

# Treatment outcome of Singapore residents with pulmonary tuberculosis in the first year after introduction of a computerised treatment surveillance module

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## ABSTRACT

**Introduction:** A key intervention of the Singapore Tuberculosis Elimination Programme (STEP) was the introduction in 2001 of a computerised treatment surveillance module (TSM) for the real-time monitoring of the treatment progress of the country's notified tuberculosis (TB) cases until a final outcome. We report the treatment outcome as at December 31, 2002 for the cohort of Singapore residents with new and relapsed pulmonary TB in whom treatment was commenced in 2001.

**Methods:** Each TB notification will activate the TSM, which requires a return on the patient's treatment progress, treatment delivery mode and the treating physician's management decision at each clinic visit to the STEP Registry until an outcome is reached.

**Results:** There were 1,354 Singapore residents with new or relapsed pulmonary TB who started treatment in 2001. Of these, 620 (45.8 percent) underwent directly-observed therapy (DOT) at their nearest polyclinic. As at December 31, 2002, 79 percent of patients completed treatment, nine percent died (two percent from TB), nine percent interrupted treatment (they were either lost to follow-up or refused treatment), 1.8 percent were still on treatment, 0.6 percent left the country, and 0.5 percent had permanent cessation of treatment due to drug reactions. Factors associated with treatment completion were Chinese ethnicity (odds-ratio [OR] 1.5, 95 percent confidence interval [CI] 1.1-2, p-value is 0.02), age younger than 65 years (OR 1.8, 95 percent CI 1.3-3.0, p-value is 0.003) and the use of DOT (OR 3.1, 95 percent CI 2.3-4.1, p-value is less than 0.05).

**Conclusion:** The findings from the TSM's first year provide a baseline for future programme evaluation.

**Keywords:** directly observed therapy, pulmonary, treatment outcome, tuberculosis.

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## INTRODUCTION

Recording and reporting of the treatment outcome of tuberculosis (TB) cases constitutes one of the five elements of the World Health Organisation (WHO) - recommended Directly-Observed Treatment - Short Course (DOTS) strategy<sup>(1)</sup>. Although Singapore has had a national TB notification registry since the 1950s, there had been no systematic reporting of treatment outcome, nor surveillance of the treatment progress of the country's TB cases until 2001. The Ministry of Health had, in 1997, launched the Singapore TB Elimination Programme (STEP)<sup>(2,3)</sup> to address the decade-long stagnation in the country's TB incidence rate<sup>(4)</sup>. Singapore's annual TB incidence rate has since steadily declined from 57 per 100,000 in 1998 to 40.8 per 100,000 resident population in 2003<sup>(5)</sup>.

A major activity of STEP was the setting up of a computerised treatment surveillance module (TSM) to monitor "real-time" the treatment progress of each notified TB case treated in Singapore until an outcome is reached. The system achieved nation-wide coverage by January 2001. We report the treatment outcomes as at December 31, 2002 for new and relapsed pulmonary TB cases among Singapore residents who commenced treatment in 2001, the first year of nationwide implementation of TSM.

## METHODS

The notification of TB is mandated by law in Singapore. Each notified TB case will activate the TSM, which requires periodic returns on the patient's treatment progress to be submitted by the treating physician at every clinic review (generally recommended to be monthly), until an outcome is achieved. The treatment surveillance forms (MD 117) are submitted directly (usually via fax) to the

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**Table I. Outcome by treatment delivery mode (DOT versus non-DOT).**

	Total n=1,354	Non-DOT n=734	DOT n=620	p-value
Completed treatment	1,072 (79.2%)	519 (70.7%)	553 (89.2%)	<0.001
Treatment interrupted (lost to follow-up/ refused treatment)	120 (8.9%)	95 (12.9%)	25 (4.0%)	<0.001
Treatment interrupted (drug reaction)	7 (0.5%)	5 (0.7%)	2 (0.3%)	0.3
Died (from TB/ other causes)	122 (9%)	96 (13.1%)	26 (4.2%)	<0.001
Still on treatment	25 (1.8%)	14 (1.9%)	11 (1.8%)	0.9
Transferred out	8 (0.6%)	5 (0.8%)	3 (0.5%)	0.4

STEP registry on a real-time basis.

The TSM captures the patient's progress, the treating physician's management decision at each clinic visit, and the final outcome. For the purpose of this analysis, cases on DOT were defined as those who attended the government polyclinics where the medicine was swallowed under the direct observation of the polyclinic nurses. All other cases were classified as non-DOT cases. If the patient was to be transferred to another treatment centre, details of that treatment centre, and the scheduled appointment date at that centre would be captured.

The designated final outcomes were: "treatment completed", "death" (and cause of death), "treatment interrupted due to treatment refusal or default" ("lost to follow-up"), "treatment interrupted due to drug reaction" and "transferred out" (i.e. left the country). A patient on non-DOT was considered to be adherent to treatment according to the attending physician's judgment. For a patient on DOT, adherence was determined by the polyclinic medication records. The final treatment regimen utilised was also captured. We analysed the treatment outcome as at December 31, 2002 for Singapore residents with notified new or relapsed pulmonary TB in whom treatment was started between January 1 and December 31, 2001.

Descriptive summary measures of central tendency and frequency of the study variables were computed as appropriate. Bivariate categorical data were analysed using  $\chi^2$  or Fischer's exact test, whichever is appropriate. All factors showing an association with treatment outcome, in univariate analysis, were introduced in a step backward logistic regression. All statistical tests performed were two-tailed and statistical significance was defined by a

p-value of less than 0.05. Statistical analysis was carried out by using Statistical Package for Social Sciences (SPSS) version 9.0 (Chicago, IL, USA).

## RESULTS

The majority of TB patients in Singapore are treated in the public sector. In 2001, 50.2% of the country's TB cases were treated at the TB Control Unit (TBCU) and 35.5% at the five government restructured general hospitals, while 4.7% were treated by chest physicians in private practice, and 3.3% by the Singapore Anti-TB Association<sup>(6)</sup>. The treatment centre was not known in 6.3% of patients.

There were 1,646 Singapore residents notified with new and relapsed TB in 2001<sup>(5)</sup>. Among these, 108 (6.6%) were not started on TB treatment: 84 cases died without having started treatment, six refused treatment, and 18 cases had no reasons given for non-treatment. There were thus 1,538 cases (all types of TB) who were started on TB treatment and for whom treatment outcome data were available. Of these, 1,354 were pulmonary TB cases, comprising 1,189 (88%) new cases and 165 (12%) relapsed cases. 64% (872/1,354) were culture-positive cases; of these, 32% (283/872) were sputum AFB smear positive.

The treatment outcome reported is the final outcome as at December 31, 2002, i.e. at one year after December 31, 2001, the last enrolment date. Of the 1,354 pulmonary TB cases under treatment surveillance, 1,072 (79.2%) completed treatment, 26 (1.9%) died from TB, 96 (7.1%) died of other causes or did not have their cause of death indicated, 120 (8.9%) had interrupted treatment (they refused treatment or were lost to follow-up), 25 (1.8%) were still on treatment, eight (0.6%) were transferred out (i.e. left the country), and seven (0.5%) had treatment interrupted due to drug reaction.

620 (45.8%) patients received treatment under DOT at their nearest polyclinic. The treatment outcome according to treatment delivery mode (DOT versus non-DOT) is shown in Table I. Patients treated under DOT had a statistically significantly higher treatment completion rate, compared to those who did not (89.2% versus 70.7%,  $p<0.001$ ). Patients treated under the non-DOT delivery mode were significantly more likely to have treatment interruption (12.9% versus 4.0%,  $p<0.001$ ) or death as an outcome (13.1% versus 4.2%,  $p<0.001$ ).

The treatment outcome by ethnicity is shown in Table II. Persons of Malay and Indian ethnicity were more likely to interrupt treatment than those of Chinese ethnicity, with the Indians having the highest rate of treatment interruption (22%,  $n=16$ ).

**Table II. Treatment outcome by ethnic group.**

	Chinese (n=1,020)	Malay (n=245)	Indian (n=72)	Others (n=17)	p-value $\chi^2$ test, Fischer's exact test (completed treatment vs other treatment outcomes)
Completed treatment	817 (80%)	189 (77%)	51 (71%)	15 (88%)	
Treatment interrupted (lost to follow-up/ refused treatment)	69 (6.8%)	34 (13.9%)	16 (22.2%)	1 (5.9%)	<0.001
Treatment interrupted (drug reaction)	5 (0.5%)	2 (0.8%)	0	0	0.9
Died (from TB/ other causes)	102 (10%)	15 (6.1%)	4 (5.6%)	1 (5.9%)	0.5
Still on treatment	23 (2.3%)	2 (0.8%)	0	0	0.5
Transferred out	4 (0.4%)	3 (1.2%)	1 (1.4%)	0	0.2

The death rate among the Chinese was the highest among the ethnic groups at 10% (n=102), compared to 6.1% (n=15) in the Malay and 5.6% (n=4) in the Indian ethnic groups. The outcome by age is shown in Table III. The median age of patients who died during treatment (whether from TB or other causes) was statistically significantly higher than that of those who completed treatment (70 years versus 52 years,  $p<0.001$ ). New TB cases had a better treatment completion rate than relapsed cases (80% versus 74%); this was not statistically significant. Logistic regression analysis showed factors associated with treatment completion to be Chinese ethnicity (OR 1.5, 95% CI 1.1-2,  $p=0.02$ ), age<65 years (OR 1.8, 95% CI 1.3-3.0,  $p=0.003$ ) and the use of directly-observed therapy (DOT) (OR 3.1, CI 2.3-4.1,  $p<0.05$ ) (Table IV).

## DISCUSSION

The first year's data from the TSM revealed a national treatment completion rate of 79%, which falls short of the WHO targets of 85% for smear-positive cases in developing countries and 95% in industrialised countries<sup>(7)</sup>. Our treatment completion rate is also lower than that reported in the UK<sup>(8)</sup>, Italy<sup>(9)</sup>, and the Netherlands<sup>(10)</sup>. Factors associated with higher likelihood of successful treatment were Chinese ethnicity, age <65 years and the use of DOT.

The death rate in our treatment surveillance cohort of 2001 was disturbingly high at 9%, and this was a major factor for treatment non-completion among patients of Chinese ethnicity. We had shown that death occurred mostly among the elderly TB patients: the median age of patients who died during

**Table III. Treatment outcome by age.**

	Median age (years)	p-value Mann-Whitney test (completed treatment versus other treatment outcomes)
Completed treatment	52	
Treatment interrupted (lost to follow-up/ refused treatment)	57	0.002
Treatment interrupted (drug reaction)	73	0.24
Still on treatment	58	0.18
Died (from TB/ other causes)	70	<0.001
Transferred out	70	0.25

**Table IV. Patient characteristics and treatment factors related to successful treatment outcome (2001) (Logistic regression).**

	Adjusted OR	95% CI	p-value
Chinese ethnicity	1.5	1.1 - 2	0.02
Age <65 years	1.9	1.3 - 3.0	0.003
Treatment delivery mode DOT (as final delivery mode)	3.1	2.3 - 4.1	<10 <sup>-6</sup>

treatment (whether from TB or other causes) was 70 years (whereas the median age for those who completed treatment was 52 years) (Table III).

Despite having the best treatment completion rate among the ethnic groups, the death rate was highest among the Chinese at 10%, versus 6.1% and 5.6% in Malays and Indians, respectively. This can be attributed to the higher absolute number of TB cases among the elderly of the Chinese ethnic majority in Singapore, in whom death was more likely. Furthermore, the poorer treatment completion rate among the Malays and Indians was a reflection of their higher treatment interruption rate, compared to the Chinese. As the TB incidence rate in Singapore shows a striking increase with age<sup>(6)</sup>, the relatively high death rate may not be entirely surprising. Nevertheless, this issue should still be addressed – while TB was reported as the cause of death in 2%, concomitant TB disease may still have contributed to mortality in the remaining 7% of patients who had death as their treatment outcome. We need to further evaluate the circumstances of death in our patients, particularly to ascertain if these deaths were in any way related to delayed TB diagnosis or the adverse effects of TB medications.

Another significant finding was that patients of Malay and Indian ethnicity were more likely than the Chinese patients to interrupt their TB treatment. This finding is consistent with that of a survey on treatment defaulters carried out at the Singapore TB Control Unit in 1996, before STEP was launched<sup>(11)</sup>. There is an evident need for increased outreach and educational activities within these communities to raise the awareness of TB as a public health concern.

While DOT is recommended as the standard of care by international organisations such as the American Thoracic Society, the World Health Organisation and the Union<sup>(1,12,13)</sup>, this treatment delivery mode may not be well accepted by patients, or even certain physicians. It has been argued that there has not been any evidence from randomised controlled trials that the use of DOT compared to self-administered treatment (SAT) has achieved superior treatment outcomes<sup>(14,15)</sup>. However, in field/programme conditions, the use of DOT has been shown to achieve good cure rates and to decrease the incidence of drug resistance and relapse in the community<sup>(16-18)</sup>. Therefore, a major strategy adopted by STEP was the promotion of outpatient DOT administered at the public health clinic nearest the patient's home.

Since 1998, DOT has been utilised in about 70% of cases treated at the TBCU, the national referral centre where 50% of the country's cases are managed. DOT was, however, not used by the other treatment centres in Singapore in 2001. Thus,

of the 1,354 pulmonary TB cases treated nationwide in 2001, only 620 (46%) received treatment under DOT. In Singapore, DOT is administered on an outpatient basis and requires the patient to attend his or her nearest polyclinic for its administration. It may be argued that patients who were not treated under DOT were likely those who were physically unable to attend their nearest outpatient polyclinic because of their underlying poorer health status, and that their poorer treatment outcome could be attributed to this. However, after removing the cases who died during treatment, the treatment completion rate was still better in the DOT group than the non-DOT group (93% versus 81%). The significantly higher treatment completion rate of 89% for patients treated under DOT compared to 70.7% for patients treated under non-DOT conditions lends support for the wider use of this treatment delivery mode.

The treatment outcome data from the first year of nationwide implementation of the TSM has identified important areas for intervention and improvement. We now also have a baseline upon which the programme can build to monitor and improve its performance.

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