



## Epidemiological Research

### Studies in progress:

#### Mortality among a cohort of TB patients treated under RNTCP from a rural area in India

##### Objectives:

1. To measure the mortality rates among the cohorts of TB patients in a rural area such as Tiruvallur;
2. To measure the excess general mortality among the cohorts of TB patients;
3. To identify high-risk groups for mortality among TB patients;
4. To study the trend of mortality rates over successive annual cohorts of TB patients;

##### Methods:

##### Study design:

This is a retrospective cohort study.

##### Study population:

The study population consisted of 3429 patients (2469 males and 960 females) registered with Velliyur TB Unit (TU), Tiruvallur district, Tamil Nadu, in the years 2000, 2001, 2002 and 2003. They were treated under the RNTCP and were all retrospectively followed-up from the day of the start of treatment to either the date of interview (for the survivors), or the date of death (for the dead).

There were 2729 (79.6 per cent) survivors and 700 (20.4 per cent) deaths.

##### Study duration:

May 2005 to February 2006.

Data analysis is in progress.

##### Mortality surveys in Andhra Pradesh and Orissa

This is a Government of India Project (Central TB Division) funded by Global Fund Against AIDS, TB and Malaria (GFATM). The total budget sanctioned for this project is Rs. 85 lakhs.

##### Objectives:

1. To estimate crude mortality rate in the state of Andhra Pradesh.
2. To estimate TB mortality rate among the general population aged  $\geq 15$  years.

##### Sample Size:

380,000 for both the States

##### Sampling design:

The sampling frame consisting of a list of villages (rural) and towns (urban) were obtained from the Directorate of Census Operations. In the rural areas, villages were the sampling units. In the urban areas, sampling units were from the census enumeration block. The total sample size of 380,000 will be selected from 380 sampling units. All these sampling units have been selected by a simple random method without replacement.



## **Methodology:**

Health workers registered the study population by house-to-house enumeration. During registration, the household number, names of the members, age in completed years and gender were recorded in the household form. In addition, information on occurrence of death in each household was recorded. All household forms that report deaths will be handed over to the supervisors for detailed verbal autopsy to ascertain the cause of death.

## **Verbal Autopsy:**

All deaths identified during enumeration were probed in detail by the supervisors through verbal autopsy from a close relative / neighbour / friend to ascertain the cause of death. Supervisors are specially trained to undertake verbal autopsy. Verbal autopsy is an investigation of train of events, circumstances, symptoms and signs of illness leading to death through interviews of relatives or associates of the deceased.

## **Andhra Pradesh:**

The survey began during the first week of September, 2005.

Surveys in five districts, Mahabub Nagar, Khammam, Krishna, Vizianagaram and Prakasam were completed. The survey is in progress in Chittoor district.

Cumulative coverage: Units-370; Population-3,76,742; Deaths-2114.

## **Orissa:**

The survey began in the last week of October 2005.

Surveys in six districts namely, Cuttack, Jagathsinghpur, Kendra Para, Sundargarh, Deogarh and Gajapati have been completed. Survey is in progress in Bargarh and Rayagada districts.

Cumulative coverage: Units-330; Population-3,34,417; Deaths-1612.

## **Model DOTS Project:**

Directly Observed Treatment Short course (DOTS), a global strategy for control of TB is being implemented in India in a phased manner since 1997. The epidemiological impact of this strategy in high burden countries is not known. To understand this, the TB Research Centre, is undertaking an epidemiological impact study in five blocks of Tiruvallur district, Tamil Nadu. This is the same area where the BCG trial was done. Therefore, epidemiological data on TB is available even before DOTS has been implemented. The project has its technical support from the World Health Organization (WHO) and financial support from United States Agency for International Development (USAID). Started in May 1999, the project has the involvement of TRC in the following areas:

- a) Training
- b) Epidemiological survey of TB disease and infection
- c) Bacteriological and molecular epidemiological studies and
- d) Operational research.



### **Training:**

Good quality training is essential for the successful implementation of any programme. Therefore TRC has been identified as a nodal centre for training in RNTCP. During the training period, 53 Medical Officers (Tr), 41 Medical Officers, 59 Senior Treatment Supervisors, 19 Senior TB Laboratory Supervisors, 13 Laboratory Technicians and nine microbiologists, have been trained.

### **Studies completed:**

#### **Assessment of quality of life of TB patients treated under the DOTS programme**

##### **Background:**

Information on health related quality of life (HRQoL) of treated TB patients is very sparse.

##### **Objective:**

To assess the HRQoL of TB patients, one year after treatment completion.

##### **Method:**

Patients registered under the programme (July 2002-June 2003) in one tuberculosis unit (TU), South India, one year after the successful completion of treatment were interviewed. Data on HRQoL was collected using the modified SF-36 questionnaire, covering physical, mental, social and economic well being. Scores were given for all domains and the total well being score was the average of all these domains.

##### **Results:**

Of the 436 TB patients interviewed, overall well being score was 72, on a scale of 100. The mean scores for different domains were: social (84), physical (74), mental (68) and economic (62). The total well being score was significantly less (70) for patients aged  $\geq 45$  years and for non literate patients (68). Persistence of symptoms was observed among 40 per cent of the patients. The total score was (65) in this group was significantly lower compared to persons without symptoms (77).

##### **Conclusion:**

The HRQoL was significantly impaired among those with persistent symptoms. This information is vital for developing the targeted communication strategies.

#### **Smear-positive TB patients at 2-3 years after initiation of treatment under a DOTS programme in a district, south India**

##### **Background:**

The DOTS strategy aimed at least 85 per cent cure rate and a case detection of at least 70 per cent. This reduces chances of failure, relapses and prevents the harbouring of Multi Drug Resistant TB (MDR-TB).

TRC monitored the programme in one TU in Tiruvallur district intensively, for 5 years since its implementation in 1999. This was done by using different operational studies and generated valuable data. But the status report of cases treated under a DOTS programme is yet to be looked into. This information would show ways and means of reducing mortality and morbidity.



## **Objective:**

To investigate how cases 2-3 years after the initiation of treatment under DOTS in the same area are faring.

## **Methodology:**

Smear-positive TB patients registered for treatment during the year 2002 and 2003 formed the study population. Those who were declared successfully treated, defaulted or failed were under a follow-up at 3 and 2 years respectively, after the initiation of the treatment. Two sputum specimens were collected from those who were available at the time of the visit by the health worker at their residence.

## **Results:**

A total of 1171 smear positive cases were registered for treatment during the period 2002-2003. Of these, 1113 cases were eligible for follow up and among the 1088 cases that were followed up, 148 expired, 54 migrated and 46 cases could not be contacted. Sputum sample was collected from the remaining 840 cases. The overall mortality rate was 15 per cent and among the remaining, 18.6 per cent (156 of 840) remained positive.

## **Conclusion:**

The mortality and those who had active TB was higher among smear positive cases, followed up at 2-3 years after the initiation of treatment.

## **Studies in progress:**

### **Epidemiological Impact Study: Community survey of TB infection and disease**

#### **Background:**

DOTS programme was implemented in Tiruvallur district, Tamil Nadu in May 1999. To assess the epidemiological impact of the DOTS strategy, the TB Research Centre is carrying out a series of sample surveys to estimate the prevalence of disease and infection in this district. The study covers a population of 5, 80,000.

#### **Aims:**

To study the trends over time for both disease and infection and thereby, to measure the impact of DOTS implementation.

#### **Methods:**

All adults  $\geq 15$  years have been included. They have been screened by two methods, namely, elicitation of symptoms and X-ray examination. Two samples of sputum specimen were collected from those who were either symptomatic and/or X-ray abnormal suggestive of TB. These specimens were processed for smear and culture and those who became bacteriologically positive, were referred for anti-TB treatment provided they satisfied the RNTCP guidelines.

All children included in the tuberculin survey, were tuberculin tested with purified protein derivative (PPD) 1TU RT23 vials. The reaction sizes were read after 72-96 hours.



## Results:

Two disease surveys, each with two and half year duration, were completed. The second resurvey is in the completion stage.

Coverage in the current survey is above 90 per cent for all investigations – namely symptoms, X-ray and sputum examination as seen in Table 7. So far, 284 persons have been diagnosed with smear/culture positive TB.

**Table 7: Coverage of various investigations**

Activities	2 <sup>nd</sup> resurvey
Eligible for symptom and X-ray	96075
Symptom screening	88341 (92%)
X-rayed	87211 (91%)
Sputum eligible	11175
Sputum collected	10514 (94%)

The prevalence of the disease from the two completed surveys, have shown a decline in TB prevalence. This demonstrates the effectiveness of the DOTS implementation, and a more rapid reduction in the prevalence of disease compared to that during the pre-DOTS period. (A precise estimate of the decline will be available only after an analysis and after the completion of the second resurvey).

Based on the existing data generated from Tiruvallur and elsewhere, the burden of TB in India for the year 2000 was estimated at 8.5 million (95 per cent C.I: 6.3-10.4) of which 3.8 million were bacillary cases, 3.9 million abacillary cases and 0.8 million extra-pulmonary cases.

In the third tuberculin survey among 27,199 children eligible for tuberculin testing, 25,935 (95 per cent) were test read.

From among 8329 unvaccinated children, 499 (6.0 per cent) were found to be infected using the cut-off at 12 mm. The acute respiratory tract infection (ARTI) was estimated to be 1.2 per cent. The ARTI estimates in the two tuberculin surveys conducted earlier are 1.6 per cent and 1.4 per cent respectively. There was a significant decline in the trend of TB infection ( $P < 0.001$ ). The annual decline estimated from the first to the third survey is six per cent.

## Conclusion:

DOTS implementation is associated with a substantial reduction in the prevalence and risk of TB infection amongst children.

## Risk of TB infection and disease in different economic strata

### Background:

Tuberculosis affects the poorest people in the world. Ninety five per cent of the new TB cases every year are in developing countries. Most researchers agree on the general association between TB and socio economic conditions, but no direct cause and effect relationship has been demonstrated.



### **Aim:**

To estimate TB infection and disease rates in the community and relate these to the economic status of the population.

### **Methods:**

The study is being carried out amongst the same population where the disease survey has been undertaken. This is to evaluate the prevalence of the disease. All households in a village included for the survey, will be visited. The head of the family/informant will be identified and the purpose of the survey will be explained to him/her. Their cooperation therefore is being requested for the interview using the semi-structured questionnaire. This will also reveal their socio-economic status (standard of living index). Data collection started in February 2004. So far, 28,702 households have been interviewed and coverage for the interview has been around 95 per cent. The study is going on.

### **Reliability of involving community Volunteers as DOT Providers**

#### **Background:**

DOTS, the main strategy of RNTCP, are the best method currently available to control TB. After seeing the problems being faced by the Government, the role of the DOT providers has been recognized. Therefore decentralizing TB control measures beyond health facility by using Community Volunteers to act as DOT providers to facilitate administration of regular and complete treatment, has been initiated. Identifying a good DOT provider is a challenge. It was proposed to visit and interview all the DOT providers including community volunteers identified as DOT providers and the patients treated by them currently, to obtain detailed information on their practices.

#### **Aim:**

1. To assess the reliability and accountability of Government health workers and community volunteers as DOT providers.
2. Acceptability of community providers by patients.

#### **Methods:**

Community volunteers engaged as DOT providers during two cohort periods in one TU at Tiruvallur district and those at the Chennai Corporation formed the study population. DOT providers and their patients are interviewed by trained field workers using semi structured questionnaires. These aid in getting information about their practices and problems encountered while acting as DOT provider.

In the rural area, data collection was completed for 201 providers and 377 patients while in the urban area, it has been completed for 52 providers and 55 patients.

### **Factors that lead to hospitalization of TB patients**

#### **Background:**

The RNTCP endorses domiciliary treatment under the direct observation of health care staff. Even though hospitalization is recommended in special cases, a large number of beds in the various hospitals throughout the country are still utilized by



TB patients. Though the DOTS strategy is considered a cost effective method of intervention, large numbers of patients still seek inpatient care. As a result of this, considerable resources are spent on care and attention for these patients.

#### **Aim:**

To see why there is hospitalization of TB patients in the RNTCP implemented areas.

#### **Methods:**

As many as 450 hospitalized TB patients were proposed to be included in the study from select hospitals (TB sanatorium at Tambaram, TB hospital at Otteri, Chennai and TB sanatorium at Madurai).

A pilot study was initiated in February 2005 and based on this the questionnaire was modified. So far, 117 patients have been interviewed. The study is in progress.

#### **Private practitioners and TB: Patient perceptions**

##### **Background:**

In the pre RNTCP era, it was found that patients who started anti-TB treatment (ATT) with Private Practitioners (PPs), switched over to the public sector. This is because there have been many financial problems. After implementation of the RNTCP, perceptions on TB treatment with PPs, their awareness of DOT, and reasons for choice of treatment are not known. Therefore a study on the patient's perceptions in TB treatment would come in handy.

##### **Aims:**

To discover:

1. The proportion of patients treated by the PPs in the study population
2. Reasons for switching over to public sector after being treated by PP
3. The perceptions of patients on PPs

##### **Methods:**

The study is being conducted among patients attending urban (Choolaimedu TU, Chennai), rural (Tiruvallur TU), specialized TB hospital (Tambaram TB sanatorium) and in Kancheepuram district.

All patients are interviewed using a semi-structured pre-coded interview schedule. So far, 442 patients from rural, 426 from urban, 281 from TB sanatorium and 102 from Kancheepuram have been interviewed.

#### **Evaluation of the impact of RNTCP on the socio-economic status of TB patients and their families**

##### **Background:**

An earlier study from TRC, before the implementation of DOTS, has reported that the direct and indirect costs of the TB epidemic come to at least \$3 billion (Rs 13,000 crores) every year. Patients suffering from TB incurred a total loss of \$99 (Rs.3469) while shopping for diagnosis and treatment. Indian workers with TB lost an average of 83 workdays. This study is aimed at estimating the long term economic impact of the TB control programme after 5 years of the implementation of the DOTS programme.



## **Objectives:**

To measure the total costs for patients enrolled in the programme and to estimate the economic and non-economic benefits of the programme to patients, family and the nation.

## **Methods:**

All those chosen for the study and diagnosed with TB were started on treatment during the Jan – March 2006 formed the study population. So far, 260 patients have been interviewed. The study is in progress.

## **Socio-economic study of those suspected with TB present at the health care at Tambaram Sanatorium and in Kancheepuram district**

### **Background:**

Even though DOTS with the objective of providing decentralized diagnostic and treatment services is in place in Tamil Nadu for the last seven years, those with suspected TB from all over the state seek care at Tambaram Sanatorium. And over the years the out patient attendance has not come down.

For the patients, this involves traveling long distance, loss of income, stay during inpatient treatment and incurring expenditure. This may be due to lack of awareness or non acceptability of diagnostic and treatment facilities available locally among patients and or the referring practitioners.

### **Aim:**

To understand the reasons and the socio economic profile of those suspected with TB coming to the Tambaram sanatorium during a three - month cohort period.

### **Methodology:**

The study is being conducted at the government TB sanatorium Tambaram, Chennai. A semi-structured pre-coded interview schedule is used to collect relevant information regarding demographic, socio economic profile. In all, 2021 persons have been interviewed. The analysis is in progress.

## **Multi-Drug Resistance-TB (MDR-TB) management in the community – a field report from south India**

### **Background:**

Emergence of MDR-TB is a potential threat to the success of TB control. Patients diagnosed with MDR-TB in the study area, were managed by TRC under programme conditions.

### **Aim:**

To document the experience in the management of MDR-TB patients identified in the RNTCP implemented rural area of Tamil Nadu.

### **Methods:**

#### **Diagnosis of MDR-TB:**

For all TB patients registered for treatment under the RNTCP in the rural area, 2 additional sputum samples were collected within a week of starting the treatment. Patients were referred by an NGO if they suspected MDR-TB and 2 sputum specimens were collected at TRC for these patients. All specimens were processed at TRC for culture and drug susceptibility testing.



### Treatment procedures:

Any patient identified with MDR-TB, was referred to TRC, Chennai, for initiating a second line treatment. Before registering for treatment, all patients underwent a detailed clinical, sociological assessment and laboratory investigations. They were started on an appropriate second line drug treatment regimen, based on drug susceptibility. After initiation of treatment, patients were advised hospitalization for at least a minimum period of one month, to monitor the drug tolerance pattern.

### Results:

Patients identified with organisms resistant to both, INH and RMP (MDR-TB), with or without resistance to other drugs, were treated with one of the following regimen (Table 7a):

**Table 7a: Drug Regimens**

Regimen	Number of patients
S <sub>3</sub> /K <sub>3</sub> OfI <sub>7</sub> , Eth <sub>7</sub> , Emb <sub>7</sub> , Z <sub>7</sub>	46
Individually tailored	20
Total	66

Among 66 patients, 12 were resistant to two drugs i.e. INH & RMP. In 34 patients, organisms were resistant to one or two of the first line drugs in addition to INH & RMP (S/EMB). In the remaining 20 patients, resistance pattern included second line drugs (Eth, OFX, and K).