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Economic evaluations of diagnosis and treatment programmes for tuberculosis in developing countries: a review

This paper reviews recent economic evaluations of diagnostic pathways and treatments of TB in poorly resourced and highly burdened countries. The limited number of studies and their methodological weaknesses make it difficult to draw strong policy conclusions, especially in the field of diagnosis. The evidence points to a possible gain in cost-efficiency by moving from the Ziehl-Neelsen staining method to fluorescence microscopy and from three to two sputum examinations. Nevertheless, further research is indispensable. Concerning treatment, the community-based DOTS approach has proved more cost-effective than the conventional approach. With respect to other treatment alternatives, less evidence is available, but two promising possibilities are the expansion of DOTS by collaboration with the private sector and the introduction of second-line drugs for chronic disease.

Economische evaluaties van diagnose- en behandelingsprogramma's voor tuberculose: een literatuuroverzicht

De voorliggende studie geeft een overzicht van economische evaluatiestudies gepubliceerd in de periode 2000-2004 met betrekking tot diagnose en behandeling van tuberculose in landen met een hoge incidentie en een laag tot gemiddeld inkomen. Er kunnen geen sterke beleidsconclusies afgeleid worden. Het aantal studies dat gevonden werd is beperkt en bovendien methodologisch relatief zwak, voornamelijk wat betreft diagnose. De evidentie wijst in de richting van een mogelijke efficiëntie-winst wanneer afgestapt wordt van de Ziehl Neelsen kleuring naar fluorescentiemicroscopie en van drie naar twee sputum analyses. De resultaten moeten echter nog bevestigd worden in verder onderzoek. Wat behandeling betreft, bewijzen de resultaten dat een, door de gemeenschap gesuperviseerde DOTS-behandeling, kosten-effectiever is dan de conventionele benadering. Voor andere behandelingsalternatieven is er minder evidentie ter beschikking; verdere uitbreiding van DOTS door samenwerking met de private sector en de introductie van tweedelijnsgeneesmiddelen voor chronische ziekte lijken echter veelbelovend pistes.

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Tuberculosis (TB) is one of the most serious infectious killers of all time. Deformities in the skeletons of Egyptian mummies suggest that the disease has existed since antiquity (Morell 1994).

The current first-line TB drugs (isoniazid, rifampicin, pyrazinamide, streptomycin and ethambutol) have been available for the past 30 years and can provide cure rates of 95% (Dye *et al* 2002: 438). Yet the burden of TB is still immense, especially in developing countries.

According to the World Health Organization there were 8.8 million new cases of TB and about two million TB deaths in 2002. The incidence of TB is growing globally at 1.1% per year. Most cases are found in South East Asia, but the per capita incidence and mortality rates are by far the highest in Africa (where the incidence growth rate is about 10%). The most important cause of this increasing incidence is HIV/AIDS; 30 to 40% of TB cases in Africa are HIV-positive, and in some countries up to 70%.[1]

The current situation is clearly paradoxical: TB has reached epidemic proportions in developing countries despite the availability of effective drugs.

During the nineties the WHO tried to alleviate the situation by introducing a new strategy known as DOTS[2] (directly observed treatment short course). It still is the cornerstone for TB control internationally and has been introduced in a variety of countries with great success. Geographical coverage of DOTS, however, is not all. In Uganda for example, the whole population is covered by DOTS but only 50% of the estimated cases are detected (Raviglione 2003: 10, 11), mainly because of a lack of efficient, cheap methods of diagnosis.

Current methods for detecting and diagnosing TB in developing countries still rely heavily on centuries-old technology. Diagnosis on the basis of culture is referred to as "the gold standard" but requires equipment that is seldom available in resource-poor settings and involves a delay of six to ten weeks before the results become available. During this time, the patient is likely to transmit the infection to close contacts,

1 <www.who.int>

2 DOTS combines five elements: political commitment, microscopy services, drug supplies, surveillance and monitoring systems, and the use of highly efficacious regimes with direct observation of treatment.

thereby increasing the burden of disease. It is estimated that the average person with active TB will infect between 10 and 15 people every year (Walker 2001: 1100-3). Sputum smear microscopy, where a patient's sputum is examined under a microscope, is the principal method of diagnosis in developing countries. It is a cheap, swift procedure but it is less sensitive than culture, especially among HIV-positive patients (Walker 2001: 1101; Kivihya-Ndugga *et al* 2004: 1164). Nucleic acid amplification technologies are already available but are often expensive and/or less reliable. In order to ascertain whether they offer a potential solution, their cost-effectiveness should be analysed (Dowdy *et al* 2003).

Patients who are correctly diagnosed with TB should complete eight months of treatment with first-line drugs. According to the WHO (2004c), on average 6.2% of new smear-positive cases registered in 2001 in high-burden countries defaulted under DOTS strategy and 10% under non-DOTS strategy. Non-compliance can sometimes be much higher: Khan *et al* (2002), for example, found rates of 25% for men and 15% for women while Nganda *et al* (2003) reported rates of 41.5% for smear-negative and extra-pulmonary cases. The reasons cited for failing to complete treatment were the high cost in travel and time (OBoyle *et al* 2002).

The cure rate among registered cases in these high-burden countries was 77%, while a further 6.7% completed treatment under DOTS, giving a reported overall treatment success rate of 84%. Under non-DOTS systems, the overall treatment success rate in high-burden countries amounts to 34%: a 20% cure rate plus a further 14% treatment completion rate (WHO 2004c).

Patient non-adherence and improper diagnosis cause multi-drug-resistant (MDR) TB to emerge.[3] Treatment of MDRTB requires longer and more expensive second-line drugs. Currently, most patients with MDRTB are not identified until they have failed with one or more courses of conventional therapy over a period of months to years. This results in the selection of drug-resistant populations of bacteria and the continued transmission of MDR strains (Espinal 2003). The most

3 Multi-drug-resistant TB (MDRTB) refers to patients infected with TB bacteria resistant to at least isoniazid and rifampicin.

recent global report on resistance to anti-TB drugs performed by the WHO/IUATLD (WHO 2004a) reveals the presence of MDRTB in most of the settings surveyed, especially in Eastern Europe. To control the emerging cases of MDRTB the WHO conceived the DOTS-plus strategy in 1998. DOTS-plus is intended as a supplement to standard DOTS-based programmes in settings with high MDR prevalence. New diagnostic tools are being developed for swifter identification of patients infected with MDRTB. Developing countries would welcome new diagnostic tools which are simple and cheap.

Like most diseases that mainly affect the poor, TB suffers from underfunding. However, with the WHO's declaration of TB as a global emergency and its commitment to detecting 70% of new infectious TB and to curing 85% by 2005, more resources are becoming available.

In 2002, a global fund to fight AIDS, TB and malaria became operational.[4] Pledges and contributions to date amount to about 6 billion USD. Experts agree, however, that much more is needed to prevent and treat these diseases.

Since resources are scarce and the impact of TB is enormous, it is of the utmost importance that cost-effectiveness be considered in the design of new strategies, especially in developing countries. As Walker & Stevens (2003: 365) state, inefficient allocation of resources exacts a much higher penalty in terms of foregone health benefits in the developing world than elsewhere. Cost-effectiveness studies have already proved their relevance in evaluating TB control. In a review article on the cost-effectiveness of TB programmes, Fryatt (1997) concludes that effective, shorter rifampicin-based regimens are more cost-effective from the perspective of both the provider and the household. Ambulatory care was found to be more cost-effective than hospital care from the user's perspective, while the results are mixed from the provider's perspective. These findings make policy changes relating to shortening treatment (up to six or eight months for primary TB patients and up to more than 12 months for re-treatment patients) defensible from an economic point of view. This review, however, provides a snapshot of the evidence at a certain point in time. Other economic evaluations of TB control have been undertaken. Although some recent reviews focus on the role

4 <www.theglobalfund.org>

of economic studies in TB control (Walker & Stevens 2003; Floyd 2003), none of these analyse the available evidence on cost-effectiveness.

The present study assembles all the recent cost-effectiveness or cost-utility studies in the field of TB control in poorly resourced and high-burden countries. Although a previous review article on the cost-effectiveness of TB programmes (Fryatt 1997) covers the period up to 1995, we choose to start our review in 2000. This apparent discontinuity is defensible because Fryatt (1997) includes only studies dealing with treatment whereas we also include studies on diagnosis. Moreover, the discussion of studies dating from the mid-nineties is of limited use in assessing the current situation. The situation has changed substantially with respect to the cost of diagnosis and treatment, the prevalence of TB, and the comorbidities associated with it, especially its relationship with HIV/AIDS. All studies will be summarised in a standard way and critically assessed. We hope to highlight ways in which current practices can be improved and identify areas for further study.

1. Methods

The Dare, NHS EED, and HTA databases from the University of York as well as Medline were searched for publications from the year 2000 to the present (December 2004).[5] The following search criterium was used to screen titles and abstracts : "((“cost effect*” OR “cost-effect*” OR “cost util*” OR “cost-util*” OR “economic evaluation” OR economics) AND (TB OR tuberculosis))". In addition, the WHO publications on TB were screened.[6] From the Medline search we had 137 hits. We retained all original economic evaluation studies related to diagnosis or treatment of TB in high-burden, and low- or middle-income countries. Countries with an overall TB incidence in excess of 100/100.000 per year (WHO estimates)[7] were regarded as high burden while the World Bank classification of low or middle income of 2002 GNI per capita less than $9,076 was utilised (*World Development Report* 2004). Original

5 <http://www.york.ac.uk/inst/crd/crddatabases.htm>

6 <http://www.who.int/docstore/gtb/publications/index.html>

7 <http://www.who.int/GlobalAtlas/DataQuery/browse.asp?catID=011600000000&lev=3>

economic evaluation studies were defined as those reporting first-hand results of the outcomes and costs of at least two alternatives. Dutch, English, Spanish, French and German articles could be retained. First, titles and abstracts (if available) were carefully read, then the full text was used to further refine the search results. This was done by two independent reviewers.

2. Results

Seventeen articles that met the inclusion criteria were retrieved, relating to seventeen separate analyses.[8] Fourteen were retrieved from the Medline search; two further studies (one publication) from the WHO publications, and one additional study from the article references. All but two were cost-effectiveness analyses. Most evaluations (ten in total) were performed in (sub-Saharan) African countries; six in Asia and only one in Latin America. Four studies considered different diagnostic options while the others related to alternative treatment options.

We shall now proceed to review the methodology and the conclusions of the various studies, dealing separately with the subsets: those studies relating to diagnostic alternatives and those relating to treatment alternatives.

2.1 Economic evaluations of diagnosis

A first step in TB control is, of course, a correct diagnosis, so that treatment may commence on those who really need it and no funds are wasted on others. This is self-evident but less easy to achieve. Various factors may negatively affect the situation, including the accuracy of the test (specificity and sensitivity), the time taken to obtain results, the complexity of the test, and its cost. In this section, we will consider the available economic evidence to guide our prioritisation of diagnostic alternatives.

2.1.1 Alternatives compared, research design and viewpoint

Among the economic evaluations that were retrieved using the specifications described above, four studies focused on the diagnosis of pul-

8 One article contained two different analyses, whereas two other articles reported the same study.

monary tuberculosis. All of these were performed in Africa. Three studies concentrated on detection of smear-positive TB, whereas one concentrated on diagnosis of smear-negative TB. These studies are listed in Table 1 with authors and year of publication, the country and period of study, the alternatives considered, the research design, the sample size and the type of analysis.

For countries with limited resources, international guidelines from the WHO and the IUALTD recommend sputum smear microscopy as the principle method for the diagnosis of active TB and advise that three sputum smears should be examined for all suspected cases. For smear-negative cases, chest X-rays are taken. However, examining three sputum smears for each TB suspect generates a huge workload for hospital laboratory staff in resource-poor countries with a high burden of TB. In addition, several studies have found the third sputum examination to have a relatively low incremental yield. Therefore, alternative diagnostic algorithms are explored and compared.

Two studies (Harries *et al* 2000 and Walker *et al* 2000) compare the incremental yield (and cost) of examining an additional sputum smear with the Ziehl-Neelsen staining method. Sputum smear-negative cases are followed by a chest X-ray. Harries *et al* 2000 uses data from one laboratory where during two consecutive six-month periods three sputum smears (first period) and two sputum smears (second period) were screened. This pre-post comparison without randomisations or even control variables precludes any convincing conclusions as we cannot be sure that the two populations were comparable. A further methodological weakness is the lack of a reference standard (*eg* a test in a second laboratory on a duplicate sample or with a better-performing technique) to verify the specificity and sensitivity of the test. In Walker *et al* (2000), the incremental yields of screening one, two and three smears are calculated, using data obtained from a single laboratory. Again, the lack of a reference standard is a great methodological weakness. Kivihya-Ndugga *et al* (2003) compare detection of smear-positive TB using routine Ziehl-Neelsen staining with examination by fluorescence microscopy (both methods using one, two and three smears), followed by a chest X-ray for suspects who are smear-negative. The results of these strategies are validated by comparing them with the so-called gold-standard (*ie* culture on Löwenstein-Jensen slopes) to

Table 1: Overview of economic evaluations of TB diagnosis (2000-2004)

Authors	Year pub	Country; year of data collection	Alternatives	Methodology	Sample (n)	Type of study	Viewpoint
Harries *et al*	2000	Malawi; 1998	Diagnosis of pulmonary TB on the basis of 3 sputum smears (1) versus new strategy: 2 sputum smears with ZN staining method (2)	Before and after comparison in 1 laboratory	2258	CEA	Not stated (laboratory)
Walker *et al*	2000	Zambia; 1997-1998	Diagnosis of pulmonary TB on the basis of one sputum smear (1) versus 2 sputum smears (2) versus 3 sputum smears (3) with ZN direct staining method	Test results from 1 laboratory	1423	CEA	Health provider (=laboratory)
Kivihya-Ndugga *et al*	2003	Kenya; 2000-2001	Diagnosis of pulmonary TB with detection of smear-positive cases based on ZN of 1 sputum sample (1) 2 sputum samples (2), 3 sputum samples (3), or based on FM of 1 sputum sample (4), 2 sputum samples (5), 3 sputum samples (6), each followed by CXR if sputum results are negative	Duplicate testing on same sample with culture as gold standard (Lowenstein-Jensen slopes) and CXR reread (blinded first result)	993	CEA	Not stated (societal)
Albert	2004	South Africa; not stated	Current diagnostic practice consisting of CXR, and if suspect 2 sputum samples, for smear and culture (1), versus FastPlaqueTB and culture of all suspects (2), versus FastPlaque TB testing of all suspects and culture on specimens with a negative FastPlaqueTB result (3), versus FastplaqueTB of all suspects (4), in NEW SMEAR-NEGATIVE suspects (two negative sputum smears)	Model; patient characteristics and test performance from 1 study	853	CEA	Health provider

ZN: Ziehl-Neelsen
FM: fluorescence microscopy
CXR: chest X-ray

assess the sensitivity and specificity of the smear procedures. The Ziehl-Neelsen test was performed in one laboratory while a duplicate sample was used in a second laboratory for examination by fluorescence microscopy and culture. Albert (2004) compares the South African National TB Control Programme (NTCP) algorithm for diagnosis of pulmonary TB in smear-negative suspects, which is based on chest X-ray (founded on WHO guidelines), with three strategies (FASTPlaque TB[9] and culture of all smear-negative suspects versus FASTPlaqueTB testing of all smear-negative suspects and culture on specimens with a negative FASTPlaqueTB result versus FASTPlaqueTB of all smear-negative suspects) using a new rapid test (FASTPlaqueTB). The different options are analysed on the basis of a model. The use of this model allows for comparison of the various possible diagnostic algorithms. One should bear in mind, however, that the model is based on data from only one study.

Reviewing the various studies, the methodological weaknesses are striking. Only Kivihya-Ndugga *et al* (2003) can be considered to have a reliable research design.

Two studies (Walker *et al* 2000 and Albert 2004) take the viewpoint of the health provider. Harries *et al* (2000) and Kivihya-Ndugga *et al* (2003) do not explicitly mention their viewpoints, but they can be identified as "laboratory" (Harries *et al* 2000) and "society" (Kivihya-Ndugga *et al* 2003), respectively.[10]

9 *FASTPlaque*TB, a phage-based test which is currently being marketed by Biotec, detects TB from sputum specimens. The Phage Amplification uses bacteriophage (bacterial viruses approximately 10 millionths of a cm long) to report the presence of target bacterial cells in a sample. The test takes two days to yield results and is technically simple to perform.

10 The "viewpoint" refers to the perspective from which costs are calculated. If the perspective of the health service provider is chosen, the analysis focuses only on the costs incurred by the provider. If a patient perspective is taken, the focus is on costs to the patient, such as out-of-pocket costs, travel costs, loss of income, and so on. A societal viewpoint considers all costs; this is the preferred viewpoint since it is the most comprehensive.

2.1.2 Measures of effectiveness and cost

All four studies are cost-effectiveness studies. The effectiveness measures used, the cost categories included and the values for these variables are summarised in Table 2. In order to make the costs comparable, we recalculated them in $2004 values and added these in brackets in column 5. Where necessary, cost figures were first converted to US$ on the basis of the exchange rate (Federal Reserve, annual rates)[11] and then actualised to 2004 (July) prices on the basis of the CPI (Bureau of Labour statistics).[12] The cost-effectiveness results are also expressed in $2004 values (column 6).

Ultimately, we would like to know the impact of different diagnostic pathways on the health of the patient and on the costs involved. The cost-effectiveness of TB diagnosis therefore depends not only on the characteristics of the diagnostic technique, but also on the effectiveness and cost of treatment and the impact of non-treatment or delayed treatment on the health of patients and their contacts. The data needed to make such an overall evaluation are numerous; none of the studies surveyed in this review is so ambitious. They all have a more limited scope, taking the number of TB cases diagnosed as the outcome measure; Harries *et al* (2000) is restricted to the number of smear-positive cases, Albert (2004) to smear-negative cases, while Walker *et al* (2000) and Kivihya-Ndugga *et al* (2003) deal with all TB cases. This limits the comparison of the results, meaning that we cannot compare whether it is more worthwhile to invest in better diagnosis or in better treatment. Moreover, there is the risk of ignoring the issue of false negative or false positive results. Worst of all, Harries *et al* (2000) and Walker *et al* (2000) do not even distinguish between true and false positives.

As could be expected with a narrow outcome measure and a limited perspective (except in the case of Kivihya-Ndugga *et al* 2003), the cost categories analysed are also limited. Only the costs of diagnosis, and sometimes even only part of these are considered. One therefore needs to be very cautious in interpreting the results.

11 <http://www.federalreserve.gov/releases/g5a/>
12 <http://www.bls.gov/home.htm>

Table 2: Results of economic evaluations on TB diagnosis

Study	Effectiveness measure	Results	Cost categories	Results (US$2004 second quarter)	C/E -ratio (US$2004)	Discount rate	Remarks
Harries *et al* 2000	Number of smear-positive PTB cases diagnosed	(1) 305 (58%) (2) 303 (54%)	Consumable costs of laboratory examination	US$1997 (1) 731 (851) (2) 521 (607)	(2) is dominant: same effectiveness and lower cost	N/A	Incomplete analysis
Walker *et al* 2000	Number of TB cases diagnosed	(1) 128 (2) 153 (3) 166	Medical costs associated with diagnosis of TB	US$, year not stated, 1998? (1) 583.4 (2) 1166.9 (3) 1750.3	Average cost/case detected (1) 0.52 (2) 8.73 (3) 12.08 Incremental cost/case detected (1) 5.22 (2) 26.7 (3) 51.4	3%	Incomplete analysis
Kivihya-Ndugga *et al* 2003	Number of cases correctly detected (smear-positive and smear-negative)	(1) 512 (2) 515 (3) 513 (4) 512 (5) 515 (6) 516	Medical costs associated with diagnosis of TB and patient costs	US$, year not stated, 2001? Per 1000 suspects for diagnosis of TB (1) 15723 (16677) (2) 18787 (19927) (3) 20951 (22222) (4) 15433 (16369) (5) 19097 (20256) (6) 21754 (23074)	Average cost/TB case detected (inclusive savings treatment costs false positve versus (3) in brackets) (1) 32.6 (46.9) (2) 38.7 (37.2) (3) 43.3 (43.3) (4) 38.0 (27.9) (5) 39.2 (36.0) (6) 44.7 (41.6)	Not stated	Sensitivity analysis confirms the results
	Number of correctly detected smear-positive cases	(1) 177 (2) 307 (3) 334 (4) 373 (5) 430 (6) 433		per 1000 suspects for diagnosis of smear-positive TB (1) 13730 (14563) (2) 17058 (18093) (3) 19282 (20452) (4) 15139 (16058) (5) 18095 (19193) (6) 20273 (21503)	Average cost/smear-positive TB case detected (inclusive of savings) (1) 82.3 (74.8) (2) 58.9 (54.5) (3) 61.2 (61.2) (4) 43.1 (39.5) (5) 44.7 (42.7) (6) 49.6 (48.5)		

Table 2: Results of economic evaluations on TB diagnosis (continued)

Study	Effectiveness measure	Results	Cost categories	Results (US$2004 second quarter)	C/E -ratio (US$2004)	Discount rate	Remarks
Albert 2004	Number of true positive cases	(1) 39 (2) 54 (3) 54 (4) 26	Medical costs associated with diagnosis of TB	US$, year not stated, 2003? (1) 20079 (20635) (2) 18581 (19095) (3) 18312 (18819) (4) 14740 (15148)	Not calculated in study; own calculations Cost/true positive case detected: (1) 529 (2) 354 (3) 348 (4) 583 Marginal analysis not done; own calculations (4) 583 (vs doing nothing) (3) 131 (vs 4) (=18312-14740)/(54-26) (1) and (2) dominated	Not used	Model includes unrealistic assumptions

In Harries *et al* (2000) and Walker *et al* (2000) costs are limited to laboratory costs. According to Harries *et al* (2000) a change from three sputum smear examinations to two would reduce the cost of consumables such as reagents and slides ($0.23 for one sputum smear in 1997) and would leave other costs (eg staff equipment, transport, and overheads) unchanged. Therefore the authors only calculate the total cost of consumables for a strategy with three smears versus one with two smears. In $2004 these amount to $851 and $607 respectively. Walker *et al* (2000) distinguish between capital costs (buildings and equipment), which are annualised using a 3% discount rate, and recurrent costs (supplies and labour costs of staff) to calculate the average cost per smear ($0.41, year not stated). The total cost of using three smears versus two or one is calculated as the average cost multiplied by the number of smears analysed. In this way the authors assume that capital costs and equipment costs are also fully variable, which is a very unrealistic assumption. Kivihya-Ndugga *et al* (2003) consider all diagnosis-related costs, both medical costs (labour, materials and equipment) and patient costs (examinations, transport, loss of income) for the use of Ziehl-Neelsen testing and fluorescence microscopy, with one, two and three sputum smears. The study includes a sensitivity analysis to assess the effect of changes in X-ray use, the prevalence of culture-positive TB, staff workload and the cost of investment and labour. Albert (2004) uses costs for acidfast bacilli (AFB) smear microscopy, chest X-rays and clinic visits, from published data, and adds costs for consumables, reagents, labour and overheads. The model calculates the cost per 1000 smear-negative TB suspects tested for the four diagnostic algorithms.

2.1.3 Results and discussion

Harries *et al* (2000) and Walker *et al* (2000) conclude that using two instead of three sputum smears represents a more efficient use of resources. This conclusion is a bit premature, however, given the many caveats relating to the studies: dubious methods of measuring effectiveness, no accounting for false positive cases, only laboratory costs being considered and a disputable method of calculating costs is disputable.

Kivihya-Ndugga *et al* (2003) conclude that fluorescence microscopy is more cost-effective than Ziehl-Neelsen testing and leads to savings for both patients and health facilities. Using three rather than two sputum smears (with fluorescence microscopy) only detects an additional 0.7% of smear-positive cases, hence the use of fluorescence microscopy on two sputum specimens is recommended. Some sensitivity analyses confirm these results. HIV testing was also undertaken and a logistic regression (accounting for sex and age) was performed on culture-positive TB patients to assess the impact of HIV status on the performance of the various tests. The results show that the sensitivity of fluorescence microscopy is higher than that of the Ziehl-Neelsen testing, while their specificity levels are equally high. HIV status did not have a significant impact on the performance of fluorescence microscopy. Some important conclusions can be drawn from the study. First, it is important to include all costs: since laboratory costs constitute only a small proportion of total costs (around 17%), no firm conclusions can be drawn on the basis of these costs alone. Secondly, it is equally important to consider the treatment costs of false positives. Different diagnostic algorithms may lead to different numbers of false-positive patients and their treatment costs can offset the differences in diagnosis costs. Thirdly, on the basis of this study, fluorescence microscopy on the basis of two sputum smears should be preferred for diagnosis. Although this result seems robust on the basis of a sensitivity analysis, it should be confirmed by other analyses.

Albert (2004) calculates the medical costs of the four specified diagnostic pathways (including lab tests, chest X-rays, and clinic visits), but the study is not very clear on the cost categories included (equipment, buildings, overheads, etc) nor is the year of cost calculation given. After attributing costs to every step of the various algorithms, the author assumes (and simulates) that every smear-negative TB suspect will complete the entire procedure, enabling him to calculate the total cost of the four alternatives. But it is rather unrealistic to assume that all patients will complete the entire diagnostic algorithm. Once again, no costs are attached to false positive and false negative cases. The author concludes that the second algorithm enables detection of 28% more cases than the NTCP algorithm, and at a lower total cost. Moreover, he argues that the algorithms which incorporate the use of FASTPlaqueTB are

simpler, faster and require fewer clinic visits on the part of the patients. The results are confirmed in a sensitivity analysis. The results of this new diagnostic test are therefore promising, but need to be confirmed. The results are based on the test performance of only one study, and do not incorporate the full range of costs.

2.2 Economic evaluations of treatment alternatives

Thirteen studies were found on the treatment of TB in low- or middle-income countries. The studies were all performed in high-burden countries, and eight of them in the top 22 high-burden countries according to the WHO. Most of the evaluations were done in Africa[13] and Asia[14] and one in Latin America (Suarez *et al* 2002). The studies are listed in Table 3. A brief description of the alternatives compared, the research design and the sample size, the type of analysis and the viewpoint taken are given in the table. Table 4 describes the effectiveness measures used and their values, as well as the cost categories and results as stated in the article and as recalculated to $2004 values, together with the cost-effectiveness results.

2.2.1 Alternatives compared, research design and viewpoint

At the moment, the Directly Observed Treatment short course (DOTS) is the most generally recommended strategy for the treatment of TB. One of the components of the DOTS approach is that patients are observed while taking their medication, usually by health workers in the health facility or hospital (WHO 2002); another is the use of highly efficacious short-course treatment. Although DOTS was introduced by the WHO in 1991 and has been promoted since as the most cost-effective strategy, five studies choose to compare this approach with the pre-existing situation.[15] One study compares the standardized short-course therapy with individualised treatment after susceptibility testing (Jacobs *et al*

13 Cf Wilton *et al* 2001; Floyd *et al* 2003; Moalosi *et al* 2003; Nganda *et al* 2003; Okello *et al* 2003; Xu *et al* 2001.

14 Cf Xu *et al* 2000; Islam *et al* 2002; Jacobs *et al* 2002; Khan *et al* 2002; WHO 2004b(1); WHO 2004b(2).

15 Cf Xu *et al* 2000; Wilton *et al* 2001; Jacobs *et al* 2002; Nganda *et al* 2003; Okello *et al* 2003.

Table 3: Overview of economic evaluations of TB treatment (2000-2004)

Authors	Year pub	Country; region type; year of data collection	Alternatives	Methodology	Sample (n)	Type of study	Viewpoint
Xu *et al*	2000	China; Region type not stated 1994	DOT (1) versus non-DOT treatment (2) for newly registered smear-positive cases (no further details given)	Model	n=794	CUA	Not stated (healthcare provider?)
Wilton *et al*	2001	South Africa; region type; year data collection not stated	DOT (1) versus conventional therapy (2) (no further details given)	Model (Monte Carlo simulation)	N/A	CEA	Not stated (healthcare payer?)
Islam *et al*	2002	Bangladesh; rural July 1996-June 1997	DOT through healthcare facilities (first 2-3 months: patients receive drugs weekly, following 6-5 months: patients collect drugs monthly) (1), versus through CHW (new patients; first 2-3 months: CHW observes patient swallow drugs, following 6-5 months: patients collect drugs weekly; retreatment: patients are observed the entire period) (2), for pulmonary and extra-pulmonary TB in adults and children	Retrospective, comparison of 2 'similar' districts, each using an alternative (no randomisation)	(1) 186 (2) 185	CEA	Healthcare provider
Jacobs *et al*	2002	Russian Federation; rural and urban 1995-1996 effect; 1997 costs	Russian approach with individual treatment according to primary susceptibility testing (including surgery and adjunct/pathogenic therapies) (1), versus WHO standardised SCC (2)	Prospective randomised controlled trial	(1) 155 (2) 155	CEA	Societal
Khan *et al*	2002	Pakistan; rural and urban 1997-1998	DOT via health workers at health centre (1a) or community centre (1b), versus via a family member (2), versus unsupervised treatment (3), for new cases of sputum positive pulmonary TB	Prospective, Randomised controlled trial	(1a) 46 (1b) 73 (2) 107 (3) 111	CEA	Societal
Suarez *et al*	2002	Peru; urban and rural 1997-1999	DOT standardised 18-month regimen with second-line drugs (1a), or 1a plus option of individualised regimen for non-responders (1b), or 1b plus MDR-testing for non-responders and standardised 2nd-line drugs for MDR-patients (1c), versus isoniazid monotherapy (2), for chronic tuberculosis patients	Cohort and model for long-term effects	466	CEA CUA	Public sector

Table 3: Overview of economic evaluations of TB treatment (2000-2004) (continued)

Authors	Year pub	Country; region type; year of data collection	Alternatives	Methodology	Sample (n)	Type of study	Viewpoint
Floyd, Nyirenda *et al*	2003	Malawi; urban 1997-1998	Hospital admission if necessary and DOT for first 2 months at health facility or by community member (1), versus hospital admission if necessary and no DOT (2), for new SMEAR-NEGATIVE patients AND Hospital admission if necessary or chosen and DOT at health facilities for first 2 months (3), versus hospital admission for first 2 months of treatment and no DOT afterwards (4), for new SMEAR-POSITIVE patients	Overall before-and-after comparison	(1) 1329 (2) 1258 (3) 1492 (4) 916	CEA	Societal
Moalosi *et al*	2003	Botswana; urban 1997	Home-based care with drug collection on a daily or weekly basis from nearest clinic by caregivers (1), versus hospitalisation (2), for chronically ill TB patients	Historical cohort study	(1) 50 (2) simulated	CEA	Societal
Nganda *et al*	2003	Kenya; rural, until September 1997 (1), from October 1997 (2)	DOT supervision by health facility or community volunteer for first 2 months, unsupervised for next 6 months, with drug collection once a month (1), versus hospitalisation for first month, unsupervised for next 11 months with drug collection once a month (2), for new SMEAR-NEGATIVE and EXTRA-PULMONARY patients AND hospitalisation if necessary, and DOT supervision by health facility or community volunteer for first 2 months, unsupervised for next 6 months, with drug collection once a month (3), versus hospitalisation for first 2 months, unsupervised next 6 months with drug collection once per month (4), for new SMEAR-POSITIVE patients	Overall before-and-after comparison	Not mentioned	CEA	Societal
Okello *et al*	2003	Uganda; rural 1995-January 1998 (1), January 1998-1999 (2)	Hospitalisation for first 2 weeks followed by either community-based care with DOT supervision during whole treatment or (patient choice) further hospitalisation until 2 months and unsupervised treatment for next 6 months (1), versus hospitalisation for first 2 months, unsupervised for next 6 months (2), for new SMEAR-POSITIVE pulmonary patients	Overall before-and-after comparison	Not mentioned	CEA	Societal