

Costs of tuberculosis disease in the EU – a systematic analysis and cost calculation

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Summary (200 words)

Without better vaccines it is unlikely that tuberculosis (TB) will ever be eliminated. An investment of about €560 million is considered necessary to develop a new, effective vaccine in the European Union (EU). Less is known, however, about the costs of TB disease in the EU. We performed a systematic review of literature and institutional websites addressing the 27 EU members to summarize cost data. We searched Medline, EMBASE and Cochrane bibliographies of relevant articles.

Combining direct and indirect costs, we arrived at average per-case TB costs in the old EU-15 states plus Cyprus, Malta and Slovenia of €10,282 for drug-susceptible TB, €57,213 for multidrug resistant (MDR)-TB and €170,744 for extensively drug resistant (XDR)-TB. In the remaining new EU states costs amounted to €3,427 for susceptible TB and €24,166 for MDR-TB/XDR-TB. For the 70,340 susceptible TB cases, 1,488 MDR-TB and 136 XDR-TB cases notified in 2011 total costs of €536,890,315 accumulated in 2012. For the same year, the 103,104 disability-adjusted life years (DALYs) caused by these cases, when stated in monetary terms, amounted to a total of €5,361,408,000.

Thus, the resulting economic burden of TB in the EU clearly outweighs the cost of investing in more efficient vaccines against TB.

1. Introduction

Although vaccination with Bacille Calmette-Guérin (BCG), the only available vaccine, has been shown to decrease the risk of severe forms of TB in young children (disseminated TB and TB meningitis) [1], it is ineffective in preventing the infectious pulmonary TB that occurs mainly in adults and remains the primary source of TB transmission. Currently, 12 vaccines have already been taken into phase I or II clinical trials, with the aim of replacing the present BCG vaccine or at enhancing immunity induced by BCG [2,3], and with the hope of licensing at least one new vaccine by 2018 [4].

An investment of about €560 million is considered necessary to achieve this result in the EU [5]. In its effort for funding, the Tuberculosis Vaccine Initiative (TBVI) has proposed an investment model [6] to close the financial gap and speed up the development of those new TB vaccines. The economic calculation that follows shows that the annual cost of TB in the EU clearly outweighs the total cost of developing new vaccines.

Looking at the cost of TB in Europe, confusion may arise as to the definition of the region. A much-used estimation of the TB-related costs in Europe in the EASAC study [7] comes from the European Lung White Book, which placed these in 2003 at €2.1 billion in the European Region as defined by the World Health Organization (WHO), i.e. comprising 53 member states including the EU, EU-associated and Former Soviet Union (FSU) countries [8]. However, some details of that cost calculation have not been provided and thus it is challenging to provide a more explicit, reasonable cost calculation of TB disease focussing on the current 27 member states of the EU.

Numerous publications [e.g. 9, 10] stress the dramatic increase of MDR-TB and XDR-TB in the world. According to estimates of the WHO of the total of 8.7 million new cases in 2011 an estimated 3.7% had MDR [11], defined as resistance to at least the two most powerful first-line anti-TB drugs isoniazid and rifampicin, and about 58,000 cases involved XDR, adding resistance to any fluoroquinolone and at least one of the three injectable anti-TB drugs (amikacin, capreomycin or kanamycin) to MDR.

Fifteen of the 22 countries considered “MDR-TB high burden” belong to the WHO Europe Region [12]. In 2011 the number of cases tested for MDR-TB in Europe was 84,140, of which 68% delivered a positive bacteriological result [13].

The highest rates of MDR-TB, up to 26% among new cases and up to 65% among previously treated cases, are seen in the countries of the FSU [14, 15], which together had an estimated 66,000 reported cases in total in 2010 [16].

According to a recent document of the WHO Regional Office for Europe [17] the total number of notified XDR-TB patients in the WHO European Region have almost tripled, from 132 in 2008 to 344 in 2009.

For 2011, the European Centre for Disease Prevention and Control (ECDC) and WHO Regional Office for Europe Surveillance report [18] mentions 1,518 MDR-TB cases and 136 XDR-TB cases. This confirms that drug-resistant TB is an important problem, especially because it is well known to be associated with a relatively low treatment success rate [19, 20] and, as shown in our calculations below, a significant increase in treatment cost. Accordingly, in every economic analysis the increasing cost of MDR-TB has to be included according to its respective proportion among all TB cases arising in the EU.

The historical summary of the Wolfheze workshops and their consensus documents with recommendations on TB control activities in the EU [21] highlights the ultimate target of TB elimination, defined as a TB incidence of less than one case per million population [22]. As it must be recognised that, following current trends, Europe is unlikely to achieve elimination of the disease by the target date of 2050 [23, 24], we urgently need new vaccines, on top of better diagnostics [25, 26] and new drugs [27, 28, 29]. With respect to economic considerations, the aim of the present study was to evaluate the costs associated with TB disease in order to determine whether they outweigh the investment needed to generate a new vaccine.

2. Working methods

2.1 Calculating direct and indirect costs

Firstly, we performed a systematic literature review, followed by the extraction of direct as well as indirect costs of TB. Direct costs include costs for the medical treatment of TB (medication, laboratory, hospitalization and outpatient visits) and indirect costs represent productivity loss because of TB-induced sick days off-work.

From this we gathered information on the following cost components for drug-susceptible TB, MDR-TB and XDR-TB

- 1.) Duration of hospitalization and inpatient cost per day
- 2.) Outpatient cost
- 3.) Cost of medication
- 4.) Cost due to loss of productivity
- 5.) Year in which the costs were assessed or collected

If there was more than one cost calculation for a country the most current version was chosen in the review. It was the aim of our study to show current TB costs, so the price year of this study was 2012. Consequently, all costs arisen in different EU-countries and years were adjusted to 2012 values using the Harmonised Index of Consumer Prices (HICP) for the euro area countries [30] and the results were summarized.

Cost of public health surveillance, especially costs of contact tracing, screening risk groups, preventive treatment of persons latently infected by *Mycobacterium tuberculosis* and activities of national reference laboratories and institutes were out of the scope of this analysis.

We searched Medline, Embase, Health Economic Evaluations Database, Centre for Review and Dissemination (CRD)/National Health Service Economic Evaluation Database (NHSEED), the Cost-Effectiveness Analysis Registry, the European Network of Health Economic Evaluation Databases and the Cochrane Central Register of Controlled Trials (CENTRAL; Cochrane Library 2013, issue 3, through March 15, 2013) for studies published using the following search terms in different combinations:

“Tuberculosis” OR “TB disease” OR “MDR-TB” OR “drug resistant TB” OR “drug resistant tuberculosis” OR “multidrug resistant TB” OR “multidrug resistant tuberculosis” AND “cost” OR “cost-effectiveness” OR “economic” OR “burden”.

No restrictions were made with respect to language, study design, or data collection (prospective or retrospective). Secondary references cited by the studies and review articles retrieved from the databases were reviewed. In addition these terms were translated in the respective languages of all 27 EU member states for web research using internet search services provided by “Google” and “Yahoo” in order to receive results from country-specific governmental or regional papers from the respective national statistical offices and authorities.

2.2 Calculating of DALYs and conversion to monetary terms.

DALYs represent the loss of the equivalent of one year of full health due to a specific disease, in this case due to TB. Briefly, they are the sum of life years lost (YLL) due to premature mortality, i.e. the number of deaths due to TB multiplied by the standard life expectancy at the age at which death occur, and of the years lived with the disability (YLD), the latter gained by multiplying incident TB cases by treatment duration and disability weight for the condition: $DALY = YLL + YLD$.

The basic formula for calculation of YLL and YLD on a population basis are as follows: $YLL = [n/r] (1 - 1-e^{-rL})$, where n = number of deaths, L = life expectancy at age of death (years) and r = discount rate; $YLD = [I \times DW \times L (1-e^{-rL})]/r$, where I = number of incident cases, DW = disability weight and L = duration of disability (years).

For practical purposes we calculated the difference between life expectancy and average age at death from TB, summed across the EU-27 population and incorporated a 3% discount rate as well as a non-uniform age weighting (see full equations in the Supplement [31]). In line with the Global Burden of Disease (GDB) study [32] we used an average disability weight for TB disease of 0.271. YLD were calculated separately for susceptible TB ($L=0.5$ years) and MDR-TB ($L=2$ years).

Finally, the resulting DALYs were multiplied by the long-established estimate of the European Commission of €52,000 as value of one life-year lost (VOLY) [33], derived from citizens' responses to willingness-to-pay questionnaires on the topic of air pollution mortality, which remains unadjusted in consideration of the fact that the TB burden weighs more heavily on the poorer EU member states than it does on the former EU core members [34].

Results

3.1 Direct costs

In the selection process 4,278 citations and 247 websites were identified, of which only 12 scientific articles [36-38, 41-47, 49, 50] and 2 websites [35, 48] were eligible for final inclusion, as they contained specific information on at least one of the cost components as listed above. To take into consideration the gaps in Gross Domestic Product (GDP) per capita between the 27 present EU member countries, we presented separately the results for the EU-15 states (member countries of the EU prior to the accession of twelve candidate countries on 1 May 2004 comprising the following 15 countries: Austria,

Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, United Kingdom) and the other 12 countries which have since joined (see table 1 for figures of total treatment costs and table 2 for the key features of all 12 studies included in our review):

a) EU-15 member states:

Total costs of TB treatment for drug-susceptible and/or MDR-TB/XDR-TB could be obtained from the following countries:

3.1.1 United Kingdom (UK)

Aggregated governmental NHS data were available for the UK in which neither a partitioning between hospital inpatients and outpatient visits was provided nor cost of medication was separately documented [35]. The total direct cost of treatment of a 'normal' case of TB has been calculated to be around GBP5,000 in 2009 (equivalent to €5,864) and cost of treatment of a drug-resistant case between GBP50,000 and GBP70,000 or more per patient (equivalent to €58,624 and €82,096, respectively). This estimate is less than assessed in previous calculations from White et al. [36] presenting costs of GBP6,040 for a susceptible TB case and GBP60,000 for a MDR-TB patient 9 years earlier.

3.1.2 France

In France the direct cost for a susceptible TB case have been calculated at €5,231.81 for the year 2007 [37] including medication costs of €268.20.

The cost figure for medication only is in line with the governmental estimation of medication costs [38] between €250 and €450 for the treatment of 6 months short course therapy. In addition, for the year 2009 a cost range between €27,330 and €44,235 is shown for treatment of MDR-TB and €46,614 of XDR-TB. However these figures only refer to therapy duration of 12 months and therefore drastically underestimate the costs adding up during the therapy course as required by the previous [39] and current WHO guidelines [40]. These propose a treatment duration for MDR-TB patients of a minimum length of 18 and 20 months after culture conversion, respectively, i.e., usually a total of 24 months.

3.1.3 Italy

Bocchino et al. [41] investigated the treatment costs of TB taking into account all 'fixed' expenses (€200.45 per day for hospitalization and €50.12 per day for any outpatient visit) and by adding the cost of drugs, tests and procedures for each case. The resulting annual costs arising in 2002 varied between €7,364 for the first quartile of the IQR (interquartile range) interval (IQR 25) and €20,194 for IQR 75 with median costs of €13,413, but these costs also included 19% MDR-TB cases. Thus, the amount of the lowest quartile IQR 25, representing only a quarter of the way through the list of all the cost data, i.e. €7,364, was chosen as cost for treating susceptible TB.

3.1.4 Spain

For Spain the cost of hospitalization and the total TB cost can be extrapolated from the study of Montes-Santiago et al. [42] calculating an amount of €8,175.33 with 70% (€6,279.31) for hospitalization costs in the year 2006.

3.1.5 Finland

Recalculated from the detailed unit costs given for the year 2000 the mean costs for a six-month treatment comprising inpatient stay of only 14 days the costs per susceptible TB case amount to €6,673.10 [43].

3.1.6 Germany

The newest data for direct costs for Germany by Diel et al. [44] presented combined weighted inpatient/outpatient costs of €7,363.99 for susceptible TB and €52,259 for MDR-TB per patient with an average duration of hospitalization of 30 days for susceptible cases and 86 days for MDR-TB cases. The costs for XDR-TB patients were not included in this cost analysis, but according to Blaas et al. [45] in 2004-2006 the costs of treating XDR-TB patients in Germany amounted to more than €170,000 per patient. As assessed in another German survey, the mean treatment duration of XDR-TB cases as inpatients was 202 ± 130 days [46].

3.1.7 The Netherlands

In a most recent, retrospective analysis based on 1,138 patients with Non-MDR-TB and 20 with MDR, de Vries et al. calculated the total cost per patient. Costs due to susceptible TB amounted to €7,854, of MDR-TB to €44,250 and of XDR-TB to €139,500 [47].

Cost data for TB medication, but no figures for additional inpatient or outpatient costs, were available for the following two countries:

3.1.8 Belgium

According to the Belgian Lung and Tuberculosis Association (BELTA), the cost of medication per TB case for 2012 ranges from €368 for a susceptible TB case (six months), €14,307 to €41,229 for a MDR-TB case (18 or 24 months) and €67,067 for an XDR-TB case (24 months) [48].

3.1.9 Austria

For 2008 there is an estimate of medication costs which amounts to €277.50 for susceptible TB and €22,291 for MDR-TB in 2008 [49].

To estimate the TB patient costs of countries for which total cost data are not available we used for a susceptible TB the average of the aforementioned costs for susceptible TB. Thus, the assumed average direct costs (after adjusting for the year 2012) are €7,848 for Austria, Belgium, Denmark, Ireland, Greece, Luxemburg, Portugal and Sweden (see Table 1). An identical approach with respect to MDR-TB/XDR-TB results in average costs of €54,779 and €168,310, respectively.

b) New EU member states:

3.1.10 Estonia

In a recent publication by Floyd et al. [50] in Estonia, one of the smallest of the FSU countries with a population of 1.3 million in 2010, the average costs per patient treated for MDR-TB including XDR-TB were assessed to be US\$8,974 or €8,530 (US\$1=14.7 Kr; €1=15.65 Kr) in Estonia from a health system perspective in 2003. Of note, second-line anti-TB drugs are purchased at favorable conditions for Estonia by the Global Drug Facility (GDF) established by WHO to help low- and middle-income countries access first- and second-line drugs at the lowest-possible price, thus the medication costs per

MDR-TB patient are only US\$2,219 in 2003 (€2,084, adjusted to 2012: €3,082). Most EU countries are not eligible for these prices, but new member such as Estonia, Romania and Bulgaria are. No figures are provided for susceptible TB and XDR-TB. In Floyd's analysis, 192 hospital days for MDR-TB patients were included at US\$30.50 (€28.65) for the first 60 days.

However, inpatient cost per day as low as €28.65 is very unlikely to cover the up-to-date cost in 2012. Already for 2005, the WHO figures [51] show inpatient bed costs per day (representing the "hotel" component of hospital cost only, i.e., excluding drugs and diagnostics) for Estonia of US\$95.24, US\$124.25 and US\$169.71 for primary, secondary and tertiary level respectively, corresponding with €76.57, €99.90 and €136.45 respectively (according to an average exchange rate of 1US\$=€0.804 in 2005). Adjusted to 2012 the hospitalization costs in Estonia are €105.59 per day at a primary level. Therefore, we use the Estonia figure of €105.59 per hospital day at a lowest (primary) level as an average cost estimate; direct cost of treating a MDR-TB or XDR-TB patient in Estonia consequently adds up to 192 days times 105.59 (€20,273) plus medication cost of €3,082, i.e., a total of €23,355.

Cost estimates for susceptible TB patients are completely lacking in the new EU states. According to the European Hospital morbidity database [52] the average length of hospital stay due to TB varies between 28 days (Slovakia) and 91 days (Lithuania) but there is no information which proportion of TB patients will in fact be hospitalised and data for Estonia, Romania and Bulgaria are not assessed at all; in addition medication costs are mentioned nowhere in the literature.

A reasonable approach of cost estimation would be comparing the Gross Domestic Products (GDP) between EU countries: The 15 "old" member states that were part of the EU before 2004 plus Cyprus, Malta and Slovenia have a comparable GDP. The average GDP per capita [53] in 2011 for these countries was €28,979 varying between €16,100 for Portugal to €82,000 for Luxemburg. In the 9 remaining countries, on average, the GDP per capita is about one third of that GDP amounting to €9,358 [54].

Accordingly, we estimate the total costs of treating a susceptible TB case in the new EU member states to be one third of the mean in the old EU member states (€7,848), i.e. € 2,616.

3.2 Charging for indirect costs

To these figures for direct treatment costs, a sum for the loss of productivity that TB causes, must be added to arrive at total cost. The only precise calculation for loss of productivity due to TB in Europe was found in a study of the cost of TB in Germany by Diel et al. [44]. In this study, loss of productivity is calculated at €2,313 per case (adjusted to 2012: €2,434) regardless of drug susceptibility, since drug-resistant cases only represent 2.1 % of the total number of cases and some MDR-TB patients might go to work even when still under treatment. As different figures are not provided in any other study, it seems reasonable to use this amount as average for all cases in countries that were part of the EU before 2004 and Cyprus, Malta and Slovenia; the latter three have GDP closer to EU-15 than the other new members and are usually seen as belonging to the “high income” European countries [53].

To calculate cost of productivity loss for the 9 remaining countries we considered a third of the amount we used for the 18 other EU members as shown above for direct cost, i.e. €811 that have to be added for each patient to the respective direct cost.

3.3 Combining direct and indirect TB cost

For the EU-18 (EU-15 plus Cyprus, Malta and Slovenia) the calculations above would result in the following total average cost of TB per case, including cost of treatment and loss of productivity:

- Susceptible cases: €10,282
- MDR-TB: €57,213
- XDR-TB: €170,744

The total average cost of TB in the 9 remaining “new” countries then becomes:

- Susceptible cases: €3,427
- MDR-TB: €24,166
- XDR-TB: €24,166

Original cost data as presented in the respective publications and the averages mentioned in the calculations above were used to calculate the total cost of TB in the EU

as shown in table 2. According to these calculations, the cost of TB in the EU adds up to over €537 million per year. It is conspicuous that in the “new” EU member states (as far as any assessment is possible at all) the cost of treating an XDR-TB case is only about one-seventh of that in the other EU states. This is largely due to the fact that more expensive medications such as linezolid, used to treat XDR-TB in wealthier countries, are not available at discounts and therefore not affordable to the newer EU members. However, this does not have much influence on the total costs because of the low number of 136 XDR-TB cases notified in the whole EU. Beside the lower medication cost, the main reason of the difference is the much lower inpatient costs in those countries: Whereas the number of inpatient treatment days is comparable, e.g. in Germany with 202 hospital days for XDR-TB patients and 192 days in Estonia, the inpatient cost of €296.31 per day in Germany differ substantially with the €105.59 per day in Estonia. It can be expected that in the future inpatient per day costs and consequently the cost of treating XDR-TB in the EU will increase, considering the current gap between inpatient costs for TB patients and those assigned to other diseases: According to an analysis of Organisation for Economic Co-operation and Development (OECD) data by McKinsey [54] the average inpatient costs per day in the EU-15 states, irrespective of the type of disease, are in general much higher, varying between €533 (Germany) and €1,639 (Denmark).

3.4 Monetary value of DALYs

In 2010, the most recent year for which data is available, the mean age of TB patients (notified cases) was 45.1 years, unchanged since 2001 [12]. Life expectancy in the EU-27 states, combined for both sexes, was 79.7 [55]. Mortality in new, laboratory-confirmed pulmonary TB cases has been reported in the European Centre for Disease Prevention and Control (ECDC)/WHO report [12] to be 6.6% as treatment outcome and 13% for culture confirmed new MDR-TB after treatment duration of 24 months. Thus, the number of deaths due to susceptible TB and MDR-TB/XDR-TB were 4,642 ($70,340 \times 0.066$) and 211 ($1,624 \times 0.13$), respectively, summing up to a total of 4,854 deaths (rounded) in 2012.

The calculated YLL (detailed formula in Excel provided as Supplement) were 90,478.56 and the calculated total of YLD were 11,592.032 (susceptible TB) plus 1,033.026 (MDR-

TB/XDR-TB). Multiplication of the aggregated 103,104 DALYs (rounded) by €52,000 per VOLY resulted in a total of €5,361,408,000.

1. Discussion

Our objective was to review and summarize the available evidence on cost and the cost components of TB and MDR-TB/XDR-TB in the European Union. However, despite of a growing flood of epidemiological publications on TB and MDR-TB, aggregated TB costs in the individual EU member countries are sparse and information on the attributable cost components that may act as cost drivers is often incomplete.

Due to different health systems in the EU, there are considerable differences in refunding expenditures of diagnostics and treatment, and what makes the assessment of TB costs methodologically even more complicated is the fact that every country has its own way of monitoring and registering costs. Furthermore, they clearly depend on the generally differing pricing of pharmaceutical companies for identical drugs in the respective countries and the degree of eventual sponsoring by non-profit organizations such as the GDF. Thus, with respect to the target cost components listed above, the data provided are quite heterogeneous. Indeed, there are only two studies providing weighted cost data for both, susceptible TB and MDR/XDR-TB [44, 47] in which the cost components had been comprehensively deduced from all the country-specific economic sources. For the majority of countries there were no data available at all making an extrapolation necessary.

Nevertheless, despite the limitations of our review, the best available cost data are part of the evidence needed for budgeting and financing the expansion of TB services, especially with respect to scaling-up MDR-TB treatment. The increase of the number of cases of MDR- and XDR-TB is a real health threat but also causes an important concern about the rise of the cost of TB, globally as well as in the EU. TB represents a high cost for the EU; summing up to nearly €537 million each year according to our conservative cost calculations and based on the ECDC/WHO Regional Office for Europe number of cases in the year 2011. Although TB rates are decreasing slightly, drug-resistant strains are on the rise, bringing an increase in cost of treatment. No mention is made of MDR-TB and XDR-TB for 2011 in either Malta and Slovenia, and only in 12 out of the 27 EU-

countries are XDR-TB cases reported, although we can assume that such cost-driving cases were present in at least some of those countries.

We are aware that our calculations underestimate the real overall cost of TB in the EU. The study of de Vries et al. [47], the only one fully assessing costs due to TB cases as well as general costs, demonstrates that the costs due to TB of €29.49 million in 2009 in the Netherlands are mainly, by 61%, due to surrounding costs such as surveillance, screening of high risk-groups, follow-up and treating of contacts and BCG vaccination. The “net”-costs in UK only for detecting and treating LTBI and BCG vaccination in 2006 were estimated to be GBP10.405 million (€15.264 million adjusted to 2012) by calculations of the National Institute for Health and Clinical Excellence [56] indicating that costs directly linked to TB disease are meaningful but only a fraction of its whole financial impact.

Without new tools to control the disease, it is unlikely the cost of TB will go down. With respect to the development of new vaccines, for example, TBVI’s funding model proposes an investment of €560 million spread over 10 years. This cost is only slightly higher than the current cost of TB disease in the EU for only one year based on 2011 cases, but, using a minimal discount rate of 3%, the net-present value of an investment of €537 million at the end of 10 years would be about €722 million.

Furthermore, taking into account the monetary equivalent of more than €5,3 billion for the 103,104 DALYs caused by the TB cases notified in 2011, there is no doubt that the economic burden of TB provides good rationale for investing in the development of new, safe and efficacious vaccines. In line with the new EU standards for TB care [57] such an investment could clearly contribute to fulfil the goal of eliminating TB in the future.

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Figure 1: Flow of study selection

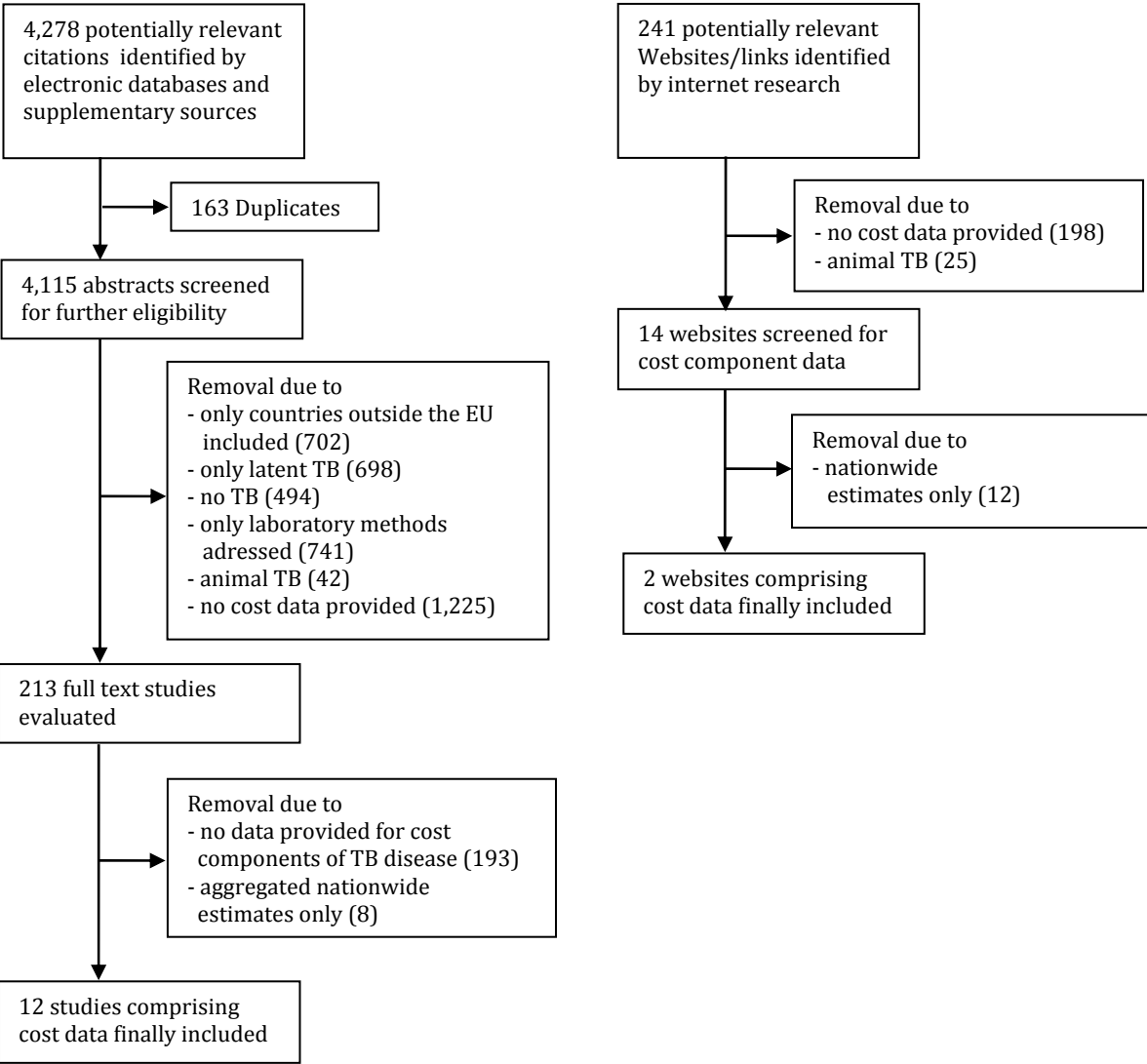


Table 1: Countries for which total direct (treatment) TB costs are available (costs in € adjusted to 2012)

Costs per case	Susceptible TB	MDR-TB	XDR-TB
EU-15 member states			
France	5,691	NA	NA
Germany	7,751	55,003	188,466
UK	6,234	62,343	NA
Netherlands	8,340	46,990	148,136
Italy	9,294	NA	NA
Finland	8,242	NA	NA
Spain	9,384	NA	NA
Mean value	7,848	54,779	168,310
New EU members			
Estonia	2,616	15,344	15,344

NA: not available

Table 2: Characteristics of EU studies included in the systematic review

Study (first author, year, country)	Method used	Setting	Data available	Reference year for costs	Type of TB assessed	Sampling	Comments
NHS, 2009†, UK [22]	Pooled routine data	Governmental assessment	Total treatment costs	2009	“normal” and drug-resistance TB	NA	No distinction between in- and outpatients
White, 2000, UK [23]	Retrospective analysis	Hospital data: St Bartholomew’s, London	Total treatment costs of adult HIV-negative patients	2000	Susceptible and MDR-TB	9 MDR-TB and 18 susceptible TB patients matched by age group and ethnicity 1996-1999	Local data, not representative of UK
Deuffic-Burban, 2010, France [24]	Modelling per patient	Unit costs obtained from French registers, drug costs from the pharmacy records of Tourcoing Hospital	Total treatment costs	2007	Susceptible TB only	NA	Figures embedded in cost-effectiveness analysis of LTBI diagnostics
French National Assembly, 2011‡, France [25]	Pooled routine data	Governmental assessment	Medication costs only	2009	Susceptible TB, MDR-TB and XDR-TB	NA	–
Bocchino, 2006, Italy [28]	Retrospective analysis	Division of Respiratory Medicine of the University of Tor Vergata, ‘L Spallanzani’, Rome	Total treatment costs of adult HIV-negative patients	2002	Susceptible TB and MDR-TB	Review of the medical records of 92 TB cases 2000-2003	Local data, not representative of Italy
Montes-Santiago, 2010, Spain [29]	Retrospective analysis	Recalculation of governmental data (weighted averaging)	Total treatment costs	2006	Susceptible TB only	Evaluation of routine data	TB patients assigned to the respective diagnosis-related groups (DRG)
Rajalahti, 2004, Finland [30]	Retrospective analysis	Combined annual data of two University Hospital Districts	Total treatment costs	2000	Susceptible TB only	27 culture-proven pulmonary TB patients	Local data, not representative of Finland

Diel, 2012, Germany [31]	Modelling per patient	Weighted averaging of cost data, separately provided for children and adults	All types of costs calculated	2010	Susceptible and MDR-TB	All TB cases reported in 2010 included	Epidemiological data and unit costs assessed according to the German public health insurance system
Blaas, 2008, Germany [32]	Retrospective analysis	Averaging of individual cost occurring in the University Hospital Regensburg	Total treatment costs	1998-2003	XDR-TB only	4 XDR- TB patients 1998-2003	–
Eker, 2008, Germany [33]	Retrospective analysis	27 participating hospitals	Duration of hospitalisation	NA	MDR-XDR-TB patients only	177 MDR-TB and 7XDR-TB cases 2004-2006	37% of all culture-confirmed TB cases in Germany included
de Vries, 2013, The Netherlands [34]	Retrospective analysis	Costs derived from the official RIVM and KNCV data	Total treatment costs	2009	Susceptible, MDR-and XDR-TB	1,138 patients with Non-MDR-TB and 20 with MDR-/XDR-TB	Complete countrywide review
Belgian Lung and Tuberculosis Association, 2012, Belgium [35]	Pooled routine data	Governmental assessment	Medication costs only	2012	Susceptible TB, MDR-TB and XDR-TB	NA	–
Rumetshofer, 2008, Austria [36]	Retrospective analysis	Pharmacy records of the Otto-Wagner-Hospital, Vienna	Medication costs only	2008	Susceptible TB, MDR-TB and XDR-TB	NA	–
Floyd, 2012, Estonia [37]	Retrospective cohort analysis	Average cost per patient treated according to WHO guidelines	Total treatment costs	2003	MDR-TB only	Cohort of 149 TB cases (enrolled 2001-2002) followed	

NA: Not available

†Last modified date 16 June 2009

‡registered 9 June 2011

Table 3: Table of pooled costs of TB disease (direct costs and loss of productivity) in the EU*

	No. TB cases 2011 ¹	No. susceptible TB cases	No. MDR-TB cases ¹	No. XDR-TB cases ¹	Cost per susceptible TB case	Cost per MDR-TB case	Cost per XDR-TB case	Total cost due to susceptible TB cases	Total cost due to MDR-TB cases	Total cost due to XDR-TB cases	Overall total cost
Austria	687	662	19	6	10282	57231	170744	6806684	1087389	1024464	8918537
Belgium	1044	1026	15	3	10282	57213	170744	10549332	858195	512232	11919759
Bulgaria	2407	2352	55		3427	24166	24166	8060304	1329130	0	9389434
Cyprus	54	53	1		10282	24166	170744	544946	24166	0	569112
Czech R	600	591	7	2	3427	24166	24166	2025357	169162	48332	2242851
Denmark	381	378	3		10282	57213	170744	3886596	171639	0	4058235
Estonia	341	249	78	14	3427	24166	24166	853323	1884948		2738271
Finland*	325	320	5		10676	57213	170744	3416320	286065	0	3702385
France	4942	4902	40		8668	57213	170744	42490536	2288520	0	44779056
Germany*	4316	4260	56		10185	57487	190880	43388100	3219272	0	46607372
Greece	489	482	5	2	10282	57213	170744	4955924	286065	341488	5583477
Hungary	1445	1438	7		3427	24166	24166	4928026	169162	0	5097188
Ireland	425	422	3		10282	57231	170744	4339004	171693	0	4510697
Italy	3521	3434	81	6	11728	57213	170744	40273952	4634253	1024464	45932669
Latvia	885	778	95	12	3427	24166	24166	2666206	2295770	289992	5251968
Lithuania	1904	1555	296	53	3427	24166	24166	5328985	7153136	1280798	13762919
Luxemburg*	26	24	2		10282	57213	170744	246768	114426	0	361194
Malta	33	33			10282	24166	170744	339306	0	0	339306
Netherlands*	1007	992	15		10774	49424	150570	10687808	741360	0	11429168
Poland	8478	8436	41	1	3427	24166	24166	28910172	990806	24166	29925144
Portugal	2540	2518	22		10282	57213	170744	25890076	1258686	0	27148762
Romania	19212	18682	500	30	3427	24166	24166	64023214	12083000	724980	76831194
Slovakia	399	396	3		10282	24166	24166	4071672	72498	0	4144170
Slovenia	192	192			3427	24166	24166	657984	0	0	657984
Spain	6762	6720	41	1	11818	57231	170744	79416960	2346471	170744	81934175
Sweden	586	569	17		10282	57213	170744	5850458	972621	0	6823079
UK	8963	8876	81	6	8558	64777	170744	75960808	5246937	1024464	82232209
	71964	70340	1488	136				480568821	49855370	6466124	536890315
¹ Numbers from ECDC AND WHO Europe Tuberculosis Surveillance and Monitoring in Europe 2013, cases in 2011 www.ecdc.europa.eu											
Blanc boxes: no data available in ECDC AND WHO Europe Tuberculosis Surveillance and Monitoring in Europe 2013											

*cost of 2011 TB cases adjusted to the year 2012