

Cost-comparison of different management policies for tuberculosis patients in Italy

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Although in developing countries the treatment of tuberculosis (TB) cases is among the most cost-effective health interventions, few studies have evaluated the cost-effectiveness of TB control in low-prevalence countries. The aim of the present study was to carry out an economic analysis in Italy that takes into account both the perspective of the resource-allocating authority (i.e. the Ministry of Health) and the broader social perspective, including a cost description based on current outcomes applied to a representative sample of TB patients nationwide (admission and directly observed treatment (DOT) during the initial intensive phase of treatment); a cost-comparison analysis of two alternative programmes: current policy based on available data (scenario 1) and an hypothetical policy oriented more towards outpatient care (scenario 2) (both scenarios included the option of including or not including DOT outside hospital admission, and incentives) were compared in terms of cost per case treated successfully. Indirect costs (such as loss of productivity) were included in considerations of the broader social perspective.

The study was designed as a prospective monitoring activity based on the supervised collection of forms from a representative sample of Italian TB units. Individual data were collected and analysed to obtain a complete economic profile of the patients enrolled and to evaluate the effectiveness of the intervention. A separate analysis was done for each scenario to determine the end-point at different levels of cure rate (50–90%).

The mean length of treatment was 6.6 months (i.e. patients hospitalized during the intensive phase; length of stay was significantly higher in smear-positive patients and in human immunodeficiency virus (HIV) seropositive patients). Roughly six direct smear and culture examinations were performed during hospital admission and three during ambulatory treatment. The cost of a single bed day was US\$ 186.90, whereas that of a single outpatient visit ranged, according to the different options, from US\$ 2.50 to US\$ 11. Scenario 2 was consistently less costly than scenario 1. The cost per case cured for smear-positive cases was US\$ 16 703 in scenario 1 and US\$ 5946 in scenario 2. The difference in cost between the cheapest option (no DOT) and the more expensive option (DOT, additional staff, incentives) ranged from US\$ 1407 (scenario 1, smear-negative and extrapulmonary cases) to US\$ 1814 (scenario 2, smear-positive cases). The additional cost to society including indirect costs ranged from US\$ 1800 to US\$ 4200. The possible savings at the national level were in the order of US\$ 50 million per year.

In conclusion, cost-comparison analysis showed that a relatively minor change in policy can result in significant savings and that the adoption of DOT will represent a relatively modest economic burden, although the real gain in effectiveness resulting from DOT in Italy requires further evaluation.

Voir page 474 le résumé en français. En la página 474 figura un resumen en español.

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Introduction

The competition of health programmes for limited economic resources within national health systems has spawned an abundance of studies on economic evaluation in health care. Economic evaluation is the comparative analysis of alternative courses of action in terms of costs and consequences, and is most useful when preceded by evaluation of efficiency and effectiveness (1). In the last few years a slowdown or reversal in the decline of tuberculosis (TB) rates has been observed in industrialized countries, the reasons being mainly attributed to increased immigration, poverty, intravenous drug abuse, and infection with human immunodeficiency virus (HIV) (2, 3). WHO is promoting a strategy of TB control based on rapid

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case detection predominantly through case finding among symptomatic patients self-reporting to health services and supervised administration of standardized short-course chemotherapy, preferably on an ambulatory basis (4). Although in developing countries the treatment of TB cases is among the most cost-effective health interventions, there have been few analyses of the cost-effectiveness of TB control in low-prevalence countries (5, 6). The aim of the present study was to perform an economic analysis in Italy, where TB control efforts were recently revitalized (7), both from the perspective of the resource-allocating authority (i.e. Ministry of Health) and in the broader social context. This study comprises (i) a cost description based on present policy applied to a significant sample of TB patients nationwide (admission and directly observed treatment (DOT) during the initial intensive phase of treatment); and (ii) a cost-comparison analysis of two alternative programmes: current policy and a policy oriented more towards outpatient care (both offering the option of including or not including DOT outside hospital admission, plus incentives) were compared in terms of cost per case cured. The cost-comparison analysis included indirect costs (such as loss of productivity) in considerations of the broader social perspective.

Methods

Setting and coverage

In Italy (in 1995: population, 57.2 million; notified TB cases: 9.8 per 100 000 all types; 2.5 per 100 000 new sputum smear-positive), decentralized TB control efforts based on regional programmes started operating in 1990 (7). As part of the first TB project of the Istituto Superiore de Sanità (technical branch of the Ministry of Health), data from a national network of TB units belonging to the AIPO (Italian Society of Hospital Pneumologists) network were collected prospectively beginning in 1995.

Data were collected from 41 TB-reporting units nationwide, selected on the basis of their willingness to participate, the geographical location of the units (15 in the north, 13 in the centre, and 13 in the south and islands) and their features (17 outpatient units, 10 inpatient units, 14 in- and outpatient units). The network, with a catchment area of 20 million inhabitants, covered about one-quarter of all TB cases notified in Italy every year. Additional information on the TB units and on treatment outcomes is summarized in Table 1.

Forms, timeliness, and flow of reporting

All patients detected at the participating units from 1 January to 31 December 1995 were enrolled. Two notification forms were used to perform the economic analysis: (i) a quarterly report form on TB treatment results and examinations performed (aggregated data); and (ii) an individual form.

After the staff had received appropriate training, all completed forms were sent by participating units to both the coordinating centre (Tradate, Varese) and the area supervisors (north: *L.S.*, Novara; centre: *L.N.*, Firenze; south/islands: *B.F.*, Cagliari) at the completion of treatment on a quarterly basis, according to the WHO cohort analysis method to evaluate treatment results (8).

The form for aggregated data was based on the WHO standardized form (9). The individual form was designed to provide a complete profile of the patients enrolled and to evaluate the effectiveness of the intervention (diagnostic data, 14 items; follow-up data, 13 items; outcomes, 8 items).

Supervision

The participating units were directed on a monthly basis by the area supervisors and, if necessary, by the coordinating unit staff. A meeting of the principal investigators and coordinators was held on a quarterly basis. All errors or inconsistencies found in the forms were corrected during the supervisory visits.

General principles

The costs derived from the cohort study (Table 2; see Cost description for details) were applied in each scenario (see Scenarios for details).

A separate analysis was carried out for each scenario to determine the end-points. The future consequences of a wider application of outpatient care (reduced need for buildings and personnel time) was not evaluated in monetary terms. An exchange rate of US\$ 1 = 1720 Italian lire was used. All costs were adjusted for inflation as of 30 June 1997 (International Financial Statistics, 1997). TB case definitions and regimen abbreviations were in line with those recommended by WHO (10).

The role and cost of Calmette-Guérin bacillus (BCG) vaccination and chemoprophylaxis in preventing TB were not examined.

Cost description

Drug costs were based on prices approved by the Italian Ministry of Health in 1997 (1, 11-14). Costs were divided into fixed costs (buildings, diagnostic facilities, salaries, overhead) and variable costs (food, TB and non-TB drugs, examinations). All fixed and variable costs were calculated per bed day (BD) and per outpatient visit (OPV) in health units of different levels in 1997 to determine their average value. The equivalent annual cost was calculated amortizing the initial capital outlay over a useful life of 30 years (buildings) and 5 years (diagnostic facilities) (1). The gross salaries of health personnel were derived from the budget of each health facility evaluated, based on the national contract for health personnel (1 min with a chest physician = US\$ 0.402; 1 min with a nurse = US\$ 0.204) (15-17). The personnel time necessary to perform the different TB activities was derived from published standards (14, 15).

Overhead costs (heating, telephone, electricity, other examinations and services), calculated from the budgets of the different health facilities, were allocated based on the extent of floor space of the departments and laboratories concerned (1). The cost of TB and non-TB drugs was calculated separately in the model. The cost of examinations per BD and OPV was calculated by multiplying the unit cost of examinations by their number stratified by BD/OPV. The number and types of examinations performed in a single BD/OPV were derived from the individual data records of the database.

In each scenario fixed and variable costs were calculated separately for pulmonary smear-positive, smear-negative, and extrapulmonary patients.

Regimen categories

The regimen categories used in the model were as follows: new cases of smear-positive pulmonary TB and other newly diagnosed seriously ill patients with severe forms of TB (WHO category I); relapse, returning after default, and failure smear-positive TB patients (WHO category II); and new cases of smear-negative pulmonary TB and other newly diagnosed patients with TB not included in category I (WHO category III) (8).

Analysis of cost-comparison

End-point. Two scenarios were compared in terms of cost per case treated successfully (denominator: number of patients cured + treatment completed, according to the WHO definition) (18). The case-finding policy presently used in Italy (passive screening and active screening in high-risk groups) was used in both scenarios.

Scenarios

Scenario 1. This scenario represented the current policy of managing TB patients, based on available data, as derived from the first part of the study (mean

Table 1. Characteristics of TB units and treatment results of the baseline scenario, stratified by in- and outpatients, Italy, 1995

| | Inpatients | Outpatients |
|---|------------|-------------|
| Total no. of units | 24 | 17 |
| No. in catchment area (>100 000 population) | 18 | 15 |
| No. in catchment area (<100 000 population) | 6 | 2 |
| No. of patients | 365 | 317 |
| % of patients | 53.5 | 46.5 |
| Treatment success (%) | 73 | 95.2 |
| Deaths (%) | 7.1 | 0 |
| Failures (%) | 0.5 | 0.3 |
| Defaulters (%) | 12.3 | 3.8 |
| Transferred out | 7.1 | 0.7 |

values applied: smear-positive patients admitted for 2 months; smear-negative and extrapulmonary patients admitted for 1.5 months; total treatment duration 6.5 months, standardized treatment regimens prescribed for 88% of patients, no DOT outside hospital admission; see Cost description in Results for details).

Scenario 2. The second scenario (hypothetical) was more oriented towards outpatient care (50% of smear-positive patients and 10% of smear-negative or extrapulmonary cases admitted for 1 month, total treatment duration 6 months, standardized regimens prescribed for all patients).

In both scenarios the regimen was administered daily, and "no DOT" means no DOT outside hospital admission.

Options. The two scenarios were compared in the context of the following options: (i) no DOT; (ii) DOT for all patients, no additional staff (the number of patients receiving DOT in the different units does not justify additional staff); and (iii) DOT for all patients, additional staff (the number of patients receiving DOT in a single large unit justifies additional staff). To calculate the personnel-related

Table 2. Distribution of examinations performed during hospital stay and ambulatory treatment, number per BD and OPV and their unit cost among 992 TB patients, Italy, 1995

| Examination | Inpatients | | | Outpatients | | | Unit cost (US\$) |
|-----------------------|------------|--------------------|-----------------|-------------|--------------------|------------------|------------------|
| | Mean | Standard deviation | BD ^a | Mean | Standard deviation | OPV ^b | |
| Ambulatory visit | — | — | — | 4.26 | 2.29 | 0.024 | 44 |
| Laboratory visit | 5.65 | 9.07 | 0.11 | 7.26 | 4.67 | 0.042 | 6.5 |
| Chest X-ray | 3.98 | 4.42 | 0.078 | 3.28 | 2.29 | 0.019 | 69.7 |
| PPD test ^c | 0.42 | 0.49 | 0.082 | 0.54 | 0.54 | 0.031 | 6.1 |
| Direct smear | 3.33 | 3.33 | 0.065 | 5.91 | 6.79 | 0.034 | 5.1 |
| Culture | 2.46 | 2.50 | 0.048 | 5.88 | 6.71 | 0.034 | 10.3 |
| Fibrobronchoscopy | 0.11 | 0.34 | 0.002 | 0.03 | 0.18 | 0.00017 | 87.2 |
| Computer tomography | 0.14 | 0.37 | 0.0027 | 0.05 | 0.25 | 0.00029 | 290.7 |
| Other examinations | 0.12 | 0.40 | 0.0023 | 0.24 | 0.86 | 0.0014 | 116.3 |

^a BD = bed day.

^b OPV = out-patient visit.

^c PPD = purified protein derivative or tuberculin test.

cost needed to perform DOT on all patients, we multiplied the average nurse time by the number of patients. Total nurse time was divided by unit annual nurse time (95 040 minutes) to determine the number of additional nurses needed for DOT in the sample examined (1). Finally, the total cost of personnel gross salaries was divided by the number of directly observed treatment intakes expected. The cost of two home visits to 10% of patients was also included. For both options requiring DOT, the possibility of including or not including incentives for patients was explored (one meal, US\$ 5 per OPV) (19).

A final projection was made to evaluate the potential savings of scenario 2 over scenario 1 at the national level, by multiplying the unit savings obtained (separately for smear-positive, smear-negative, and extrapulmonary cases) by the total number of cases diagnosed in Italy in 1995 (1933 smear-positive, 1824 smear-negative, and 1404 extrapulmonary) (20, 21).

Perspective. In exploring the broader social perspective, indirect costs were added to the costs calculated from the perspective of the resource allocating authority using the human capital approach. Indirect costs were estimated according to the mean national monthly gross salary derived from the national statistics (11, 17), similar to the approach used in an economic study recently published in Italy (salary per day of work lost: US\$ 75) (14). Indirect costs were applied to patients admitted to hospitals in both scenarios. (In scenario 1, indirect costs were applied for the entire duration of the hospital stay. Scenario 2 assumed that no patient was allowed to work during the first 30 days of treatment.) Because the majority of patients who died (72%) were aged >65 years, the economic value of their deaths was not included in the model.

Sensitivity analysis

Sensitivity analysis was conducted on the variables when a result was uncertain to test the robustness of the study results (1). In particular, all fixed and variable costs determining the cost per case treated

successfully in scenario 2 were progressively increased (and those of the less cost-effective scenario 1 decreased) until a similar cost-effectiveness was obtained at different levels of success rate. The standard value of success rate applied in the model was 77.3% for smear-positive and 86.9% for smear-negative and extrapulmonary, corresponding to current outcomes in the sample studied, including both new and retreatment cases (16). In addition, the following percentages of success were included in the model: 90%, 80%, 70%, and 50%.

Statistical analysis

Data were stratified by smear and HIV serostatus, sex, and age groups (< 65 years and > 65 years). After verifying the data distribution, we compared the mean values of the variables using an unpaired *t* test. To make multiple comparisons we used the Bonferroni corrected *t* test. A *P* value <0.05 was considered to be statistically significant.

Results

Complete profiles were obtained for 682 patients, 365 admitted for the intensive phase and 317 treated on a fully ambulatory basis (Table 1).

Cost description. When all patients were considered, the mean length of treatment was 198.9 ± 87.9 days. No significant difference was observed between smear-positive and smear-negative or extrapulmonary patients. The mean length of ambulatory treatment was 171.6 ± 91.1 days. The mean length of hospital admission (calculated for patients who were admitted) was 51.1 ± 48.9 days. The length of hospital stay was significantly higher (*P* < 0.002) for smear-positive patients (6.31 ± 51.2 days) than for smear-negative or extrapulmonary patients (41.2 ± 44.7 days; *P* < 0.001). The length of hospital stay was significantly higher than the average value among HIV seropositive TB patients (82.4 days), whereas no difference was found for males (52.1 days) and older patients (52.3 days).

Table 3. Cost per case cured (US\$) in sputum smear-positive cases under different options and percentages of treatment success from the perspective of the funding agencies in scenario 1 (current policy, based on available data) and scenario 2 (hypothetical, more oriented towards outpatient care), Italy, 1995

| Option ^a | Success rate 50% | | Success rate 70% | | Success rate 77.3% ^b | | Success rate 80% | | Success rate 90% | |
|---------------------|------------------|--------|------------------|------|---------------------------------|------|------------------|------|------------------|------|
| | Scenario | | Scenario | | Scenario | | Scenario | | Scenario | |
| | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |
| 1 | 25 503 | 8799 | 18 173 | 6267 | 16 494 | 5690 | 15 973 | 5511 | 14 181 | 4893 |
| 2 | 25 827 | 9195 | 18 403 | 6552 | 16 703 | 5946 | 16 176 | 5759 | 14 362 | 5113 |
| 3 | 26 448 | 9954 | 18 846 | 7093 | 17 105 | 6437 | 16 565 | 6234 | 14 707 | 5535 |
| 4 | 27 177 | 10 845 | 19 365 | 7728 | 17 576 | 7014 | 17 021 | 6792 | 15 112 | 6030 |
| 5 | 27 798 | 11 604 | 19 808 | 8268 | 17 978 | 7505 | 17 410 | 7268 | 15 458 | 6452 |

^a 1 = No DOT; 2 = DOT, no additional staff, no incentives; 3 = DOT, additional staff, no incentives; 4 = DOT, no additional staff, incentives; 5 = DOT, additional staff, incentives.

^b Success rate currently observed in Italy (new + retreatment cases).

The mean length of treatment of patients ($n = 17$) treated on a fully ambulatory basis was 202.4 ± 65.8 days (there was no significant difference between smear-positive and smear-negative or extrapulmonary patients). The treatment outcomes of patients admitted or treated on a fully ambulatory basis are summarized in Table 1.

The average number of examinations performed and their unit cost are summarized in Table 2. The cost of TB drugs per day (derived from national health system prices) was as follows: smear-positive patients, initial phase: US\$ 1.70, continuation phase: US\$ 1.10; smear-negative or extrapulmonary patients, initial phase: US\$ 1.30, continuation phase: US\$ 1.10 (12).

The unit cost of 1 BD was US\$ 186.90. The unit cost of 1 OPV, according to the different options selected, was as follows: no DOT: US\$ 2.50; DOT, no additional staff: US\$ 3.70; DOT plus additional staff: US\$ 6; DOT plus incentives but no additional staff: US\$ 8.70; DOT plus additional staff plus incentives: US\$ 11.

Cost-comparison analysis. The cost per case cured from the perspective of the resource allocating authority is summarized in Table 2 (smear-positive cases) and Table 3 (smear-negative and extrapulmonary cases). The cost per case cured was consistently higher at each level of cure rate for scenario 1 compared with scenario 2.

According to current policy (no DOT, no incentives), the cost per case cured was as follows: scenario 1: US\$ 16 703 for smear-positive and US\$ 11 438 for smear-negative and extrapulmonary cases; scenario 2: US\$ 5946 for smear-positive and US\$ 2448 for smear-negative and extrapulmonary cases. The difference between the cheapest (no DOT) and the more expensive option (DOT, additional staff and incentives) ranged from US\$ 1407 (scenario 1, smear-negative and extrapulmonary cases) to US\$ 1814 (scenario 2, smear-positive cases).

The lowest cost was found for the "no DOT" option and the 90% success rate (scenario 1: US\$ 14 181 for smear-positive and US\$ 10 752 for smear-negative and extrapulmonary cases; scenario 2: US\$ 4892 for smear-positive and US\$ 2108 for smear-negative and extrapulmonary cases). The highest cost was found for the "DOT plus additional staff plus incentives" option and the 50% success rate (scenario 1: US\$ 27 797 for smear-positive and US\$ 21 923 for smear-negative and extrapulmonary cases; scenario 2: US\$ 11 603 for smear-positive and US\$ 6808 for smear-negative and extrapulmonary cases).

Considered from the broader social perspective, the additional cost per case cured (including indirect costs) was US\$ 4159 for smear-positive and US\$ 2792.20 for smear-negative and extrapulmonary cases in scenario 1; and US\$ 2079.90 and US\$ 1864.10, respectively, in scenario 2. From the perspective of the resource allocating authority, the potential savings achievable at the national level,

shifting from scenario 1 to scenario 2, ranged from US\$ 49.1 million (the "DOT plus additional staff plus incentives" option) to US\$ 50.6 million ("no DOT" option) a year.

Sensitivity analysis. Sensitivity analysis strongly supported the hypothesis that scenario 1 is more costly than scenario 2. At the mid-level of cure rate selected, the cost per case cured of scenario 1 approaches that of scenario 2 with the following adjustments:

- reducing the cost of 1 BD in scenario 1 to 26% or increasing the cost of 1 OPD in scenario 2 to 2150% (no DOT);
- reducing the cost of 1 BD in scenario 1 to 26% or increasing the cost of 1 OPD in scenario 2 to 930% (DOT without additional staff or incentives);
- reducing the cost of 1 BD in scenario 1 to 27% or increasing the cost of 1 OPD in scenario 2 to 670% (DOT plus incentives but without additional staff); and
- reducing the cost of 1 BD in scenario 1 to 28% or increasing the cost of 1 OPD in scenario 2 to 540% (DOT plus additional staff plus incentives).

The results were consistent when sensitivity analysis was performed applying the other percentages of success.

Discussion

The aim of our study was to analyse potential provider cost reductions through programme restructuring (22) by means of cost description, based on the present policy of treatment of TB patients in Italy and a cost-comparison analysis of two alternative programmes, the current policy based on available data (scenario 1) versus an hypothetical scenario more oriented towards outpatient care (scenario 2). The results of our study are outlined below.

- In Italy the mean treatment length was 6.6 months, the majority of TB patients were hospitalized during the intensive phase, and the length of hospital stay was significantly higher for smear-positive patients and HIV seropositives. On average, roughly six direct smear and culture examinations were performed during the hospital stay and about three over the course of ambulatory treatment. The cost of 1 BD was US\$ 186.90, whereas that of 1 OPV ranged from US\$ 2.5 to US\$ 11, depending on the different options.
- Scenario 1 was consistently more costly than scenario 2. Based on current project outcomes, the cost per case cured for smear-positive cases was US\$ 16 703 in scenario 1 and US\$ 5946 in scenario 2. The difference between the cheapest option (no DOT) and the most expensive option (DOT plus additional staff plus incentives) ranged between US\$ 1407 (scenario 1, smear-negative and extrapulmonary cases) and US\$ 1814 (sce-



nario 2, smear-positive cases). Considering the broader social perspective, the additional costs (including indirect costs) ranged from US\$ 1800 to US\$ 4200. The possible saving at the national level was about US\$ 50 million per year.

Although the study did not aim to evaluate the quality of treatment, there have been some indications of significant improvement in TB control in Italy in the recent past. In 1995, the duration of treatment was only slightly longer, and the percentage of treatment success slightly lower, than that suggested by internationally recognized standards (10, 20). This improvement may in part be attributed to the active role of the AIPO and the tuberculosis project of the Istituto Superiore di Sanità and the Ministry of Health (7). As expected, detailed analysis of admission policies revealed two distinct behaviours: the TB units that replaced the previous TB dispensaries (dismantled by law in 1978) were used to treat all patients, when possible, on a fully ambulatory basis (in our sample, 72 sputum smear-positive and 245 smear-negative and extrapulmonary cases), whereas the units equipped with beds (internal medicine, chest, or infectious disease departments) admitted patients during the intensive phase of treatment.

There are two plausible reasons for the lower cure rates observed in patients admitted:

- the majority of patients with problems (severe TB, low compliance, drug abuse, HIV serostatus, etc.) are hospitalized, and their subsequent poor performance brings down the overall rate; and
- after patients are discharged, hospital-oriented TB services face greater difficulties than do ambulatory services in making home visits and tracing defaulters (e.g. less experienced and dedicated staff, fewer contacts with leaders of immigrant communities, etc.).

In a recent study (Nutini et al., personal communication, 1998) findings from a questionnaire were used to estimate the mean hospital stay in a national sample of TB units in Italy, as follows: 39 days for smear-positive, 26 days for smear-negative, and 29 days for extrapulmonary TB cases. The fact that (i) in our study the hospitalization length was significantly lower for noninfectious TB patients and (ii) in Nutini's study (performed after the approval of the new disease-related groups (DRG) system to finance the health system) the hospitalization length had decreased demonstrates the progressive influence of economic constraints on hospital admitting policy in Italy.

An international comparison of our data and those of other industrialized countries was, unfortunately, not possible, since to the best of our knowledge published studies on this topic are available only for the USA (6).

The number of examinations performed (Table 1) is in general consistent with the national recommendations (bacteriological examinations at diagnosis and at 1, 2, and 6 months later; chest X-ray

at diagnosis, and at 2 and 6 months later; laboratory examinations at diagnosis and at 1 month later; at least a clinical follow-up visit on a monthly basis) (7), although the number of laboratory tests was still higher and that of microbiological tests lower than expected.

The cost of hospital admission was, as expected, the main determinant of the difference in cost between scenarios 1 and 2. Since the actual rates of hospitalization observed in the cohort study were used in the cost calculations, and the patients hospitalized are more severe, our results might be biased in favour of outpatient care.

Surprisingly, the cost increase observed in going from the no DOT option to the different DOT options (Table 2 and Table 3) did not exceed US\$ 1814 per case cured. This cost represented about one-fifth of the average savings that can be achieved, reducing the length of hospital stay (e.g. US\$ 10 473 was the difference between scenarios 1 and 2 under the most expensive outpatient option — DOT plus additional staff and incentives). Because the percentage of success achieved in Italy with virtually no DOT outside hospital admission approached the WHO target of 85%, the exact role of DOT in further improving cure rates was difficult to evaluate.

Individual data, including risk factors and treatment outcomes, have been available from the AIPO network since 1995, and multivariate analysis can therefore be used to identify predictors of default, in future selective uses of DOT in groups at higher risk.

We used current project outcomes to determine the standard value of success rates. Furthermore, a hypothetical success range of 50–90% was explored (Tables 1–4). In order to facilitate comparison of different scenarios, further studies are required to estimate success rates for each scenario individually.

Sensitivity analysis showed that scenario 2 was less costly over the entire range of cure rates explored. In particular, the difference in cost per case cured under the different options was not relevant in the success range 70–90% (Table 3 and Table 4), a reasonable range for Western European treatment programmes (6).

The present cost-comparison study, assessing resource inputs (costs) and the gains (effectiveness, explored in a wide range of hypothetical possibilities, including the observed success rates) of alternative programmes, assists decision-making by programme managers and policy-makers (1).

In a recent review article, economists agreed that the following elements constituted good practice in analyses of the type we have presented here (6): a clear statement of the alternatives compared; a detailed description of how cost and effects were evaluated; the use of marginal analysis; a statement of point of view; proper discounting; and sensitivity analysis.

Table 4. Cost per case cured (US\$) in sputum smear-negative and extrapulmonary cases under different options and percentages of treatment success from the perspective of the funding agencies in scenario 1 (current policy, based on available data) and scenario 2 (hypothetical, more oriented towards outpatient care), Italy, 1995

| Option ^a | Success rate 50% | | Success rate 70% | | Success rate 80% | | Success rate 86.3% ^b | | Success rate 90% | |
|---------------------|------------------|------|------------------|------|------------------|------|---------------------------------|------|------------------|------|
| | Scenario | | Scenario | | Scenario | | Scenario | | Scenario | |
| | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |
| 1 | 19 374 | 3799 | 13 829 | 2712 | 12 115 | 2376 | 11 230 | 2202 | 10 752 | 2108 |
| 2 | 19 734 | 4224 | 14 086 | 3015 | 12 340 | 2641 | 11 438 | 2448 | 10 952 | 2344 |
| 3 | 20 424 | 5038 | 14 579 | 3596 | 12 772 | 3151 | 11 838 | 2920 | 11 335 | 2796 |
| 4 | 21 234 | 5994 | 15 157 | 4279 | 13 279 | 3749 | 12 308 | 3474 | 11 785 | 3327 |
| 5 | 21 924 | 6809 | 15 560 | 4860 | 13 710 | 4258 | 12 708 | 3946 | 12 168 | 3779 |

^a 1 = No DOT; 2 = DOT, no additional staff, no incentives; 3 = DOT, additional staff, no incentives; 4 = DOT, no additional staff, incentives; 5 = DOT, additional staff, incentives.

^b Success rate currently observed in Italy (new + retreatment cases).

Our study satisfies all these criteria including marginal analysis if we consider, as suggested by Siegel et al. (23), that "third party" payments can be used as an approximation of marginal costs.

One limitation of our study is the methodology used to estimate indirect costs, since we aggregated possible individual losses of income into a lost production for the society as a whole. Further studies taking into consideration age and employability of TB patients, unemployment rate, and the marginal product of labour are warranted to clarify the issue in more detail.

A second limitation of the study design is that it is not possible to estimate the true effectiveness (treatment success) of scenario 2, which may of course limit any shift towards outpatient care of TB patients.

The methodology used was similar to that recently used in an economic analysis carried out in the Russian Federation (24), but our study had two main advantages: (i) the actual number of examinations (and not an estimate) performed nationwide was applied in the model; and (ii) the effectiveness (percentage of success) was measured on a significant sample and not estimated. In both studies, the cost of hospital admission, which is relevant for determining the less costly scenario, was calculated and not simply estimated using a "per diem" value.

Although in both studies the economic consequences of applying the less costly scenario were not examined in monetary terms, in the present study monetary terms are of limited relevance, since a significant proportion of our patients were already being treated on a fully ambulatory basis. Among nine economic studies analysed by Fryatt (6), only one compared self-administered versus directly observed treatment in a country with a low prevalence of TB (25, 26). Because DOT is currently used on a minority of TB patients in Italy, we have included different options for implementing it (with and without additional staff, with and without incentives) to add further elements useful for defining future policy at the national level.

In conclusion, our cost-comparison analysis showed that a relatively minor change in policy can produce significant savings (about US\$ 10 000 per patient, up to US\$ 50 million per year at the national level) and that adopting DOT will represent a relatively modest economic burden (approximately US\$ 1500 more per patient), although the real gain in effectiveness in Italy requires further study. ■

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Résumé

Analyse comparative des coûts de différentes politiques de traitement de la tuberculose en Italie

L'OMS préconise une stratégie de lutte antituberculeuse qui repose sur un dépistage rapide, généralement chez des sujets asymptomatiques qui se présentent d'eux mêmes aux services de santé, et sur l'administration, sous surveillance, d'un traitement chimiothérapeutique standardisé de brève durée, de préférence en ambulatoire. S'il a été démontré que le traitement de la tuberculose figure parmi les interventions sanitaires qui offrent le meilleur rapport coût-efficacité dans les pays en développement, le rapport coût-efficacité de la lutte antituberculeuse dans les pays où la prévalence de la maladie est faible n'a pas été souvent analysé.

L'objet de la présente étude était d'entreprendre en Italie, où l'on a récemment relancé la lutte antituberculeuse, une analyse économique conduite à la fois du point de vue de l'autorité pourvoyeuse des fonds (c'est-à-dire le Ministère de la Santé) et dans une perspective sociale plus vaste. A cette fin, on a d'une part établi une description du coût de la stratégie actuelle appliquée à un échantillon statistiquement significatif de malades dans l'ensemble du pays (hospitalisation et traitement sous surveillance directe au cours de la phase intensive de début), d'autre part effectué une analyse comparative du coût de deux options, à savoir (scénario 1) la stratégie actuelle reposant sur les données disponibles, et (scénario 2) une stratégie hypothétique davantage axée sur les soins en ambulatoire. Pour cela, on a comparé les coûts de ces deux stratégies par cas traité avec succès (nombre de malades guéris et de traitements menés à bien d'après la définition de l'OMS). Dans les deux scénarios, deux options étaient possibles : application ou non de la chimiothérapie sous surveillance directe en ambulatoire, et incitations. Les coûts indirects (perte de productivité, par exemple) ont été pris en compte pour l'analyse comparative conduite dans une perspective sociale plus vaste.

L'étude a été conçue comme une activité de surveillance prospective reposant sur la collecte, sous supervision, de formulaires auprès d'un échantillon représentatif d'unités de lutte antituberculeuse en Italie. On a recueilli et analysé des données sur chaque cas afin d'établir le profil économique des sujets de l'étude et d'évaluer l'efficacité des interventions. Pour chaque

scénario, on a procédé à une analyse distincte afin de déterminer le résultat pour divers taux de guérison (de 50 à 90%; d'après les valeurs standard actuelles, 77,3% pour les cas à frottis positif et 86,9% pour les cas à frottis négatif et extrapulmonaires).

Les résultats de l'étude ont été les suivants :

- La durée moyenne du traitement a été de 6,6 mois, la majorité des malades a été hospitalisée au cours de la phase intensive et la durée de l'hospitalisation a été sensiblement plus élevée pour les malades à frottis positif et pour les malades positifs pour le VIH. En moyenne, on a pratiqué environ six examens directs de frottis et de cultures au cours de l'hospitalisation et trois au cours du traitement en ambulatoire. Le coût de la journée d'hospitalisation était de US \$186,90 alors que celui d'une visite en consultation externe se situait, selon les différentes options, entre US \$2,50 et US \$11.
- Le coût du scénario 2 s'est révélé bien inférieur à celui du scénario 1. Le coût par cas à frottis positif traité avec succès était de US \$16703 dans le scénario 1 et de US \$5946 dans le scénario 2. La différence de coût entre l'option la moins coûteuse (pas de traitement ambulatoire sous surveillance directe) et l'option la plus coûteuse (traitement sous surveillance directe, personnel supplémentaire et incitations) se situait entre US \$1407 (scénario 1, cas à frottis négatif et extrapulmonaires) et US \$1814 (scénario 2, cas à frottis positif). Le coût supplémentaire (tenant compte des coûts indirects) établi dans une perspective sociale plus vaste se situait entre US \$1800 et US \$4200. Les économies susceptibles d'être dégagées au niveau national étaient de l'ordre de US \$50 millions par an.

L'analyse comparative des coûts a ainsi montré qu'une modification relativement mineure de la stratégie de traitement peut donner lieu à des économies importantes (environ US \$10 000 par malade et jusqu'à US \$50 millions par an au niveau national) et que le traitement ambulatoire sous surveillance directe ne représente qu'un fardeau économique relativement modeste (environ US \$1500 par malade), encore que le gain réel d'efficacité qu'il offre en Italie reste à évaluer.

Resumen

Análisis comparativo de los costos de distintas políticas de tratamiento de la tuberculosis en Italia

La OMS promueve una estrategia de lucha contra la tuberculosis (TB) basada en la detección rápida de los casos, fundamentalmente mediante la identificación de los afectados entre los pacientes sintomáticos que

acuden por propia iniciativa a los servicios de salud, y en la administración supervisada de quimioterapia normalizada de corta duración, preferiblemente en régimen ambulatorio. Aunque en los países en desarrollo el

tratamiento de los casos de tuberculosis se ha revelado como una de las intervenciones más eficaces en relación con el costo, son escasos los estudios efectuados acerca de la relación costo-eficacia de la lucha antituberculosa en los países de baja prevalencia de la enfermedad.

El objetivo del presente estudio consistió en realizar un análisis económico de esa índole en Italia — donde recientemente se había revitalizado la lucha contra la tuberculosis— tanto desde la perspectiva de la autoridad asignadora de recursos (esto es, el Ministerio de Salud) como desde el punto de vista de las repercusiones sociales generales. El estudio incluye *i*) una descripción de los costos correspondientes a la aplicación de la actual política a una muestra estadísticamente significativa de enfermos tuberculosos a escala nacional (ingreso y tratamiento bajo observación directa (DOT) durante la fase intensiva inicial del tratamiento); *ii*) un análisis comparativo de los costos de dos programas alternativos: la política actual basada en los datos disponibles (escenario 1), y una política hipotética más orientada a la atención ambulatoria (escenario 2); se procedió a comparar una y otra en lo que atañe al costo por caso tratado con éxito (lo que incluye a los pacientes curados y a los que acaban el tratamiento, según la definición de la OMS). En los dos escenarios existía la posibilidad de incluir o no el DOT fuera del hospital, así como de usar incentivos. A la hora de determinar las repercusiones sociales generales, el análisis de comparación de costos incluyó los costos indirectos (como la pérdida de productividad).

El estudio se concibió como un proceso de vigilancia prospectivo a partir de una recopilación supervisada de formularios de una muestra representativa de unidades antituberculosas italianas. El análisis de los datos individuales reunidos permitió obtener un perfil económico completo de los pacientes implicados y evaluar la eficacia de la intervención. Se analizó por separado cada escenario para determinar la variable de evaluación a diversas tasas de curación (50-90%; las

tasas corrientes eran de 77,3% para los pacientes con frotis positivo y de 86,9% para los pacientes con frotis negativo y tuberculosis extrapulmonar).

A continuación se resumen los resultados del estudio.

- En Italia la duración media del tratamiento era de 6,6 meses, la mayoría de los enfermos tuberculosos eran hospitalizados durante la fase intensiva, y la duración de la estancia hospitalaria era considerablemente mayor en los pacientes con frotis positivo y en los VIH-positivos. Como promedio, se efectuaban aproximadamente seis exámenes de frotis directo y de cultivos durante la estancia hospitalaria, y tres durante el tratamiento ambulatorio. El costo diario de una cama de hospital era de US\$ 186,90, mientras que el de una visita ambulatoria ascendía, según la opción, a entre US\$ 2,50 y US\$ 11.
- El escenario 2 fue sistemáticamente más económico que el escenario 1. Actualmente, el costo por caso con frotis positivo curado es de US\$ 16 703 en el escenario 1, y de US\$ 5946 en el escenario 2. La diferencia de costo entre la opción más barata (sin DOT) y la más cara (DOT, personal adicional e incentivos) osciló entre US\$ 1407 (escenario 1, casos con frotis negativo y extrapulmonares) y US\$ 1814 (escenario 2, casos con frotis positivo). Los costos sociales adicionales (incluidos los costos indirectos) se situaron entre US\$ 1800 y US\$ 4200. Las posibles economías a nivel nacional fueron del orden de US\$ 50 millones anuales.

Así pues, el análisis de comparación de costos muestra que un ligero cambio de la política puede traducirse en economías importantes (unos US\$ 10 000 por paciente, hasta US\$ 50 millones al año a nivel nacional) y que la adopción del DOT supone una carga económica relativamente discreta (aproximadamente US\$ 1500 por paciente); no obstante, es necesario seguir evaluando el aumento real de eficacia asociado al DOT en Italia.

References

1. **Drummond MF, Stoddart GL, Torrance GW.** *Methods for the economic evaluation of health care programmes.* Oxford University Press, Oxford, 1989.
2. **Raviglione MC et al.** Secular trends of tuberculosis in Western Europe. *Bulletin of the World Health Organization*, 1993, **71**: 297–306.
3. **Raviglione MC, Snider E, Kochi A.** Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. *Journal of the American Medical Association*, 1995, **273**: 220–226.
4. **WHO Tuberculosis Programme.** *Framework for effective tuberculosis control.* Geneva, World Health Organization, 1994 (Unpublished document WHO/TB/94-179: 1–13).
5. **Murray CJL, Styblo K, Rouillon A.** Tuberculosis in developing countries: burden, intervention, and cost. *Bulletin of the International Union against Tuberculosis and Lung Disease*, 1990, **65**: 2–20.
6. **Fryatt RJ.** Review of published cost-effectiveness studies on tuberculosis treatment programmes. *International journal of tuberculosis and lung disease*, 1997, **2**: 101–109.
7. **Migliori GB et al.** Evaluation of the impact of guidelines on tuberculosis control in Italy. *Monaldi archives for chest disease*, 1996, **51**: 204–209.
8. *Tuberculosis surveillance and monitoring.* Geneva, World Health Organization, 1991 (Unpublished document WHO/TB/91.163: 1–18).
9. **WHO Tuberculosis Programme.** *Managing tuberculosis at district level. A training course.* Module A5. Geneva, World Health Organization, 1994.
10. **WHO Global Tuberculosis Programme.** *Treatment of tuberculosis. Guidelines for national programmes.* Geneva, World Health Organization, 1997 (Unpublished document WHO/TB/97.220: 1–77).
11. [Annual Report, State of Italy, 1993]. Italian Institute of Statistics (ISTAT), Rome, 1994 (in Italian).
12. **Migliori GB et al.** Economical aspects of tuberculosis control in Italy. *Rassegna di Patologia dell'Apparato Respiratorio*, 1994, **S/1**: 67–70.

13. [Practical guide for determination of tariffs. Analysis: policy, management and health organizations]. *Notiziario SNABI*, 1995, **7**: 274–304 (in Italian).
14. **Neri M et al.** Economic analysis of two structured treatment and teaching programs on asthma. *Allergy*, 1996, **51**: 313–319.
15. **Arossa W, Petrozzi L, Colorizio V.** Working proposal for chemoprophylaxis, vaccination, and contact tracing management. *Rassegna di Patologia dell'Apparato Respiratorio*, 1994, **9/S1**: 45–47.
16. **Ambrosetti M et al.** Tuberculosis treatment results in Italy (1995–1996). *International journal of tuberculosis and lung disease*, 1997, **5**: S71
17. *Introducing Italy, 1994*. Rome, Italian Institute of Statistics (ISTAT), 1994.
18. **Veen J et al.** Standardised treatment outcome monitoring in Europe. Recommendations of the Working Group of WHO and IUATLD. *Third European Workshop on Tuberculosis Control in Low Prevalence Countries, Noordwijk, Netherlands, 15–20 June 1997*.
19. **Salomon N et al.** Implementation of universal directly observed therapy at a New York City hospital and evaluation of an outpatient directly observed therapy program. *International journal of tuberculosis and lung disease*, 1997, **5**: 397–404.
20. **WHO Global Tuberculosis Programme.** *Global tuberculosis control. WHO report 1997*. Geneva, World Health Organization, 1997 (Unpublished document WHO/TB/97.225).
21. **EuroTB (CESES/KNCV) and the national coordinators for tuberculosis surveillance in the WHO European Region.** *Surveillance of tuberculosis in Europe. Report on the feasibility study (1996–1997). Tuberculosis cases notified in 1995*. Saint-Maurice, France, European Centre for the Epidemiological Monitoring of AIDS (CESES), 1997.
22. **Barnum NH.** Cost savings from alternative treatments for tuberculosis. *Social science and medicine*, 1986, **23**: 847–859.
23. **Siegel JE et al.** Recommendations for reporting cost-effectiveness analyses. *Journal of the American Medical Association*, 1996, **176**: 1339–1341.
24. **Migliori GB et al.** Cost-effectiveness analysis of different policies of tuberculosis control in Ivanovo Oblast, Russian Federation. *Bulletin of the World Health Organization*, 1998, **76**: 475–483.
25. **Cohn DL et al.** A 62-dose therapy for pulmonary and extra-pulmonary tuberculosis. A twice-weekly directly observed, and cost-effective regimen. *Annals of internal medicine*, 1990, **112**: 407–415.
26. **Iseman MD, Cohn DL, Sbarbaro JA.** Directly observed treatment of tuberculosis. We can't afford not to try it. *New England journal of medicine*, 1993, **328**: 576–578.