

# Risk Factors for Default in the Population of DOTS Plus Patients in Tomsk Oblast, Russia

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## Introduction

- Prolonged 18-24 months of treatment of multi-drug resistant TB generally results in higher default rate than short-course chemotherapy, ranging between 11% and 48% in different projects.<sup>1,2,3,4,5,6</sup> Incomplete treatment can lead to continued transmission of tuberculosis and higher rate of death among defaulters.
- Tomsk MDR TB treatment program was launched in 2000. The results of the first cohort, which consisted of patients enrolled between September 2000 and September 2002, were encouraging: the cure rate reached 77% while the proportion of defaulters was 12%.<sup>7</sup>
- Further expansion of the program has resulted in the growing number of incomplete treatments. The default rate reached 28.1% in 2003. Since the default rate substantially jeopardized the cure rate, more insight was given to the investigation of the reasons and search for new approaches to handle the problem.

## Methods

We conducted a cohort study to evaluate the major risk factors for default among MDR TB patients in the civilian and prison sector of Tomsk oblast, Russia

**Figure 1. Tomsk oblast is located in Western Siberia, Russia.**



## Study Population:

This study included all cases of MDR TB who were enrolled on DOTS Plus treatment program between September 10th, 2000 and November 1st, 2004 in Tomsk Oblast.

## Data Collection:

- We collected data from standardized forms completed prospectively by TB providers, and performed chart reviews to verify and complete data.
- The presence of official diagnosis of chronic alcoholism and drug addiction was recorded. In addition the information about alcohol and drug abuse during treatment was obtained from the patients' charts.
- Severe disease was defined as a presence of bilateral and cavitary process in the lungs.
- Presence of severe side effects was described as any of the following: nephrotoxicity, hepatotoxicity, hypokalemia, depression, psychosis and seizure.
- Adherence was monitored daily for each medication prescribed. Adherence was defined as the proportion of doses received out of the total doses prescribed
- Final treatment outcomes definitions by the MDR-TB Working Group were used for this study. Therefore, default was defined as treatment interruption for two or more months for any reason.

## Statistical analyses:

- We conducted univariable analyses for binary and continuous variables using Chi-squared and Student's t-tests, respectively. We used ANOVA to identify categorical variables associated with default.
- Logistic regression models were used to identify risk factors for default.

## Results

- Six hundred thirty six patients were enrolled in the program within the study period, 200 of them started treatment in the penitentiary sector and 438 patients were in the civilian sector.
- Twenty five (12.5%) of 200 patients have defaulted in penitentiary sector and 105 (24%) of 438 defaulted treatment in the civilian sector.
- The prevalence of HIV in the cohort was 5 (0.8%) of 638 patients.

**Table 1. MDR TB cohort treatment characteristics in civilian and penitentiary sectors.**

| Characteristics                         | Civilian sector N=438 |                     |         | Penitentiary sector N=200 |                     |         |
|---|-----------------------|---------------------|---------|---------------------------|---------------------|---------|
|   | Defaulter n (%)       | Non-defaulter n (%) | p-value | Defaulter n (%)           | Non-defaulter n (%) | p-value |
| Age > median                            | 61 (58.1)             | 183 (55.0)          | 0.5726  | 11 (44.0)                 | 68 (38.7)           | 0.6236  |
| Female*                                 | 19 (18.1)             | 89 (26.73)          | 0.0739  | -                         | -                   | -       |
| Married                                 | 45 (42.9)             | 180 (54.1)          | 0.0456  | 2 (8.0)                   | 23 (13.1)           | 0.4682  |
| Unemployed*                             | 40 (38.1)             | 89 (26.7)           | 0.026   | -                         | -                   | -       |
| Absence of homeownership*               | 16 (15.2)             | 16 (4.8)            | 0.0003  | -                         | -                   | -       |
| Previously incarcerated*                | 56 (53.3)             | 106 (31.8)          | <0.0001 | -                         | -                   | -       |
| Alcoholism or drug addiction diagnosis  | 72(68.6)              | 147 (44.1)          | <0.0001 | 11(44.0)                  | 81 (46.3)           | 0.8306  |
| Alcohol or drug abuse during treatment* | 85 (81.0)             | 194(58.3)           | <0.0001 | -                         | -                   | -       |
| Severe disease                          | 72 (71.3)             | 199 (60.3)          | 0.0458  | 17 (68.0)                 | 103 (59.2)          | 0.4013  |
| History of previous default             | 23 (21.9)             | 33 (9.9)            | 0.0013  | 2 (8.0)                   | 11 (6.3)            | 0.7456  |
| Initial XDR TB                          | 3 (2.9)               | 17 (5.2)            | 0.3236  | 1 (4.4)                   | 7 (4.2)             | 0.9676  |
| Presence of severe side effects         | 11(10.5)              | 71(21.3)            | 0.0131  | 5 (20.0)                  | 45 (25.7)           | 0.5381  |
| Adherence less than average             | 64 (61.5)             | 99 (29.8)           | <0.0001 | 17 (70.8)                 | 69 (41.3)           | 0.0067  |
| City inhabitant (versus rural)*         | 70 (66.7)             | 170 (51.1)          | 0.0051  | -                         | -                   | -       |
| Hospital as a last treatment place*     | 55 (52.4)             | 73 (21.9)           | <0.0001 | -                         | -                   | -       |
| Not a citizen of Tomsk oblast**         | -                     | -                   | -       | 9 (36.0)                  | 47 (26.9)           | 0.3421  |
| Being released from prison**            | -                     | -                   | -       | 16 (64.0)                 | 33 (18.9)           | <0.0001 |
| Time of enrollment by year              |                       |                     |         |                           |                     |         |
| 2000- 2001                              | 10 (11.8)             | 75 (88.2)           |         | 1 (1.7)                   | 57 (98.3)           |         |
| 2002                                    | 14 (16.9)             | 69 (83.1)           | 0.0005  | 9 (12.7)                  | 62 (87.3)           | 0.0042  |
| 2003                                    | 37 (30.6)             | 84 (69.4)           |         | 11 (22.4)                 | 38 (77.6)           |         |
| 2004                                    | 44 (29.9)             | 103 (70.1)          |         | 4 (19.1)                  | 17 (80.9)           |         |

\* These variables were assessed only in the civilian sector. MDR TB project was launched in Male prison, with no access to alcohol and drugs. Other factors were not applicable to prisoners due to their specific status.  
\*\* These variables were assessed only in penitentiary sector.

•Severity of disease and side effects did not play a role but both were significant in the univariate analysis.

•The major risk factors for default in the civilian sector were urban settlement, alcohol or drug abuse, previous incarceration and a later year of enrollment. Absence of homeownership was marginally significant.

•During treatment defaulters tended to have a shorter hospital stay→175.7±28.7 [mean ± SD] days as compared with non-defaulters with a mean of 289.1±21.7 days, p<0.0001. Default was also associated with the hospital being the last treatment place.

•In the penitentiary sector "being released" while on treatment and the year of enrollment were the major risk factors for default. Being diagnosed with alcoholism or drug dependence did not influence adherence of inmates.

•Being a citizen of another region rather than Tomsk oblast showed significance in analyses for 49 individuals, who were released from prison. In the multivariate analyses, this variable showed marginal significance for the whole cohort of prisoners.

## Discussion

- Our study has confirmed findings from other sites about the relationship between alcohol/drug abuse, homelessness, previous incarceration and default. It is also shown that one, existing hospitals lack the capacity to keep these patients on treatment and two, ambulatory care is not able to organize proper treatment after patients are discharged from the hospital.
- One of the ways to handle this problem is to follow the experience from countries with similar problems, which actually managed to improve adherence through convenient options for treatment (including home treatment), extensive social support, availability of alcohol/dependence treatment and, in extreme cases, compulsory isolation of patients.

•The major factors for default within the penitentiary sector are left behind the scope of this study since no demographic and clinical variables have shown significance. High level of default among released patients was associated with non Tomsk residence and can be addressed through detention of prisoners in prisons located close to patient's civilian residence as well as through better coordination of TB care between different oblasts (regions) in the civilian sector.

•Later year of enrollment was associated with increased risk for default. This can partly be explained by the enrollment of "good" patients at the beginning of the project and the increased flow of patients with social problems later on. Another explanation is the inability of the TB system to handle the growing number of patients with the expansion of the project.

**Table 2. Multivariate analyses of risk factors associated with default**

| Characteristic                  | Civilian sector Multivariate OR (95% CI) | Penitentiary sector Multivariate OR (95% CI) |
|---------------------------------|--|--|
| Age > median                    | 0.99 (0.58; 1.71)                        | 1.11 (0.44; 2.83)                            |
| Female                          | 0.84 (0.43; 1.66)                        | -  |
| Married                         | 0.77 (0.46; 1.29)                        | 0.43 (0.09; 2.19)                            |
| Unemployed                      | 1.17 (0.69; 1.98)                        | -  |
| Absence of homeownership        | 2.11 (0.90; 4.95)                        | -  |
| Previously incarcerated         | <b>1.71 (0.98; 2.97)</b>                 | -  |
| Alcohol or drug abuse           | <b>2.75 (1.53; 5.31)</b>                 | -  |
| Severe disease                  | 1.21 (0.68; 2.15)                        | 1.73 (0.65; 4.65)                            |
| History of previous default     | 1.24 (0.63; 2.43)                        | -  |
| Presence of severe side effects | 0.40 (0.19; 0.85)                        | -  |
| City inhabitant (versus rural)  | <b>2.83 (1.68; 4.81)</b>                 | -  |
| Not a citizen of Tomsk oblast   | -  | 2.79 (0.93; 7.79)                            |
| Being released from prison      | -  | <b>10.84 (3.98; 29.52)</b>                   |
| Late year of enrollment         | <b>1.35 (1.05; 1.73)</b>                 | -  |

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