

Factors Associated with Default from Multidrug-Resistant Tuberculosis Treatment, South Africa, 1999-2001

Final results from a case-control study in 5 provinces

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Table of contents

Page #	Item
3	Introduction
5	Methods
7	Questionnaire
8	Sample size
8	Data analysis
8	Results
8	Sampling frame
9	Response rate
10	Mortality
10	Comparing responders and non responders
11	Demographic characteristics of responders
11	MDR TB treatment characteristics
12	Mobility of respondents
12	Social characteristics
12	MDR TB treatment experience
13	Use of traditional healers
13	Health service characteristics
14	Opinions about health services
14	Knowledge of MDR TB and TB
15	Self-reported side effects
16	Province specific differences
16	Multivariate analysis
17	Self-reported attitudes about default among defaulters
17	Self-reported reasons for defaulting treatment among defaulters
17	Discussion
22	Conclusions/Recommendations
24	Role of funding source
24	Ethical approval
24	Acknowledgments
25	References
27	Other related articles
28-57	Tables 1-26

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Introduction

In the past decade, South Africa has experienced a rapid escalation of tuberculosis (TB) incidence, with new cases rising from less than 100 per 100,000 persons in 1990 to 558 per 100,000 in 2003. In the 2002 Report on Global TB Control, the World Health Organization (WHO) ranked South Africa 3rd in the world in terms of reported TB incidence for 1999 and 7th in terms of absolute number of persons with active TB.[1] Health services are currently burdened by more than 200,000 new tuberculosis patients per year, of whom 60% are estimated to be infected with HIV.[2]

As in all countries, TB control program conditions play an important role in the rise or fall of TB disease, as well as in the development of drug resistance. The World Health Organization's global TB control strategy includes measures to minimize the number of patients who fail to adhere to treatment.[3] Political commitment to the expansion of DOTS has recently strengthened in South Africa. National coverage was estimated to be 77% in 2000, up dramatically from 22% in 1998,[1] but serious escalations in TB preceded these initiatives.

At present, the estimated proportion of TB cases in South Africa identified as multidrug-resistant tuberculosis (MDR TB, resistant to at least isoniazid and rifampicin) is relatively low, ranging from 1.6% (range 1.0 – 2.6%) among new cases to 6.6% (4.0-13.9%) among retreatment cases, depending on the province.[4-6] However, this proportion corresponds to a large and expensive-to-treat caseload of roughly 4,000-6,000 MDR TB treated patients each year. Treatment for MDR TB is more lengthy, toxic, and expensive than for drug-susceptible TB, and cure rates are often lower. Failure to adhere to MDR TB therapy may result in primary transmission of MDR TB in the community, amplify resistance to second-line drugs, and increase the odds of failure in subsequent treatment attempts.[7]

In South Africa, the National Tuberculosis Control Program has adopted a strategy of standardized treatment for MDR TB patients.[8] The Medical Research Council (MRC) of South Africa, together with the National Tuberculosis Program (NTP), have designed a national-scale study to monitor and evaluate treatment outcomes of patients placed on this standardized treatment regimen.

This study has been designed to take place under national tuberculosis control program conditions and is referred to as the DOTS-Plus study.

The Centers for Disease Control and Prevention (CDC), together with the Medical Research Council (MRC) of South Africa, have conducted preliminary analyses of culture conversion rates and outcomes among MDR TB patients receiving standardized treatment prior to the implementation of the national DOTS-Plus study.[9-10] The objective was to assess early markers of standardized treatment efficacy and effectiveness among pre-DOTS-Plus study patients. The authors identified high culture conversion rates (81%) among those who were generally adherent (defined as non-defaulters, and not taking short interruptions into account), but moderate treatment efficacy rates (cure and completion versus death and failure, defaulters excluded) of 45%. The major reason for the low level of overall conversion and treatment success was the high rate of patient default (36%-45%).

For the purposes of the above study, a patient was classified as a defaulter for the treatment outcome if they had two months or more interruption from the treatment regimen, as per MDR TB default definitions (defined by the WHO Working Group on MDR TB).[11] Short breaks in treatment less than two consecutive months in length were labeled as treatment interruptions, but not classified as treatment default. For the current study we adhered to the same definitions.

It is poorly understood why TB and MDR TB patients stop taking therapy. Personal stresses, such as the need to earn money, alcoholism, pessimism, poor previous experiences with TB treatment, and family migration, have been regularly cited by TB staff, but health care restructuring and health care service limitations also seem to play a role in deterring adherence. Additionally many patients, in particular those with MDR TB, seem to be interrupting treatment and dying at home soon thereafter, although the frequency with which this occurs is unknown. Identifying and addressing preventable risk factors for non-adherence is a critical task in the early stage of MDR TB standardized treatment expansion, otherwise poor compliance may result in ineffective treatment and community spread of resistance to second-line anti-TB drugs.

CDC technical assistance was requested to assist in conducting an evaluation of factors associated with non-adherence among patients receiving treatment for MDR TB. This case-control investigation to identify patient-level and provider-level factors for non-adherence to MDR TB treatment was conducted in 2003-2004. It is our hope that the findings can be used to improve patient compliance with MDR TB treatment in South Africa and minimize its continued spread. These results will assist the South Africa National TB Control Program in strengthening existing strategies for improving adherence among all TB patients and introduce new strategies to maintain adherence among the growing pool of MDR TB patients being treated under the national standardized MDR TB treatment guidelines.

Knowledge of factors associated with patient default could assist healthcare workers in identifying the particular personal stressors that inhibit compliance with MDR TB treatment, as well as provider-level impediments to achieving treatment completion. It is hoped that the findings of this investigation will also be used to develop a demonstration site that pilots the use of innovative case management approaches to ensure treatment completion among MDR patients, such as what has been previously attempted in the Western Cape.[12-14] Interventions developed from the investigation findings may serve to improve patient retention and thus close the gap between the potential high efficacy of standardized MDR TB treatment and low effectiveness. Data collected for this study should not be generalized outside South Africa.

We conducted this study in order to 1) Identify patient-level factors associated with default from South Africa's standardized MDR TB DOTS-Plus program; 2) Identify provider-level factors associated with default from South Africa's standardized MDR TB DOTS-Plus program; 3) Quantify knowledge of TB and MDR TB among MDR TB patients; and 4) Estimate the mortality rate among MDR TB treatment defaulters following their interruption of treatment (not actual program defaulters).

Methods

We conducted an unmatched, questionnaire-based, case-control study among adult persons aged 18 years and older diagnosed with MDR TB between

October 1, 1999 and September 30, 2001, and for whom MDR TB treatment was initiated. Data was collected from four sites: one with low HIV prevalence (Eastern Cape), one with high HIV prevalence (KwaZulu Natal), one from an area that has provided standardized treatment to MDR TB patients (North West) and has very few defaulters, and one from an area that has traditionally provided individualized treatment and case management to MDR TB patients (Western Cape). A fifth province (Mpumalanga) with high HIV prevalence was added later. In the case of Western Cape and KwaZulu Natal area, our study period ran from February 2000 to September 2001 because DOTS-Plus standardized therapy started later in the Western Cape. Prior to October 1999, treatment of MDR TB was erratic in South Africa, and treatment methods varied widely between provinces and hospitals.

We selected patients from MDR TB treatment register lists generated by each province's MDR TB referral hospital. Information provided included patient name, address, and the hospital or clinic where MDR standardized therapy was initiated and last administered. In each of these provinces, all MDR TB patients are referred to one hospital for initial administration of MDR TB therapy. Due to logistical limitations, we restricted our interviewers to look for patients living within 200 kilometers of the hospital.

We defined cases as MDR TB patients 18 years or older who initiated standardized MDR TB therapy but subsequently defaulted. We defined controls as MDR TB patients who initiated MDR TB treatment and were considered to have completed a full treatment course (either cure or completion or failure). Patients who transferred out of the province were not included. In each province, we excluded prison MDR TB patients or wards of state, and children. The exclusion of children was due to lack of data on effective methods for treating MDR TB in children in South Africa.

Patients who died during treatment were excluded from the final analysis, as they were not 'at risk' for defaulting for the duration of treatment. Patients who defaulted and later died were identified during the study and counted either as misclassified defaulters (those who interrupted treatment and died within 2 months of treatment cessation) or defaulters who later died. Both were excluded from the final analysis but were recorded.

Data from the TB registry included basic demographic information, dates of MDR treatment registration, use of clinic and hospital for treatment initiation and completion, and treatment outcome. The variable “treatment outcome” was used to identify whether the patient completed a full course of therapy (usually 18 months) or whether the patient defaulted during that year.

Full-time study interviewers hired in each province worked out of the MDR TB referral hospital, which houses the registry of MDR TB patients. They all attended a 2-day interviewer skills workshop held in collaboration with the BOTUSA field unit from Botswana, where a comparable case-control study was performed. In the workshop, there was a strong emphasis on reading the questions without extraneous prompting or suggestions. To avoid interviewer bias, the interviewers hired did not know the patients and were not associated with the health services.

The interviewers who administered the questionnaire used registry address information to locate the patient, explain the study, and request written informed consent in the patient’s native language (e.g. Xhosa, Zulu, Tswana, Afrikaans or English). If the study coordinator could not locate the patient using the address, he/she investigated using the patient’s local clinic register and members of the Local Authority health staff. The interviewers strongly encouraged defaulters who were found to return to the health clinic to be evaluated for a return to MDR TB treatment. If the investigation found that the patient had died, this was recorded.

Questionnaire

A questionnaire was developed in English and then translated into the other home South African languages (Xhosa, Zulu, Tswana, and Afrikaans) and back-translated into English to evaluate the quality of translation. The questionnaire was modified using two focus groups of staff nurses and current hospital patients. Modifications were made to reflect consensus from the focus groups.

This study was conducted using a face-to-face, administered questionnaire. The questionnaire consisted of a mixture of open-ended, multiple choice, and yes/no questions. Questions were asked to establish demographic and social characteristics, health service experience, clinical characteristics, TB/MDR TB knowledge, and self-reported reasons for defaulting (if applicable).

Sample size

Sample size was calculated so that, within a single site, a 25% difference between cases and controls would result in a statistically significant odds ratio of greater than 2.8 with confidence level of 95% and power of 80%, if 30% of controls had the exposure of interest. Achieving this level of site-specific power allowed us to detect a statistically significant odds ratio of 1.8 across all sites, with the same 30% exposure among controls if a 15% difference existed between cases and controls. Based on these power calculations, 50 cases and 100 controls were needed from each site for this study. Because it was likely that defaulting patients would be harder to find, these numbers were inflated to 75 cases and 150 controls per site.

Data analysis

Data were entered into an Epi Info 6.04 database (Dean et al., 1997) and analyzed with SAS 8.02 (SAS Institute 2004), using techniques appropriate for a case control study. We compared cases and controls on various demographic, behavioral, social and clinical factors. We analyzed the differences in proportions using the Mantel-Haenszel chi-squared test or Fisher's exact test where appropriate. For data not normally distributed, we compared differences in medians using the Wilcoxon rank-sum test. We performed multivariate logistic regression analysis using SAS generalized linear models (*proc genmod*) to assess the association of multiple factors with being a case patient (defaulter), and to calculate adjusted odds ratios. We used variables in multivariate analysis that were significant at a p value less than 0.22 level in univariate analysis, and we performed the Hosmer-Lemeshow goodness-of-fit test to assess our regression models. For all statistical tests, we considered a p value of <0.05 as statistically significant.

Results of investigation

Sampling frame

We were provided with a list of 262 defaulting patients and 408 treatment completers from the MDR TB treatment hospitals in the five provinces of the study who were diagnosed and started treatment during the study period. Of the 262 defaulters, investigation by the interviewer found that 35 (13%) had actually

completed treatment, and were therefore reclassified as controls for the purposes of the study. (Table 1) Of the 408 completers, 42 (10%) were found to have actually defaulted from treatment and were classified as cases. Rates of reclassification for each province are also presented in Table 1. Of note, 19% of controls in the Eastern Cape were reclassified as cases, and 22% of cases were reclassified as controls in Mpumalanga and Western Cape. After reclassification there were 269 cases and 401 controls available for investigation.

Table 2 shows the outcome as listed in the MDR TB register for the cases and controls. All cases, with the exception of 18 persons (7%) who were listed as having died, and one with unknown outcome, had the outcome of default. Among the 401 treatment completers, 90% had been cured or completed therapy, 7% had failed, and 3% were recorded as having died in the MDR TB register.

Table 3A lists the locations where the patients investigated for interview were located. Most patients came from the Eastern Cape, Western Cape, and KwaZulu Natal. Of note, Northwest Province contributed only 4 cases to the study. Interviewers were more successful in locating and interviewing controls (68%, range 59%-83%) than they were in locating and interviewing cases (36%, range 24%-49%) (Table 3B). Overall, only 55% of those in the sampling frame were included in the study, reflecting the difficulty in locating previous TB patients. In Table 3C, we show that the ratio of cases interviewed to the total interviewed was very low in Northwest Province.

Response rate

Interviewers were instructed to attempt to locate all 670 persons available for interview. Table 4 shows the results of their efforts of patient tracking and interviewing. Overall, of the 269 persons confirmed as defaulters and assigned to the case group, 96 (36%) were located, consented, and were interviewed. Not surprisingly, we could not find 89 persons (33%) who had either moved or had an address that was not found. Four percent of cases refused to be interviewed. Among 401 controls, 274 (68%) were located, consented, and were interviewed. In addition, 79 controls (20%) were not found and could not be interviewed. The response rate varied by province, as seen in Table 4.

Mortality

We found that 74/269 cases (27%) and 44/401 controls (11%) were reported to have died. Their reported causes of death are listed in Table 5. The most common causes of death were TB, MDR TB, and pulmonary failure (likely TB). For many patients, the cause of death was unknown (46% of cases, 23% of controls). Of the 74 cases who were reported to have died, the date of death was reported for 47 (65%). Of these 47, 9 (19%) were reported to have died within 2 months after stopping MDR TB treatment. These patients were probably misclassified as defaulters, and were in fact “actual deaths.” The remaining 38 (81%) patients died more than 2 months after defaulting and can be classified as “actual defaulters.” The median length of time to death after the last recorded visit was 235 days (7.5 months), with a range of 13-1281 days (0.5-3.5 years). Patients who were reported to have died were excluded from further analysis.

Comparing responders and non responders

We were able to collect minimal data on those who refused to be interviewed, or whom we otherwise could not find or had died. Table 6 compares basic demographic data between the persons interviewed and not interviewed. Responders were less likely to have defaulted (Unadjusted Odds Ratio [UOR] 0.3, 95% Confidence Interval [CI] 0.2-0.4) and were slightly less likely to be male. The ages between the two groups were similar. Responders were also more likely to have started their treatment at a clinic versus a hospital (UOR 1.9, 95% CI 1.3-3.0). The type of facility where treatment was initiated, and whether the patient was admitted for treatment, were similar. In both groups nearly all patients had pulmonary MDR TB. A greater proportion of responders defaulted during the early continuation phase than nonresponders (60% versus 46%).

Results of interviews of responders

The remaining results concern the interviews performed on 96 cases and 274 controls who had not died, were located, consented to be interviewed, and completed an interview for our study.

Demographic characteristics

Among the 96 cases who consented to be interviewed, the median age was 36 years old (range 19-61 years), versus 35 years old among the 274 controls (range 18-67) ($p = 0.94$). (Table 7) When stratified by gender, men were older than women (38 years versus 31.5 years, $p < 0.001$) but there was no significant difference in ages between cases and controls within gender groups.

Most patients were male (59% of cases, 61% of controls), single or widowed (68% of cases, 62% of controls), reported being Christian (90% of cases, 92% of controls), and had one or more children (84% of cases, 85% of controls). (Table 8) Living arrangements between cases and controls were similar. Being born outside of South Africa (UOR 5.9, 95% CI 1.1-32.8), and self-reporting an ethnicity other than black African (UOR 1.7, 95% CI 1.1-2.8) were significantly associated with MDR TB treatment default.

Regarding socioeconomic characteristics that we were able to evaluate, a significantly greater proportion of cases reported not owning a radio (UOR 2.5, 95% CI 1.5-4.4), a television (UOR 1.6, 95% CI 1.0-2.6), or their dwelling (UOR 1.6, 95% CI 1.03-2.7). (Table 9) Education levels between cases and controls were similar, with roughly half having at least a primary school education (53% of cases, 50% of controls). Slightly over half of patients reported being employed (59% of cases, 55% of controls), with the majority of patients reporting non-skilled employment. A significantly higher proportion of cases (14%) reported missing treatment due to demands of employment compared to controls (5%) (UOR 3.0, 95% CI 1.05-8.3).

MDR TB treatment characteristics

The time between treatment initiation and the date the cases were last seen in clinic is known for 70 patients. Of these, 13% defaulted within the first 3 months of treatment, 17% defaulted between 3 and 6 months, 31% defaulted between 6 and 12 months, and 39% defaulted after receiving 12 months of treatment.

Most patients were admitted to initiate MDR TB treatment (93% of cases, 88% of controls), and received initial treatment at a government facility (53% of cases, 61% of controls). (Table 10) However, more cases reported their treatment initiation being focused at a clinic than at a hospital (UOR 1.7, 95% CI 1.0-2.9).

Though information on treatment regimens was limited to the initial drugs used, we found that a significantly higher proportion of cases (85%) were given ethambutol in their initial regimen than were controls (73%) (UOR 2.1, 95% 1.1-4.0). The most common drugs used at initiation were kanamycin (94% of cases, 95% of controls), pyrazinamide (94% of cases, 97% of controls), and ethionamide (93% of cases, 97% of controls). A higher proportion of cases (38%) reported having a history of TB treatment default than controls (30%), but the difference was not significant.

Mobility of respondents

A higher proportion of cases (26%) reported moving at least once in the year before starting treatment than controls (17%), but the difference was not significant (UOR 1.7, 95% CI 0.96-3.0). (Table 11) However, changing residence during MDR TB treatment was significantly associated with default (UOR 2.3, 95% CI 1.2-4.6). Of those who moved during treatment, a higher proportion of cases than controls reported missing treatment due to moving (UOR 10.8, 95% CI 1.1-102.8).

Social characteristics - Alcohol, drug use, and prison history

Reporting any alcohol use during treatment was significantly associated with treatment default (UOR 1.7, 95% CI 1.02-2.9), as was reporting smoking marijuana or mandrax during treatment (UOR 8.7, 95% CI 3.0-25.2), and entering and spending time in prison during treatment (UOR 3.9, 95% CI 1.5-10.2). (Table 12) Among those who used alcohol, however, more controls (48%) reported heavy alcohol drinking (3 or more drinks in 1 day) than cases (28%) but the difference was not significant.

MDR TB treatment experience

Several questions were asked of respondents concerning their experience of having MDR TB, and how they felt about their relationship to others during treatment. (Table 13) Several personal characteristics were significantly associated with treatment default, among them feeling ashamed about having MDR TB (42% versus 30%, UOR 1.7, 95% CI 1.04-2.8), reporting lacking enough food to eat during treatment (50% versus 38%, UOR 1.7, 95% CI 1.04-2.7), and reporting feeling that they did not have enough support from others during treatment (17% versus 8%, UOR 2.3, 95% CI 1.2-4.8). Although up to

90% of cases and controls had told others about their diagnosis, a large proportion reported depending on others for food and shelter (57% of cases, 48% of controls), receiving treatment support from persons other than health care workers (HCWs) (81% of cases, 83% of controls), and feeling supported by family during treatment (89% of cases, 91% of controls). At least a third of cases (34%) and a quarter of controls (26%) reported feeling ignored or neglected because of having MDR TB, but the difference was not significant.

Use of traditional healers

A slightly higher proportion of cases (16%) reported consulting a traditional healer than did controls (11%).(Table 14) Of the 45 patients who did, the median number of healers consulted was 1 (range 1-4). Cases more commonly consulted herbalists (43%), and controls more commonly consulted faith healers (45%), but these differences were not significant. Over half of respondents who saw a traditional healer reported being given treatment, but less than half took it at the same time as their MDR TB treatment. Herbs and tonics were the most common treatments given (88% of cases treated, 62% of controls treated). Only one patient who received treatment from a traditional healer reported being told to stop their TB medicines.

Health service characteristics

Cases and controls responded that that it took a median of 30 days from when they first felt ill to when they were seen by a provider for their MDR TB episode.(Table 15) Both groups reported attending a median of 1 clinic for their treatment, although 24% of cases and 25% of controls reported going to 2 or more. Most cases and controls walked to their MDR TB clinic appointments. Sixteen percent of cases and 21% of controls reported it took more than one hour to get to their clinic, and 97% of cases and controls reported waiting less than one hour at their clinic to be seen by the doctor or nurse. There were no significant differences in travel time or waiting time between the groups. However, a greater proportion of cases than controls felt that the clinic hours were inconvenient for them (10% versus 4%, UOR 2.8, 95% CI 1.0-7.6).

A significantly larger proportion of cases were never given MDR TB treatment without direct supervision (86% versus 74%, UOR 2.2, 95% CI 1.2-4.3).(Table 16) If they were, it was usually being given their pills to take on their own. More

than half of respondents were given DOT one pill at a time, although 21% of cases and 37% of controls were given their pills in plastic bags. Four-fifths of cases and controls also received food from the clinic.

Opinions about health services

Queries about satisfaction with the health service revealed stark differences between cases and controls. A significantly greater proportion of cases had an unsatisfactory opinion about the attitude of the health care workers they encountered (13% versus 2%, UOR 9.6, 95% CI 3.0-30.5). (Table 17) A higher proportion of cases than controls did not feel that the health care workers treated them with respect (8% versus 2%, UOR 6.2, 95% CI 1.8-21.1). As a result, a larger proportion of cases than controls reported missing treatment doses due to poor health care worker attitude.

Although the level of trust of health care workers, the clinics, and hospitals was over 90% in both cases and controls, a significantly larger proportion of cases did not trust the hospital (6% versus 1%, UOR 5.0, 95% CI 1.2-21.2) or the clinic (10% versus 2%, UOR 7.0, 95% CI 2.1-24.0) that they attended. (Table 17) In the end, a far larger proportion of cases than controls did not feel that the treatment made them feel better (22% versus 2%, UOR 12.1, 95% CI 4.7-31.2).

Knowledge of MDR TB and TB

Although full knowledge of TB pathogenesis and spectrum of disease are not crucial to finishing a course of medicine, it is a reflection of how well patients' are being educated about their illness. Three-quarters of patients reported that they knew they would be taking treatment for a year (72% of cases, 78% of controls), although more controls than cases reported being told why they might have to take treatment for one year (86% versus 73%, UOR 2.3, 95% CI 1.3-4.2). (Table 18) Fourth-fifths of cases, and 86% of controls, reported being given health information about MDR TB by a health care worker. Of those that received information, 10% of cases and 1% of controls did not feel it was useful (UOR 12.4, 95% CI 2.5-61.1). Only eight percent of cases and 4% of controls felt they didn't receive enough information (UOR 2.4, 95% CI 0.8-7.6).

Receiving information translated into moderately high levels of understanding about curing and preventing MDR and TB, as well as the possibility of dying from

either. Ninety-three percent of cases and controls felt it was possible to cure TB and MDR TB. (Table 18) Fewer cases than controls felt that it is possible to prevent MDR TB (84% versus 90%, UOR 0.6, 95% CI 0.3-1.3), and fewer cases than controls felt they might die from MDR (70% versus 80%, UOR 0.6, 95% CI 0.4-1.04).

Table 19 lists the responses given by cases and controls concerning their knowledge about the cause of MDR TB. The most common responses were “not taking TB medicine properly,” “being near other people with MDR TB,” and “poor nutrition.” More cases than controls reported they didn’t know the cause of MDR TB (32% versus 23%, UOR 1.7, 95% CI 0.99-2.8). A smaller proportion of cases than controls felt that “smoking and drinking” (24% versus 22%, UOR 1.1, 95% CI 0.7-2.0), and “HIV/AIDS” was the cause (3% versus 14%, UOR 0.2, 95% CI 0.06-0.7). Ten percent of patients reported “bad TB treatment by doctors and nurses” as the cause. A small minority of patients responded with answers such as “evil spirits,” “dust and smoke,” “poisons,” and “cold weather.”

Respondents answered in a consistent manner when asked about the cause of TB. (Table 20) Nearly half of cases and controls felt “being near other people with TB” was the cause, with significant proportions reporting “poor nutrition” and “germs” as well. A significantly smaller proportion of cases than controls blamed “bad air” (13% versus 24%, UOR 0.5, 0.2-0.9). One-fifth blamed “smoking and drinking,” with fewer responses for “HIV/AIDS,” “cold weather,” “unhygienic conditions,” “dust and smoke,” and “poisons.” A significantly higher proportion of cases blamed “witchcraft” (5% versus 1%, UOR 4.9, 95% CI 1.2-21.2), although the number was small.

Self-reported side effects

Cases reported experiencing side effects from MDR TB treatment, both daily and less than daily, at slightly higher proportions than controls but the differences were not significant. (Table 21) Forty-seven percent of cases and 42% of controls reported side effects on a daily basis (UOR 1.2, 95% CI 0.7-2.1). More than three-quarters of cases and controls spoke to health care workers about their side effects, but only a smaller proportion of cases took medicine to alleviate the symptoms of side effects (37% versus 53%, UOR 0.5, 95% CI 0.3-0.9). Less than 10% talked to traditional healers or took traditional medicine. However, a far

greater proportion of cases reported that they interrupted their MDR TB treatment at any time due to side effects (37% versus 6%, UOR 9.6, 95% CI 4.3-21.6).

The types of side effects reported are listed in Table 22. The most common side effects reported were nausea (57% of cases, 59% of controls), vomiting (47% of cases, 42% of controls), sore buttocks (19% of cases, 21% of controls), fatigue (21% of cases, 26% of controls), and skin rash (19% of cases, 19% of controls). There were no significant differences in side effect types between cases and controls except one: more cases than controls reported abdominal pain (19% versus 8%, UOR 2.6, 95% CI 1.2-5.8) as a side effect.

Province specific differences

Table 23 shows the variables that were significant in univariate analysis stratified by province. Table 23A stratifies the provinces by Cape Provinces versus all others, and Table 23B stratifies the provinces by Western Cape Provinces versus all others. Odds ratios are presented as unadjusted with *p* values, and then adjusted by province in the final column.

There are a few differences among variables between the provinces. For example, not owning a radio, not owning a television, and changing residence during treatment were more common in the northern provinces. Reporting not having enough support during treatment, and feeling ashamed of having TB were more common in the Cape provinces, especially the Eastern Cape. Smoking marijuana or mandrax during treatment was equally prevalent in all provinces. As we do not have the power to do a separate province specific analysis, any provincial separation between northern/eastern provinces and the Cape provinces for use as a confounding variable will be imperfect. We prefer Table 23A to demonstrate the existence of confounding by province, as there are more pronounced differences using this separation.

Multivariate analysis

Adjusting for age and sex, variables that were positively and independently associated with being a case patient (defaulter) were reporting smoking marijuana or mandrax during treatment (Adjusted Odds Ratio [AOR] 17.9, 95% CI 4.7-68.5), having an unsatisfactory opinion about the attitude of the health care workers (AOR 12.6, 95% CI 2.7-58.6), not owning a radio (AOR 3.4, 95% CI

1.6-7.1), changing residence at least once during treatment (AOR 3.2, 95% CI 1.4-7.6), residing in the Eastern or Western Cape provinces (AOR 2.4, 95% CI 1.2-4.8), reporting any alcohol use during treatment (AOR 2.1, 95% CI 1.1-4.0), and reporting feeling that they might die from MDR TB (AOR 0.4, 95% 0.2-0.8) (protective).(Table 24)

Self-reported attitudes about default among defaulters

Among the 96 cases of treatment default that consented to our study and were interviewed, 2% reported stopping in the first month, 19% reported stopping by the fourth month after treatment initiation, and 55% reported stopping in the early continuation phase (month 5-12).(Table 25) The remaining defaulted between month 12-18, or could not recall. Half reported that experiencing side effects had a role in stopping MDR TB treatment. In addition, 42% reported that not knowing enough about MDR TB had a role in stopping treatment. One quarter reported that a health care worker's poor attitude, and the lack of support or encouragement, had a role in stopping treatment. Only 12% reported that other people had played a role.

Self-reported reasons for defaulting treatment

Among the 96 cases of default interviewed, the most common reason cited for stopping treatment was that "the pills gave me side effects" (26%).(Table 26) Other reasons cited between 10%-20% of respondents included "I felt better," "I didn't like to be away from family so long," "I didn't think I had MDR TB," "I thought I was taking pills for too long," "I could not afford transport to the clinic," and "the health care staff treated me poorly." Following these reasons, socioeconomic reasons were cited, "I didn't want to lose my job," "I had to look for a job," and "I was not getting any better."

Discussion

This case-control investigation into the reasons for treatment default from MDR TB treatment by adult patients in South Africa, 1999-2001, provides multiple layers of information about patient, provider, and health system-level factors that may influence patients' adherence to MDR TB treatment. First, we discovered that 13% of treatment defaulters (our cases) and 10% of treatment completers were improperly classified in the MDR TB registers we examined. The proper

recording of treatment outcome is of enormous importance in a country like South Africa, with an emerging problem of MDR TB in the midst of a large human immunodeficiency virus (HIV) epidemic. Misclassification bias, even on the order of 10% seen here, can markedly skew “good outcomes” (treatment success of 70-75%) to “modest” outcomes (treatment success of 60-65%). Though these patients were treated before the onset of the electronic reporting system used in the DOTS-Plus country-wide study currently run by the Medical Research Council, it points to the need for vigilance in quality data reporting, recording, and data entry.

Second, not surprisingly, our investigators uncovered a significant death rate among defaulters and those completing MDR TB treatment in our sampling cohort. One quarter of patients (27%) who were classified as defaulters were in fact found to have died after the last contact with their MDR TB clinic. Twenty percent of those we found death dates for had died within 2 months after stopping treatment, and were thus “actual deaths.” If these cases had been completely followed up and their treatment outcome properly classified, the reported death rate from MDR TB would likely be higher.

We were also unable to contact another 33% of treatment defaulters, likely due to internal migration or death. Therefore the “actual death rate” among those undergoing treatment for MDR TB may not be known, but it is likely higher than the 25% reported in recent MDR TB outcome studies in South Africa. It is not known what proportion of those we were unable to find were too ill with TB or another disease to report for TB treatment, or if they were relatively well when they defaulted and subsequently died. If the cause of death among the 74 cases and 44 controls reported to have died is any indication, the overwhelming reason for death is TB. This could be due to TB alone or HIV-associated illness.

Misclassification and loss of follow-up leads to underestimates of the true impact of MDR TB on the population. It is unknown what role HIV infection played in the high death rate and high rate of non-response, but it is likely not insignificant. HIV seroprevalence in South Africa is high (HIV-1 seroprevalence of 24.5% among pregnant women attending public health services in 2002),^[15] with an estimated 5.5 million HIV-infected persons.^[16] Among the MDR TB population, roughly

35% of the patients (among the 65% tested) are thought to be co-infected with HIV.[6]

We identified four major areas associated with treatment default in the patients we interviewed. The most significant factors we found associated with treatment default were related to the quality of the patient-provider relationship, including transmission of accurate information about MDR TB. Our multivariate model showed that defaulters were nearly ten times more likely to report dissatisfaction with health care worker attitudes. They were also ten times more likely to report missing treatment due to health care worker attitudes. They reported being treated disrespectfully six times more frequently than controls. Twice as many cases reported not being told why they would receive treatment for one year for MDR TB, and of the 80% who reported being given information by the health care worker, cases reported finding this information not useful ten times more frequently than controls. Though it is possible that a small proportion of defaulters went into treatment with preconceived negative feelings about the health care services, this bias is unlikely to account for such an overwhelming disparity of opinion.

Importantly, our model showed that substance use during treatment, such as smoking marijuana or mandrax, was more than ten times more likely to be reported by cases than controls. The use of alcohol on an occasional or regular basis was also more commonly reported by cases. Cases were four times more likely to report entering and spending time in prison during MDR TB treatment than controls. When defaulting is related to another unmeasured underlying causal factor that results in prison time, or if spending time in prison causes treatment default is not clear from this study.

Lack of support from family and friends during treatment also appears to be crucial. Our multivariate model showed that cases were less likely to report feeling that they might die from MDR TB. Twice as many cases reported a lack of social support from family or friends during treatment. This is often reflective of the stigma they feel is attached to TB, the amount of support they feel in disclosing their disease to others, and of being seen as a TB patient by friends and family.

Socioeconomic factors such as access to transport, available work, monetary resources, and access to food were also significant. In our multivariate model, not owning a radio was three times more common in cases than controls. This variable could be a marker of low socioeconomic status, and could reflect access to expendable income as well as access to information. Our model also showed that cases reported changing their residence during treatment three times more often than controls. More cases than controls reported lacking enough food to eat at times during their treatment. Past studies have shown that removing all structural barriers to care greatly enhances patients' adherence to TB treatment.[17]

When cases were directly asked why they defaulted treatment, the most common response was that side effects were either too common or too much to deal with. There was a small significant difference in the frequency of side effects reported between cases and controls, but no significant difference in the types of side effects experienced in both groups. Interestingly, these variables were not found to be independently associated with treatment default in our multivariate analysis.

It is possible that patients' discomfort in having MDR TB, the associated stigma of having TB, and a poor experience in the health care setting may translate into a lowered tolerance to side effects from medication. The outward expression of these difficulties in treatment could be perceived by patients to be medication side effects. How patients perceived the severity of the side effects they experienced, their ability to tolerate them, and the amount of support they received in dealing with side effects were not fully measured in this study, but likely played a role in patients when deciding whether or not going through MDR TB treatment with side effects is "worth it."

Lastly, it cannot be discounted that some patients find the health services too difficult to access. Cases were nearly three times more likely to report that the operating hours of their TB clinic were not convenient for them. However, structural reasons (over and above the attitude of health care workers toward patients) for treatment default did not emerge in our study as overarching issues.

Other self-reported reasons for default were consistent with significant factors found in our univariate case-control analysis. The most common reasons were a

reported lack of education about the length of MDR TB treatment, forced separation from family, the perception that number of pills and length of treatment was excessive, transport costs to get to their clinic, not feeling welcomed by health care workers, and the demands of looking for work and keeping this employment to earn money.

Factors that were not associated with default among our patients interviewed include the age and sex of the patient, their particular employment role, their living situation, waiting times at the clinic, and specific knowledge about the causes of MDR TB and whether it is felt to be a killer. Overall, knowledge of what causes TB and MDR TB was quite good. We conclude that specific cultural beliefs and values placed on TB are likely not as important as the actual amount of support patients receive in completing their treatment course.

This study has multiple limitations. Due to the nature of the study design, exposures being assessed as risk factors for default were collected retrospectively, using patient self-reported data. These data are subject to recall bias, which may cause either differential or non-differential misclassification of exposure. Unfortunately, we had to allow enough time to pass since the end of the last patients' treatment course to identify the proper cohorts to study in each province. Allowing so much time to pass inevitably resulted in many patients moving or otherwise making themselves more difficult to locate. The irony of the study is that we were attempting to investigate the reasons why people became lost to follow up, precisely among the people that were more likely to be lost to follow up. Our inability to locate only one-third of the treatment defaulters on our cohort list will limit any generalizations.

In addition, we cannot ascertain the true temporal association between the factors measured and the actual treatment default (outcome). As stated above, it might be true that persons who take drugs and have problems with the law have a higher chance of defaulting from treatment as they begin, but for these patients we should redouble our efforts in helping them complete therapy, otherwise they will spread MDR TB through close contact with more persons with similar social backgrounds and behaviors. We also do not have any data on possible incentives or enablers that patients might have received during treatment that may have affected their adherence patterns.

Lastly, the overall sample size was ultimately too low to draw any country-wide conclusions, let alone province-specific conclusions. If another quantitative study on treatment default were to be attempted, our suggestion would be to build into the sample size calculation the possibility that 50% of patients will not be found.

Conclusions/Recommendations

Based on the findings of this case-control study into factors associated with MDR TB treatment default, we are able to conclude the following:

1. The quality of the patient-provider (including nursing staff) relationship is an important component of MDR TB treatment completion. Among some patients disturbances in the quality of this relationship may play a role in their decision to permanently default from treatment.

Recommendations

- a. Consider strengthening training, supervision, and support of health care providers of TB and MDR TB patients to avoid burnout and workload overburden.
 - b. Consider continuing education for health professionals on the importance of the patient-provider relationship, and the importance of a good provider attitude in care.
2. Support from family and friends is a crucial component of completing treatment, which includes confronting stigma attached to TB and MDR TB, and reducing discrimination felt by patients in their communities.

Recommendations

- a. Consider supporting patients' care and treatment package to include components such as family support sessions, closer individual case management, substance abuse counseling, and treatment support (transport vouchers and food vouchers).
- b. Consider public education campaigns to reduce stigma attached to MDR TB to facilitate community engagement with the disease.

3. Side effects from anti-MDR TB drugs negatively impact patients' ability to complete the full course of treatment.

Recommendations

- a. Consider strengthening of patient support of drug side effects, including supportive counseling and management by nurses as well as physicians.

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Ethical approval

This analysis was approved as non-human subjects research by the Office of the Associate Director for Science at the U.S. Centers for Disease Control and Prevention (CDC).

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Table 1. Results of reclassification of cases and controls with MDR TB, 5 provinces, South Africa, 1999-2001

All provinces

Category in TB register	Reclassified as Cases	Reclassified as Controls	Not reclassified	Total
Defaulter/Case	--	35 (13%)	227 (87%)	262
Completed treatment/Control	42 (10%)	--	366 (90%)	408
Total	42	35	593	670

Eastern Cape

Category in TB register	Reclassified as Cases	Reclassified as Controls	Not reclassified	Total
Defaulter/Case	--	4 (5%)	69 (95%)	73
Completed treatment/Control	29 (19%)	--	127 (81%)	156
Total	29	4	196	229

KZN

Category in TB register	Reclassified as Cases	Reclassified as Controls	Not reclassified	Total
Defaulter/Case	--	5 (7%)	64 (93%)	69
Completed treatment/Control	4 (4%)	--	97 (96%)	101
Total	4	5	161	170

Mpumalanga

Category in TB register	Reclassified as Cases	Reclassified as Controls	Not reclassified	Total
Defaulter/Case	--	9 (23%)	30 (77%)	39
Completed treatment/Control	0 (0%)	--	15 (100%)	15
Total	0	9	45	54

Northwest

Category in TB register	Reclassified as Cases	Reclassified as Controls	Not reclassified	Total
Defaulter/Case	--	0 (0%)	4 (100%)	4
Completed treatment/Control	0 (0%)	--	42 (100%)	42
Total	0	0	46	46

Western Cape

Category in TB register	Reclassified as Cases	Reclassified as Controls	Not reclassified	Total
Defaulter/Case	--	17 (22%)	60 (78%)	60
Completed treatment/Control	9 (10%)	--	85 (90%)	9
Total	9	17	145	69

Table 2. Outcome results as listed in register, after reclassification of cases and controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Final Category	Cure	Complete	Fail	Default	Died*	Unknown	Total
Case	0	0	0	250 (93%)	18 (7%)	1	269
Control	196 (49%)	163 (41%)	29 (7%)	0	13 (3%)	0	401
Total							670

*listed as defaulter or completer in register, though outcome was marked as 'died,' excluded from final analysis

Table 3A. Location of cases and controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Final Category	Eastern Cape	KwaZulu Natal	Mpumalanga	NW Province	Western Cape	Total
Case	98	68	30	4	69	269
Control	131	102	24	42	102	401
Total	229	170	54	46	171	670

Table 3B. Cases and controls interviewed by province, as ratio of those eligible to be interviewed

Province	Cases+Controls interviewed /eligible for study		Cases interviewed/ cases eligible		Controls interviewed/ controls eligible	
	Number	Percent	Number	Percent	Number	Percent
Eastern Cape	120/229	52	33/98	34	87/131	66
KwaZulu Natal	75/170	44	16/68	24	59/102	59
Mpumalanga	32/54	59	12/30	40	20/24	83
Northwest	33/46	72	1/4	25	32/42	76
Western Cape	110/171	64	34/69	49	76/102	75
Total	370/670	55	96/269	36	274/401	68

Table 3C. Proportion of cases interviewed out of cases and controls interviewed, by province

Province	Ratio of cases interviewed/ cases+controls interviewed	
	Number	Percent
Eastern Cape	33/120	28
KwaZulu Natal	16/75	21
Mpumalanga	12/32	38
Northwest	1/33	3
Western Cape	34/110	31
Total	96/370	26

Table 4. Response rate of interviewer investigation after reclassification of cases and controls with MDR TB, 5 provinces, South Africa, 1999-2001.

All provinces				
Characteristic	Cases	Percent	Control	Percent
Contacted, consented to participate	96	36	274	68
Contacted, did not consent	10	4	4	1
Reported to have died	74	27	44	11
Not contacted, address not found	46	17	36	9
Not contacted, moved from address	36	13	30	8
Unknown	7	3	13	3
Total	269	100	401	100

Eastern Cape				
Characteristic	Cases	Percent	Control	Percent
Contacted, consented to participate	33	34	87	66
Contacted, did not consent	1	1	0	0
Reported to have died	40	41	27	21
Not contacted, address not found	11	11	5	4
Not contacted, moved from address	12	12	10	8
Unknown	1	1	2	1
Total	98	100	131	100

KZN				
Characteristic	Cases	Percent	Control	Percent
Contacted, consented to participate	16	24	59	58
Contacted, did not consent	1	1	0	0
Reported to have died	15	22	6	6
Not contacted, address not found	26	38	26	25
Not contacted, moved from address	6	9	4	4
Unknown	4	6	7	7
Total	68	100	102	100

Mpumalanga Characteristic	Cases	Percent	Control	Percent
Contacted, consented to participate	12	40	20	82
Contacted, did not consent	3	10	0	0
Reported to have died	7	23	1	4
Not contacted, address not found	3	10	1	4
Not contacted, moved from address	5	17	2	8
Unknown	0	0	0	0
Total	30	100	24	100

Northwest Characteristic	Cases	Percent	Control	Percent
Contacted, consented to participate	1	25	32	76
Contacted, did not consent	1	25	0	0
Reported to have died	2	50	7	17
Not contacted, address not found	0	0	0	0
Not contacted, moved from address	0	0	3	7
Unknown	0	0	0	0
Total	4	100	42	100

Western Cape Characteristic	Cases	Percent	Control	Percent
Contacted, consented to participate	34	49	76	74
Contacted, did not consent	4	6	4	4
Reported to have died	10	14	3	3
Not contacted, address not found	6	9	4	4
Not contacted, moved from address	13	19	11	11
Unknown	2	3	4	4
Total	69	100	102	100

Table 5. Reported cause of death after reclassification among 74 cases and 44 controls with history of MDR TB who were reported to have died after treatment, 5 provinces, South Africa, 1999-2001.

Cause	Cases N=74		Controls N=44	
	Number	Percent	Number	Percent
Pulmonary TB	22	30	13	30
MDR TB	11	15	3	7
Respiratory failure	3	9	4	4
Pneumonia	1	1	3	7
Natural causes	1	1	3	7
Maternal death	1	1	0	0
Haemoptysis	1	1	0	0
Cor Pulmonale	0	0	2	5
Cardiac death	0	0	2	5
Cardiomegaly	0	0	1	2
Cardiac TB	0	0	1	2
Renal failure	0	0	1	2
Severe diarrhea	0	0	1	2
Unknown	34	46	10	23

Table 6. Comparing characteristics between those interviewed and those not interviewed, among patients with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Responders N=370		Nonresponders N=300		Unadjusted Odds Ratio 95% CI
	Number	%	Number	%	
Status					
Case	96	26	173	58	0.3 (0.2-0.4)
Control	274	74	127	42	1.0
Median age (range)	35 (18-67)		35 (18-76)		$p = 0.70^*$
Gender					
Male	225	61	205	68	0.7 (0.5-1.0)
Female	145	39	95	32	1.0
Facility where treatment initiated					
Clinic	79	21	37	12	1.9 (1.3-3.0)
Hospital	291	79	263	88	1.0
Type of facility where treatment initiated					
Non-Governmental	153	41	131	44	0.9 (0.7-1.2)
Governmental	217	59	169	56	1.0
Admitted for MDR TB treatment					
Yes	328	89	271	92	0.7 (0.4-1.2)
No	39	11	23	8	1.0
Disease classification					
Pulmonary	365	100	293	99	--
Extrapulmonary	0	0	1	.5	
Both	0	0	2	.5	
Among those that defaulted treatment, the phase of treatment when patient defaulted					
First month	2/96	2	12/173	8	
Month 2-4	18/96	21	30/173	21	
Early continuation (5-12)	53/96	60	68/173	46	
Late continuation (13-18)	15/96	17	36/173	25	
Unknown	8/96	--	27/173	--	

* Wilcoxon rank-sum test

Results of Cases and Controls Interviewed in Study

Table 7. Age distribution of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases (n=96)	Controls (n=273)*	<i>p</i> value [†]
Median age			
All (range)	36 (19-61)	35 (18-67)	0.94
Median age by gender			
Men (range)	37 (20-61)	38 (18-66)	0.66
Women (range)	31 (19-61)	32 (18-67)	0.70

* One person's age was unknown

† Wilcoxon rank-sum test

Table 8. Demographic characteristics of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Gender					
Male	57/96	59	168/274	61	0.9 (0.6-1.5)
Female	39/96	41	106/274	39	1.0
Country of birth					
Other	4/96	4	2/274	1	5.9 (1.1-32.8)
South Africa	92/96	96	272/274	99	1.0
Location of interviewee					
Cape provinces (E/W)	67/96	70	163/274	59	1.6 (0.9-2.6)
KZN/Mpumalanga/NW	29/96	30	111/274	41	1.0
Religion					
Christian	86/96	90	249/272	92	0.8 (0.4-1.7)
Non christian	10/96	10	23/272	8	1.0
Ethnicity					
Other	42/91	46	86/260	33	1.7 (1.1-2.8)
Black African	49/91	54	174/260	67	1.0
Marital status					
Married/union	31/96	32	105/274	38	0.8 (0.5-1.3)
Single/widow	65/96	68	169/274	62	1.0
Children					
More than 3	36/96	38	116/274	42	0.9 (0.4-1.9)
1-2	45/96	47	116/274	42	1.1 (0.5-2.3)
None	15/96	16	42/274	15	1.0
Live alone	3/96	3	9/274	3	0.9 (0.3-3.6)
Live with family	74/96	77	224/274	82	0.8 (0.4-1.3)
Live with partner	19/96	20	37/274	14	1.6 (0.9-2.9)
Live with a friend	4/96	4	8/274	3	1.4 (0.4-4.9)
Live with children	54/96	56	150/274	55	1.1 (0.7-1.7)
Live with coworker	2/96	2	11/274	4	0.5 (0.1-2.3)

Table 9. Socioeconomic characteristics of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Do not own cattle	95/96	99	265/274	97	3.2 (0.4-25.8)
Do not own goats	95/96	99	263/274	96	4.0 (0.5-31.2)
Do not own radio	29/96	30	40/274	15	2.5 (1.5-4.4)
Do not own a television	37/96	39	78/274	29	1.6 (1.0-2.6)
Do not own a house	48/96	50	103/274	38	1.6 (1.03-2.7)
Education level					
1° school or less	51/96	53	136/272	50	1.1 (0.7-1.8)
2° school or more	45/96	47	136/272	50	1.0
Employment					
Employed	56/95	59	150/274	55	1.2 (0.7-1.9)
Unemployed	39/95	41	124/274	45	1.0
Of those employed:					
Occupation					
Non skilled	34/56	61	78/148	53	1.4 (0.7-2.6)
Skilled	22/56	39	70/148	47	1.0
Income					
<R1000/mo	32/49	65	79/140	56	1.3 (0.7-2.9)
>R1000/mo	27/49	35	61/140	44	1.0
Missed treatment due to employment					
Yes	8/56	14	8/150	5	3.0 (1.05-8.3)
No	48/56	86	142/150	95	1.0

Table 10. Treatment characteristics of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Facility where treatment initiated					
Clinic	27/96	28	52/274	19	1.7 (1.0-2.9)
Hospital	69/96	72	222/274	81	1.0
Type of facility where treatment initiated					
Non-Governmental	45/96	47	108/274	39	1.4 (0.8-2.2)
Governmental	51/96	53	166/274	61	1.0
Admitted for MDR TB treatment					
Yes	89/96	93	239/271	88	1.7 (0.7-4.0)
No	7/96	7	32/271	12	1.0
Received kanamycin at initiation	90/96	94	261/274	95	0.8 (0.3-2.0)
Received pyrazinamide at initiation	90/96	94	266/274	97	0.5 (0.2-1.3)
Received ofloxacin at initiation	76/96	79	237/274	87	0.6 (0.3-1.1)
Received ethionamide at initiation	89/96	93	266/274	97	0.4 (0.1-1.1)
Received ethambutol at initiation	82/96	85	201/274	73	2.1 (1.1-4.0)
Received cycloserine at initiation	11/96	12	69/274	25	0.4 (0.2-0.8)
Received ciprofloxacin at initiation	18/96	19	34/274	12	1.6 (0.9-3.0)
Received clofazamine at initiation	1/96	1	2/274	1	--
Facility where treatment stopped					
Hospital	29/90	32	63/271	23	1.6 (0.9-2.7)
Clinic	61/90	68	208/271	77	1.0
Ever stop taking TB treatment before having MDR					
Yes	36/94	38	81/271	30	1.4 (0.9-2.4)
No	58/94	62	190/271	70	1.0

Table 11. Mobility of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Number of times changed residence in the year before starting MDR TB					
At least once	24/92	26	46/266	17	1.7 (0.96-3.0)
Never	68/92	74	220/266	83	1.0
Changed residence during MDR TB treatment					
Yes	16/95	17	22/272	8	2.3 (1.2-4.6)
No	79/95	83	250/272	92	1.0
If changed residence: Median number of times changed residence during treatment (range)	1 (1-4)		1 (1-4)		$p = 0.63^*$
Missed treatment due to changing residence					
Yes	6/16	38	1/19	5	10.8 (1.1-102.8)
No	10/16	63	18/19	95	1.0

* Wilcoxon rank-sum test

Table 12. Alcohol use, drug use, and prison history of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Any alcohol use during treatment					
Yes	33/86	38	66/248	27	1.7 (1.02-2.9)
No	53/86	62	182/248	73	1.0
Alcohol use stratified					
Daily drinker	3/86	4	4/248	2	2.6 (0.4-14.2)
Occasional Drinker	30/86	35	62/248	25	1.7 (0.9-2.9)
Non-drinker	53/86	62	182/248	73	1.0
If alcohol user:					
3 or more drinks in 1 day					
Yes	8/29	28	29/61	48	0.4 (0.2-1.1)
No	21/29	72	32/61	52	1.0
Missed treatment due to alcohol use					
Yes	4/30	13	9/60	15	0.9 (0.2-3.1)
No	26/30	87	51/60	85	1.0
Smoked marijuana or mandrax during treatment					
Yes	13/82	16	5/235	2	8.7 (3.0-25.2)
No	69/82	84	230/235	98	1.0
If smoker:					
Missed treatment due to smoking					
Yes	2/11	18	0/5	0	--
No	9/11	0	5/5	100	
Spent time in prison during treatment					
Yes	10/94	11	8/270	3	3.9 (1.5-10.2)
No	84/94	89	262/270	97	1.0
If prison history:					
Missed treatment due to prison					
Yes	5/9	56	5/8	63	0.8 (0.1-5.2)
No	4/9	44	3/8	37	

Table 13. Personal experience with MDR TB of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Told someone that they had MDR					
Yes	82/94	87	243/270	90	0.8 (0.4-1.6)
No	12/94	13	27/270	10	1.0
Felt ashamed about MDR					
Yes	39/93	42	80/268	30	1.7 (1.04-2.8)
No	54/93	58	188/268	70	1.0
Felt ignored or neglected b/c had MDR TB					
Yes	32/93	34	69/262	26	1.5 (0.9-2.4)
No	61/93	66	193/262	74	1.0
Depended on others for food and shelter					
Yes	55/96	57	132/274	48	1.4 (0.9-2.3)
No	41/96	43	142/274	52	1.0
Lacked enough food to eat during treatment					
Yes	48/96	50	100/267	38	1.7 (1.04-2.7)
No	48/96	50	167/267	62	1.0
Denied food or shelter b/c of having MDR TB					
Yes	7/95	7	13/269	5	1.6 (0.6-4.1)
No	88/95	93	256/269	95	1.0
Reported receiving support by non HCWs					
Yes	77/95	81	222/269	83	0.9 (0.5-1.7)
No	18/95	19	47/269	17	1.0
Felt supported by family during treatment					
Yes	84/94	89	247/271	91	0.8 (0.4-1.8)
No	10/94	11	24/271	9	1.0
Felt did not have enough support during treatment					
Yes	15/87	17	22/270	8	2.3 (1.2-4.8)
No	72/87	83	248/270	92	1.0
Felt influenced by others to stop treatment					
Yes	2/96	2	5/274	2	1.1 (0.2-6.0)
No	94/96	98	269/274	98	1.0

Table 14. Use of traditional healers among 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Saw a traditional healer during treatment					
Yes	15/96	16	30/273	11	1.5 (0.8-2.9)
No	81/96	84	243/273	89	1.0
If saw Traditional Healer: Median number of healers seen (range)	1 (1-2)		1 (1-4)		<i>p</i> = 0.54*
Type of healer seen					
Faith healer	4/14	29	13/29	45	--
Herbalist	6/14	43	7/29	24	--
Sangoma	4/14	29	9/29	31	
Given treatment by traditional healer					
Yes	8/13	62	17/28	61	--
No	5/13	38	11/28	9	
Type of treatment given					
Purgative	0/8	0	3/17	19	--
Emetic	1/8	13	3/17	19	--
Herb/tonic	7/8	88	10/17	62	
Took treatment at the same time as MDR TB treatment					
Yes	2/9	22	11/18	61	--
No	7/9	78	7/18	39	
Traditional healer asked them to stop treatment					
Yes	1/9	11	0/18	0	--
No	8/9	89	18/18	100	
Missed treatment due to traditional healer					
Yes	2/9	22	0/18	0	--
No	7/9	78	18/18	100	

* Wilcoxon rank-sum test

Table 15. Health service characteristics of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Median length of time from when patient first felt ill to time seen by the doctor (range)	30 (1-365)		30 (0-730)		$p = 0.99^*$
Median number of different clinics the patient attended for MDR TB treatment (range)	1 (0-4)		1 (0-3)		$p = 0.07^*$
How did they get to the health facility					--
Car	4/91	4	36/271	13	
Taxi	9/91	10	51/271	19	
Bus	6/91	7	16/271	6	
Bicycle	0/91	0	1/271	1	
Walk	52/91	57	151/271	56	
Other	20/91	22	16/271	6	
Time to get to the health facility					
< 30 minutes	33/74	45	100/255	39	1.3 (0.7-2.2)
30-60 minutes	29/74	39	102/255	40	1.0 (0.6-1.7)
> 1 hour	12/74	16	53/255	21	1.0
How much time spent waiting at clinic					
Did not wait	28/68	41	91/256	36	1.3 (0.7-2.3)
< 1 hr	38/68	56	156/256	61	0.8 (0.5-1.4)
> 1 hr	2/68	3	9/256	4	1.0
Were hours convenient					
No	7/70	10	10/261	4	2.8 (1.0-7.6)
Yes	63/70	90	251/261	96	1.0

* Wilcoxon rank-sum test

Table 16. DOT and support characteristics of 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Take treatment without direct supervision					
No	82/95	86	202/274	74	2.2 (1.2-4.3)
Yes	13/95	14	72/274	26	1.0
If took pills without direct supervision: Given pills by HCW to take alone					
Yes	12/12	100	59/67	88	--
No	0/12	0	8/67	12	
How did the HCW or DOTS supporter give you your pills?					
One at a time	58/84	69	149/273	55	--
Pill bottles	8/84	10	19/273	7	
Plastic bags	18/84	21	101/273	37	
Blister packs	0/84	0	4/273	1	
Ever receive food from the clinic					
No	46/78	59	142/271	52	1.3 (0.8-2.2)
Yes	32/78	41	129/271	48	1.0

Table 17. Self-reported opinions about health service and staff, by 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Opinion about the HCW attitude					
Not Satisfactory	12/96	13	4/272	2	9.6 (3.0-30.5)
Satisfactory	84/96	87	268/272	98	1.0
Did HCWs treat you with respect?					
No	8/95	8	4/274	2	6.2 (1.8-21.1)
Yes	87/95	92	270/274	98	1.0
Missed treatment due to HCW attitude					
Yes	16/95	17	5/273	2	10.9 (3.9-30.6)
No	79/95	83	268/273	98	1.0
Trust the HCW					
No	3/93	3	4/270	2	2.2 (0.5-10.1)
Yes	90/93	97	266/270	98	1.0
Trust the hospital					
No	5/91	6	3/259	1	5.0 (1.2-21.2)
Yes	86/91	94	256/259	99	1.0
Trust the clinic					
No	8/83	10	4/268	2	7.0 (2.1-24.0)
Yes	75/83	90	264/268	98	1.0
Thought treatment made them feel better					
No	20/93	22	6/271	2	12.1 (4.7-31.2)
Yes	73/93	78	265/271	98	1.0

Table 18. Knowledge of MDR TB among 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Knew taking treatment would be a year					
No	26/94	28	61/273	22	1.3 (0.8-2.3)
Yes	68/94	72	212/273	78	1.0
Told why receiving treatment for 1 year					
No	25/92	27	37/270	14	2.3 (1.3-4.2)
Yes	67/92	73	233/270	86	1.0
Given information by the HCW					
No	18/95	19	39/273	14	1.4 (0.8-2.6)
Yes	77/95	81	234/273	86	1.0
If given information					
Information was useful					
Not useful	7/70	10	2/225	1	12.4 (2.5-61.1)
Useful	63/70	90	223/225	99	1.0
Received enough information re: MDR TB					
No	5/62	8	8/225	4	2.4 (0.8-7.6)
Yes	57/62	92	217/225	96	1.0
Felt that it is possible to cure MDR TB	56/60	93	229/243	94	0.9 (0.3-2.7)
Felt that it is possible to prevent MDR TB	52/62	84	206/229	90	0.6 (0.3-1.3)
Felt that they might die from MDR TB	61/87	70	213/268	80	0.6 (0.4-1.04)
Felt that it is possible to cure TB	75/79	95	260/264	99	0.3 (0.07-1.2)
Felt that they might die from TB	63/91	69	213/271	79	0.6 (0.4-1.04)

Table 19. Self-reported responses to query about the cause of MDR TB by 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.*

Characteristic	Cases N=96		Controls N=274		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Not taking TB medicine properly	41	43	141	52	0.7 (0.4-1.1)
Being near other people with MDR TB	36	38	114	42	0.8 (0.5-1.4)
Don't know	31	32	61	23	1.7 (0.99-2.8)
Poor nutrition	20	21	68	25	0.8 (0.5-1.4)
Smoking and/or drinking	18	19	68	25	0.7 (0.4-1.3)
Having HIV/AIDS	3	3	37	14	0.2 (0.06-0.7)
Bad TB treatment by doctors and nurses	10	10	24	9	1.2 (0.6-2.6)
Evil Spirits	5	5	5	12	3.0 (0.8-10.4)
Dust and smoke	1	1	7	3	0.4 (0.05-3.3)
Poisons	1	1	7	3	0.4 (0.05-3.3)
Cold weather	1	1	6	2	0.5 (0.05-4.0)
Drug resistance	1	1	5	2	0.6 (0.07-4.9)
Unhygienic conditions	1	1	3	1	--
Bad air	1	1	2	1	--
Poor immunity	1	1	1	0	--
Stress	1	1	2	1	--
Witchcraft	1	1	0	0	--
Weak drugs	0	0	3	1	--
Poor working conditions	1	1	1	0	--
Changing one's residence	0	0	1	0	--
Chemicals	0	0	1	0	--
Depression	0	0	1	0	--
Ignorance	1	1	1	0	--
Self-neglect	0	0	1	0	--
Sharing utensils	0	0	1	0	--
Fluid in the lungs	0	0	1	0	--
Heredity	0	0	1	0	--

* Categories not mutually exclusive, percentages will add up to more than 100%

Table 20. Self-reported responses to query about the cause of TB by 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.*

Characteristic	Cases N=96		Controls N=274		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Being near other people with TB	43	45	138	50	0.8 (0.5-1.3)
Poor nutrition	34	35	116	42	0.7 (0.5-1.2)
Germs	32	33	106	39	0.8 (0.5-1.3)
Bad air	12	13	66	24	0.5 (0.2-0.9)
Smoking and/or drinking	23	24	59	22	1.1 (0.7-2.0)
Having HIV/AIDS	10	10	39	14	0.7 (0.3-1.5)
Don't know	13	14	34	12	1.1 (0.6-2.2)
Cold weather	13	14	20	7	2.0 (0.9-4.2)
Unhygienic conditions	7	7	12	4	1.7 (0.7-4.5)
Dust and smoke	2	2	8	3	0.7 (0.1-3.4)
Poisons	2	2	7	3	0.8 (0.2-4.0)
Witchcraft	5	5	3	1	4.9 (1.2-21.2)
Taboo	2	2	2	1	--
Evil Spirits	2	2	1	0	--
Poor immunity	0	0	3	1	--
Stress	0	0	3	1	--
Chemicals	1	1	1	0	--
Crowded living conditions	0	0	2	1	--
Cattle	0	0	2	1	--
Self-neglect	1	1	0	0	--
Wet clothes	1	1	0	0	--

* Categories not mutually exclusive, percentages will add up to more than 100%

Table 21. Self-reported side effects from MDR TB among 96 cases and 274 controls with MDR TB, 5 provinces, South Africa, 1999-2001.

Characteristic	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
How often had side effects					
Ever	68/83	82	181/255	71	1.9 (0.96-3.6)
Never	15/83	18	74/255	29	1.0
Side effects stratified					
Daily	39/83	47	107/255	42	1.2 (0.7-2.1)
Less than daily	29/83	35	74/255	29	1.3 (0.8-2.3)
Never	15/83	18	74/255	29	1.0
If had side effects:					
Talked to HCW					
Yes	53/68	78	149/180	83	0.7 (0.4-1.5)
No	15/68	22	31/180	17	1.0
Took medicine to feel better					
Yes	25/67	37	95/179	53	0.5 (0.3-0.9)
No	42/67	63	84/179	47	1.0
Talked to traditional healer					
Yes	4/64	6	4/173	2	2.8 (0.7-11.6)
No	60/64	94	169/173	98	1.0
Took traditional medicine					
Yes	5/62	8	4/168	2	3.6 (0.9-13.9)
No	57/62	92	164/168	98	1.0
Stopped treatment due to side effects					
Yes	24/65	37	10/174	6	9.6 (4.3-21.6)
No	41/65	63	164/174	94	1.0

Table 22. Most common reports among 68 cases and 181 controls reporting side effects from MDR TB treatment, 5 provinces, South Africa, 1999-2001.*

Side effect	Cases		Controls		Unadjusted Odds Ratio 95% CI
	Number	Percent	Number	Percent	
Nausea	39	57	107	59	--
Vomiting	32	47	76	42	--
Sore buttocks	13	19	38	21	--
Fatigue	14	21	45	26	--
Skin rash	13	19	34	19	--
Joint pain	9	13	33	18	--
Headache	11	16	24	13	--
Hearing problems	9	13	19	11	--
Visual problems	4	6	10	6	--
Dizziness	3	4	12	7	--
Abdominal pain	13	19	15	8	2.6 (1.2-5.8)
Diarrhea	12	18	6	3	--
Jaundice	9	13	1	1	5.5 (0.5-61.2)
Psychiatric problems	1	2	10	6	--
Injection abscess	1	2	3	2	--
After taste in mouth	0	0	0	0	--
Bad dreams	0	0	1	1	--
Chest pain	1	2	0	0	--
Constipation	3	4	0	0	--
Dyspnoea	0	0	2	1	--
Heartburn	1	2	0	0	--
Hot flashes	0	0	2	1	--
Incontinence	0	0	0	0	--
Insomnia	0	0	2	1	--
Kidney disease	0	0	1	1	--
Loss of appetite	0	0	2	1	--
Nose bleeding	0	0	0	0	--
Palpitations	0	0	1	1	--
Swelling chest	0	0	1	1	--
Swollen feet	0	0	3	2	--
Trembling	1	2	1	1	--
Weight loss	1	2	1	1	--

* Patients were not limited to one answer, therefore percentages will add up to more than 100%

Table 23A. Significant variables by province, unadjusted odds ratios (UOR) and adjusted odds ratios (AOR) (adjusted for province), 96 cases and 274 controls with MDR TB, South Africa, 1999-2001.

	Eastern Provinces (Mpumalanga+NWP+KZN)					Cape Provinces (Eastern and Western)					All provinces combined	
	Cases		Controls		Stratum specific OR + P value	Cases		Controls		Stratum specific OR + P value	UOR + P value	AOR, 95% CI
	Num	%	Num	%		Num	%	Num	%			
Country of birth												
Other	2/28	7	2/79	3	3.0	2/67	3	0/163	0	NA	5.3	5.9 (1.01-34.1)
South Africa	26/28	93	77/79	97	0.28*	65/67	97	163/163	100		0.04	1.0
Do not own radio	16/28	57	16/79	20	5.3	12/67	18	16/163	10	2.0	2.7	3.0 (1.7-5.5)
Own a radio	12/28	43	63/79	80	0.0002	55/67	82	147/163	90	0.09	0.0005	1.0
Do not own a television	18/28	64	28/79	35	3.3	18/67	27	36/163	22	1.3	1.7	1.8 (1.1-3.0)
Own a TV	10/28	36	51/79	65	0.008	49/67	73	127/163	78	0.43	0.04	1.0
Do not own a house	20/28	71	45/79	57	1.9	28/67	42	47/163	29	1.8	1.7	1.8 (1.1-3.0)
Own a house	8/28	29	34/79	43	0.18	39/67	58	116/163	71	0.06	0.04	1.0
Changed residence during MDR TB treatment												
Yes	10/28	36	8/79	10	4.9	6/66	9	11/161	7	1.4	2.4	2.5 (1.2-5.1)
No	18/28	64	71/79	90	0.002	60/66	91	150/161	93	0.55	0.01	1.0
Any alcohol use during treatment												
Yes	8/26	31	13/76	17	2.2	25/59	42	44/141	31	1.6	1.8	1.7 (1.02-3.0)
No	18/26	69	63/76	83	0.14	34/59	58	97/141	69	0.13	0.03	1.0
Smoked marijuana or mandrax during treatment												
Yes	4/26	15	2/76	3	6.7	9/55	16	3/130	2	8.3	7.7	7.7 (2.6-22.5)
No	22/26	85	74/76	97	0.04*	46/55	84	127/130	98	0.001*	0.0001	1.0
Spent time in prison during treatment												

Yes	5/28	18	3/77	4	5.4	5/65	8	3/161	2	4.4	4.7	4.8 (1.7-13.8)
No	23/28	82	74/77	96	0.03*	60/65	92	158/161	98	0.05*	0.002	1.0
Felt ashamed about MDR												
Yes	10/26	38	31/78	40	0.9	29/66	44	46/160	29	1.9	1.5	1.6 (0.9-2.6)
No	16/26	62	47/78	60	0.90	37/66	56	114/160	71	0.03	0.09	1.0
Lacked enough food to eat during treatment												
Yes	13/28	46	20/78	26	2.5	35/67	52	74/158	47	1.2	1.5	1.5 (0.9-2.4)
No	15/28	54	58/78	74	0.04	32/67	48	84/158	53	0.45	0.08	1.0
Felt did not have enough support during treatment												
Yes	4/26	15	7/79	9	1.9	11/60	18	14/161	9	2.4	2.2	2.2 (1.1-4.5)
No	22/26	85	72/79	91	0.45*	49/60	82	147/161	91	0.04	0.03	1.0
Opinion about the HCW attitude												
Not Satisfactory	0/28	0	1/77	1	NA	12/67	18	2/163	1	17.6	11.4	11.3 (3.1-40.7)
Satisfactory	28/28	100	76/77	99		55/67	82	161/163	99	<0.0001*	0.001	1.0
Did HCWs treat you with respect?												
No	0/27	0	2/79	3	NA	8/67	12	1/163	1	21.9	7.4	7.4 (1.9-28.5)
Yes	27/27	100	77/79	97		59/67	88	162/163	99	0.0002*	0.0008	1.0
Missed treatment due to HCW attitude												
Yes	0/28	0	0/79	0	NA	16/66	24	4/162	2	12.6	12.2	12.6 (4.0-39.6)
No	28/28	100	79/79	100		50/66	76	158/162	98	<0.0001*	0.0001	1.0
Trust the hospital												
No	2/27	7	2/78	3	3.0	3/63	5	1/149	1	7.4	4.4	4.7 (1.1-20.3)
Yes	25/27	93	76/78	97	0.27*	60/63	95	148/149	99	0.08*	0.03	1.0
Trust the clinic												
No	2/24	8	1/79	1	7.1	6/58	10	1/158	1	18.1	12.7	12.9 (2.7-63.0)
Yes	22/24	92	78/79	99	0.13*	52/58	90	157/158	99	0.002*	0.0001	1.0
Felt that they might die from MDR TB	19/25	76	62/78	79	0.8	42/61	69	130/158	82	0.7	0.6	0.6 (0.3-0.98)
	6/25	24	16/78	21	0.71	19/61	31	28/158	18	0.26	0.04	1.0

* Fishers exact 2-tailed P value

Table 23B. Significant variables by province, unadjusted odds ratios (UOR) and adjusted odds ratios (AOR) (adjusted for province), 96 cases and 274 controls with MDR TB, South Africa, 1999-2001.

	All Provinces except Western Cape					Western Cape Province					All provinces combined	
	Cases		Controls		Stratum specific OR + P value	Cases		Controls		Stratum specific OR + P value	UOR + P value	AOR, 95% CI
	Num	%	Num	%		Num	%	Num	%			
Country of birth												
Other	2/61	3	2/166	1	2.8	2/34	6	0/76	0	NA	5.3	5.9 (1.01-34.1)
South Africa	59/61	97	164/166	99	0.29*	32/34	94	76/76	100		0.04	1.0
Do not own radio	21/61	11	18/166	11	4.3	7/34	21	14/76	18	1.1	2.7	3.0 (1.7-5.5)
Own a radio	40/61	89	148/166	89	<0.0001	27/34	79	62/76	82	0.79	0.0005	1.0
Do not own a television	28/61	46	45/166	27	2.3	8/34	24	19/76	25	0.9	1.7	1.8 (1.1-3.0)
Own a TV	33/61	54	121/166	73	0.007	26/34	76	57/76	75	0.87	0.04	1.0
Do not own a house	32/61	53	70/166	42	1.5	16/34	47	22/76	29	2.2	1.7	1.8 (1.1-3.0)
Own a house	29/61	47	96/166	58	0.17	18/34	53	54/76	71	0.06	0.04	1.0
Changed residence during MDR TB treatment												
Yes	11/60	18	14/164	9	2.4	5/34	15	5/76	7	2.4	2.4	2.5 (1.2-5.1)
No	49/60	82	150/164	91	0.04	29/34	85	71/76	93	0.17	0.01	1.0
Any alcohol use during treatment												
Yes	26/58	45	40/160	25	2.4	7/27	26	17/57	30	0.8	1.8	1.7 (1.02-3.0)
No	32/58	55	120/160	75	0.005	20/27	74	40/57	70	0.71	0.03	1.0
Smoked marijuana or mandrax during treatment												
Yes	9/56	16	3/157	2	9.8	4/25	16	2/49	4	4.5	7.7	7.7 (2.6-22.5)
No	47/56	84	154/157	98	<0.0003*	21/25	84	47/49	96	0.17*	0.0001	1.0
Spent time in prison during treatment												
Yes	5/61	8	3/164	2	4.8	5/32	16	3/74	4	4.4	4.7	4.8 (1.7-13.8)
No	56/61	92	161/164	98	0.04*	27/32	84	71/74	96	0.05*	0.002	1.0

Felt ashamed about MDR													
Yes	24/58	42	50/163	31	1.6	15/34	44	27/75	36	1.4	1.5	1.6 (0.9-2.6)	
No	34/58	58	113/163	69	0.14	19/34	56	48/75	64	0.42	0.09	1.0	
Lacked enough food to eat during treatment													
Yes	28/61	46	66/165	40	1.3	20/34	59	28/71	39	2.2	1.5	1.5 (0.9-2.4)	
No	33/61	54	99/165	60	0.42	14/34	41	43/71	61	0.06	0.08	1.0	
Felt did not have enough support during treatment													
Yes	7/52	13	7/164	4	3.5	8/34	24	14/76	18	1.4	2.2	2.2 (1.1-4.5)	
No	45/52	87	157/164	96	0.02	26/34	76	62/76	82	0.54	0.03	1.0	
Opinion about the HCW attitude													
Not Satisfactory	2/61	3	1/164	1	5.5	10/34	29	2/76	3	15.4	11.4	11.3 (3.1-40.7)	
Satisfactory	59/61	97	163/164	99	0.18*	24/34	71	74/76	97	0.0001*	0.001	1.0	
Did HCWs treat you with respect?													
No	3/60	5	2/166	1	4.3	5/34	15	1/76	1	12.9	7.4	7.4 (1.9-28.5)	
Yes	57/60	95	164/166	99	0.12*	29/34	85	75/76	99	0.01*	0.0008	1.0	
Missed treatment due to HCW attitude													
Yes	3/61	5	0/166	0	NA	13/33	39	4/75	5	11.5	12.2	12.6 (4.0-39.6)	
No	58/61	95	166/166	100		20/33	61	71/75	95	<0.0001*	0.0001	1.0	
Trust the hospital													
No	3/59	5	2/164	1	4.3	2/31	6	1/63	2	4.3	4.4	4.7 (1.1-20.3)	
Yes	56/59	95	162/164	99	0.12*	29/31	94	62/63	98	0.25*	0.03	1.0	
Trust the clinic													
No	3/48	6	1/163	1	10.8	5/34	15	1/74	1	12.6	12.7	12.9 (2.7-63.0)	
Yes	45/48	94	162/163	99	0.04*	29/34	85	73/74	99	0.01*	0.0001	1.0	
Felt that they might die from MDR TB													
Yes	35/54	65	127/162	74	0.5	26/32	81	65/74	88	0.6	0.6	0.6 (0.3-0.98)	
No	19/54	35	35/162	22	0.05	6/32	19	9/74	12	0.37	0.04	1.0	

* Fishers exact 2-tailed P value

Table 24. Multivariate Logistic Regression Analysis for Treatment Default Among 77 MDR TB Case Patients and 222 Control Patients, South Africa, 1999-2001.

Characteristic	All 5 provinces †	
	Adjusted Odds Ratio 95% CI	<i>p</i> value
Age		
36 years or more	1.5 (0.8-2.7)	0.18
Less than 36 years	1.0	
Gender		
Female	1.6 (0.8-3.0)	0.18
Male	1.0	
Smoked marijuana or mandrax during treatment		
Yes	17.9 (4.7-68.5)	<0.001
No	1.0	
Opinion about the HCWs attitude		
Not Satisfactory	12.6 (2.7-58.6)	0.001
Satisfactory	1.0	
Own a radio		
No	3.4 (1.6-7.1)	0.008
Yes	1.0	
Changed residence during MDR TB treatment		
Yes	3.2 (1.4-7.6)	0.05
No	1.0	
Location of interviewee		
Cape provinces (East/West)	2.4 (1.2-4.8)	0.01
KZN/Mpumalanga/NW	1.0	
Any alcohol use during treatment		
Yes	2.1 (1.1-4.0)	0.05
No	1.0	
Felt that they might die from MDR		
Yes	0.4 (0.2-0.8)	0.05
No	1.0	

† Patients with any missing values excluded from multivariate analysis, total n = 77 cases and 222 controls.

Table 25. Self-reported attitudes among 96 MDR TB treatment defaulters

Question	Number	Percent
Phase of treatment when patient defaulted		
First month	2/96	2
Month 2-4	18/96	19
Early continuation (month 5-12)	53/96	55
Late continuation (month 13-18)	15/96	16
Unknown	8/96	8
Felt that experiencing side effects had a role in stopping MDR TB treatment		
Very much	26/73	36
A little	10/73	14
Not much	10/73	14
Not at all	27/73	37
Felt not knowing enough about MDR TB had a role in stopping MDR TB treatment		
Very much	24/85	28
A little	12/85	14
Not much	10/85	12
Not at all	39/85	46
Felt a health worker's attitude had a role in stopping MDR TB treatment		
Very much	14/93	15
A little	8/93	9
Not much	8/93	9
Not at all	63/93	68
Stopped taking MDR TB treatment because of lack of support or encouragement		
Very much	12/85	14
A little	8/85	9
Not much	10/85	12
Not at all	55/85	65
Felt other people's influence had a role in stopping your MDR TB treatment		
Very much	5/77	7
A little	4/77	5
Not much	3/77	4
Not at all	65/77	84
Stopped taking MDR TB treatment because they changed residence		
Yes	8/92	9
No	84/92	91

Table 26. Self reported reasons for defaulting among 96 MDR TB treatment defaulters, 5 provinces, South Africa, 1999-2001.

Reason	Number	Percent*
The pills gave me side effects	24	26
I felt better	16	17
I didn't like being away from family so long	13	14
I thought I was taking pills for too long	12	13
I didn't believe I had MDR TB	12	13
I could not afford transport to the clinic	11	12
The health care staff treated me poorly	10	10
I didn't want to lose my job	9	9
I had to look for a job/money	9	9
I was not getting any better on treatment	9	9
The clinic was too far for me to travel to	6	6
I didn't like taking pills every day	6	6
I was too busy with family obligations	5	5
I moved around too much	5	5
Not sure	4	4
The clinic ran out of medicine	4	4
I was depressed and gave up	4	4
I did not get enough treatment support	4	4
I was drinking alcohol too much	3	3
I could not get time off of work	3	3
I forgot to come in for treatment	2	2
I went to prison	1	1
I did not have time, too busy	1	1
I had to go back to school	1	1
Traditional healer told me to stop	1	1
I didn't think it was important	1	1

* Patients were not limited to one answer, therefore percentages will add up to more than 100%