COST SAVINGS FROM ALTERNATIVE TREATMENTS FOR TUBERCULOSIS

by

Howard N. Barnum

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Population, Health and Nutrition Department
World Bank

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ABSTRACT

The cost effectiveness of short course tuberculosis treatment regimes using Rifampicin (R) or Ethambutol (E) is calculated and compared to long course regimes based on Thiacetazone and Isoniazid (TH). Although Rifampicin and Ethambutol are more costly per case treated they are only about one-half the cost of Isoniazid based regimes per person effectively treated. This result is primarily derived from higher patient compliance with the short course regimes. In addition, ambulatory treatment, where practical, is approximately one-third the cost per person effectively treated of combined regimes using initial two-month inpatient and subsequent outpatient care. Applied to 1982 data for Botswana, the analysis reveals that treating 80% of patients through ambulatory R and E regimes would have reduced total health expenditures for tuberculosis care by two-thirds compared to inpatient regimes based on TH, and the number of people complying and cured would have doubled.

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Introduction

This paper estimates the cost effectiveness of tuberculosis treatment in Botswana using short treatment regimes based on the antimycobacterial drugs, Rifampicin or Ethambutol, compared to long treatment based on Isoniazid. The cost effectiveness of Rifampicin and Ethambutol is not self evident given that Isoniazid is, currently, only a fraction of the cost of the short treatment drugs. For example, a current reference manual for tropical diseases [5] states,

"Rifampicin is a bactericidal agent whose effectiveness and safety approximate that of isoniazid, but whose use in developing countries has been limited by high cost.", and

"Ethambutol is an effective and well tolerated bacteriostatic agent", but, "relatively high cost has limited the use of this agent in many parts of the world."

However, the relatively high cost of Rifampicin and Ethambutol should not preclude their use in developing countries because treatment regimes based on these drugs may be less costly per unit of effect. The relative cost effectiveness of a treatment is related to (a) achieving higher compliance

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rates with the short term treatments and (b) substitution of ambulatory for inpatient care, and, to a lesser extent, on (c) the slightly higher bacteriological effectiveness of Ethambutol and Rifampicin. All of these factors can vary by community depending on customs, attitudes, health care practices, the operational environment, transport, and the prevalence of resistant strains [17]. Thus, cost effectiveness must be examined in the context of a given program. In this paper an analysis of a newly introduced program in Botswana is carried out based on estimates of compliance behavior, practicality of using ambulatory care, bacteriological effectiveness and program costs.

Tuberculosis is a major health problem in Botswana with an incidence of 2.87 cases per thousand population and a total of 2705 notified cases in 1982 [2]. Prior to 1984 treatment of tuberculosis used an average of 90 days of inpatient care per case treated and annually absorbed nearly 20% of total government expenditures on institutional health care [18]. In 1984 the government began implementation of a revised treatment program to reduce the cost of treatment through the replacement of inpatient with outpatient care and the use of alternative drugs having a shorter treatment period. The change in treatment is made possible by appropriate field worker training that will allow the entire treatment to be given as ambulatory care to eighty percent of TB patients. The remaining twenty percent of patients, either because of the severity of the infection or the distance lived from the treatment center, will continue to be given at least 2 months of inpatient therapy.

Analysis of the cost savings from the revised treatment of tuberculosis proceeds by first specifying the alternative treatment regimes, then
identifying the most cost effective regimes and, finally, calculating the difference in total cost between the current regime and the cost effective alternative.

**Alternative Treatment Regimes**

There are three drug treatment alternatives to be evaluated\(^1\). First is the use of streptomycin (S) and a combination (TH) of thiacetazone and isoniazid for two months, followed by sixteen months of TH alone. Second is the use of streptomycin (S), isoniazid (H), rifampicin (R) and pyrazinamide (Z) during the first two months followed by six months of H and ethambutol (E) alone. Third is the use of SHRZ during the first two months (as under the second alternative) followed by four months of HR alone. Each of these alternatives can be carried out through either two months of inpatient care while the daily streptomycin injections take place with the remainder of the treatment being given as outpatient care, or entirely as outpatient care. This gives a total of (3x2=) 6 alternative regimes. In addition, we evaluate as a seventh regime the practice, being supplanted by the new program in Botswana starting from 1984, of using an average of three months inpatient care (STH) followed by 15 months of ambulatory care (TH).

**Compliance**

Compliance has been a serious problem with the Botswana TB program. Of all patients starting a course of treatment approximately 20% have dropped

\(^1\)The bacteriological effectiveness of these treatments has been extensively examined in the literature [4,6,7,9,13].
out after 6 months, 40% after 12 months, and 50% after 18 months. This low level of compliance accords with observations from programs in other countries. For example, the twelve month default rate for tuberculosis treatment has been estimated to be approximately 60% in Kenya and 90% in Ethiopia [16]. A failure to complete and comply with treatment has been identified as one of the most serious difficulties in implementing effective treatment programs [5,8,11]. Common reasons for premature discontinuation of therapy are behavioral or environmental in basis and include patient perceived clinical improvement, lack of transportation, other illness or injury, or work inconvenience. Very few patients discontinue treatment because of drug intolerance or lack of improvement on therapy. Shorter treatment programs have been demonstrated to have lower failure rates from behavior based non compliance [3,15].

The reduced compliance with longer programs must be taken into account in an evaluation of costs. The compliance behavior can be closely modeled by use of the formula

\[ N_t = d_0 e^{-d_1(t-s)} \]

where \( N_t \) is the proportion of patients still complying with the treatment after \( t \) months, given that ambulatory treatment is started in month \( s \). This formula, giving compliance as a declining exponential, has been used satisfactorily in the evaluation of family planning programs and other health activities where patient adherence to a specified regime is a function of time [1,14]. Compliance behavior for the Botswana program, can be approximated with the parameters \( d_0 \) and \( d_1 \) set to 1 and .04.
Costs

The cost of each regime can be calculated by an accounting of inpatient costs \( c_1 \), outpatient costs \( c_A \), drug costs \( c_S, c_{TH}, c_H, c_R, c_Z, c_E \) and the cost of X-ray \( c_X \) and sputum \( c_L \) tests. Costs include personnel time, material and supplies, transport, drugs and annualized value of equipment.

The cost of the separate elements of treatment were obtained from analysis of the records of the Central Medical Stores and Princess Marina Hospital in Botswana. Dropout behavior can be incorporated by multiplying the monthly cost per person starting treatment by the dropout factor, \( N_t^{-1} \).

Table 1
BOTSWANA: Unit Costs Related to Alternative Tuberculosis Treatments
(Pula, 1983 Pricesa)

<table>
<thead>
<tr>
<th>Description</th>
<th>Notation</th>
<th>Cost (Pula)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. UNIT COSTS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost/day ( b/ ) of streptomycin (1 g)</td>
<td>( C_S )</td>
<td>.120</td>
</tr>
<tr>
<td>&quot; &quot; thiacetazone (150 mg) and</td>
<td>( C_{TH} )</td>
<td>.009</td>
</tr>
<tr>
<td>isoniazid (300 mg)</td>
<td>( C_H )</td>
<td>.004</td>
</tr>
<tr>
<td>&quot; &quot; isoniazid (400 mg)</td>
<td>( C_E )</td>
<td>.107</td>
</tr>
<tr>
<td>&quot; &quot; ethambutol (25 mg/kg body weight)</td>
<td>( C_R )</td>
<td>.322</td>
</tr>
<tr>
<td>&quot; &quot; pyrazinamide (2 g)</td>
<td>( C_Z )</td>
<td>.270</td>
</tr>
<tr>
<td>Cost per X-ray ( c/ )</td>
<td>( C_X )</td>
<td>1.60</td>
</tr>
<tr>
<td>Cost per sputum test</td>
<td>( C_L )</td>
<td>1.32</td>
</tr>
<tr>
<td>Cost per inpatient day</td>
<td>( C_I )</td>
<td>14.50</td>
</tr>
<tr>
<td>Cost per ambulatory visit</td>
<td>( C_A )</td>
<td>4.10</td>
</tr>
</tbody>
</table>

\( a/ \) 1 Pula = US$(0.93).

\( b/ \) For an average adult of 50 kg weight.

\( c/ \) Cost per X-ray is P 3.20. Only 50% of those treated have access to X-ray facilities.
Given the cost of drugs, inpatient and outpatient care and X-rays and laboratory tests as summarized in Table 1, the cost per person starting each of the alternative regimes can be computed. For example, the cost of regime #1 (2 months of inpatient care using STH and 16 months of outpatient care using TH) can be represented as

$$C_1 = 60 (c_I + c_S + c_{TH}) + c_L + \sum_{t=3}^{18} B_{1t}$$

where

$$B_{1t} = (c_A + 30 c_{TH}) N_t + c_L N_t$$

on $t=4, 8, 12, 18$ on $t=12, 18$

Similar expressions were derived for regimes #2 through #7 and a computer program was used to calculate the costs. Cost per person treated for each regime are summarized in the next to last column of Table 2.

Cost effective Tuberculosis Treatment

The least expensive regime per case identified and starting treatment is #4 which uses the cheapest drugs and has the longest treatment period. However, because of bacterial adaptation to the drugs used and the high dropout rate over the long treatment period, the regime is not necessarily the least costly per case successfully treated.

Bacterial resistance to streptomycin and thiacetazone has lowered the cure rate for regimes #1, #4 and #7 to approximately .7, while the cure rate for regimes #2, #3, #5 and #6 using ethambutol or rifampicin is .9. The long treatment period for regimes #1, #4 and #7 results in fewer than 50% of people receiving treatment throughout the full 18 months required. In contrast, 85% of patients receiving the six-month treatment (regimes #3 and #6) are expected to complete the full course. The differentials in dropout
rates and cure rates are reflected in an expression of the cost effectiveness of the \( i^{th} \) regime, measured by the cost per person successfully treated, as

\[
CE_i = \frac{C_i}{r_i N_T}
\]

where \( r \) represents the cure rate and \( N_T \) represents the proportion of persons starting treatment that comply and continue treatment over the full period of \( T \) months. Estimates of cost effectiveness are given in column 4 of Table 2.

<table>
<thead>
<tr>
<th>Regime No.</th>
<th>Description (months of treatment and drug used)</th>
<th>Cost per person treated</th>
<th>Cost per person effectively treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2 mo. inpatient (STH), 16 mo. outpatient (TH)</td>
<td>938</td>
<td>2441</td>
</tr>
<tr>
<td>2.</td>
<td>2 mo. inpatient (SHRZ), 6 mo. outpatient (HE)</td>
<td>958</td>
<td>1301</td>
</tr>
<tr>
<td>3.</td>
<td>2 mo. inpatient (SHRZ), 4 mo. outpatient (HR)</td>
<td>968</td>
<td>1213</td>
</tr>
<tr>
<td>4.</td>
<td>2 mo. outpatient (STH), 16 mo. outpatient (TH)</td>
<td>306</td>
<td>863</td>
</tr>
<tr>
<td>5.</td>
<td>2 mo. outpatient (SHRZ), 6 mo. outpatient (HE)</td>
<td>323</td>
<td>475</td>
</tr>
<tr>
<td>6.</td>
<td>2 mo. outpatient (SHRZ), 4 mo. outpatient (HR)</td>
<td>337</td>
<td>457</td>
</tr>
<tr>
<td>7.</td>
<td>3 mo. inpatient (STH), 15 mo. outpatient (TH)</td>
<td>1374</td>
<td>3437</td>
</tr>
</tbody>
</table>

\( ^a \)Drug Abbreviations: S = Streptomycin  
TH = Thiacetazone and Isoniazid  
H = Isoniazid  
E = Ethambutol  
R = Rifampicin  
Z = Pyrazinamide

The most cost effective treatment is #6 using rifampicin (R) and having a treatment period of 6 months. Treatment #5, using ethambutol (E) and having a treatment period of 8 months follows closely in cost effectiveness. Although the cost of regime #4 is P 306 per person starting treatment as
opposed to P 337 for regime #6, the cost per person successfully completing treatment using #6 is only 53% of the cost per unit of effect for treatment #4.

All of the least costly treatments are given entirely through ambulatory care. Where inpatient care is necessary, the least costly treatment per unit of effect remains that using rifampicin. Regime #3, using R and 2 months of inpatient care, is less than 50% of the cost per unit of effect of regime #1 using STH and including two months of inpatient care. It is notable that all 6 alternative regimes are substantially less expensive than the pre 1984 practice, characterized by regime #7. Regime #7 is over four times the cost of the most cost effective alternative.

Cost Savings from Adoption of New Tuberculosis Treatment

In 1982 there were 2705 notified TB cases receiving treatment. At a cost of P 1374 per case under the current treatment practice (#7) the total cost to the MOH was P 3,716,700. If the most cost effective outpatient care (regime #6) had been given to eighty percent of notified cases and the most cost effective inpatient care (regime #3) given to the remaining twenty percent requiring hospitalization, the cost of treating the 2705 notified cases would have been reduced to P 1,253,000 resulting in a cost savings (or value of resources released for other uses) of P 2,463,700. In addition the number of people successfully completing treatment and cured would have increased from 1080 to 2100 using the improved regimes.

These results are sensitive to the assumption that the improved outpatient treatment could be given to eighty percent of the notified cases and improved inpatient care to the remaining twenty percent. If
difficulties in implementation arise that restrict the improved outpatient care to only 48% of notified cases and the improved inpatient care to 12% of the cases, with the remaining 40% treated under the current practice (regime #7), the cost savings would be reduced to P 1,500,000. Thus, even if the improved regimes are available to only sixty percent of the population, the cost savings would be substantial.
BIBLIOGRAPHY


