

**DRUG DELIVERY PROBLEMS TO TB PATIENTS IN
GAUTENG**

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A research report submitted to the Faculty of Health Sciences, University of the
Witwatersrand, Johannesburg, in partial fulfilment of the requirements of the degree of
Master of Pharmacy in Clinical and Hospital Pharmacy

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I, Confidence Mabena declare that the research report is my own work. It is being submitted for the degree of *Master of Pharmacy in Clinical Hospital Pharmacy* in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

C Mabena

5th day of OCTOBER, 2000

In memory of my grandfather

Johnson Tshinetise

1914-1992

ABSTRACT

After declining for many years, the incidence of tuberculosis (TB) is on the increase again. With TB resurgence there is also resistance of some TB strains to the commonly used TB drugs. This condition is known as multi-drug resistance tuberculosis (MDR TB). Among all factors that increase TB and MDR TB, treatment compliance and completion is the greatest challenge. MDR TB is mainly caused by poor adherence to TB treatment by either the patient or the prescriber.

In order to improve patient adherence to treatment, Directly Observed Therapy (DOT) has been implemented in many countries including South Africa. DOT means that each consumption of TB drugs by the patient is observed by a reliable person. Even with DOT in place, many patients still do not adhere to the prescribed treatment.

This study aimed at determining from health workers the following:

- Problems experienced by the health workers when giving treatment to TB patients,
- causes for non-adherence to TB treatment, and
- what could be done to make DOT more effective.

A questionnaire was used to gather information. All clinics rendering TB services in Gauteng were considered in this study. Two questionnaires were sent to each of the 138 participating clinics and had to be completed by any two health workers involved in the treatment of TB patients. Only 69 of the 276 questionnaires sent, were returned completed (25%).

Information gathered from the questionnaires revealed that patients seen at TB clinics in Gauteng came from various residential areas including townships, suburban rural and informal settlement. The Pearson chi squared test showed that there was no association between the percentage of patients who completed treatment and the number of patients seen at a clinic, or between the percentage of patients who completed treatment and the working hours at a particular clinic.

The main cause of non-compliance shown by the results of this study was that patients discontinued treatment as soon as they felt better. Other causes of non-compliance mentioned by health workers included patient denial of having TB, ignorance, long treatment periods and many drugs that were to be taken during treatment. Health workers revealed that the main problem experienced in giving treatment to TB patients was that of defaulting. The majority of these respondents suggested education as one way of making DOT more effective.

In terms of this study, it can be concluded that education on TB at various levels namely the patient, the health care worker and the community, is recommended. Education on the disease TB and its optimal treatment will improve patient compliance, decrease defaulting in delivering TB drugs to patients and make DOT more effective.

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TABLE OF CONTENTS

	Page
DECLARATION	ii
DEDICATION	iii
ABSTRACT	iv
ACKNOWLEDGEMENTS	vii
TABLE OF CONTENTS	viii
LIST OF FIGURES	x
LIST OF TABLES	xi
CHAPTER 1 - INTRODUCTION	1
1.1 Statement of the problem	1
1.2 Importance of the study	6
1.3 Aims and objectives	8
CHAPTER 2 - METHODOLOGY	9
2.1 Study design	9
2.2 Pilot study	9
2.3 Sampling method	9
2.4 Measuring instrument	10

2.5 Data processing and statistical analysis	10
2.6 Ethical considerations	11
CHAPTER 3 – RESULTS	12
CHAPTER 4 - DISCUSSION	28
CHAPTER 5	
5.1 Conclusions	37
5.2 Limitations of the study	38
5.3 Recommendations	38
APPENDIX A	40
APPENDIX B	47
APPENDIX C	48
APPENDIX D	49
REFERENCES	50

LIST OF FIGURES

Figure	Page
3.1 Number of responses received per region	13
3.2 Number of days that clinics are open per week	17
3.3 Clinics' responses on the percentage of patients who completed treatment that are cured	19

LIST OF TABLES

Table	Page
1.1 Treatment regimen for new adult TB cases	5
1.2 Treatment regimen for adult retreatment cases	5
3.1 Responses to questionnaires per region	12
3.2 Number of responses received from various regions	13
3.3 Residential areas from which most patients were seen	14
3.4 Responses of clinics from different regions on the percentage of patients who successfully completed treatment	15
3.5 Comparison between percent of patients completing treatment and the number of patients seen at a clinic	16
3.6 Comparison between working hours at the clinics and the percent of patients that completed treatment	18
3.7 Major causes of non-compliance	20
3.8 Actions taken to ensure that defaulters were convinced to resume treatment	21
3.9 Frequency of shortage of TB medicine	24

CHAPTER 1

INTRODUCTION

1.1 Statement of the problem

Tuberculosis (TB) is a chronic infection caused by *Mycobacterium tuberculosis* (1). It is generally transmitted by inhalation or ingestion of infected droplets and usually affects the lungs, although infection of multiple organ systems can occur including the kidneys, skin, middle ear, bones, joints and meninges. Inhaled organisms not successfully killed by cell-mediated immunity can spread through the blood or lymphatic system. Infected organs may not show any pathology for many years. Post-primary disease can manifest with pregnancy, stress, weakened immune system, other diseases or old age. Relapse most commonly occurs in lung apices in 85% of the patients. Highest risk for active disease is within the first two years after exposure (2). Experts estimate that one smear positive patient could infect three others before they start treatment. Those dropping out before they are cured infect ten others before they die or are retreated (3).

Tuberculosis is by far the most common notifiable disease in South Africa (SA) with 80000 to 90000 cases reported annually (4). It is also an important cause of morbidity and mortality in South Africa (5). One and a half million new cases are reported each year in Sub-Saharan Africa (6). A third of the world's population are infected with the TB organism (7,8).

After declining consistently for several decades, the incidence of TB surged after 1985. Sixty two thousand more cases, than had been predicted by the pre-1985 trend, were reported in the USA by 1993. The incidence of TB is expected to increase from 8,8 million cases in 1985 to 10,2 million cases by the year 2005. A significant proportion of these cases is due to recent transmission of infection, confirming the suspicion that untreated cases serve as a reservoir to infect others (9,10). This increase can also be due to improper adherence to treatment programmes, poor adherence by the patient, and the explosive effect of the Human Immuno Deficiency Virus (HIV) epidemic (11).

It is well recognised and has often been said that TB is the largest cause of death from a single infection worldwide (6-8,11). Three million deaths due to TB occurred in 1985 worldwide and 3,5 million deaths can be expected in the year 2000. Deaths caused by TB could be seen as failures of TB control programmes (12).

The World Health Organisation (WHO) has set specific targets aimed at successful TB control. These are 70% detection of TB cases and 85% cure of new cases. The setting of these targets was prompted by the worldwide resurgence of TB in 1985 (13).

Diagnosis of new cases is of no value if a good treatment programme is not ensured. Careful bacteriologic monitoring of treatment progress is essential to detect early failures or lack of patient adherence (14). Patient adherence or compliance refers to adherence by patients to the prescribed treatment regimen. It has been shown that chemotherapy for smear positive TB is the cheapest health intervention measure available in developing countries. It is even cheaper than

other cost-effective interventions such as measles immunisation and oral rehydration therapy (15).

TB is almost 100% curable and is 100% preventable and yet is nowhere near being eliminated in any area of the globe, including the most developed nations (8). Overall, TB control programmes in SA have a cure rate of 56% (3). Completion of anti-tuberculosis treatment is of the foremost importance in TB control programmes (16,17). The Centre for Disease Control and Prevention (CDC) calls for 90% of all TB cases to complete a recommended six months course of chemotherapy. If this treatment is completed, 90% cure rate is achieved, and fewer than 5% of treated cases will experience relapse (9).

We are now threatened by two rather serious complications affecting the TB epidemic - multidrug resistant tuberculosis (MDRTB) and Acquired Immune Deficiency Syndrome (AIDS). Resistance to standard chemotherapy for TB is an increased problem worldwide (3,18-21).

MDRTB is resistant to at least isoniazid (INH) and rifampicin (Rif). MDRTB has been associated with treatment failure and high mortality especially in those patients co-infected with HIV. The economic consequences of TB are great. Treatment of MDRTB is even more costly because of the prolonged treatment period and the number of drugs that are to be taken by the patient. Major causes of MDRTB are HIV, failure to complete therapy by patients, homelessness, migration from endemic regions, substance abuse and mismanagement by physicians (3,9,18,22). Sub-therapeutic treatment of MDRTB can kill up to 75% of its victims (18,22). History of previous inadequate treatment with anti-tuberculosis drugs and mismanagement by physicians, and not HIV are the principal factors associated with MDRTB (23,24).

Among all the factors that increase TB and MDRTB, treatment completion is the greatest challenge in TB treatment. Because TB is a chronic condition it requires prolonged treatment. The most difficult task for TB control is to persuade patients to take their prescribed medication regularly for the required duration as prescribed. For successful completion of treatment, motivation and co-operation are essential for patient's adherence. Lack of motivation could be due to ignorance about the harmful effects of TB both on the patient himself and on the community (9).

The ability to predict adherence to and completion of treatment is unreliable. Demographic variables such as occupation, level of finance and others do not reliably predict adherence to treatment. Adherence to most medical regimens is inversely proportional to the number of drugs administered, length of therapy, frequency of drug administration and the overall complexity of the treatment regimen (9).

Patients with TB take many medicines. For example the number of tablets taken by adult patients varies according to the weight of the patient. The South African Treatment Guidelines recommend that patients take treatment as summarised in table 1.1 for new cases (TB patients). The same guidelines recommend the treatment regimen in table 1.2 for retreatment cases (25).

Table 1.1 Treatment regimen for new adult TB cases

Pretreatment body weight	2 months initial phase		4 months continuation phase	
		Combination tablet RHZE 120/60/300/200mg or 120/60/300/225mg	or	Combination tablet RH 150/100mg
Less than 50kg	4 tablets		3 tablets	
More than 50kg	5 tablets		2 tablets	

R=rifampicin; H=isoniazid; Z=pyrizinamide; E=ethambutol

Table 1.2 Treatment regimen for adult retreatment cases

Pretreatment body weight	2 months initial phase		3 rd month	5 months continuation phase	
		RHZE*		streptomycin	RHZE*
Less than 50kg	4 tablets	750mg	4 tablets	3 RH and 1 E tablets	
More than 50kg	5 tablets	1000mg	5 tablets	2 RH and 3 E tablets	

*Same strength as in table 1.1.

Note that in table 1.1 and table 1.2, treatment is taken once daily, 5 times per week.

Certain circumstances may necessitate a 3 times a week regimen, whereby the use of a 3 times a week regimen should be approved and co-ordinated at provincial level. The use of fixed-dose combinations are encouraged to enhance patient adherence, reduce the risk of inappropriate monotherapy and to shorten the duration of treatment (3,25). An American textbook mentions that rifampicin and isoniazid are just as effective if given together for 9 months (26).

1.2 Importance of the study

Between 20% and 50% of all TB patients do not complete their treatment (27). Defaulting from treatment does not only lead to MDRTB but to relapse, delaying in smear conversion from positive to negative, spreading of the bacteria and increasing the number of TB patients. Non-adherence or poor compliance is also regarded as the principal cause of failure of treatment of TB because patients remain infectious and can develop resistant organisms (5,16).

Adherence requires accessible and appropriate health care. To increase the probability of treatment completion, directly observed therapy (DOT) has been recommended as a standard of care to TB patients. DOT requires that a responsible observer observe each ingestion of medicine by the patient (3,5,16,18,19). The Minister of Health in South Africa called for a countrywide implementation of DOT in 1996 (3). Even with DOT in place, patients still do not always complete treatment (28). In light of this, several specific strategies have been used. Some strategies aim to change the behaviour of health personnel, which includes training, motivation and supervision. Others are directed at the patients and they include education, reminders and prompts to reattend and financial incentives to return for treatment (27).

The success of observation is likely to depend on how attractive it is to both the observer and the patient and not on the act of observation. For example, patients at Hlabisa village in South Africa are attracted partly by the fact that DOT costs less than going to a hospital for treatment. In Bangladesh, attraction is through payment of a bonding incentive between patients and community health workers (6).

The WHO and the International Union Against Tuberculosis and Lung Diseases (IUATLD) had previously advocated a strategy of hospital admission for the first 2 months of treatment, primarily as a way of ensuring adherence. This strategy was effective until recently. However, the epidemic of HIV and TB is such that hospital based care is no longer feasible. From 1985 to 1995 bed occupancy in some hospitals in Sub Saharan Africa reached 400%. Therefore, DOT and not hospitalisation, is advocated to promote adherence (6).

The critical aims of completion of treatment are to avoid persistent infectious state on the part of the patient and higher rates of treatment failure, relapse and drug resistance (1,29). Efficient detection of TB cases and completion of therapy remain central to TB control (29). However there are many reasons for non-adherence to TB treatment.

1.3 Aims and objectives

The main aim of this study was to determine what problems are encountered by health workers in delivering (administering or giving) treatment to TB patients. This was to be achieved by questioning health workers on the following:

- What problems do they encounter when giving drugs to TB patients?
- What are the causes of non-adherence to TB treatment by TB patients?
- What could be done to make DOT more effective.

CHAPTER 2

METHODOLOGY

2.1 Study design

This was a mail survey carried out in Gauteng province. Gauteng is divided into 5 regions namely: Central Wits, East Rand, Pretoria, Vaal and West Rand. Because of the low response rate that is associated with mail surveys, all clinics that provide TB services (178 clinics) were included in this study. The study was carried out over four months (March 1999 to July 1999).

2.2 Pilot study

A pilot study was undertaken and the questionnaire (measuring instrument) was sent to four clinics in Pretoria in order to find out if the questionnaire was easy to complete and how long it would take to complete it.

2.3 Sampling method

The 1996 list (the most current list at the time of conducting this study) of TB service providers from the Department of Health in Gauteng was used to select the sample group for this study. All the clinics that were listed (178 clinics) were included in the sample. Two questionnaires per clinic were mailed and they were to be completed by any two health workers involved in the treatment of TB patients. The reason for sending two questionnaires per clinic was to increase the response

questionnaires than if only 1 questionnaire is addressed to a specific person in a certain clinic.

Before the questionnaires were sent, clinics were contacted telephonically and asked permission to conduct the research at their facilities. The telephone numbers used were also found in the 1996 list of TB service providers. Not all clinics gave permission, some could not be reached by telephone. The questionnaires were mailed accompanied by a letter introducing the researcher, aims and objectives of the research and stating that participation is voluntary (example of the letter is reproduced in Appendix B). The questionnaires were sent to those clinics that gave permission as well as to those that could not be reached telephonically. Two hundred and seventy six (276) questionnaires were sent to 138 clinics i.e. two questionnaires per clinic.

2.4 Measuring instrument

A questionnaire was designed to be used as a data gathering tool. A copy of the questionnaire used is attached in Appendix A.

2.5 Data processing and statistical analysis

Each clinic was allocated a specific code which was marked on the particular clinic's questionnaire. This was done in order to determine which clinics had not returned their questionnaires. On receiving the responses, the codes on the questionnaires were matched to the clinic that was allocated that specific code. Clinics were given up to six weeks to return the questionnaires. After six weeks another pair of questionnaires was sent to those clinics that neither returned the completed questionnaires nor the blank ones. If only one questionnaire was returned from a

particular clinic, the second pair of questionnaires was not sent to that clinic. The clinics that received the second set of questionnaires were given 4 weeks to respond. After 4 weeks all the completed questionnaires which had been returned were regarded as data for this research.

The questionnaire data were analysed with the help of statisticians from the Medical Research Council in Pretoria, using the Epi Info programme.

2.6 Ethical considerations

The post-graduate committee and the research and ethics committee of the University of the Witwatersrand have approved the protocol for this research. See Appendices C and D for letters (certificates) of approval.

CHAPTER 3

RESULTS

The overall questionnaire response (return) was poor even after the second pair of questionnaires were sent. Out of the expected 276 responses, only 69 completed questionnaires were received (i.e. 25%). The comparison between the number of questionnaires sent and those received is shown in Table 3.1

TABLE 3.1: Responses questionnaires per region

Region	Number of questionnaires sent	Questionnaires returned blank	Questionnaires Completed	Percent completed
Central Wits	56	3	5	8,9%
East Rand	98	2	24	24,5%
Pretoria	40	3	16	40,0%
Vaal	48	0	14	29,2%
West Rand	34	3	10	29,4%
TOTAL	276	11	69	

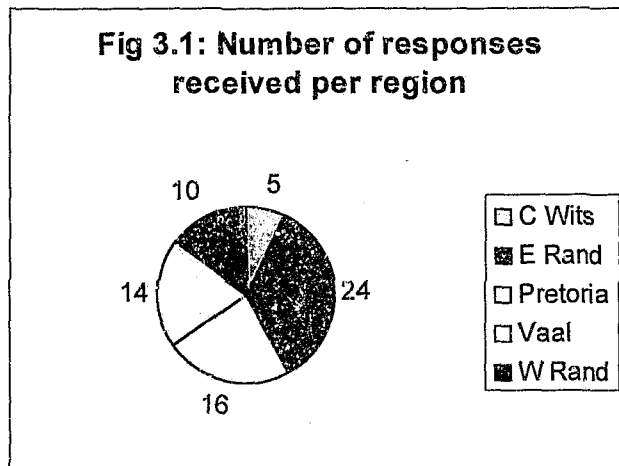
Eleven (11) questionnaires were returned blank and 69 were completed. Since a 1996 list of clinics was used, the poor response might be due to the possibility that some clinics might have closed down or some changed addresses. Six questionnaires were returned to the sender because they did not reach their destinations. Twenty one clinics completed both questionnaires and 27 completed only one questionnaire.

Question1: In which region is your clinic located?

Of the completed questionnaires 7,2% were from Central Wits, 34,8% from East Rand, 23,3% from Pretoria, 20,3% from Vaal and 14,5 % from West Rand. The distribution of responses from various regions is indicated in table 3.2.

TABLE 3.2: Number of responses received from various regions.

REGION	CLINICS	PERCENTAGE
Central Wits	5	7,2%
East Rand	24	34,8%
Pretoria	16	23,2%
Vaal	14	20,3%
West Rand	10	14,5%
TOTAL	69	100,0%



Question 2: From which areas do most of your patients come from?

Patients from different types of residential areas visited the clinics in Gauteng. The different areas are indicated in table 3.3.

TABLE 3.3: Residential areas from which most patients were seen

TYPE OF AREA	NUMBER OF CLINICS	PERCENTAGE
Suburban	12	17,4%
Township	47	68,1%
Informal Settlement	39	56,5%
Rural	10	14 %
Industrial	1	1,5%

Note: Any particular clinic could see patients from more than one type of area, hence percentages may add up to more than 100%.

Question 7: According to your clinic's statistics, what percentage of your TB patients complete their course of treatment (medication)?

Some clinics reported that 50% or less of their patients had completed treatment. Table 3.4 shows the percentage of patients who completed treatment, according to the regions where they were seen (P=0,26).

TABLE 3.4: Responses of clinics from different regions on the percentage of patients who successfully completed treatment.

REGION	PERCENTAGE PATIENTS WHO COMPLETED TREATMENT				TOTAL
	91-100 %	76-90 %	51-75 %	50% or less	
Central Wits	1 (20,0%)	2 (40,0%)	2 (40,0%)	0 (0,0%)	5
East Rand	2 (8,3%)	16 (66,7%)	4 (16,7%)	2 (8,3%)	24
Pretoria	6 (37,5%)	4 (25,0%)	3 (18,8%)	3 (18,8%)	16
West Rand	2 (14,3%)	4 (28,6%)	6 (42,9%)	2 (14,2%)	14
Vaal	1 (10,0%)	5 (50,0%)	4 (40,0%)	0 (0,0%)	10
TOTAL	12 (17,4%)	31 (44,9%)	19 (27,5%)	7 (10,1%)	69

Question 3: How many TB patients visit your clinic for consultation per month?

Question 7: See previous page for this question.

The number of patients seen at a clinic per month was compared to the percentage of patients who completed treatment). Table 3.5 determines if the two variables were related. The value of the Pearson chi squared with 9 degrees of freedom ($p=0,71$), which showed that the percentage of patients who completed treatment was not related to the number of patients seen at a particular clinic.

TABLE 3.5: Comparison between percent of patients who completed treatment and the number of patients seen at a clinic.

Number of Patients seen monthly	PERCENTAGE OF PATIENTS WHO COMPLETED TREATMENT				
	91-100%	76-90%	51-75%	50% or less	TOTAL
Less than 50	8 (25,0%)	14 (43,7%)	7 (21,9%)	3 (9,4%)	32
50-99	2 (16,7%)	6 (50,0%)	4 (33,3%)	0 (0,0%)	12
100-200	0 (0,0%)	6 (50,0%)	4 (33,3%)	2 (16,7%)	12
More than 200	2 (15,4%)	5 (38,5%)	4 (30,8%)	2 (15,4%)	13
TOTAL	12 (17,4%)	31 (44,9%)	19 (27,5%)	7 (10,1%)	69

Question 4: How many nursing staff and other health care workers employed at your clinic are engaged in TB services?

Of all the respondents, only 4 mentioned that they had more than 5 health workers involved with the treatment of TB patients, one respondent did not give a response to this question.

Question 5: How many days a week is your clinic open?

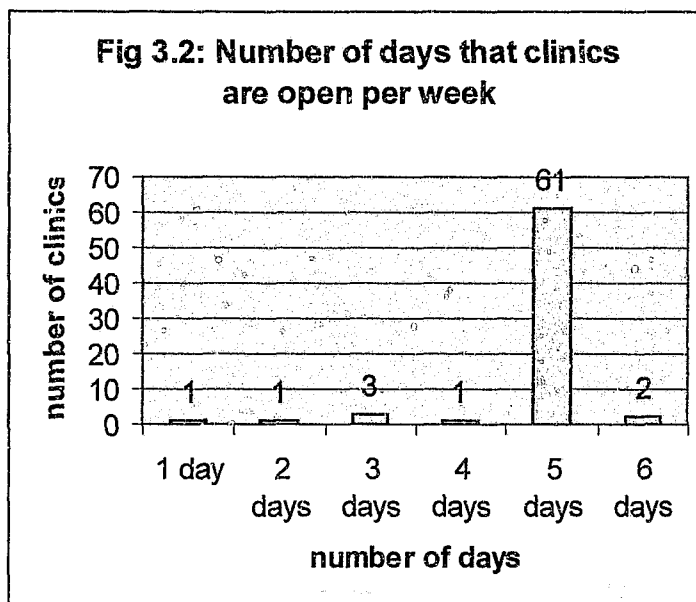


Figure 3.2 shows that the majority of clinics are open for 5 days per week.

Question 6: For how long are your clinics open per day or session?

None of the clinics that responded was open for less than 4 hours per day. Eighty four percent ($n = 58$) were open for 4-8 hours every working day and sixteen percent ($n = 11$) were open for more than 8 hours. A comparison was made between the working hours at a clinic and the percentage of patients who completed their TB treatment (question 6 and 7). Analysis of the data gave the Pearson chi squared as 5,57 with 3 degrees of freedom ($p=0,135$). The results are shown in Table 3.6.

The Pearson chi squared test showed that there was no association between the percentage of patients who completed treatment and the working hours. However, it was observed that greater proportion of clinics with shorter working hours indicated that at least 76% of their patients completed treatment.

TABLE 3.6: Comparison between working hours at the clinics and the percent of patients that completed treatment.

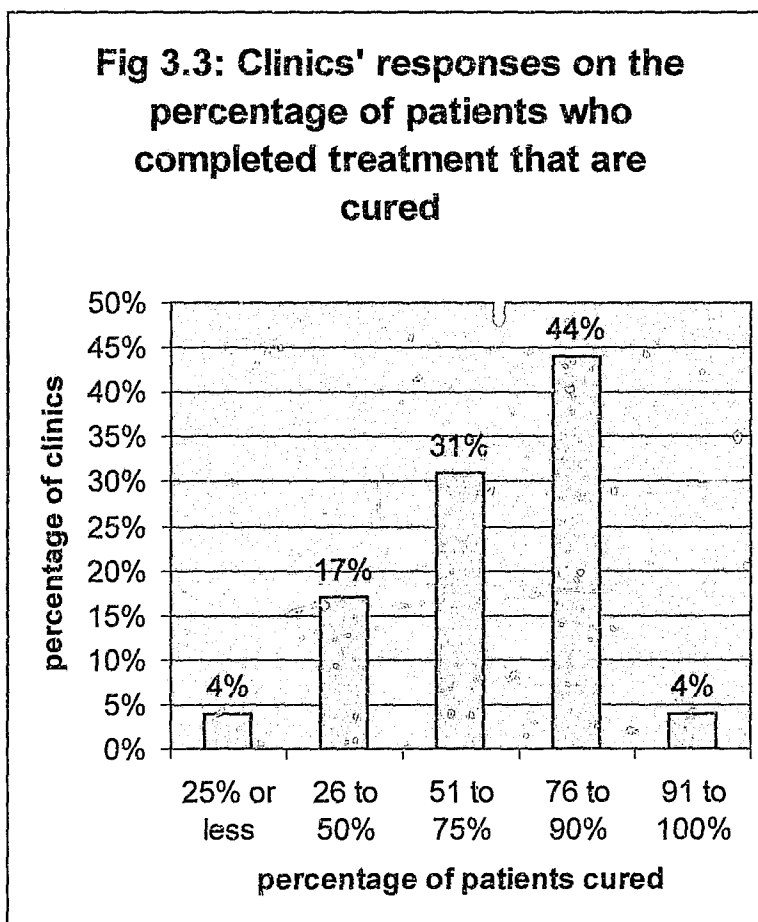
Working hours	PERCENT OF PATIENTS WHO COMPLETED TREATMENT				TOTAL
	91-100%	76-90%	51-75%	50% or less	
4 to 8 hours	10 (17,2%)	29 (50,0%)	13 (22,4%)	6 (10,3%)	58
More than 8 hours	2 (18,2%)	2 (18,2%)	6 (54,6%)	1 (9,1%)	11
TOTAL	12 (17,4%)	31 (44,9%)	19 (25,5%)	7 (10,1%)	69

Question 8: Are all of your patients who finish treatment cured?

Fourty six respondents mentioned that not all TB patients who completed treatment were cured, 22 said that all patients completing TB treatment were cured and 1 did not respond.

Question 9: If the answer to question 8 is no, what is the percentage of patients that are cured?

Figure 3.3 shows the percentage of patients who completed treatment that were cured – those clinics that responded that all patients completing treatment were cured did not respond to this question



Question 10: From your point of view, what are the main causes of non-compliance to TB treatment that you encounter in your clinic?

According to the respondents the main cause of non-compliance in TB patients was that patients stop treatment because they felt better. Table 3.7 indicates the main causes of non-compliance.

TABLE 3.7: Major causes of non-compliance.

CAUSE	NUMBER OF CLINICS (%)
Patients feeling better	56 (81,2)
Denial of having TB	36 (52,2)
Ignorance	33 (47,8)
Long period of treatment	31 (44,9)
Staying far from clinic	23 (33,3)
Lots of medicines taken	21 (30,4)
Poverty	21 (30,4)
Patients visiting without transfer letters	17 (24,6)

Note: Any particular clinic could have more than one cause of non-compliance, hence percentages may add up to more than 100%.

Some respondents also mentioned that some employers denied their workers permission to visit the clinics either for consultation or for receiving treatment. They also did not want to give medication from the workplace. Some employers even went to the extent of retrenching TB sufferers.

Question 11: How do you trace defaulters?

Whenever there were patients who did not take medicines regularly, health workers traced them a) telephonically, b) visiting the patients at home, c) contacting the person who supervises the patient in taking treatment or d) writing letters to the patient. One respondent mentioned that their clinic was too busy therefore they did not trace defaulters.

Question 12: How do you convince defaulters to continue taking their medicines?

After finding the patients who defaulted from treatment, the health workers convinced them to resume with treatment by the actions indicated in Table 3.8.

TABLE 3.8: Actions taken to ensure that defaulters were convinced to resume treatment.

ACTION	NUMBER OF CLINICS (%)	
Health education	65	(94,2)
Enforce DOT	53	(76,8)
Involve treatment supporters	40	(58,0)
Involve patients in TB projects	18	(26,1)
Threaten by reporting to police	2	(2,9)

Another respondent mentioned that patients should be admitted to hospital in order for them to resume treatment.

Question 13: After finding defaulters, do they continue with treatment?

Twenty two (39,2%) responded that after finding defaulters they always resumed treatment.

Forty seven (68,1%) responded that defaulters would sometimes resume treatment.

Question 14: Do you give all your DOT from your clinic?

Thirteen (18,8%) of the respondents mentioned that they gave all the TB treatment directly from the clinic. These respondents were asked to go directly to question 19.

Question 15: Where else is DOT given?

The respondents that did not give all their DOT from the clinics mentioned that they used family members, doctors, teachers, employers, neighbours or community members to give treatment.

Question 16: Do the people or institutions in question 15 give feedback about the patients whom they supervise in taking TB medication?

Question 17: How often do they give feedback?

Of all the clinics that gave DOT outside the clinic 9 (16,1%) did not get feedback from the treatment supervisors on whether the patient was compliant (question 16). The majority of DOT supervisors communicated with the clinic only when there was a problem (question 17).

Question 18: If they do not give feedback, how do you know if the patient is taking treatment as prescribed?

In order to determine whether the patient was taking treatment, the health workers at those clinics that did not get feedback did one of the following:

1. Contacted the patient if he did not show up on the expected return date (n=10).
2. Checked if the treatment observer had marked the patient retained card (n=8).
3. Visited the home of the patient, asked the patient or the treatment observer if the patient was taking treatment regularly as prescribed and checked the quantity of the remaining medicines (n=6).
4. Contacted the treatment observer and enquired if the patient was taking medicine or asked the

patient on the next visit (n=6).

5. Asked the patient to bring the remaining medicines on the next clinic visit to the clinic. The medicine remaining was counted and compared with the quantity that should have been in the container (n=2).
6. One respondent mentioned that they depended on sputum conversion from positive to negative.

(Note: Respondents gave more than one answer, hence n may add up to more than 9).

Question 19: Do you encounter situations where a patient comes from other clinics to your clinic without medication?

Forty eight of the respondents said that they encountered situations where patients came from other clinics without TB medicines. Twenty said that they never encountered such a situation. One respondent did not respond to that question.

Question 20: If the answer to question 19 is yes what do you do?

Those who indicated that they saw patients from other clinics, said that in such situations they did one of the following:

1. Contacted the clinic where the patient came from, got the patient and medication history, then continued with treatment (n=15).
2. Continued with treatment if patient had a treatment card or a referral letter (n=12).
3. If the patient had neither of the above, the patient was asked about his/her medication

history and continued with treatment as described by the patient (n=12).

4. Investigated and then treated according to the Standard Treatment Guidelines from the Department of Health (n=8).
5. Sent the patient back to the clinic where he/she came from (n=2).

(Note: one clinic gave more than one answer, hence n is greater than 48).

Question 21: Do you ever run short of TB drugs?

The response to this question is as shown in Table 3.9.

TABLE 3.9: Frequency of shortage of TB medicine.

	NUMBER OF CLINICS	PERCENTAGE
Never	56	82,4%
Once a year	5	7,4%
Twice or more a year	7	9,9%
TOTAL	68	100,0%

One clinic did not respond to this question. The longest period that clinics were without TB treatment was up to one month.

Question 22: What do you do if you run short of TB drugs?

Question 23: How long does it take to get new stock if you've run out of TB medicines?

When clinics were out of stock they either borrowed from the neighbouring clinics or hospitals, or contacted the distributor to supply them with the required medicines. The majority of the respondents mentioned that they were able to receive stock within one day.

Question 24: What other problems do you encounter with giving TB medicines to patients?

The problems encountered by health workers when giving TB drugs were:

1. Defaulting from taking treatment because there were too many tablets to be taken as well as a painful injection (n=15).
2. Defaulting because of side effects resulting from taking TB drugs (n=6).
3. Patients complained that TB drugs made them feel hungry and they did not have money to buy food (n=5).
4. Lack of co-operation from employers (n=4).
5. Patients who refused to be supervised at clinics (n=2).
6. No dosage form for children (n=2).
7. Migration from one place to another (n=2).
8. Patients discharged from hospitals did return to clinics to continue treatment (n=2).
9. Poor understanding on how to take the medicines (n=1).
10. Shortage of staff which made DOT impossible at some clinics (n=1).

11. Social problems e.g. drinking (n=1).

(Note: Some respondents did not respond to this question, hence n is less than 69).

Question 25: In your opinion what do you think must be done to make DOT more effective, and how?

Most respondents answered the question of “what must be done to improve DOT” and “how it could be done” similarly (question 25). Eight (11,6%) of the returned questionnaires had no response to this question. The remainder responded as follows:

1. Educate the patient, health care workers and the whole community about the disease (n=30).
2. Involve the community by erecting DOT stations closer to where the patients live (n=18).
3. Involve health workers in the private sector, for example general practitioners and pharmacists (n=4).
4. Control the relationship between the patient and the treatment supervisor (n=4).
5. Good support throughout treatment (n=4).
6. Motivate patients by addressing the stigma attached to TB (n=4).
7. Motivate patients by involving cured ex-TB patients (n=3).
8. Provide transport to take the patients to the clinic or provide mobile clinics to reach the patients (n=3).
9. Establish feeding schemes (n=2).
10. Start “fast queues” so that TB patients should not wait for too long at the clinics (n=2).

11. Have good relations with employers so that they can supervise patients or release them to visit the clinics when necessary (n=2).
12. DOT to be given at the clinic, due to the perception of some patients that only nurses will be able to give them the correct medicines (n=2).
13. Encourage patients to visit the clinic more often even if it is not their return date (n=1).
14. The possibility of a single dose per day treatment should be investigated (n=1).

(Note: Some respondents gave more than one answer, hence n is greater than 61.

8 respondents did not respond to this question)

CHAPTER 4

DISCUSSION

The response rate to this study was low. Only 69 questionnaires (25%) of the 276 that were sent out were completed and returned. Mail surveys are associated with a low response (30). Since a 1996 list of TB services was used to select the sample, this might have contributed to the low response. Some clinics might have changed addresses or some might have been closed down. However the 1996 list was the most current list available at the time of conducting this research.

The percentage of patients who completed treatment was compared to the working hours at the clinics. The Pearson chi squared test showed that the two variables were not related ($p=0,135$). There was a pattern observed in this comparison though. The majority of the clinics that were open between 4 and 8 hours per day (67,2%) had more than 75% of patients who had completed treatment. Only 36,4% of the clinics that were open for more than eight hours per day indicated that more than 75% of their patients completed treatment. Due to the small sample size, a conclusion cannot be drawn from this observation.

Forty six respondents (67%) mentioned that not all of the patients who completed treatment were cured. Of these clinics 48% mentioned that more than 75% of the patients who completed therapy were cured. The South African TB control programme has as its target a 85% cure rate (12). Only 65% of all the respondents stated that more than 75% of the patients who completed TB treatment were cured. Compared to the figure expected by the TB control programme, the cure rate obtained was low. TB is said to be approximately 100% curable (8,31), yet this study

showed that some patients who completed treatment were not cured. In the absence of MDRTB, 6 months treatment of TB can cure a great majority of patients. The obvious reason why TB is so prevalent is that only a minority of TB patients complete their treatment (32). These patients might not be taking treatment correctly, are not thoroughly supervised or might be suffering from MDR TB.

A few clinics mentioned that they were sometimes without TB drugs. The longest period that clinics were without TB drugs was one month. In these situations clinics borrowed drugs from the nearest health facility or contacted the distributor to supply them with the required medicines. The government must ensure regular supply of drugs at no cost to the patient (32). Situations where clinics are without drugs may result in non-compliance to treatment by the patient. In addition non-compliance result from inadequate provision and administration of medication by the health system (5).

Eighty one percent (81%) of the health care workers who participated in this study revealed that the major cause of non-compliance in TB patients was that patients discontinued treatment because they felt better. It was also stated in other studies that the sensation of feeling cured due to the resolution of symptoms, even though treatment has not been completed has been found to be the most common reason of discontinuation of treatment (1,16). This is coupled with the ignorance of the consequences that result from interrupting treatment. Interrupted treatment leads to resistance of mycobacteria to the drugs used in the treatment of TB (1).

Clinical improvement in patients on appropriate treatment is seen after 2 weeks and is characterised by decreased coughing, increase in weight, decrease in fever, increase in appetite and an increase in the sense of well being. Another cause for non-compliance mentioned by respondents was that patients complained of hunger and that they did not have food. One of the symptoms of TB is lack of appetite. As patients are on treatment TB symptoms subside and appetite increases (33). Some respondents suggested that feeding schemes be introduced, which would address to some extent the problem of patients complaining of an increased appetite, due to medication consumption. Patients will therefore be more compliant and take their medication as prescribed.

In studies where incentives were used, compliance with TB regimen was improved. Among incentives identified as successful in the USA, were food parcels, clothing, bus tokens and free transportation (34). In order to encourage patients to take TB drugs, incentives should be given only to those patients who come for their medication. Giving incentives appear to be more effective for patients trying to balance TB treatment completion with poverty, hunger, unemployment, HIV infection and substance abuse (9).

Denial of having TB was marked as a major cause for noncompliance by 52,2 % of the respondents. As long as the patients do not accept the fact that they are suffering from TB, they will see no reason for taking TB medication. The denial of having TB might be caused by the stigma attached to TB because most people regard tuberculosis as a shameful disease (35).

Ignorance was mentioned by 47,8% of the respondents as another cause for defaulting from

treatment. Lack of motivation to take TB medication could be due to ignorance of the harmful effects that TB could have on the patient himself/herself and the community (1). An untreated TB sufferer will usually die within 2 years and will infect ten people before dying (3).

Respondents mentioned other reasons for patients to interrupt treatment, namely: poverty, patients living far from clinic and visiting without transfer letters. The majority of respondents mentioned that they got patients coming from other clinics without medication. Most of them mentioned that they continued treatment immediately or after investigation. Some employers did not allow their employees to visit the clinics to obtain medication as well as refused to observe patients, which caused non-compliance since the patients did not have time to visit the clinic.

According to 44,9% of the respondents, patients discontinue treatment because of a long treatment period while 30,4% of them indicated the many drugs that have to be taken as a cause of non-compliance. To assist patients, DOT has been implemented in South Africa since 1996. The treatment period of TB is shorter than the regimens used in some developing countries. Prior to 1 October 1999, patients treated for TB for the first time had to take more tablets than what is currently being taken. Patients weighing less than 50kg had to take 6 tablets daily compared to only 4 which are now taken and patients weighing more than 50kg had to take 8 tablets daily as compared to the 5 tablets that are now taken (25,36). Some countries treat TB patients with streptomycin 1g, INH 15mg and pyridoxine 10mg twice weekly for 12 months. This regimen has a nearly 100% cure rate in the absence of resistance (33). Fixed combination drugs are also given. The advantage being that drugs are not given separately and the risk of resistance is decreased. The WHO and IUATLD recommend the use of fixed dose combination drugs with demonstrated

bioavailability (8).

The health workers mentioned that defaulting from treatment was one of the problems they experienced when it came to giving TB drugs to patients. Defaulting was said to be due to many tablets, painful injections and side effects. Combination drugs are used in South Africa. TB patients take up to 5 tablets daily, depending on their body weight and only patients who are retreated, receive streptomycin injections. If patients were compliant there would be no need for retreating TB.

According to health workers, they also encountered the following problems in giving treatment to TB patients: defaulting, patients refusing to be observed at clinics when they take medication, migration of patients, shortage of staff, disappearance of patients after being discharged from hospitals, poor understanding of how to take medication and no co-operation from employers.

Another problem was that some patients refused to be observed at the clinics when taking treatment. A solution would be for these patients to indicate who they prefer to observe them taking their treatment. There was a response that a good interpersonal relationship must be ensured between the patient and the treatment supervisor in order for patients to adhere to treatment. Other patients did not understand how to take medication and observation would be important for these patients. They should either come to the clinic daily for medication or should get a responsible person to supervise them when taking medication.

The person chosen to be a DOT supervisor should also be educated on TB and should be committed, since TB treatment is a long time process and there are many different factors to be considered. The patients should also receive good support from the treatment supervisor throughout treatment. A study done in South Africa showed that adhering to treatment was enhanced by the use of voluntary health workers (DOT supervisors) who were well motivated and respected by the patient as well as the community (36). If the community is involved in DOT, the problem of staff shortages could be partly solved, because the health care workers will then be able to spend time with those patients who really need their attention.

From the results obtained education seemed to be the most important way of improving DOT. The respondents mentioned that the patient should be educated intensively on his/her first visit. Most problems encountered with TB treatment arose from lack of information on the disease. If patients knew the importance of completing the course of treatment and the consequences that may result from untreated TB, they would not interrupt treatment (1). If the TB patients, when discharged from hospitals are informed of the importance of continuing with treatment they would regularly go to the clinics to continue with treatment. Education should also focus on motivating patients to adopt a behaviour beneficial to their health and to take responsibility for their own health (35).

Another suggestion made to improve DOT was to involve patients in TB projects, to make use of cured ex-TB sufferers as treatment supporters, to promote good relations with the patient and provide education. For DOT to be successful, it requires well-motivated patients who appreciate the importance of regular treatment. Poor compliance was reported to be a direct consequence of a health care system in which adequate motivation to the patient is not provided (35). When patients are educated they will realise that treatment given by DOT supervisors or treatment supporters, is similar to treatment given by the nurses at the clinics (32).

The respondents mentioned that the community should also be educated about the disease for them to know that TB is not a shameful disease, that they can volunteer as treatment givers and that they can support TB patients. With education to the community, some employers would know the importance of treating TB and they might then be willing to help observe the patient taking medication, or would allow them to go to clinics for treatment. The community can be reached at community meetings, during visitations at the clinics and through the press. Reichman partly blames the press for the high incidence of TB because of the lack of interest in awareness campaigns on TB (8).

It was also mentioned that DOT can be improved by giving further training to health workers. Topics that could be covered in this training include how to relate better to TB patients, TB as a disease, new developments and the management of TB. Training and ongoing support at clinics are important for effective and sustained TB control efforts. Staff involved with TB patients should be trained in correct diagnosis, treatment as well as monitoring of TB patients (31). With diabetes, hypertension, pneumonia and other typical illnesses, the responsibility of getting cured affects only

the health of the patient. However, with TB, the patient's problem is affecting the health of the community. It is the health worker and ultimately the society who need to assist and encourage TB patients to adhere to treatment. If TB is not cured, the disease will spread and resistance to TB drugs will occur (1).

Some respondents mentioned that DOT could be improved by making it more accessible to the patient. They said that involving health workers in the private sector, erecting DOT stations and involving the community and providing mobile clinics could do this. This would alleviate the problem that patients default from treatment because of long queues, lack of transport patients living far from the clinic. The presence of "fast queues" at the clinics was mentioned as a factor that might improve DOT. If patients know that there will not be a long waiting period at the clinic, the chances that they might come to take medication are better.

Another problem encountered by health workers was that patients relocate during their treatment period. These patients defaulted from treatment more often than patients who did not relocate. In order to improve DOT it was suggested that patients should also be motivated to remain in one area throughout treatment. This is not to punish the patient, but makes it easier to trace patients if there is a problem and to monitor the progress of the patient. Patients who relocate during the course of treatment may be at an increased risk for interrupted and/or incomplete treatment. Relocation of patients has contributed to several outbreaks of MDR TB in the USA and may facilitate the spread of MDR TB to different areas (10,17).

Through this study we were able to determine the problems encountered by health workers in delivering TB treatment to patients. The main problem according to health workers was defaulting which was caused by many factors. The main reason for non-compliance was that patients stopped treatment as soon as they felt better. From the responses received, it can be surmised that defaulting is mainly due to lack of knowledge about the disease, on the part of patients, the community as well as health care workers.

CHAPTER 5

5.1 CONCLUSIONS

From the results of this study it may be concluded that non-compliance was caused mainly by patients who stopped treatment as soon as they felt better. Other causes of non-compliance were ignorance, patients living far from clinics, long treatment periods, many drugs that have to be taken, poverty, denial of having TB, patients relocating without transfer letters and employers who are not co-operative.

The main problems health care workers are faced with is defaulting from treatment. They further encounter lack of co-operation from employers, shortage of staff, poor understanding of patients on how to take medicines, poverty, patients discharged from hospitals and not returning to clinics to continue treatment, patients who do not want to take medicines from the clinic and the lack of a dosage form for children.

According to the health care workers, the most important way to make DOTS more effective is to educate health care workers, patients and the community as a whole.

5.2 LIMITATIONS OF THE STUDY

Limitations to this study were due to the fact that the survey was directed at health workers only. The information gathered was the self-report of the respondents, therefore the validity and reliability of the clinic's data is questionable. If patients were interviewed or given a questionnaire to complete, more information could have been obtained. The small sample size as well as the use of mail survey has also contributed to the weakness of this study in that the response was poor.

5.3 RECOMMENDATIONS

With the above findings in mind, I would recommend the following:

1. That the population of South Africa be educated about TB, its treatment, effects of non-compliance on treatment and the consequences that will ensue from not treating the patient. With education, the community will know that TB is not a shameful disease and the TB patients will be encouraged to take treatment. Employers will co-operate either by giving treatment or by letting employees suffering from TB go to the clinic. Patients will know the importance of continuing with treatment and those discharged from hospitals will go to the clinics for follow-up treatment. Health care workers should get further training on the diagnosis and treatment of TB. This will result in early diagnosis of the disease and proper management to prevent problems like MDR TB. Health care workers will relate better to patients and it will be easier to encourage patients to continue with treatment.
2. Involve the community in giving DOT through training TB counselors/treatment supporters. If the community is involved, it will not be necessary for patients to go far to get medication and the workload of health care workers will be reduced to some extent. Patients will also get

treatment from people with whom they can relate to best. If cured ex-TB patients are giving DOT this might motivate the current patients to take their medicines.

3. The problem of lack of transport could be resolved by the provision of mobile TB clinics to go to the community.
4. Feeding schemes should be introduced in order to provide nutritional food to those patients with a perceived need because of an increase in appetite which result from medication consumption. This might encourage those patients to continue taking their medicines.
5. Further studies should be carried out at the clinics after implementation of the above recommendations to determine if adherence to TB treatment has improved.
6. The implementation of social support services by utilising support groups e.g. Church groups and TB "cell groups" as well as the help of social workers for motivation, moral support and family bonding.
7. The observation made of clinics with shorter working hours having patients with better compliance to treatment, could be further investigated.

APPENDIX A**DRUG DELIVERY PROBLEMS TO TB PATIENTS IN GAUTENG**

Please mark the appropriate box(es) with a tick

1. In which region is your clinic located?

Central Wits	<input type="checkbox"/>
East Rand	<input type="checkbox"/>
Pretoria	<input type="checkbox"/>
Vaal	<input type="checkbox"/>
West Rand	<input type="checkbox"/>
Other (Please specify)	<input type="checkbox"/>
	<input type="checkbox"/>

2. From which areas do most of your patients come from

Suburban	<input type="checkbox"/>
Township	<input type="checkbox"/>
Informal Settlement	<input type="checkbox"/>
Rural	<input type="checkbox"/>
Others (Please Specify)	<input type="checkbox"/>
	<input type="checkbox"/>

3. How many TB patients visit your clinic for consultation per month?

Less than 50	
50-99	
100-149	
150-200	
More than 200	

4. How many nursing staff and other health care workers employed at your clinic are engaged in TB services?

5. How many days a week is your clinic open?

6. For how long are your clinics open per day or session?

Less than 4 hours	
4-8 hours	
More than 8 hours	

7. According to your clinic's statistics, what percentage of your TB patients complete their course of TB treatment (medication)?

91% to 100%	
76% to 90%	
51% to 75%	
26% to 50%	
25% and less	

8. Are all of your patients who finish their TB treatment cured?

Yes	
No	

9. If the answer to question 8 above is no, what is the percentage of patients that are cured?

25% or less	
26% to 50%	
51% to 75%	
76% to 90%	
91% to 100%	

10. From your point of view, what are the main causes of non-compliance to TB treatment that you encounter in your clinic?

Ignorance	
People living far from the clinic	
Patients visiting without transfer letters	
Denial of having TB	
Patient stops treatment because he feels better	
Period of treatment is too long	
Poverty	
Lots of medicines to be taken	
Other (Please Specify)	

11. How do you trace defaulters?

Home visits	
Telephonical	
Contacting employer / teacher	
Writing letters	
Other (Please Specify)	

12. How do you convince defaulters to continue taking their medicine?

Health education on TB and its complications	
Enforce direct observed therapy	
Find a reliable treatment supporter	
Threaten them by reporting them to the police	
Involve them in TB projects	
Other (Please Specify)	

13. After finding defaulters, do they continue with treatment?

Always	
Sometimes	
Never	

14. Do you give all your DOT direct from your clinic?

Yes	
No	

If the answer to question 14 is yes, go directly to question 19.

15. If the answer to question 14 is no, where else is DOT given?

Doctor	
Teacher	
Employer	
Others (If ... Specify)	

16. Do the people or institutions in question 15 above give feedback about the patients whom they supervise in taking TB medication?

Yes	
No	

17. How often do they give feedback?

Daily	
Weekly	
Monthly	
Whenever there is a problem	
Other (Please Specify)	

18. If they do not give feedback, how do you find if the patient is taking medicines as

19. Do you encounter situations where a patient comes from other clinics to your clinic without medication?

Yes	<input type="checkbox"/>
No	<input type="checkbox"/>

20. If the answer to question 19 is yes what do you do?

21. Do you ever run short of TB medicines?

Never	<input type="checkbox"/>
Once in a year	<input type="checkbox"/>
Twice in a year	<input type="checkbox"/>
Four times a year	<input type="checkbox"/>
Monthly	<input type="checkbox"/>

If the answer is never, go directly to question 24.

22. What do you do if you run short of TB medicines?

23. How long does it take to get new stock if you've run out of TB medicines?

24. What other problems do you encounter with giving TB medicines to patients?

25. In your opinion what do you think must be done to make DOT more effective , and how?

APPENDIX B**SAMPLE OF THE LETTER THAT WAS ATTACHED TO THE QUESTIONNAIRE**

PO BOX 340
Atteridgeville
0008
10 March 1999

Sister in Charge

I am studying towards M.Pharm degree with Wits University. As part of the degree's requirements I am doing a research project in TB.

We are faced with a large number of multi-drug resistant tuberculosis (MDR TB) cases and still there are people who do not take their TB medicines as prescribed. Research has shown that non-compliance is the major cause of MDR TB. The main purpose of this study is to find out what causes non-compliance and what can be done to improve compliance in TB patients.

Enclosed herein are two copies of the questionnaire that is intended to get the solution to the above problem. The questionnaire could be completed by the sister in charge and any other sister involved with TB patients or any health care workers involved with TB patients. I would appreciate it if you could complete the questionnaires and mail them in the enclosed envelopes before 21 April 1999. Even if you do not wish to fill in the questionnaires please return blank questionnaires to the addressee (this is for statistical purposes).

Please note that participation is voluntary.

Thank you
Confidence Mabena

APPENDIX C

08 October 1998

Ms C Mabena
50 Rathoekuyana Street
ATTERIDGEVILLE
0008

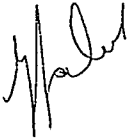
Dear Ms Mabena,

M PHARM(CLINICAL HOSPITAL) - APPROVAL OF AMENDED PROTOCOL
ENTITLED "DRUG DELIVERY PROBLEMS TO TB PATIENTS IN GAUTENG".

I have pleasure in advising you that the Postgraduate Committee has approved your amended protocol for confirmation of continuation of candidature.

It is noted that ethics clearance is still awaited for your proposed research.

Yours sincerely,



MRS G GABRIEL
FACULTY OFFICER (POSTGRADUATE)
FACULTY OF HEALTH SCIENCES

cc: Professor I Moodley
Professor A Gous

APPENDIX D

49

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)
Ref: R14/49 Mabena

DIVISION OF THE DEPUTY REGISTRAR (RESEARCH)	
RECEIVED	1999 -02- 02
FILE:
ACTION:

CLEARANCE CERTIFICATE PROTOCOL NUMBER M980908

PROJECT Drug Delivery Problems Of Tuberculosis Patients In Gauteng

INVESTIGATORS Miss C Mabena

DEPARTMENT Dept of Pharmacy, Faculty of Health Sciences

DATE CONSIDERED 980925

DECISION OF THE COMMITTEE *

Approved unconditionally

DATE 990125 CHAIRMAN.....*P E Cleaton-Jones*.....(Professor P E Cleaton-Jones)

* Guidelines for written "Informed consent" attached where applicable.

c c Supervisor: Prof A Gous
Dept of Dept of Pharmacy, Faculty of Health Sciences

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DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and ONE COPY returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee.

DATE 10-02-1999 SIGNATURE*C. M. M. M. M.*.....

PROTOCOL NO.: M 980908

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

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