Patient and family costs associated with tuberculosis, including multidrug-resistant tuberculosis, in Ecuador

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SUMMARY

BACKGROUND: There is little published information on the costs of multidrug-resistant tuberculosis (MDR-TB) for patients and their families in low- or middle-income countries.

METHODS: Between February and July 2007, patients with microbiologically confirmed active TB who had received 2 months of treatment completed an interviewer-administered questionnaire on direct out-of-pocket expenditures and indirect costs from lost wages. Clinical data were abstracted from their medical records.

RESULTS: Among 104 non-MDR-TB patients, total TB-related patient costs averaged US$960 per patient, compared to an average total cost of US$6880 for 14 participating MDR-TB patients. This represents respectively 31% and 223% of the average Ecuadorian annual income. The high costs associated with MDR-TB were mainly due to the long duration of illness, which averaged 22 months up to the time of the interview. This resulted in very long periods of unemployment. Most patients experienced a significant drop in income, particularly the MDR-TB patients, all of whom were earning less than US$100/month at the time of the interview.

CONCLUSION: Direct and indirect costs borne by patients with active TB and their families are very high in Ecuador, and are highest for patients with MDR-TB. These costs are important barriers to treatment completion.

KEY WORDS: multidrug-resistant tuberculosis; MDR-TB; economic impact; patients’ costs
fees are waived, although they must continue to pay for tests other than acid-fast bacilli smears, and for treatment other than TB medications. If hospitalized, patients also pay for diagnostic tests and treatment, as well as per diem fees, although the per diem fees are waived if they are diagnosed with active TB.

Within Guayas we selected 22 clinics, representing 55% of all Ministry of Health clinics in the province. These were both rural and urban, to ensure a more representative patient sample, but did not include the more remote clinics because of limited funds for transportation. At these clinics, all patients who had started initial or retreatment therapy for active TB between 6 to 12 weeks earlier, or were on treatment of any duration for confirmed MDR-TB, were approached to participate.

Data collection
Consenting patients completed an interviewer-administered questionnaire in Spanish on direct and indirect expenses from the time of onset of TB symptoms until the interview. Clinical data and information on previous treatment were abstracted from their medical records. Patients were considered to have confirmed MDR-TB if drug susceptibility testing (DST) showed resistance to at least isoniazid (INH, H) and rifampin (RMP, R). In Ecuador, DST is performed only for patients who have failed or relapsed after standardized retreatment. Patients treated with the standardized initial or retreatment regimens therefore do not undergo DST; these are defined as non-MDR patients.

The questionnaire was initially adapted from a World Bank questionnaire addressing the economic impact of adult fatal illness, and modified for TB and used in TB cost studies in Canada, the United States, Haiti, and Dominican Republic,7,19 and subsequently in seven other countries.11,20,21 The interviewer (VAR) received standardized training on questionnaire administration.

The questionnaire asked about out-of-pocket expenditures for any health services or for accessing these services, such as travel costs, registration and paperwork fees, consultation fees, costs for blood tests, medications, X-ray examinations, food, or any other expenses. The questionnaire also asked about patients’ lost income due to disability, unemployment due to illness, time spent waiting for or receiving care, and time for travel to clinics or hospitals. During hospitalization, patients were assumed to have lost 8 potential work hours per day. Indirect costs also included the time spent by family members accompanying patients on out-patient visits, or in hospital.

The questionnaire was organized into three main sections: in the first section, patients were asked about costs incurred from the time of the first health encounter with any provider, including nurse, physician, or pharmacist, up to the time of the start of treatment (pre-treatment period). This included physician fees, laboratory or radiologic tests, and medications for which the patients had to pay. The second section covered costs incurred from the start of treatment up to the time of the interview (treatment period). This included visits for medical follow-up evaluations, as well as those required for taking DOT. The third section enquired about the impact on income, loans, additional help paid for, and other impacts throughout the course of illness.

All patients with confirmed MDR-TB had previously been treated for TB. For these patients, the interval between the onset of TB-related symptoms and questionnaire completion ranged from 12 to 27 months, limiting the accuracy of recall of costs related to these earlier episodes of TB. These patients therefore did not complete the pre-treatment section of the questionnaire.

Ethics
The study was approved by an ethics committee of the McGill University Health Centre Research Institute, and by the director of the TB control program of the Province of Guayas, Ecuador.

Data analysis
Data were entered into Microsoft Access XP (Microsoft, Redmond, WA, USA). Statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC, USA).

Costs were calculated for the two main phases of the illness, pre-treatment and treatment, as defined above. Sub-totals and totals for each type of cost were calculated as the product of the patient-reported cost parameter (e.g., consultation fee) and frequency (e.g., number of clinic visits). For each patient, the total number of hours spent traveling, waiting, receiving health services, hospitalized, disabled, or unemployed due to TB illness were summed to provide an estimated total hours of work lost. Indirect costs were estimated by multiplying this total by the estimated average hourly wage in Ecuador, using methods previously described and justified elsewhere.7,11,19–21 In brief, the hourly wage was calculated from the average per capita gross national income in Ecuador22 divided by 2496 h worked per year (48 h per week for 52 weeks). All costs are reported in 2007 $US (the official currency of Ecuador since 2001). Pre-treatment costs of MDR-TB patients were calculated by multiplying the number of previous treatment episodes times the average total costs for the diagnosis and treatment of non-MDR-TB patients.

RESULTS
In total, 14 patients with MDR-TB and 104 patients without MDR-TB were interviewed between February
and July 2007. These represented all patients with MDR-TB (at any stage of treatment), and all other TB patients who had been on treatment for 1–3 months at the time the interviewer visited the selected clinics. All 14 MDR-TB patients had smear-positive *Mycobacterium tuberculosis*, as did all but one of the non-MDR-TB patients. As seen in Table 1, 71% of the MDR-TB patients were female, with a mean age of 38 years (range 18–51). Of the non-MDR-TB patients, 38% were female, with a mean age of 34 years (range 14–68). A significant proportion of patients had comorbid illnesses, with HIV/AIDS (human immunodeficiency virus/acquired immune-deficiency syndrome) and diabetes being the most common conditions.

Three MDR-TB patients had received an unknown initial treatment regimen from a private provider, following which they received the World Health Organization (WHO) recommended standardized initial treatment regimen (2HRZE/4H3R3), followed by the WHO standardized retreatment regimen (2HRZES/1HRZE/5H3R3).  

Among non-MDR-TB patients, the average interval from onset of patient symptoms and first encounter with any health service, including government health center, pharmacy or private clinic (patient delay) was 3.7 months, while the average interval from the first visit to the diagnosis of TB (health system delay) was an additional 2 months. For MDR-TB patients, the average total duration of TB illness from onset of first symptoms until the start of therapy was 22 months. This included a delay of 4.5 months between presentation for care of the current TB illness episode and initiation of MDR-TB therapy. Most of this health system delay was due to delays in receiving laboratory results confirming MDR-TB.

Of the non-MDR-TB patients surveyed, 47 (45%) were earning US$100–500/month before the TB diagnosis, which was 43% of the MDR-TB patients were earning US$100–500/month, and one (7%) >US$500/month before the first TB diagnosis. Many patients experienced an important drop in income during their TB illness; 84% of non-MDR-TB patients and 100% of MDR-TB were earning <US$100/month at the time of the interview (Table 2). This was mainly due to unemployment from direct disability or the

Table 1  Demographic, socio-economic and clinical characteristics of patients studied

<table>
<thead>
<tr>
<th></th>
<th>Non-MDR-TB patients (n = 104)</th>
<th>Confirmed MDR-TB patients (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male 64 (62) Female 40 (39)</td>
<td>Male 4 (29) Female 10 (71)</td>
</tr>
<tr>
<td>Age, years</td>
<td>18–24 19 (18) 25–34 33 (32)</td>
<td>18–34 18 (17) 35–44 29 (28)</td>
</tr>
<tr>
<td>Form of TB</td>
<td>Pulmonary smear-positive 103 (99)</td>
<td>Pulmonary smear-negative 1 (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extra-pulmonary 0</td>
</tr>
<tr>
<td>Classification of treatment history</td>
<td>New case 84 (81)</td>
<td>Retreatment, default 3 (3)</td>
</tr>
<tr>
<td></td>
<td>Retreatment, failure 2 (2)</td>
<td>Retreatment, relapse 15 (15)</td>
</tr>
<tr>
<td>Comorbid illnesses</td>
<td>None 44 (42)</td>
<td>Any 60 (58)</td>
</tr>
<tr>
<td>Household size, persons</td>
<td>Alone 8 (8)</td>
<td>2–3 21 (20)</td>
</tr>
<tr>
<td>Education</td>
<td>None 4 (4)</td>
<td>Primary school 39 (38)</td>
</tr>
<tr>
<td>Current employment status</td>
<td>Employed 40 (38)</td>
<td>Unemployed 64 (62)</td>
</tr>
</tbody>
</table>

MDR-TB = multidrug-resistant TB; TB = tuberculosis; HIV = human immunodeficiency virus; AIDS = acquired immune-deficiency syndrome.

Table 2  Changes in personal income from before TB diagnosis up to the time of the interview

<table>
<thead>
<tr>
<th>Monthly income pre-diagnosis, US$</th>
<th>Current monthly income, US$</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>48* 1* 0* 1</td>
</tr>
<tr>
<td>100–500</td>
<td>35† 12* 0* 0</td>
</tr>
<tr>
<td>500–1000</td>
<td>3† 1† 0* 0</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>0† 0† 2† 0</td>
</tr>
<tr>
<td>MDR-TB patients</td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>7* 0* 0* 0</td>
</tr>
<tr>
<td>100–500</td>
<td>6† 0* 0* 0</td>
</tr>
<tr>
<td>500–1000</td>
<td>1† 0† 0* 0</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>0† 0† 0† 0</td>
</tr>
</tbody>
</table>

* No change or increase.
† Decrease in income.

Z = pyrazinamide; E = ethambutol; S = streptomycin. Numbers before the letters indicate the duration in months of the phase of treatment; numbers in subscript indicate the number of times the drug is taken each week.
recommendation of their physician, or due to being fired because of the TB diagnosis.

Information about costs incurred by patients prior to their first diagnosis of TB could only be collected for non-MDR patients (Table 3), because this period was too long ago for MDR patients to recall many details. The majority of patients’ pre-diagnosis costs were related to hospitalization before active TB was recognized. As seen in Table 4, the largest sources of direct costs for MDR patients were for non-TB medications (vitamins, antacids, anti-nausea), and travel for clinic-based DOT, which accounted for respectively 41% and 33% of direct costs during the treatment period. In total, non-MDR patients incurred average costs of $960 compared to $6880 for MDR-TB patients, i.e., more than seven times higher (Table 5). These totals were equivalent to respectively 31% and 22.3% of the average annual per capita income in Ecuador. The greatest economic losses came from lost income related to time not working, accounting for 85% of the total costs for the confirmed MDR patients, compared to 60% of total costs for the non-MDR patients.

**DISCUSSION**

In Ecuador, the total TB-related costs for patients with non-MDR-TB accounted for 31% of the average...
Ecuadorian annual income. Total costs were seven times higher for MDR-TB patients, mostly because they lost much more time from work due to prolonged illness and treatment. These high costs represent a potential barrier to completion of treatment for MDR-TB patients, and could impoverish these patients long after treatment is completed.

This study had a number of strengths, including the use of a detailed and standardized interviewer-administered questionnaire which has been used in several other studies. Over 100 non-MDR-TB patients participated, enhancing the precision of cost estimates for this group. All 118 questionnaires were administered by one interviewer, ensuring comparability of results between MDR-TB and non-MDR-TB patients. Interviews with non-MDR-TB patients were conducted within 1–3 months of diagnosis, enhancing accuracy of recall of the events leading up to the diagnosis, as well as events after initiation of therapy. However, because of the much longer and more complicated treatment history of MDR-TB, we limited detailed questioning to the current treatment period. In particular, this meant we could not obtain detailed cost information for the period before the initial TB diagnosis.

Nevertheless, the study had several limitations. The number of MDR-TB patients was small. Although this was adequate to detect striking differences in direct and indirect costs, a larger scale study would be valuable to confirm these findings, examine more carefully why these high costs occur, and begin to examine how patients and families cope with these catastrophic costs. Income was not directly ascertained because we had previously found this approach too intrusive. Instead we asked about income ranges; this was well accepted by respondents and informative, as it demonstrated important reductions in income following TB illness. To estimate income lost, we used average per capita income in Ecuador. This value—of US$246 per month—fell near the midpoint of the range of US$100–500 monthly which was the pre-TB income reported by about half of all respondents. As there are other methods of giving value to work time lost, we also reported total time lost from work, facilitating comparison with other studies that have assigned a value to work time lost in different ways. A final weakness is that some of the non-MDR-TB patients may have had unrecognized MDR-TB. This is most likely among failures of initial therapy. However, only two of the non-MDR-TB patients were failures and therefore this misclassification should have been modest.

To our knowledge, this is the first study to report directly gathered patient and household total costs in patients with MDR-TB, compared to other TB patients. One previous study estimated direct costs of MDR-TB only, and a second estimated indirect costs from hospitalization or death due to MDR-TB. Several studies have described the important economic impact of non-MDR-TB. In Thailand, the poorest segment of the population was most affected by a substantial reduction in income: almost one third had to take out bank loans or sell assets to pay for TB-related expenses. In China, the poorest were also disproportionately affected by TB, and were forced to sell productive assets, or were forced into migrant labor. In Tanzania, 68–98% of total costs were due to patients’ loss of income related to reduced capacity to work; this far exceeded health system costs.

The most important finding of this study was the important economic burden imposed by TB on all patients and families, and the much greater burden created by MDR-TB. The greater burden of MDR-TB was due to several factors: first, the total duration of illness was much longer, averaging a total of 40 months from symptom onset to end of MDR therapy, compared to an estimated average of 12 months for non-MDR cases. Second, the cost per month was US$172 for MDR-TB, compared to US$82 for the other patients, which meant an ever increasing debt as the months passed. MDR-TB patients had greater barriers to employment, as they were hospitalized for the initial intensive phase of therapy for up to 6 months, and thereafter had to attend every day (and sometimes twice daily) for clinic-based DOT. As a result, none of the MDR-TB patients were working full time at the time of the interview. By contrast, many of the non-MDR-TB patients were still able to work, having never been hospitalized and on thrice weekly supervised therapy.

In a review, Russell noted that expenditure of more than 40% of monthly income is considered catastrophic, and that most studies report TB-related expenditures that are close to that threshold. We found that all MDR-TB patients bore costs far in excess of this threshold, at a level equivalent to the estimated household costs due to AIDS in several regions of sub-Saharan Africa. This economic burden will create substantial pressure on MDR-TB patients to find work, which would make treatment adherence more difficult. It is important to recognize that we only interviewed ‘survivors’, i.e., patients on MDR-TB treatment, and not the families of patients who had died. These costs therefore represent an underestimate of the burden on families as we did not include estimates of the economic impact of premature death from MDR-TB, which according to one study incurs a much greater economic burden. (We speculate whether this ‘survivor effect’ may explain why women accounted for 71% of the MDR-TB patients but only 39% of the non-MDR-TB group, as women may have been more likely to survive with MDR-TB.)

One of the most important findings in this study is that the interval between the first diagnosis of active TB and the institution of effective MDR-TB therapy averaged 22 months. During this time, patients
received more than two full courses of therapy, and did not work. This finding suggests that an important way to reduce the economic burden of MDR-TB on patients would be to reduce the time between the onset of TB illness and the institution of effective MDR-TB treatment through earlier DST. The second intervention would be to reduce hospitalization and a third would be to shift from clinic-based to community-based DOT, so that patients could return to work sooner. Another possible intervention would be to provide some financial or nutritional support.

Although confirmation of these findings would be important, this study suggests that TB-related costs for patients and their families in Ecuador are high, and catastrophically high for patients with MDR-TB. Measures that could reduce this economic burden include earlier DST, reduction of hospitalization, and provision of community-based DOT for MDR-TB patients.

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References

INTRODUCTION: Les informations sont limitées concernant les coûts de la tuberculose à germes multirésistants (TB-MDR) pour les patients et leurs familles dans les pays à revenus faibles ou moyens.

MÉTHODES: Entre février et juillet 2007, les patients atteints de tuberculose (TB) active confirmée par l'examen microbiologique, qui avaient bénéficié de 2 mois de traitement, ont complété un questionnaire administré par l'interviewer concernant leurs dépenses directes « de leur poche » et les coûts indirects provenant de pertes de salaires. Les données cliniques ont été prélevées dans leurs dossiers médicaux.

RÉSULTATS: Chez 107 patients TB non MDR, les coûts-patient totaux liés à la TB ont été en moyenne de 960 $US par patient par comparaison avec un coût total moyen de 6880 $US pour 14 patients TB-MDR qui ont participé à l’enquête. Ceci représente respectivement 31% et 223% des revenus annuels moyens en Equateur. Les coûts élevés associés à la TB-MDR ont été dus principalement à la longue durée de la maladie qui a été en moyenne de 22 mois jusqu’au moment de l’interview. Ceci a entraîné des périodes prolongées de chômage. La plupart des patients ont subi une importante perte de revenus, particulièrement les patients TB-MDR, qui dans l’ensemble gagnaient moins de 100 $US par mois au moment de l’interview.

CONCLUSION: Les coûts directs et indirects supportés par les patients atteints de TB active et par leurs familles sont très élevés en Equateur et sont les plus élevés chez les patients atteints de TB-MDR. Ces coûts représentent d’importantes barrières à l’achèvement du traitement.