

Cost for Tuberculosis Care in Developed Countries: Which Data for an Economic Evaluation?

Leopoldo Trieste and Giuseppe Turchetti

ABSTRACT. Tuberculosis (TB) seems to be eradicated in developed countries. However, current migration flows and increasing use of immunosuppressive and biologic drugs for rheumatic diseases are increasing the risk of latent TB and TB onset for citizens of developed countries. Because little is known about the economic burden of TB in developed countries, we set out to describe the order and dimension of the costs of TB care in developed countries. A review of the literature indicated that the cost for anti-TB therapy is about \$2000 US per patient. Costs of drugs associated with standard therapy for active TB [2HRZE/4HR, i.e., 2 months of isoniazid (H), rifampin (R), pyrazinamide (Z), and ethambutol (E), followed by 4 months of HR] are about \$600. Standard therapy for latent TB care costs about \$80 for 9H and \$256 for 4R, respectively. However, these data are very limited because of the horizon of analysis and because data are strongly localized. It can be concluded that in developed countries, available data on TB care costs are insufficient for detailed analysis of the economic burden of TB. (J Rheumatol Suppl. 2014 May; 91:83–5; doi:10.3899/jrheum.140107)

Key Indexing Terms:

ACTIVE TUBERCULOSIS CARE LATENT TUBERCULOSIS ONSET
COST DEVELOPED COUNTRIES

Over recent decades, tuberculosis (TB) has become very rare in developed countries^{1,2,3,4}. However, demographic changes, migration flow, increasing use of immunosuppressive and biologic drugs for the treatment of many diseases, reduced effectiveness of bacillus Calmette Guérin vaccination, and multidrug-resistant TB^{1,2} are increasing the risk of latent TB and TB onset for citizens of developed countries³. In spite of this, few data are available on the economic burden of TB in these countries.

With respect to TB prevalence, the World Health Organization (WHO, 2013)⁴ reported differences based on per-capita annual income because the percentage of TB onsets strongly decreases with increasing income. In 2000, the percentages of TB onset were 48, 38, 10, and 1.2 per 100,000 population, for low-, lower middle-, upper middle-, and high-income populations, respectively. Similarly, the percentage rate of reduction of TB-related mortality over 10 years (2000–2011) seems to be influenced by per-capita income. Considering 10-year variations of TB onset on 100,000 population with respect to 2000 data, reductions of 25%, 43%, 42%, and 31% have been estimated for high-, upper middle-, lower middle-, and low-income populations, respectively. These data suggest that, with a low incidence of the disease, the low reduction of cases may be associated

with small investments in prevention and treatment of the disease.

With respect to the economic dimension, available data on costs for TB care often come from underdeveloped⁵ and developing countries⁶. For a number of economic and societal reasons, these data are not useful for indicating TB and costs of TB treatment in developed countries.

Results

Treatment of active TB is based on drug treatment that is differentiated between adults and children (Table 1).

A metaanalysis by Ziakas and Mylonakis⁷, which includes American and Canadian studies, indicates a monthly cost of US \$1.50 for isoniazid (INH) therapy and \$101.40 for rifampin (RIF). Indirect measures of cost for TB

Table 1. Drug consumption in the treatment of TB in adults and children (2HRZE/4HR).

Patient	Drug	Dose, mg/ml	Maximum Daily Dose	Length, mos
Adults	H	5	300	6
	R	10	600	6
	Z	15–30	2000	2
	E	15–25		2
Children	H	10–20	300	6
	R	10–20	600	6
	Z	15–30	2000	2
	E	15–25		2

2HRZE/4HR: 2 months of isoniazid (H), rifampin (R), pyrazinamide (Z) and ethambutol (E), followed by 4 months of HR; TB: tuberculosis.

From the Istituto di Management, Scuola Superiore Sant'Anna, Pisa, Italy. L. Trieste, PhD; G. Turchetti, PhD, Istituto di Management, Scuola Superiore Sant'Anna.

Address correspondence to L. Trieste, Istituto di Management, Scuola Superiore Sant'Anna, Piazza Martiri della Libertà 33, 56127 Pisa, Italy. E-mail: l.trieste@sssup.it

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

care derive from studies that compared cost effectiveness of alternative therapies, such as the rigorous cost-effectiveness analysis by Jasmer, *et al*⁸, on the use of 2 months RIF and pyrazinamide (RZ) versus 9 months of INH for latent TB care. They found that the 2 alternatives are comparable in terms of effectiveness, but RZ costs \$273 more per patient than INH. On the cost side of their evaluation, the authors found that the first 2 months of RZ therapy cost \$640 per patient in a baseline case (based on \$184, \$164, \$292 for medication, laboratory testing, and nursing/physician costs, respectively). The first 6 months of INH treatment cost \$347 per patient (based on \$14 for medication, zero costs for laboratory testing, and \$333 related to nursing/physician care; some of these data are also reported in Table 2).

Based on the data of Ziakas and Mylonakis, and Jasmer, *et al*^{7,8} [excluding ethambutol (E) because consolidated data are not available] and the length of therapy (Table 1), we can give some indications of the dimension of direct costs for care of active TB in developed countries (Table 2).

Costs reported in Table 2 are comparable with indications from the WHO report of 2013 suggesting about \$2000 for treatment of TB. However, Menzies, *et al*⁹ reported \$19,906 and \$845 per active and latent TB care, respectively, with an average cost of \$300 per contact screened.

In detail, therapy costs restricted to drugs for 2 months of INH, RIF, RZ, and E, followed by 4 months of INH and RIF, are also reported in Menzies, *et al*⁹ with a distinction between care of active and latent TB in a study focused in Canada, which shows that costs for latent TB care are about one-seventh of the costs for active TB care.

Costs for hospitalization and investigations and tests related to TB care are reported in the study by Menzies, *et al*, showing that a tuberculin skin test unit costs \$9.13 for material and \$5.00 for labor⁹. Data are lacking with respect to indirect costs.

In spite of a reappraisal of TB in developed countries, particularly among selected patient subsets such as immunosuppressed patients, patients with rheumatic diseases, and elderly populations, the literature is lacking on recent economic evaluations that could guide detailed cost-effectiveness analysis. Although some may argue that these

analyses may have little effect given the still relatively low prevalence of TB in developed countries and the relatively low mortality rate, with the development of new immunosuppressive therapies [e.g., anti-tumor necrosis factor (TNF) drugs in rheumatic diseases] and extended migratory flows, it is likely that the economic implications of TB care will assume a growing importance. In particular, with respect to rheumatic diseases, in view of the costs of anti-TNF therapies, the inclusion of TB costs could allow a more complete cost-effectiveness analysis of different therapeutic approaches^{10,11,12,13}.

We have introduced here the theme of TB care in developed countries, by presenting a synthesis of results and data currently available. Recent and future trends in the onset of TB in developed countries warrant more effort in studying the economic burden of TB.

REFERENCES

1. Fitzpatrick C, Floyd K. A systematic review of the cost and cost effectiveness of treatment for multidrug-resistant tuberculosis. *Pharmacoeconomics* 2012;30:63-80.
2. World Health Organization. Multidrug and extensively drug-resistant TB (M/XDR-TB) 2010 global report on surveillance and response. Geneva: WHO Press; 2010.
3. Steffen R, Menzies D, Oxlade O, Pinto M, de Castro AZ, Monteiro P, et al. Patients' costs and cost-effectiveness of tuberculosis treatment in DOTS and non-DOTS facilities in Rio de Janeiro, Brazil. *PLoS One* 2010;5:e14014.
4. WHO. World Health Statistics, Part III: Global Health Indicators; 2013. [Internet. Accessed February 20, 2014.] Available from: www.who.int/gho/publications/world_health_statistics/EN_WHS2013_Part3.pdf?ua=1
5. Trends in tuberculosis—United States, 2012. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep* 2013;62:201-5.
6. KNCV. Literature Review/Discussion Paper. KNCV Tuberculosis Foundation; 2008. [Internet. Accessed February 27, 2014.] Available from: <http://predoc.org/download/docs-201978/201978.doc>
7. Ziakas PD, Mylonakis E. 4 months of rifampin compared with 9 months of isoniazid for the management of latent tuberculosis infection: a meta-analysis and cost-effectiveness study that focuses on compliance and liver toxicity. *Clin Infect Dis* 2009;49:1883-9.
8. Jasmer RM, Snyder DC, Saukkonen JJ, Hopewell PC, Bernardo J, King MD, et al. Short-course rifampin and pyrazinamide compared

Table 2. Direct costs associated with active care for tuberculosis, per patient.

Costs (US\$)	INH, 6 mos	RIF + Z 2 mos + RIF 4 mos	E Therapy	Reference
Drugs	9.0 or 14.0	184 + 4*101.40	48.6	Ziakas and Mylonakis, 2009 ⁷ Jasmer, et al, 2004 ⁸
Laboratory testing	0	164*3 ^a		Menzies, et al, 2008 ⁹ , but considering 2004 data
Human resource involved in therapy	333	292*3 ^a		Ziakas and Mylonakis, 2009 ⁷ Ziakas and Mylonakis, 2009 ⁷
Total	\$342 or \$347	\$1957.60	\$48.60	\$2348.20 or \$2353.20

^aRelated human resources and laboratory testing costs for 2 mos. RIF + Z therapy included for the additional 4 mos of RIF. INH: isoniazid; RIF: rifampin; Z: pyrazinamide; E: ethambutol.

- with isoniazid for latent tuberculosis infection: a cost-effectiveness analysis based on a multicenter clinical trial. *Clin Infect Dis* 2004;38:363-9.
9. Menzies D, Oxlade O, Lewis M. Cost for tuberculosis care in Canada. *Can J Public Health* 2008;99:391-6.
 10. Turchetti G, Scalone L, Della Casa Alberighi O, Mosca M, Montella S, Cortesi PA, et al. The rationale of pharmacoeconomic analysis in rheumatologic indications. *Clin Exp Rheumatol* 2012;30 Suppl 73:S64-71.
 11. Furneri G, Mantovani LG, Belisari A, Mosca M, Cristiani M, Bellelli S, et al. Systematic literature review on economic implications and pharmacoeconomic issues of rheumatoid arthritis. *Clin Exp Rheumatol* 2012;30 Suppl 73:S72-S84.
 12. Palla I, Trieste L, Tani C, Talarico R, Cortesi PA, Mosca M. A systematic literature review of the economic impact of ankylosing spondylitis. *Clin Exp Rheumatol* 2012;30 Suppl 73:S136-S141.
 13. Cortesi PA, Scalone L, D'Angiolella L, Belisari A, Fusco F, Olivieri I, et al. Systematic literature review on economic implications and pharmacoeconomic issues of psoriatic arthritis. *Clin Exp Rheumatol* 2012;30 Suppl 73:S126-S131.