TITLE

THE EVALUATION OF TRENDS AND COMPARISON ANALYSIS OF THE ROLES OF DIRECTLY OBSERVED TREATMENT (DOT) SUPPORTERS IN TB TREATMENT OUTCOME AT THANDUKUKHANYA COMMUNITY HEALTH CENTRE FROM 2000-2005

By: Dr. Joven Jebio Ongole

Student Number: 0411758T

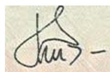
Submitted to the Department of Epidemiology and Biostatistics, School of Public Health, University of Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Science Epidemiology and Biostatistics

Date submitted: 24 April 2012

Promoter: Dr. Ronel Kellerman

DECLARATION

I, Dr. Joven Jebio Ongole, hereby declare that the work on which this research report is based, is original (except where acknowledgement indicates otherwise) and that neither the whole work nor any part of it has been, or is to be submitted for another degree at this or any other university.

Signed: 

Place: University of Witwatersrand, School of Public Health

Date: 24 April 2012

DEDICATION

I dedicate this work to my dear wife, Mrs. Janet Oloya Ongole and our three daughters Janice, Jessica and Jasmine whose constant support, understanding and endurance helped me throughout my study as a part- time post graduate student of Epidemiology and Biostatistics. This was more so when I was working on this research project

My gratitude also goes to my parents who educated me.

ABSTRACT

Introduction

TB is a high burden disease (prevalence: 940/100,000 in 2006) with high morbidity and mortality in South Africa and the primary health care facilities are well position to provide primary TB care in accordance to the national TB control guidelines and achieve desired treatment outcome targets. This study followed the TB management at Thandukukhanya clinic from 2000-2005 and found among others that the number of TB cases tripled, the TB cure rate progressively declined and DOTS support dwindle over the six years.

The study was motivated by 26% decline in TB cure rate at Mkhondo sub-district from 2003 – 2005 and 76% increase in TB default in the same period. The TB cure rate in 2005 was 37% compared to 85% national target. The poor treatment outcome prevails despite availability of DOTS support in the program. In addition, the number of drug resistant TB has increased in the past years and extremely drug resistant TB emerged in the past three years in South Africa.

Study Objectives

1. To describe the trend of TB at Thandukukhanya clinic from 2000 -2005.
2. To analyse TB treatment outcomes of TB cases from 2000-2005.
3. To conduct comparison analysis of TB cases with and without treatment supporters.

Methods

This retrospective study was performed at Thandukukhanya, a day clinic at Mkhondo Sub-District, Mpumalanga South Africa. I reviewed health records of TB cases registered at Thandukukhanya clinic from 2000 to 2005. The records were reviewed consecutively starting with first registered patients in 2000 and ended with the last registered case in 2005. Information from the facility retained TB card was verified with that in the TB register and this was done for all cases. Data was captured and entered, edited and analysed using Epi-Info version 3.5. Further analysis was performed in Stata10. The TB cure rate and treatment interruption rate was obtained from electronic TB register at the sub-district. Analysis evaluated the TB trend, treatment outcomes and DOTS support. Graphs were constructed in MS. Excel and tables in Ms. Words.
The researcher ensured privacy and confidentiality of information was maintained at all times. The permission to conduct the study was granted by Mkhondo Municipality Health Directorate

and Witwatersrand University provided ethical clearance. The cost of the study was undertaken by researcher.

Materials and Methods

This was a cross-section study design, with data sourced from the TB register and patients' TB cards retained at the clinic for a period 2000-2005. The researcher collected, captured and collated all data for the study. Record in the TB register was used to verify correctness of data in patients TB card. Data collected was entered, stored and cleaned in Epi-Info 3.5 version and Analysis was performed using Stata10 Statistical packages. Graphs were constructed in MS. Excel and tables in Ms. Words. The researcher maintained privacy and confidentiality of information by denying access to anyone else and managing all data process. The Mkhondo Municipality Health Directorate gave permission to conduct the study and ethical clearance was provided by Wits University. The cost of the study was met by researchers.

Results

Objective one

Of 861 cases in the study, 858 were analysed and three dropped due to inadequate data. The children under 15 years of age made up 4% of cases. The number of tuberculosis cases increased 3.7 times (67 in 2000 Vs 249 in 2005) during the study. Except for the first year that males cases were more than females and in second year that females cases were more, both sex were equally affected by TB. However, the sex ratio was different by age groups, being equal (1:1) in <15 years group, more females (0.68:1) in 15-34 years group and more males (1.5:1) in >35 years. Majority of cases were registered in age group 20-34 years.

Fewer educated cases were treated for tuberculosis compared to uneducated (46.78% Vs 53.22%) and fewer employed cases were treated compared to unemployed (6.92% Vs 93.08%).

The proportion of smear negative tuberculosis cases increased during the study and became dominant over smear positive in 2004 to 2005. The proportion of re-treatment TB cases registered increased 5-fold and the majority had previously completed treatment without confirming cure.

At the beginning of the study, TB was predominantly diagnosed by bacteriologic method, but declined (86.57% in 2000 vs 10.45% in 2005) and X-ray was predominant in the last two years of the study.

The sputum conversion smear done declined from 83.58% in 2000 to 43.15% in 2005 but proportion of cases converted remained stable between 92-97%.

Objective two:

33.69% of tuberculosis cases were cured of TB infection (target 85%) while 38% completed treatment course without confirming sputum conversion. 12.9% died of TB during treatment while 10% interrupted treatment. 0.82% failed TB treatment while 3.39% transferred to another facility before completing treatment.

Having DOTS support during treatment (OR: 2.4, CI: 1.7 – 3.25, p=0.0001) and tertiary education (OR: 4.47, CI: 1.02-19.6, P=0.047) were significantly associated with TB cure. Having single marital status (OR: 0.26, CI: 0.11 – 0.59, P=0.001), being widowed (OR: 0.075, CI: 0.007-0.71, P=0.025), having relative as DOTS supporter (OR: 2.16, CI: 0.99-4.66, P=0.05) and being in age group 31-40 years (OR: 0.61, CI: 0.39 -0.95, P=0.031) were significantly associated with completing tuberculosis treatment course.

Being in age group 31-50 years (OR: 3.6 CI: 1.28-10.09, p=0.015) was significantly associated with tuberculosis death but having education (primary OR: 0.50, CI: 0.27-0.92, p=0.026 and secondary OR: 0.22, CI: 0.11-0.42, p=0.001) were significantly associated with low risk of tuberculosis death. Having no education (OR: 5.59, CI: 1.38 – 22.54, p=0.016), extra-pulmonary tuberculosis (OR: 5.24, CI: 2.67 – 10.29, p= 0.001), X-ray diagnosis (OR: 6.46, CI: 3.5 – 11.9, p= 0.001) and being age 31-40 years (OR: 5.59, CI: 1.38 – 22.54, p= 0.006) were significantly associated with tuberculosis treatment interruption and having DOTS support (OR: 0.29, CI: 0.12 – 1.29, p= 0.001) during treatment protected from treatment interruption.

Having DOTS support during treatment (OR: 2.61, CI: 1.89 – 3.59, p=0.0001), being educated (OR: 1.86, CI: 1.37 – 2.53, p=0.0001) and young age <30 years (OR: 1.20, CI: 1.05 – 1.35, p=0.006) were strongly associated with tuberculosis treatment cure. Being married (OR: 1.48, CI: 1.00-2.219, p=0.049) and older age >30 years (OR: 0.8, CI: 0.71 – 0.93, p=0.002) predicted tuberculosis treatment completion. Having no education (OR: 2.00, CI: 1.26 – 3.16, p=0.003), being married (OR: 3.46, CI: 1.83 – 6.55, p=0.0001), female gender (OR: 1.58, CI: 1.03 – 2.43, p=0.035), older age (>30 years) (OR: 0.68, CI: 0.56 – 0.84, p=0.0001) and residing > 2km away from the clinic (OR: 0.52, CI: 0.34 – 0.87, p=0.003) predicted tuberculosis mortality. Having no DOTS support (OR: 5.05, CI: 3.07 – 8.32, p=0.0001) and no education (OR: 1.77, CI: 1.10 – 2.84, p=0,017) predicted tuberculosis treatment interruption.

8.3). Objective three

In the comparison analysis of DOTS support, 61% of the tuberculosis cases in the study were DOTS supported during treatment. The DOTS support declined from 95.59% in 2002 to 73.21% in 2003, reaching a low 27.31% in 2005. 52.4% of DOTS support was supported by trained TB treatment supporters, followed by community health workers with 40.5% and clinic nurse < 10%.

DOTS support was strongly associated with treatment cure (OR: 2.39, CI: 1.74-3.27, p=0.001) and fewer treatment interruption (OR: 4.78, CI: 2.92 – 7.83, p= 0.0001). The community health workers and relatives were the two DOTS groups associated with treatment interruption, while there was increased in treatment interruption in cases supported by relatives (OR: 2.04, CI: 1.17 – 3.6, p=0.011).

The trained TB treatment supporters was the only group with statistically significant association with low risk of TB deaths (OR: 0.39, CI: 0.22 – 0.69, p=0.007) and this association was protective.

Cases treated with positive pre-treatment sputum smear were 7.8 times (OR: 7.8, CI: 2.2-26.6, p=0.0001) likely to have DOTS support than those without and educated cases were less likely to be supported (OR: 0.7, CI: 0.53 – 0.93, p=0.015).

Cases newly diagnosed for TB were more likely to be dotted (OR: 2.18, CI: 1.4 -3.3, p=0.0001) compared to re-treatment cases (OR: 0.12, CI: 0.02 – 0.58, p=0.009).

Cases were 2.4 times (OR: 2.4, CI: 1.7 – 3.3, p=0.0001) likely to be cured if treated with DOTS support than without and only 0.2 times (OR: 0.2, CI: 0.13- 0.34, p=0.0001) likely to interrupt treatment.

Education (OR: crude 2.30, adjusted 0.91) and employment (OR: crude 2.30, adjusted 0.86) confounded DOTs support and protected cases against TB death and age was a confounding factor in both treatment interruption (OR: crude 4.47, adjusted 5.46) and completion (OR: crude 4.77, adjusted 5.46).

9.0). Discussion of findings

The study found that over the six years, the number of cases enrolled for treatment increased 4-fold, treatment completion rate increased, mortality increased, treatment interruption increased but DOT support declined. The 4-fold increase in number of TB cases in the study was not an isolated event, but reflected an increased trend in the Mkhondo sub-district, Gert Sibande district, Mpumalanga Province and the South Africa. The finding that TB affected males and females equally in children, more females in the middle young adults and more males in older group was consistent with findings in Uganda, USA and Sweden.

The high proportion of TB infection in age group 25-45 is a cause of concern, because in addition to being economically and reproductive efficient group, they are also prone to HIV infection (ANC Survey 2007) and it is the only age group that had rising trend of tuberculosis in the study.

According to result, the treatment outcomes indicators were favourable until 2002, but progressively became unfavourable reaching the lowest point in 2004 and recovered slightly in 2005. It was in part contributed by decline in sputum smear done, increased proportion of cases diagnosed by X-ray and the decline in DOTS support for cases on treatment.

The DOTS support was low and even decreased during the study. In addition, the TB treatment outcomes indicators varied by the DOTS group. The cases supported by trained TB supporters had lower cure rate compared to those supported by nurses and community health workers and could have been due to fact that quality of DOTS support vary with provider group due to different level of training. The training for community health workers and clinic nurses are comprehensive, while trained TB supporters is narrow and basic on DOTS. The relative are not trained but given short education during consultation and health education in the clinic waiting area.

There was no particular DOTS provider that continuously supported TB cases during the study period. Many had breaks during the study. The DOTS support by clinic nurses waned in 2003.

As already proven by WHO and other previous studies, DOTS support was associated with treatment success, with the groups supported by DOTS registering higher cure rate, treatment completion and fewer treatment interruption. However, DOTS support had no effect on TB mortality and this finding is supported by Kayelitshsa study in Western Cape.

Conclusion

The following conclusions were drawn from the study. The TB case load tripled, affected age group 25-34 years than others and affected males and females equally. The smear negative TB increased and X-ray diagnosis increased above smear diagnosis in the last two years. While sputum conversion done declined, the percentage of sputum conversion remained high and stable. The re-treatment TB cases remained low with modest increase in the last year.

While the overall TB cure rate was low (33%) and progressively declined from 4.63% in the beginning of the study to 24% at the end of the study, the treatment completion, mortality and treatment interruption increased. The TB treatment failure, transferred and moved cases remained low and stable throughout the study.

While five categories of supporters provided DOTS support during the study, the overall DOTS support was low, progressively declined and was paradoxically related to TB cure rate. Except for community health workers whose trend matched that of cure rate, no other DOTS categories had effect on the trend TB cure rate. The rise in relatives as DOTS supporter decreased mortality and stopped decline in TB cure. Overall, the tuberculosis cure rate was significantly higher and treatment interruption lower among cases with DOTS support compared to those without. DOTS support did not affect mortality and treatment failure in the study.

Recommendation

1. All TB patients should be done sputum smear for TB diagnosis and conversion to increase cure rate at Thandukukhanya clinic.

2. The young adults 25-34 registered highest of cases number and should be targeted with TB education, infection prevention and DOTS support.

3. All patients should be provided DOTS support to improve treatment outcome indicators (increase cure rate and reduce treatment interruption and mortality).

4. Recommend operation research further studies aim to determine reason for differences seen in the treatment outcome indicators from different DOTS providers.

5. Recommend the findings of this study be applied to TB management in Mkhondo sub-district to improved TB management.

ACKNOWLEDGEMENTS

I wish to express my sincere thanks to the following:

1. Almighty for keeping me safe during the long drive to and from the course venue at Wits University, Health Science Faculty

2. Dr. Ronel Kellerman, Specialist in the Department of Epidemiology and Biostatistics. She provided valuable effort in helping me develop the protocol to final approval and write up of this research report.

3. The Director of Health and administration of Mkhondo Municipal Council for issuing me authority to conduct the research at their facility, Thandukukhanya Clinic.

4. The HAST (HIV, AIDS, STI and TB) Coordinator for providing all the registers from which I collected data.

5. The management of Elizabeth Glaser Paediatric AIDS Foundation, especially Felice Apter, for approving part-time study during my employment with them.

6. The Medical Manager, Dr. BM Wankya for granting study leaves to during the last year of my study.

7. Mrs. Lindy Mataboge, the course coordinator and Lawrence Mpinga, the research coordinator for all the valuable communications and feedbacks during the course.

I wish to tank all those not mentioned by name that directly or indirectly contributed in the study. Your efforts were valuable.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

NOMENCLATURE

AIDS	Acquire Immune Disease Syndrome
CHC	Community Health Centre
CHW	Community Health Worker
DOTS	Directly Observed Treatment Short Course
DOH	Department of Health
HIV	Human Immune Virus
HAST	HIV, AIDS STI and TB
Km	Kilometres
MDR	Multi-Drug Resistant
NTCP	National Tuberculosis Control Program
SA	South Africa
STI	Sexually Transmitted Infections
TB	Tuberculosis
TTTS	Trained TB DOTS supporters
WHA	World Health Assembly
WHO	World Health Organisation
MDR-TB	Multiple Drug Resistant Tuberculosis
X-DR-TB	Extreme Drug Resistant Tuberculosis

CHAPTER ONE

In this chapter the background to the study is presented, followed by problem statement and justification for the research, research question, and study objectives. The chapter ends with literature review and common terms used in the TB program.

1.0). Background

This study was conducted to determine the TB trends, analyse treatment outcomes and perform comparison analysis of DOTS (Directly Observed Treatment Short course) in the TB program at Thandukukhanya clinic from 2000 – 2005

The TB cure rate at Mkhondo sub-district was 37% in 2005 and there was concern that the TB cure rate as well as other treatment outcomes could have declined over a number of years due to poor TB management without having given due interventions. Thandukukhanya clinic was chosen to conduct the study because it large catchment population made of formal and informal settlements of an estimated 19,902 people [1]. The facility won TB award in 2000 and 2001 and maintained well documented TB register and patients retained TB cards.

In 2006, it was generally known that although the number of TB cases was increasing, the treatment cure and success rate were lower than the national target and that DOTS support programme which started in 1996 in South Africa was associated with high case detection rate but appeared to not have improved cure and treatment success rates in the national TB control programme. Locally, though the TB cure rate was known to be very low, the trends of cases in the TB programme as well as the effect of DOTS support on treatment outcomes were unknown. This study therefore was designed to determine the trends in the TB programme and to understand the role of DOTS support on TB treatment outcomes.

1.1). Global TB perspective

According to WHO report of 2006, nearly one-third of the global population is infected Mycobacterium tuberculosis and at risk of developing the disease[2]**.** Worldwide 8.5 million people develop active tuberculosis every year causing about 2 million deaths and TB remains the leading cause of death in low income countries[3]**.** Globally over 90% of TB deaths occur in the developing world and of these about 75% are the most economically productive age group (15-54 years) [4].

In 1994, WHO Stop TB set a global target for countries to achieve in managing TB and was adopted by South Africa. The cure rate for cases diagnosed with sputum was set at 85%, the detection of new cases at 70% and treatment interruption at < 5%[5].

1.2). South African Perspective

South Africa has high TB prevalence rate of 544/100,000 cases per year[6] and ranked 8th in the world in 2006. The TB notification rate increased by about 3% in 2006 due to improved reporting and better case-finding[7]**.** The treatment success rate also increased from 67 to 70% (target 85%) over the same period[8]. The cure rate was 56% (target 80%) in 2005 (SA NTCP report 2006) and low cure rate contributed to the emergence of MDR and XDR and high TB mortality[9].

1.3.0). Direct Observed Treatment Short Course (DOTS)

World Health Organisation (WHO) declared TB a public health emergency in 1993 and was this followed by the launch of DOTS in 1995 as an internationally recommended strategy for controlling TB by using five elements[10]: Government commitment to TB control (policy and financing), diagnosis through bacteriology and effective laboratory network, standardised short course chemotherapy with full patient support throughout treatment, uninterrupted supply of quality-assured drugs and recording and reporting to measure patient and programme outcomes.

By 2006, over 19 million people with TB benefited from effective DOTS support and it was attributed to a 20% reduction in TB prevalence worldwide[11]. India and China rapidly scaled up DOTS programs and today are success stories in TB control.

1.3.1). DOTS in South Africa

In South Africa, the DOTS programme started in 1996 and reached 100% coverage in 2003. But the coverage fell to 94% in 2005[12]. Due to the DOTS program, the TB notification and detection increased to over 70%, but the program had no impact on cure rate and treatment success over years and unclear trend on mortality. In general, TB case notification continued to rise as case-finding and reporting improved. The unfavourable outcomes (not evaluated, transferred, defaulted, failed and died) decreased from 40% in 1999 to 30% in 2004. The target set for unfavourable outcome in the National TB Control Program is 15% [13].

1.3.2). DOTS in Mpumalanga Province

Like the national trend, the TB mortality and incidence increased in Mpumalanga Province from 1999 - 2003[14]. There was no data available for mortality and incidences for Mpumalanga province after 2003 (Health Trust System 2005).

1.3.3). DOTS in Mkhondo Sub-district

Despite establishing DOTS program in the sub-district in 1999, the TB cure rates decreased from 63.7% in 2003 to 42.8% in 2004 and 37% in 2005 (Mkhondo) . The TB treatment defaulters increased from 3.4% in 2003 to 6% in 2005. During this period, the DOTS was provided by The clinic nurses, community health workers, trained TB treatment supporters, relatives and teachers provided DOTS support from 2000-2005.

1.4.0). Statement of the problem and justification for the research

1.4.1). Problem statement

Despite an established DOTS program in Mkhondo sub-district since 1999, the cure rate fell by 26% in two years (from 63% in 2003 to 37% in 2005) and far below the expected 85% target. The TB default rate increased by 76% within the same period

1.4.2). Justification for the study

Tuberculosis (TB) is the leading cause of death in the world from a bacterial infectious disease. The disease affects 1.8 billion people per year which is one-third of the entire world population[15]**.** In South Africa, TB is a major public health problem and according to WHO TB Report 2008, South Africa had nearly 453,929 new TB cases in 2006, with an incidence rate of an estimated 940 cases per 100,000 populations – a major increase from 338 per 100,000 populations in 1998[16]. In addition, the number of drug resistant TB has increased in the past years and extremely drug resistant TB emerged in the past few years in South Africa.

In Mkhondo sub-district, TB cure rate decreased by 26% in two years despite an established DOTS support program suggested poor management. By determining the trends of TB, analysing treatment outcome and conducting comparison analysis of DOTS support from 2000-2005 in Thandukukhanya TB program, the study will come with recommendation to optimise TB management at the clinic and municipality.

1.5). Research Question

Is there a significant change in the trends of TB cases, treatment outcome and DOTS support in the TB program at Thandukukhanya clinic from 2000 – 2005?

Is there a difference in TB treatment outcomes in patients with DOTS supporters to no DOTS supporters?

1.6). Study Objectives

1. To describe the trend of cases, sputum smears done and smear positive cases by year.
2. To compare the rates of treatment outcomes (cure, completion, interruption, failure and deaths) of TB cases from 2000-2005
3. To conduct comparison analysis of TB treatment outcomes in cases with and without treatment supporters.

1.7.0). Literature Review

1.7.1). Global and South African TB trend and burden

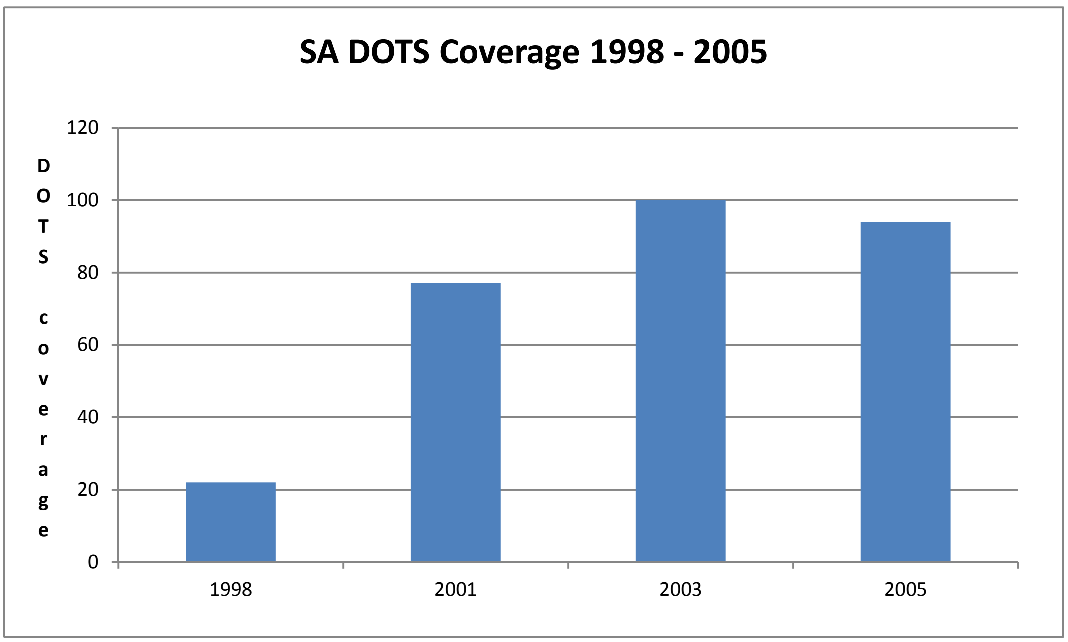
With regards to the global tuberculosis burden and trend, according to the WHO (TB) report, 1.75 and 1.9 million deaths resulted from tuberculosis in 2005 and 2007 respectively and HIV was the single most important factor determining the increased incidence of TB in the past 10 – 15 years and led to rapid increases in the incidence of TB and HIV infection increases the risk of dying from TB[16]. Over 90% of TB deaths occur in the developing world, with about 75% in the most economically productive age group (15-54 years) [4].

In 1990s the WHO supported by other organisations promoted DOTS as a TB control strategy and this proved to be effective in achieving an overall cure rate of nearly 80% (range 70 – 90%)[17]. DOTS strategy was a direct outcome of WHO operational research that made it possible to carry out case-finding, chemotherapy and patient monitoring effectively without hospital care (WHO Geneva 1997)[18].

The DOTS programme was originally aimed to successfully treat 85% of new active (smear-positive) TB cases and detect 70% of such cases by the year 2000 (WHO report 2003). The target for treatment success was reset to successfully treat 85% of new active TB cases by 2005, because many countries missed the target. Global DOTS coverage increased from 3% in 1993 to 12% in year 2000 and 85% in 2005, reaching 10.8 million new smear positive cases.

The tuberculosis burden in South Africa was not different from the global one. The progress towards TB control in South Africa (ranked in 9th place for estimated number of cases globally in 2006) had mixed achievements between 1998 and 2001[19]. In 2000 treatment success was 66% and increased to 72% in 2001 (both below WHO 85% DOTS targets). The DOTS population coverage increased from 22% in 1998 to 77% in 2003, 100% in 2003 and levelled to 94% in 2004.

Figure 1: DOTS coverage in South Africa 1998 - 2005



The TB notification rate in South Africa of all cases/100,000 increased from 338 in 1998 to 349 in 2000, then to 540 in 2004 due to improved case detection and notification.

The notification rate of new smear positive cases/100,000 pop increased from 157 in 2000 to 191 in 2003 and 265 in 2005[20]. The case detection rate (new smear positive) decreased from 90% in 1998 to 82% in 2004 while the DOTS detection rate increased from 22% in 1998 to 72% in 2001 and 103% in 2005. The DOT success rate decreased from 74% in 1998 to 66% in 2000 and 70% in 2004 and this was lower than the 85% target set by world Health Organisation.

According to data from South Africa (1994 to 2001), the trend of TB in South Africa was driven by poverty, HIV/AIDS, multi-drug resistant TB, insufficiently resourced health system and weak link in TB control at staff level in facilities. Patient's factors such as ignorance, delay in seeking care, non-adherence and interruption of treatment were other factor that contributed to the poor treatment outcome.

The 2006 TB report by Department of Health South Africa found continuous failure to adhere to treatment led to low smear conversion rates and high re-treatment and high staff turnover in facilities have interrupted TB treatment in facilities.[21]. In the same report, the national cure rate increased from 49.9% in 1995 to 68% in 2004 (target 85%). But the cure rates varied in provinces with Western Cape (65.3%) being the highest and KwaZulu Natal (24.7%) the lowest[22].

In South Africa, the TB control is decentralised to the district health system with the basic unit for TB control and management being individual primary care facility, supported by the district hospital and the treatment supporters in the community. The TB services are provided for free (including diagnosis and treatment), helping to ensure access for all patients. The nurse at the clinic plays an important role in patient care, supported by DOTS supporter to supervise treatment in the community where the patient resides. Maintaining the TB register and regularly reporting keys data is important in determining treatment outcome in any facility. However, the same data should be utilised by the facility to monitor trend, treatment outcome and DOTS performance against treatment outcomes and trend over time.

Table 1: DOTS coverage, case detection and treatment success in South Africa 1995 – 2005

DOTS	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Coverage %	0	0	13	22	66	77	77	98	100	93	**94**
Notification(all cases) /100,000 pop/year	-	-	15	50	201	193	262	457	484	546	**549**
Notification rate (new smear+/100.000pop/year	-	-	10	37	121	137	155	210	248	256	**253**
Case detection (all new cases, %)	-	-	2.9	9.4	35	36	44	7	75	82	**82**
Case detection rate (new smear+, %)	-	-	5.0	1.8	57	62	67	88	101	104	**103**
Treatment success (new smear+, %)	-	69	73	74	60	66	65	68	67	70	-
Re-treatment success (smear+, %)	-	67	68	71	47	52	53	53	52	56	-
Case detection (all cases)	-	-	2.9	9.4	35	36	44	70	75	82	**82**
Case detection (new cases)	**-**	**-**	**5.0**	**18**	**57**	**62**	**67**	**88**	**101**	**104**	**103**

Source: WHO Report 2007 Global TB control

In general, TB case notification continued to rise as case-finding and reporting has improved. The unfavourable outcomes (not evaluated, transferred, defaulted, failed and died) decreased from 40% in 1999 to 30% in 2004, but remained above the set target of 15% in the National TB Control Program [13].

According to the World Health Organization's (WHO's) Global TB Report 2009, South Africa had nearly 460,000 new TB cases in 2007, with an incidence rate of an estimated 948 cases per 100,000 populations – a major increase from 338 cases per 100,000 populations in 1998. Since South Africa adopted DOTS (the internationally recommended strategy for TB control) in 1996, all districts have implemented the core DOTS components, although coverage varies widely within and among districts. Despite South Africa's investments in TB control, progress toward reaching programme objectives has been slow; however, new data suggest that for the first time, in 2006, South Africa reached (and surpassed) the DOTS case detection target of 70% and increased to 78% in 2007. DOTS treatment success increased from 65% t in 2001 to 74% in 2006, somewhat lower compared with other African countries that have high HIV/AIDS prevalence rates and few resources[14].

1.7.2). Mpumalanga Perspective

In Mpumalanga Province, like the national trend, the TB mortality and incidence increased in the province from 1999 -2003[14]. There was no data available for mortality and incidences for TB in the province after 2003 (Health Trust System 2005).

Table 2: TB incidence – National Program compared to Mpumalanga Province

Year	Incidence of TB, all cases/100,000		Mortality of TB cases %	
	National	Mpumalanga	National	Mpumalanga
1999	360	174	6.9	**8**
2000	178	349	7.7	-
2001	426	224	8.9	**8.5**
2002	497	207	10.2	**11.2**
2003			**12**	-

Source: Health Trust System 2005

1.7.3). Mkhondo Sub-district perspective

Despite implementing DOTS in the TB program Mkhondo sub-district in 1999, the TB cure rates continued to spiral downward (63.7% in 2003 vs. 42.8% in 2004 and 37% in 2005) and the TB treatment defaulters upward (3.4% in 2003 vs. 6% in 2005), despite the fact that five DOTS group provided treatment support: clinic nurses, community health workers, trained TB treatment supporters, relatives and teachers (Mkhondo TB report, 2006)

1.7.4). Literature from South African and other countries studies

Many studies related to TB trends, treatment outcomes and DOTS have been conducted in South Africa and other countries and findings varied. Simon Lewin et al conducted a randomised cluster clinical trial in primary health care clinics in Cape Town, South Africa. The study assessed whether adding training interventions for clinic staff to usual DOTS strategy would affect outcomes of TB treatment in primary health care clinics with treatment success rates below 70%. They found a small increase in treatment success (4.8%s) and cure rate 10.4% and concluded that participatory training on TB outcome in primary care facility did not appear to improve TB outcomes[15].

In another study, Salla Munro et al conducted systematic review of qualitative studies to understand factors considered important by patients, caregivers and health care providers in contributing to TB medication adherence in SA. The structural factors including poverty and gender discrimination, social context, health service factors and personal factors were four major factors that affected adherence and concluded that patient adherence to medication was influenced by the interaction of a number of factors[16].

In a separate study by Salla Atkins et al in Cape Town Metropolitans clinics which evaluated whether poor tuberculosis outcomes improved if usual DOTS is enhance by model of ART support – training clinic staff, treatment adherence counselling and assessment of patient’s living conditions at home and providing treatment buddy and lay care workers to support self-supervised tuberculosis treatment. After two months, the study found that TB smear conversion rate increased significantly compared with comparison site but did not improve cure and treatment success rates above that of comparison sites. They concluded DOTS combined with enhance adherence model appeared to have limited effect on cure and treatment success rates[17].

In Gauteng Province, a retrospective study by Peter Odour investigated the role played by treatment supporters in promoting patients' treatment outcomes in six TB clinics of Ekurhuleni Metropolitan Municipality. A descriptive research design was used to study TB patients who were registered in the clinics in April and May 2006. Interviews were conducted on 216 new adult patients six months after their registration at clinics, all 30 treatment supporters of those who had supporters and the staff responsible for TB at the six clinics at which the patients were registered. Results showed that significantly more supported patients achieved successful outcomes than patients who did not have supporters [18].

A study in India to elicit reasons for treatment default from a cohort of TB patients under revised national TB control program and their DOT providers found DOTS being inconvenient and led to treatment default[19].

Jimmy Volmink and Paul Garner in Cochrane review compared DOT with self- administration of treatment or different DOT options for people requiring treatment for clinically active tuberculosis or prevention of active disease. The results of randomized controlled trials conducted in low-, middle-, and high-income countries provided no assurance that DOT compared with self-administration of treatment has any different treatment outcome for tuberculosis[20].

S. Ntshanga et al, assessed impact of DOTS since the inception of DOTS in South Africa in 1996, by evaluating the DOTS programme in the priority facilities of the four TB crises districts (EThekwini, UMgungundlovu, UMzinyathi and UThungulu) in the province of KwaZulu-Natal. A semi-structured questionnaire was used to interview TB nurses and community DOT supporters. On average, priority facilities in districts that have high DOT coverage had better cure rates compared with those that have low DOT coverage ($\beta = 0.818$, 95% CI 0.023–1.614; $P = 0.045$). The fewer the number of patients allocated to a DOT supporter the higher the cure rates ($\beta = -1.984$; 95% CI –3.88 to 0.086; $P = 0.041$). These findings suggest that cure rates can be improved if DOT is implemented appropriately[21].

1.7.5). Terminologies used in TB management

In the study, some terms were used and the definitions are provided below in order for the reader to understand them.

Trend – a general direction in which something is developing or changing or - change that develops in a general direction.

Case finding – refers to the number of cases per unit time (per month, quarter or year). It is used to compare with previous time period and calculate rate per population at risk.

It is an indication of size of the problem, trend (increase in cases over time in one place), work load and rate (conventionally per 100,000 populations) so that it can relate to other districts, provinces, national, other countries.

Proportion of smear positive TB – refers to the proportion of all pulmonary TB cases are smears positive and indicate serious (advanced), infectious TB (number of cases of smear positive TB/all cases of pulmonary TB)

Smear conversion rate – Is a case monitoring indicator and refers to proportion of TB patients on treatment whose sputa have converted (positive to negative) by the end of three months. For new cases this is the 2 month conversion plus those who converted at 3 months. It is the 3 month conversion for re-treatment cases (number of new smear positive TB cases who are negative at 3 months/number of new cases who were smears positive at the start of treatment). It is an indicator of success in treatment so far, but not overall outcome. The target is 85% conversion at 3 months for new cases and lowers for re-treatment.

Treatment outcome – Refers to indicators that defines TB treatment outcome at the end of the course of treatment. These indicators are:

Cure – a patient who has completed the full course (6 or 8 months, depending in category) and who was sputum smear negative after 2 months of treatment and at the end of treatment (number smears negative at 2 or 3 months and end of treatment/ all smear positive at diagnosis that completed full course of treatment)

Completed treatment – a patient who has completed the full course but bacteriological conversion is not proven (number of smear who completed treatment, no conversion sputum/number of cases treated)

Interrupted treatment – a patient interrupted treatment for a cumulative period of 42 days during treatment (number of TB cases who missed treatment of total of 2 months/number of TB cases treated)

Failed treatment – a patient who remains smear positive at the end of treatment (number of TB cases positive at end of treatment/ number of TB cases treated)

Died – a patient who dies during the course of treatment of TB or not of TB (number of TB cases who died during treatment/ number of TB cases treated)

Transferred elsewhere – a patient who is formally transferred to another health service outside the district

New smear positive cure rate – is the proportion of all new smear positive patients who are cured. It is the single most important indicator of TB control programme (number of new smear positive patients cured/ number of new smear positive patients registered and treated)

New smear positive treatment completion rate – is the proportion of all new smear positive patients who complete treatment (number of new smear positive patients completed treatment/number of new smear positive patients registered and treated)

DOTS supporter – is a relative, teacher, clinic nurse, community health worker, trained TB supporter, volunteer or other person ensuring adherence and compliance for the duration of TB treatment.

DOTS rate – is the proportion of patients on treatment that have a treatment supporter and which type. Indicates application of basic principle of TB treatment and is programme management indicator for a defined period of time (proportion of patients with treatment supporter/ all TB cases on treatment)

DOT (Directly Observed Treatment Short Course) is a World Health Organisation (WHO) recommended strategy to assist adherence to TB treatment. DOTS strategy is a community based program based on case-finding, chemotherapy and patient monitoring.

CHAPTER TWO: METHODOLOGY

2.0). Introduction

This chapter presents the materials and methods used to carry out the study which includes description of the study area, the study design used, study population, inclusion and exclusion criteria sample size, study variables, study limitation, bias, data management and ethical consideration.

2.1). Demographic and socio-economic description of the study location

Thandukukhanya clinic is a primary health care facility in the suburb of Piet Retief town, Mkhondo sub-district administrative municipality, Gert Sibande district in Mpumalanga Province, South Africa. Mkhondo sub-district borders Swaziland in the north and KwaZulu Natal province in the south and west, both of these have a high burden of tuberculosis. The clinic serves Ethandu settlement composed of both formal and informal housing and variable municipality water and electricity services. The catchment population of the clinic is 21,000 people (Mkhondo population stat 2006) out of 148,000 people in the sub-district. The population is relatively young and grew rapidly since the demographic election in 1994 due to migration from rural areas in search of jobs and from neighbouring province and countries. The main economic activities are farming, forestry, coal mining and small and medium size businesses.

2.2). Study Design:

The study used an analytical cross-sectional design using records of TB cases from Thandukukhanya clinic from 2000- 2005. The analysis of data was both descriptive and analytic. The descriptive analysis demonstrated the trends and patterns in TB cases by demographic characteristic (age, sex, marital status, education status, distance from the clinic, residence and employment), clinical characteristics (site of infection, method of TB diagnosis, presence of alcohol acid bacilli, treatments category and smear conversion), and the identification of risk factors associated with TB treatment outcome and treatment (DOTS) support. The analysis also included factors confounding DOTS support in determining treatment outcomes.

2.3). Study Population

The Study population were all patients treated at Thandukukhanya clinic from 2000 to 2005 and the sample population included all cases registered in the TB register and had facility retained TB card.

2.5). Inclusion Criteria and Exclusion Criteria

All TB cases registered every year at Thandukukhanya clinic from 2000-2005 were included as study participant in the study, except those with missing records

2.4). Study Sampling

No sampling technique was applied to select TB cases from 2000- 2005 at Thandukukhanya clinic to study. All TB cases were included in the study and recruited consecutively starting with the first case registered in 2000 and ending with the last case in 2005. The cases were then grouped into those with and without treatment (DOTS) supporters to conduct comparison analysis of TB treatment outcomes with DOTS support. At 95% level of significance, a sample size of 504 cases is (336 unexposed, 168 exposed to DOTS) required to demonstrate significant difference in TB treatment outcome in cases unexposed and exposed to DOTS support.

2.6.0). Study Variables

The study variables included in this section was divided into demographic, exposure, outcome and confounding variables.

2.6.1). Demographic variables:

Age – age in years was continuous variable measured in years but categorised for analysis.

Sex – categorical variable defined as male or female.

Distance from clinic – continuous variable measured in kilometres from the clinic to place of residence. It was categorised into three groups for analysis: <2, 2-5 and >5km groups.

Marital status – categorical variable and was defined as single, married, separated, and widowed.

Educational status – categorical variable defined as the level of education attained by the patient at the time of registration for treatment.

Employment status – categorical variable defined as employed or unemployed.

2.6.2). Exposure variables:

Treatment (DOTS) supporters – defined as persons offering TB treatment support and supervision during treatment in the community which the participant lived. In this study, they were clinic nurses, community health workers, relatives, teachers and trained TB supporters.

Treatment category – categorical variable defined as new or re-treatment cases.

TB site – categorical variable, defined as pulmonary or extra-pulmonary.

TB diagnosis method – categorical variable defined as clinical, radiological or bacteriological method of diagnosis.

2.6.3). Outcome variables:

Cured - patient who is smear-negative at, or one month prior, to the completion of treatment and also on at least one previous occasion (SA TB policy guidelines 2009)

Treatment completed - patient who has completed treatment but without proof of cure, smear results are not available on at least two occasions prior to the completion of treatment.

Treatment failure - patient that remains or is again smear-positive at five months after starting treatment

Died - patient who dies for any reason during the course of TB treatment

Transferred - patient who has been transferred to another reporting unit (e.g. district) and for whom the treatment outcome is not known

Moved -patient who is moved to another facility within the same district

Treatment failure - patient that remains or is again smear-positive at five months after starting treatment

Treatment interruption - patient who treatment was interrupted for more than two consecutive months before the end of the treatment period

2.6.4). Confounding variables:

The following variables were analysed for confounding of DOTS support for treatment outcome: marital status, employment status and education status.

2.7). Study limitations and bias

This was a cross-sectional study and looked at events at the point in time and it was not possible to determine incidence. In addition, the study used clinic records and it was not possible to interview cases to verify information in the record. Incomplete records could have caused bias but only 4 out of 861 cases were excluded due to incomplete data. It was clinic based and could have not been representative of cases in the community. Some patients could have gone to private providers.

2.8.0). Data Management

2.8.1) Data Source

The sources of data was facility retained TB cards and registers at the clinic.

2.8.2) Computer Programs

Epi-info (2002) statistical software was used to design data collection sheet (MakeView), enter, clean and store data. Analysis was conducted using *Stata Supercooled version 10*. Graphs were drawn in MS Excel.

2.8.3). Data Collection

The data collected was captured in a pre-design data sheet (see appendix 1) and entered and stored into Epi-info 2002 Statistical Software.

2.8.4). Validity

The researcher managed all data process: collection, entry, cleaning and analysis. The data collected was captured and cleaned in Epi-Info Statistical package. The cleaning process was conducted by identifying missing data and verifying against records in the patient chart with that in the register.

2.8.5). Data Analysis

Data was analysed using Stata 10statistical software. The trend was analysed by tabulating frequencies and using chi square to test significance in the trend. The mean, range and standard deviation was used to analyse age and distance. Chi Square was used to test statistical significance of the categorical variables. Odd ratio was used to analyse association between treatment outcome and response variables and to test factors confounding DOTS support in relation to cure, died, interrupted treatment and completed treatment. Multivariate analysis (logistic regression) was used to determine the relationship between treatment outcome and multiple response variables. The stepwise regression was used sort out factors that predict treatment outcome and to test interactions of response variables.

2.9.) Ethical Consideration

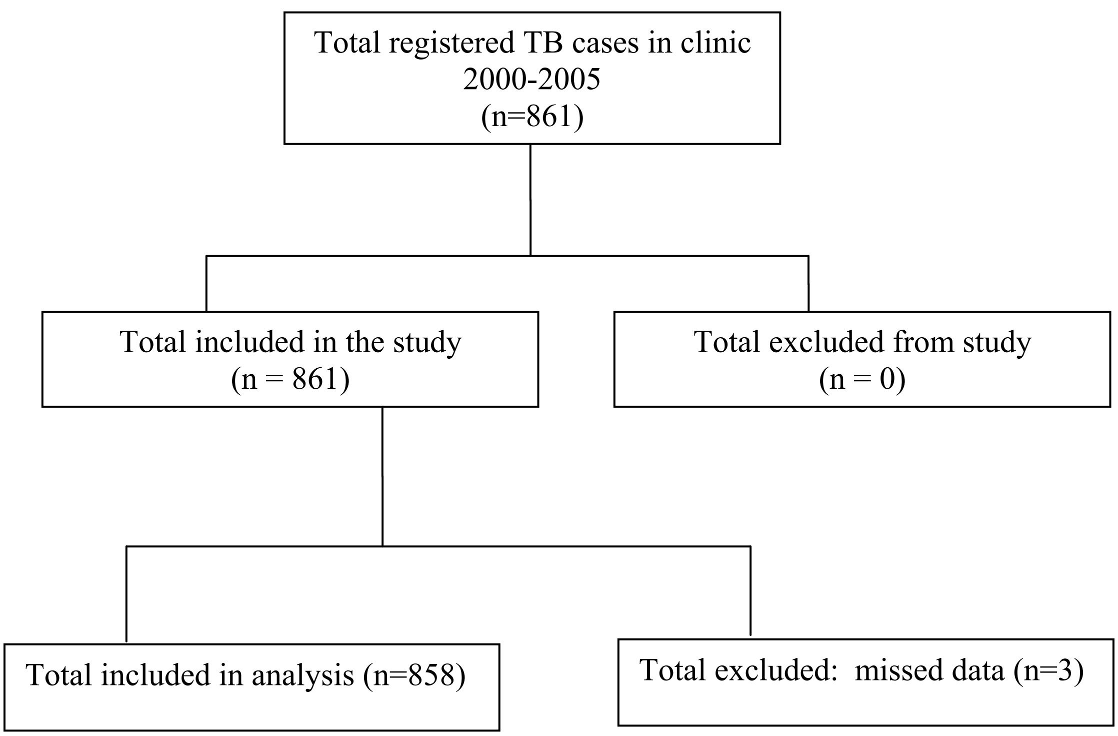
A written permission to conduct study and access information from patient record and TB register was obtained from the Health Director at Mkhondo Health District. The individual consent was not required since records were used. Confidentiality and anonymity of information was maintained at all times. The Ethic Committee and the Committee for Research on Human Subjects of the University of Witwatersrand approved the study and was implementation after the approval – number M061133

CHAPTER THREE: RESULTS

3.0). Introduction

This chapter presents the results of the analysis for the study in three sections according to the objectives. In the first section (objective 1) the descriptive analysis of demographic and clinical factors is provided. . The next section (objective 2) present results of analysis of treatment outcomes. In addition to the descriptive analysis, bivariate and multivariate analyses were performed. In the final section (objective 3), is a comparison of DOTS support as well as factors confounding DOTS in treatment outcomes. The results of bivariate, multivariate and confounding analyses are presented in second and third section. The flow diagram below shows the sampling of study population and inclusion in the analysis.

Fig 2: Flow diagram showing sampling of the study participants for analysis

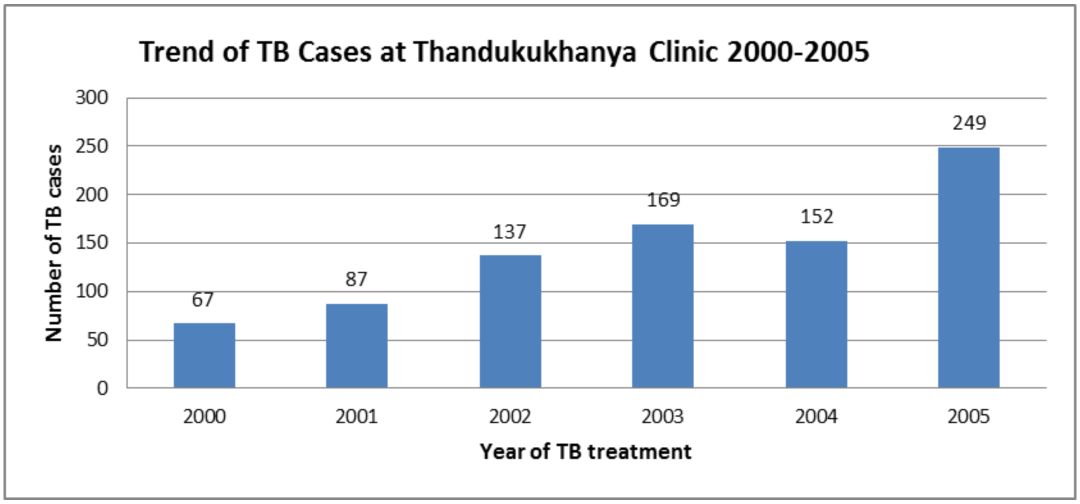


3.1.0.). Descriptive Analysis (Objective 1)

3.1.1). General description of the study population

Figure below show the distribution of TB cases by year, showing a steady increase every year except in 2004.

Figure 3: Distribution of TB cases every year 2000-2005 at Thandukukhanya Clinic



The table below shows demographic characteristics of TB cases by age, sex and distance from the clinic and number of cases missing in every year of the study. Of 861 TB cases recruited in the study, 858 were analysed while three excluded due to insufficient data.

Table 3: Demographic characteristics of the population: age, sex, and distance from clinic in every year (missing cases by year included)

Variables		Total	2000	2001	2002	2003	2004	2005	P-value
All cases		861	67	84	137	169	152	249	
Cases analysed		858	67	84	136	169	152	247	
Missing cases		0	0	0	1	0	0	2	
Age in years	**Total**	**851**	**65**	**84**	**137**	**167**	**151**	**247**	P=0.828
	<5	10(1.18)	0(0)	1(1.19)	2(1.46)	2(1.20)	1(0.66)	4(1.62)	
	5 – 14	24(2.82)	0(0)	1(1.19)	2(1.46)	3(1.80)	4(2.65)	14(5.67)	
	15 –24	184(21.62)	15(23.80)	22(26.19)	28(20.44)	41(24.55)	29(19.21)	49(19.84)	
	25 – 34	290(34.08)	23(35.38)	29(34.52)	42(30.66)	59(35.33)	56(37.09)	81(32.79)	
	35 - 44	216(25.38)	17(26.15)	16(19.05)	44(32.12)	39(23.35)	37(24.50)	63(25.51)	
	45- 54	88(10.34)	8(12.31)	10(11.90)	13(9.49)	17(10.18)	17(11.26)	23(9.31)	
	>54	39(4.58)	2(3.08)	5(5.95)	6(3.59)	6(3.59)	7(4.64)	13(5.26)	
Sex	**Total**	**857**	**67**	**84**	**136**	**169**	**152**	**249**	P=0.869
	Male	422(49.24)	35(52.24)	36(42.86)	66(48.53)	86(50.89)	75(49.84)	124(49.80	
	Female	435(50.76)	32(47.76)	48(57.14)	70(51.47)	83(49.11)	77(50.66)	125(50.20)	
Distance from the clinic in Km	**Total**	**856**	**67**	**84**	**137**	**169**	**152**	**247**	P=0.02
	0 - 1.9	284(33.18)	12(17.91)	29(34.52)	40(29.20)	54(31.95)	52(34.21)	97(39.27)	
	2 – 5	558(65.19)	54(80.60)	54(64.29)	95(69.34)	113(66.86)	98(64.48)	144(58.30)	
	>5	14(1.64)	1(1.49)	1(1.19)	2(1.46)	2(1.18)	2(1.32)	6(2.43)	

The p-values in the table are for Chi Square test to determine if difference in variables existed among different years

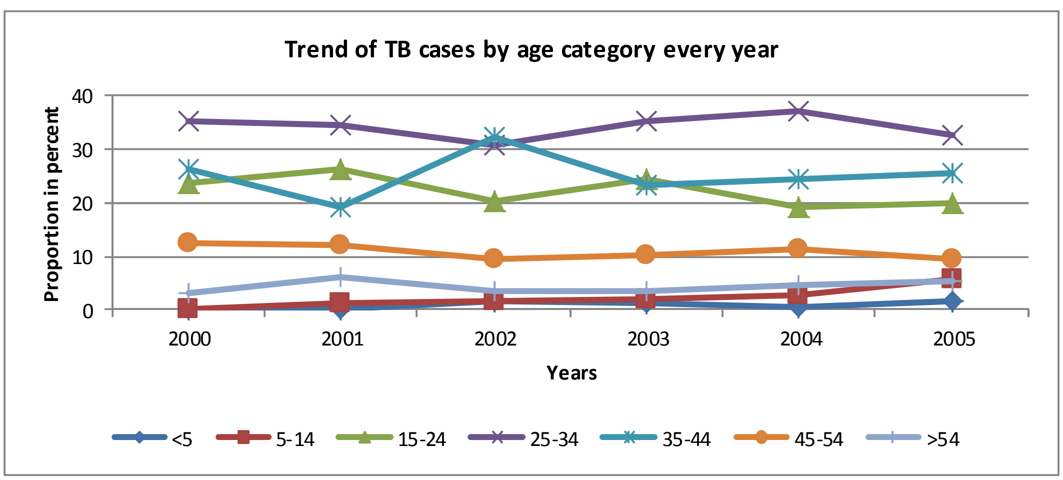
3.1.2). Age

This was a continuous variable but was also categorised for purpose of analysis. Of the 858 cases included in the analysis, 851 were analysed. The age range was 1 – 77 years, with a mean of 33 years and 78.6% of the cases were in the age group 20 – 40 years.

The proportion of cases by age category in every year was highest in the age group 25-34 years, followed by 35 -44 years (25.38%) and then 15-24 years (21.62%). In the three age categories above, there was variation in cases every year: in the 15-24 years it increased in 2001, decreased in 2002 then increased in 2003 followed by a decrease in 2004 and an increase again in 2005; in the 25-34 years the trend decreased from 2001 – 2002, followed by an increase in 2003-2004 and a decrease in 2005 and in the 35-44 years an initial ion of TB cases in age categories decreased in 2001 was followed by an increase in 2002, then another decreased in 2003 and remained stable until 2005.

The proportion of TB cases in age categories < 5, 5-14, 45-54 and > 54 years remained lowed in every year of the study, with small increases or decreases in trend demonstrated. In the <5 years age group, cases increased in 2002, followed by adecreased in 2003-2004 and an increased in 2005; in the 5-14 years there was an increased in 2001, stabilised from 2002-2004 and finally a moderate increase in 2005; in the 45-54 years there was a decreased in 2001 -2002, stable in 2003, an increase in 2004 and a decrease in 2005; in the category >54 years, there was an increase in 2001, then a decrease in 2002, stabilising in 2003 and increasing gently in 2004 – 2005. The 5-14 and >54 years were the only age categories which demonstarted an increase in TB cases in 2005.

Figure 4: Distribution of TB cases by age group 2000 - 2005



3.1.3). Sex

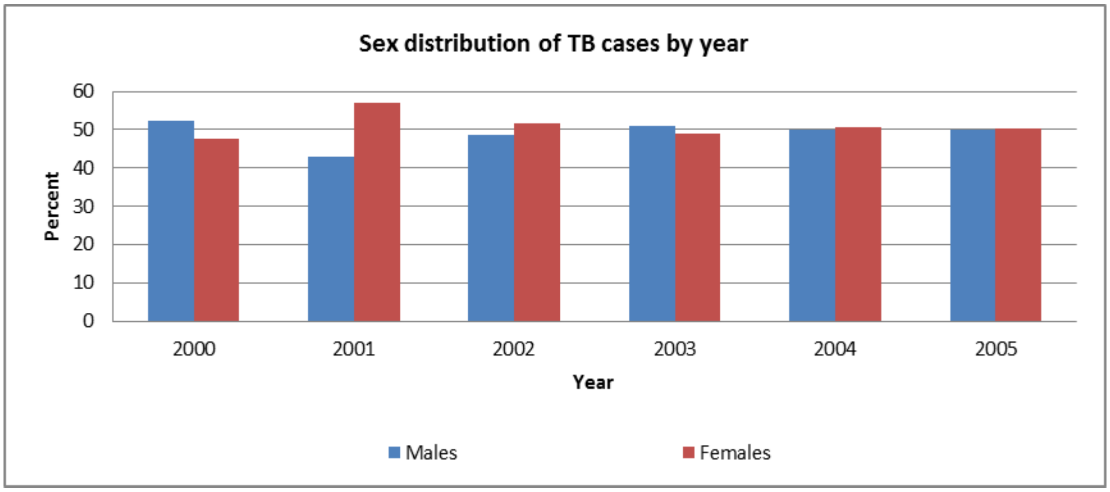
Of the 861 TB cases in the study, 856 were analysed for sex and five excluded due to missing data on sex. Of those analysed 422(49.24%) cases were males, 435(50.76%) females, with the male to female ratio of 0.97. The male: female ratio in <15 years was1:1, more females in 15-34 years (0.68:1.00) and more males in >35 years (1.5:1).

Table 4: the sex distribution of TB cases by age groups 2000 - 2005

Age in years	Males	Females	Ratio (M:F)
0 – 4	5	5	**1:1**
5 – 14	12	12	**1:1**
15 – 24	59	124	**0.47:1**
25 – 34	137	153	**0.89:1**
35 – 44	123	93	**1.3:1**
45 – 54	61	27	**2.3:1**
>54	22	17	**2.3:1**
All cases	422	435	**0.97:1**

The pattern of distribution of cases by gender varied by year with percentage of males higher than females in 2000 and 2003

Figure 4: Sex distribution of TB cases 2000-2005



3.1.4). Distance from Clinic

Distance from the clinic is a continuous variable measured in kilometres but it was also categorised into three groups 0-1.9km, 2-5km and >5km) for purpose of analysis. Of the 858 cases, 856 were analysed and 2 excluded due to missing data on distance. The mean distance was 2.3km (range 1- 50Km); 98.36% of cases resided less than 5 km from the clinic and only 1.64% resided > 5km from the clinic. The proportion of TB cases residing from the clinic by category in every year changed.

Table 5: Demographic characteristics of TB cases by education, employment and marital status 2000 -2005

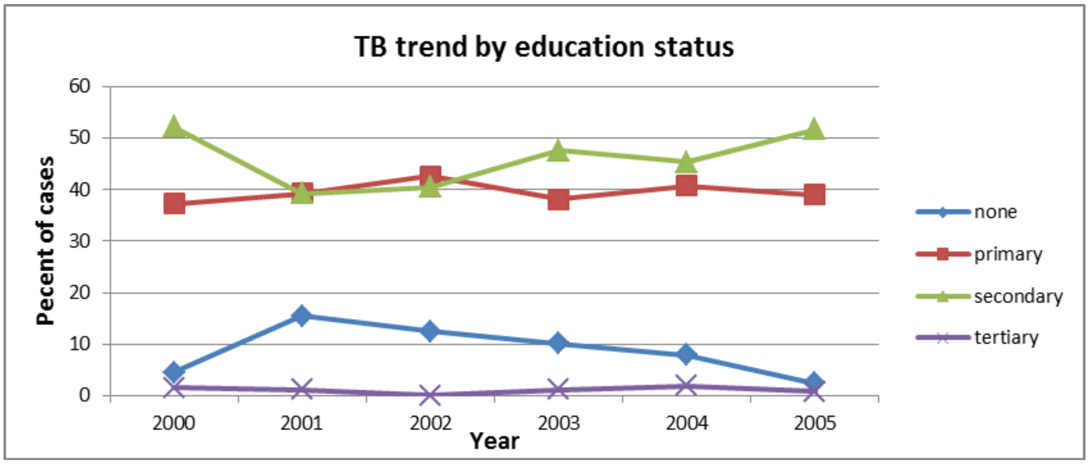
Variables		Total cases	2000	2001	2002	2003	2004	2005	P=value
Education status	**Total**	**853**	**67**	**84**	**137**	**168**	**152**	**246**	P=0.022
	Not known	39(4.57)	3(4.48)	4(4.76)	6(4.41)	5(2.98)	6(3.95)	15(6.10)	
	None	68(7.97)	3(4.48)	13(15.48)	17(12.5)	17(10.12)	12(7.89)	6(2.44)	
	Primary	338(39.62)	25(37.31)	33(39.29)	58(42.65)	64(38.10)	62(40.79)	96(39.02)	
	Secondary	399(46.78)	35(52.24)	33(39.29)	55(40.44)	80(47.62)	69(45.39)	127(51.63)	
	Tertiary	9(1.06)	1(1.49)	1(1.19)	0(0.00)	2(1.19)	3(1.97)	2(0.81)	
Employment status	**Total**	**853**	**67**	**84**	**136**	**168**	**152**	**249**	P=0.304
	Unemployed	794(93.08)	65(97.01)	82(97.62)	126(92.65)	53(91.07)	139(91.45)	229(93.09)	
	Employed	59(6.92)	2(.2.99)	2(2.38)	10(7.35)	15(8.93)	13(8.55)	17(6.91)	
Marital status	**Total**	**853**	**67**	**84**	**136**	**168**	**152**	**246**	P=0.348
	Not known	29(3.40)	1(1.49)	3(3.57)	5(3.68)	5(2.98)	4(2.63)	11(4.47)	
	Single	603(70.69)	47(70.15)	65(77.38)	97(71.32)	128(76.19)	101(66.45)	165(67.07)	
	Married	212(24.85)	19(28.36)	14(16.67)	31(22.79)	32(19.05)	47(30.92)	69(28.05)	
	Widowed	7(0.82)	0(0.00)	2(2.38)	2(1.47)	2(1.19)	0(0.00)	1(0.41)	

The p-values in the table are for Chi Square test to determine if difference in variables existed among different years

3.1.5). Education Status

Education status was a categorical variable that referred to the level of education of a TB case at registration. Of the 853 cases analysed for education status, 746 (87.46%) were educated while 107(12.54%) were not (none and unknown). Of those educated, 399(46.78%) had secondary, 338 (39.62%) primary, and 9(1.06%) tertiary education. The proportion of uneducated TB cases increased in the first year and progressively decreased from 2002-2005, while the proportion of TB cases with tertiary education remained nearly constant throughout the study period. The proportion of TB cases with secondary education decreased in the first year, remained constant in 2002 and increased from 2003 – 2005, while the proportion of TB cases with primary education increased in 2001 - 2002, then decreased in 2003, increased again in 2004 and finally decreased in 2005.

Figure 5: Trend of cases by education status 2000-2005



3.1.6). Employment status

Employment status was a categorical variable referred to whether a TB case was employed or unemployed. Of the 853 cases, 794 (93.08%) were unemployed, while 59 (6.92%) were employed. The proportion of employed and unemployed cases remained the same in the first two years followed by a decrease in the unemployed group and an increase in employed group from 2003- 2004. There was a small increase in the unemployed group and a decrease in the employed group in 2005.

3.1.7). Marital status

Marital status was a categorical variable with four sub-variables: not known, single, married and widowed. Of the 858 cases, 853 cases were analysed while five were excluded due to missing data on marital status. Of those analysed, 603(70.69%) of cases were single, 212 (24.85%) married, 29(3.4%) unknown and 7(0.82%) widowed. The proportion of married TB cases decreased while TB cases that of single increased from 2000 – 2004 but reversed in 2005. The proportion of widowed cases and of unknown marital status remained low and constant throughout the study, except for a small increase in the unknown cases in 2005.

3.2.0) Description of the clinical variables

The clinical variables included in the study are TB treatment category (new and re-treatment), TB infection site (pulmonary or extrapulmonary), TB diagnostic method (bacteriology, X-ray and others) and alcohol acid fast bacilli in sputum (smear positive or negative). The re-treatment categories was further categorised into re-treatment after cure, treatment completion, treatment failure, and treatment interruption. In the table below, the clinical characteristics of TB cases by treatment category, infection site, diagnostic methods and alcohol acid Fast bacilli (AAFB) at Thandukukhanya clinic 2000- 2005 are provided.

Table 6: Distribution of TB cases by treatment category and site of infection at Thandukukhanya clinic 2000 to 2005

Variables		Total	2000	2001	2002	2003	2004	2005	P-value
TB treatment category	**Total**	858	67	84	137	169	152	249	0.0001
	New cases	754(87.83)	58(86.57)	80(95.24)	129(94.16)	142(84.02)	141(92.76)	204(81.93)	
	Re-treatment cases (total)	104(12.12)	9(13.43)	4(4.76)	8(5.84)	27(15.98)	11(7.24)	45(18.07)	
	Re-treatment (cure)	47(5.48)	1(1.49)	2(2.38)	1(0.13)	12(7.10)	9(5.92)	22(8.84)	
	Re-treatment (completion)	20(2.33)	7(10.45)	0(.0.00)	1(0.73)	9(5.33)	0(0.00)	3(1.20)	
	Re-treatment (failure)	11(1.28)	0(0.00)	0(0.00)	1(0.73)	2(1.18)	0(0.00)	8(3.22)	
	Re-treatment (interruption)	26(3.03)	1(1.49)	2(2.38)	5(3.65)	4(2.37)	2(1.32)	12(4.82)	
TB infection site	Total	854	67	83	137	167	152	247	0.133
	Pulmonary	804(94.15)	66(98.51)	76(91.57)	126(91.97)	155(92.26)	148(97.37)	233(94.33)	
	Extra-pulmonary	50(5.85)	1(1.49)	7(8.43)	11(8.03)	13(7.74)	4(2.63)	14(5.67)	
	Converted	440(51.17)	56(83.58)	51(67.86)	70(51.09)	84((50.00)	64(42.11)	107(43.15)	
	Not converted	27(3.15)	5(7.46)	4(4.76)	2(1.46)	3(1.79)	4(2.63)	9(3.63)	
	Smear missed	238(27.80)	3(4.48)	9(10.71)	36(26.28)	43(25.60)	48(31.58)	99(39.92)	
	Not applied	153(17.87)	3(4.48)	14(16.67)	29(21.17)	38(21.17)	36(23.68)	33(13.31)	
	Total	856	67	84	137	168	152	248	

3.2.1). TB treatment Category

Treatment category is a categorical variable that referred to new or re-treatment cases. In the re-treatment group, four sub-variables were studied, namely re-treatment after cure, re-treatment after completion of treatment, re-treatment after treatment failure and re-treatment after interruption of previous TB treatment.

Out of 858 analysed 754(87.83%) were new TB cases and 104(12.17%) re-treatment. Of the re-treatment cases, 47(45.2%) were TB cases previously cured with treatment, 26(25%) interrupted treatment, 20(19.23%) completed treatment course and 11(10.58%) previously failed treatment.

The trend varied every year in the study for both new and re-treatment cases. The new cases increased in 2001, then decreased in 2002-2003, followed by an increase in 2004 and a decrease in 2005, while the re-treatment decreased in 2001, increased in 2002-2003, then decreased in 2004 and again increased in 2005.

3.2.2). Site of TB infection

Site of TB infection was a categorical variable that referred to pulmonary or extra-pulmonary tuberculosis. Of the 854 cases analysed, 804(94.14%) were pulmonary TB and 50(5.85%) extra-pulmonary. The proportion of TB case with pulmonary decreased in 2001, then remained stable until 2004 before increasing in 2005, while the extra-pulmonary TB increased in 2001, then remained stable until 2004, followed by decrease in 2005.

Table 7: Distribution of TB cases by diagnostic methods, AAFBs and TB smear conversion at Thandukukhanya clinic 2000 to 2005

Variables		Total	2000	2001	2002	2003	2004	2005	P-value
TB Diagnostic method	Total	858	67	84	137	169	152	249	0.0001
	Bacteriology	486(56.64)	58(86.57)	69(82.14)	79(57.66)	98(57.99)	80(52.63)	102(40.96)	
	X-ray	341(39.74)	7(10.45)	12(14.29)	50(36.50)	64(37.87)	67(44.08)	141(56.63)	
	Others	31(3.61)	2(2.99)	3(3.57)	8(5.84)	7(4.14)	5(3.29)	6(2.42)	
AAFBs in sputum	Total	486	43	49	74	82	77	159	0.0001
	Positive	290(59.75)	40(94.74)	41(84.62)	47(63.92)	42(51.85)	35(45.54)	82(51.44)	
	Negative	196(40.25)	3 (5,26)	8(15.38)	27(36.08)	40(48.15)	42(54.46)	77(48.56)	
TB smear conversion	Total done	465	61	55	72	87	68	116	P=0.0001
	Converted	440(51.17)	56(83.58)	51(67.86)	70(51.09)	84((50.00)	64(42.11)	107(43.15)	
	Not converted	27(3.15)	5(7.46)	4(4.76)	2(1.46)	3(1.79)	4(2.63)	9(3.63)	
	Smear missed	238(27.80)	3(4.48)	9(10.71)	36(26.28)	43(25.60)	48(31.58)	99(39.92)	
	Not applied	153(17.87)	3(4.48)	14(16.67)	29(21.17)	38(21.17)	36(23.68)	33(13.31)	
	Total	856	67	84	137	168	152	248	

3.2.3). TB diagnostic Method

The TB cases were diagnosed by bacteriology, radiography and others (biopsy and clinical symptoms and signs). The number of TB cases diagnosed by clinical symptoms and signs and biopsy were small and were combined for analysis.

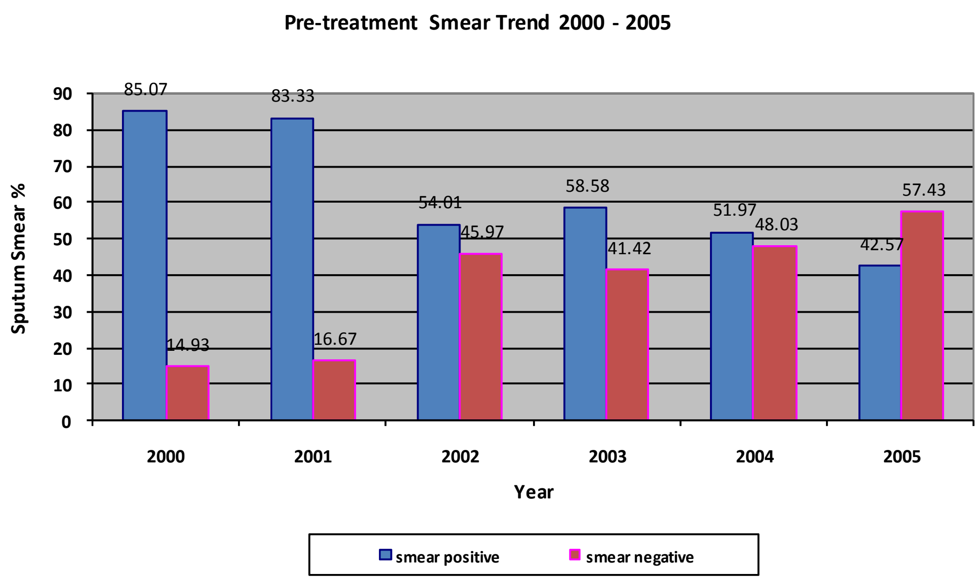
Of the 850 cases analysed, 486(56.64%) were diagnosed by bacteriology, 341(39.74%) by X-ray and 31(3.61%) by others. There was a significant change in method of diagnosis during the study period (p=0.0001). The proportion of TB cases diagnosed by bacteriological method decreased by 52.7%, while X-ray increased by 46.2% between 2000 and 2005.

3.2.4). AAFBs (Alcohol Acid Fast Bacilli)

This was a categorical variable that referred to TB cases with acid alcohol fast bacilli (AAFB) positive or negative sputum smear at diagnosis. Of the 486 cases analysed, 290(59.75%) were smear positive and

196(40.25 %) smear negative for AAFB. There was a small increase in smear negative and similar small increase in smear positive cases in 2001, followed by a sharp rise in 2002 in smear negatives and a small decrease in 2003. The proportion of cases with positive smears increased in 2003, followed by progressive decrease in 2004 through to 2005. The proportion of smear negative cases was higher than smear positive in2005.

Figure 6: Distribution of positive and negative TB cases every year at Thandukukhanya Clinic



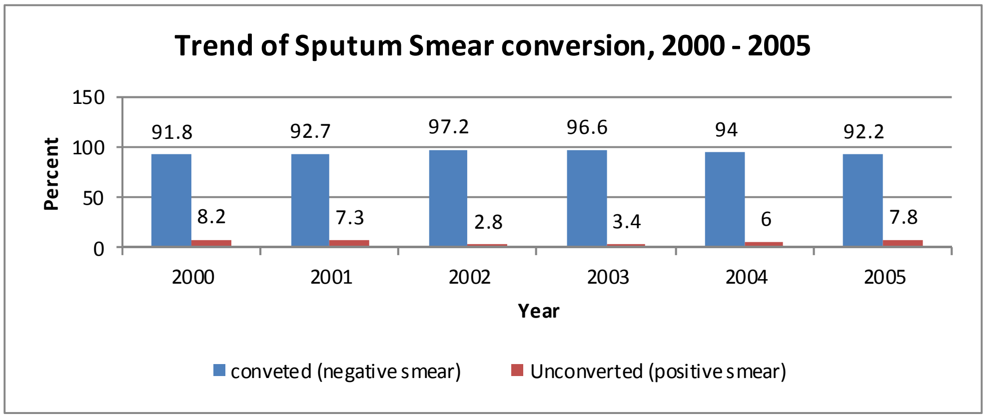
3.2.5). TB smear conversion

Table 8: Distribution of TB cases by sputum smears conversion at Thandukukhanya clinic 2000-2005

Variable	2000	2001	2002	2003	2004	2005	Total	p-value
Negative smear	56(91.80)	51(91.8)	70(92.7)	84(97.2)	64(94.1)	107(92.2)	440(94.2)	0.607
Positive Smear	5(8.20)	4(8.2)	2(7.3)	3(2.8)	3(3.4)	9(7.8)	27(5.8)	
Total	61	55	72	88	68	116	467	

TB sputum conversion is a categorical variable and refers to case that started treatment smear positive and converted to smear negative with treatment. Of the 858 cases analysed, 467(54.5%) were done smear conversion test, of which 440 (94.2%) converted while 27(5.8%) remained unconverted. The proportion of TB cases that converted smear negative increased until 2003, then decreased gradually to 2005, while unconverted cases(smear positive) decreased until 2003, then increased gradually from 2004- 2005.

Figure 7: Trend of TB sputum smear conversion at Thandukukhanya Clinic 2000- 2005



3.3.0) Objective 2: the analysis of TB treatment outcomes

3.3.1). Introduction

This section provided analysis of treatment outcomes in the TB cases registered at clinic from 2000-2005. Of the seven standard TB treatment outcomes in the study, only cure, completed treatment, died and interrupted treatment were analysed, while treatment failure, moved and transferred were excluded due to a small number, accounting to less than 5% of the cases. The descriptive analysis of treatment outcomes is followed by bivariate analysis and multivariate analysis.

3.3.2). Description of TB Treatment Outcomes

3.3.2.1) Treatment Outcomes

There were seven treatment outcomes treatment outcomes were of seven sub-categories: cured (finished TB treatment course and cure confirm by bacteriology), completed treatment (finished TB treatment course but not confirmed by bacteriology), died (case died during the course of TB treatment), transferred (left treatment initiating site to continue at another facility within health district), moved (left initiating site to continue treatment outside health district), treatment failure (patient remained sputum smear positive at the end of treatment course), and treatment interruption (patient missed 42 or more days during treatment course).

Table 9: Frequency distribution of treatment outcome at Thandukukhanya clinic

Treatment outcome	Frequency	Percentage
Completed treatment	335	39.74
Cured	284	33.69
Died	109	12.93
Interrupted treatment	86	10.20
Transferred	29	3.44
Failed treatment	07	0.82
Moved	06	0.70
Missing	**15**	**1.74**

Of 843 analysed, 335(39.74%) completed treatment, 284 (33.69%) cured, 109(12.93%) died, 86(12.93%) interrupted treatment and 29 (3.44%) transferred, 6(0.70%) moved and 7(0.82) failed treatment. Due to the small of patients who transferred, moved or failed treatment, the three outcome variables were excluded from further analysis.

Table 10: Frequency distribution of TB cases by treatment outcome 2000 – 2005

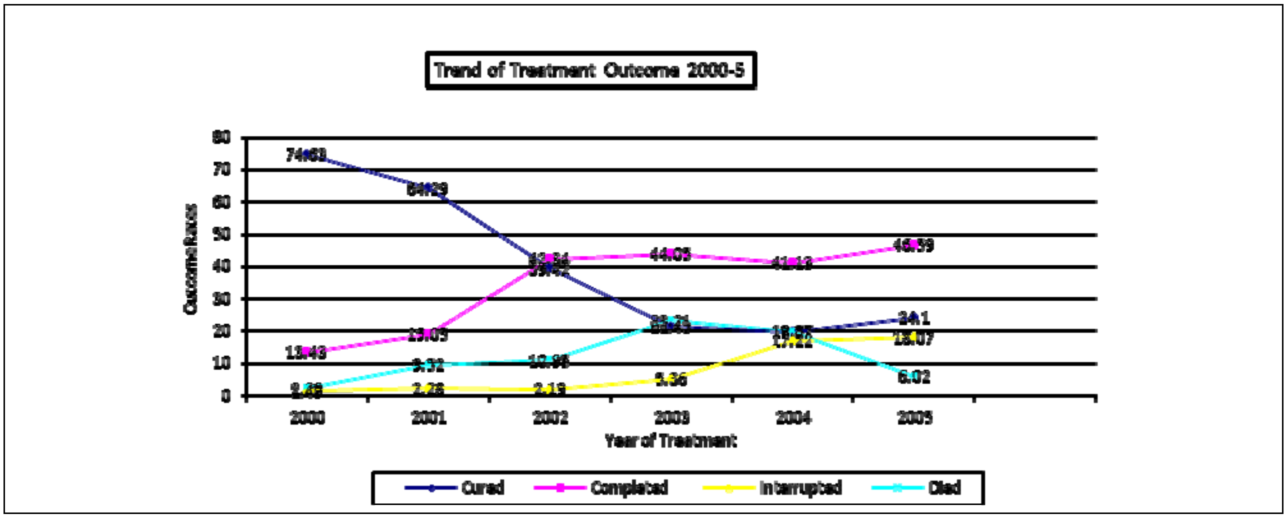
Treatment outcome	2000	2001	2002	2003	2004	2005	p-value
Completion	9 (13.43)	16(19.05)	58(42.34)	73(43.45)	62(40.79)	115(46.37)	0.0001
Cured	50(74.63)	54(64.29)	54(39.42)	36(21.43)	30(10.74)	60(20.19)	0.0001
Died	2(2.29)	8(9.52)	15(10.95)	39(23.21)	30(19.74)	15(6.05)	0.0001
Moved	0(0.00)	0(0.00)	1(0.73)	2(1.19)	1(0.66)	2(0.81)	0.704
Transfer	4(5.97)	3(3.57)	4(2.92)	8(4.76)	2(1.32)	8(3.23)	0.621
Treatment failure	1(1.49)	1(1.19)	2(1.46)	0(0.00)	0(0.00)	3(1.21)	0.506
Treatment interruption	1(1.49)	2(2.3)	3(2.19)	9(5.36)	26(17.11)	45(18.15)	0.0001

Table 11: New and Re-treatment TB cases at Thandukukhanya Clinic 2000 - 2005

Variable	**Completion**	**Cured**	**Died**	**Moved**	**Transferred**	**Treatment failure**	**Treatment interruption**	**Total**
New TB cases	302 (40.11)	252 (33.47)	92 (12.5)	5 (0.66)	23 (3.05)	5 (0.66)	72 (9.56)	753 (87.97)
Retreatment TB Cases	31 (38.90)	33 (31.07)	17 (16.50)	1 (0.97)	6 (5.83)	2 (1.94)	14 (13.59)	103 (12.03)
Total	**333**	**284**	**109**	**6**	**29**	**7**	**86**	**856**

There was no significant differences in TB treatment outcomes among retreatment compared to new cases (p=0.217). However, the proportion of retreatment cases that interrupted treatment was twice that of new cases.

Figure 8: Line graph showing trend of treatment outcome indicators 2000-2005



The TB cases presented different trend of treatment outcomes during the study period. The cure rates decreased from 2000-2004 and only increased in 2005, while the treatment completion rates increased throughout the study period except in 2004 that it decreased. The TB death increased from 2000 – 2003 and decreased in 2004-2005. The proportion of cases that interrupted treatment was low and stable from 2000 to 2003 but increased in 2004 to 2005.

3.3.1.1). Inferential Analyses: Bivariate and Multivariate.

Bivariate and multivariate regression analyses were carried out to investigate association between TB treatment outcomes and a number of exposure variables. The summary estimates of regression analysis was an odds ratio computed using the Mantel-Haenszel and logistic regression statistic tests models. While both significant and non-significant results are displayed, only those significant have been interpreted in details. Only significant factors in bivariate analysis were included in the multivariate model. In the tables below the results of both bivariate and multivariate analyses are displayed separately for treatment outcomes: cure, completed treatment, interrupted treatment and died.

3.3.1.2). Interpretations - TB Cure

According to the results, tertiary education, DOTS support by trained TB treatment supporter or relative was positively associated with TB cure in the bivariate analysis. The TB cure was 2.4 times likely in DOTs supported (OR=2.4, p= 0.001, CI 1.75 – 3.3).

TB cure was not significantly associated with any age categories. But compared to age category 15-19 years, TB cases in age category 20-39 years were 1.6 times likely to cure (OR= 1.6, p=0.412, CI 0.54 - 4.4), 1.6 times in 40-59 years (OR= 2.4, p=0.121, CI 0.79 – 6.9) and 1.7 times in ≥ 60 years (OR= 1.7, p=0.518, CI 0.34 – 8.2).

TB cure was not associated with distance from the clinic, but cases residing 2- 4 km from the clinic were 1.43 times likely to cure from TB compared to those less than < 2km (OR 1.43, p= 0.038, CI 1.0 – 2.01).

The DOTS support provided by relatives or trained TB treatment supporters were positively associated with TB cure. The cases was 0.3 times likely to be cured of TB if supported by relative (OR = 0.29, p=0.003, CI 0.13 – 0.65) and 0.4 times by TTTS (OR=0.41, p=0.04, CI 0.23 – 0.75).

Tertiary education was positively associated with TB cure and cases with tertiary education were 4.6 times likely to be cured compared to those with no education (OR=4.6, p=0.041, CI 1.06 – 20). In addition, being married was non-significantly associated with TB cure and married cases were 1.3 times likely to cure compared to those of single marital status (OR=1.3, p=0.07, CI 0.97 – 1.86).

In the multivariate regression model, variables that were significant in the bivariate model were included for analysis to control for confounding effect. In the multivariate model, only one factor remained significant with strong association with TB cure. This variable DOTS support positively associated with TB cure (OR=0.65, p=0.020, CI 0.44 – 0.9).

Age categories, relatives as DOTS supporter, and having tertiary education that were initially significantly associated with TB cure in bivariate analysis model were dropped. There was strong association between DOTS support and TB cure in multivariate model, even after adjusting for age, distance from the clinic, DOTS provider type, being married and tertiary education.

Table 12: Bivariate and Multivariate regression analysis of TB Cure

Variables	Bivariate Model (p-value, 95% interval)			Multivariate Model (p-value, 95% interval)		
Treatment Outcome Cure						
Variables	**OR**	**CI**	**p-value**	**OR**	**CI**	**p-value**
Age						
15 - 19	1			1		
20 - 39	1.6	0.54 – 4.4	0.412	1.4	0.4 – 4.2	0.495
40 - 59	2.4	0.79 – 6.9	0.121	3.1	0.9 – 10.2	0.054
> 59	1.7	0.34 – 8.2	0.518	3.2	0.52 – 19	0.199
Sex						
Female	1			1		
Male	1.3	0.78 – 1.38	0.811	0.6	0.3 – 1.2	0.144
Distance from clinic						
<2km	1			1		
2-4 km	**1.43**	**1.01 – 2.01**	**0.038**	1.3	0.6 – 2.9	0.497
5+ km	0.87	0.27 – 2.81	0.820	1.3	0.12 – 14.7	0.814
Treatment category						
New	1			1		
Retreatment	0.88	0.59 – 1.37	0,590	0.58	0.2 – 1.6	0.313
TB Infection site						
Extra-pulmonary	1			1		
Pulmonary	**6.6**	**2.3 – 18.6**	**0.001**	0.75	0.13 - 41	0.889
Smear conversion						
Negative	1			1		
Positive	1.13	0.50 – 2.53	0.760	0.78	0.06 – 9.3	0.849
Treatment supporters						
No DOTS supporter	1			1		
DOTS Supporter	**2.4**	**1.75 – 3.3**	**0.001**	**0.64**	**0.44 – 0.9**	**0.020**
Treatment supporters type						
Clinic nurse	1			1		
CHWs	0.98	0.5 – 1.84	0.95	0.37	0.12 – 1.3	0.117
Relatives	**0.29**	**0.13 – 0.65**	**0.003**	1.1	0.15 – 7.3	0.948
Teachers	0.41	0.03 – 4.8	0.485	Dropped	Dropped	Dropped
TTTS	**0.41**	**0.23 – 0.75**	**0.04**	7.2	0.001 - 50	0.660
Education status						
None	1			1		
Primary	0.93	0.53 – 1.6	0.806	0.33	0.06 – 169	0.184
Secondary	1.3	0.81 – 2.3	0.225	0.89	0.17 – 4.7	0.890
Tertiary	**4.6**	**1.06 - 20**	**0.041**	5.8	0.07 - 468	0.427
Employment Status						
Employed	1			1		
Unemployed	1.2	0.68 – 2.06	0.547	4.3	0.9 – 19	0.05
Marital Status						
Single	1			1		
Married	**1.3**	**0.97 – 1.86**	**0.07**	10.61	0.19 – 1.9	0.400
Widowed	0.6	0.31 – 1.43	0.24	1.03	0.10 - 10	0.978

1= Reference group in each variable

3.3.1.3). Interpretation of TB treatment outcome- Completed treatment

Completed treatment is a TB treatment outcome if smear positive cases finish treatment course without being done sputum to confirm absence of TB bacilli and ideally is expected to be zero in TB program.

In the bivariate model, age and being married were factors significantly associated with completed treatment as an outcome.

All age categories showed positive association with TB treatment completion and applied to all age categories: 20- 39 (OR 0.24, p=0.0001, CI: 0.11 -0.49) 40 -59years (OR=0.24, p=0.001, CI: 0.1 – 0.82) and 60+ years (OR=0.28, p=0.001, CI: 0.09 – 0.86).

The average distance to the clinic was 3.2 km and TB cases that resided 2-4km from the clinic was positively associated with TB treatment completion and cases were only 0.57 times likely to complete TB treatment compared to those that resided < 2km (OR 0.57, p= 0.0001, CI: 0.04 – 0.11).

Being categorise as pulmonary TB was associated with completion of treatment, even though it non-significant relationship. The cases were 0.10 times likely to complete TB treatment compared to extra-pulmonary (OR=0.10, p-0.001, CI: 0.11– 0.38).

Being married was positively associated with TB treatment completion and married cases were 1.3 likely to complete treatment compared to single marital status (OR=1.3, p=0.008, CI: 1.0 – 1.7). The relationship between married and treatment completion was not statistically significant

In the **multivariate regression model**, variables that were significant in the bivariate model were included for analysis to control for confounding effect. In the multivariate model, of the six factors, three remained significant with strong association with treatment completion. These variables were age (20-39, 40-59 and >60), positive smear at conversion and being married. The evidence of association with age category 45-54years (OR 0.1, p=0.003, CI: 0.02 – 0.47) and positive smear conversion (OR=3.4, p=0.0001 CI: 1.9 -6.1) was very strong in the multivariate model. The variable age categories 0-14 and 15-24 years, distance (2-4km) from the clinic, bacteriological diagnosis and pulmonary site of infection were dropped in the multivariate model, when controlled for other factors.

Three new variables that had no significant association with treatment completion in bivariate model were significant in the multivariate model. These variables are primary education (OR=2.6, p=0.046, CI: 1.2 – 5.6), secondary education (OR=4.2, p=0.007, CI: 1.5 – 11.9) and widowed marital status (OR=6.9, p=0.006, CI: 1.7 – 27). The evidence of association in multivariate model was very strong with secondary education status.

Table 13: Bivariate and Multivariate regression analysis of TB treatment completion

Variables	Bivariate Model (p-value, 95% interval)			Multivariate Model (p-value, 95% interval)		
Treatment Outcome : Completed Treatment						
Variables	**OR**	**CI**	**p-value**	**OR**	**CI**	**p-value**
Age						
15-19	1			1		
20-39	0.82	0.3 – 2.4	0.664	0.86	0.3 – 2.6	0.789
40-59	1.14	0.6 - 2.1	0.567	0.33	0.6 – 2.0	0.860
> 60-	1.20	0.3 – 8.2	0.721	0.18	0.4 – 1.9	0.747
Sex						
Female	1			1		
Male	0.98	0.74 – 1.29	0.895	1.6	0.9 – 2.6	0.077
Distance from clinic						
<2km	1			1		
2-4 km	**0.57**	**0.4 – 0.82**	**0.003**	0.6	0.3 – 1.1	0.104
5+ km	0.55	0.17 – 1.78	0.316			
Treatment category						
New	1			1		
Retreatment	0.15	0.42 – 1.02	0.059	0.79	0.3 – 1.7	0.630
TB Diagnostic method						
Xray	1			1		
Bacteriology	**0.09**	**0.07 – 0.137**	**0.0001**	0.54	0.12 – 2.4	0.426
TB Infection site						
Extra-pulmonary	1			1		
Pulmonary	**0.21**	**0.11 – 0.38**	**0.001**	0.67	0.3 – 1.7	0.418
Smear conversion						
Negative	1			1		
Positive	**0.10**	**0.01 – 0.78**	**0.028**	**3.4**	**1.9 – 6.1**	**0.0001**
Treatment supporters						
No DOTS supporter	1			1		
DOTS Supporter	0.82	0.61 – 1.09	0.187	0.96	0.78 – 1.2	0.710
Treatment supporters type						
Clinic nurse	1			1		
CHWs	0.6	0.3 – 1.19	0.152	0.9	0.7 – 1.2	0.710
Relatives	1.9	0.9 – 4.14	0.085	0.55	0.3 – 1.2.	0.148
Teachers	3.5	0.3 – 41	0.319	0.58	0.2 -1.6	0.278
TTTS	1.2	0.6 – 2.12	0.615	1.4	0.04 - 50	0.848
Education status						
None	1			1		
Primary	1.13	0.66 – 1.95	0.656	**2.6**	**1.01 – 6.7**	**0.046**
Secondary	1.2	0.7 – 1.95	0.454	**4.2**	**1.5 – 11.9**	**0.007**
Tertiary	0.52	0.1 – 2.7	0.442	3.6	0.22 - 41	0.398
Employment Status						
Employed	1			1		
Unemployed	0.76	0.44 – 1.28	0.305	1.5	0.5 – 4.2	0.472
Marital Status						
Single	1			1		
Married	**1.3**	**1.01 – 1.7**	**0.008**	**2.5**	**1.2 – 5.6**	**0.021**
Widowed				**6.9**	**1.7 – 27.4**	**0.006**

1= Reference group in each variable

3.3.1.4). Interpretation of TB treatment outcome – Interrupted treatment

Five variables showed evidence of association with TB treatment interruption in bivariate model analysis. These variables were pulmonary site of infection, treatment (DOTS) support, community health workers (CHWs) and primary education. Except for primary education, all the significant variables above had protective association against treatment interruption. The TB cases with pulmonary infection, DOTS support and DOTS supported by CHWs were positively associated treatment interruption. The cases were 0.2 time likely to interrupt treatment if they had pulmonary TB compared to extra-pulmonary TB (OR=0.21, p=0.001, CI: 0.11 -0.38); were 0.7 times likely to interrupt treatment if they had DOTS supporters compared to cases that did not (OR=0.7, p=0.001 CI: 0.6 – 0.8) and were 0.2 time likely to interrupt treatment if supported by CHWs compared to clinic nurses (OR=0.23, p=0.001, CI: 0.1 – 0.54).

The TB cases with primary education was negatively associated with treatment interruption and cases were 4.5 time likely to interrupt treatment compared to those with no education (OR=4.5, p=0.028, CI: 0.021 – 15). However, the relation was not statistically significant association considering that the CI remained wide and overlapped value 1. 0.

The association of treatment interruption with DOTS support and relatives and CHWs as DOTS supporters were significantly associated in the multivariate model. The cases were 48 times less likely to interrupt treatment if they had supporters compared if they did not (OR=48, p=0.0001, CI: 22-104). The association with CHWs as supporters was strong and cases were 1.9 times less likely to interrupt treatment compared to clinics nurses as supporters (OR 1.9, p=0.0001, CI: 1.8 – 2.1). The an association between TB treatment interruption and relatives as DOTS supporters and cases were 2.1 times less likely to interrupt treatment if they were supported by relatives compared to clinic nurses (OR=2.1, p=0.0001, CI: 1.7 – 4.9).. Male cases were 3.2 times likely to interrupt treatment compared to females (OR: 3.2, p=0.022, CI: 1.2 – 8.5)

Table 14: Bivariate and Multivariate regression analysis of TB treatment interruption

Variables	Bivariate Model (p-value, 95% interval)			Multivariate Model (p-value, 95% interval)		
Treatment Outcome : Interrupted TB treatment						
Variables	**OR**	**CI**	**p-value**	**OR**	**CI**	**p-value**
Age						
15-19	1			1		
20-39	0.64	0.5 – 4.8	0.559	0.6	0.6 – 8.9	0.661
40-59	0.57	0.4 – 3.8	0.600	1.1	0.4 -.3.4	0.806
>59	1.1	0.4 – 3.4	0.839	1.2	0.3. – 4.1	0.826
Sex						
Female	1			1		
Male	01.4	0.9 – 2.2	0.132	**3.2**	**1.2 – 8.5**	**0.022**

Distance from clinic						
<2km	1			1		
2-4 km	0.72	0.4 – 1.3	0.285	0.7	0.2 – 2.1	0.495
5+ km	1.42	0.3 – 6.4	0.653			
Treatment category						
New	1			1		
Retreatment	1.4	0.8 – 2.7	0.215	0.6	0.07 – 5.2	0.637
Sputum Smear at Diagnosis						
Positive	1			1		
Negative	0.8	0.5 – 1.6	0.626	1.3	0.04 – 4.4	0.867
None	1.6	0.8 – 3.0	0.182	0.9	0.23 – 3.2	0.829
TB Diagnostic method						
Xray	1			1		
Bacteriology	0.31	0.04 – 2.3	0.256	0.73	0.02 - 21	0.861
TB Infection site						
Extra-pulmonary	1			1		
Pulmonary	**0.21**	**0.11 – 0.38**	**0.001**	0.67	0.3 – 1.7	0.418
Smear conversion						
Negative	1			1		
Positive	1.09	0.4 – 2.8	0.847	0.8	0.17 – 3.9	0.814
Treatment supporters						
No DOTS supporter	1			1		
DOTS Supporter	**0.7**	**0.6 – 0.8**	**0.001**	**0.48**	**0.22 – 0.71**	**0.0001**
Treatment supporters type						
Clinic nurse	1			1		
CHWs	**0.23**	**0.1 – 0.54**	**0.001**	**1.9**	**1.8 – 2.1**	**0.001**
Relatives	0.51	0.2 – 1.30	0.143	**2.1**	**1.7 – 4.9**	**0.0001**
Education status						
None	1			1		
Primary	**4.5**	**0.021 – 15**	**0.021**	**6.7**	**0.8 – 55**	**0.028**
Secondary	2.4	0.8 – 6.9	0.108	1.1	0.25 – 4.9	0.884
Tertiary	1.6	0.5 – 4.5	0.418	0.5	0.08 – 3.1	0.458
Employment Status						
Employed	1	0.40 – 2.00	0.800	1	0.09 – 9.5	0.953
Unemployed	0.90			0.9		
Marital Status						
Single	1	0.4 – 1.14	0.174	1	0.15 – 2.4	0.481
Married	0.74			0.6		

1= Reference group in each variable, TTTS: Trained TB Treatment Supporters, CHWS: Community Health Workers

3.3.1.5). Interpretation of TB –treatment outcome died

Six variables showed significant evidence of association with TB death in the multivariate model. These variables are distance (2-4km) from the clinic, smear positive conversion smear, DOTS support by trained TB treatment supporter, primary education or secondary education and being married. The association with positive conversion smear showed very strong evidence. The case were 1.9 times likely to die if they had positive conversion smear than if they had negative smear (OR=1.9, p=0.0001, CI: 1.5 – 2.4). The association with distance from the clinic and secondary education status showed strong evidence. Cases were 2.4 times likely to die from TB if they resided 2-4km from the clinic compared to residing <2km (OR = 2.4, p=0.002, CI: 1.2 -2.8) and were 0.25 times less likely to die if they had secondary education compared to those with no education (OR= 0.25, p=0.001, CI: 0.13 – 0.46). The association with secondary education was protective from TB death.

The association with being married, primary education status showed evidence and married cases were 0.4 times less likely to die from TB compared to single status (OR=0.4, p=0,011, CI: 0.28 – 0.84). The cases with primary education status were 0.55 time less likely to die compared to those with no education (OR=0.55, p=0.05, CI: 0.3 1.0) and those supported by trained TB treatment supporters were 2.8 times more likely to die compared to those supported by clinic nurses. Being married TB cases or had primary education were positively associated TB death.

In multivariate model, nine variables were either positively or negatively associated with TB death. Four of these variables were retained from the bivariate model (residing 2-4km from the clinic, positive conversion smear, secondary education status and being married) and five were variable that had no significant association in the bivariate model (male sex, age 35 - 44 years, 45-54 years, DOTS support and unemployed status).

The association with positive conversion smear and secondary education showed very strong evidence. The cases were 0.21 times less likely to die if they had secondary education compared to no education (OR=0.21, p=0.0008, CI: 0.07 - 0.67). The cases were 0.4 times less likely to die from TB if the resided far from the clinic (>2 km) from the clinic compared with those residing < 2km (OR=0.4, p=0.002, CI 1.5 – 5.6). The association with male sex, age categories 20-39 and 40-59 years, DOTS support, unemployed status and being married showed evidence. The cases were 7.6 time likely to die if in age category 40 -59 years than 15-19 years (OR=7.6, p=0.028, CI: 1.3 -46).

The male TB cases were positively associated with TB death and male cases were 0.4 times likely to die from TB compared to females (OR=0.4, p=0.010, CI: 0.2 – 0.8) in multivariate model. This association was non-significant in bivariate model. Being married or unemployed was also positively associated with death and cases were 0.23 time likely to die from TB if they were unemployed compared to employed (OR=0.23, p=0.013, CI: 0.07 – 0.73) and were 0.27 time less likely to die if married compared to if single (OR=0.27, p=0.010, CI: 0.1 – 0.73).

There was no significant association between DOTS support and death and cases were 1.4 times more likely to die if they had DOTS support compared to those without (OR=1.4, p=0,049, CI: 1.0 – 1.8)..

Table 15: Bivariate and Multivariate regression analysis of TB outcome - Died

Variables	Bivariate Model (p-value, 95% interval)			Multivariate Model (p-value, 95% interval)		
Treatment Outcome : Died						
Variables	**OR**	**CI**	**p-value**	**OR**	**CI**	**p-value**
Age						
15-19	1			1		
20-39	1.5	0.5 – 4.5	0.412	1.4	0.5– 4.3	0.495
40-59	2.3	0.8 – 6.9	0.121	3.2	0.9 - 10	0.054
>59	1.7	0.3 – 8.2	0.518	3.2	0.5 - 18	0.199
Sex						
Female	1			1		
Male	0.69	0.4 – 1.03	0.076	**0.4**	**0.2 – 0.8**	**0.010**
Distance from clinic						
<2km	1			1		
2-4 km	**1.8**	**1.2 – 2.8**	**0.008**	**2.8**	**1.5 – 5.6**	**0.002**
5+ km	2.2	0.6 – 8.11	0.231	**8.5**	**1.0 - 66**	**0.040**
TB Diagnostic method						
Xray	1			1		
Bacteriology	1.9	0.4 – 1.11	0.156	0.8	0.006 – 1.23	0.070
TB Infection site						
Extra-pulmonary	1			1		
Pulmonary	1.5	0.6 – 3.7	0.435	2.7	0.72 – 16.21	0.142
Smear conversion						
Negative	1			1		
Positive	**1.9**	**1.54 – 2.44**	**0.0001**	**5.9**	**2.8 – 12.3**	**0.0001**
Treatment supporters						
No DOTS supporter	1			1		
DOTS Supporter	1.1	0.76 – 1.76	0.487	**1.4**	**1.0 – 1.8**	**0.049**
Treatment supporters type						
Clinic nurse	1			1		
CHWs	1.24	0.4 – 4.0	0.716	1.5	0.5 – 4.7	0.452
Relatives	0.9	0.2 – 4.1	0.958	0.7	0.2 – 3.2	0.697
TTTS	**2.8**	**0.9 – 8.2**	**0.05**			
Education status						
None	1			1		
Primary	**0.55**	**0.3 – 1.00**	**0.05**	0.63	0.23 – 1.7	0.371
Secondary	**0.25**	**0.13 – 0.46**	**0.001**	**0.21**	**0.07 – 0.67**	**0.008**
Tertiary	0.36	0.04 – 3.03	0.344	0.88	0.05 - 14	0.928
Employment Status						
Employed	1			1		
Unemployed	1.02	0.47 – 2.2	0.959	**0.23**	**0.07 – 0.73**	**0.013**
Marital Status						
Single	1			1		
Married	**0.4**	**0.28 – 0.84**	**0.011**	**0.27**	**0.1 – 0.73**	**0.010**
widowed	0.9	0.4 – 2.3	0.932	0.85	0.2 – 3.9	0.846

1= Reference group in each variable

3.4.0). Objective 3: the comparison analysis of TB cases with and without DOTS supporters

3.4.1) Introduction

The objective 3 is the comparison analysis of TB treatment outcome in cases with and without DOTS support at Thandukukhanya clinic from 2000 - 2005. In this section, the descriptive analysis of DOTS support, bivariate analysis, multivariate analysis and analysis of confounders is presented. The teachers as DOTS supporters was limited to three school children and excluded from further analysis. The TB cases transferred (29, 3.39%) and moved (6, 0.70%) during the study period contributed less than 5% of cases and were excluded from further analysis due to small number. Of the 858 cases included in the analysis, 856 were analysed for DOTS support and two were excluded due to missing data.

.

3.4.2). Descriptive analysis of treatment (DOTS) support

The table below shows frequency and proportion of support at Thandukukhanya clinic in every year from 2000 – 2005

Table 16: frequency and distribution of DOTS support at Thandukukhanya clinic 2000 – 20005

Variable	Total	2000	2001	2002	2003	2004	2005	p-value
DOTS supporter	**525 (61.18%)**	63 (94.05%)	80 (95.24%)	131 (95.62%)	123 (73.21%)	59 (48.72%)	167 (27.02%)	P=0.0001
No DOTS supporter	**333 (38.72%)**	4 (5.95%)	4 (4.76%)	6 (4.38%)	45 (26.79%)	93 (61.18%)	181 (72.98%)	
Total	**858**	**67**	**84**	**137**	**168**	**152**	**248**	

Of the 858 TB cases, 61.18% had DOTS supporter while 38.72% did not. The DOTS support was high and nearly constant in the first three years. However, from 2003, the DOTS support sharply declined reaching lowest level of 27.02% in 2005, the last year of study. Meanwhile, the proportion of TB cases without DOTS support sharply increased in 2003 and peaked in 2005 at 72.98%. The majority of TB cases treated from 2004 to 2005 did not have DOTS support. However, there was significant difference in the trend of DOTS support during the study period (Pearson Chi^2, p=0.0001)

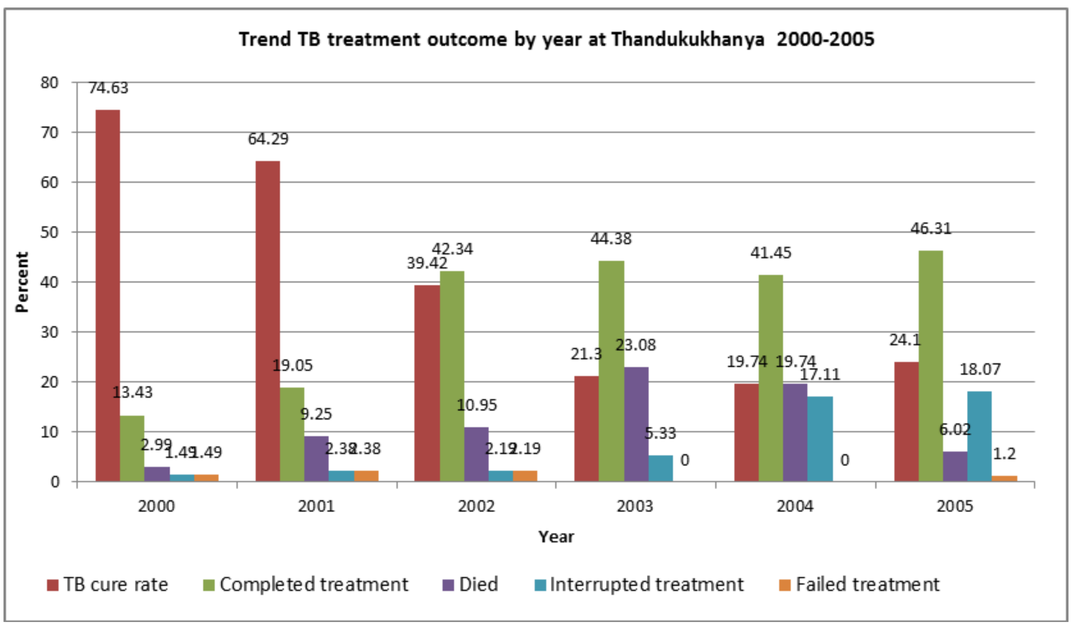
Table 17: TB Treatment outcome by DOTS supporters at Thandukukhanya Clinic

Treatment Outcomes	Clinic nurse	CHW	Relative	Teachers	TTTS	Total	p-value
Completed treatment	18 (33.96)	35 (25.38)	30 (52.63)	2 (66.67)	110 (56.41)	333 (38.90)	**0.0001**
Cured	30 (56.22)	73 (54.07)	15 (26.32)	1 (33.33)	92 (33.45)	284 (33.18)	
Died	4 (7.55)	12 (8.89)	4 (7.02)	0 (0)	50 (18.18)	109 (12.73)	
Moved	0 (0)	0 (0)	1 (1.75)	0 (0)	2 (0.73)	6 (0.70)	
Transferred	0 (0)	6 (4.44)	1 (1.75)	0 (0)	8 (2.91)	29 (3.39)	
Treatment failure	1 (1.89)	2 (1.48)	0 (0)	0 (0)	2 (0.73)	7 (0.82)	
Treatment Interruption	0 (0)	7 (5.19)	6 (10.53)	0 (0)	11 (4.00)	86 (10.50)	
Total	**53 (10.13)**	**135 (15.81)**	**57 (10.90)**	**3 (0.57)**	**275 (52.58)**	**856 (100)**	

TTTS: trained TB Treatment Supporters; CHW: Community Health Workers

Of 525 TB cases provided DOTS support, ,52.58%, were supported by trained TB supporters, 15.81% by community health workers, 10.13% by the clinic nurses, 10.90% by relatives and 0.57% by teachers.

Figure 9: The changes in treatment outcomes at Thandukukhanya clinic from 2000-2005 (moved, transferred & treatment failure excluded)



The figure showed a paradox between DOTS support and treatment outcome. Despite high and stable DOTS support until 2002, the TB cure rate sharply declined while treatment completion and cases that died increased. From 2003 – 2005, the DOTS support sharply declined but cure rate continued to fall in 2003 but stabilised in 2004 – 2005. At the same time, TB treatment completion and mortality stabilised while DOTS support declined. In the final year of the study, the DOTS support continued to drop while cure rate and treatment completion increased and mortality decreased.

Table18: the trend of treatment DOTS supporters at Thandukukhanya clinic 2000 – 2005

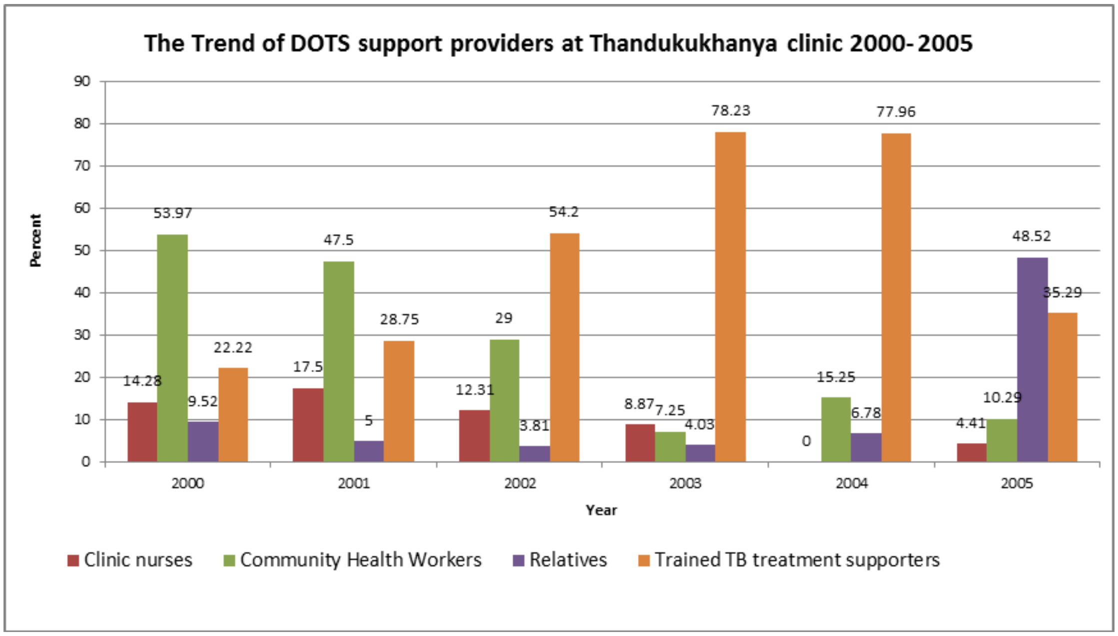
Variables	2000	2001	2002	2003	2004	2005	Total
Clinic nurses	9 (14.28)	14 (17.50)	16 (12.31)	11 (8.87)	0 (0.00)	3 (4.41)	**53 (10.13)**
Community Health Workers (CHWs)	34 (53.97)	38 (47.50)	38 (29.00)	9 (7.25)	9 (15.25)	7 (10.29)	**135 (25.81)**
Relatives	6 (9.52)	4 (5.00)	5 (3.81)	5 (4.03)	4 (6.78)	33 (48.52)	**57 (10.90)**
Teachers	0 (0)	1 (1.25)	1 (0.76)	1 (0.8)	0 (0.00)	0 (0.00)	**3 (0.57)**
Trained TB Treatment Supporters	14 (22.22)	23 (28.75)	71 (54.20)	97 (78.23)	46 (77.96)	24 (35.29)	**275 (52.58)**

In 2000, the majority of TB cases were provided with treatment support by community health workers (53.9%), followed by trained TB supporters (22.22%), then clinic nurses (14.28%) and least by relatives (9.52%). The teachers did not provide any support in 2000.

From 2001 the DOTS support provided by clinic nurses initially increased, but decreased in 2002, reaching zero in 2004 and then a small increase in 2005. The proportion of TB cases supported by the CHWs decreased from 2001 to 2003, followed by an increase in 2004 and a decreased in 2005. The support by relative remained nearly constant from 2000 to 2004 and only increased in 2005 and by trained TB treatment supporters increased from 2000 to 2004 but decreased in 2005.

In 2001 the largest percentage of patients were supported by CHW (47.5%) as compared to 2005 when the most patients were supported by relatives (48.52%)

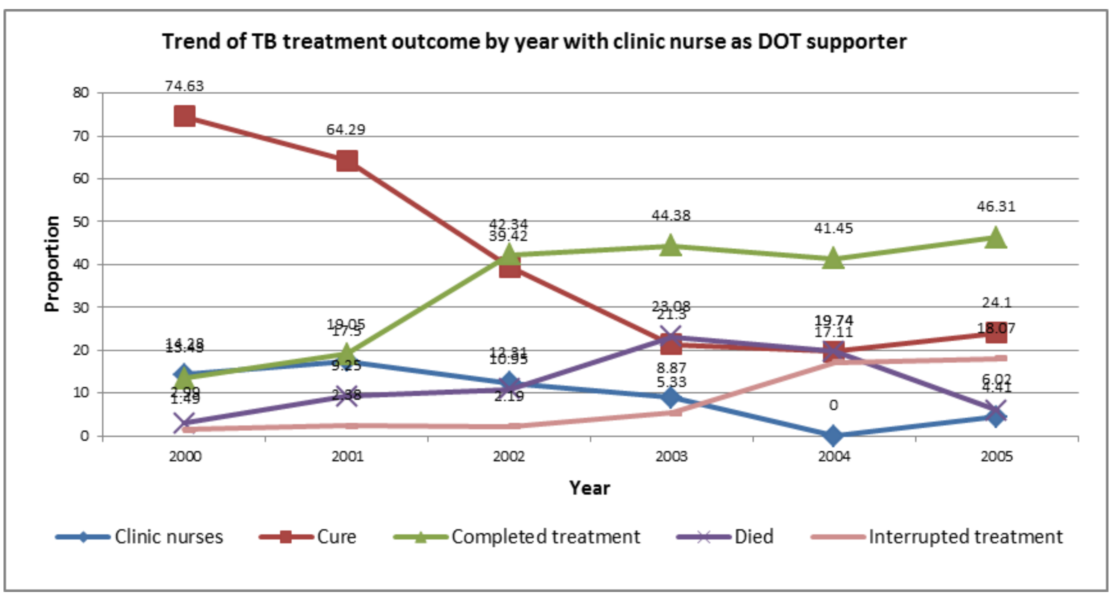
Figure 10: Trend of DOTS support providers at Thandukukhanya clinic 2000 - 2005



3.4.3). DOTS support and outcome variable Completed treatment

TB treatment completion rate increased in 2001- 2002, along similar slope with trained TB treatment supporters but the relationship was inverse from 2003 -2005. While the trained TB treatment support continued to increase, the treatment completion rate levelled in 2003- 2004 and increased slightly in 2005. The support by community health workers, teachers, clinic nurses and relatives did not match the trend of TB treatment completion during the study.

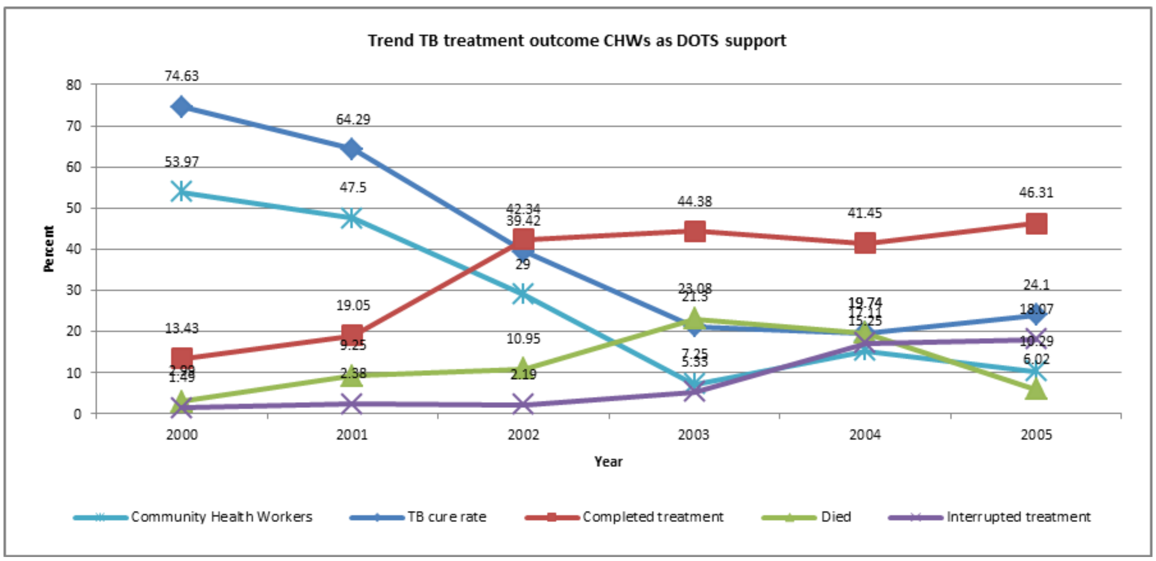
Figure 11: trend of TB treatment outcomes with clinic nurse as DOTS supporter 2000-2005



3.4.4). DOTS support and TB outcome cure

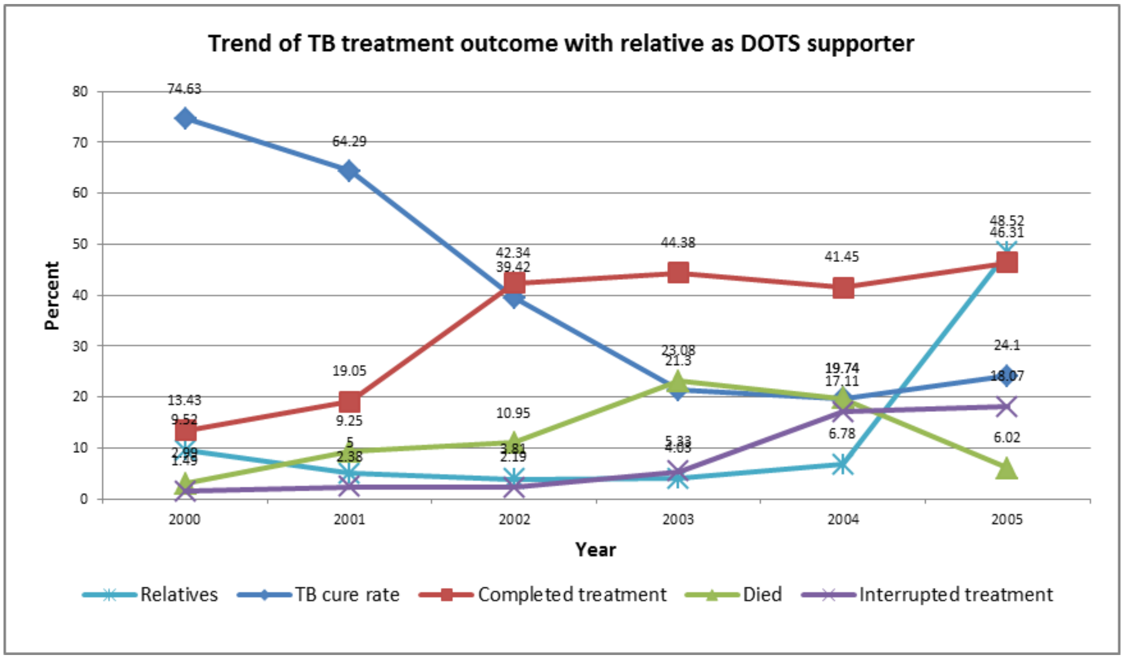
The cure rate decreased from 74.65% in 2000 to 24.3% despite DOTS support and there was a close link between community health workers and TB cure rate for all years except in 2005. As the proportion of TB cases supported by community health workers decreased from 2000 – 2003, the cure rate decreased with similar gradients and as the proportion of cases supported by community health workers increased in 2004, the cure rate stabilised in 2004 and increased in 2005. There was no trend between cure rate and other DOTS support group: The cure rate decreased despite increase in the proportion of TB cases supported by trained TB supporters and in 2005 the cure rate increased despite a decrease in support by trained TB treatment supporters (TB treatment supporters had inverse relationship with cure rate. The cure rate trend was not affected by the DOTS support offered by clinic nurses, relatives and teachers.

Figure 12: Trend of TB treatment outcomes with CHWs as DOTS supporter at Thandukukhanya 2000-2005



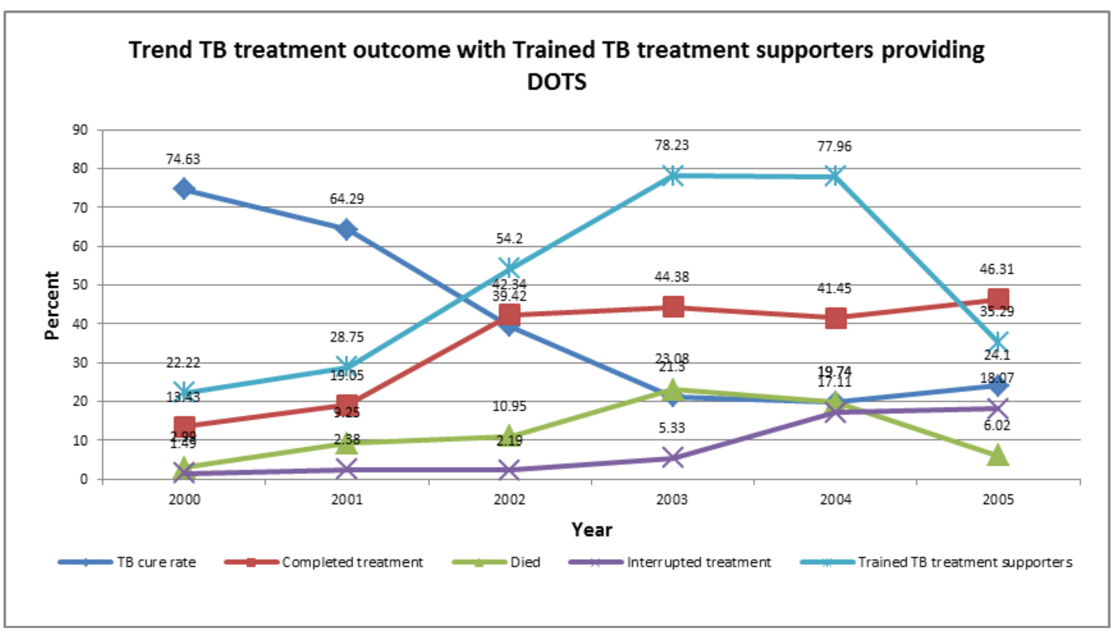
The mortality from TB increased despite increase in the proportion of trained TB treatment supporter in the program and only decreased in 2005, perhaps due to increase in the DOTS support by relatives.

Figure 13: Trend of TB treatment outcomes with relatives as DOTS supporters 2000-2005



The TB treatment interruption remained low and increased in 2003 – 2005, and this trend matched the increased and decrease in the proportion of trained TB treatment supporters. The trained TB treatment supporters seemed to have kept treatment interruption low.

Table 14: Trend of TB treatment outcomes with trained TB treatment supporters as DOTS supporters at 2000 – 2005



3.4.5). Bivariate and Multivariate Analysis

The bivariate and multivariate analyses were conducted to show the relationship between TB treatment outcomes and DOTS support. Table below presents the results of bivariate and multivariate model analyses.

3.4.6). Interpretation of bivariate and multivariate model

TB cure and treatment interruption were the two TB treatment outcomes that showed significant association with DOTS support in both bivariate and multivariate models. The cases were 2.1 time likely to be cured compared than complete treatment if they had DOTS support (OR=2.1, p=0.0001, CI: 1.4-2.8). The cases were 0.27 times less likely to interrupt treatment compared to complete treatment if they had DOTS supporters (OR=0.27, p=0.0001, CI: 0.16 – 0.46) and this was positive association.

In the multivariate model, after controlling for age, marital status, education, smear conversion, sex, distance from the clinic, and employment, both cure and treatment interruption were retained. As in the bivariate analysis, the rest of the treatment outcomes showed no significant association with DOTS support. The TB treatment outcomes was twice likely to be cure than complete treatment if they had DOTS support (OR=2.0. p=0.006, CI: 1.2 – 2.3) and were 0.2 time less likely to default treatment if they had DOTS. The association with treatment interruption remained positive in the multivariate model (OR=0.2, p=0.0001).

The multivariate analysis was performed to include other variables other than treatment outcome variables. The variables distance (2-4km) from the clinic, re-treatment TB, bacteriology diagnosis, primary education and secondary education showed evidence of association with DOTS support. The association with distance (2-4km) from the clinic, retreatment TB and secondary education showed strong association: the cases were 2 times more likely to be supported by DOTS if resided 2-4 km from the clinic compared to < 2km (OR=2, p=0.0001, CI: 1.4 – 2.9). In addition, cases were 0.5 times less likely to have DOTS support if they were re-treated for TB compared to new TB case (OR=0.5, p=0.0001, CI: 0.3 – 0.6) and were 0.3 times less likely to be DOTS supported if had secondary education compared to no education (OR=0.3, p=0.0001, CI: 0.2 – 0.5).

The association with bacteriology diagnosis and primary education was significant and cases were 1.58 time more likely to be supported by DOTS if they were diagnosed by sputum smear (bacteriology) compared to X-ray diagnosis (OR=1.58, p=0.003, CI: 1.2 – 2.1) and were 0.4 times less likely to be supported by DOTS if they had primary education compared to no education (OR=0.4, p=0.003, CI: 0.2 – 0.7).

A multivariate model analysis was conducted to show association of variables other than treatment outcomes with DOTS support. Four variables: distance (2-4km) from the clinic, retreatment TB type, primary education and secondary education retained significant association in multivariate analysis when controlled for possible confounding factors. The cases were 1.9 times more likely to have DOTS support if they resided >2km from the clinic compared to <2km (OR=1.9, p=0.001, CI: 1.3 – 2.9), were 0.5 times less likely to be DOTS supported if they were re-treatment TB compared to new TB cases (OR=0.5, p= 0.0002, CI: 0.3-0.6), 0.4 times less likely to have DOTS support if they had primary education compared to no education (OR=0.4, p=0.010, CI: 0.16 – 0.77) and 0.3 times less likely to have DOTS support if they had secondary education compared to no education (OR=0.3, p=0.001, CI: 0.11 – 0.6). The cases were 0.5 times less likely to be DOTS supported if they had pulmonary TB compared to extra-pulmonary TB (OR=0.5, p=0.038, CI: 0.11 – 0.6).

Table 19: Table of bivariate and multivariate models of DOTS support

Variables	Bivariate Models (p=values, 95% confidence Intervals)			Multivariate Models (p=value, 95% confidence Intervals)		
	OR	**CI**	**P-value**	**OR**	**CI**	**P-value**
Treatment outcomes						
Completed treatment	1			1		
Cured	**2.1**	**1.4 – 2.8**	**0.0001**	**2.0**	**1.2 – 3.3**	**0.006**
Died	1.3	0.8 – 1.9	0.287	1.0	0.6 – 1.8	0.773
Moved	0,7	0.14 – 3.6	0.678	0,5	0.09 – 3.3	0.509
Transferred	0.8	0.36 – 1.62	0.482	0.9	0.4 – 2.0	0.804
Failed treatment	1.7	0.34 – 9.2	0.496	1.8	0.3 – 10	0.508
Interrupted treatment	**0.27**	**0.16 – 0.46**	**0.0001**	**0.2**	**0.13 – 0.42**	**0.0001**
Age						
0 – 14	1			1		
15 – 24	**0.27**	**0.1– 0.6**	**0.006**	**0.2**	**0.06 – 0.5**	**0.001**
25 – 34	**0.25**	**0.1- 0.6**	**0.003**	**0.1**	**0.06 – 0.5**	**0.0001**
35-- 44	**0.25**	**0.1 - 0.6**	**0.003**	**0.1**	**0.05 – 0.5**	**0.001**
45 – 54	**0.23**	**0.1 – 0.6**	**0.003**	**0.2**	**0.05 – 0.54**	**0.003**
55+	**0.30**	**0.1- 0.8**	**0.026**	0.2	0.7 – 1.4	0.995
Sex						
Female	1			1		
Male	0.9	0.7 – 1.2	0.671	0.8	0.6 – 1.3	0.657
Distance from clinic						
<2	1			1		
2-5	**2.0**	**1.4 – 2.9**	**0.0001**	**1.9**	**1.3 – 2.9**	**0.001**
>5	0.3	0.1 – 1.2	0.101	**0.3**	**0.08 – 1.00**	**0.047**
Treatment category						
New	1			1		
Re-treatment	**0.5**	**0.3 – 0.6**	**0.0001**	**0.5**	**0.3 – 0.6**	**0.0002**
TB infection site						
Extra-pulmonary	1			1		
Pulmonary	0.6	0.3 – 1.2	0.155	**0.5**	**0.24 – 0.9**	**0.038**
Smear at diagnosis						
Positive	1			1		
Negative	1.44	0.9 – 2.0	0.051	0.5	0.17 – 1.8	0.350
TB diagnosis method						
X-ray	1			1		
Bacteriology	**1.58**	**1.2 – 2.1**	**0.001**	2.2	0.7 - 70	0.196

Smear Conversion						
Negative	1			1		
Positive	1.0	0.4 – 2.3	0.974	0.9	0.4 – 2.3	0.870
Education status						
None	1			1		
Primary	**0.4**	**0.1 – 0.7**	**0.003**	**0.4**	**0.16 – 0. 77**	**0.010**
Secondary	**0.3**		**0.0001**	**0.3**	**0.11 – 0.6**	**0.001**
Tertiary	0.4	**0.2– 0.5**	0.278	0.3	0.05 – 1.6	0.147
		0.1 – 1.9				
Employment status						
Employed	1			1		
Unemployed	1.2	0.7 – 2.1	0.400	0.87	0.5 – 1.6	0.688
Marital Status						
Single	1			1		
Married	0.8	0.6 – 1.1	0.127	0.7	0.4 – 1.2 0.2 –	0.119
Widowed	0.7	0.4 -1.4	0.347	0.5	1.2	0.115

1= Reference group in each variable

3.4.7). Confounding Analysis – Assessing Confounding Effects

None of the TB treatment outcomes became significant or insignificant after adjusting for age, sex, distance from the clinic, education status, marital status and employment status. This multivariate model showed that age, sex distance from the clinic, education status, marital status and employment status had no confounding effect on DOTS support for the treatment outcome seen in the analysis. Also none of the factors became significant in the multivariate model.

CHAPTER FOUR: DISCUSSION

4.0). Introduction

This chapter summarises and discuss the findings of the study. The chapter starts with the study limitation and bias, followed by major findings and then secondary findings. Finally the findings are compared to the literature.

4.1.0). Study limitations

The limitations of the study were divided up into epidemiological, technical and statistical.

4.1.1. Epidemiological

This was a clinic based study and the cases were not representative of all TB cases in the community as it excluded patients treated in private practice and company clinics. But since TB drugs were only stocked in the public sector at the time, the cases from private and company clinics were likely registered at the clinic and the study was therefore most probably representative.

4.1.2). Technical

It was a cross-sectional study that looked at events a point in time and was not able give the sequence of events; infer causality and separate cause from effect because exposure and outcome variables were conducted at the same time.

The study used records at the clinic as source of data or information; it could have been affected by incomplete information. The records at the clinic were largely complete, with only three out of 861 cases excluded from analysis due to incomplete data. This was a small number to affect results.

4.1.3). Statistical

The limitation due to small sample size was overcome by large number of participants in the study. Of the 861 cases studied, 858 were analysed and provided accurate estimations of parameters during analysis.

4.2.0). Bias

4.2.1). Selection bias

The selection bias was avoided by including all patients in the TB register into the study unable to measure incidence and causation. But due to large number of study participants, the findings of the study finding can be generalised to the population of Mkhondo sub-district.

Being a facility based study; TB cases treated outside could have made findings not representative of the population. This was assumed to be small due to small private sector and restricted availability of drugs at the public sector.

Since it was a cross-sectional study, it was not possible to determine case definition of TB patient at the time of initiating treatment, as some patients were sputum smear negative. The study could have included patients treated as TB case while case definition could have excluded the patient.

4.2.2). Information bias could have arisen due to the incomplete records collected from the register and patient cards, but records were complete and captured by the researcher himself..

4.2.3). Confounding bias: The study analysed outcomes of TB treatment excluding patients transferred and moved outside the initiating site in the final outcome analysis. However, this groups was small in sum total (<10 cases, 0.011%) to affect the overall results of the study.

4.3.0). Major findings of the study

The number of TB cases showed an increasing trend during the study, with the number of cases rising every year during the study except in 2004.Overall, TB cases at Thandukukhanya clinic increased by 3.7 fold with the highest increase in 2005.

The overall TB cure rate at the clinic was very low (33.69%) and showed significant decrease every successive year except in 2005 (p=0.0001). The TB treatment failure rate was very low (0.82%) and stayed stable in every year, except in 2005 when it reached 3%. There was only a minor increase in proportion of cases that failed treatment during the study (p=0.506). The TB mortality was high (12.93%), with significant increase every year except in 2005 (p=0.0001). Overall, TB mortality increased by 8.6 fold during the study. The treatment interruption was high (10.20%) and increased 12 fold during the study (p=0.0001). The treatment interruption only started to increase in 2003 and increased every year until 2005. The majority of cases had completed treatment without conformation of cure by bacteriology (39.74%) and treatment completion rate increased 4 fold during the study, especially from 2003 – 2005. TB outcomes of moved (0.70%) and transferred (3.44%) contributed a small proportion of TB cases neither had any significant change in trend in the period of the study (respective p=values: 0.704, 0.621).

The overall treatment (DOTS) support in the programme was not only low (61% of cases had DOTS support), but significantly declined during the study compared to TB cases without DOTS support (p=0.0001). Though DOTS support remained constant from 200-2002, it decreased from 95.24% in 2003 to 27.02% in 2005.

DOTS support was significantly associated with an increase in TB cure (p=0.006) and low treatment interruption (p=0.0001) but had no effect on TB mortality (p=0.509).

The DOTS providers in the program changed in the period of the study, leading to different treatment outcomes. Of the five DOTS provider categories, the cases supported by relatives (p=0.003) and trained TB treatment supporters (TTTS) (p=0.040) were more likely to be cured; no DOTS supporter category was significantly associated with outcome completed treatment. The community health workers (p=0.001) and trained TB treatment supporters (0.0001) were significantly less likely to interruption TB treatment. The cases supported by trained TB treatment supporters were significantly more likely to die from TB (p=0.05).

4.4.0).Other findings by demographic factors

4.4.1). Findings by age:

The age category 25-34 years had the highest proportion of TB cases in every year with little variation during the study except in 2002. Overall, TB affected the younger age groups with 60% of TB cases in age range 25-44 years of age ((34.08% in 25-34and 25.38% in 35-44).

There was non-significant association between any age categories with treatment (DOTS) support and DOTS supporter type. However, TB cases in age categories above 3 4 years were significantly associated with TB treatment outcome completed treatment but not cure. TB mortality or treatment interruptions were not associated with age.

4.4.2). Findings by sex

Except for 2002 when more males and in 2003 when more female were treated for TB infection, the proportion of males to females was nearly equal. When the total number of patients was compared by age, ratio of males to females was, equal in children, more females in young adults and more males in older adults and elderly. The male was equal to female cases in 0-14 years (1:1), more females in 15 – 34 years (0.68:1) and more males in > 35 years (1.5:1). There was no evidence that showed sex was association with DOTS support, but evidence showed strong association with treatment interruption (p=0.022)

4.4.3). Findings by distance from the clinic

The majority of TB cases (99.37%) resided within 5 km from the clinic with no significant change in trend during the study. The cases residing 2-4 km from the clinic had were more likely to complete TB treatment and cure and provided DOTS support during treatment. There was a strong and significant of association with between cases residing 2-4km from the clinic with TB treatment completion (p=0.003), cure (p=0.0.038) and DOTS support (p=0.002).

4.4.4). Findings by education status

The majority of cases were educated (88%), with 40% primary, 47% secondary and 1% tertiary education and the trend was maintained in every year in the study. There was significantly low level of DOTS support in case with primary (p=0.010) and secondary education (0.001) compared to those uneducated. Likewise, mortality was low in cases with secondary education (p=0.001). However, compared to uneducated cases, those with primary education status were more likely to interruption TB treatment (p=0.028), suggesting primary education is unfavourable for TB treatment compliance.

4.4.5). Findings by employment status

Overall 93% of TB cases were unemployed and while there was a decreased of cases in the unemployed category from 2003 to the end of the study, there was an increased in the employed group in the same period. The unemployed category had low risk of TB mortality compared to employed and showed strong evidence (p=0.013).

4.4.6). Findings by marital status

The mortality risk from TB was low in married cases compared to those with single status and the evidence of this association was strong (0.010) and married cases were more likely than single to be cured of TB (p=0.007) or complete TB treatment (p=0.021).

4.4.7). Findings by TB treatment category

In total, 88% of cases were new TB patients while 12% were re-treatment. The proportion of new cases treated at the clinic increased in the first year and decreased progressively during the study period while the proportion of re-treated cases increased. The number of he re-treatment cases increased three-fold during the study. The re-treatment cases were less likely to have DOTS support compared to new cases (p=0.0002) and the majority of re-treatment cases were those previously cured of TB infection (45%).

4.4.8). Finding by TB site

There was only a slight increase in extra-pulmonary TB in the first three years and fluctuated in the last three. The cases with extra-pulmonary TB infection were significant less likely to interruption treatment (p=0.0001) compared to those with pulmonary TB. But cases with extrapulmonary TB were significantly less likely to be provided DOTS supported compared to pulmonary cases (p=0.038).

4.4.9). Findings by diagnostic methods

The majority of TB cases were pulmonary and diagnosed bacteriological confirmation of bacilli in the sputum (56.64%). However, there was a steady decline in bacteriological diagnosis every year during the study and a simultaneous increase in X-ray diagnosis, becoming a dominant diagnostic method in 2005. Compared to cases diagnosed by X-ray, those diagnosed by sputum smear were more likely to be provided DOTS support (p=0.001) during treatment.

4.4.10). AAFB in sputum

The majority of cases were sputum smear positive at registration (59.75%) but this steadily declined every year except in 2005. At the same time, the smear negative TB cases increased 10-fold during the same period and made up the majority of cases in 2004. Compared to smear negative TB cases, those smear positive were significantly more likely to die of TB (p=0.049).

4.5.0). Comparing study finding with findings of other studies

The rise in tuberculosis at Thandukukhanya Clinic was not an isolated trend at the facility. The Mkhondo sub-district (Mkhondo Sub-district TB report 2007)[22] and Gert Sibande district (Gert Sibande TB report 2008)[23] TB program reports both confirmed a rise in the number of TB cases by 30% and 22% respectively from 2003 to 2006. In addition, literature from Centre for Disease Control and Prevention (MMWR) [24] and study published in lancet both confirmed the rise in tuberculosis in Kwa-Zulu Natal, including outbreak of extremely resistant tuberculosis strain associated with HIV infected persons[25].

An increase trend of TB cases was documented in Khayelitsha in Western Cape between 2000 -2006 and found a four-fold increase in the number of cases[26]. However, nationally, the increase was only 1.9 fold from 2000 -2005 in a report by National TB Control Program[27]. The increase in Khayelitsha and Thandukukhanya clinic was similar despite the fact that Khayelitsha clinic group were HIV population with higher risk of TB co-infection. The HIV status was not included in this study. The small increase in the national figure could be due to difference in the population group in the report.

The study found sex difference existed among TB cases from the age 15 years above: more females between 15 – 34 years and more males from 35 years (p=0.017). This is different from the findings by World Health Organisation (WHO) in which global tuberculosis incidence rates are higher for males at all ages in most setting except in childhood that is higher in females with exception for high prevalence areas (WHO Fact Sheet, Gender and Health) [27, 28]. For example in Africa which is a high prevalence area, the female to male ratio increases from childhood up to age of 45-54 years and decrease until age of 65 years [27]. The sex differentials in prevalence rates begin to appear between 10 and 16 years of age, and remain higher for males than females thereafter. Just like in WHO report, the sex difference emerged after 14 years in this study but unlike WHO findings, the TB rates was higher in females before 35 years and reversed thereafter. The differences could be have been due to different population group targeted by the study compared to those in the WHO report, different risk face by males and females, traditional and cultural practices, roles of males and females in the community and practices of seeking medical treatment

The study found TB infection was high among the young age group and is supported by the finding by Statistics South Africa, that found the notification of TB and mortality due to TB was highest in age group 25-50 years in 2003[30]. This is the age group that are of reproductive age and economically viable and TB infection can negatively affect both aspects.

The study found an increase in sputum smear negative TB cases and a similar finding was noted in Khayelitsha in Cape Town, where there was steady increase in smear negative TB cases from 2000 – 2006 and decrease in smear positive TB cases from 2003[31]. In a policy report for recommendation of prevention of infectious disease in Western cape in 2007, smear negative TB was found to have increased by 46% in age group 25-34 years and by 45% in 35-44 years in data compiled from clinics, excluding hospitals[32]**.** The increase in high proportions of cases with smear negative TB are most likely due to the increase in associated with HIV in both this study and in Western Cape. In Kenya, smear negative TB cases reached 70% in 2006 and was associated with HIV co-infection[33].

The increase in smear negative TB cases could have in part been due to high HIV prevalence in the area that increased from 21% in 2003 to 37.9% in 2006 (HIV and Syphilis survey among antenatal mothers).
In Mkhondo sub-district, the HIV prevalence was 42% in 2006 (ANC survey 2006) and could partly explained the increased number of smear negative cases, since the TB bacilli load is scanty is HIV infected patients.

In this study the majority of TB cases that were re-treated previously cured as opposed to default treatment (OR= 3.3). This was a different finding from a study in Western Cape community study that found defaulting treatment was the only risk factor for being retreatment patient (OR = 4.10)[35,36]. The difference with this study could be due to the fact the communities in Western Cape and Thandukukhanya though are both South African, but are different in the prevalence of tuberculosis, including default rate, living conditions, cultural practices and study location and design (Western Cape study was prospective community based and the Thandukukhanya Clinic was cross sectional clinic based). The defaulted patients could have died and therefore did not come back to the facility.

In this study, 54% of TB cases converted smear negative and was lower than national average of 65- 68%. According to national TB Control program guidelines of 2000 and 2007 documents, all patients on treatment are expected to convert. But in South Africa, the sputum conversion with treatment was low but stable, 65% and 68% for all cases (new and retreatment) in 2004 and 2005 respectively [38]. The conversation rate in the study is lower than national average perhaps due to difference in the population from which data was obtained.

The proportion of cases cured decreased while the proportion of cases that completed treatment and died increased, more especially from 2002. The increase in treatment interruption only started in 2004 and continued to the end of the study. The reason for the increase in treatment interruption could not be identified from this study.

The study found that cure rate was associated with DOTS support, education and young age. A prospective study in Syria that found the tuberculosis cure rate was significantly higher among the younger and more literate patients[41]. Despite the fact that the two studies were conducted in different population, culture and using different designs, the finding were similar. However, Syrian study did not mention DOTS supporters.

A similar finding was documented in Ethiopia, where hospital cohort study found age <25 years was significantly associated with treatment success and age >25 years was associated with treatment interruption[41], not treatment completion like in this study. There was no link to being married with either treatment interruption or completion in Ethiopian study.

The study found that TB mortality was high in TB cases of young age, no education, married and female gender. In USA (Hawai'i) mortality was high in older age group of 45-65 years (Hawai'i 2006 Statistics). In South Africa, age group 25-54 has high mortality but the same age group is also heavily affected by HIV/AIDS (ANC survey 2007), a lethal combination with TB infection.

The study found a difference in treatment outcome among DOTS supporters. This was also confirmed by a prospective study in KwaZulu Natal found that the difference in treatment outcome among cases provided DOTS support by traditional healers compared to others. The treatment completion was high (89%) and mortality low (6%) for those supervised by traditional healers compared for others with 67% (p=0.002) and 18% respectively (P = 0.04). 5% of cases supervised by others transferred while none for traditional healer. The traditional healers were more successful because of generally high levels of satisfaction, easy access to them by patients and short waiting time when attending treatment[43]. Though this study did not include traditional healers as DOTS supporters, the study in Kwa Zulu Natal highlighted the difference in treatment outcomes by different DOTS providers.

Smear negative TB cases were twice more likely to interrupt treatment compared to positive smears. This finding was collaborated by CAPRISA centre study in Durban, Kwa Zulu Natal.

Cases with positive pre-treatment sputum smear were 7.8 times (CI: 2.2-26.6, p=0.0001) more likely to have DOTS support than those with negative smears and were more likely to be cured or completed treatment A study in Somaliland by Ahmed Haji Omar (Tuberculosis and TB Co-infection) confirmed poor treatment outcome among smear negative TB cases compared to smear positive cases, due in part to supervision by DOTS providers[44].

The cure rate was higher among TB cases with DOTS support compared to those without. A retrospective study in USA, San Francisco County, patients treated by directly observed therapy at the start of therapy (n = 149) had a significantly higher cure rate compared with patients treated by self-administered therapy (n = 223) (the sum of bacteriologic cure and completion of treatment, 97.8% versus 88.6%, p < 0.002), and decreased tuberculosis-related mortality (0% vs. 5.5%, p = 0.002)[45].

In South Africa, a study in KwaZulu Natal (Ethikiwini and Umgungundlovu districts) found TB cure rates high in districts and facilities with high DOTS coverage compared to those with low DOTS coverage (β=0.818, 95% CI 0.023-1.614; p=0.045) and concluded that cure rate can be improved if DOTS is implemented appropriately[28].

There was no significant factor confounding treatment support for treatment outcomes in this study. But an Indonesian study in Jakarta found urban residence confounded DOTS in TB cure[32], and was different finding from this study that found education and employment confounded DOTS support and was associated with treatment completion and low treatment interruption. Though this study did not explore urban residence, employment was not a confounding factor.

Chapter Five

5.0). Conclusion and Recommendations

5.1). Conclusions:

Though this was a cross-sectional study design, the number of participant was large and the records were complete with only five cases excluded from the study. The study biases and limitations were few and did not affect the overall results. This enabled considerable information to be adduced from the study and reach the following conclusion and recommendations.

TB an important disease burden in the community and showed an increasing trend in the number of cases, suggesting TB will continue to rise in the community, especially in the 25-54 years group. This group, which is the most economically active group showed both high disease burden as well as increasing trend of TB registration.

In general, the program performed well in the first three years of the study and produced indicators that measured well with the national targets. This could not be sais of the last three years that showed very low cure rate, high mortality, low DOTS support, low conversion smear done and adoption of X-ray to diagnose TB.

Though the study showed no sex difference in TB registration after 2003, there was no sex difference by age in <15 years but females were more affected in 15-34 years and the males in >34 years.

Although most TB cases resided within 5 km from the clinic, there was evidence that registered cases were mainly concentrated within 2km in the early period of the study but spread further away in the last three years. This suggests that TB was spreading to the wider community and reaching the areas previously less affected.

The educated TB cases that constituted 90% of cases showed mixed treatment outcomes- strong association with treatment interruption, low mortality and low DOTS support. The low DOTS support could explain the treatment interruption in educated cases, but not mortality, since DOTS support had no effect on TB deaths in the study

The results showed that TB increased in the employed group and the risk of death from TB was higher in the employed group compared to the unemployed. Unlike the employed group, the risk of death from TB was also low in the married group compared to single. But married cases were likely to complete treatment course without confirming sputum conversion.
For unexplained reason by this study, the new cases were likely to have DOTS support than re-treatment cases, despite the fact that retreatment cases increased and majority previously cure of TB.

Despite the increased in extra-pulmonary TB and the low level of DOTS support compared to pulmonary type, it was associated with low risk of treatment interruption in the study.

The method of TB diagnosis not only change from predominantly bacteriological in the first four years of the study to X-ray method in the last two years, the case were more likely to have DOTS support if the diagnosis is bacteriological. The more the cases were diagnosed by X-ray, the less the DOTS support.

Compared to smear positive, smear negative TB cases increased during the study, but the mortality was higher in the smear positive cases, especially if they did not convert during treatment.
Though the sputum smear conversion rate remained high throughout the study, the sputum smear conversion done decreased and cases that did not convert with treatment had high mortality.

Although DOTS support reached only 61% of cases and steadily declined during the study, it was associated with high cure rate and low treatment interruption. However, DOTS support did not have an effect on mortality.

The TB cure rate was low (33.69%) and there was no correlation between the decline trend of cure rate and that of DOTS support in the study. This is despite the fact that TB cases with DOTS support had higher cure rate.
The study findings compares well with studies in South Africa, African and non-African countries. In the same period, TB cases increased nationally and also in studied conducted in KwaZulu Natal and Khyelisha in Western Cape. Studies in Khayelisha and Kenya found an increase smear negative TB cases attributed to HIV epidemic, a similar finding to this study. The DOTS support was associated with TB cure in WHO study and study in Syria. Like in this study, the DOTS support types each produced different treatment outcomes in KZN study. Like in this study, the CAPRISA study found smear negative cases were likely to interrupt treatment compared to smear positive.

However, there were also differences room this study. In Khayelisha patients that defaulted previous treatment and not those that cured were in the re-treatment category. In Syria, DOTS was associated with education and young age. In this study, DOTS had association with age but with no education. The WHO study found sex ratio by age among cases not comparing to this study, but only for ages above 14 years. The sex ratio was the same in both studies in 0-14 years but was the reverse in 15-34 (more males) and > 34 years (more females).

5.2). Recommendations

The findings provide support for role DOTS in TB treatment success and confirms sputum smear as gold stand for pulmonary TB diagnosis. The study therefore recommends that DOTS support to all TB patients to improve the both the low cure rate and high treatment interruption found in the study.

Since the cure rate depends on the sputum smear for TB diagnosis, the study recommends sputum smear for all patients to improve TB cure rate and treatment success.

DOTS support was provided by five providers with different treatment outcomes. The design could not determine the reason and further study is needed to answer question why each DOTS provider produced TB treatment outcomes different from others

Additional studies are required to determine reason for the low treatment failure rate in the despite low DOTS support.

The study recommends that these findings are applied to TB programs outside Mkhondo sub-district.

References

1. Mkhondo Sub-district TB report 2007.

2. Gert Sibande District TB Report 2008.

3. [2, 3, 4, 5] World Health Organisation: Global TB Report 2006.

4. [6, 7, 8, 9]South African National TB Control Program: TB Report 2007.

5. [10, 11]World Health Stop TB: Global TB Report 2008.

6. A.N. Martinz, J.T. Rhee, PM Small and M.A. Behr. Sex differences in the epidemiology of tuberculosis in San Francisco. International Journal of Tuberculosis and Lung Disease. 2000; 4(1):26-31.

7. Borgdorff MW, Nagelkerke NJ, de Haas, Van Soolingen D. Transmission of mycobacterium tuberculosis depending on age and sex cases. American Journal of Epidemiology. 2001; 154(10); 934-43.

8. P. Nsubuga, J.L. Johnson, A. Okwera et al. Gender and HIV associated pulmonary tuberculosis: presentation and outcome at one year after beginning anti-tuberculosis in Uganda.

9. 9. Holmes CB, Housler H and Nunn. A review of sex differences in epidemiology of tuberculosis. International Journal of Lung Disease. (2):96-104.

10. 10. Diwan VK, Thorson A. Sex, gender and tuberculosis. The Lancet. 1999; 353(9157):1000-1.

11. 11. Hudelson, P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. Tuberculosis Lung Disease. 1996; 77(5):391-400.

12. 12. Henry M, Blumberg. Tuberculosis: Epidemiology-infectious disease. Medscape Today. ACP medicineonline. 2002.

13. Fourie P.B, Donald P.R. Epidemiology of tuberculosis. TB in childhood. Pretoria. Van Schails publishers. 1999.

14. Fourie B, Weyer K. Epidemiology. World Health Organisation (WHO) review of the tuberculosis situation in South Africa. Geneva: WHO, 1996.

15. Toro P, Coetzee D, Stein Z et al. TB epidemiology in Gugulethu, HIV endemic community outside Cape Town, South Africa. Anti-retroviral therapy 2003(8).

16. Karin Weyer. TB epidemiology and intervention case study: South Africa. Bulletin of World Health Organisation.2007 85(5).

17. Verver S, Warren R.M, Nulda Bayer et al. American Journal of Respiration and Critical Care Medicine. 2005; 171:143-5.

18. J. Cacho, A. Perez, Cano T et al. Recurrent tuberculosis from 1992 to 2004 in a metropolitan area. European Respiratory Journal 2007; 30:333-7.

19. Lindiwe Mvusi. Information equals better cure rates. WWW. Health-e.org.za

20. Levent Kart, Deniz Akduman, Remzi Altin et al. Fourteen-year trend of tuberculosis dynamics in the Northwest of Turkey. Respiration. 2003; 70:468-74.

21. D.L Stephen, L.G. Baker, K. Middelkoop, L. Meyer and R. Wood. Impact of HIV infection on the tuberculosis in peri-urban community of South Africa: The need for age-specific interventions. Clinical Infectious Disease. 2006; 42:1040-7.

22. E. Bumburidi, S. Ajeilat, A. Dadu et al. Progress towards TB control and determinants of treatment outcomes. Kazakhstan, 2000-2002. MMWR. Apr. 2006; 55(01):11-5.

23. Estifanos B. Shargie and Bernt Lindtjorn. DOTS improve treatment outcomes and service coverage for TB in South Ethiopia: a retrospective trend analysis. BMC Public Health 2005; 5:62.

24. Tuberculosis treatment success under DOTS. WHO. WHOSIS (WHO statistical Information System). 2006.

25. Report on the Integration of TB and HIV services in Site B Khayelitsha February 2005. Médecins Sans Frontières Infectious Disease Epidemiology Unit, School of Public Health and Family Medicine, University of Cape Town.

26. World Health Organization. Global tuberculosis control annual reports from 1997 to 2008. Geneva, Switzerland: WHO. http://www.who.int/tb/publications/en/ Accessed 20 April 2008.

27. M. Colvin, L. Gumede, K. Grimwade, D. Macher, D. Wilkinson. Contribution of traditional healers to rural tuberculosis programme in Hlabisa, South Africa. International Journal of tuberculosis Lung Disease. 2003; 7(9):S86-9.

28. Holmes C B, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis 1998; 2: 96–104.

29. M-E Jiménez-Corona[1], L García-García[1], K DeRiemer[2], L Ferreyra-Reyes[1] et al. Tuberculosis. Gender differentials of pulmonary tuberculosis transmission and reactivation in an endemic area. BMJ & British Thoracic Society; 2006.

30. Statistic South Africa: 2007

29. Paul Chinnock. Gender and TB: socio-cultural aspects. International Journal of Tuberculosis and Lung Disease. 3 Jul 2008.

30. Beatrice Nojilana, Rosana Norman, Desiréé Pieterse and Michelle Schneider. Initial estimates from the South African National Burden of Disease Study, 2000. MRC Policy Brief No. 1, March 2003.

31. Infectious Disease and Epidemiology Unit, School of Public Health and Family Medicine, University of Cape Town. City of Cape Town Health Services. Report on the Integration of TB and HIV Services in *Ubuntu* clinic (Site B), Khayelitsha. Médecins Sans Frontières. November 2007.

32. Beverly Draper David Pienaar Warren Parker Thomas Rehle. Recommendations for Policy in the Western Cape Province for the prevention of Major Infectious Diseases, including HIV/AIDS and Tuberculosis. Final report June 2007.

33. John Mansoer, Suzanne Scheele, Katherine Floyd, Christopher Dye, Joseph Sitieneic & Brian Williams. New methods for estimating the tuberculosis case detection rate in high-HIV prevalence countries: the example of Kenya. Bull World Health Organ 2009; 87: 186–192.

34. [34,40,43] Hamed Haji Omar Askar. Tuberculsosi and HIV Co-infection in Two Districts in Somaliland. Academic dissertation.University of Tampere Finland. 2008.

35. Den Boon, Saskia; van Lill, Schalk W.P.; Borgdorff, Martien W.; Enarson, Donald A.; Verver, Suzanne. High prevalence of tuberculosis in previously treated patients, Cape Town, South Africa. Emerging Infectious Diseases; August 1, 2007

36. Suzanne Verver, Robin M Warren, Zahn Munch et al. Transmission of tuberculosis in a high incidence urban community in South Africa. International Journal of Epidemiology, Volume 33, 2 (351-7)

37. Meaza Demissie, Bernt Lindtjorn, and Yemane Berhane. Patient and health service delay in the diagnosis of pulmonary tuberculosis in Ethiopia. *BMC Public Health* 2002, 2:23i:10.1186/1471-2458-2-23.

38. Floyd K, Blanc L, Raviglione M, Lee J-W. Resources required for global tuberculosis control. *Science* 2002; 295:2040-2041

39. Amornrat Anuwatnonthakate, Pranom Limsomboon, Sriprapa Nateniyom et al. Directly Observed Therapy and Improved Tuberculosis Treatment Outcomes in Thailand. PLoS ONE 3(8): 2008.

40. [41]H. Bashour and F. Mamaree. Gender differences and tuberculosis in the Syrian Arab Republic: patients'attitudes, compliance and outcomes. Eastern Mediterranean Health Journal, Vol. 9, No. 4, 2003 (757)

41. [42]Estifanos Biru Shargie, Bernt Lindtjørn. Determinants of Treatment Adherence Among Smear-Positive Pulmonary Tuberculosis Patients in Southern Ethiopia. PLoS Medicine, February 2007 Issue

42. [43]Hawai'i State Department of Health. Tuberculosis Control Program. 2006 Statistics