Survival rates of past-tuberculosis patients during the pandemic and the factors affecting it

- a mixed methods study.

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Abbreviations

TB: Tuberculosis

DS-TB: drug sensitive TB

RNTCP: Revised National Tuberculosis Control Programme

NTEP: National Tuberculosis Elimination Programme

SF36: Short Form 36

QOL: Quality of life

MDR TB: Multidrug resistant TB

HR: Hazard ratio

Abstract

Objectives: This study was done to estimate the survival rates, factors affecting mortality and quality of life among residents of Vellore and Tiruvannamalai districts who have completed treatment for drug sensitive tuberculosis between 2015 and 2020 under the RNTCP or NTEP.

Methods: A mixed methods study was adopted. A historical cohort study was done to estimate the survival rates among patients who have completed treatment. The line list of eligible patients was retrieved from Nikshay and their current health status was assessed through telephonic interviews, after obtaining verbal consent.

A cross sectional study was done among survivors to assess their quality of life. The SF36 was administered through a face-to-face interview on a subset of patients who consented for home visits. Overall mental status and physical status scores were calculated for all participants.

To explore the medical and non-medical factors that contribute to death in those who have completed TB treatment, in- depth interviews were conducted among families who have lost someone between March and October 2022. This was done using a verbal autopsy tool developed by the NTEP team in Tamil Nadu. Through purposive sampling 30 families were chosen and interviewed. The main themes emerging were extracted.

Results: A total of 20,032 eligible individuals were identified and 9415 individuals consented to be interviewed. Overall survival in this group was found to be 85.4%. Annual survival rates, from 2017 have been around 95%. Death rates when adjusted for age category and calendar period did not show a higher death rate in 2020, during the COVID lockdown. Standardised mortality ratio was calculated to be 441% when comparing the death rates among this cohort and the residents of Kaniyambadi block implying that people with a history of treated TB are at a 4 times higher risk of dying when compared to the public. Two hundred and forty survivors were screened using the SF36 revealing poor mental health scores in 23.33% (95%CI 17.98-28.6%) and poor physical health scores in 25.42% (95%CI 19.91-30.93%) of the survivors. Thirty families were interviewed in depth using the verbal autopsy tool. The thematic analysis revealed that medical factors included chronic diseases such as uncontrolled diabetes, hypertension, cardiovascular disease, chronic kidney disease, chronic respiratory conditions arising from tuberculosis, physical disability, and cancer. Social isolation, substance abuse, affordability of care and delays in recognising the need for care and seeking care were also issues that led to the death of some of the individuals.

Conclusion: Survival rates have been stable between 2017 and 2020 with no change during the COVID lockdown of 2020. However, individuals with a history of treated TB have a 4.4 times higher risk of dying than the general population. People who have discontinued treatment, men and individuals in older age groups are at a higher risk of poor outcomes. Also, with almost a quarter experiencing some form of mental or physical issue it may be useful to see if regular follow ups can improve their health status.

Primary objective:

To estimate the survival rates among those who successfully completed treatment for drug sensitive TB, under the National TB Elimination Programme between 2015 and 2020 in Vellore and Tiruvannamalai districts of Tamil Nadu.

Secondary objectives:

1. To study the association of clinical and other socio-demographic factors on long term survival and annual survival rates.
2. To understand the quality of life of those alive individuals after getting affected with TB.
3. To explore in depth the causes of death and the medical and non-medical factors that contributed to adverse outcomes in some patients with tuberculosis.

Literature review

TB control in India: India remains as the country with the highest burden of TB globally. (1) The Revised National Tuberculosis Control Programme (RNTCP) was renamed the National Tuberculosis Elimination Programme (NTEP) and now aims to reduce TB incidence by 80% and TB related mortality by 90% by 2025, five years ahead of the Sustainable Development Goal target, a commitment the state of Tamil Nadu has promised to work towards. (2), (1), (3)
After the National Strategic Plan (2017-2025) was established, multiple strategies were rolled out to detect all TB cases (through up scaling of diagnostics, universal drug sensitivity testing and screening of high-risk populations) and to treat all TB cases (through ensuring good support systems, free universal daily regimen and drugs for all TB cases, patient friendly adherence monitoring systems and social welfare scheme including nutritional schemes). The case detection rate was highest in 2019 but the pandemic resulted in a setback in TB control across the world.

Mortality rates and survival among TB patients

TB deaths, according to WHO, are deaths among patients with TB while on treatment irrespective of cause. Most TB deaths occur within the first 8 weeks of initiating treatment and are considered early deaths. They are usually severe forms of TB and require more comprehensive clinical care. (4) A study in Andhra Pradesh has shown that patients newly treated for TB had a 6% risk of dying in the first year since diagnosis. (4) In terms of long-term survival, two studies done in Tamil Nadu have shown an increased risk of death among those who have completed treatment when compared to the general population. One study done in 2006 found the general excess mortality rate among TB patients was *6 times* more than that of the general population and in a cohort study that followed up patients for 10 years found that mortality in the TB cohort was 2.3 times higher than in the age-matched general population. (5), (6)

Potential impact of COVID and the lockdown on TB control and survival of patients with TB

Provisional data from 84 countries compiled by the WHO showed that the number of people who availed of TB care in 2020 had dropped by 29% when compared with 2019. (7) In India there was a 59% decrease in case notification rate in 2020 when compared to 2019, as seen on Nikshay and in Tamil Nadu this was 68 %. (8) Undernutrition contributes to 32-44% of incident TB cases in India and during the lockdown there was a worsening of all socioeconomic determinants of Tuberculosis. Overcrowding, under nutrition and disruptions in health services have the potential to reverse some of the gains in TB control in the last few years. The under reporting and disruption in TB services have been estimated to result in a 13% increase in the death rate in India. (8) According to the WHO TB deaths have gone up for the first time in a decade due to the COVID pandemic. (9)

Nikshay

Nikshay is a case-based web based real time patient management system which offers the programme managers the ability to monitor their patients in real time. Nikshay digitized the TB register which was maintained at the Tuberculosis Unit level (TU), for all TB Nikshay & TB Surveillance cases initiated on treatment within the TU. This allowed patient-wise granular information to be available at all levels of the reporting system and simultaneously be used for monitoring and evaluation.
It captures all the components of services delivery to both DSTB and DRTB patients in both public as well as private sector patients such as:
- Demography details of the patients

- Treatment initiation status

- Laboratory tests

- Treatment adherence/ compliance of the patient

- TB comorbidity status

- Treatment outcome

The online application NISHAY has been in use in the state of Tamil Nadu since 2018 Direct benefit transfers such as
- i. Nikshay Poshan Yojana (NPY) to patients,

- ii. Incentive to Treatment Supporters

- iii. Notification Incentive to Private Providers and

- iv. Transport incentives to Tribal TB patients are recorded on this portal. (1)
Nikshay allows patients to be monitored and followed up effectively.

Quality of life of people who have completed treatment for Tuberculosis and residual disability.

Quality of life is a broad and complex multidimensional concept that incorporates physical, social, psychological, economic, spiritual and other domains. It is therefore difficult to define and measure but may be broadly described as individuals' perceptions of their position in life in the context of the culture and value systems in which they live. One tool used to measure the quality of life is the SF36.

This gives scaled scores across eight domains – Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health, and two summary scores – Physical Component Score and Mental Component Score. A study done in India showed that patients with TB had a higher prevalence of depression, 23.7% when compared to the general population, 6.8%. Quality of life of people living with long-term diseases has been shown to reflect the quality of care received. SF 36 measures the quality of life in 8 dimensions and provides a score ranging from 0-100. (10) The long-term impact of successful TB treatment on QOL is not clear. A few studies show that the overall QOL in patients previously treated 1–2 years back was largely like that in the general population. Other investigators report substantial impairment in QOL, even several years after The TB control programme has now been providing direct transfers to support nutrition and this information was help inform the policy related to social welfare measures that may be needed for TB patients.

Role of verbal autopsies causes of deaths among patients who have completed treatment for TB.

Death certificates have not been able to capture the actual non-medical contributors to death and assess delays in health care. (11) Current national policy is to conduct verbal autopsies to understand the causes of death among those on treatment for MDR TB to identify potential programmatic deficiencies in the diagnosis and treatment of tuberculosis. (12)

Justification of the study

The course of TB control in India has been both positively impacted by implementation of important strategies and at the same time negatively impacted by the pandemic. So, quantifying the survival rate among the cohort who has successfully completed treatment is important from a programme point of view. Also understanding the long-term health impact will help inform the kind of social welfare measures that need to be developed.

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a. **Setting:** This study was done in Vellore and Tiruvannamalai districts of Tamil Nadu.

b. **Participants:**

Inclusion criteria for the quantitative part of the study

Part 1: To estimate survival rates:
- Adult patients who were registered for TB treatment under the RNTCP or NTEP between 2015 and 2020 on Nikshay.
- With a residential address, at the time of enrolment, within Tamil Nadu and
- Have completed treatment for drug sensitive TB.

Part 2: To estimate the quality of life of patients who have completed TB treatment,
- Patients from the above cohort who are alive and currently residing in either Vellore or Tiruvannamalai districts.
-

Detailed diagrammatic Algorithm of the quantitative part of the study.

All patients registered on Nikshay was downloaded.

- Drug sensitive TB
- those who have completed the TB treatment - between 2015 and 2020.
- at time of enrolment residents of Tamil Nadu
- for the QOL part of the study - currently residing in Vellore or Tiruvannamalai districts

↓

Using phone numbers registered on Nikshay they were contacted, and verbal consent was taken to check on their status.

↓

By simple random sampling, from the existing list, 240 people were selected and screened using the SF36.

Qualitative part of the study: in depth interviews – verbal autopsies

Deaths that occurred among the cohort being followed up were recorded and a separate list was maintained for deaths that occurred between March and October 2022. The families that permitted us to visit them at homes were interviewed after written informed consent was taken**.**

Inclusion criteria for the qualitative part of the study

Deaths occurring among the above-described cohort between March and October 2022

Exclusion criteria
None

c. **Variables being measured:**

Outcomes measured were the following:
    a. Current status –
        i. currently alive: For those alive survival time was measured. Survival time was calculated as the time between diagnosis of TB treatment and the date of death or date of interview. This was one as the date of completion of treatment was not available for many of the patients.
    b. Dead: Date of death and the level of certainty of the date of death was recorded for all those reported to have died.
    c. Quality of life was measured using the SF 36 and mean scores for each domain was calculated.

d. **Data Sources/measurement:**

Baseline details of patients at the time of enrolment for TB treatment were obtained from Nikshay.

Current status was measured using a standardized questionnaire administered by an interviewer through a telephonic interview.
Quality of life was measured using the SF36 form, through a face-to-face interview.

Verbal autopsies were done using a semi structured interviewer administered questionnaire. This was administered by doctors and the in-depth interview was conducted with the family member or friend who was with the patient at the time of the death.

Data entry: All data collected by telephonic interviews was recorded on Microsoft Excel as the interview was being conducted and then to REDCap immediately.

SF36 was collected on paper forms by the field workers and then entered on REDCap by the data analyst. Verbal autopsies were collected on paper forms and then entered on Microsoft Excel.

Data analysis: Data were analyzed using Stata version16.

Bias: To reduce interviewer bias the structured questionnaires were standardized. Selection bias was minimised by ensuring that a minimum of 3 attempts were made to contact all eligible participants to assess survival. Simple random sampling was done to reduce selection bias while studying the quality of life. To minimise recall bias all verbal autopsies were done prospectively and as soon as possible. Verbatim notes were captured, compiled, and categorised under themes within the same week.

Sample size:

Quantitative part of the study

Part 1. To estimate survival rates, **all** eligible individuals was be followed up.

Part 2. To study the quality of life of people who have completed TB treatment.

Using the formula $n=1.96^2pq/d^2$, where p (prevalence) from previous studies which have shown that 24% can have poor mental scores, aiming for an absolute precision of 6 a sample size of 202 was calculated.

(Aggarwal, Quality of life with Tuberculosis, Journal of Clinical Tuberculosis and Other Mycobacterial Diseases, volume 17, Dec 2019)

Qualitative part

To explore in depth the causes of death 30 verbal autopsies were done by purposive sampling.

Analysis of Quantitative variables:

Data from Nikshay was be downloaded on Microsoft Excel. Primary data collected by the study team was done on REDCap, exported and analysed on Stata version16.

Statistical methods:

Annual survival rates were reported for every cohort. Kaplan Meier plots were prepared and hazard ratios along with 95% confidence intervals and p-values were reported for various risk factors. Using a Lexis expansion, survival rates for each age group were stratified based on the calendar year as well. Risk factors explored included the gender of the patient, age category of the patient, presence of diabetes/ HIV positivity at the time of diagnosis, completion of therapy, occurrence of COVID after completing treatment and previous history of TB. To compare the death rates among this group and the general population an indirect standardization was done, comparing this cohort to the residents Kaniyambadi block.

SF 36 was scored in 2 stages. First, all the responses were given a numeric score, as given below, where higher scores indicate better health status.

Question number	Responses*	Score
1, 2, 20, 22, 34, 36	1 →	100
	2 →	75
	3 →	50
	4 →	25
	5 →	0
3, 4, 5, 6, 7, 8, 9, 10, 11, 12	1 →	0
	2 →	50
	3 →	100
13, 14, 15, 16, 17, 18, 19	1 →	0
	2 →	100
21, 23, 26, 27, 30	1 →	100
	2 →	80
	3 →	60
	4 →	40
	5 →	20
	6 →	0
24, 25, 28, 29, 31	1 →	0
	2 →	20
	3 →	40
	4 →	60
	5 →	80
	6 →	100
32, 33, 35	1 →	0
	2 →	25
	3 →	50
	4 →	75
	5 →	100

Precoded response choices as printed in the questionnaire.

Scores were then generated for each of the following eight domains by calculating the average of a certain subset of questions.

Scale	Number of items	Questions to be considered for the domain
Physical functioning	10	3 4 5 6 7 8 9 10 11 12
Role limitations due to physical health	4	13 14 15 16
Role limitations due to emotional problems	3	17 18 19
Energy/fatigue	4	23 27 29 31
Emotional well-being	5	24 25 26 28 30
Social functioning	2	20 32
Pain	2	21 22
General health	5	1 33 34 35 36

Overall physical component score was calculated by taking the average of the physical functioning score, general health, bodily pain experienced and limitations in role due to physical pain. Those with a score of less than 50 were classified as having poor physical health.

Overall mental component score was calculated by taking the average of the scores for vitality, social functioning, emotional wellbeing, and role limitation due to emotional health. Those with a score of less than 50 were classified as having poor mental health.

(https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form/scoring.html)

Scores for men and women were compared using the independent T test.

The verbal autopsy narratives were analysed by identifying certain themes. Specific details related to medical and non-medical factors that contributed to the death of the individual were extracted.

Results and discussions

A total of **20,032** individuals over the age of 15, treated for drug sensitive tuberculosis (TB) in health care facilities located in either Vellore or Tiruvannamalai districts between January 2015 and December 2020 were eligible to participate in the study. The table below gives the year wise description of the study populations baseline characteristics, with column percentages.

The population eligible to participate in the study consisted mostly of men (67.59%), people with newly diagnosed TB (90.41%) and people with pulmonary TB (76.68%). The proportion testing positive for diabetes mellitus at the time of diagnosis was 4.1% in 2017 and this has increased every year and with 23.51 % of patients testing positive in 2020. (Table1)

Part 1: Descriptive statistics of eligible population

Table 1: Baseline characteristics at diagnosis, with column percentages (n=20032)

Demographic characteristics	Subgroups	Year of diagnosis of Tuberculosis						Total (n=20032)
		2015 (n=663)	2016 (n=1559)	2017 (n=2661)	2018 (n=4918)	2019 (n=6147)	2020 (n=4084)	
Age group	<=20 years	50 (7.54%)	104 (06.67%)	182 (0.84%)	406 (8.26%)	477 (7.76%)	328 (8.03%)	1547 (7.72%)
	21-40 years	251 (37.86%)	620 (39.77%)	945 (35.5%)	1757 (35.73%)	2032 (33.06%)	1,458 (35.7%)	**7063 (42.98%)**
	41-60 years	275 (41.48%)	614 (39.38%)	1126 (42.31%)	1969 (40.04%)	2552 (41.52%)	1,671 (40.92%)	8207 (40.97%)
	61-80 years	83 (12.52%)	216 (13.86%)	402 (15.10%	754 (15.33%)	1042 (16.95%)	607 (14.86%)	3104 (15.5%)
	Above 80 years	4 (0.60%)	5 (00.32%)	6 (0.23%)	32 (0.65%)	43 (0.7%)	20 (0.49%)	110 (0.55%)
	Missing	0(0%)	0(0%)	0(0%)	0(0%)	1 (0.02%)	0(0%)	1(0.005%)
Gender	Female	228 (34.39%)	520 (33.35%)	802 (30.14%)	1587 (32.27%)	1931 (31.41%)	1413 (34.06%)	6481 (32.35%)
	Male	435 (65.61%)	1039 (66.65%)	1859 (69.66%)	3329 (67.86%)	4209 (68.47%)	2668 (65.33%)	**13539 (67.59%)**
	Transgenders	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.04%)	7 (0.11%)	3 (0.07%)	12 (0.06%)

Demographic characteristics	Subgroups	Year of diagnosis of Tuberculosis						Total (n=20032
		2015 (n=663)	2016 (n=1559)	2017 (n=2661)	2018 (n=4918)	2019 (n=6147)	2020 (n=4084)	
HIV	Non-reactive	NA	NA	2185 (82.11%)	3005 (61.6%)	5615 (91.35%)	3898 (95.45%)	14703 (73.40%)
	Reactive	NA	NA	45 (1.69%)	160 (3.25%)	247 (4.02%)	184 (4.51%)	636 (3.17%)
	Unknown	NA	NA	431 (16.20%)	1753 (35.64%)	277 (4.51%)	2 (0.05%)	2463 (12.3%)
	Missing	663 (100%)	1559 (100%)	0 (0%)	0 (0%)	8 (0.13%)	0 (0%)	2230 (11.13%)
Diabetes	Yes	NA	NA	109 (4.1%)	327 (6.65%)	1022 (16.63%)	960 (23.51%)	2418 (12.07%)
	No	NA	NA	611 (22.96%)	1794 (36.48%)	4692 (76.03%)	3112 (76.20%)	10207 (50.95%)
	Unknown	NA	NA	352 (13.23%)	87 (1.77%)	14 (0.23%)	1 (0.02%)	454 (2.27%)
	Missing	663 (100%)	1559 (100%)	1589 (59.71%)	2,710 (55.10%)	421 (6.85%)	11 (0.27%)	6953 (34.71%)
Type of diagnosis	Microbiologically confirmed	331 (49.92%)	831 (53.3%)	1943 (73.02%)	3249 (66.06%)	4221 (68.67%)	2813 (68.88%)	13388 (66.3%)
	Clinically confirmed	146 (22.02%)	289 (18.54%)	718 (26.98%)	1669 (33.94%)	1926 (31.33%)	1271 (31.12%)	6019 (30.05%)
	Missing	186 (28.05%)	439 (28.16%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	625 (3.12%)

Demographic characteristics	Subgroups	Year of diagnosis of Tuberculosis						Total (n=20032)
		2015 (n=663)	2016 (n=1559)	2017 (n=2661)	2018 (n=4918)	2019 (n=6147)	2020 (n=4084)	
Type of case	New	593 (89.44%)	1349 (86.53%)	2339 (87.9%)	4346 (88.37%)	5626 (91.52%)	3858 (94.47%)	18111 (90.41%)
	Retreatment	70 (10.56%)	210 (1.47%)	322 (12.10%)	572 (11.63%)	521 (8.48%)	226 (5.53%)	1921 (9.59%)
Site of disease	Pulmonary	488 (73.6%)	1169 (74.98%)	2256 (84.78%)	3852 (78.32%)	4699 (76.44%)	2896 (70.91%)	15360 (76.68%)
	Extrapulmonary	175 (26.4%)	390 (25.02%)	405 (15.22%)	1059 (21.53%)	1443 (23.47%)	1134 (27.77%)	4606 (22.99%)
	Missing	0	0	0	7 (0.14%)	5 (0.08%)	54 (1.32%)	66 (0.33%)
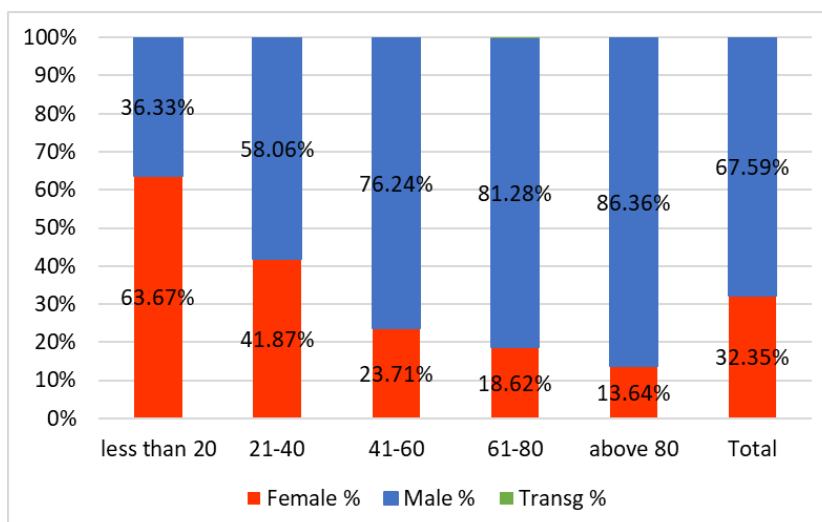
Figure 1: Age and sex distribution at baseline (n=20032)

The youngest age group of less than 20-year-olds comprised of a larger proportion of women, but this decreased in increasing age bands. The mean age of women was 10 years younger than that of men.

Part 2: Outcome of follow up.

A total of **9415** individuals were contactable and gave consent to participate in the study.

Table 2: Response to phone calls by year of diagnosis (n=20,032)

Year of diagnosis of TB	No. of subjects	Response to phone call					
		Did not answer	Did not consent to participate	If minor parental consent obtained	Incorrect phone number	Verbal Consent given	Total
2015	n	232	6	0	266	159	663
	%	34.99%	0.9%	0%	40.12%	23.98%	100%
2016	n	543	14	0	585	417	1,559
	%	34.83%	0.9%	0%	37.52%	26.75%	100%
2017	n	781	62	0	848	970	2,661
	%	29.35%	2.33%	0%	31.87%	36.45%	100%
2018	n	1,712	42	2	801	2,361	4,918
	%	34.81%	0.85%	0.04%	16.29%	48.01%	100%
2019	n	2,088	56	2	954	3,047	6,147
	%	33.97%	0.91%	0.03%	15.52%	49.57%	100%
2020	n	1,094	34	3	499	2,454	4,084
	%	26.79%	0.83%	0.07%	12.22%	**60.09%**	100%
Total	n	6,450	214	7	3,953	9,408	20,032
	%	32.2%	1.07%	0.03%	19.73%	46.96%	100%
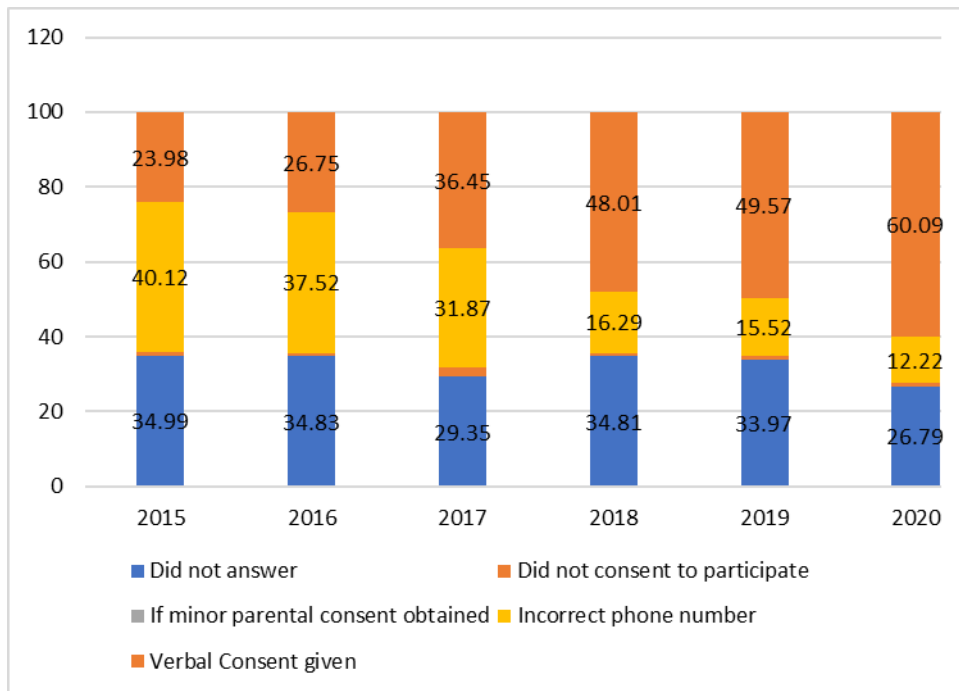
Figure 2: Response to phone calls by year of diagnosis (n=9415)

The proportion of people contactable increased with every year and 60% of those diagnosed in 2020 could be followed up. (Table 2)

Part 3: General characteristics of individuals who were followed up.
A total of 9415 people consented to participate in the study, 159 from 2015, 417 from 2016, 970 from 2017, 2363 from 2018, 3049 from 2019 and 2457 from 2020. Of all participants 66.28% were men, average age of women was 41.16 (SD 16.28), average age of men was 50.59 (SD 15.41), 99.3% confirmed to have had a history of tuberculosis and 91.05% reported that they had completed at least 6 months of medication and 6% reported that they had had more than one episode of TB in their lifetime. (Table 3)

Though a majority of those followed up were men (66.28%) an almost equal proportion of men and women from the list of eligible individuals were contactable with 49.56% of women and 46.78% of men on the eligible list being followed up. Only 8.33% of transgenders from the eligible list were followed up.

The youngest age group had a larger proportion of women and with every successive age band the proportion of men increased. The age sex distribution pattern is very similar to the pattern seen in the eligible group. The men were on average 9 years older than the women. (Figure 3).

Table 3: General characteristics of individuals followed up (n=9415)

Demographic characteristics	Subgroups	Year of follow up						Total (n=9415)
		2015 (n=159)	2016 (n=417)	2017 (n=970)	2018 (n=2363)	2019 (n=3049)	2020 (n=2457)	
Age group	<=20 years	2 (1.26%)	1 (0.24%)	14 (1.44%)	57 (2.41%)	92 (3.02%)	101 (4.1%)	267 (2.84%)
	21-40 years	52 (32.7%)	158 (37.89%)	305 (31.44%)	751 (31.78%)	982 (32.21%)	876 (35.52%)	3,123 (33.17%)
	41-60 years	65 (40.88%)	165 (39.57%)	410 (42.27%)	979 (41.43%)	1,247 (40.90%)	990 (40.15%)	**3,850 (40.89%)**
	61-80 years	33 (20.75%)	83 (19.90%)	232 (23.92%)	539 (22.81%)	677 (22.20%)	473 (19.18%)	2,035 (21.61%)
	Above 80 years	7 (4.4%)	10 (2.40%)	9 (0.93%)	37 (1.57%)	51 (1.67%)	26 (1.05%)	140 (1.49%)
Gender	Female	58 (36.48%)	141 (33.81%)	317 (32.68%)	799 (33.81%)	997 (32.7%)	862 (35.08%)	3,174 (33.71%)
	Male	101 (63.52%)	276 (66.19%)	653 (67.32%)	1,564 (66.19%)	2,052 (67.3%)	1,594 (64.88%)	6,240 **(66.28%)**
	Transgenders	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.04%)	1 (0.01%)
Confirms history of TB	Yes	157 (98.74%)	412 (98.8%)	957 (98.66%)	2,344 (99.2%)	3,029 (99.34%)	2,450 (99.72%)	**9,349 (99.3%)**
	No	2 (1.26%)	5 (1.2%)	13 (1.34%)	19 (0.8%)	20 (0.66%)	7 (0.28%)	66 (0.7%)
Patient reported outcome	Completed treatment	135 (84.91%)	371 (88.97%)	866 (89.28%)	2,128 (90.06%)	2,788 (91.44%)	2,284 (92.96%)	**8,572 (91.05%)**
	Incomplete treatment	22 (13.8%)	41 (9.8%)	91 (9.4%)	216 (9.1%)	241 (7.9%)	166 (6.8%)	777 (8.3%)
	Not sure	2 (1.26%)	5 (1.20%)	13 (1.34%)	19 (0.80%)	20 (0.66%)	7 (0.28%)	66 (0.70%)
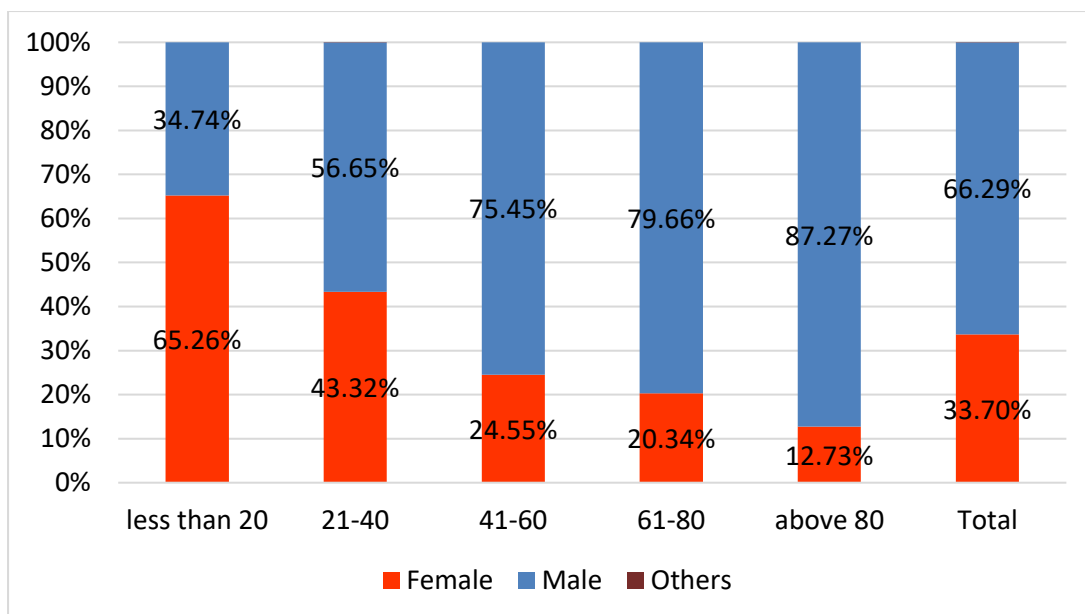
Figure 3:Age and gender distribution among those followed up (n=9415)

At the time of follow up 22.46% of the patients reported to have diabetes mellitus and 9.47% reported having hypertension. The proportion of people with comorbid conditions was higher among those who had already died. It is likely that those who were unwell had more opportunity to be in contact with the health care system and have therefore been diagnosed with these conditions. As the date of onset of these comorbidities their impact on survival cannot be commented on. (Table 4)

Many of those with chronic diseases were seeking care in government hospitals and therefore incurred no additional expenses. However, those visiting private hospitals spent even up to Rs.8000/- per month on treatment for diabetes. (Table 5)
Out of all the participants 88.5% owned a gas stove, 77.4% owned some amount of land and 63.3% owned some type of vehicle. The most common type of insurance owned was CMCHIS. However, we do not know the extent of the coverage and whether the insurance covers post tuberculosis complications. (Table 7)

Table 4: Last known medical history of the participants (n=9415)

Current medical status of individuals	Responses	Frequency		Percentage
		Among those currently alive	Among those who have died	
Presence of diabetes mellitus	Yes	1780(22.06%)	335(24.89%)	2115(22.46%)
	No	6236(77.28%)	924(68.65%)	7160(76.05%)
	Don't know	53(0.66%)	87(6.46%)	140(1.49%)
Presence of hypertension	Yes	699(8.66%)	193(14.34%)	892(9.47%)
	No	7315(90.66%)	1066(79.20%)	8381(89.02%)
	Don't know	55(0.68%)	87(6.46%)	142(1.51%)
Presence of ischaemic heart disease/ any heart disease	Yes	128(1.59%)	55(4.09%)	183(1.94%)
	No	7,904(97.96%)	1,194(88.71%)	9,098(96.63%)
	Don't know	37(0.46%)	97(7.21%)	134(1.42%)
Presence of COPD/asthma	Yes	326(4.04%)	143(10.62%)	469(4.98%)
	No	7697(95.39%)	1117(82.99%)	8814(93.62%)
	Don't know	46(0.57%)	86(6.39%)	132(1.4%)
Presence of chronic liver disease	Yes	20(0.25%)	30(2.23%)	50(0.53%)
	No	8011(92.28%)	1221(90.71%)	9232(98.06%)
	Don't know	38(0.47%)	95(7.06%)	133(1.41%)
Presence of Chronic kidney disease	Yes	51(0.63%)	70(5.02%)	121 (1.29%)
	No	7979(98.88%)	1181(87.74%)	9160 (97.29%)
	Don't know	39(0.48%)	95(7.06%)	134(1.42%)
History of COVID	Yes	142(1.76%)	22(1.63%)	164(1.74%)
	No	7,873(97.57%)	1,249(92.79%)	9,122(96.89%)
	Don't know	54(0.67%)	75(5.57%)	129(1.37%)
No. of doses of COVID vaccine received	0	1159(14.4%)	1062(78.9%)	2221(23.6%)
	1	799(9.9%)	81(6.0%)	880(9.3%)
	2	5529(68.5%)	131(9.7%)	5660(60.1%)
	3	495(6.1%)	3(0.2%)	498(5.3%)
	Don't know	87(1.1%)	69(5.1%)	156(1.7%)

Table 5: Patient incurred health expenditure per month on chronic diseases.

Chronic disease	No. of people on treatment	Range (INR)	Mean (SD)	Median (IQR)
Diabetes mellitus	2115	0-8000	541.44(878.60)	50 (0-800)
Hypertension	892	0-5000	272.63(521.33)	0(0-400)
Ischemic heart disease or any other chronic heart disease	183	0-20,000	1361.36(3117.51)	100(0-1500)
Chronic liver disease	52	0-20,000	2818.18 (5824.01)	1000(0-2000)
Chronic kidney disease	123	0-40,000	5482.14 (8997.08)	1750(0-6250)
COPD	469	0-25000	584 (7607.71)	0(0-500)

Current socio-economic status

Table 6: Socioeconomic status - ownership of specific commodities

Personal belongings	Yes (%)	No (%)	Prefer not to say (%)
Gas stove	8330 (88.5%)	683 (7.3%)	402 (4.3%)
Land	7285 (77.4%)	1734 (18.4%)	396 (4.2%)
Vehicle	5964 (63.3%)	3048 (32.4%)	403 (4.3%)
Cattle/poultry/animal related business	1986 (21.1%)	7025 (74.6%)	404 (4.3%)

Table 7: Socioeconomic status - ownership of health insurance

Type of insurance owned	Yes (%)	No (%)	Prefer not to say (%)
CMCHIS	4772 (50.7%)	4154 (44.4%)	459 (4.9%)
Ayushman Bharath/PMJAY	558 (5.9%)	8396 (89.2%)	461 (4.9%)
Private	135 (1.4%)	8821 (93.7%)	459 (4.9%)
Others	103 (1.1%)	8849 (94.0%)	463 (4.9%)

Part 4: Survival results

Out of the 9415 individuals followed up 85.7% were currently alive. Of those diagnosed in 2020, 90.68% are still alive and 65.41% of the 2015 cohort are currently alive. (Table 8)

Of the 9415 people who consented to participate in the study 28 were found to have died before their date of diagnosis with TB recorded in Nikshay. The remaining 9386 were used in the survival analysis out of which 1318 people have died. Observation time ranged from 2 days to 7.84 years, mean duration of survival was 3.29 years (SD 1.31 years).

Table 8: Survival status of individuals by year of diagnosis (n=20032)

| Year of diagnosing TB | Total eligible patients requiring follow up | Status | | | Proportion alive among those who could be contacted (n=9415) |
		Alive	Died	Status unknown (unable to f/u patient)	
2015	663	104	58	501	65.41%
2016	1,559	325	101	1,133	77.94%
2017	2,661	756	226	1,679	77.53%
2018	4,918	2,003	369	2,546	84.64%
2019	6,147	2,664	400	3,083	87.24%
2020	4,084	2,232	238	1,614	90.68%
Total	**20,032**	**8,084**	**1,392**	**10,556**	**85.70%**

As expected, a larger proportion of people from the 2020 cohort are currently alive when compared to the earlier cohorts.

Table 9:Annual survival rates in each cohort

| Year of diagnosis | Cumulative Survival rates | | | | |
	1 year	2 years	3 years	4 years	5 years
2015	88.70%	83.00%	79.20%	76.10%	71.10%
2016	93.00%	88.90%	85.30%	83.60%	81.20%
2017	95.10%	88.70%	85.50%	82.00%	77.30%
2018	95.70%	91.80%	88.00%	84.70%	
2019	95.80%	91.90%	88.20%		
2020	95.40%	92.00%			

On analysing the annual survival rate also, it was seen that since 2017 the first-year post treatment survival rate was around 95%, like a previous study done in Andhra Pradesh where it was found to be 94%. The low rates in the earlier years may be related to the low number of patients we were able to follow up from 2015 and 2016.

Table 10: cause of death in each observation period

Time of observation	Cause of death category			
	Infectious diseases	**Injuries**	**Non communicable disease**	**Unsure**
0-2 years	386 (47.2%)	36 (4.4%)	349 (42.7%)	46 (5.6%)
2-4 years	129(31.0%)	28 (6.7%)	231 (55.5%)	28 (6.7%)
4-6 years	17(22.4%)	9 (11.8%)	42 (55.3%)	8 (10.5%
>6 years	2 (40.0%)	0 (0%)	3(60%)	0 (0%)

The cause of death was classified as either due to infectious diseases, non-communicable disease and injuries. This was done the principal investigator by using the information provided by the relatives. In some situations, this was comprehensive and, in some situations, very little information was available. From the information provided infectious diseases seem to contribute to poor outcomes in the first 2 years and then most of the deaths are due to non-communicable diseases.

Of all participants 1.7% reported to be on treatment for TB at the time of follow up (Table 11)

Table 11: Currently on Treatment for TB – (participant reported)

Response	Frequency	Percent
Yes	130	1.7
No	7867	97.4
Prefer not to say/ don't know	72	0.9
Total	8069	100.0

Bivariable analysis:

Men seemed twice as likely to die than women, and COVID positivity did not impact survival. This could also be possible as the date of COVID positivity was not included in the analysis.
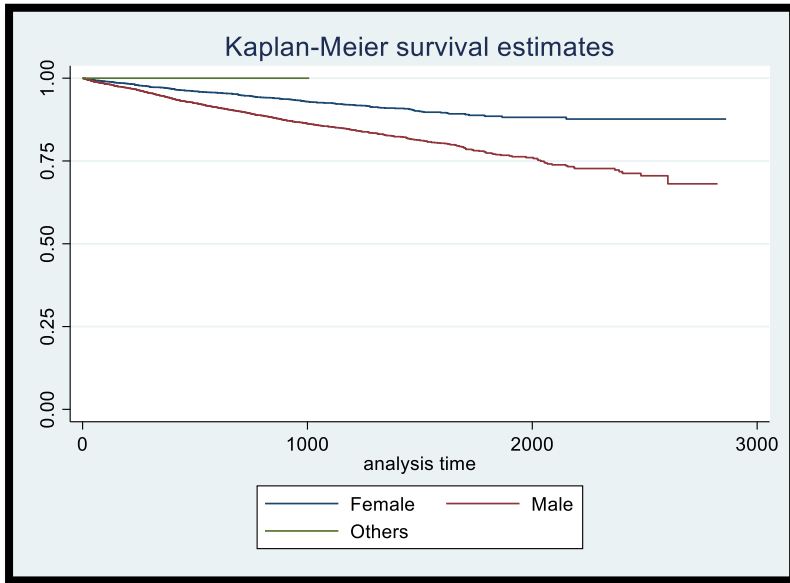
Figure 4: Gender and survival
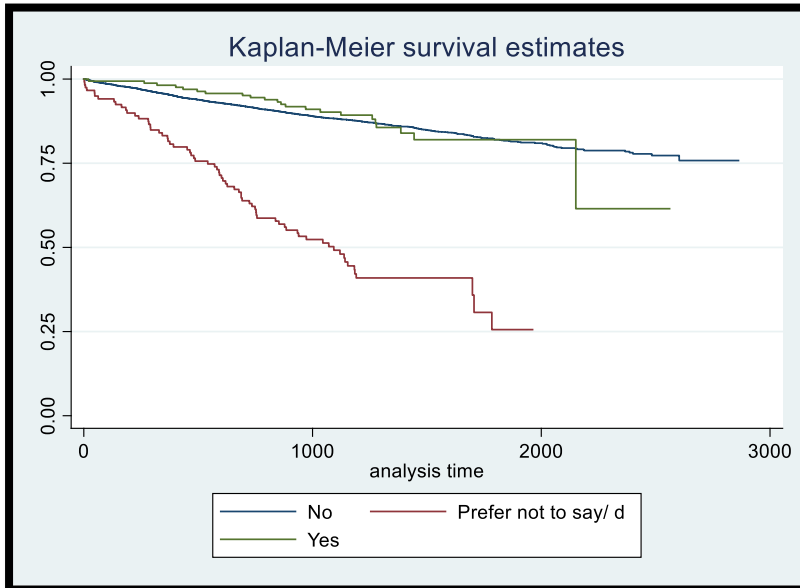
Figure 5: COVID positivity and survival
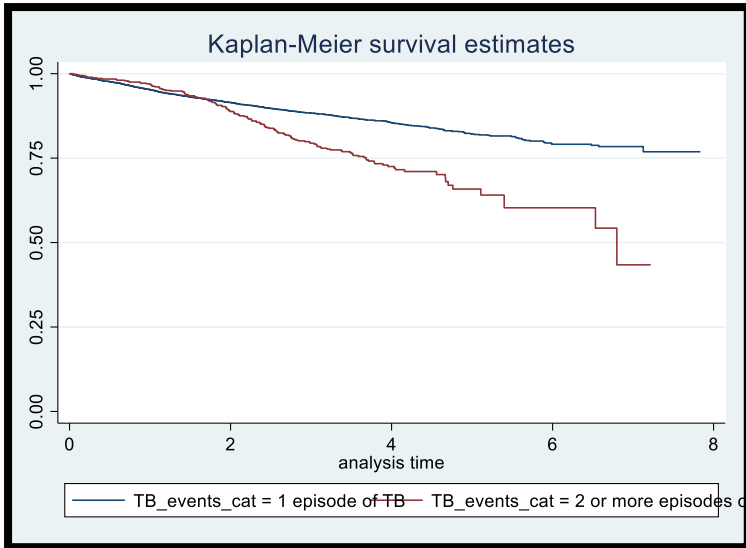
Figure 6: Survival by no. of episodes of TB
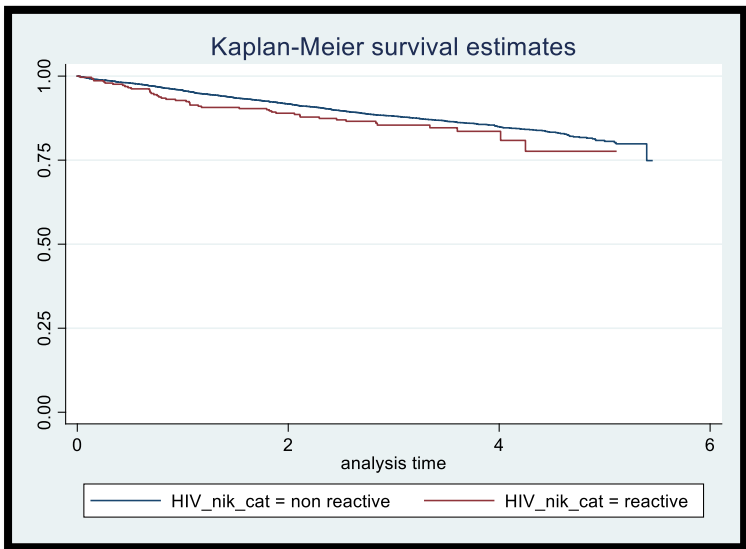
Figure 7: Survival by HIV positivity at diagnosis

Participants with a history of having 2 or more episodes of TB were more likely to die than those with only one episode of TB. HIV positivity showed no impact on survival, and this could be because this cohort included only those who had drug sensitive TB and completed treatment. The HIV positive patients who may have died while on treatment, defaulted due to adverse drug events or developed MDR TB are not included in this cohort.

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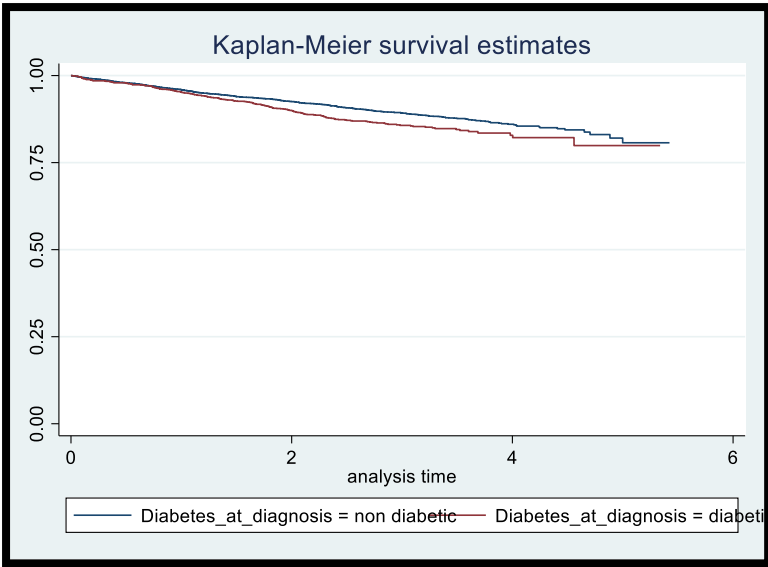
Figure 8: Survival by presence of diabetes at diagnosis
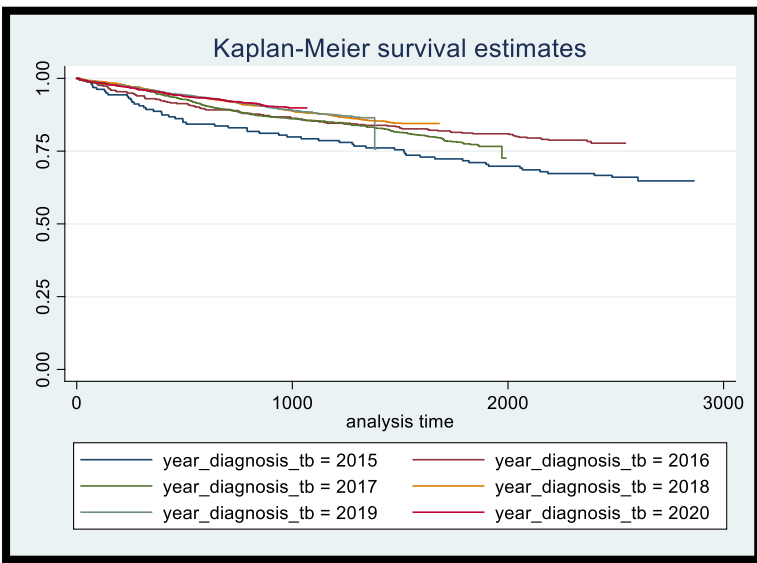
Figure 9: Survival by year of diagnosis of TB

The Kaplan Meier curve showing survival by year of diagnosis showed that the earlier years, 2015 and 2016, had a slightly higher death rate and this may be due to the low number of participants available from these years.

Table 12: Summary of bivariable analysis

Risk factors	Hazard ratio	95%CI	P value
Male Gender	2.06	1.81-2.36	<0.001
Having 2 or more episodes of TB	1.91	1.61-2.27	<0.001
Diabetes Mellitus at the time of diagnosis	1.31	1.12-1.55	0.001
HIV at the time of diagnosis	1.25	0.93-1.70	0.144
Patient reported that they have not completed at least 6 months of treatment	9.23	8.24-10.35	<0.001

Table 13: Hazard ratios for various age categories

Age category	Hazard ratio	[95% CI]		P value
		Lower limit	Upper limit	
<=20 years	ref			
21-30 years	0.77	0.38	1.56	0.462
31-40 years	2.24	1.14	4.41	0.02
41-50 years	3.36	1.73	6.54	<0.001
51-60 years	5.15	2.66	9.98	<0.001
61-70 years	6.90	3.56	13.38	<0.001
71-80 years	9.30	4.76	18.19	<0.001
81-90 years	12.40	6.11	25.13	<0.001
>90 years	11.89	3.66	38.61	<0.001

Table 14: Survival rates in each age category (n=9387)

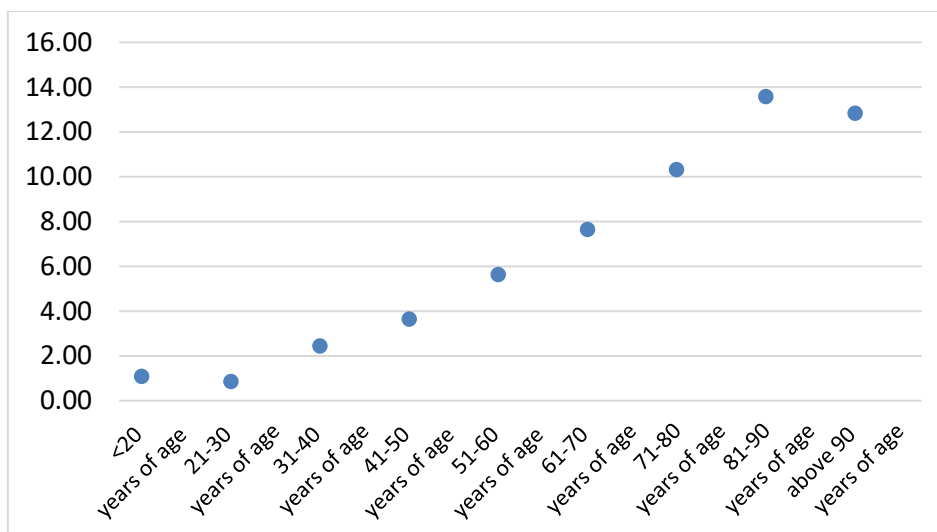| Age category at follow up	Alive	Dead	Total	Person years of observation	Age specific death rates (per 1000 person years)
<=20 years	258(96.63%)	9(3.37%)	267	831.18	10.83
21-30 years	1,595(97.02%)	49(2.98%)	1,644	5741.18	8.53
31-40 years	1,356(91.68%)	123(8.32%)	1,479	5043.77	24.39
41-50 years	1,658(87.96%)	227(12.04%)	1,885	6241.40	36.37
51-60 years	1,608(81.83%)	357(18.17%)	1,965	6349.88	56.22
61-70 years	1,131(76.32%)	351(23.68%)	1,482	4590.71	76.46
71-80 years	381(68.9%)	172(31.1%)	553	1667.52	103.15
81-90 years	75(58.14%)	54(41.86%)	129	397.72	135.8
above 90 years	7(63.64%)	4(36.36%)	11	31.16	128.4
Total	**8,069(85.7%)**	**1,346(14.3%)**	**9,415**	**30894.52**	**42.66**

Figure 10: Age specific death rates per 100 person years

On stratifying for age, it was found that the death rates showed a J shaped curve with high rates in the youngest group which slightly dips and then increases over successive years.

The age specific death rates were compared across Vellore and Tiruvannamalai districts and similar rates were noted (Table 15 and 16). The remaining 333 participants belonged to other districts.

Table 15: Age specific death rates in Vellore district

Age category at follow up	Alive	Dead	Total	Person years of observation	Age specific death rates (per 1000 person years)
<=20 years of age	165(96.49%)	6(3.51%)	171	528.81	11.34
21-30 years of age	982(96.94%)	31(3.06%)	1013	3661.75	8.19
31-40 years of age	859(91.58%)	79(8.42%)	938	3315.19	23.53
41-50 years of age	1031(88.12%)	139(11.88%)	1170	3993.58	34.56
51-60 years of age	967(80.85%)	229(19.15%)	1196	4012.9	56.82
61-70 years of age	703(76.16%)	220(23.84%)	923	2946.37	72.97
71-80 years of age	243(69.23%)	108(30.77%)	351	1116.11	93.18
81-90 years of age	42(53.16%)	37(46.84%)	79	251.23	143.29
above 90 years of age	4(57.14%)	3(42.86%)	7	21.17	141.68
Total	**4996(85.43%)**	**852(14.57%)**	**5848**	**19847.11**	**42.93**

Table 16: Age specific death rates in Tiruvannamalai district

Age category at follow up	Alive	Dead	Total	Person years of observation	Age specific death rates (per 1000 person years)
<=20 years of age	85(96.59%)	3(3.41%)	88	273.4	10.97
21-30 years of age	511(96.96%)	16(3.04%)	527	1718.86	8.73
31-40 years of age	444(91.93%)	39(8.07%)	483	1540.9	24.66
41-50 years of age	570(87.42%)	82(12.58%)	652	2042.53	39.66
51-60 years of age	595(82.87%)	123(17.13%)	718	2174.24	54.27
61-70 years of age	403(76.04%)	127(23.96%)	530	1552.24	78.60
71-80 years of age	130(68.06%)	61(31.94%)	191	518.93	115.62
81-90 years of age	30(65.22%)	16(34.78%)	46	131.31	121.85
above 90 years of age	2(66.67%)	1(33.33%)	3	5.86	170.60
Total	**2770(85.55%)**	**468(14.45%)**	**3238**	**9958.28**	**45.59**

Table 17:Multivariable analysis for survival

Category	Subgroup	Adjusted HR	95%CI	P value
Gender	Female	*Ref*		
	Male	1.24	1.08-1.43	0.003
Age category	1-20 years of age	*Ref*		
	21-40 years of age	3.52	1.96-6.32	<0.001
	41-60 years of age	8.41	4.73-14.97	<0.001
	61-80 years of age	18.67	10.47-33.28	<0.001
	above 80	23.50	11.37-48.59	<0.001
Past history of TB	>=2 episodes	1.06	0.88-1.27	0.55
Diabetes at the time of diagnosis	Diabetic	0.98	0.86-1.11	0.75
Duration of treatment – patient reported	>6 months of treatment	8.43	7.47-9.51	<0.001

A predictive model was generated to identify the main risk factors for poor survival. Risk factors identified in the bivariable analysis were introduced in the multivariable model. Incomplete treatment and age remained strong risk factors for poor survival outcomes and gender seems to be a confounding factor as men were all almost 10 years older than the women at diagnosis and at follow up.

Impact of calendar year on death rate
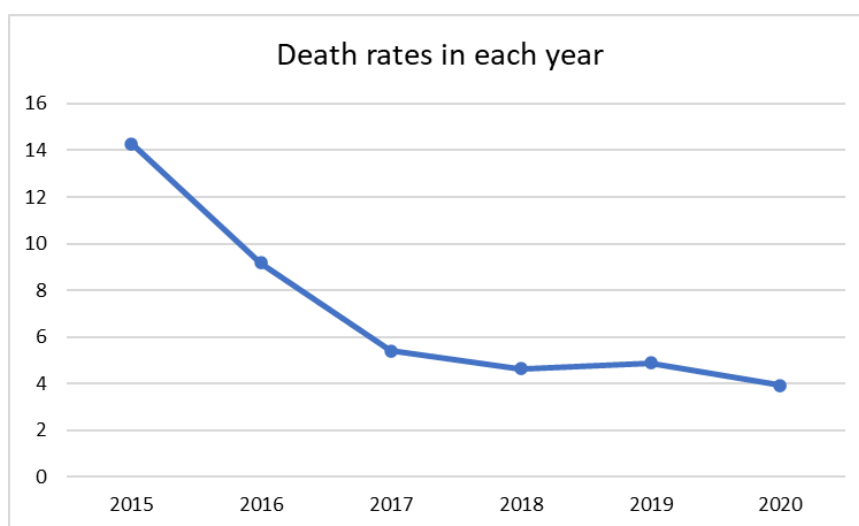
Figure 11: Death rates in each year

The death rates were found to be the highest in 2015 and has gradually reduced with every succeeding year. After stratifying this on age at diagnosis a similar pattern was seen, which as that the highest death rate was seen in 2015 with a gradual decrease through the next few years. This could possibly be due to the very few numbers available for 2015 and 2016.

All age groups had comparable death rates during all calenda years between 2017 and 2020.
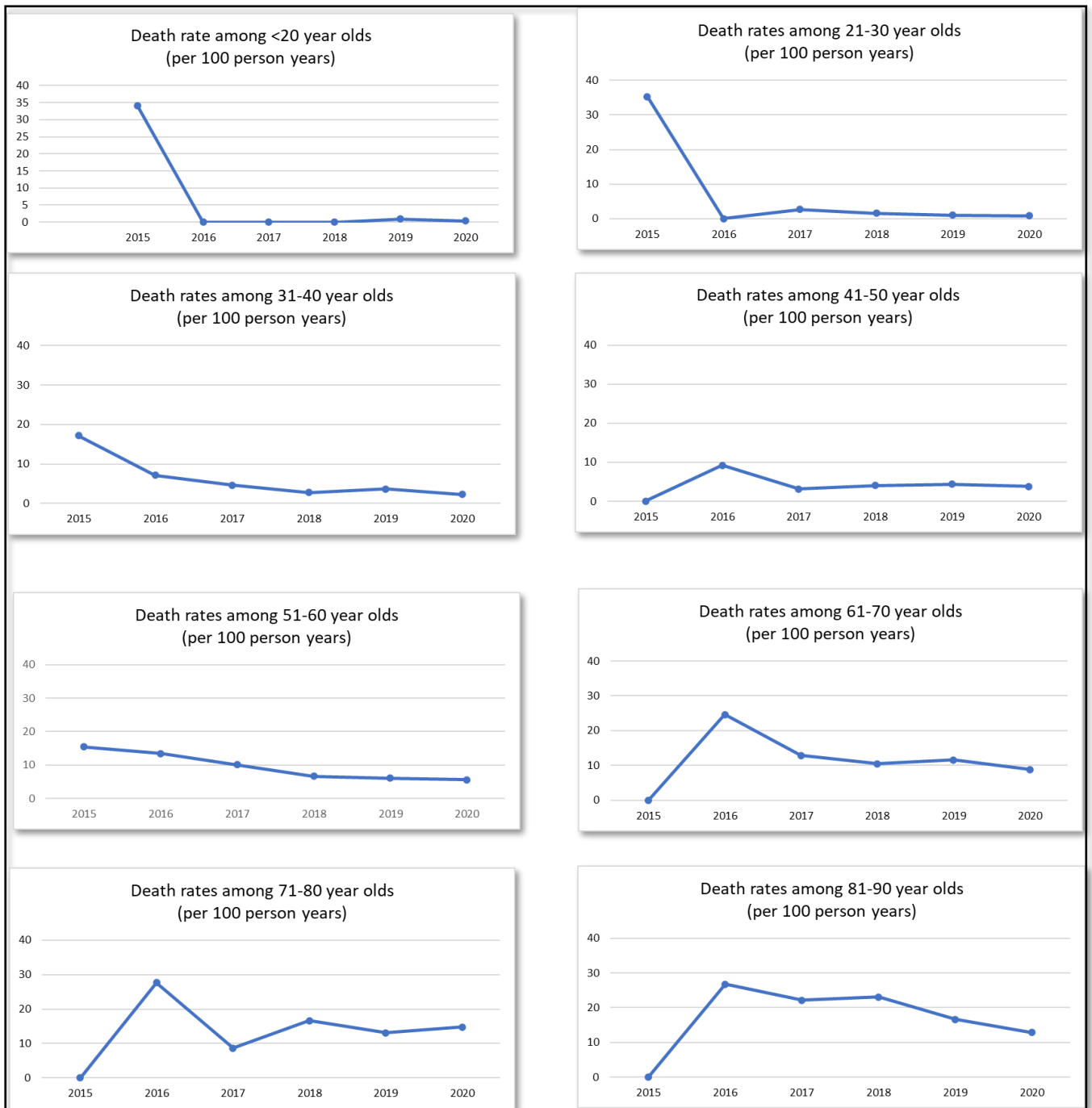
Figure 12:Death rates stratified on age and calendar time.

Age standardized mortality rates.

Table 18: Mortality Data for Kaniyambadi block in 2020

Age group	No. of people	No. of deaths observed	Death rates per 1000 people
<=20 years	8118	8	0.985
21-30 years	18959	28	1.477
31-40 years	19782	39	1.971
41-50 years	16403	77	4.694
51-60 years	14096	131	9.293
61-70 years	9736	185	19.001
71-80 years	5434	252	46.375
Above 80 years	2728	210	76.979

If the cohort of individuals, who have completed TB treatment in the past, experience the same death rate that the residents of Kaniyambadi experience then the expected deaths that could have been recorded are given in the table below.

Total observed deaths 1346 and expected deaths as calculated to be 305.13 giving an age standardized mortality rate of 441.12%. This implies that those who have completed treatment experience a 4.4 times greater risk of dying than the general population.

Table 19: Expected deaths in Observed cohort, indirect standardization.

Age group	Age specific death rate in Kaniyambadi (Per 1000 person years)	Number of person years of observation in each age group in the TB cohort	No. of expected deaths in the TB cohort if they experienced the same death rate as residents of KNB block
<=20 years	0.99	831.18	0.82
21-30 years	1.48	5741.18	8.48
31-40 years	1.97	5043.77	9.94
41-50 years	4.69	6241.40	29.30
51-60 years	9.29	6349.88	59.01
61-70 years	19.00	4590.71	87.23
71-80 years	46.37	1667.52	77.33
Above 80 years	76.98	428.88	33.01

Part 5: Quality of life of patients who have completed treatment for DS-TB.

Two hundred and forty individuals were randomly selected from those who were willing to be visited at home. Of those interviewed 162 (67.5%) were men, with a mean age of 51.45 years (SD 14.84)

Table 20: General characteristics of those screened using SF36 (n=240)

Characteristic	Subgroup	Frequency	Percentage
Gender	Female	80	33.3
	Male	160	66.7
District in which they currently reside	Tiruvannamalai	107	44.58
	Vellore	133	55.42

Responses to SF36

General health

Table 21: Responses to general health questions (n=240)

Question number	Question	Response	Frequency	Percentage
1	In general, would you say your health is	Excellent	51	21.25
		Very Good	77	32.08
		Good	93	38.75
		Fair	17	7.08
		Poor	2	0.83
2	Compared to one year ago, how would you rate your health in general now	Much better now than one year ago	72	30.00
		Somewhat better now than one year ago	111	46.25
		About the same	26	10.83
		Somewhat worse now than one year ago	26	10.83
		Much worse than one year ago	5	2.08

Table 22:Limitations of activities (n=240)

| Question number	Activities	Not limited at all	Limited a little	Limited a lot
3	Limitation of moderate activities	74	86	80
4	Limitation of Vigorous activities	127	91	22
5	Lifting groceries	167	55	18
6	Climbing several flights of stairs	85	63	92
7	Climbing one flight of stairs	155	61	24
8	Bending kneeling or stooping	130	85	25
9	Walking more than a mile	120	61	59
10	Walking several blocks	114	66	60
11	Walking one block	171	60	9
12	Bathing or dressing yourself	214	19	7
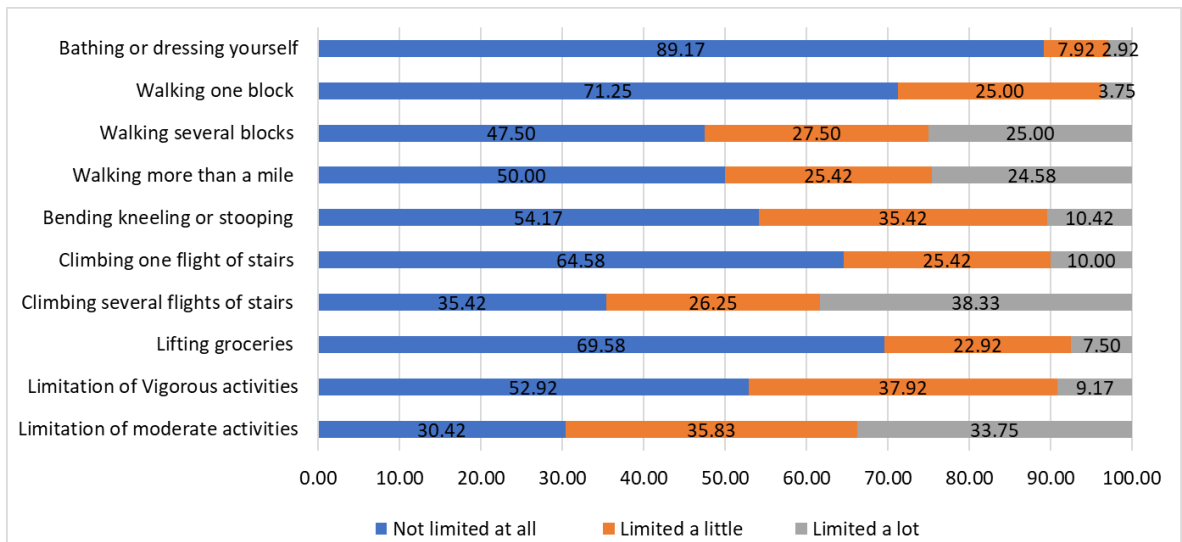
Figure 13:Distribution of responses regarding limitation of physical activities in percentages (n=240)

Table 23:Physical health problems (n=240)

Question number	During the last 4 weeks, have you had any of the following problems with your work or other daily activities because of your physical health?	Yes	No
13	Cut down on the amount of time you spent on work or other activities	115	125
14	Accomplished less than you would like	115	125
15	Were limited in the kind of work or other activities	110	130
16	Had difficulty performing the work or other activities	129	111

Table 24:Emotional health problems (n=240)

Question number	During the last 4 weeks, have you had any of the following problems with your work or other daily activities as a result of any emotional problems?	Yes	No
17	Cut down on the amount of time you spent on work or other activities	86	154
18	Accomplished less than you would like	113	127
19	Did'nt do work or other activities as carefully as usual	71	169

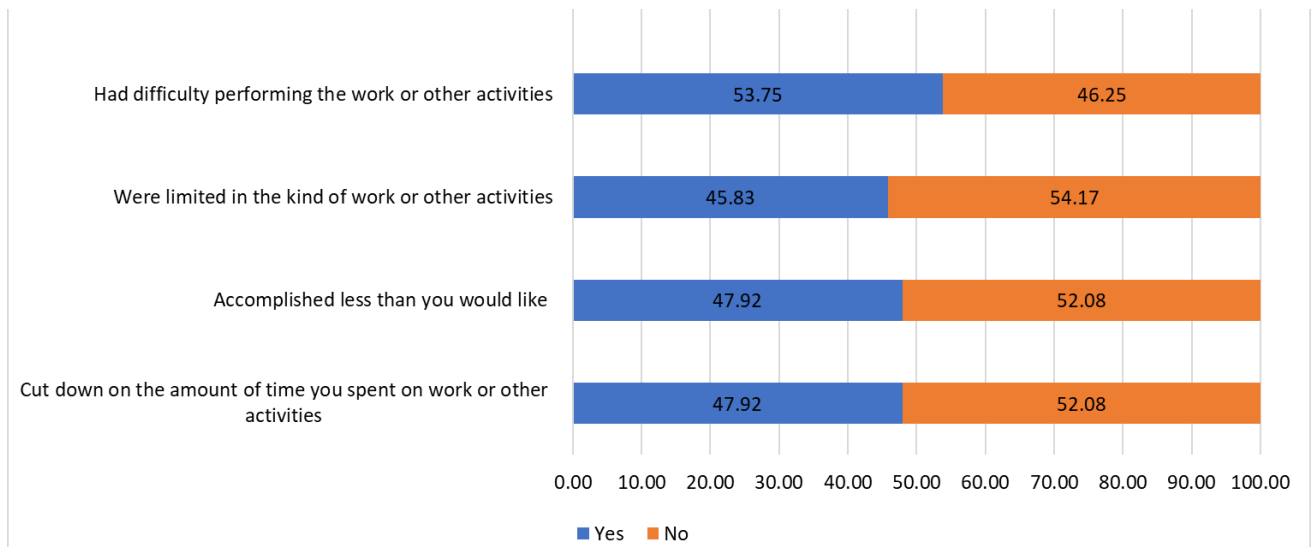*Figure 14:Role limitation due to physical problems (n=240)*

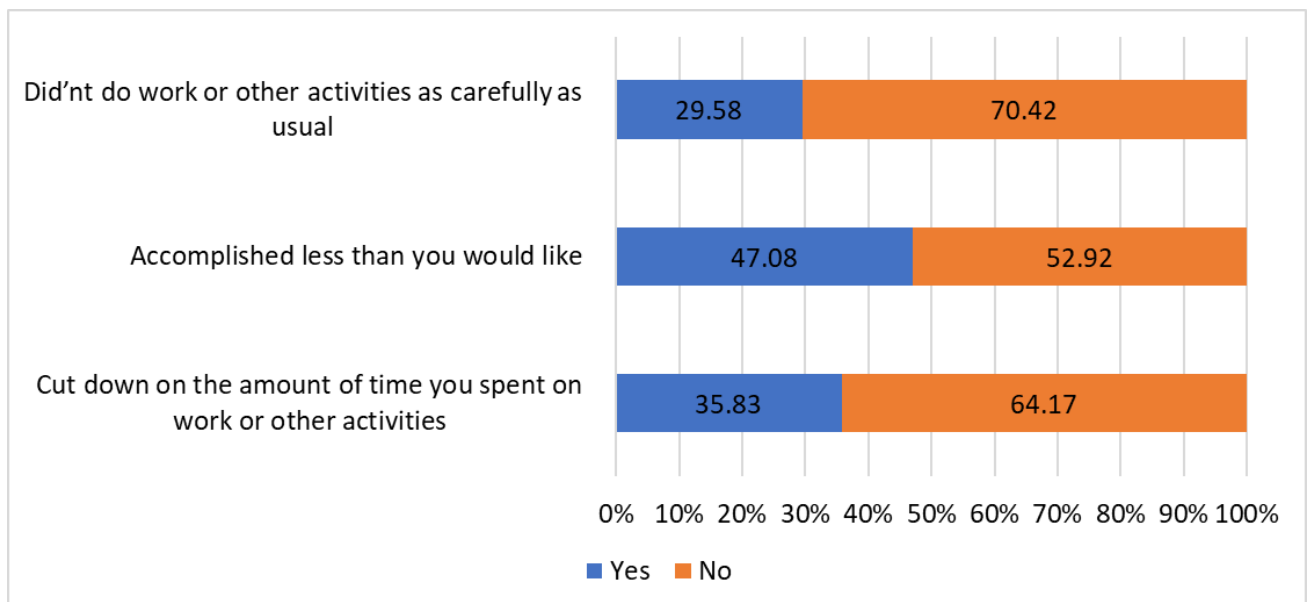*Figure 15:Role limitation due to emotional problems (n=240)*

Question 20: Social activities

Table 25:Restrictions in social activities (n=240)

Response	Frequency	Percentage
Not at all	153	63.75%
Slightly	37	15.42%
Moderately	23	9.58%
Severe	21	8.75%
Very severe	6	2.5%

Pain

Table 26:Experience of Pain

Question number	Question	Response	Frequency	Percentage
21	How much bodily pain have you experienced in the last 4 weeks?	None	101	42.08
		Mild	29	12.08
		Moderate	42	17.5
		Severe	24	10
		Very Mild	36	15
		Very Severe	8	3.33
22	During the past 4 weeks, how much did pain interfere with your normal work?	Extremely	6	2.5
		Quite a bit	22	9.17
		Moderately	36	14.58
		A little bit	37	15.42
		Not at all	140	58.33

Energy and emotion

Table 27:Level of energy and emotion experienced in the last 4 weeks.

| Question number	Question	All of the time	Most of the time	A good bit of the time	Some of the time	A little bit of the time	None of the time
23	Did you feel full of pep	37	64	26	66	31	16
24	Have you been a nervous person	5	18	24	50	43	100
25	Have you felt so down in the dumps that nothing could cheer you up	2	14	15	40	71	98
26	Have you felt calm and peaceful	31	53	43	62	31	20
27	Did you have a lot of energy	20	42	39	52	45	42
28	Have you felt down hearted and blue	6	17	12	46	73	8
29	Did you feel worn out	4	14	21	53	57	91
30	Have you been a happy person	30	67	35	47	44	17
31	Did you feel tired	6	23	30	31	63	87
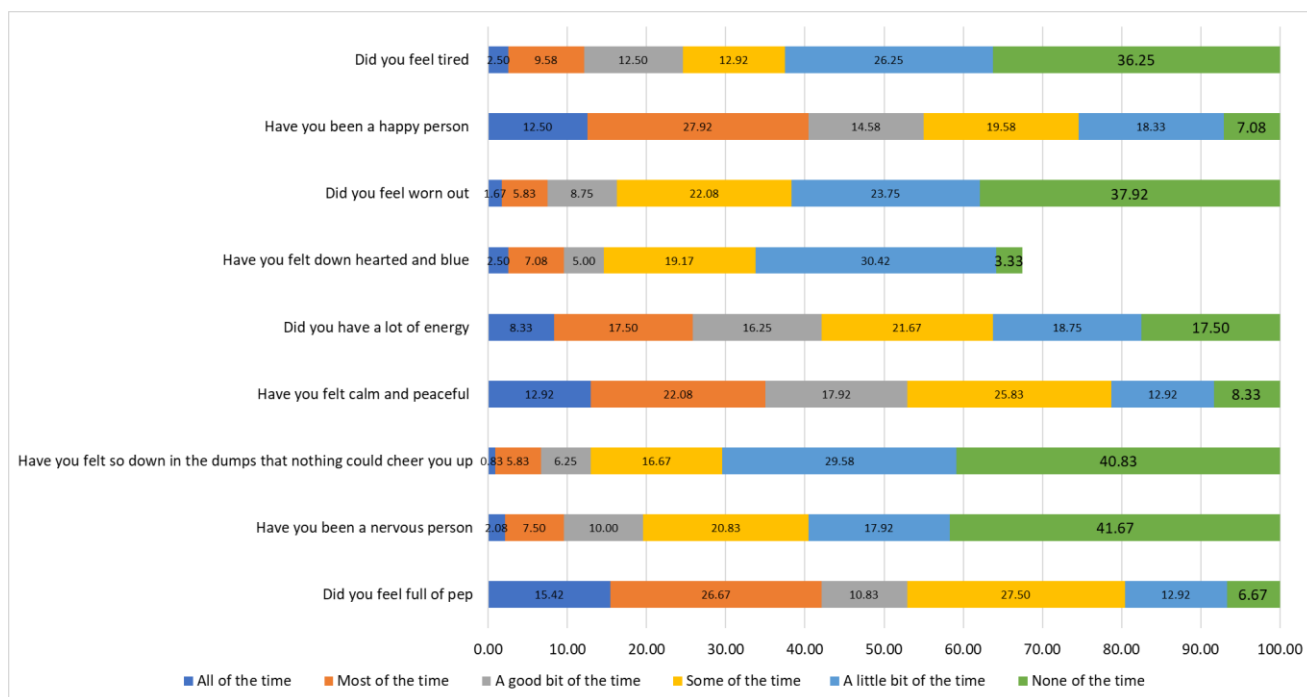
Figure 16:Levels of energy and emotion

Question 32: Social activities

Table 28:During the past 4 weeks how much of the time has your physical health or emotional problems interfered with your social activities.

Response	Frequency	Percentage
All of the time	13	5.42
Most of the time	25	10.42
Some of the time	29	12.08
A little bit of the time	43	43.0
None of the time	130	130

General health

Table 29:How true/ false is each of the following statements?

| Question no.	Question	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33	I seem to get sick a little easier than other people	23 (9.58%)	67 (27.92%)	6 (2.5%)	56 (23.33%)	88 (36.67%)
34	I am as healthy as anyone I know	89 (37.08%)	84 (35.00%)	9 (3.75%)	40 (16.67%)	18 (7.5%)
35	I expect my health to get worse	13 (5.42%)	24 (10%)	32 (13.3%)	52 (21.67%)	119 (49.58%)
36	My health is excellent	93 (38.75%)	80 (33.33%)	10 (04.17%)	35 (14.58%)	22 (09.17%)
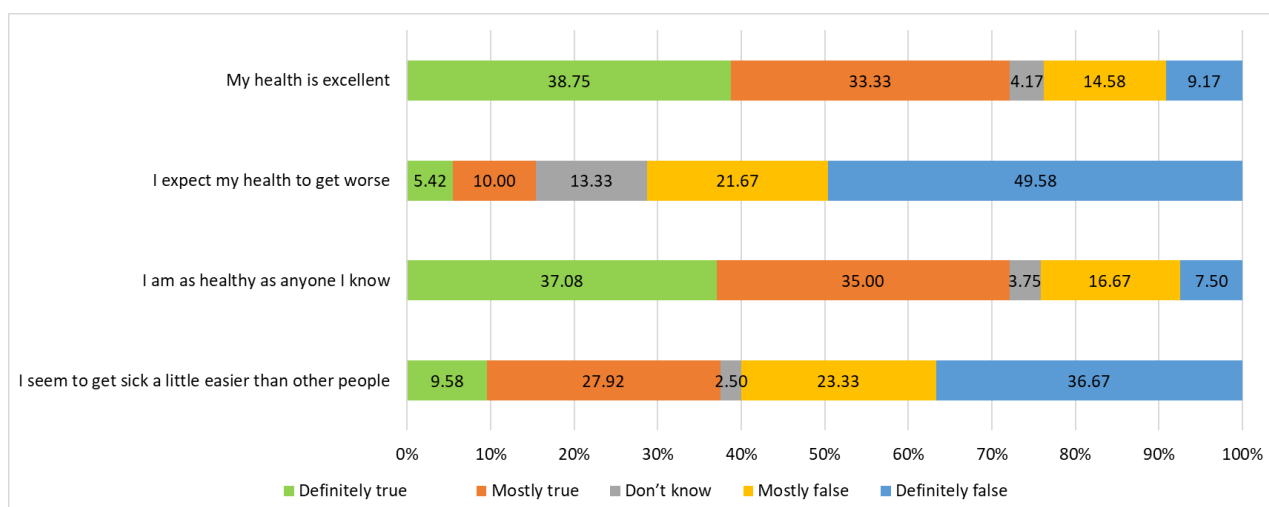
Figure 17:Distribution of responses regarding limitation of physical activities

Table 30: Average scores in each domain (n=240)

Domain	Mean	SD	Minimum	Maximum
General health	69.98	27.37	0	100
Physical functioning score	51.15	43.65	0	100
Limitations due to physical health	62.50	38.22	0	100
Limitations due to emotional health	62.02	23.16	0	100
Energy and Fatigue	67.32	20.04	0	100
Emotional well being	79.27	26.27	0	100
Social functioning	74.91	28.39	0	100
Pain	68.54	24.97	0	100

Table 31:Overall scores

	Range	Mean (SD)	Proportion with low score (95%CI)
Physical component score	3.75-100	66.14(24.99)	25.42% (19.91-30.93%)
Mental component score	3.13 -100	67.78(22.21)	23.33% (17.98-28.6%)

Overall physical component score was calculated by taking the average of the physical functioning score, general health, bodily pain experienced and limitations in role due to

physical pain. Those with a score of less than 50 were classified as having poor physical health.

Overall mental component score was calculated by taking the average of the scores for vitality, social functioning, emotional wellbeing, and role limitation due to emotional health. Those with a score of less than 50 were classified as having poor mental health. The numbers found here are comparable with other studies done in India.

Part 6: Findings from the verbal autopsies

Thirty in-depth interviews were conducted between 12 August 2022 and 5 December 2022. Immediate family members were available for most of the interviews. (Table 32) The index patients were aged between 27 and 86 years of age, were mostly men (93.3%), residents of Vellore district (80%). Almost two thirds of them had a history of consuming alcohol or smoking tobacco. Almost all the patients had a diagnosis of pulmonary tuberculosis, 13% had a history of previously treated TB and 26% reported that they had defaulted on treatment. (Table 33 and 34)

Table 32:Characteristics of the respondents

Characteristics	Subgroups	Frequency	Percentage
Relationship to the deceased	Spouse	13	43.33%
	sibling	3	10.00%
	Parent	1	3.33%
	Daughter /son	11	36.67%
	Granddaughter/ grandson	1	3.33%
	household member	1	3.33%
Did they live with the patient at the time of their death	Yes	22	73.33%
	No	4	13.33%

Families were visited at home and all available documents were examined. However, many had been burnt during the patient's funeral. Also, there were situations where hardly any medical documents were available, and each member of the family had a different narrative around the cause of death. Not all members of the family were aware of the diagnosis of TB in the index patient which made the interviews very challenging as multiple people had to be interviewed to understand the complete picture.

Table 33:General and disease characteristics of the index patients

General characteristics	Subgroups	Frequency	Percentage
Age group	21 to 40	3	10.00%
	41 to 60	10	33.33%
	61 to 80	14	46.67%
	above 80	3	10.00%
Educational status	Illiterate	7	23.33
	Primary	9	30.00
	Middle	7	23.33
	Intermediate	1	3.33
	High	5	16.67
	Higher secondary	1	3.33
	Graduate	0	0.00
Marital status	unmarried	3	10.00
	married	21	70.00
	widow	1	3.33
	widower	4	13.33
	separated/divorced	1	3.33
Occupation	unemployed	5	16.67
	daily wage	13	43.33
	skilled	8	26.67
	professional	0	0.00
	farmer	2	6.67
	retired	2	6.67
History of smoking	Yes	20	66.67
	No	10	33.33
History of alcohol consumption	Yes	19	63.33
	No	11	36.67
Year of diagnosis of the index case of tuberculosis	2017	1	3.33
	2018	8	26.67
	2019	9	30.00
	2020	12	40.00
Type of TB as reported on NIKSHAY	Pulmonary	30	100%
	Extrapulmonary	0	0
	Both	0	0
	Not sure	0	0
Type of patient	New	26	86.67
	Previously treated	4	13.33
Did the patient default	Yes	8	26.67
	No	22	73.33

Table 34:Medical history of the index patients

Medical condition	Subgroup	Frequency	Percentage
History of diabetes mellitus	Diabetes on OHAs	11	36.67
	Diabetes on insulin	1	3.33
	not known / not diabetic	18	60.00
History of hypertension	Hypertensive on tablets	10	33.33
	not known/ not hypertensive	20	66.67
Other comorbidities	COPD /asthma	8	26.66
	cancer	1	3.33
	HIV/AIDS	0	0.00
	Stroke	1	3.33
	cardiac	1	3.33
	others	2	6.67
	none	15	50.00
History of smoking	Yes	20	66.67
	No	10	33.33
History of alcohol consumption	Yes	19	63.33
	No	11	36.67
Year of diagnosis of the index case of tuberculosis	2017	1	3.33
	2018	8	26.67
	2019	9	30.00
	2020	12	40.00
Type of TB as reported on NIKSHAY	Pulmonary	29	96.67
	Extrapulmonary	1	3.33
	Both	0	0
	Not sure	0	0
Type of patient	New	26	86.67
	Previously treated	4	13.33
Did the patient default	Yes	8	26.67
	No	22	73.33
Total no. Of Episodes of TB experienced	1	12	54.55
	2	8	36.36
	3 or more	2	9.09
Place of death	Hospital	10	33.33
	On the way to the hospital	2	6.67
	Home/ non-hospital location	18	60.00

The various factors contributing to the death of these individuals are as follows:

a. Direct medical causes:

    i. Non communicable diseases: The most common cause of death in this group was related to chronic diseases such as diabetes and hypertension. Though many of them were on treatment for the same they were not controlled sufficiently. Some experienced complications related to these chronic diseases such as myocardial infarctions, strokes, diabetes related soft tissue infections requiring amputations, and renal failure.

    ii. Tuberculosis and tuberculosis related causes

        a. Incomplete treatment: Some families were uncertain regarding the duration of the treatment recommended for tuberculosis. A few families reported that they had been informed directly by health care workers that the duration of treatment required was less than 6 months, in some cases as short as 2 months. So, they thought their relatives had completed treatment when in fact they had taken only 2-3 months of treatment. Some patients found it difficult to complete care due to reasons related to alcohol abuse.

        b. Recurrent pulmonary tuberculosis

        c. Post TB-related lung diseases: Chronic obstructive lung disease with acute infective exacerbations, COPD with cor pulmonale were some of the diagnoses noted on medical records. In some cases, family members were told by the treating physician that the lungs were damaged due to TB.

    iii. Physical impairments: Impairments such as deafness, speech impediments and loss of limb are problems resulting in decreased ability to express health needs and difficulty in accessing health care.

    iv. Other medical causes: Injuries

Table 35:Primary cause of death according to hospital records

Cause of deaths according to hospital records	Frequency
COPD	4
Diabetes related complications	1
Cancer	1
TB related complications	1
Others	1
Not available	22

Table 36: Primary cause of death according to the verbal autopsy

Cause of death from Verbal autopsy	Frequency
DM & HTN related complications/ CKD/ MI stroke	10
Chronic respiratory symptoms (COPD/ haemoptysis)	6
TB related	5
Cancers	3
Others	3
Not sure	2

b. **Personal habits:** Chronic substance abuse with alcohol, tobacco and ganja were reported in some cases and in most situations' family members had recognized this as a problem but were either unable to help the person or distanced themselves from the patient. None of the patients who reported substance abuse had accessed or attempted treatment for the same.

c. **Family and social issues:** Some patients had complicated family issues and were estranged from their families for various issues resulting in a delay in accessing health care. All these causes had an impact on the patient's finances, nutrition, mental health, and severity of substance abuse resulting in a deterioration of health status.
   i. Property disputes
   ii. Marrying outside the caste
   iii. Death or separation from the spouse resulting in poor nutritional status, worsening of substance abuse and
   iv. Elderly parents living away from their children.

d. **Health system related issues**:
   i. Delay in taking the patient to the hospital or deterioration of patient by the time the decision was made. At times patient were referred by grassroot level health care workers but the patients need for higher care was identified at a late stage.
   ii. Delay in referring patient from small clinic to higher centre as it was a Sunday, there were no doctors available, and the traffic was very heavy.
   iii. Some patients had chronic conditions like diabetes and hypertension which were not controlled.
   iv. Patients can see care in certain facilities only if they are offered concessional care.
   a. Some patients have been diagnosed with advanced stages of certain conditions, poor prognosis had been explained to relatives and so they were not taken to the hospital for further care.

Summary of key findings:

1. Annual survival rates, from 2017 have been around 95%.
2. Death rates when adjusted for age category and calendar period did not show a higher death rate in 2020, during the COVID lockdown.
3. Standardised mortality ratio was calculated to be 441% when comparing the death rates among this cohort and the residents of Kaniyambadi block implying that people with a past history of treated TB are at ta 4 times higher risk of dying when compared to the general public.
4. Poor survival was seen among patients who had discontinued treatment (HR 8.43, 95%CI 7.47-9.51), higher age groups and men (HR 1.24, 95%CI 1.08-1.43)
5. Among the survivors, poor mental health scores were found in 23.3% (95%CI 17.98-28.6%) and poor physical health scores were found in 25.42% (19.91-30.93%).
6. Medical cause of mortality among the patients with a previous history of tuberculosis include.
   a. TB related issues such as incomplete treatment, recurrent pulmonary tb, post tb related lung disease and chronic respiratory conditions
   b. Non communicable diseases such as diabetes, hypertension, and cancers also contributed to the overall mortality.
   c. Social isolation, substance abuse, affordability of care and delays in recognising the need for care and seeking care were also issues that led to the death of some of the individuals.

Challenges and limitations:

1. Quantitative part of the study: The survival rates have been calculated based on the responses of those who could be contacted. However, the inability to contact almost half of the patients impacts the generalisability of these findings.

2. Qualitative part of the study: The exact and complete picture of the individual's disease condition and treatment are difficult to gather as the course of the disease and treatment is typically spread across many months or years and some details have never been openly revealed to certain members of the family, including the spouse. So, the details need to be acquired through multiple sources – multiple family members, records and those involved in the treatment process. Limited information was available for certain people with poor family support. They either had no evaluation of their final symptoms or were found dead. Many of the families had burnt all medical reports along with the patients' belongings after their death.

1. Annual check of pulmonary functions and screening for post TB lung disease.
2. Strengthening of care for NCD (Non-Communicable Diseases) services in the primary health care centres for patients with a previous history of TB.
3. Linking certain patients or rehabilitation services for substance abuse
4. The post TB 2 year follow up initiative that has been implemented by the programme from 2022 will be useful in collating the various problems people experience as the follow up will be done prospectively.