EU.

International systematic reviews into treatment outcomes of MDR-TB showed worse outcomes compared to fully susceptible TB, as expected, with 62% of the pooled patients having a successful outcome. Also high proportions of default and other unsuccessful outcomes were reported. [41,42]. However, the majority of these reports were from middle or high-incidence countries outside the EU.

Treatment outcome criteria

Monitoring the outcome of treatment through a minimum set of outcome parameters is essential in order to evaluate the effectiveness of the intervention, i.e. a short-course anti-tuberculosis chemotherapy and for comparison within and between countries [4]. Since 1998 WHO/IUALTD consensus on standardised TOM categories and definitions for fully susceptible TB in Europe exists [4,5], with updates [43], also in the context of the European framework for tuberculosis control and elimination in countries with a low incidence [44] Although these TOM definitions are widely used in the literature, there are differences in the details that can affect interpretation of the outcomes and international comparability of results is still limited by insufficient standardisation [38,39]. Some countries use treatment outcome categories adapted from but not similar to the WHO and European standards. For example the UK uses a modified set of definitions and does not use the category 'default' but employs the categories 'treatment stopped' (i.e. a patient found to have stopped treatment by himself for a reason not mentioned in other categories) or 'treatment not completed (no reason)' (i.e. a patient was reported not to have completed treatment but the reason was unknown). In the published UK literature the presentation of these outcome categories varies, i.e. they are not shown as a uniform set of outcomes [14,16,21,32]. An adjusted set of criteria, i.e. slightly modifying the WHO and European standards, was proposed from the UK for high income low-incidence countries, especially those with a high mortality among elderly TB patients,

more clinical appropriate for alterations in the management of patients. On these adjusted outcome categories successful outcomes in the UK increased from 77% to 88% [21].

Methods used to analyse the outcome of treatment for MDR-TB were standardised in 2005, enabling international comparisons [10]. Before the introduction of these definitions some countries experienced problems with the inadequate length of follow-up of 12 months for MDR-TB cases [10]. MDR-TB standard definitions were designed for cohort assignment (new MDR-TB, MDR-TB previously treated with only first-line drugs and MDR-TB previously treated with second-line drugs), patient categorisation (smear and culture conversion) and the six previously standardised treatment outcomes [4]. These definitions were used in the majority of the 14 reports from the 6 countries identified. One of the studies discussed the definitions from the perspective of overall programme performance evaluation in countries where MDR-TB treatment is fully integrated into programme practice [33]. In the Baltic states, the relatively high prevalence of primary MDR-TB contributed to low success rates [43], as indicated earlier for the WHO European region [42].

Comparison with central database

For 2008 [45] 24 out of 30 EU/EEA countries reported TOM data for culture-confirmed pulmonary TB to TESSy, compared to 22 for 2007 [3] and 21 for 2006. Five of the 24 reporting countries stated that more than 10% of the cohort starting TB treatment had unknown outcomes. Treatment outcomes for MDR-TB after 24 months were reported by 15 countries for 2007 [3], and by the same 15 countries for 2008 [45]. Out of the 6 non-reporting countries for 2008 two (Liechtenstein and Luxembourg) will represent only a small number of patients. The omission of TOM data from France, Greece, Italy and Spain is of greater concern. In a recent survey Luxemburg and Italy indicated they do not collect data on TOM at the national level while France and Spain reported they collect TOM data at the national level [46]. It is not clear why these data are not reported to TESSy but in the survey both France

and Spain indicated difficulties with the completeness of the data. An interesting observation is that from Italy and Spain, indexed and non-indexed local, regional or sentinel studies on TOM are published, for example from the AIPO-SMIRA or National Tuberculosis Project network in Italy [47-50] or the SEPAR network in Spain [51,52].

Treatment outcome in demographic or clinical subgroups in the population

The published literature gave a fragmented and heterogeneous presentation of TOM data for demographic or clinical subgroups in the EU/EEA. For variables such as age group, pulmonary TB and MDR-TB, TESSy provides much more standardised and complete information and appears superior as a data source to systematic literature review and meta-analysis.

Treatment outcome in vulnerable subgroups in the population

Unsuccessful outcomes have been associated with socially excluded groups, such as some immigrants, asylum seekers, homeless persons, injecting drug users and alcoholics [39], and therefore data on these marginalised subgroups are relevant for TOM analysis.

This systematic review reflects that only few of the included national studies, mostly retrospective, i.e. restricted to specific variables [27], published TOM data on marginalised subgroups in the population, often reporting a single outcome, i.e. death or default [19,26,36]. These limited data are probably incomplete and will not be representative for the EU. A recent survey demonstrates the availability of some variables relevant to TOM analysis of vulnerable subgroups in the EU/EEA in a reasonable number of member states, such as prisoners (17 countries) and asylum-seekers, drug addicts, alcoholics, undocumented persons and immune suppressed patients (10-14 countries) [46].

In the EU/EEA undocumented migrants are a specific vulnerable group, often from high-endemic countries, which, in combination with a history of destitution, can result in high TB

incidence rates. Because of eviction, e.g. a transfer in the context of the Dublin Agreement, they can contribute to a high proportion of unsuccessful outcomes because of unavailable final results [23].

TOM depends on the collaboration of local physicians and they are more likely to cooperate to provide the requested information when it is simple, concise and of immediate obvious general interest [6]. Obtaining complete and uniform information on these risk factors will require a trade-off between expansion of routine surveillance versus limiting the collected data to a minimum, especially in those low-incidence countries where TB services are generally an integrated part of the overall health care system, rather than a distinct specialised programme or service [16,21,53]. To answer more complex questions on vulnerable subpopulations it was advised previously to use specifically designed surveys [6].

Further consideration should be given to TOM data collection on socially marginalised groups in the EU/EEA countries allowing more standardised and complete analysis of treatment outcomes, preferably including reporting of TOM in vulnerable population groups in national reports and to TESSy.

TOM critical issues

This literature review did not provide extensive information on critical TOM issues, gaps and challenges. A limited number of publications gave some suggestions for improvements. Main critical issues identified related to the TOM system were registration of mortality in the elderly and registration of failure. Critical issues have been addressed in detail in a separate report presented to ECDC [46].

Conclusion

Surveillance is an integral part of TB control, its contribution essential to inform the programme on what is going on and what public health response is urgently needed but is still suboptimal in Europe [54,55]. Standardised routine reporting under harmonised definitions and outcome categories to a centralised database is key for an EU-wide surveillance system, including TOM, as well as challenges to improve completeness, timeliness, comparability and trend analysis.

Our systematic review indicates that PubMed/MEDLINE and EMBASE indexed studies are not a suitable instrument to describe TOM processes, methods, policies and practices. They do not produce TOM results representative for the general population or for demographic, clinical and social subgroups in the 30 EU/EEA countries. They provide little information on useful TOM variables not available in TESSy. TESSy should portray the most representative picture of TB treatment outcomes in the EU/EEA, providing all countries report TOM data annually, guided by ECDC and national focal institutes, and based on standardised and complete local data collection. While TESSy focuses on routine TOM in the general population, the treatment outcome of cases among specific marginalised and vulnerable subgroups, some available in EU/EEA countries' TB registers, are of specific public health importance and general public health interest and thus, relevant for publication in peer reviewed journals.

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Figure 1: Flow diagram of selection process of articles included in the systematic review
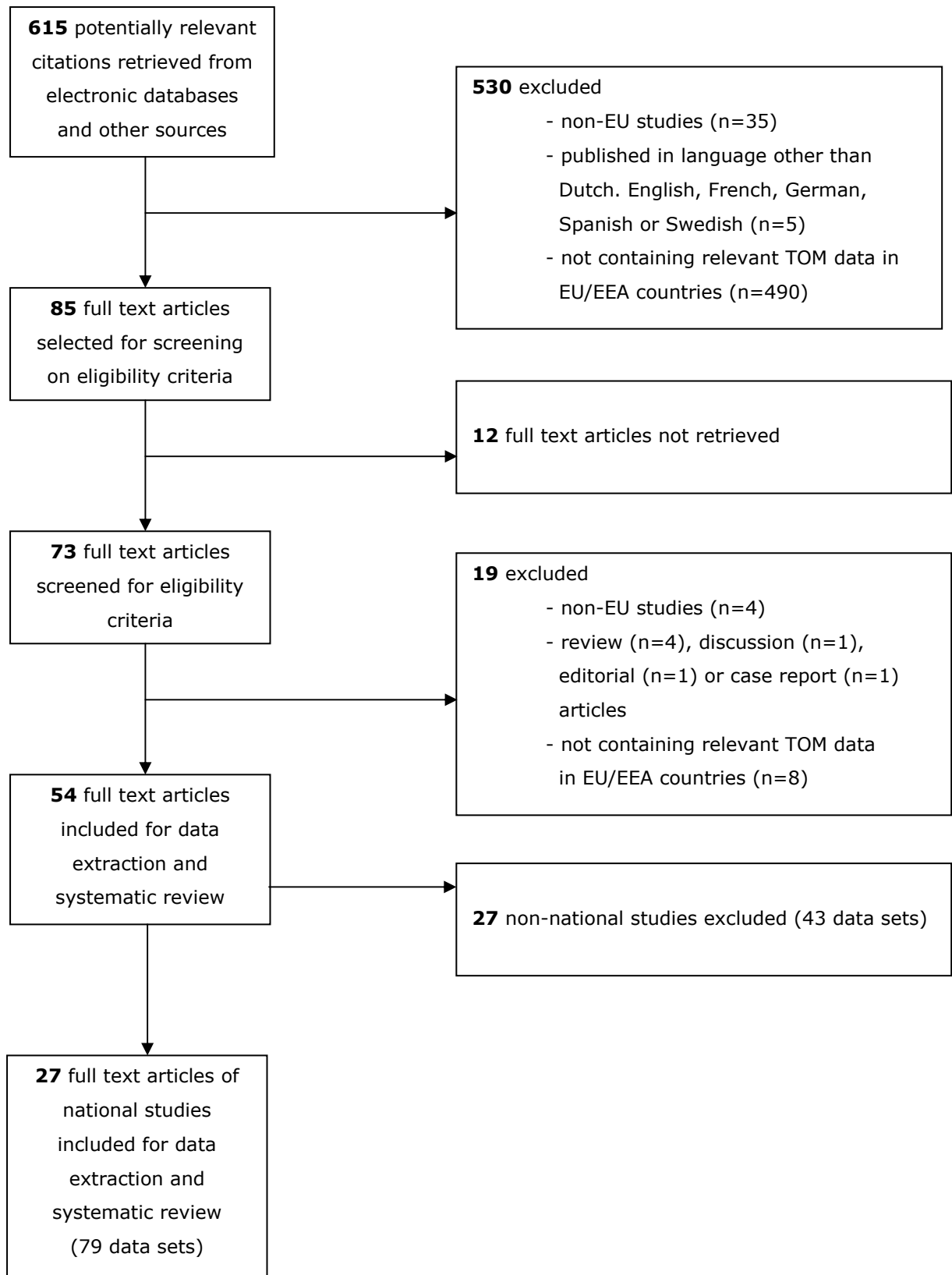
Table 1 Selected national studies on Treatment Outcome Monitoring (TOM) in the EU/EEA countries, with first author, country, type of TB described, publication year, study period, sample size and TOM categories with patients reported

Number in References	First Author	Country	Type of TB	Year of publication	Study years	Sample size	TOM categories with patients reported
13	Abubakar	United Kingdom	XDR TB	2009	1995-2008	8	Death, Ongoing*
14	Abubakar	England and Wales	Paediatric TB	2008	2001-2005	1941	Completed, Died, Transferred out, Ongoing, Lost-to-follow-up, Unknown, Stopped
15	Anderson	Scotland	MDR TB	2009	2000-2007	11	Completed, Ongoing, Lost-to-follow-up, Unknown
16	Antoine	England, Wales and Northern Ireland	All TB	2007	2001	5139	Completed, Died, Transferred out, Ongoing, Lost-to-follow-up, Unknown, Treatment stopped, Treatment incomplete
17	Bang	Denmark	Culture-confirmed relapse TB,	2010	1992-2005	54	Success (= cured + completed), Failed, Died, Default
18	Bang	Denmark	MDR TB	2010	1992-2007	29	Cured, Completed, Default, Transferred out, Unknown, Success (after initial defaulting)
19	Borgdorff	the Netherlands	All TB with treatment < 1 year	2000	1993-1997	6690	Completed, Died, Default, Transferred out
20	Bwire	the Netherlands	All bacteriologically confirmed TB	2000	1993-1996	3217	Success (= cured + completed), Died, Default, Transferred out
21	Ditah	England, Wales & Northern Ireland	All TB	2008	2001-2002	10684	Cured, Completed, Died, Transferred out, Ongoing, Lost-to-follow-up, Unknown
22	Falzon	19 (2000) / 20 (2001) EU/EEA countries	New pulmonary culture-confirmed TB	2006	2000-2001	23909	Success (= cured + completed), Died, Default, Transferred out
23	Guled Farah	Norway	New pulmonary culture-confirmed TB	2005	1996-2002	655	Cured, Completed, Failure, Died, Default, Transferred out

24	Geerligs	the Netherlands	MDR TB	2000	1985-1998	44	Cured, Died, Ongoing
25	Holtz	Latvia	Pulmonary MDR TB	2006	2000	167	Cured, Completed, Failure, Died, Default
26	Kliiman	Estonia	All pulmonary culture-confirmed TB	2010	2003-2005	1107	Cured, Completed, Failure, Died, Default
27	Kliiman	Estonia	All pulmonary XDR TB	2009	2003-2006	54	Cured, Completed, Failure, Died, Default
28	Leimane	Latvia	All pulmonary MDR TB	2005	2000	204	Cured, Completed, Failure, Died, Default
29	Lockman	Estonia	New pulmonary pan-susceptible and MDR TB	2001	1994-1996	92	Cured, Failure, Died, Stopped
30	Marica	Romania	New culture-confirmed TB and new sputum-smear positive TB	2009	2006	Not reported	Cured (proportion), Completed (proportion)
31	Nathanson	Estonia and Latvia	MDR-TB	2006	2000-2001 (Latvia); 2001 (Estonia)	291	Cured, Completed, Failure, Died, Default
32	Ormerod	England and Wales	Pulmonary and lymph node TB (including deaths)	2003	1998 (first 6 months)	1337	Cured, Completed, Failure, Died, Default, Transferred out, Lost-to-follow-up
33	Riekstina	Latvia	New bacteriologically confirmed pulmonary TB	2007	2002	934	Cured, Completed, Failure, Died, Default, Transferred out, Ongoing
34	Romanus	Sweden	All TB	2000	1994-1995	676	Cured, Died, Default, Transferred out, Ongoing, Unknown, Initial defaulting, Stopped

35	Trnka	Czech Republic	New bacteriologically confirmed pulmonary TB	2001	1998	731	Cured, Completed, Failure, Died, Default, Transferred out, Unknown
36	Vasankari	Finland	Treated culture-confirmed pulmonary TB	2007	1995-1996	629	Cured, Completed, Died, Transferred out, Stopped
37	Leimane	Latvia	MDR TB	2007	2000-2003	820	Cured (proportion), Failure (proportion), Died (proportion), Default (proportion)
38	Falzon	19 EU countries	New pulmonary culture-confirmed TB	2007	1999-2003	17253	Success (proportion), Died (proportion)
3	Manissero	22 EU/EEA countries	All pulmonary culture-confirmed TB	2010	2007	36377	Success (= cured + completed), Failure, Died, Default, Transferred out (including Unknown), Ongoing

* Ongoing = Still on Treatment

Table 2 Number of data sets (n=79=100%) with Treatment Outcome categories reporting ≥ 1 patient and the proportion of the total number of data sets, with minimum and maximum proportion

Treatment outcome category	Number of data sets with ≥ 1 patient reported (%)	Minimum - maximum proportion of patients reported (%)
Cured	53 (67.1)	(10.0 - 89.0)
Completed	43 (54.4)	(1.1 - 88.4)
Failed	49 (62.0)	(0.2 - 68.0)
Died	69 (87.3)	(0.7 - 28.3)
Defaulted	56 (70.9)	(0.8 - 29.0)
Transferred out	31 (39.2)	(0.3 - 11.7)
Ongoing*	25 (31.6)	(0.3 - 66.7)
Unknown	15 (19.0)	(1.6 - 27.3)
Success[¶]	20 (25.3)	(6.9 - 88.6)
Lost to follow-up	10 (12.7)	(3.1 - 9.1)
Stopped	8 (10.1)	(0.8 - 7.6)
Treatment incomplete	4 (5.1)	(0.2 - 0.3)

*: Ongoing = still on treatment; [¶]: Success = cured + completed

Table 3 Published treatment outcome monitoring (TOM) reports on culture-positive pulmonary TB in EU/EEA countries, potentially comparable with previously reported WHO EU and EU TOM success rates

Author	Country	Type of TB	Year(s)	Success (%)	WHO EU 2000/2001 (%) [22]	EU 1999/2003 (%) [38]	EU 2007 [3]
Antoine	UK	Culture positive pulmonary TB	2001	77	N.R.	65	77
Guled Farah	Norway	New culture positive pulmonary TB	1996-2002	83	78/86	NR	78
Kliiman	Estonia	New culture positive pulmonary TB	2000-2005	87	73/68	70	61
Kliiman	Estonia	Retreatment culture positive pulmonary TB	2000-2005	60	NR	NR	47
Marica	Romania	New culture positive pulmonary TB	2006	86	NR	NR	85
Riekstina	Latvia	New culture positive pulmonary TB	2002	84	76/77	78	82
Trnka	Czech Republic	New culture positive pulmonary TB	1998	71	69/69	75	72
Romanus	Sweden	Smear-positive pulmonary TB	1994/1995	69	79/62	84	66

NR: not reported

Table 4 Published treatment outcome (TOM) monitoring reports of MDR TB in EU/EEA countries, potentially comparable with previously reported WHO EU and EU TOM success rates

Author	Country	Type of TB	Year(s)	Success (%)	EU 2007 [3]
Anderson	UK	MDR	2000-2007	18.2	NR
Geerligs	Netherlands	MDR	1985-1998	75	NR
Holtz	Latvia	MDR	2000	64.7	61.3
Nathanson	Latvia	MDR	2000/2001	68.5	61.3
Leimane	Latvia	MDR	2000-2003	67	61.3
Nathanson	Estonia	MDR	2001	65.2	45.3
Romanus	Sweden	MDR	1994/1995	33	NR

NR: not reported