A study to determine the Palliative Care Needs of Patients with Drug Resistant Tuberculosis in the Southern sub-district of Cape Town

Research of

Dr Shannon Odell

(Clinical Investigator)

MBChB (UCT), DCH, Dip.Obst, Dip.Pall.Med

ODLSHA001

*****

Submitted for partial completion of Masters of Philosophy in Palliative Medicine

Department of Family Medicine

University of Cape Town

2016/2017/2018

*****

Principal investigator/Supervisor

Dr René Krause

Senior Lecturer in Public Health and Family Medicine (UCT)

MBChB, M.Fam Med, M.Phil(Pall.Med), Post-graduate Diploma Health care education

*****

Co-Supervisor

Dr Liz Gwyther

Senior Lecturer in Public Health and Family Medicine (UCT)MBChB, M.Phil(Pall.Med)

ACKNOWLEDGEMENTS

The researcher would like to thank her family – Craig, Abigail and Noah for their patience, understanding, encouragement and unconditional love, and her parents for their belief and support.

The researcher is grateful to Tozama Manga for her dedication in the community serving DR-TB patients and for her on-the-ground input.

This work is dedicated to STW.

---

*

DECLARATION OF OWN WORK:

I, Shannon Ann Odell, hereby declare that the work on which this thesis is based is my original work and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. Advice regarding appropriate biostatistical tests and analysis was received from Jordache Ramjith, Lecturer and Biostatistician in the Division of Biostatistics and Epidemiology at the UCT School of Public Health and Family Medicine.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 13 February 2018

“Born there”

A poem by Dr Curi Kim(1)

(This poem was inspired by a patient with drug-resistant tuberculosis)

Birth geography
Tied tight to longevity
But when might is right
What rights are given that might
Right the balance of the world
No rites can heal this
Hideous haemoptysis
If a mite of care
The mighty felt to fight white
Plague, then this I needn’t write

TABLE OF CONTENTS:

FIGURES

TABLES

APPENDICES

ACRONYMS

ADR: Adverse Drug Reaction

APCA: African Palliative Care Association

APCA-POS: African Palliative Care Association – Palliative Outcome Score

ARVs: Anti-Retroviral medication

ATLA: American Theological Library Association

BCH: Brooklyn Chest Hospital

CCW: Community Care Worker

CD4: "Cluster of Differentiation 4" T-lymphocytes

CI: Confidence Interval

CINAHL: Cumulative Index to Nursing and Allied Health Literature

de novo: Latin, meaning "afresh"

DG: Disability Grant

DOTS: Directly Observed Treatment Schedule

DPM: D.P. Marais Hospital

DR-TB: Drug-Resistant Tuberculosis

DR-12: Health related quality of life score

DS-TB: Drug-Sensitive Tuberculosis

EBSCO: Elton B. Stephens Co – collection of databases

ECOG: Eastern Co-operative Oncology Group

et al: Latin, "and others"

GHQ12: General Health Questionnaire 12

HBC: Home-Based Care

HCP: Health Care Professional

HIV: Human immunodeficiency Virus

HPCA: Hospice Palliative Care Association of South Africa

HREC: Human Research Ethics Committee

HRQoL: Health Related Quality of Life

in vitro: Latin "in glass"; in artificial environment

IQR: Inter-Quartile Range

IUATLD: The International Union against Tuberculosis and Lung Disease

LTFU: Lost To Follow-Up

MDR-TB: Multi-Drug Resistant Tuberculosis

MEDLINE: Medical Literature Analysis and Retrieval System Online

MeSH: Medical Subject Headings

MOTT: Mycobacteria Other Than Tuberculosis

N/A: Not applicable

NGO: Non-governmental organization

NTM: Non-Tuberculosis Mycobacteria

NTP: National Tuberculosis Program

OR: Odds Ratio

PDQ: Patient Dignity Question

per se: Latin, "as such"

POS: Palliative Outcome Scale

Pre-XDR-TB: Pre-eXtensively Drug-Resistant Tuberculosis

PTB: Pulmonary Tuberculosis

PubMED: "Pub" Public/ Publisher; "Med" refers to MEDLINE database

q: question

QoL: Quality of Life

RR-TB: Rifampicin-Resistant Tuberculosis (also described as mono-resistant)

SF-36: Short Form 36 Health Survey

SPICT: The Supportive and Palliative Care Indicators Tool

STROBE: "Strengthening The Reporting of Observational Studies in Epidemiology"

TB: Tuberculosis

TDR-TB: Totally Drug-Resistant Tuberculosis

UCT: University of Cape Town

verbatim: Latin, meaning "word for word"

WHO: World Health Organization

WHOWHOL-BREF: abbreviated version of the World Health Organization Quality of Life-100 instrument

XDR-TB: EXtensively Drug-Resistant Tuberculosis

ABSTRACT

Introduction

The Palliative Care needs of patients with Drug-Resistant Tuberculosis (DR-TB) are under-researched, yet pertinent in the management and control of DR-TB. Most literature reviewed focused on treatment schedules, outcomes, transmission, drug adherence, drug side effects and further drug-resistance.

Aim

The aim was to determine the palliative care needs of patients infected with DR-TB living in the Southern sub-district of Cape Town.

The Objectives

The objectives were to determine the quality of life and symptom burden of DR-TB patients and to assess for correlation between these variables and palliative care needs.

Methodology

In this cross-sectional study, twenty-eight participants were posed a culturally sensitive questionnaire designed by the researcher, that comprised: demographic questions, Likert-type questions for the African Palliative Care Association – Palliative Outcome Score (APCA-POS) tool, Eastern Co-operative Oncology Group (ECOG) score, a symptom checklist and open patient dignity questions. Quantitative and qualitative data of the respondents' quality of life, functional status and burden of symptoms in the preceding week were ascertained. Pre-determined numerical scores in the Likert-type questions were deemed indicative of palliative care need.

Results

Quantitative and qualitative analysis of the data showed that each participant had a palliative care need: be it either (or a combination of) unmet clinical, psychological, social and/or spiritual needs - despite being at differing stages of the DR-TB disease trajectory. These needs required contextualizing within the respondents' communities where socio-economic issues were prevalent. Predominant physical complaints were tiredness (79%), joint pain (64%), confusion (61%) and shortness of breath (51%). Respondents' also experienced a loss of autonomy, poor self-value and financial insecurity. Fifty percent of patients interviewed required urgent further management and referral to the local clinic.

Conclusion

Despite the small cohort of patients and possible recruitment bias, this research concurred that a palliative care approach be adopted from the point of DR-TB diagnosis and throughout the treatment period – regardless of treatment outcome; and that DR-TB patients had significant unmet palliative care needs that affected their quality of life, functional status and dignity, regardless of whether pain was present.

CHAPTER 1

Introduction

1.1 Background

Robert Koch identified *Mycobacterium tuberculosis* on the 24th March 1882. (2) This bacterium was responsible for "consumption" (the older description of pulmonary tuberculosis) and the "White plague of Europe" (a depiction of its devastating effect on seventeenth to nineteenth century England, America and Europe).(3) Even today, 135 years since discovery, *Mycobacterium tuberculosis* infection is the leading natural cause of death in South Africa(4) and it remains one of the top ten causes of death worldwide in 2015 (5) – resulting in the deaths of three people per minute.(6)

Tuberculosis has also been described "like the multi-layered mystery of the famous Russian doll. No sooner do we think we understand it, than a new form, as baffling and menacing as ever, appears to confound us."(3) This "White Plague" has morphed into two categories: drug-sensitive (DS-TB) and drug-resistant tuberculosis (DR-TB). Table 1 on page 12 provides definitions for DS-TB and DR-TB.

Figure 1: Russian Matryoshka nesting dolls(7)

1.2 The development of DR-TB

Patients either acquire DR-TB infection *de novo* from a DR-TB contact* (implying person-to-person transmission), or their DS-TB infection may develop subsequent drug resistance due to poor adherence

*A "contact": any person who has been exposed to an index patient(8)

to standard anti-tuberculosis medication, sub-optimal treatment due to health-system or patient-related factors (such as drug stock shortfalls, poor implementation of treatment guidelines or transport costs(9)), pharmacokinetic variability (even with excellent adherence and stringent supervision(10)) or the circulation of counterfeit drugs. (11,12)

In the South African context, other contributing factors have been implicated: poor therapeutic relationships between patients and health care personnel (HCP), inadequate adherence counselling, inadequate contact tracing and follow-up of DR-TB cases and restricted access to health care.(8)

A more profound basis for the development of DR-TB, was the indictment made by the University of Cape Town (UCT)'s Professor Dheda and international colleagues: that DR-TB had resulted "essentially [as] a consequence of a systematic violation of human rights arising from the failure to develop pharmaceuticals for this neglected disease." (13,14)

1.3 The Emergence of DR-TB

Progressively, DR-TB has been further sub-divided to encompass Rifampicin-Resistant (RR-TB), Multi-Drug Resistant (MDR-TB), extensively drug-resistant (XDR-TB), extremely drug-resistant(15) and totally drug-resistant tuberculosis (TDR-TB). The definition for drug resistance beyond extensively drug-resistant tuberculosis has not yet been agreed upon amongst the international community. (15) Table 1 below explains the sub-divisions of DR-TB according to their resistance patterns.

Table 1. Definitions for Drug-resistant TB(16)

Acronym	Definition	Resistance pattern
DR-TB	Drug-resistant TB	Resistance to any TB drug
RMR-TB	Rifampicin mono-resistant TB	Resistance to rifampicin and susceptibility to isoniazid
MDR-TB	Multi-drug resistant TB	TB resistant to isoniazid and rifampicin
RR-TB	Rifampicin-resistant TB	TB resistant to rifampicin, regardless of resistance to other drugs
PreXDR-TB	Pre-extensively resistant TB	MDR-TB with resistance to either a fluoroquinolone OR a second-line injectable
XDR-TB	Extensively drug-resistant TB	MDR-TB with resistance to both a fluoroquinolone AND a second-line injectable drug

MDR-TB had first been recognised in the United States in 1976, (17) and in the proceeding forty years had come to be reported in a further 153 countries. (18) MDR-TB describes *Mycobacterium tuberculosis* infection exhibiting *in vitro* resistance to both first-line drugs, Isoniazid and Rifampicin.

(19) The medical literature described MDR-TB as a "leading killer", (20) an "epidemic", (21) a "public health menace", (22) "a dirty disease", (20) a "global threat" (21) and a "real and present danger for the developed nations". (23) Those tuberculosis patients with MDR-TB have been considered as being "some of the most vulnerable persons", (24) "therapeutically destitute" (25) and "hopeless". (25)

The term XDR-TB first appeared in 2006 in a report jointly published by the US Center [*sic*] for Disease Control and Prevention (CDC) and the World Health Organization (WHO). (26) Recent medical literature described XDR-TB as a "burgeoning global health crisis" (15) and a "new threat" (15) that "has a high mortality rate regardless of HIV status". (15)

The term DR-TB is used in this research study to include mono-, multi-, pre-extensively, extensively and totally drug resistant tuberculosis.

1.4 The Incidence of DR-TB

In 2014 the WHO estimated that 480 000 people developed MDR-TB worldwide and that there were an estimated 190 000 deaths from MDR-TB. (27) South Africa's incidence of laboratory-confirmed R-R/MDR-TB cases in 2014 was 18 734. (28)

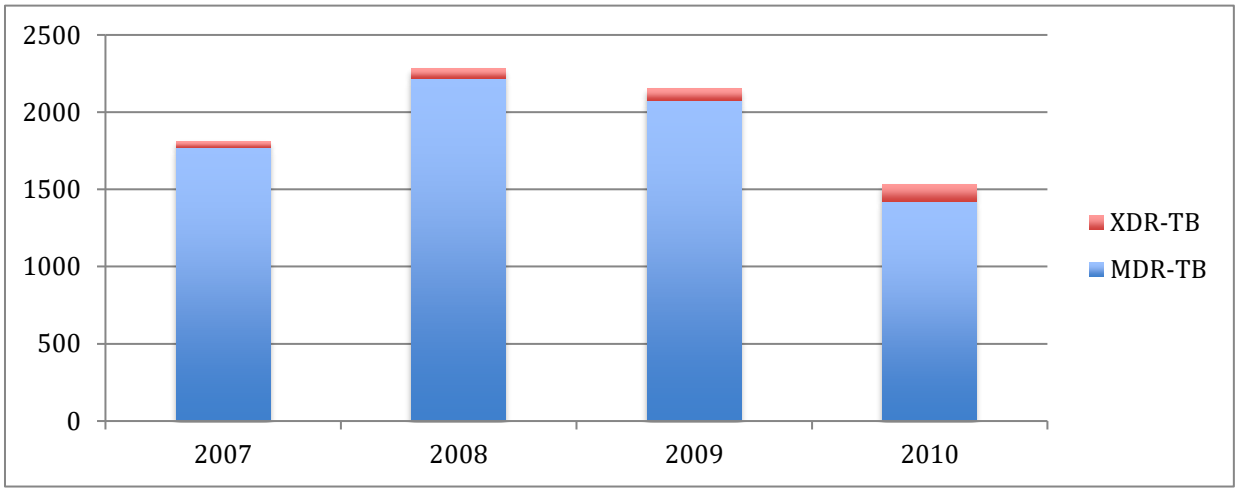
According to the WHO Global Tuberculosis Report 2015, (29) 1.8% of new TB cases notified globally were MDR-TB, and 6.7% of re-treatment TB cases were MDR-TB. XDR-TB had been reported in 105 countries in 2015 and an estimated 9.7% of people with MDR-TB had XDR-TB. (27)

The WHO Global Tuberculosis Report 2016 (5) considered South Africa to be a high burden TB country, ranking 6th in 2015, with a total TB incidence of 454 000. South Africa had the highest HIV-positive TB incidence (258 000). This Report estimated 480 000 new cases of MDR-TB and an additional 100 000 people with RR-TB who were newly eligible for MDR-TB treatment. South Africa was one of fourteen countries that had the highest TB, MDR-TB and TB-HIV incidence.

Figures released recently in the WHO Global Tuberculosis Report 2017, (30) indicated that in South Africa: 3.4% of new TB cases were found to be MDR/RR-TB and 7.1% of previously treated cases (30); globally, the percentages were 4.1% and 19% respectively. (30) An estimated 600 000 incident cases of MDR/RR-TB were reported worldwide in 2016- 490 000 of which were MDR-TB and approximately 240 000 deaths due to MDR-TB. In that same year, the average proportion of MDR-TB cases globally with XDR-TB was 6.2%.

The schematic below depicts the incidence of MDR-TB and XDR-TB in the Western Cape from 2007-2010. (31) MDR-TB and XDR-TB data relevant to the Western Cape subsequent to 2010 was not available.

Figure 2: Drug resistant TB statistics for the Western Cape: 2007-2010(31)



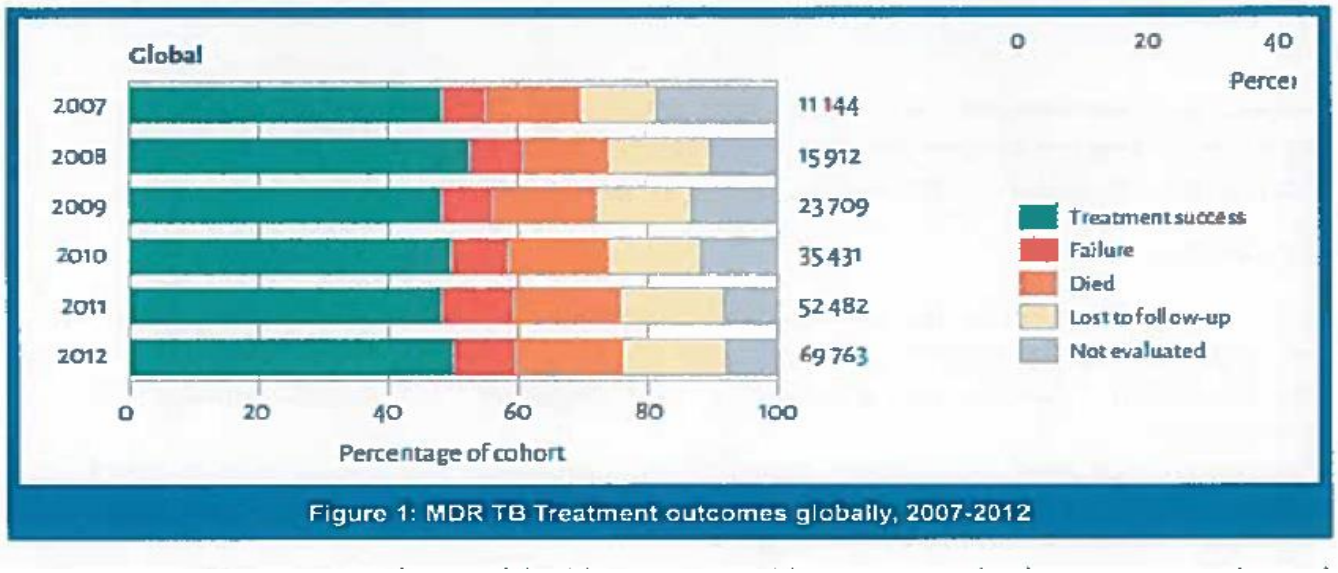
In South Africa, 80% of MDR-TB(32) and an increasing proportion of XDR-TB(33) infections are acquired *de novo*. The emergence of additional resistance to the drugs available in the national programme to manage XDR-TB has resulted in patients who are essentially untreatable. (34) Some patients have nowhere to go and remain in TB facilities in South Africa. (15) Pietersen *et al*. (33) reported that since 2008 in the Western Cape, approximately 100 of such patients had been discharged back into the community – for reasons such as absence of effective drugs, treatment futility, scarce resources and insufficient bed space. (15) In their communities, these incurable XDR-TB cases continued to live for a number of months (more than 50% survived for an average of 16 months(34)) and continued to engage in family, community and work life. (15) These discharged patients, however, remain infectious and potential vectors for transmission (35) - thereby threatening to undermine national and international TB control efforts. (34) Having had TB drugs discontinued, the need for palliative care is acute and maintaining contact with the health system critical. (14) However, these patients often find themselves abandoned by HCPs and in a "careless void". (25) This was sensationalized in a national newspaper in December 2016, reporting: *"TB sufferers sent home to die, and perhaps to kill*". (36)

1.5 Treatment Outcomes and Mortality

Undoubtedly, DR-TB is a "life-threatening condition" (37) upon diagnosis, with an extended course and unpredictable prognosis. (21) According to Dheda *et al* the number of drugs a *Mycobacterium tuberculosis* isolate was resistant to independently predicted mortality - therefore, DR-TB patients had poorer outcomes than those ptients with DS-TB. (13,15) They noted that DS-TB patients had higher survival and cure rates than MDR-TB patients and similarly, MDR-TB had higher successful cure rates than XDR-TB. (15)

The schematic below illustrates the global MDR-TB treatment outcomes from 2007 to 2012 – and demonstrates that the treatment success rate remained relatively unchanged in this time period.

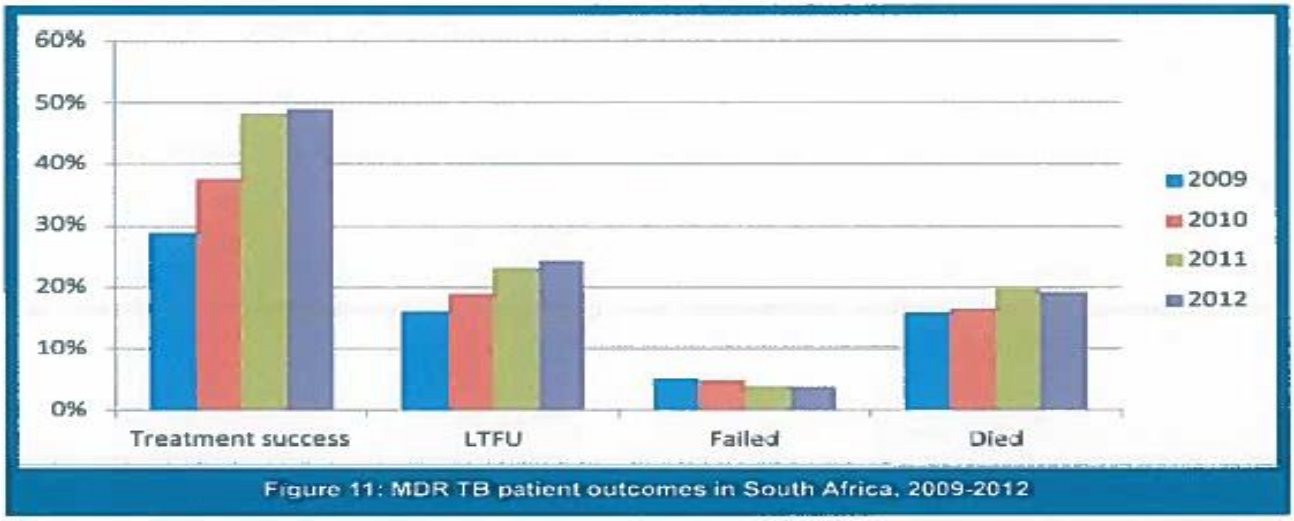
Figure 3: Global MDR-TB treatment outcomes: 2007-2012 (38)



The latest treatment outcomes data for South Africa showed a treatment success rate of 81% for new and relapse DS-TB (2015 cohort), 54% for MDR/RR-TB (2014 cohort) and 27% for XDR-TB (2014 cohort). (30) Globally, the treatment success rates for the same parameters were 83%, 54% and 30% respectively. (30)

As compared to the global treatment success rates over a similar period, the schematic that follows shows an encouraging improvement in treatment success rates. However the number of patients lost to follow up and those dying increased year on year.

Figure 4: South African MDR-TB treatment outcomes: 2009-2012(38)



In the Western Cape, the treatment success rate of DR-TB patients had marginally improved year on year, however in 2012 remained less than 30% - see Figure 5. (39)

Figure 5: Western Cape DR-TB outcomes: 2009-2012(39)

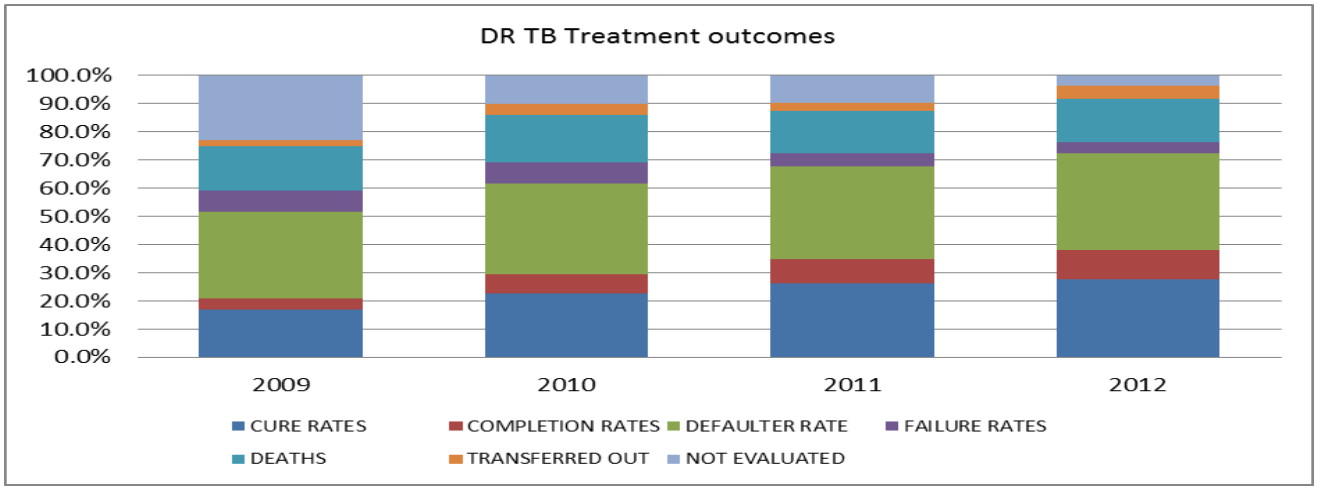
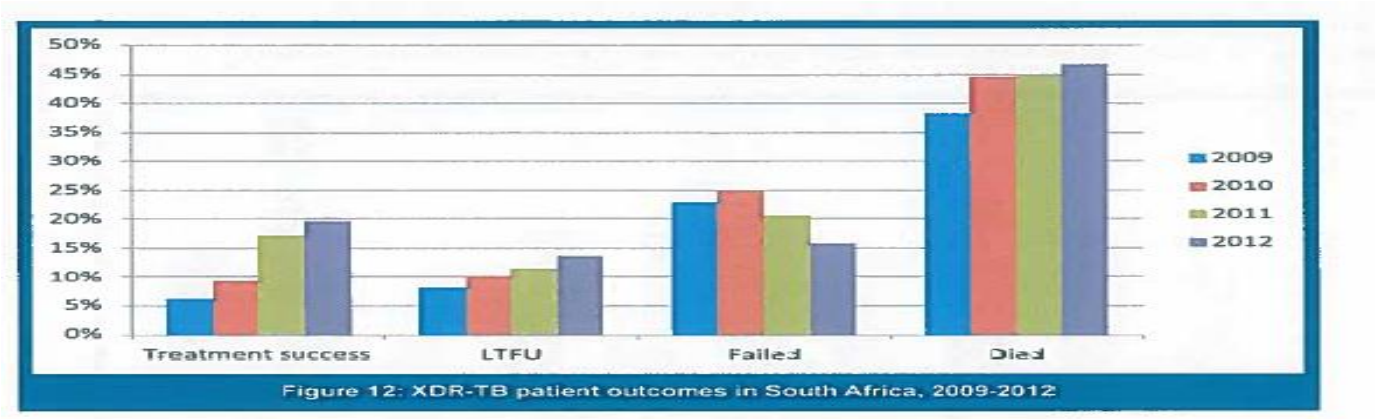


Figure 6 illustrates the worse outcomes for XDR-TB nationally.

Figure 6: South African XDR-TB treatment outcomes: 2009-2012(38)



The sturdiness of the global, national and local health systems is potentially jeopardised by the DR-TB epidemic (21) - with this "profound challenge" (40) in the management and containment of DR-TB having been likened to "defusing… a time bomb". (25) In order to institute the necessary "effective and humane response", (21) Abubakar and colleagues urged for "major conceptual change and visionary global leadership". (23)

1.6 Treatment regimens

"Effective" DR-TB regimens are obligated to aim for cure and include targeted anti-tuberculosis drugs recommended by WHO and national guidelines, with a large number of active drugs (particularly later-generation fluoroquinolones). The regimen must be individualised according to the patient's *Mycobacterium tuberculosis* isolate and concomitant medical conditions, with concurrent use of anti-retrovirals (ARVs) if HIV-positive. A community-based model of care is recommended. (15)
The WHO Global Tuberculosis Report 2016 (5) recommended that "RR-TB" and "MDR-TB" patients be grouped together and collectively referred to as MDR/RR-TB. (5) These MDR/RR-TB patients were to be treated with the second-line MDR-TB regimen. (41) Historically, DR-TB treatment was prolonged (lasting approximately 20 months), expensive (swallowing approximately 45% of the South African national tuberculosis management budget), (42) required toxic drugs and offered a low success rate for cure. (29) In May 2016, the WHO launched new guidelines for the management of MDR-TB with the recommendation of a shorter 9 to12 month regimen. (43) This shorter regimen has promised to cost less, have lower mortality, lower loss to follow-up rates and potentially achieve a success rate of >90%.(5)

Subsequently, the shorter regimen was rolled-out to Cape Town patients on 01.10.2017 and initiated at primary health care clinics. Unlike the WHO recommendations, the local rollout program also included pregnant patients, those with mild extra-pulmonary disease and previously fully treated and cured MDR-TB patients whose isolate remained sensitive to second line drugs. (Naidoo, G. 2018, personal communication, February 6).

The efficacy and durability of this new regimen is still being investigated.(44)

1.7 The Challenge

The treatment challenges and "patient-level factors" (35) have to be addressed as they influence the adherence, continuity of care, treatment outcomes and ultimately infectious control of DR-TB. (22)

The WHO identified DR-TB as an adult disease that required palliative care (45): In Isaakidis' study in Mumbai, India, patients and their families described DR-TB as "the worst of the worst illnesses" and its treatment "worse than the disease itself". (46) The response to the suffering caused by the DR-TB epidemic, according to Harding *et al.* needed to be both "effective and humane" (21) and Lopez *et al* (47) suggested that effective care include recognising the dignity and individuality of the person with TB – thereby investing in knowing the patient and not merely their diagnosis. (47)

The Oxford Dictionary defined "*humane*" as: "having or showing compassion or benevolence" or "inflicting the minimum of pain". (48) The WHO definition of palliative care encapsulates the requisite "humane" response: *"Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychological and spiritual".* (49)

The WHO definition of Palliative Care (49) offered reasons why DR-TB patients would benefit from receiving palliative care, in that it:

- "provides relief from respiratory distress, pain and other symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten nor to postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patients' illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;
- enhances quality of life, and may also positively influence the course of illness; and
- is applicable early in the course of illness, in conjunction with second-line anti-TB medication, with the main therapy intended to prolong life through cure".(50)

The last point related to when palliative care would be applicable in DR-TB management. The benefits of early integration of palliative care in the course of a life-threatening illness, was investigated by Temel *et al* in their study entitled, *"Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer*". (51) "Early" implementation was interpreted as at the time of diagnosis - and palliative care was found to lead to significant improvements in both quality of life and mood.

In DR-TB patients, the pragmatic timing of palliative care integration is an imperative ethical obligation for national health departments with limited resources. The WHO promulgates a “needs-based” model of palliative care, rather than a “prognosis-based” model. (52) That does note imply that palliative care be postponed until the identification of risk factors for mortality in DR-TB.

With regards to the delivery of effective care, Mason and colleagues urged HCPs to have a “greater competency in understanding the social and cultural dimensions that impact TB patients.” (53) Furthermore, instituting a “humane” response requires TB to be recognized as “more than just a biomedical phenomenon”, (20) as it also undermines the TB patient’s “sense of self and personhood”. (47) TB must be fully comprehended for the suffering it inflicts upon those already burdened by poverty, overcrowding, malnutrition and inadequate health care access. (20) Thus, a humane response demands a holistic, palliative care approach to appreciate the DR-TB patient’s perspective within their community and context.(54,55)

In it’s 2016 Treatment Guidelines for Drug-Resistant Tuberculosis policy, the WHO recommended that “palliative and end-of-life care in patients with very advanced resistance patterns” be a research priority and that more studies be conducted on health-related quality of life.(5)

This research study evaluated the impact of DR-TB and its treatment on the quality of life and burden of symptoms experienced by DR-TB patients in the southern sub-district of Cape Town. The findings contributed to knowing more about the multi-dimensional palliative care needs of DR-TB patients and allowed the researcher to assess for correlation between the entities of quality of life and symptom burden to the need for palliative care. This study aimed to highlight the necessity and ethical obligation for palliative care services to be made available in the southern sub-district of Cape Town (and beyond).

The Clinical Investigator is referred to as the “researcher” and the Principal Investigator as the “supervisor” in the text, with the terms “participants”, “patients” and “respondents” used interchangeably to refer to the DR-TB patients who participated in the study.

This introductory chapter provided background on the emergence of DR-TB, the challenge its treatment poses and the poor treatment outcomes reported historically. The need for palliative care alongside curative treatment strategies has been introduced and its merits documented. The next chapter reviews the international and local literature pertaining to quality of life, functional status, symptom burden and palliative care issues experienced by DR-TB patients.

CHAPTER 2

Literature Review

2.1 Overview

Chapter 2 presents the findings of an extensive literature search on DR-TB and Palliative Care - and exposed the paucity of data on the palliative care needs of DR-TB patients. The literature findings of the general benefits of palliative care, the optimal timing of integration of palliative care and the causes of clinical deterioration of DR-TB patients are discussed within the context of a low-resource setting, with emphasis on cultural sensitivity. Palliative Care needs were further investigated with respect to literature pertaining to quality of life, functional status and symptom burden of DR-TB patients – and the assessment tools utilised in this regard. This formed the basis of the questionnaire designed for this research study. The rationale proposed by the researcher was validated by the corpus of literature.

2.2 Literature search methodology

A Literature search was undertaken using the EBSCO host database platform: Africa-wide information, ATLA Religion database with ATLASerials, CINAHL and MEDLINE. The keywords and phrases used to search thematically included: “quality of life”, “symptom burden”, “multi-drug resistant tuberculosis”; “MDR-TB”; “TB”; “tuberculosis”, “extensively drug-resistant tuberculosis”, “XDR-TB”; “psychosocial”, “stigma”, “palliative medicine”; “palliative care”; “Western Cape”; “South Africa”; “morbidity”; “adverse drug reactions”; “cultural competency” and “dignity”. The literature reviewed was not limited to all these keywords being present simultaneously as the body of literature would have been too small. Additional articles were found by scanning reference lists found in the initial search and those cited in journal articles. The *Oxford Textbook of Palliative Medicine*(56) was also referred to.

Other resources that were consulted to broaden knowledge of DR-TB were the MDR-TB treatment guidelines set out by the South African Department of Health’s National TB management guidelines, (19) the Companion Handbook to the WHO Guidelines for the Programmatic management of Drug-Resistant Tuberculosis, (50) The Patient’s Charter for Tuberculosis Care, (57) the Declaration on Palliative Care for MDR/XDR Tuberculosis (see Appendix 1), (37) Hospice Palliative Care Association (HPCA) of South Africa’s Guidelines for providing palliative care to patients with tuberculosis, (58) the End TB Strategy (2016-2035) (see Appendix 2), (59) the Western Cape Annual Progress Report 2014/15: Provincial Strategic Plan 2012-2016, (39) Drug Resistant Tuberculosis in South Africa: findings from a nationwide survey, 2012-2014, (60) and the Report of the Evaluation of South Africa

Drug-resistant TB programme and its implementation of the Policy Framework on Decentralised and De-institutionalised management of Multidrug resistant TB. (38) Drug-resistant Tuberculosis by the Lancet Respiratory Medicine Commission, March 2017 (61) was an excellent resource. To gauge the magnitude of the DR-TB problem globally and locally, statistical data available in the Global Tuberculosis Report 2015, (29) 2016, (5) and 2017, (30) Global TB Fact sheet 2015 (27) and the Western Cape Mortality profile (62) were consulted.

Various websites were visited: tbsouthafrica.org; The International Union against TB and Lung disease (IUATLD) www.theunion.org; www.who.int/tb. The researcher also attended the Advanced course, "Meeting the challenge of drug resistant tuberculosis" held in Cape Town on 24-26 March 2017. The conference afforded opportunity to hear leaders in the field of DR-TB discuss treatment challenges and new drug developments. Despite the focus on curative management, there was active discussion regarding the dilemma of untreatable TB and debate regarding sanatoria or community-based palliative care.

2.3 Gaps in the Literature

Following this comprehensive search, it was evident that the palliative care needs of DR-TB patients were poorly represented within the literature - despite DR-TB's irrefutable life-threatening nature and four-decade existence. The mainstay of the literature reflected public health prerogatives. Volumes of literature were available regarding the epidemiological, microbiological and genetic make-up of DR-TB, future vaccine and drug development, adverse drug reactions, the global extent of the DR-TB problem and the clinical outcomes reported for DR-TB. (63)

Nonetheless, there was limited research of the patients' experience of DR-TB and the psychosocial context of DR-TB. (22) The impact of DR-TB infection and its treatment on the patients' quality of life, (64) functionality, (65) spiritual wellbeing (63) and the nature and severity (21,66) of their palliative care needs were neglected in the literature.

The researcher noted that the literature concerning quality of life of DR-TB patients placed more focus on the adverse drug reactions of the DR-TB treatment and not the combined effect of the infectious disease process and the drug therapy. Many studies evaluated the symptom burden and quality of life of patients co-infected with HIV and DR-TB, but not of DR-TB alone. Further knowledge gaps were noted in the symptom prevalence and burden of DR-TB patients(21) and the reasons for DR-TB patients dying, irrespective of HIV status or phase of treatment.(67)

In addition, the researcher was unable to locate an assessment tool for determining palliative care needs of DR-TB patients, nor able to find a scoring system for evaluating the TB patient's degree of morbidity.(68) Furthermore, the DR-TB literature did not yield realistic suggestions for implementation of palliative care according to an assessment of needs.

Several countries with the highest incidence of DR-TB were not well represented in the English literature - particularly Russia, China and India. This was evident in Bauer's systematic review(24) where three potentially relevant Russian articles were excluded from analysis. Thomas *et al* described the shortage of studies originating in low and middle-income countries as a "dearth". (22)

2.4 Palliative care needs

A relevant South African study published in the latter part of 2016, entitled, *"What palliative care-related problems do patients with drug-resistant or drug-susceptible tuberculosis experience on admission to hospital? A cross-sectional self-report study"* (66) was reviewed. The authors (Harding *et al.*) commented that their literature search had also failed to identify data on patient-reported palliative care needs in DR-TB patients.

Their study utilised a self-report questionnaire that included the African APCA POS tool to identify the most burdensome problems in the physical, psychological, social and spiritual domains. The aim was to compare palliative care-related problems in DS-TB versus DR-TB patients when these patients were admitted to hospital. However, the circumstances for admission were different: DS-TB patients were admitted for TB complications and DR-TB patients for initiation of treatment (prior to decentralised management).

In the researcher's opinion, use of the term "palliative-care related problems", might hold negative connotations for those unfamiliar with palliative care - creating the impression of a separate, additional, onerous entity to care providers. The introductory paragraph described a number of TB, MDR-TB and XDR-TB statistics without clear context, and included a disingenuous statement that, "Palliative care is needed for those who may die from their TB infection, especially XDR-TB". (66) The Declaration on Palliative Care and MDR/XDR-TB, (37) proposed that palliative care be integrated alongside the prevention and treatment of MDR/XDR-TB, and from the time of diagnosis until the patient reached cure or the end of life – and thus regardless of treatment outcome.

The study's findings were possibly limited by sampling bias and underestimation of symptoms by excluding those too ill to participate. This exclusion was based on a professional nurse's clinical

judgment, which was not quantifiable and perhaps not reproducible. With consecutive sampling these ill patients were prohibited from being re-approached when feeling more able, which excluded the yield of valuable information of those with potentially the greatest "problems". Another limitation was that other co-morbidities or confounding variables on functional performance were not included. The inclusion criteria did not state whether patients had pulmonary or extra-pulmonary TB or whether patients were admitted for other complications (such as HIV) and were subsequently found to have TB. Interviews were done within 7 days of admission and although improvement might have occurred having started treatment (contrasting Chang *et al*'s systematic review findings that symptomatic improvement only started 2-3 weeks into treatment(63)) - other research pertaining to DR-TB found that the treatment (especially the injectables) *per se* caused increased morbidity, (69) which was not mentioned in this study.

The study did not mention any delays for the hospital admission of DR-TB patients (due to bed availability) and thus a delay in treatment. (More recently in South Africa, DR-TB treatment initiation has been decentralised with the aim of starting treatment within five day of diagnosis(19)).

Separate DS and DR-TB African APCA POS scores were not reported in the paper for the comparitive scores to be seen. The researcher had reservations about the reasonability of drawing conclusions about DR-TB patients' palliative care needs by comparing newly admitted DS-TB patients experiencing complications, with DR-TB patients forcibly admitted to hospital for treatment initiation.

Harding *et al.'*s study found that the "worry"question in the APCA POS scored the worst for the full sample of DS-TB and DR-TB patients; and that the diagnosis of DR-TB was predictive of lower (better) scores for both total POS and Factor I (physical and psychological wellbeing). That would imply that DR-TB patients experienced fewer palliative care needs than DS-TB patients. Bauer, (24) Brown, (69) Ahmad,(64) and Sharma's(70) studies contradicted these findings and therefore the researcher questioned the validity of this study design.

Regardless of the study's shortfalls, it identified some of the multidimensional problems TB patients (both DS and DR-TB) experienced when admitted to hospital and advocated for the training of HCPs to assess and manage these complex problems in the inpatient setting. Importantly the authors also mentioned the necessity of addressing palliative care problems within the community prior to admission to hospital and after discharge, to ensure continuity of care.

The scarcity of palliative care needs literature with respect to DR-TB re-directed the focus of the literature search to studies relevant to the evaluation of quality of life, functional status, symptom burden and dignity maintenance in DR-TB patients – the combination of which would estimate palliative care need in this research. Some of the key articles found in the literature search have been discussed below - some relate to TB broadly, some to DS-TB from which inferences regarding DR-TB can be made, and others to DR-TB specifically.

2.5 Quality of life in TB patients

Quality of life (QoL) or Health Related Quality of Life (HRQoL) assessment is an important health outcome. It is relevant in understanding the impact of TB(24) and its treatment on the patients' subjective sense of overall wellbeing. (71)

Chang *et al*'s systematic review entitled "*Quality of life in tuberculosis: A review of the English language literature*" (63) published in 2004 was informative. The authors recognised that little literature was available on TB patient's quality of life and illness burden, as well as QoL variations with respect to being on treatment or achieving cure. They suggested that knowing more about these entities would "improve treatment regimens, adherence to treatment, functioning and well-being of people with TB." (63) No mention was made in the selection criteria of whether DR-TB literature was included (although this is presumed as DR-TB treatment was mentioned further on) – and no distinction was made between DS-TB and DR-TB in their results or comments. Sixty articles met their inclusion requirements from their search on PUBMED using 12 appropriate medical subject headings (MeSH) terms. The authors' initial definition of QoL focused on physical and psychosocial health, social and role functioning and self-perceptions of health – but led to the concession in the reviewing process that "TB-specific QoL domains" (63) of spiritual and financial wellbeing, should have been included. The authors divided their literature findings into the following domains: somatic symptoms; physical, psychological, social and emotional functioning; role function, general health perceptions, as well as spiritual and financial wellbeing. Chang's systematic review did not find any studies describing the impact of TB symptoms, diagnosis or drug therapy on functional status. (63) At the time of their review, a TB-specific QoL instrument was not available and Chang *et al* advised future investigators to use "generic QoL instruments or batteries of available instruments." (63) So too, they emphasised that in resource-limited settings (thus relevant to the study in the southern sub-district of Cape Town), financial and spiritual domains should be included. The authors admitted to having unanswered questions with respect to whether the QoL differed between DS-TB and DR-TB patients and whether QoL contributed to the development of resistant disease.

In 2013, a systematic review by Bauer *et al*(24) was published that continued on from Chang *et al*'s work. It sought to understand and quantify the impact of TB and was titled, "*Systematic review and meta-analysis of the impact of tuberculosis on health-related quality of life."* (24) The authors considered publications in which QoL was self-reported and quantitatively assessed, and compared patients with active and latent TB infection, those with ongoing respiratory symptoms after TB treatment and healthy controls. TB was considered broadly, regardless of whether classified as DS-TB or DR-TB. Their literature search was extensive in terms of databases and length of time (over fifty years), yet had dissimilar studies and literature compared to Chang *et al*, despite using the same or similar MeSH terms. The reviewers identified thirty-four different HRQoL and health utility instruments and noted that the most commonly used tool was the Short Form 36 Health Survey (SF-36).

Twenty five percent of the studies that Bauer *et al* analysed used a longitudinal design and only one included MDR-TB patients (33% of cohort in Aydin *et al*'s study(72) and used the General Health Questionnaire 12 (GHQ 12)). Twenty-four studies conducted a quantitative assessment of HRQoL, three studies used up to four(55) tools, and most studies were cross-sectional. Bauer *et al* performed a quality rating on each cohort study according to the STROBE statement (which provided a checklist of items that should be included in observational studies(73)) and noted that assessment of HRQoL in TB patients was limited. (24) Bauer *et al* granted that not including qualitative studies within their review (as it was beyond the scope of the study) omitted valuable insights for HCPs into patients' experiences and needs in specific settings, and advised that further qualitative studies should supplement their quantitative information. Their review revealed that the greatest improvement in HRQoL occurred during the first 2-3 months of treatment in those patients with active TB and also concluded that MDR-TB patients' experiences probably differed substantially from those with DS-TB.

Further work on QoL assessment in TB patients was done by Brown *et al*.. (69) They evaluated the range of tools previously used, in their article entitled, *"Health status and quality of life in tuberculosis,"* published in 2015. They discussed thirty-two tools employed in QoL TB literature – varying from general to disease or symptom-specific instruments. They acknowledged that different instruments evaluated different aspects of TB but noted that there were no tools designed specifically to assess QoL for TB patients *per se*, and in particular not for DR-TB patients. Brown *et al* concluded that QoL would be particularly impaired in MDR and XDR-TB due to a number of factors: "the complexity and duration of treatment, high rates of adverse events, additional stigmatisation, difficulties with family life, fertility and employment" (69) - ear-marking these patients for urgent assessments of QoL especially when undergoing treatment. This would suggest that a specific DR-TB QoL assessment tool be required.

Having reviewed a large number of QoL tools, Brown *et al* commented that it was impossible to calculate a single numerical value that represented the impact of TB on an individual and they tabulated what the ideal TB QoL instrument would look like. (69) This was informative in the development of the questionnaire utilised in this research study. Chapter 3 discusses this further.

Both Bauer and Brown mentioned the DR-12 instrument used in Dhingra's study (*"Health related quality of life (HRQL) scoring (DR-12 score) in tuberculosis – additional evaluative tool under DOTS").* (74) DR-12 was purportedly a TB-specific QoL instrument comprising two domains: symptoms and socio-psychological and exercise adaptation. However, Guo *et al* in "*Measuring health-related quality of life in tuberculosis: a systematic review",* (75) questioned the methods used by Dhingra to claim strong construct validity of this instrument and pointed out weak statistical analysis.

The researcher found one English article relating specifically to QoL in DR-TB: *"Quality of life of Multi Drug Resistant Tuberculosis Patients: a Study of North India,"* (70) published in *Acta Medica Iranica* in 2014 by Sharma *et al*..Theirs claimed to have been the first study to compare QoL of MDR-TB and PTB (taken to mean DS-TB) – and the first the researcher found that compared QoL to a control group. However, the article did not mention the socio-demographics of the control group nor the number of control participants. They recruited both PTB(50%) and MDR-TB(50%) patients, and interviewed outpatients at a tertiary hospital using the WHOWOL BREF scale (Abbreviated version of the World Health Organization Quality of life -100 Assessment tool). Inclusion criteria were unclear but alluded to newly diagnosed patients being excluded.

They found that the QoL of MDR-TB patients was lower than DS-TB and controls, and that all domains of QoL were affected - psychological, social and environmental (which related to physical safety and financial security). Sharma *et al* advised that a valid, TB-specific QoL instrument be designed, but did not elaborate on the reasons for the WHOWOL BREF scale being inadequate. This was a culturally representative study of Northern India that mentioned: "*lakhs*" (a measurement of a thousand people), difficulty arranging marriages for TB sufferers, and that MDR-TB patients were required to fund their own treatment. Most of the cited references were studies from lower socio-economic countries – India, Pakistan, Honduras and Vietnam.

Mention must be made of Ahmad *et al.*'s prospective study, *"Effects of Multidrug Resistant Tuberculosis Treatment on Patients' Health Related Quality of Life: Results from a follow up study"*,(64) published in 2016. They focused on the treatment regimen's impact on quality of life (as opposed to the DR-TB infection *per se*). They recruited MDR-TB patients at a TB hospital serving a

large province in Pakistan, and had participants self-complete the Urdu version of the SF-36 at their baseline visit, at 12 months and at completion of treatment. It was unclear whether patients required admission to hospital at baseline for initiation of treatment (given that the data was collected in 2012-2013) and the absence of a control group of Pakistani DS-TB patients. Instead, United States general population norms were used as per the scoring software, which was a shortcoming of the study.

Considering Brown *et al*'s "ideal" QoL study features(69) – Ahmad *et al* collected meaningful data in their longitudinal, prospective study that reported to Pakistani and global National Tuberculosis Program (NTP) managers that (a) despite the improvement of patients' HRQoL when on MDR-TB treatment, study participants still had a poor HRQoL and residual impairment at the end of TB treatment, and (b) during treatment, many MDR-TB patients were susceptible to depression.(64)

There was an underlying sentiment in the literature that QoL instruments be culturally representative and developed using population groups with similar cultural and socio-demographic backgrounds to the average TB patient. (75)

2.6 Symptom burden in DR-TB patients

A local study, Senthilingam *et al*'s "*Lifestyle, attitudes and needs of uncured XDR-TB patients living in the communities of South Africa: a qualitative study*", (35) published in 2015, was reviewed. In this study, XDR-TB patients not on treatment in the community and irrespective of their HIV status, were interviewed telephonically (to negate infection risk). The posed questions explored their daily lives - pre and post infection with TB, the impact of the disease, life in hospital and after release, and thoughts of their future. These questions would be deemed "culturally sensitive" - which is discussed later. The study's objective was to ascertain improved models of care and identify potential routes of transmission. The study's shortfalls were the telephonic interview format, the small number of patients interviewed (twelve), the interview not being in respondents' first language and small representations of black (25%) and female (17%) patients in the study (compared to the cohort characteristics - 57% and 42% respectively).

Having thematically analysed the nine patients' and three family members' answers, Senthilingam *et al* found that patients' were concerned about the futility of treatment regimens and financial subsistence; and expressed mistrust of HCPs and a need for purpose in life. (35) Their findings affirmed that the needs of uncured XDR-TB patients, not on treatment, were not being met within the current model of care in the Western Cape and advocated for community-based palliative care support.

Thomas *et al*'s "*Psycho-Socio-Economic Issues Challenging Multidrug Resistant Tuberculosis Patients: A Systematic Review*", (22) published in 2016, gave insight on further issues affecting MDR-TB patients. This review, however, omitted valuable keywords in their original search criteria (such as "economic", "quality of life", "financial" and "spiritual" – the last two being TB-specific QoL domains described by Chang), which would have made the search more comprehensive. They mentioned that 60% of the global burden of MDR-TB disease was borne by China, India and Russia; yet, only 3 of the 15 studies reviewed were conducted in one of those countries (India) – the reasons for which were presumably due to language of publication or scarcity of research. Two of the three were part of an HIV/MDR-TB interventional study and one study was from rural South Africa. Two of the studies related to patients with concomitant MDR-TB and HIV, which found that HIV amplified the already severe psychosocial burden faced by MDR-TB patients. (46,76) Studies relating to the pharmacology of MDR-TB medications were excluded – which might have yielded further valuable information regarding adverse psychological or psychiatric drug side effects. The 15 chosen articles varied in their methodologies and did not permit formal meta-analysis. The narrative approach using "thematic synthesis" effectively reflected the MDR-TB patients' psychological and socio-economic experiences. The descriptive themes were organised into three sub-sections: (a) Psychological issues (b) Social issues and (c) Psychosocial intervention studies. Further analysis assessed the relationship between psychosocial intervention and MDR-TB outcomes (which was not the primary objective of the systematic review).

The authors concluded that there was a dire need for "feasible, innovative psychosocial and economic intervention studies" (22) that would enable DR-TB patients to better cope with their diagnosis and improve their QoL. This resonated with the urgent appeal for palliative care intervention.

Further literature was sought for the high-burden countries Russia and China using "MDR-TB", "drug-resistant TB", "quality of life", "Russia" and "China" on the databases mentioned previously – but were unsuccessful. India was not well represented in the previous systematic review, therefore literature that pertained to their psychosocial issues of DR-TB patients was sought, specifically using the EBSCO database platform as well as searching *The Indian Journal of Tuberculosis*.

An article worth mentioning is Venkatraju and Prasad's, "*Psychosocial trauma of diagnosis: a Qualitative study on rural TB patients' experiences in Nalgonda district, Andhra Pradesh*". (20) The authors' intentions were to address TB patients' psychosocial needs, having recognised that India's existing control strategy largely ignored the human and social aspect of care. (20) In this study, 110 purposively recruited, recently diagnosed TB patients (type not specified) in two rural clinics were

interviewed using a semi-structured format and asked what the single most troublesome psychosocial issue was that they experienced upon being informed they had TB. Venkatraju *et al* described the diagnosis as being traumatic in their title.

A limitation noted in this study was that the questions seemed misinterpreted by some respondents and a pilot study would have been beneficial to test the acceptability of the question. Interviews were also conducted in the respondent's first language, translated into English, (the reliability of the translation was not mentioned), and then analysed, which might not have preserved the original connotations and meaning of the answers.(77)

Qualitative content analysis showed that 37.3% of respondents experienced worry/depression, 23.6% disbelief/shock, 16.4% embarrassment/shame, 12.7% a fear of death, 9.1% fate and 0.9% relief when given the diagnosis of TB. These significant findings affirmed the Declaration on Palliative Care and MDR/XDR-TB(37): that palliative care be integrated from the time of diagnosis.

Venkatraju and Prasad recommended that TB management be "culturally sensitive" to meet the patients' psychosocial needs. (20,78)

2.7 Cultural competency

Two proponents of cultural competency and sensitivity in the literature were Epner(79) and Papadopoulos. (80) Epner described "culturally competent" clinical practice as being patient-centred, with awareness of socio-cultural issues and health beliefs important to the patient and their community. (79) Communication skills were recognised as paramount – particularly asking the patient what mattered most to them in their experience of illness and treatment.(79) A similar question was asked in the research questionnaire.

Papadopoulos defined "culturally competent" compassion as the ability to understand another's suffering and to intervene in a culturally appropriate and acceptable manner. (80) Such a HCP would not only focus on the disease and its treatment, but would also be aware of patients' psychosocial suffering, consider the patients' fears about the illness and its impact on their physical and psychosocial functioning. (20)

2.8 Functional status of DR-TB patients

Chang *et al*'s(63) systematic review did not identify any studies that examined the impact of TB disease symptoms on physical functioning (that is their the ability to perform basic activities of daily living).

Further searches in the literature found Godoy *et al*'s, "*The functional assessment of Patients with Pulmonary Multidrug-Resistant Tuberculosis*",(65) published in 2012. In this study, MDR-TB patients, after 18 months of treatment, were assessed to determine their respiratory function, functional capacity and QoL. Patients with co-morbidities affecting respiratory function were excluded. They found that 78% of their sample patients had impaired respiratory function (as assessed by formal physician-conducted pulmonary function tests and 6-minute walking test) and 78% of their sample patients reported impairment in QoL (as assessed by Airways Questionnaire 20). They stated that the ventilatory impairments impacted the functionality of the MDR-TB patients and suggested that MDR-TB patients post-treatment required continued intervention measures to help improve their QoL.

To measure functional status in pulmonary TB patients, de Vallière and Barker used a modified ECOG score and looked at the association between poor performance status and early death in patients with pulmonary tuberculosis. (68) The objective of the study was to determine whether the performance status of pulmonary TB patients at the initiation of anti-TB treatment was associated with death within two months. (68) This South African study was done in the Limpopo province in 2005. From their data, the Kaplan Meier survival curves showed an increased risk of dying with poorer performance status – greatest with performance scores of 3 or 4. (68) They commented that they were unable to identify a scoring system that evaluated TB patients' morbidity.(68)

2.9 Causes of death among DR-TB patients

Van der Walt *et al,* in 2016, noted the global scarcity of data relating to causes of death among DR-TB patients, regardless of their HIV status, both during and after treatment. (67) In 2011, Waitt and Squire's systematic review of risk factors for death in patients started on TB treatment, found that in high HIV/TB regions: HIV co-infection, atypical chest x-ray features, sputum smear-negative disease, advanced immunosuppression and malnutrition were risk factors. (81,82) In low HIV/TB burden regions the risk factors included increased age, typical features of severe TB on chest x-ray, smear positivity and socio-demographic disadvantage. (81,82)

A Cape Town study, led by Osman *et al* undertook a retrospective analysis of all adult deaths during TB treatment in the city between 2009 and 2012 to identify risk factors for mortality in relation to HIV infection.(81) This analysis did not include DR-TB patients and relied upon the accurate reporting of death at the primary health care clinic in a paper-based register. Their patient data was stratified according to HIV status and Kaplan Meier curves were generated for the time of death after starting TB treatment. Robust statistical modelling determined which demographic and clinical characteristics were linked to death. Osman *et al* found that independent risk factors for death were: being male, HIV-

positivity, being 65 years and older, having extra-pulmonary TB, or retreatment cases.(81) They mentioned culturally relevant factors that impacted mortality of patients in Cape Town such as alcohol dependence, cigarette smoking, diabetes, malnutrition and mental ill health. For those TB patients who were HIV co-infected: greater immunosupression, poor ARV uptake and opportunistic infections meant worse outcomes.

Osman *et al's* study did not include DR-TB patients, but their methodology could be replicated for DR-TB patients, with the inclusion of DR-TB defaulters and those whose treatment had failed or had been withdrawn.

2.10 The Hypothesis

The literature alluded to quality of life and symptom burden being linked by functional status. Ahmad *et al's* study stated that the functional impairment of patients was indicative of their HRQoL. (64) In another study, "*Factors associated with lower quality of life among patients receiving palliative care",* Chui *et al* found that patients with less severe physical symptoms had better functional status and QoL. (83) Similarly, a single debilitating physical symptom would likely impact their physical functioning status and in turn patients' QoL. (83) Justice *et al*'s study (which related to HIV infection) maintained that effective symptom management improved the patient's QoL by reducing the burden of symptoms experienced. (84) Therefore, quality of life, symptom burden and functional status are linked. The implication in this research study would be that the worse the physical symptoms (or symptom burden), the worse the functional status (or ECOG score(85)) - the worse the quality of life (or APCA-POS score). The Supportive and Palliative Care Indicators Tool (SPICT) identified poor performance status as an indicator of deteriorating health,(86) and Gestsdottir *et al* claimed that worsening functional status was the single strongest indicator of deterioration and death.(87) That would imply that poor functional status was related to mortality – and palliative care need. This confirmed the researcher's hypothesis that the lower the patient's quality of life and the greater the symptom burden-the more the palliative care need of the patient.

2.11 Conclusion

The Literature review gave a framework for the development of the research questionnaire and disease trajectory (discussed in Chapter 5). It also helped validate the hypothesis proposed by the researcher that the lower the patient's quality of life and greater the symptom burden-the more the palliative care need of the patient. The gaps noted in the literature corroborated the necessity of this research in the history of the *Mycobacterium tuberculosis* infection. It was emphasised in the literature review that evaluating

the quality of life, symptom burden, functional impairment and palliative care needs of DR-TB patients was important to the patient and their management strategies. Urgent strategies of care should be implemented that are effective, humane, and proportional to the needs of these vulnerable patients. (22,63,66)

The following chapter discusses the study's methodology in terms of the design and collection of data.

CHAPTER 3

Methodology

3.1 Introduction

Chapter 3 discusses the planning and implementation of the research.

3.2 Study design

This study was an observational, quantitative and qualitative, cross-sectional cohort study.

3.3 Study site

The geographical location was the Southern sub-district of Cape Town. (The sub-districts of Cape Town were re-classified subsequent to the study completion.)

Figure 7: Map of the Cape Peninsula showing clinics within the Southern sub-district

3.4 Inclusion criteria for study

- Patients infected with DR-TB (this included RMR-, RR-, MDR-, pre-XDR, XDR and TDR); regardless of whether their TB was pulmonary or extra-pulmonary.
- They should be 18 years or older.
- They should currently reside within the Southern sub-district of Cape Town.
- The participants must be able to communicate in English, Afrikaans or Xhosa.
- They must be able to give informed consent.

3.5 Exclusion criteria for study

- Those patients who had DS-TB, or DR-TB defaulters lost to follow-up.
- Patients hospitalised at the time of data collection were not included.
- Patients unable to communicate effectively.
- Patients with diminished decision-making capacity (assessed as disorientated to time, place, or person).
- Those patients currently incarcerated in Pollsmoor prison facility.

3.6 Sample size

The researcher generated a DR-TB patient list from the names provided by the City of Cape Town's MDR-TB team and the names of patients known or attending the clinics in the southern sub-district.

For completeness sake, the private pathology laboratory, Pathcare, was contacted to enquire about the prevalence of DR-TB isolates picked up in the private health sector. Pathcare tested 1162 patients in 2016 in Cape Town - Rifampicin resistance was isolated in 234 patients, Isoniazid in 160, aminoglycosides in 20 and fluoroquinolones in 33. Pathcare, however, was unable to ring fence their data for the southern sub-district. (email correspondence with Pathcare's J.Gerber on 13.06.2017, unreferenced) Patients diagnosed in private were referred to the local government clinics for ongoing management.

On the 08.03.2017, the total number of DR-TB patients within the Southern sub-district of Cape Town on paper totalled 199. Figure 8 shows the proportions of patients at each clinic. This number of patients was further reduced after eliminating those patients fulfilling exclusion criteria and others that were "treatment completed", "cured", "deceased", "discharged", and "unknown to clinic".

Figure 8. Cohort of DR-TB patients on 08.03.2017

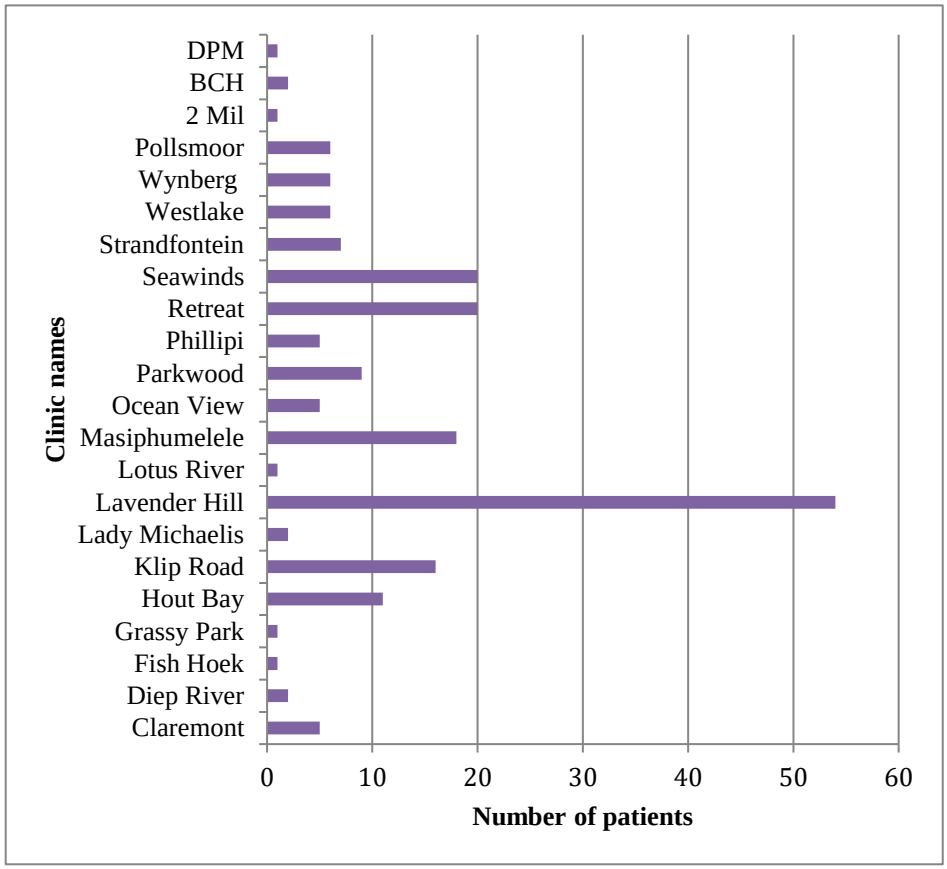


Table 2. Cohort "ledger"

Original number	Exclusions		Further exclusions		RUNNING TOTAL	Sample (%of running total)
199						
	Age <18	9			190	
	DS-TB	1			189	
	MOTT/NTM	1			188	
	Incarcerated	6			182	
	Deceased	12			170	
	Hospitalized	20			150	
			Lost to follow up/defaulter	21	129	
			Treatment completed	3	126	
			Cured	13	113	
			Relocated	4	109	
			Discharged	16	93	
			Unknown to clinic	12	81	
			Lavender Hill clinic	22	59	
			Pilot study participants	6	53	
						28 (52.8%)

Unfortunately recruiting patients from the Lavender Hill clinic became too dangerous with road and clinic closures due to taxi and gangster violence.

The number of possible patients was thus reduced to 53. The patients to be interviewed were then randomly chosen by convenience sampling, beginning at the clinics with the greatest number of DR-TB cases.

3.7 Data collection tool

An assessment tool specific to DR-TB patients' palliative care needs was not identified in the literature. The researcher developed a multidimensional questionnaire for palliative care needs, by assessing the quality of life, functional status and symptom burden of DR-TB patients. The Literature Review in Chapter 2 discussed these variables in detail.

The questionnaire was available in 3 languages: English (Appendix 5), Afrikaans (Appendix 6) and Xhosa (Appendix 7). It was forward translated from English into Afrikaans and Xhosa by first-language translators, and then back translated into English to confirm the validity of the translation. Uniquely, the questionnaire did not require retrieval of information from the patient's clinic file.

Each participant was asked questions from a paper questionnaire that included five components:

Table 3. Components of questionnaire

	Tool
Demographic details	Individual questions (researcher-designed)
Functional Status	ECOG score(85)
Quality of life	APCA African POS(88)
Symptom burden	Symptom checklist (researcher formatted)
Personhood and dignity	Modified Patient Dignity Question

3.7.1 **Demographic details** [questions 1-26]:

The demographic details of the participants provided information regarding age, socio-economic status, lifestyle habits, financial circumstances, home situation, previous TB, HIV co-infection, compliance and time of diagnosis and treatment initiation. These questions were designed by the researcher. Questions were answered by ticking a checkbox or by one-word answers.

3.7.2 The ECOG Scale of Performance Status [question 27]:

The ECOG score measured the impact of DR-TB on the patient's daily living abilities and measured their functional status. The ECOG classification consisted of six possible categories (scored 0-5) and was quick and easy to determine. This scoring system had been used in other studies of TB patients in South Africa. (68) The APCA African POS guidelines also recommended using the ECOG score in conjunction with the APCA POS assessment. (89)

3.7.3 The APCA African POS tool [questions 28-34]:

The APCA African POS tool was chosen to be a QoL measure. It had been developed to assess a patient's palliative care needs in terms of physical, psychological, social and spiritual concerns. (90) It addressed patients' optimal care requirements(89) and measured the quality of the care rendered with consecutive testing. As this research study was aimed at assessing the palliative care needs of the DR-TB patients only, single use of the tool was performed and questions 8,9 and 10 of the original APCA African POS (that related to the patient's family) were not included in this study. Single use had been discussed with the APCA African POS developers.

This tool had been validated as a research tool applicable to the South African context (88) with the acknowledgment of the HPCA of South Africa and King's College London in this regard. It was available in relevant translations (English, Afrikaans and Xhosa) for measuring the care outcomes of patients with life-threatening illnesses. (89) Advantageously, the APCA-POS questions were short and easy to administer despite the respondent potentially being very weak or ill or residing in an informal settlement. (89) The answers were scored using a 6-point Likert-type scale (from 0-5) and each score had corresponding descriptive labels and visual aid (Appendix 3). The researcher used a visual aid to complement the Likert scale and adjusted the recall period to one week instead of three days - which was permissible within the APCA African POS guideline stipulations.(89) Answers to questions 31-34 were reversed as necessary when recorded (so that "0"= best and "5"= worst score throughout).

3.7.4 Symptom list [questions 35-60]:

Justice *et al* defined the objective of a symptom index: to identify and qualify symptoms representative of clinical phenomenon to advise effectively on intervention. (84) A specific, validated DR-TB symptom checklist or scale was not found in the literature. (91) As a result, the researcher identified the most burdensome symptoms of DR-TB in the literature(22,35,77,92,93) and together with input from local DR-TB experts compiled a list. These symptoms represented issues relating not only to the DR-TB disease, but also to common adverse drug reactions, associated DR-TB related stigma and economic

burden. Financial and spiritual domains were included according to Chang *et al*'s recommendations. (63) The content validity of the symptom burden list was discussed further with the researcher's supervisor and experts within the DR-TB field.

In order to minimise recall bias, study participants were asked to remember whether in the preceding week they had experienced each symptom from the checklist and asked to rate the symptom's frequency and intensity using a visual Likert-type scale (see Appendix 4).

3.7.5 Open-ended questions [questions 61 and 62]:

These informal questions were added post pilot study - having considered Lopez *et al.*'s paper, "*Knowing about you: eliciting dimensions of personhood within tuberculosis care"*. (47) The intent was to address the individual DR-TB patient's priorities, uphold their dignity(47) and invite broader, more patient-centred concerns to be voiced. Question 62 was based on Chochinov's Patient Dignity Question, (94) and invited the respondent to "express their personhood" (47) in a "culturally sensitive" (20) manner.

3.8 Pilot study:

The face validity and reliability of the questionnaire was verified by conducting a pilot study of six DR-TB patients.

The original questionnaire – which was entirely quantitative - insufficiently captured relevant, life-changing issues for the pilot participants. Consequently, adjustments were made to a few questions and two qualitative open questions were added as discussed above.

All those approached during piloting were willing to participate. Only one of the six pilot participants required urgent referral for further medical management. The clinic doctor was available for discussion and the formal distress protocol referral form was not required. This patient required eventual hospital admission for symptom management and sadly died soon after the pilot study was completed. Another patient interviewed in the pilot study died a few months after being interviewed. Due to the procedures put in place for confidentiality it was not possible to look back at their respective questionnaires and gauge the validity of their answers in predicting their unfortunate outcomes.

The timing of the interviews coincided with their visit to the clinic. The length of time to explain the research, take consent and ask the questionnaire took between 20-27 minutes. Towards the end of the

interview, the participants seemed fatigued by the tedious verbal descriptions of the Likert-type scoring system and the visual scales were introduced to combat this as mentioned previously.

A further pilot study was not deemed necessary once these comprehensive alterations were made. Supplementary ethics approval was received from the UCT Human Research Ethics Committee (HREC). These new or altered questions were forward and back translated as previously described. The pilot study patients' answers were not included in the final data analysis.

3.9 Palliative Care need allocation

After finalising the content of the questionnaire, the researcher determined a score for each question that would rate as a "Palliative Care need". This estimation was based on the literature review, other palliative care need assessment tools (SPICT(86), Gold Standards Framework(95)), clinical intuition, palliative care training and supervisory input. The consensus was that "Palliative Care need" be defined as:

- ECOG score (q27) of 3 and above,
- APCA African POS varied with each question (q28: score 2 and above; q29: 2 and above; q30: 3 and above; q31: 2 and below; q32: 3 and below; q33: 2 and below; q34: 2 and below)
- Symptom burden list - a score of 3 and above.

This "need" allocation was not indicated on the paper copy of the questionnaire to ensure that no bias was introduced during the interview.

3.10 Training of the researcher:

The researcher ensured that she was equipped to answer any question regarding DR-TB that the study participants might have, and had a thorough understanding of each question and the scales used in answering. The APCA African POS training manual was referred to by the researcher and online support was accessed at www.pos_pal.org.

Prior to the any contact with potential DR-TB study participants, the researcher was formally "fit-tested" for an N95 mask* and the researcher ensured a sufficient supply of the requisite healthcare particulate respiratory and surgical masks.

---

* An "N95 mask" is a disposable respiratory protective device

Before starting data collection, the researcher felt confident in undertaking the research. An additional research assistant was not utilised, however a Xhosa translator (available at the clinic) was required when interviewing Xhosa-speaking patients. In these instances, the researcher expressly instructed the translator to quote the questions verbatim from the Xhosa-translated questionnaire and to interpret directly back to the researcher avoiding extrapolation.

3.11 Recruitment strategy

The clinics with the highest incidence of DR-TB were targeted initially. The clinic managers were emailed requesting permission to visit the clinic and recruit DR-TB patients - with an attached copy of the research proposal, information sheet and HREC approval reference letter. The researcher also attempted to contact the clinic managers telephonically. However, several of the clinic's email addresses and telephone numbers were out-dated, incorrect or went answered. After several attempts at contacting the various clinics and the clinic managers electronically and telephonically, the researcher attempted to meet the clinic manager on the day of visiting. Many times however, the researcher only had the opportunity to speak to the TB sister or sister-in-charge telephonically, getting the clinic manager's permission by proxy from the TB sister. On the day of visiting the clinic, the researcher supplied the TB sister with a copy of the study's information sheet with the researcher's contact details, ethics approval and UCT HREC member's contact details.

The clinic TB sisters provided the researcher with information (telephonically or in person) regarding the number of DR-TB patients attending their clinics and the patients' sputum conversion status, when patients were next due for a doctor's appointment, support group or audiology appointment and times when best to visit the clinic (with respect to injection and medication dispensing times). DR-TB patients fulfilling the inclusion criteria were then approached at their respective clinics at these times.

The researcher also liaised with the CCW/ DR-TB counsellor, and accompanied her on three occasions to known DR-TB patients' homes. These patients had been informed of the research study and consented to participation prior to the researcher's visit.

The prospective study participants were informed of the study verbally and with the help of a printed Information sheet (see Appendices 8,9,10) that was theirs to keep. Patients were invited to ask questions, raise concerns or confer with family members regarding their participation in the study.

They were then invited to participate voluntarily and informed that there would be no monetary or other incentives offered for their participating. Patients were reassured that declining participation would not result in deleterious consequences. The researcher explained her non-involvement in their clinical management and was mindful to differentiate between patient's routine standard of care to avoid any feeling of coercion. The distress protocol (see Appendix 20 and Section 3.16) was explained to the patient, and permission requested to refer by name to other HCPs should further management be necessary.

After ensuring that the trial participant understood the purpose of the research study, how the questionnaire would be administered and how data would be collected, informed consent (Appendices 11,12,13) with a witness' signature was requested in order to continue.

3.12 Data collection procedure

Clinic activities and staff duties were not interrupted as a result of this study. In the clinic environment, patients were interviewed either in an unused office or outside garden; and in the home environment in an inside sitting area to ensure privacy. The researcher was responsible for explaining the research information sheet, taking informed consent and completing the questionnaires and took care to maintain confidentiality, dignity and respect for the participants during the interview process. This included when a Xhosa translator's help was required. Before starting the questionnaire, the patient's mental capacity and their understanding of confidentiality were determined by the researcher.

Thereafter, the once-off interview proceeded, observing appropriate infection control measures - such as the use of particlate respiratory health masks, surgical masks, adequate ventilation and draft in interview area. The questions were asked in the order they appeared on the questionnaire, using visual aids to assist in answering the Likert-type questions and ensuring the researcher did not influence the participants' responses.

The participants' comments and answers were recorded on the questionnaire *verbatim* by the researcher. The researcher carefully documented anecdotal narrative data offered by the participants of their personal accounts during the interview in a non-biased way. Other additional information regarding the interview – such as the use of facemasks, the trial participant's emotional display, those present during the interview were also written down.

If the participant required further urgent management (deemed a "Palliative care Referral"), with their permission, the participant was referred back to the clinic doctor with a referral letter detailing the issues and concerns that arose during the interview (see Appendix 14). If the doctor was not available immediately, either the TB-sister was informed and the referral letter was placed in the patient's file, or the CCW/DR-TB counsellor was informed to ensure the patient be seen by the doctor as soon as possible.

The interview concluded by thanking the participant for their time and willingness to participate, and by reiterating that they keep the information sheet in a safe place and contact the researcher should there be any queries.

3.13 Data storage & confidentiality

The data was extracted from the questionnaire by the researcher only, in a private secure location, as soon after the interview as feasible. The raw data was loaded onto a password-protected computer and a cloud service was used as backup. Confidentiality was maintained by storing the questionnaire and informed consent documents in separate sealed files with no means of associating names to answers. These folders were not misplaced at any stage and were not handled by a third party. The participant's name was ticked off the compilation list to prevent duplication.

Paper copies of the completed questionnaire were locked in a secure storage facility - with access available to the researcher only. The study participant's data will be retained until the publishing of a peer-reviewed journal article. The clinical investigator takes responsibility for the storage, access and final disposal of the raw data (including data from the pilot study). This collected data will not be shared with other parties.

3.14 Data analysis

3.14.1 Quantitative data analysis

Quantitative data was entered into a bespoke Excel spreadsheet by the researcher. Statistical guidance was provided by Mr Jordache Ramjith, Lecturer and Biostatistician in the Division of Biostatistics and Epidemiology at the UCT School of Public Health and Family Medicine.

Basic statistical analysis was undertaken, such as descriptive statistics and cross-tabulation. Descriptive statistics was used to explain the study participants' demographic profiles. Mann-Whitney tests were performed to compare two independent variables and statistical significance determined. Pie charts and

bar graphs were used to represent the data visually. The ranking, frequency, percentage, prevalence and severity of symptoms were tabulated. Spearman's Rank Correlation compared variables to consider statistical significance. The mean total of symptoms and a summative measure of functional status was calculated. Cronbach's alpha analysis was used to analyse the reliability of the questionnaire, consistency and insightfulness of patients' answers – particularly with regards to psychosocial concerns. A Cronbach's alpha score of >=0.70 was considered to indicate satisfactory reliability of the scale.(69)

As mentioned previously, "Palliative Care need" was defined in each question according to a researcher-determined rating on the Likert scale. Proportions of people in need of palliative care according to their quality of life and symptom burden were determined with a confidence level of 95%. A probability below 0.05 was regarded as being statistically significant. Multiple Logistic regression was carried out to determine how quality of life, functional status and symptom burden affected Palliative Care Referral.

Results of the data analysis are presented in Chapter 4.

3.14.2 Qualitative Content analysis

Each interview was read and then re-read and all additional comments, context and descriptions given by the participants and impressions of the researcher were transcribed into the researcher's notes. This narrative data was included along with the open-ended questions (q61 and q62) in the content analysis.

Initially the qualitative analysis focused on how participants responded to each question and consistencies and differences were identified. Later, connections and relationships between questions were explored. Information was categorised according to themes and organised into coherent categories.

3.15 Ethical considerations

This study was researcher-funded and undertaken to fulfil requirements for the UCT Masters of Philosophy in Palliative Medicine. The research proposal was initially submitted to the UCT HREC for ethics approval on 25.05.2016 (reference REC 7743). After deliberation, the HREC requested clarification on a number of issues. These were sufficiently addressed with modifications to the study and full ethics approval was later granted on 12.10.2016. Further ethics approval was received from the HPCA (Appendix 15), and permission granted to undertake research at the clinics managed by the Department of Health (Appendix 16) and City of Cape Town (Appendix 17) in the southern sub-district.

After the completion of the pilot study, the title, inclusion and exclusion criteria were amended and the research proposal was submitted again to UCT HREC on 27.02.2017. DR-TB patients admitted to hospice or hospital were excluded and HPCA was later notified that further ethics approval would not be pursued. Full ethics approval from UCT HREC was received on 08.03.2017 (See Appendix 19). The Department of Health and City of Cape Town were informed.

DR-TB patients might have been vulnerable if acutely unwell, had a short life expectancy, were experiencing stigmatisation or lived in dangerous, impoverished socio-economic conditions. Additionally, trial participants might have been unemployed, have hearing impairment due to ototoxic anti-tuberculosis drugs, may find communicating difficult due to the necessity for wearing protective masks or have a low level of education and literacy. The researcher acknowledged and factored these in to the culturally sensitive manner in which patients were approached, explained informed consent and interviewed. Confidentiality was maintained throughout and patients' rights and welfare were protected.

It was the researcher's opinion that the benefits of the research to ascertain their palliative care needs outweighed the potential risks – however unrealistic expectations of benefits from participation or future palliative care services required further explanation where necessary.

3.16 Distress protocol

This safeguard was mentioned to the patient prior to their consenting to participate in the study. The patient was reassured that should they display or express physical or psychological distress during the questionnaire, then they could pause the questioning and either abandon or restart (with a rescheduled appointment time and date) the interview when they felt more able. (89) Appendix 20 detailed this procedure.

The protocol stated that should the distress warrant referral for further management, the researcher would then make arrangements to refer the patient to the appropriate personnel at the local clinic. A referral form (Appendix 14) with the patient's name, the study's name and the clinical investigators details were included. Importantly, the protocol also stated that should the participant need to terminate the questionnaire, their further care or management would not be deleteriously affected.

Of equal importance, the protocol stated that should the researcher feel that her physical safety be in jeopardy or that infection control be insufficient, that the questionnaire be halted, and that steps described in the distress protocol be followed.

The study design and recruitment of the DR-TB patients in the southern sub-district of Cape Town has been detailed, with distress protocol and ethical considerations emphasised. The next chapter documents the results and qualitative analysis of the 28 patients recruited into the research study.

CHAPTER 4

Results of the study

4.1 Introduction

Chapter 4 presents the results of the 28 participants' answers that were collected from 24.03.2017 until 16.08.2017 (excluding April and July school holidays). These participants represented DR-TB patients at various stages of their illness trajectory, attending clinics within the Southern sub-district of Cape Town. The small sample size was a limitation of the study.

The data is presented in the same order as the questionnaire. Each answer has frequencies and percentages alongside, and graphs and charts have been added to provide a clearer visual representation for interpretation. Patients' quotes have been italicised and the English translation given in brackets where necessary.

4.2 Cohort

The table below summarises the cohort characteristics.

Table 4. Data collection and sample details

Number of subjects eligible from the target population:	53
Number of those approached and invited to participate:	29
Number recruited from those approached:	29
Number of those evaluated from recruited:	28
Number of those evaluations included in the analysis:	28
Number of people where an appointment was made for an alternative time:	1
Number of interviews where a Xhosa translator was required:	4
Number of interviews discontinued - This patient had schizophrenia and lacked mental capacity to answer questions consistently and appropriately.	1
The number of patients who wore their mask during the interview (surgical or tissue):	26
The number of times the researcher wore her mask during the 29 interviews:	29

Due to this study being descriptive, a sample size calculator was not appropriate, having discussed the sample size estimation with the UCT Biostatistician. Recruitment of patients was discontinued after 28 patients were interviewed due to data saturation, but safety concerns, time and resource constraints also contributed.

4.3 Palliative Care need assessment

In the table below, the number of participants' answers falling within the"palliative care need" range for each question have been highlighted. Section 3.9 on page 39 detailed the researcher-defined "palliative care need" scores for each question. The total number of respondents that had a palliative care need for each question are found in the far right column.

Table 5. Number of respondents scoring within the "palliative care need" range in each question

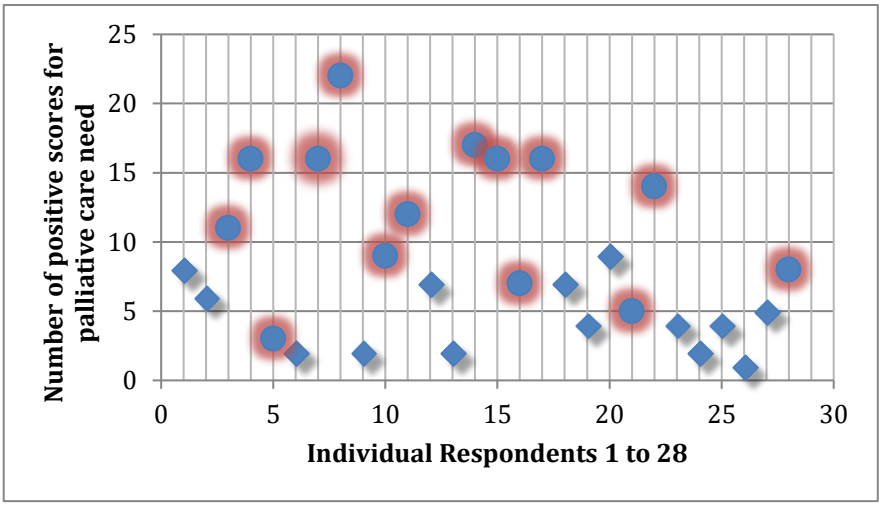
Question/Score	0	1	2	3	4	5	Total (%)
Q27				3	0	0	3 (10.7)
Q28			6	2	2	3	13 (46.4)
Q29			5	2	2	5	14 (50.0)
Q30				0	2	7	9 (32.1)
Q31				3	0	5	8 (28.6)
Q32			5	1	1	5	12 (42.9)
Q33				4	2	3	9 (32.1)
Q34				2	2	4	8 (28.6)
Q35				2	4		6 (21.4)
Q36				0	4		4 (14.3)
Q37				5	5		10 (35.7)
Q38				0	4		4 (14.3)
Q39				3	4		7 (25.0)
Q40				0	2		2 (7.1)
Q41				1	3		4 (14.3)
Q42				3	7		10 (35.7)
Q43				0	0		0 (0)
Q44				3	4		7 (25.0)
Q45				3	2		5 (17.9)
Q46				3	9		12 (42.9)
Q47				0	2		2 (7.1)
Q48				2	3		5 (17.9)
Q49				0	2		2 (7.1)
Q50				4	5		9 (32.1)
Q51				0	1		1 (3.6)
Q52				4	5		9 (32.1)
Q53				2	5		7 (25.0)
Q54				2	5		7 (25.0)
Q55				1	3		4 (14.3)
Q56				0	5		5 (17.9)
Q57				1	2		3 (10.7)
Q58				3	0		3 (10.7)
Q59				2	6		8 (28.6)
Q60				2	19		21 (75)

Furthermore, "Palliative Care need" was also determined for each study participant. The number of times a participant had an answer within the pre-determined palliative care range (or shaded area in above table), a score of "1" was given, and outside the range a score of "0". These binary scores were totalled for individual respondents and have been represented in the following figure. All participants had at least one answer within the shaded area – therefore all had a specific palliative care need. The

graph indicated that all those participants with a score of 10 or more required urgent palliative care referral on the day of their interview.

Figure 9. The "Palliative care needs" scores for individual respondents (n=28)

Range of scores: 1 to 23. (Red highlighted scores: respondents referred urgently)



4.4 Demographic details

Table 6. Answers to questions 1 to 9

Questions						
1. Age (years):	Youngest: 18		Oldest: 63		Median: 42	
2. Sex: (*n; %*)	Male: 13 (46.4%)			Female: 15 (53.6%)		
3. Citizen: (*n; %*)	South African: 27 (96.%)			Non-South African: 1 (3.6%)		
4. Lang: (*n; %*)	Afr: 11(39.3%)	English: 6 (21.4%)		Xhosa: 8 (28.6%)	Other: 3 (10.7%)	
5. Marital status: (*n; %*)	Single: 7 (25%)	Married: 8 (28.6%)	Pa'ship: 10 (35.7%)	Divorced: 0 (0%)	Widowed: 3 (10.7%)	Other: 0 (0%)
6. Ed lvl:(*n; %*)	Prim: 13 (46.4%)	S'dary: 13 (46.4%)		Tertiary: 0 (0%)	None: 2 (7.1%)	
7. Setting: (*n; %*)	Clinic: 25 (89.3%)			Household: 3 (10.7%)		
8. Dwell: (*n; %*)	Brick house: 13 (46.4%)			Informal settlement: 15 (53.6%)		
9. No. of windows	Least: 0		Max: 10		Mode: 3	

Age categories (such as those used in de Vallière and Barker's study(68)) were compared with ECOG and median APCA-POS and Symptom burden scores and statistical significance determined. The explanation of the significance of the age group 35-49 years is discussed in Section 5.2 on page 68.

Table 7. Age categories versus median ECOG, APCA-POS and Symptom burden scores

	Median ECOG	Median APCA-POS (IQR)	Med. Symptom burden (IQR)
Age 35-49 yrs (*n=14)*	1	12.5 (11)	27 (39.5)
Other age *(n=14)*	1	9 (7.75)	24 (24.5)
Median difference	0	3.5	3

Mann-Whitney test of median APCA POS score: age (35-49 years) vs other age (using online statistical analysis site: www.socscistatistics.com/tests/mannwhitney) (96) :
The *p*-value is 0.20766. The result is *not* significant at $p > 0.05$.

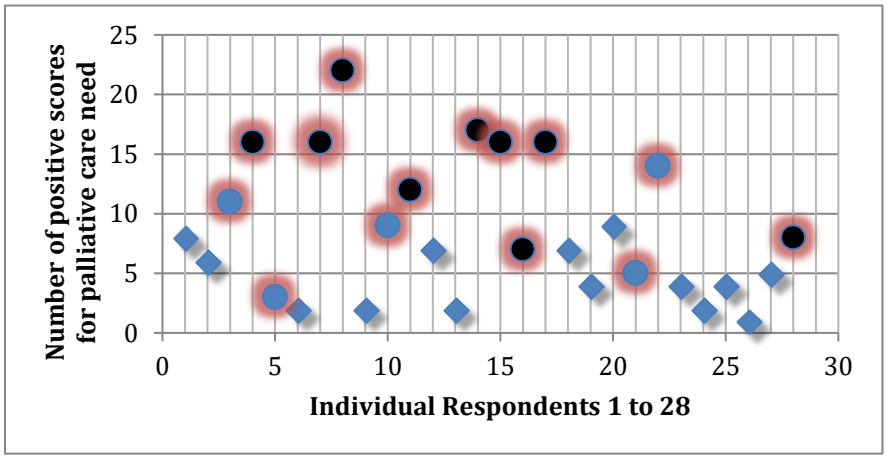
Mann-Whitney test of median Symptom burden score: age (35-49 years) vs other age (using online statistical analysis site: www.socscistatistics.com/tests/mannwhitney)(96)
The *p*-value is 0.4593. The result is *not* significant at $p > 0.05$.

The Mann-Whitney test is a non-parametric test to compare outcomes between two independent groups. (96)

This analysis showed that palliative outcome and symptom burden scores were not influenced by age.

"Palliative Care need" of the 35-49 year age group is indicated in Figure 10.

Figure 10. The "Palliative care needs" scores for individual respondents (n=28).
(Red highlighted scores: respondents referred urgently. Black dots: respondents 35-49 years)



Male and female responses were compared with median APCA-POS and median Symptom burden scores:

Table 8. Sex versus median APCA-POS and median Symptom burden score

	Median APCA-POS score (IQR)	Median Symptom burden score (IQR)
Male *(n=13)*	11 (8)	22 (21)
Female *(n=15)*	11 (13)	41 (40)
Median difference	0	19

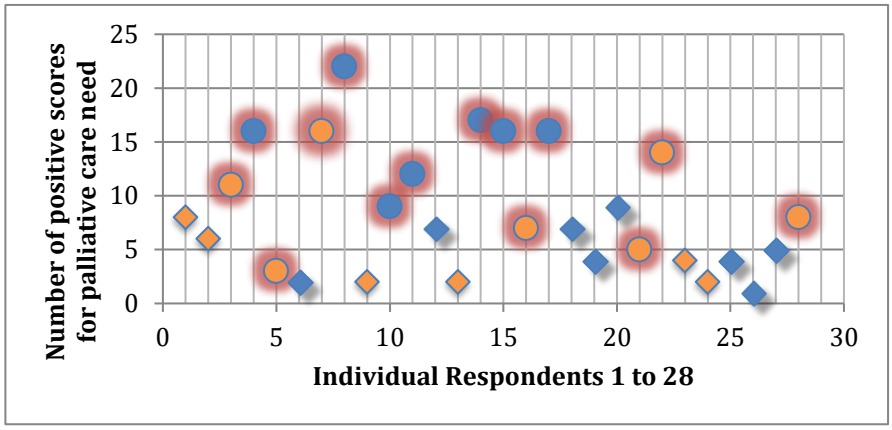
Mann-Whitney test of median APCA-POS score male vs female respondents (using online statistical analysis site: www.socscistatistics.com/tests/mannwhitney) (96) :
The *p*-value is 0.85716. The result is *not* significant at $p > 0.05$.

Mann-Whitney test of median Symptom burden score of male vs female respondents (using online statistical analysis site: www.socscistatistics.com/tests/mannwhitney) (96) :
The *p*-value is 0.101. The result is *not* significant at $p > 0.05$.

Thus, the sex of the patient did not influence their APCA-POS or symptom burden scores.

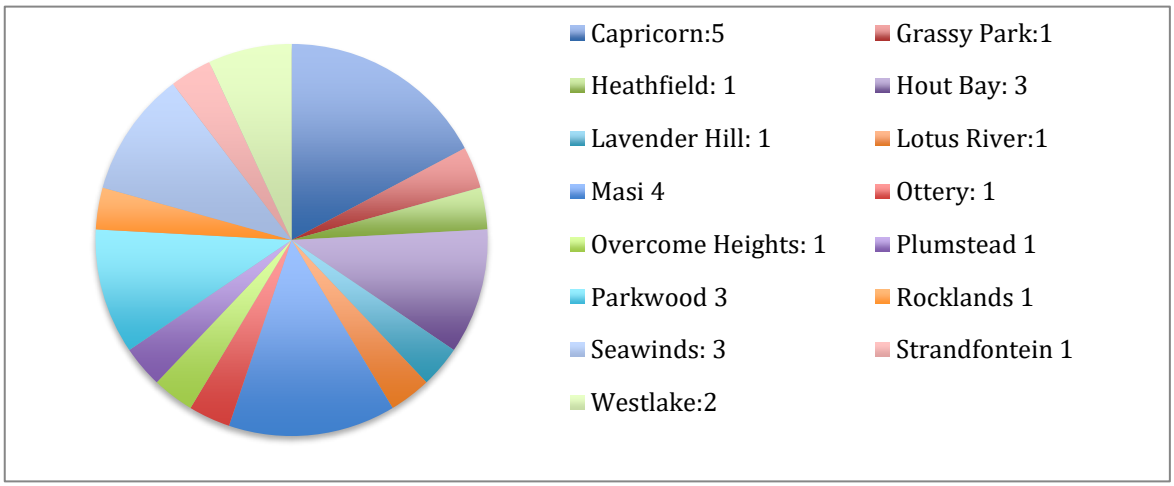
Figure 11. The "Palliative care needs" scores for individual respondents (n=28)

(Red highlighted scores: respondents referred urgently. Orange data points: Male patients)



Question 10. Suburbs where participants resided

Figure 12. Sample suburb distribution



Demographic details continued

Table 9. Answers to questions 11-26

Questions							
11. No. of people in household:	Most: 10			Mode: 4			
12. Others with TB at home: *n (%)*	Yes: 7 (25%)			No: 21 (75%)			
13. Previously had TB: *n (%)*	Yes: 18 (64.3%)		No: 10 (35.7%)		Uncertain: 0 (0%)		
14. When DR-TB diagnosed: *n (%)*	2017: 5 (17.9%)	2016: 15 (53.6%)	2015: 7 (25%)	2014: 0 (0%)	2013: 0 (0%)	2012: 0 (0%)	<2012: 1(3.6%)
15.When meds started: *n (%)*	2017: 5 (17.9%)	2016: 15 (53.6%)	2015: 7 (25%)	2014: 0 (0%)	2013: 0 (0%)	2012: 0 (0%)	<2012: 1(3.6%)
16. Currently taking meds: *n (%)*	Yes: 25 (89.3%)			No: 3 (10.3%)			
17. DR-TB status: *n (%)*	Defaulter: 2 (7.1%)		Treatment failure:1(3.6%)	Culture converted: 22 (78.6%)		Sputum positive: 3 (10.7%)	
18. HIV status: *n (%)*	Pos: 16(57.1%)		Neg:12(42.9%)	Unwilling: 0 (0%)		Unknown: 0 (0%)	
19. On ARVs: *n (%)*	Yes: 15 (53.6%)			No: 13 (46.4%)			
20. No. of tablets: *n (%)*	<10: 3 (10.7%) [0 tabs:1 (3.6%)		10-19: 7 (25%)		>20: 18 (64.3%)		
21. Problems taking meds: *n (%)*	Yes: 18 (64.3%)			No: 10 (35.7%)			
22. Smoke cigarettes: *n (%)*	Yes: 14 (50%)			No: 14 (50%)			
23. Using other drugs: *n (%)*	Yes: 2 (7.1%)			No: 26 (92.9%)			
24. Hospitalised in last year: *n (%)*	Yes: 15 (53.6%)			No: 13 (46.4%)			
25. HBC help: *n (%)*	Yes: 5 (17.9%)			No: 23 (82.1%)			
26. DR-TB affected work: *n (%)*	Yes: 18 (64.3%)		No: 8 (28.6%)		N/A: 2 (7.1%)		

HIV status was compared with median APCA-POS, ECOG and Symptom burden scores.

Table 10. HIV status versus median APCA-POS, median ECOG and median symptom burden scores.

	Median APCA-POS (IQR)	Median ECOG (IQR)	Median Symptom burden (IQR)
HIV positive:	12.5 (11.5)	1 (1)	23.5 (33.25)
HIV negative:	11 (1)	1 (1.25)	25 (7.5)
Median difference	1.5	0	1.5

Figure 13. The "Palliative care needs" scores. Red highlight: urgent referrals. Purple data point: HIV-positive pts

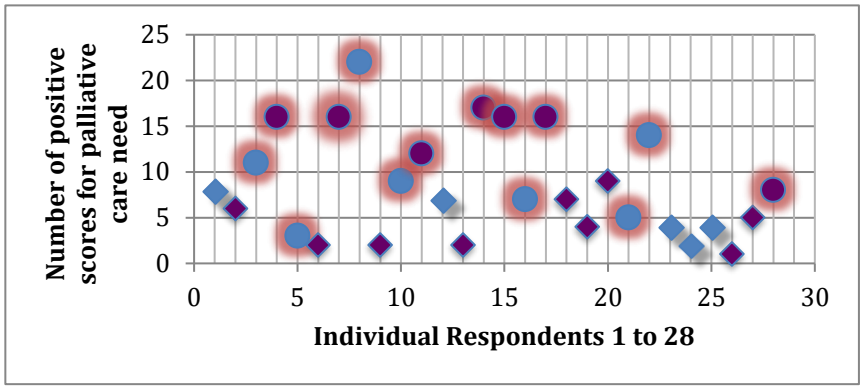


Figure 14. One patient's daily pill requirement

Patients who experienced problems with pill taking were compared to the number of pills prescribed.

Table 11. Contingency table showing "problems with taking tablets" *vs* "number of tablets required"

	<10 tabs	10-19 tabs	>20 tabs
Problems-Yes *n (%)*	1 (3.6%)	5 (17.9%)	12 (42.9%)
Problems-No *n (%)*	2 (7.1%)	2 (7.1%)	6 (21.4%)

The Contingency table below compared patients who reported DR-TB affecting their work with median APCA-POS and symptom burden scores.

Table 12. Work affected versus median APCA POS and median Symptom burden scores

	Median APCA African POS score	Median Symptom burden score
Affected work-Yes	12.5	36.5
Affected work-No	9.5	19
N/A	2.50	8

4.5 Functional status (ECOG score):

Table 13. Definition of ECOG scoring system(85) **with prevalence in current study**

ECOG score		*n* (%)
0	Fully active: able to carry on all activities without restriction	8 (28.6)
1	Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature	10 (35.7)
2	Ambulatory and capable of self-care but unable to carry out any work activities. Up and about more than 50% of waking hours	7 (25)
3	Capable of only limited self-care: confined to bed or chair 50% or more of waking hours	3 (10.7)
4	Completely disabled: cannot carry on any self-care: totally confined to bed or chair	0
5	Dead	0

The table below compared the ECOG scores with the median APCA-POS and symptom burden scores.

Table 14. ECOG scores versus median APCA-POS and median symptom burden scores

ECOG score	**Median APCA-POS score (IQR)**	**Median Symptom burden score (IQR)**
0	11 (9.25)	14.5 (16)
1	7.5 (6.25)	23 (31.25)
2	22 (13.5)	41 (30.5)
3	11 (2)	27 (10.5)
4	/	/
5	/	/

4.6 APCA African POS score

Answers to questions 31-34 were reversed as necessary when recorded (so that "0"= best and "5"= worst score throughout).

Question 28: Please rate your pain during the last week

Question 29: Have any other symptoms been affecting how you feel in the last week?

Question 30: Have you been feeling worried about your illness in the past week?

Question 31: Over the past week, have you been able to share how you are feeling with your family and friends?

Question 32: Over the past week have you felt that life was worthwhile?

Question 33: Over the past week, have you felt at peace?

Question 34: Have you had enough help and advice for your family to plan for the future?

Table 15. APCA-POS scores

APCA-POS score	Q28 *n (%)*	Q29 *n (%)*	Q30 *n (%)*	Q31 *n (%)*	Q32 *n (%)*	Q33 *n (%)*	Q34 *n (%)*
0	12 (42.9)	3 (10.7)	12 (42.9)	19 (67.9)	13 (46.4)	8 (28.6)	18 (64.3)
1	3 (10.7)	3 (10.7)	3 (10.7)	0 (0)	3 (10.7)	3 (10.7)	2 (7.1)
2	6 (21.4)	7 (25)	4 (14.3)	1 (3.6)	5 (17.9)	7 (25)	0 (0)
3	2 (7.1)	5 (17.9)	0 (0)	3 (10.7)	1 (3.6)	4 (14.3)	2 (7.1)
4	2 (7.1)	2 (7.1)	2 (7.1)	0 (0)	1 (3.6)	3 (10.7)	2 (7.1)
5	3 (10.7)	5 (17.9)	7 (25)	5 (17.9)	5 (17.9)	3 (10.7)	4 (14.3)

The scores of those patients who had described experiencing pain were compared to those not describing pain in terms of their ECOG, median APCA-POS, median symptom burden scores and need for referral.

Table 16. Contingency table comparing "No pain" to "pain" scores

	Median APCA-POS (IQR)	Mode ECOG	Median symptom burden (IQR)	Urgent referral *n (%)*
No Pain (score 0) *n=12*	6.5(12.75)	0	12(17.5)	3(25)
Pain (score 1-5) *n=16*	11(6)	2	34.5(26)	11(68.8)

Mann-Whitney test comparing median APCA-POS (pain vs no pain): p-value is 0.09894. The result is not significant at $p > 0.05$.

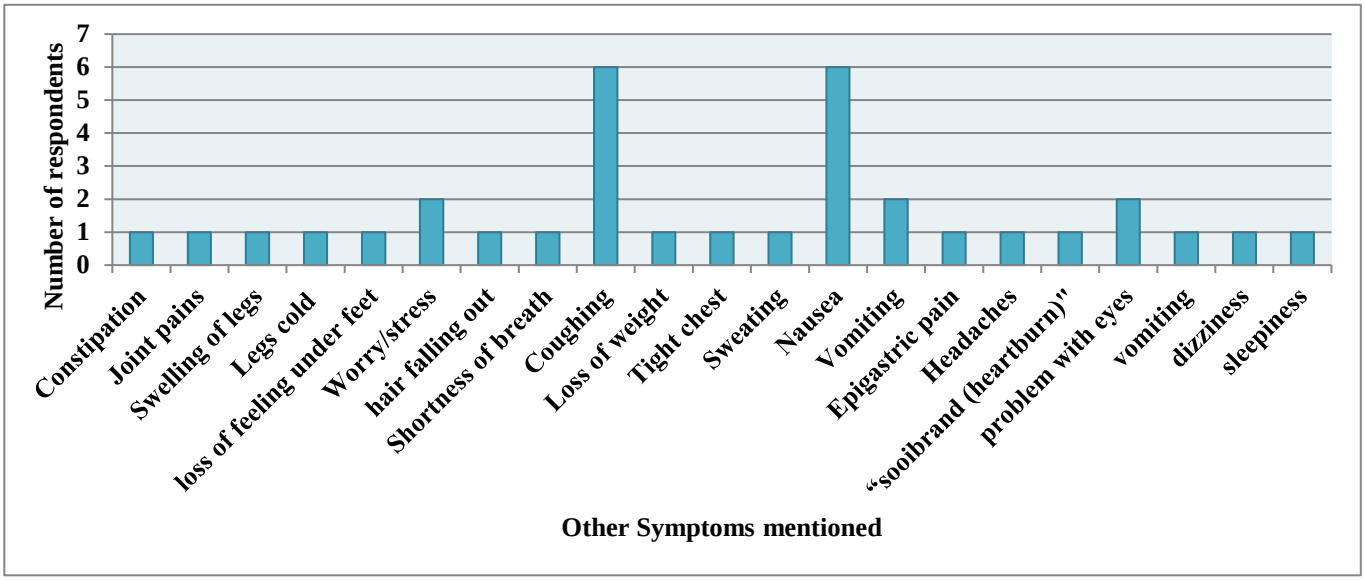
Mann-Whitney test comparing mode ECOG (pain vs no pain): The p-value is 0.00804. The result is significant at $p < 0.05$.

Mann-Whitney test comparing median Symptom burden (pain vs no pain). The p-value is 0.02034. The result is significant at $p < 0.05$. (using online statistical analysis site: www.socscistatistics.com/tests/mannwhitney) (96)

Therefore, the presence of pain influenced the ECOG and symptom burden scores, as well as the need for urgent referral.

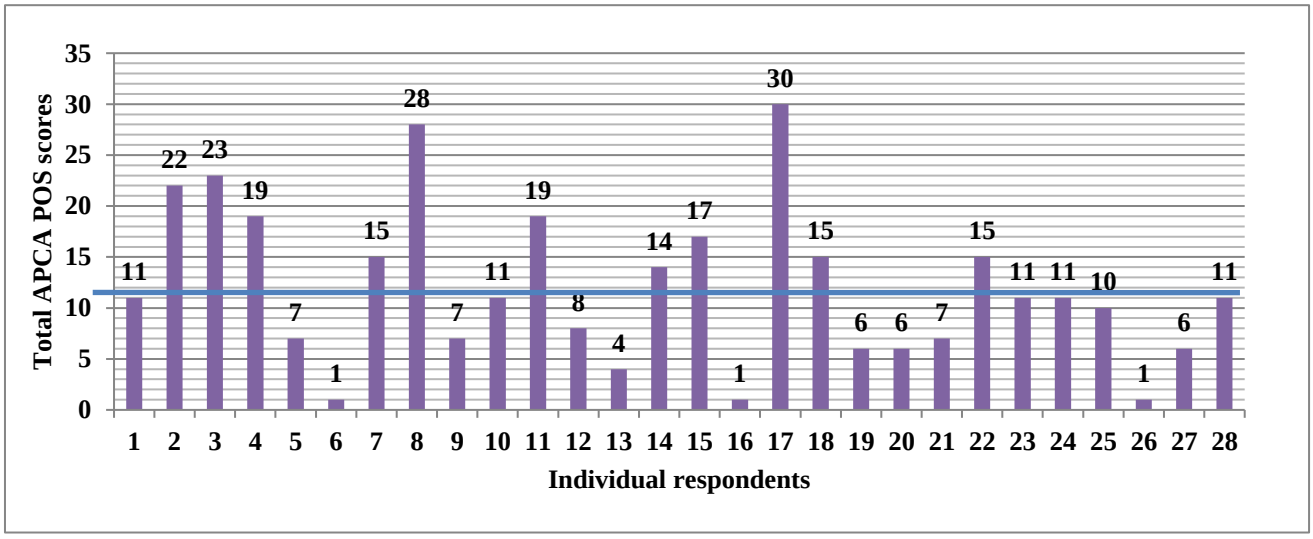
The symptoms that patients mentioned in question 29 were:

Figure 15. Prevalence of "other" symptoms



Respondents' total APCA African POS scores were calculated and are depicted in the figure below (keeping in mind that for q31 to 34 the scores were reversed). Therefore the best possible total score would be zero, and the worst possible total score 35. The blue line indicated the median score of 11.

Figure 16. Total APCA African POS scores



4.7 Symptom list

Questions 35 to 60 had been rated according to the following Likert-type scale:

Table 17. Likert-type scale

0	I do not have this symptom
1	I have this symptom, it doesn't bother me
2	I have this symptom, it bothers me a little
3	I have this symptom, it bothers me
4	I have this symptom, it bothers me a lot

Questions 35-49 related to physical symptoms. Answers are represented in the next table and graph.

Table 18. Answers to questions 35-49

Questions/ Scores	0	1	2	3	4
35: Difficulty falling or staying asleep	16 (57.1)	2 (7.1)	2 (7.1)	2 (7.1)	4 (14.3)
36: Feeling dizzy or light-headed	18 (64.3)	3 (10.7)	3 (10.7)	0 (0)	4 (14.3)
37: Fatigue or loss of energy	6 (21.4)	2 (7.1)	8 (28.6)	5 (17.9)	5 (17.9)
38: Pain, numbness or tingling in the hands or feet	17 (60.7)	4 (14.3)	3 (10.7)	0 (0)	4 (14.3)
39: Nausea or vomiting	16 (57.1)	0 (0)	4 (14.3)	3 (10.7)	4 (14.3)
40: Diarrhoea	26 (92.9)	0 (0)	0 (0)	0 (0)	2 (7.1)
41: Loss of appetite	18 (64.3)	2 (7.1)	4 (14.3)	1 (3.6)	3 (10.7)
42: Shortness of breath	13 (46.4)	0 (0)	5 (17.9)	3 (10.7)	7 (25.0)
43: Coughing up blood	28 (100)	0 (0)	0 (0)	0 (0)	0 (0)
44: Skin problems, such as rash, dryness or itching	12 (42.9)	5 (17.9)	4 (14.3)	3 (10.7)	4 (14.3)
45: Ringing in ears or loss of hearing	12 (42.9)	5 (17.9)	3 (10.7)	3 (10.7)	2 (7.1)
46: Joint pains	10 (35.7)	3 (10.7)	3 (10.7)	3 (10.7)	9 (32.1)
47: Ongoing pain at injection sites	26 (92.9)	0 (0)	0 (0)	0 (0)	2 (7.1)
48: Confusion or trouble remembering	11 (39.3)	8 (28.6)	4 (14.3)	2 (7.1)	3 (10.7)
49: Tremors, shaking or fits	23 (82.1)	1 (3.6)	2 (7.1)	0 (0)	2 (7.1)

Questions 50-60 concerned psycho-social issues and are depicted in the table and graph below:

Table 19. Answers to questions 50-60

Question	0	1	2	3	4
50: Feeling sad, down or depressed	11 (39.3)	4 (14.3)	4 (14.3)	4 (14.3)	5 (17.9)
51: Feeling suicidal	26 (92.9)	0 (0)	1 (3.6)	0 (0)	1 (3.6)
52: Feeling hopeless	16 (57.1)	1 (3.6)	2 (7.1)	4 (14.3)	5 (17.9)
53: Feeling anxious or scared	18 (64.3)	0 (0)	3 (10.7)	2 (7.1)	5 (17.9)
54: Having remorse or regret	13 (46.4)	3 (10.7)	5 (17.9)	2 (7.1)	5 (17.9)
55: Feeling like you're not coping	17 (60.7)	2 (7.1)	5 (17.9)	1 (3.6)	3 (10.7)
56: Feeling stigmatised by family, relationships are limited	21(75)	2 (7.1)	0 (0)	0 (0)	5 (17.9)
57: Feeling stigmatised by community or discriminated against	24 (85.7)	0 (0)	0 (0)	1(3.6)	2 (7.1)
58: Feeling stigmatised by health care professionals, abandoned	23 (82.1)	2 (7.1)	0 (0)	3 (10.7)	0 (0)
59: Feeling isolated and lonely	16 (57.1)	1 (3.6)	2 (7.1)	2 (7.1)	6 (21.4)
60: Worried about finances/ money	4 (14.3)	2 (7.1)	1 (3.6)	2 (7.1)	19 (67.9)

Figure 17. Prevalence and burden of physical symptoms

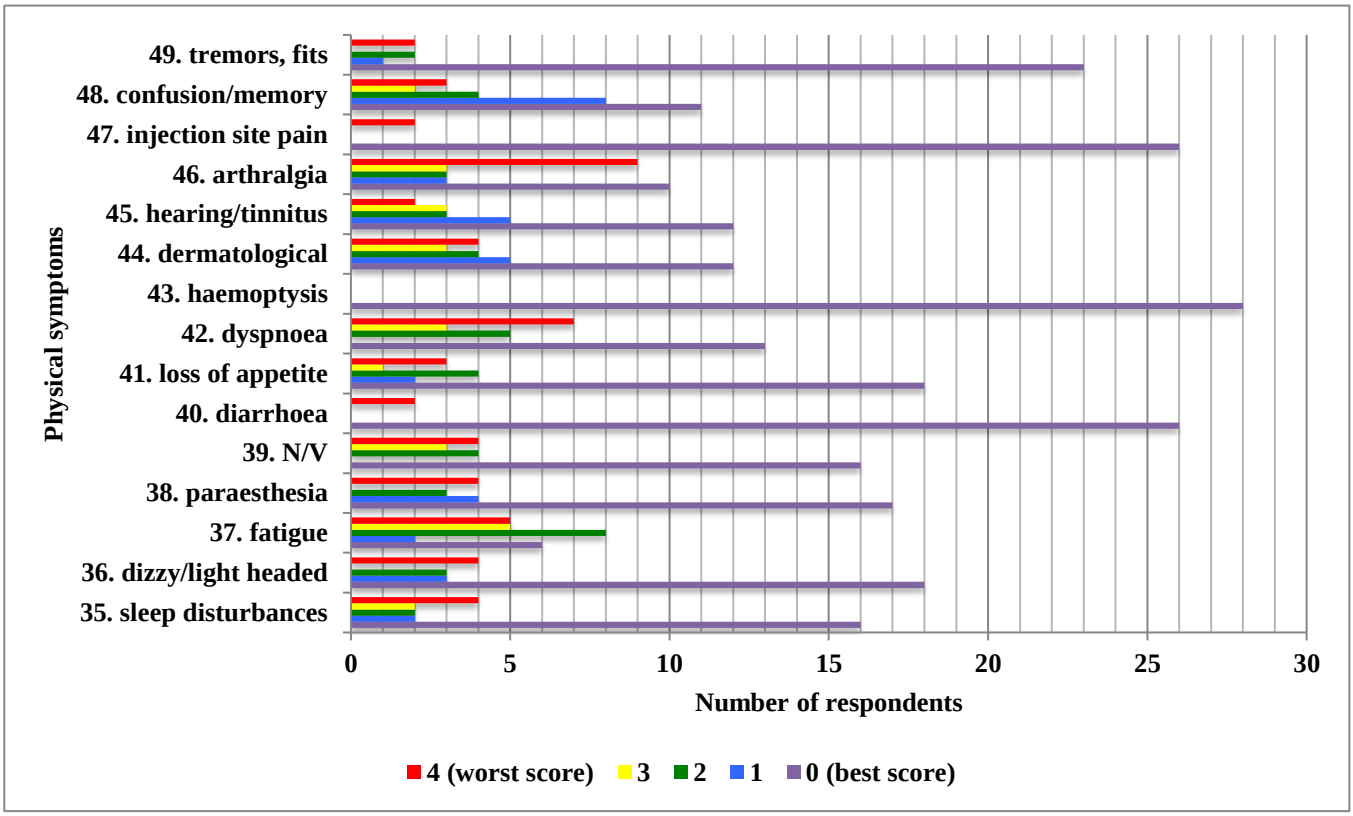
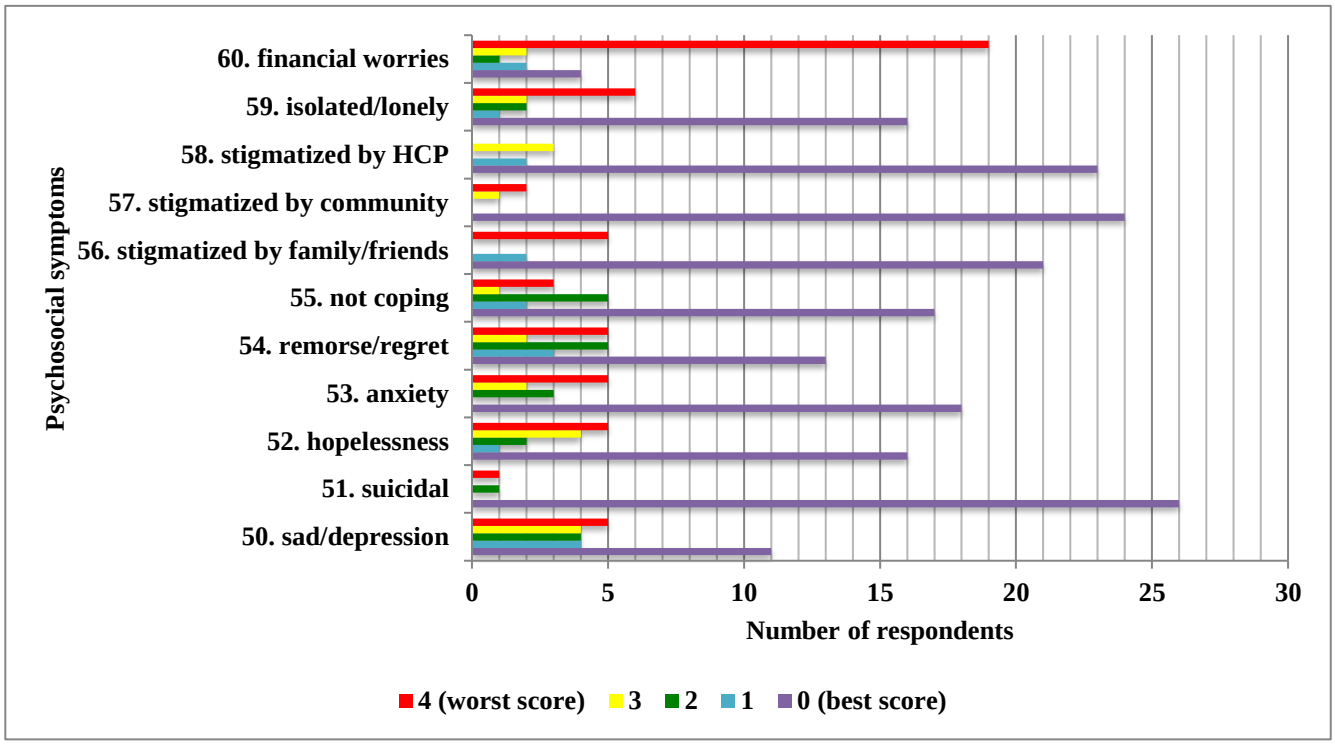


Figure 18. Prevalence and burden of psychosocial symptoms



The next contingency table compared "depression" with several variables:

Table 20. Contingency table comparing "depression" with "difficulty taking tablets", "financial worry", "suicidal ideation" and "hopelessness".

	Diff taking tabs-Yes	Diff taking tabs-No	Fin.worry-Yes	Fin.worry-No	Suicidal-Yes	Suicidal-No	Hopeless – Yes	Hopeless-No
Depressed-Y *N (%)*	14 (50.0)	3 (10.7)	14 (50)	3 (10.7)	2 (7.1)	15 (53.6)	11 (39.3)	6 (21.4)
Depressed-N *N (%)*	4 (14.3)	7 (25.0)	10 (35.7)	1 (3.6)	0	11 (39.3)	1 (3.6)	10 (35.7)

Spearman's Rank Correlation: Depression (x) vs difficulty taking tablets (y) (using online calculator found at Social Science Statistics website(97))

The value of R is 0.33776 and the two-tailed value of P is 0.07877. By normal standards, the association between the two variables *would not be considered statistically significant.*

Spearman's Rank Correlation: Depression (x) vs hopelessness (y) (using online calculator found at Social Science Statistics website(97))

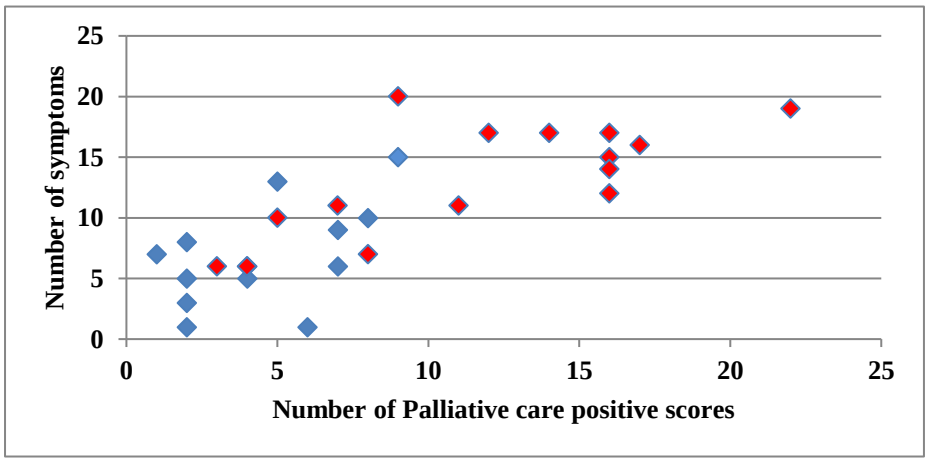
The value of R is 0.64595 and the two-tailed value of p is 0.0002. By normal standards, the association between the two variables would be *considered statistically significant*.

Spearman's Rank Correlation: Depression (x) vs financial worries (y) (using online calculator found at Social Science Statistics website(97))

The value of R is 0.28301 and the two-tailed value of p is 0.14448. By normal standards, the association between the two variables *would not be considered statistically significant*.

Each respondents' total symptom burden score was plotted. The average number of symptoms was 10.25. In the Figure below, red data points mark those respondents who were referred urgently.

Figure 19. Number of symptoms each respondent experienced



Cronbach's Alpha analysis was performed on questions pertaining to psychosocial concerns to determine the consistency of patients' answers and their insight into the questions. An alpha value above 0.7 was considered consistent. (98)

Table 21. Cronbach's alpha analysis

Items	Cronbach Alpha
All items	0.8474
Question 50 (Depression) excluded	0.7879
Question 60 (Financial worries) excluded	0.8791
Question 55 (Coping) excluded	0.8209
Question 52 (Hopelessness) excluded	0.7965
Question 53 (Anxiety) excluded	0.8293
Question 59 (Feeling isolated and lonely) excluded	0.8049

Therefore, the respondents had answered the questions consistently and reliably. Furthermore, Multiple Logistic Regression analysis was carried out to determine how quality of life, functional status and symptom burden (measurement variables, x_1, x_2 and x_3 respectively) affected Palliative Care Referral (binomial, independent variable, y: "0" no referral, "1" referral. 14 cases had y=0; 14 cases had y=1) - using online calculator found at www.statpages.info/logistic.html

Table 22. Univariable analysis *vs* multivariable analysis

	Univariable analysis				Multivariable analysis with FS				Multivariable analysis with FS (0/1)			
Var	Co-eff	P	OR	95% CI	Co-eff	P	OR	95% CI	Co-eff	P	OR	95% CI
x_1	0.1583	0.0287	1.1715	1.0166-1.3500	0.0724	0.4549	1.0751	0.8892-1.2999	0.0756	0.4289	1.0786	0.8943-1.3009
x_2 *(a)*	0.5637	0.1815	1.7571	0.7687-4.0166	0.1516	0.7879	1.1637	0.3857-3.5111				
x_2 *(b)*	0.7732	0.5485	2.1667	0.1734 27.075					0.3221	0.8312	1.3800	0.0714-26.687
x_3	0.1365	0.0042	1.1463	1.0440-1.2585	0.1254	0.0112	1.1336	1.0289-1.2490	0.1270	0.0101	1.1354	1.0306-1.2508

[Var= variable; Co-eff= co-efficient; p= p-value; OR= Odds ration; 95% CI= 95% confidence interval; FS=functional status]; x 2 (a)= functional status as scored on ECOG score; x 2 (b)= functional status as binary score :"0" is ECOG scores 0,1,2 and "1" is ECOG scores 3,4,5.

The use of the binary score of ECOG did not make a difference. Symptom burden scores showed a significant relationship to palliative care referral with a $p<0.05$.

4.8 Qualitative analysis of data retrieved from open questions

Question 61. Please tell me more about what troubles you the most?

Question 62. What else do I need to know about *you* to be able to provide good care?

The themes that emerged were:

(1) Financial concerns
(2) Concerns for Physical safety
(3) Dysfunctional social relationships
(4) Impact of DR-TB infection and treatment
(5) Concerns about HIV co-infection
(6) Patients' sense of loss of autonomy and self-worth
(7) Inadequate Therapeutic relationship

Theme (1) Financial concerns:

Several of the communities that were visited were impoverished and lacked decent infrastructure, amenities and accommodation. Many participants lived in unsafe locations and were concerned about the inadequacy of their housing. Households were often overcrowded. Participants had limited choice in where or with whom they lived due to their financial insecurity. Several patients were unable to access disability grants because of lapsed applications, missing Identity documents and asylum seeker status. The worry about the lack of money predominated: it caused stress and guilt due to the participant's inability to care and provide for their family (in terms of shelter, food, schooling and clothing) and thus fulfil parental responsibilities. Limited finances made transportation to clinics or visiting children difficult or impossible. Financial concerns worsened physical and psychological symptoms and strained relationships. Pre-existing financial constraints were exacerbated by the participant being unwell and incapacitated.

- *"Ek moet die waarheid praat – dis die geld" (I must be truthful – it's the money) – participant "AD"*
- *"I've got nothing at home" – participant "L"*
- *"Ek kan nie uitkom nie" (I can't make ends meet)- participant "O"*

Theme (2) Concerns for Physical safety:

Physical safety (personal, family, business and belongings) was a real concern for a number of participants. Their safety had been threatened by gangsterism, living in unsavoury neighbourhoods and opportunistic sexual exploitation. The safety of participants' family members was a concern when admission to BCH was considered.

- *"dinge wat ek sien nie reg vir my kind of my nie" (The things that I see [that are going on around us] are not right [beneficial] for my child or me)- participant "Y"*

Theme (3) Dysfunctional social relationships:

Several respondents had dysfunctional relationships that distracted from efforts to regain health and resulted in isolation. Some relationships were economically, physically and emotionally abusive. A few participants had been separated from their children by social circumstances –such as the recent fire in Imizama Yethu, social welfare child protection, gangsterism and their children's drug usage - and longed for contact.

- *"my familie– hulle verstoot – maak probleme vir my*" *(my family, they reject me and make problems for me)- participant "Y"*
- *"[I]can't even take my children to school"- participant "L"*
- *"Ek kry nie die liefde" (I don't get love) – participant "O"*

Theme (4) Impact of DR-TB infection and treatment:

- Participants described poorly controlled physical symptoms
  "to suffer like this, it's better for me to go [die]"- participant "R"
- The prescribed treatment, with the accompanying pill burden and side-effect manifestations affected patients
  "its scary actually" – participant "N"

Theme (5) Concerns about HIV co-infection:

For a number of HIV-positive patients, having HIV was worse than having DR-TB in that the stigma of HIV concerned them more than having DR-TB, and DR-TB was perceived as trivial compared to the fatality and incurability of HIV.

- *"As jy HIV is, is jy vrot" (If you have HIV – then you're [considered] rotten) – participant "O"*
- *"Die een maak jou gesond, die ander een maak jou dood" (This [DR-TB] you'll get better from, this [HIV] will kill you") – participant "O"*
- *Participant "O" requested a cure for HIV to be found.*

Theme (6) Patients' sense of loss of autonomy and self-worth:

Patients struggled with feeling out of control and unable to make their own decisions.

- Incapacitating physical symptoms led to a loss of independence.
  "[Die] pille maak my dronk – dan kan ek niks doen vir die dag nie" (*The pills make me feel drunk- then I can't do anything during the day)-participant "X"*
  "My life is not going to be the same again"-participant "R"
- Patients felt uncertainty for the future: they worried about being admitted to BCH, about future treatment opportunities and about not being cured.

"[there's] lots of promises for treatment, but nothing happens"- participant "G"

Some participants expressed a sense of worthlessness

- *"niks werd vir niemand nie" (["I'm] not worth anything for anybody")- participant "O"*
- *"somtyds voel ek so vuil" ("sometimes I feel so dirty"*) *– participant "P"*

Theme (7) Inadequate Therapeutic relationship:

Participants desired a more therapeutic relationship with their HCP: to be treated with respect and have their complaints addressed.

- "*om die moiete werd te voel" (To feel like I matter)- participant "E"*
- *"it is true – I'm not lying – they assume that I don't want to take my medication; but I have complained about the same problem for 6 months – and still don't feel better"- participant "R"*
- *"[I] can't swallow the tablets without eating – and [I'm] not eating at the moment" – participant "L"*

4.9 Qualitative analysis summary of all the narrative data

All the narrative data from the patients' interviews as well as questions 61 and 62 were analysed collectively and arranged into two themes or responses to patients' vulnerability. Vulnerability had led to the development of either despair or resilience. The theme relating to despair looked at the personal context and widened to include the family, community and the current health care system context. The theme relating to resilience showed attitudinal shifts and adjustments that stemmed from good therapeutic relationships and inner resolve.

Table 23. Emerging Themes from Qualitative analysis

	VULNERABILITY leading to:	
	(a) Despair	**(b) Resilience**
In personal context	Lack of autonomy Lack of dignity Spiritual pain	Adaptive medication-taking techniques Inner strength and purpose
In community context	Concern regarding Physical safety Lack of empathy/ stigma	
In family context	Weight of responsibilities Lack of empathy/ stigma	
Within Health care system	Lack of palliative care approach by HCP Negative connotations towards BCH	Valuable therapeutic relationships

Theme (a) Vulnerability/ Despair:

(1) **In personal context**

Participants despaired about their personal circumstances where there were unfulfilled wishes, poor self-determination, poor support and loss of selfhood.

Lack of autonomy:

- *"I wish for money – to have a life I can afford. If I want to do something to be able to do it" – participant "I"*
- *"without income I am lost" – participant "L"*
- *"I'm a prisoner in my own body" – participant "Z"*
- Participant "F" wanted to be able to get his salvage treatment regimen from his clinic and not be forced to be admitted to BCH.

Lack of dignity:

- *"I have to beg my neighbour for food for myself and my daughter" – participant "U"*
- *"Am I disgusting?"- participant "N"*
- *"If I die, don't tell anyone, just call my @£$%^&* children" –participant "O" recounting what her sister said before dying from MDR-TB*

Spiritual pain:

The following comments suggested spiritual suffering:

- *"I cry every day" – participant "L"*
- *"I will never have peace" – participant "U"*
- *"I'm a prisoner in my own body" – participant "Z"*

and descriptions of having lost identity, purpose and meaning:

- *"Ek voel klaar – ek is niks werd vir niemand nie" (I feel empty – I'm not worth anything to anybody) – participant "O"*
- *"Nothing comes right, nothing comes my way" – participant "L".*
- *"I don't know where I stand" – participant "G"*

Some respondents expressed their religious struggles in the context of being unwell:

- "*TB kom van die Here af"(TB comes from God)- participant "Q"*
- One patient had relinquished his Rastafarian beliefs of a herbal cure for DR-TB.

Others asked rhetorically:

- *"Why am I still taking the tablets if I'm going to vomit?" – participant "Z"*
- *"There's always the worry- is it your time?" – participant "AA"*
- *"When is this TB going to be finished?" – participant "AE"*

The persistence of some symptoms possibly indicated a spiritual component – *Participant "R"* had experienced the same symptom for 6 months.

(2) In community context:

Within participants' communities they felt isolated by fear or stigma.

Concern regarding Physical safety:

- Participant "L" claimed to be watched by her son's rival gang members.
- Attendance at the clinic was obstructed by gang rivalry and danger.
- "*The 'Americans' [gang name] are here at the clinic – hulle kyk skeef aan my" (The Americans watch me suspiciously at the clinic) –participant "Y"*

Lack of empathy by community members/stigmatisation:

- *"[my] friends have run away*" *–participant "S"*
- Whilst participant "H" was in BCH, her son had been bullied and teased with taunts of his mother going to die.
- Participant "S" was deliberately turned away from the community hall when seeking refuge from a fire in her township.

(3) In family context:

Participants also felt despair and loneliness within their family unit.

Weight of responsibilities:

- *"I must be alive for my children and grandchildren" –participant "J"*
- *"I'm letting my children down, I can give [bread] today, but not tomorrow"– participant "L"*

Lack of empathy/ stigmatization:

- *"nie een van hulle het 'n phone call gemaak om te sien hoe dit gaan" ("not one family member had bothered to make a phone call to see how I was doing.")- participant "X"*
- *"You're already dead!" – participant "U"'s boyfriend of her*

(4) Within the health care system:

Participants' disappointment extended to the current health care system – occasionally with justification.

- *"find a tablet that will work for me" – participant "G"*

Lack of palliative care approach by HCP:

A holistic approach to the DR-TB patient was not always portrayed.

- *"these tablets are making me sick" – participant "M"*
- *"to suffer like this, it's better for me to go [die]"- participant "R"*
- *"who is going to look after my children [if admitted to BCH]?" – participant "U"*

Lack of dignity:

Several patients felt angry and hurt by attitudes and behaviours within the health care system that belittled them.

- *"They treat you like you're a germ" – participant "N"*
- *"Don't show people my tablets!" – participant "T"*

Negative connotations towards Brooklyn Chest Hospital

BCH was not perceived or experienced in a positive light by those anticipating admission or those previously admitted.

- *"The yellow one[tablet] – the Brooklyn one – is hard to swallow – it tastes worse and worse." – participant "S"*
- *"[you] give us spaghetti bolognaise – we don't eat that"- participant "F*" regarding culturally inappropriate meals at BCH
- *"Daar gat ek dood gaan – dis beter as ek aangaan by die huis" (I'll die there – it's better if I continue [treatment] at home) – participant "AF"*

Theme (b) Vulnerability leading to Patients' resilience:

Some patients had adapted to their diagnosis and circumstances in a positive way showing resolve, motivation and purpose. This was seen in the value placed on tablet adherence, recovery and their therapeutic relationship within the health care system.

(1) Adaptive medication-taking techniques

Several participants described an acceptance and understanding of the treatment regimen and described novel ways of taking all their required medication.

- *"ek vat die kleinjies eerste – dan wag – die capsules – hulle is die moeilikste" (I take the small ones first then wait – the capsules are the most difficult)- participant "P"*
- *"I drink it like smarties[*]" – participant "I"*
- *"I trust the clinic" – participant "S"*

(2) Inner strength and purpose:

Despite their circumstances, several patients expressed acceptance of their predicament and had found existential meaning, rising above their suffering and challenges.

- *"I'm never going to give up" – participant "I"*
- *"It is here, I must face it"- participant "F"*
- *"I'm not the only one with the disease" – participant "J"*

(2) **Therapeutic relationships:**

Some clinic staff were commended for their care.

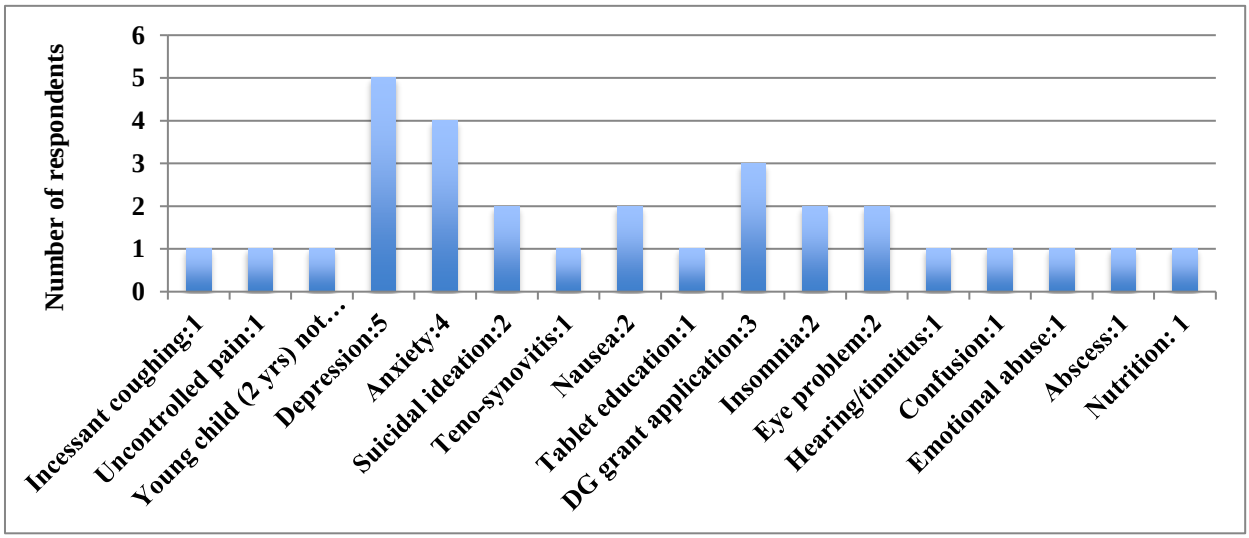
- *"Ek geniet dit eintlik om kliniek toe te kom." (I enjoy coming to the clinic actually) – participant "W"*
- *"The TB sisters have treated me with dignity – my own people don't treat me like this" – participant "Y"*

Referrals to HCPs at local clinic for further management:

Referred: *n (%)*	Yes: 14 (50%)	No: 14 (50%)

There were several issues per referral that needed addressing.

Figure 20. Reasons for palliative care referral (DG=Disability grant)



[*] "Smarties" are small, colourful candy-coated chocolates

The next chapter unpacks these results further and links this study's findings with the published literature reviewed previously.

CHAPTER 5

Discussion

5.1 Introduction

This study's aim was to determine the palliative care needs of DR-TB patients. The objectives were: to assess quality of life and symptom burden; and to assess for a link between these variables to palliative care need. The researcher demonstrated that the higher the symptom burden, the lower the quality of life and the lower the functional status, the greater the need for providing palliative care services in the southern sub-district of Cape Town.

The communities in this geographical area of Cape Town were multi-cultural, multi-lingual and differed in socio-economic status. Chapter 2 considered the difficulties of assessing palliative care needs of DR-TB patients in a culturally sensitive, demographically representative manner - when no tool existed for this purpose. Chapters 2 and 3 mentioned the research that was undertaken to tailor the questionnaire used in this study.

A discussion follows on the quantitative and qualitative findings of the research questionnaire.

5.2 Demographic details

De Vallière and Barker's study(68) considered which pulmonary TB patients were at risk of dying using a modified ECOG score - and showed that the age category 35-49 years was independently associated with a higher mortality (reasons for this were not given in the paper). In the current study, fifty percent of patients fell into this age category. Figure 9 showed that almost two-thirds of the urgent referrals were from this 35-49 year age group and that all those having a palliative care score of >15 were in this age group. Their median ECOG, APCA-POS and symptom burden scores were compared with those participants' whose ages were younger or older than 35-49 years - but was not found to be statistically significant. This study's sample size was not large enough to establish a clear relationship between this age group and high palliative care need.

Female participants scored higher in their symptom burden scores, however this was not deemed statistically significant. The median APCA-POS scores for males and females were equal. Chang *et al*'s systematic review (that referenced Banerji *et al*(99) and Hongthiamthong *et al*(100)) showed that somatic

symptoms of TB were more common in men and middle-aged individuals (63) – however that finding was not collaborated in this current study.

All but one participant was South African and this patient was a Burundian refugee. A "refugee" has a high risk of requiring palliative care support to cope with an infection such as DR-TB. (101) This participant had the highest combined stigmatisation total: stigmatised by family or friends, by the community and by health care professionals. His pre-existing language barriers and ex-prisoner status contributed to the stigmatisation he experienced.

In this study, none of the respondents had received a tertiary education. More than half of the respondents had left school before reaching Grade 7. Poor literacy had been shown to limit health literacy - exacerbating patient vulnerability, impacting health-seeking behaviour, impairing understanding of disease management, compliance and decreasing employability. (102) It therefore impacted on the person's physical, emotional, psychological and social wellbeing. The literacy of this study's cohort compared to the literacy average of the City of Cape Town was more than seven times worse(103) – which contextualised the challenges faced in preventing and managing TB in these vulnerable communities.

The questions relating to the number of windows in the patient's dwelling, number of people in the household and other people at home with TB helped gauge the living conditions of the participants and the infection risk within their households. This information contextualised the research findings. Of concern was the participant who lived with nine others (including children) in small quarters with only one window. Another participant's answers led the researcher to identify a child (younger than 5 years) not on prophylactic TB medication. The researcher was ethically obligated to refer this child to the local health authorities, which was done with the consent of the adult participant.

Almost two-thirds of this study's participants had had TB before – reflecting the burden of TB on individuals and their families. One participant (*"AF")* volunteered that he had been treated for TB six times previously and another participant (*"AE")* had had TB three times – including MDR-TB. The length of time between their previous episodes and current DR-TB infection was not elucidated, but re-treatment TB patients have been recognised as being at high risk of developing DR-TB. (8) There was one case where the current diagnosis of DR-TB had developed subsequent to defaulting from recent DS-TB.

The trial participants were at different stages of their treatment journey - which reflected the cross-sectional nature of the study and gave an indication of whether the participants were receiving injectable treatment in the initial phase. The length of time since diagnosis provided a reference point within the proposed disease trajectory (see discussion later).

The question regarding current usage of TB drugs stirred up strong emotions for three participants not currently taking medication. It highlighted the ethical complexities and challenges of DR-TB management: two patients had failed treatment and TB medication had been suspended or withdrawn. See Appendix 21 for the indications of DR-TB medication withdrawal. Both of these participants continued to live in the community.

One patient had refused admission to BCH for participation in a trial because: (a) BCH was too far away from his community and family; (b) he was concerned for his family's safety in his absence; (c) and he complained about the culturally inappropriate food at BCH *"[you] give us spaghetti bolognaise – we don't eat that!*" This patient's powerlessness and loss of autonomy in negotiating his future management caused mistrust in the therapeutic relationship and blame on HCPs. Senthilingam's findings in community-based uncured XDR-TB patients also reported mistrust of HCPs, unmet needs and the preference to receive care and treatment in the community. (35) Upshur *et al* described an individual having the potential to be both a victim and vector of disease (104) – and in this participant's instance, the ethical dilemma of justifiable forced admission was raised.

The other respondent was waiting on a salvage regimen application, having had treatment withdrawn six months prior due to treatment futility. He described a sense of abandonment and hopelessness that highlighted the disproportionate power differential between a treatment failure patient and the treating authorities.

The third patient had missed his medication for one week after a quarrel with the TB sister - who had allegedly withheld his "*pap*"(porridge) supplement. According to clinic staff, patients qualify for a porridge supplement according to their Body Mass Index and as prescribed by a dietician.

In this research study, approximately half of the trial participants were co-infected with HIV and all but one were taking ARVs currently. This respondent claimed that the clinic doctor had withdrawn her ARVs temporarily. All respondents had been tested for HIV – conforming to the South African National TB Guidelines' stipulation that all confirmed TB patients be offered HIV counselling and testing. (8) Furthermore, the guidelines stated that co-infected TB patients, irrespective of CD4 count, required

ARVs. Ideally, HIV and TB services should be integrated.

In Osman and colleagues' Cape Town study, HIV co-infected DS-TB patients were more than twice as likely to die as compared to HIV-negative patients. (81) They also found that HIV-positive women (with DS-TB) had a higher risk of death than their male counterparts. (81) Thus, the possibility of HIV-positive patients experiencing worse quality of life or worse DR-TB symptoms than HIV-negative patients was explored. Lowther *et al* had found that HIV-positive people reported experiencing lower quality of life compared to HIV negative people (notwithstanding DR-TB)-attributing this to their physical and psychological symptoms. (105) A number of studies reported that co-infection with HIV substantially increased the mortality rate of patients with MDR-TB or XDR-TB(13,15) – with HIV infection being the strongest predictor of death among MDR-TB patients.(67)

In Avong's Nigerian study of patients on MDR-TB treatment, no differences were observed in the risk of adverse events between HIV infected and uninfected patients. (106) On the contrary, Sagwa's Namibian study(107) looking at the adverse events reported by DR-TB patients on treatment, found that HIV-positive DR-TB patients experienced more moderate-to-severe adverse events compared with their HIV-negative counterparts. Sagwa recognised that HIV exacerbated the already severe psychosocial burden faced by DR-TB patients (46,76) and was an additional stressor for participants.

In this study, with a relatively small cohort of patients, HIV co-infected DR-TB patients scored slightly worse (higher) on the APCA-POS score compared to HIV-negative patients (see Table 9). Furthermore, HIV co-infected patients had similar scores for ECOG median scores compared to HIV-negative patients and scored lower in median symptom burden scores. Thus HIV co-infection did not make a significant difference to the quality of life or symptom burden of this cohort of patients.

The pill burden and the accompanying side effects were mentioned repeatedly when patients were asked what bothered them the most and were a significant finding in the thematic analysis. Pill burden is associated with poor drug regimen adherence - and both pill burden and side effects pose challenges when TB and HIV are treated concomitantly. (108) Almost two-thirds of patients were required to take more than 20 tablets each day and the same percentage found taking their tablets difficult. Some of those taking less than 20 tablets also found taking their tablets a problem.

The questionnaire in this research study did not ask specifically about adherence. Daftary and colleagues, in their study of ARV adherence of DR-TB/HIV co-infected patients in South Africa, reported that patients expressed a preference for ARVs over DR-TB treatment because of better tolerability, fewer

pills and a commitment to ART. (109) The researcher also found that some patients feared the stigma and incurability of HIV more than DR-TB (*Participant "O":"TB is nie groot nie" (TB is not [a] big [deal]"[compared to HIV])*. Potentially, improper adherence to MDR or XDR-TB treatment could amplify TB drug resistance. (109) *Participant "H"* had displayed all her tablets during the interview and exclaimed, "*I can't do it! I want to default!"* Defaulting sentiments require urgent intervention and support.

The results showed that there was no association between reports of depression and difficulty taking tablets – although DiMatteo found that depression was one of the strongest predictors of patient non-adherence to medical management. (110)

The cohort was divided equally between smokers and non-smokers. Active smoking is a known risk factor for death when having TB. (8) No correlation with smoking and increased palliative care need was found. A number of patients described members of their family that were drug users and the detrimental drug culture in which they lived. The recreational drugs mentioned were dagga[*], "tik"[^] and mandrax[$].

Participants mentioned that their inability to work had often been for extensive periods- during the six months whilst receiving injectables and up to 1 year following diagnosis. Two studies-Isaakidis *et al* and Morris *et al* respectively (46,111) - reported that DR-TB resulted in an inability to work because of drug side effects and incapacitating depression at the time of diagnosis, resulting in loss of income and diminishing responsibilities. Therefore, poorly managed symptoms and poor functional status perseverated the cycle of vulnerability and suffering.

5.3 ECOG score – an assessment of functional status

The researcher had defined "palliative care need" as a score of greater than or equal to "3" on the ECOG score. Only three respondents described themselves in that way and required referral for urgent intervention. Recall de Vallière and Barker's study which showed that patients with a performance status of "3" or "4" (at time of diagnosis and initiation of TB-treatment) had a strong association with early death. (68) However, the study's recruitment strategy and safety precautions precluded home visitations and thus introduced unavoidable sample bias.

[^] "Tik" is the South African street name for crystal methamphetamine*;

"Dagga" is a South African stree tname for the drug marijuana;

[$] "Mandrax" is the sedative-hypnotic drug methaqualone

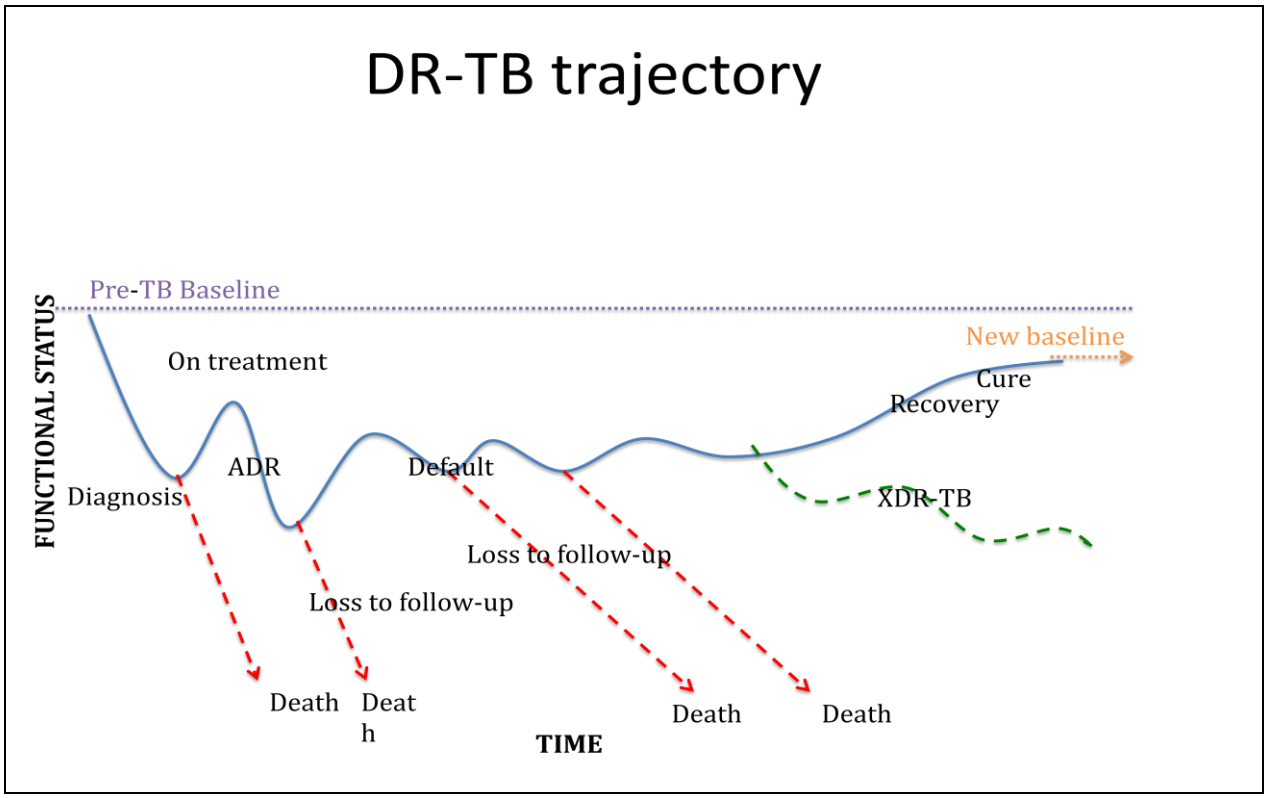
None of the respondents reported being completely disabled and unable to carry out self-care (score "4"). Within this cohort of patients, the ECOG score might have been inflated despite symptom burden, considering the large burden of parental responsibility and financial strain highlighted in the qualitative data.

In this research study, the ECOG score could not be linked meaningfully to the median APCA-POS or median symptom burden scores, due to the small sample size (*n=28).*

5.3.1 The Proposed DR-TB Disease trajectory

Plotted disease trajectories depict the impact of the disease on the individuals' functional status (such as the ECOG score). The researcher, after supervisory input, discussion with experienced DR-TB colleagues and from information gathered from the Literature Review, proposed a disease trajectory for DR-TB infection.

Figure 21. Proposed DR-TB trajectory over time



The "pre-TB baseline" functioning, as depicted in the graph, would be determined by the individual's age or co-morbidities. After DR-TB diagnosis, functional status might be impacted by the patient's symptom burden (112) or improve having started DR-TB specific treatment.

Further positive and negative fluctuations along the trajectory might be due to DR-TB complications (such as pleural effusion, TB dissemination, development of XDR-TB), medication side effects, co-morbidities or changes in psycho-socio-economic circumstances. Deterioration in health and functional status might result in constructive health-seeking behaviour or alternatively poor compliance, defaulting, loss to follow-up and further deterioration. The plummet in functional status indicated high risk of mortality and would correspond to an ECOG score of 3 or 4.(68,86)

The proposed DR-TB disease trajectory anticipated patients' potential needs and outcomes (113) and allows preparation for the care required. It highlighted the relevance of applying a palliative care approach alongside curative treatment from the time of diagnosis and reinforced the need for continuity of care. DR-TB patients might die at any point along the trajectory – death may be sudden and unforeseen (as the researcher realised with the unexpected deaths of two participants in the pilot study). As an educational tool, such a DR-TB trajectory would also help patients to cope with the illness by improving awareness and empowerment.

Functional status was shown in the literature to link QoL and symptom burden.

5.4 Quality of life evaluation

The literature indicated that TB affected quality of life both directly and indirectly. (63) The DR-TB patient's perception of QoL was a reflection of a "complex construct of influences" (55) - the DR-TB infection, anti-TB medication, "socioeconomic background and cultural context", (114) immigrant status, other co-morbid conditions, (75) financial concerns, symptom burden and spiritual issues. The once-off use of the APCA African POS score in this study gave an indication of the trial participants' quality of life.

All but three patients denied experiencing pain; but a number described experiencing overwhelming and moderate pain. The type of pain described was mostly physical but occasionally emotional.

The WHO Global Atlas of Palliative Care(45) estimated palliative care needs according to pain prevalence. In their analysis, DR-TB ranked second in overall pain prevalence (90%) after cancer (35-96%), and above HIV/AIDS (63-80%). (45) In this research study, just more than half of the participants reported experiencing pain, and therefore by the Global Atlas estimation, would imply the same percentage having palliative care needs. However, as Figure 9 indicated, the prevalence of palliative care need was far greater –each participant was determined to have a "palliative care need" in this study.

Those patients who answered "no pain/ 0" in the APCA-POS were compared with those who described having pain. Patients who had experienced a degree of pain, scored higher on their median APCA-POS, ECOG and symptom burden scores. The differing ECOG and symptom burden scores (no pain *vs* pain) were statistically significant. Despite a patient *not* reporting pain, they still had significant palliative care needs that warranted referral and escalation of care.

Recall the WHO definition of palliative care: *"Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychological and spiritual".* (49)

The researcher found that more than two-thirds of those with pain were referred urgently as well as a quarter of those reporting "no Pain/0". Thus the absence of pain did not dismiss the need for palliative care. Therefore, the researcher believes that in the context of DR-TB, the prevalence of "palliative care need" should not be estimated solely on one variable – pain prevalence. Paradoxically, however, "palliative care need" existed in the presence of only one significant variable or uncontrolled symptom.

The next question in the study indicated that respondents were bothered mostly by respiratory (shortness of breath, coughing, tight chest) and gastro-intestinal symptoms (nausea, vomiting, epigastric pain, heartburn). There was significant prevalence of these physical symptoms. The top five "other" symptoms that bothered patients in question 29 were: coughing (21.4%), nausea (21.4%), vomiting (7.1%), problems with eyes (7.1%) and stress (7.1%). Summarised, these five symptoms were due either to the tuberculosis infection, DR-TB drug side effects or socio-economic concerns.

The researcher sensed that some respondents were unable to distinguish their worry related to DR-TB from other worries, such as concomitant medical problems (such as Diabetes or HIV) or social circumstances. The "degree" of worry was moderated by confidence in the anti-tuberculosis medication- one lady denied being too worried because *"jy kry pille"(you get pills) participant "P"* – as well as by the resources available to them –"*I looked it up on my phone [internet]"* (*participant "N")* and *"other people's prayers helped"(participant "N").*

The question regarding the ability to share feelings with others hinted at their disclosing of their diagnosis and provoked strong emotions in some participants, highlighting abusive, broken or strained family relationships, limited support and social isolation. One out of the nine participants who had

difficulty sharing their feelings, reported feeling stigmatised by her family due to DR-TB. Several participants had chosen not to burden their families by withholding their diagnosis.

5.5 Assessment of patient's Symptom burden

Brown *et al* commented that, "illness … cannot be understood independently of the societies in which people live". (55) In this study, many patients were burdened by their inherent societal context, added to which were the symptoms due to DR-TB.

The dominant symptom was anxiety related to financial worry (see Figure 17). In the analysis of the qualitative data, the worsening of pre-existing social issues overshadowed the DR-TB infection *per se*. This is in keeping with Chang et *al*'s comment that "the social and emotional burden of disease can equal and even exceed the physical impact of illness". (63) The other symptoms that had high percentages - scoring "4" on the Likert scale- were joint pain (32.1%), shortness of breath (25%) and feeling isolated and lonely (21.4%).

Further discussion of each symptom category follows:

5.5.1 Physical symptoms

Chapter 2 discussed how physical symptoms were attributed to the mycobacterial infective process, concomitant illnesses or anti-tuberculosis drug side effects (see Appendix 21 for anti-tuberculosis drug abbreviations). The results showed that respondents were hampered by shortness of breath (51%, with 25% scoring "4"), but fatigue was the most frequent (79%) and severe symptom reported by trial participants. Complaints of joint pains (64%) (Z,FQs) (19) were also frequent and debilitating (32.1% scoring "4"). Symptoms such as paraesthesia (Cs,Trd,S,Km,Am,Cm,Eto/Pto,FQs), nausea and vomiting (Eto/Pro,PAS,Cm,E,Z) and visual impairment (E) could be attributed to anti-TB drug side effects (responsible agents in brackets).(18)

5.5.2 Psychological symptoms:

Seventeen of the respondents described feeling some degree of depression, with five describing it as very worrisome. Atif's study showed that MDR-TB patients on treatment were at high risk of depression at the start of treatment and even on completion of treatment. (115) Thus, even though eleven respondents denied feeling sad, down or depressed, this would need to be continually assessed throughout their disease trajectory.

The association between “Depression” and “Hopelessness” was statistically significant. Two patients had considered suicide and were referred urgently to the local clinic doctor.

Thomas *et al*’s systematic review of issues challenging DR-TB patients listed prevalent psychological issues as being: “hopelessness, fear, perceived loss of self-identity, low self-esteem, feeling of guilt, isolation and depression”. (22) In this research study, “hopelessness” and “isolation” have been described rather as spiritual issues.

5.5.3 Spiritual concerns:

Spiritual wellbeing is a vital component of the impeccable assessment in integrating the palliative care approach. Chang’s review of TB literature did not find any studies that examined the impact of TB on spiritual wellbeing. (63) Post and colleagues reported that neglecting spiritual needs might drive patients away from effective medical treatment (116) – with obvious detrimental consequences to the DR-TB patient and community.

In this study, participants were asked directly about spiritual issues. Two themes emerged: those experiencing existential pain and suffering, and those able to find meaning and purpose in the midst of their current predicament. The ability of this cohort of DR-TB patients to adapt, develop better coping mechanisms and be resilient was observed by their accessing their faith, inner strength, family and community support or therapeutic relationships.

5.5.4 Social symptoms:

Vega *et al.* (117) described a number of psychosocial concerns of DR-TB patients. They mentioned that DR-TB patients on treatment experienced fear and guilt associated with infectious risk. Likewise, several respondents in this trial expressed concern for their children’s risk of infection and had them tested for TB regularly at the clinic. An exception was participant (*“F”),* who had failed treatment, and was thus still contagious, who flagrantly did not observe infection precautions in his home and business.

Vega *et al* (117) also raised the issue of respondents having lost family members to DR-TB, which was raised by a number of patients in this study – some grieving the loss of two close family members.

Patients’ anxiety was ameliorated by their confidence in the TB tablets or their management team. Those who were feeling anxious expressed fear of the possibility of not getting better, future treatment options and the threat to physical safety for themselves and their family. At the other extreme, *Participant “U”’s* denial of anxiety was due to her sense of hopelessness and fatalism.

"Stigma" was addressed in the questionnaire by asking the respondents three questions relating to family relationships, community situations and HCP interactions, but did not differentiate the basis for stigma – be it due to HIV, DR-TB, prison history, refugee status or homelessness. The researcher had anticipated the number of respondents experiencing stigma to be greater - after Lopez *et al*'s observations that the diagnosis of TB was "often accompanied by stigma, marginalization and shame". (47) One participant (*"Y")* had even given a motivational interview for a local popular magazine regarding his experiences with DR-TB.

The researcher deliberated whether the respondents understood the abstract concept of "stigma" with the answers from the direct questions - while, the patients' anecdotal narratives indicated stigma in other ways. Some patients feared stigma or perceived there to be stigma when there was none. In other cases, stigma was "enacted" resulting in discrimination, (118) being the targets for gossip, public insults, marginalisation and public humiliation during conflict.

The patient with XDR-TB, who was not on treatment (*participant "G"),* reported not experiencing any stigma in the three categories. This was possibly inconsistent with the fact that this patient had been barred from attending the clinic because of his infectious risk.

The non-South African participant (*"T")* felt too intimidated to report his visual disturbances to the clinic and felt he was treated differently when his medication was dispensed. Senthilingam *et al*'s study(35) in the Western Cape also reported discrimination and humiliation by nurses when patients collected their medication.

Lastly, Vega *et al* also mentioned "concomitant poverty" (117) as being a significant concern of DR-TB patients. This was confirmed in both the qualitative and quantitative data of this research and witnessed on the community streets around the clinic sites. Financial insecurity influenced decision-making regarding treatment, with employment superseding DOTS attendance or BCH admission. Nonetheless, financial insecurity also affected non-DR-TB community members (would-be control subjects) with South Africa's high level of unemployment (27.7% in 2017 (119)). Existing financial vulnerabilities would be exacerbated by the diagnosis of DR-TB. DR-TB costs the individual and family(77) in terms of lost employment opportunities whilst unwell, attending the clinic for treatment or stigma by employers; and by additional expenditure such as extra transportation costs for daily clinic visits.

5.6 Limitations of the study

Time and resource constraints as well as safety concerns imposed limitations on the study in terms of sample size. The small sample size restricted the conduction of statistical analyses such as linear or logistic regression models. These models would have been useful to identify predictors of participants' concerns.

The study's confines were recruitment and measurement bias. The questionnaire did not ask about other significant co-morbidities – such as diabetes, alcoholism or cancer and the symptom burden list might have missed other important symptoms. The length of the questionnaire might have resulted in under or over reporting of symptoms.

Because financial and social burdens played a dominant role in the participants' quality of life - this study lacked the inclusion of a suitable comparison group (non-TB infected/ affected) within the southern sub-district of Cape Town with similar demographic, ethnic, cultural and socio-economic backgrounds and challenges.

All but three participants were recruited and interviewed at the clinic. This might have resulted in the exclusion of more severely ill patients who would have been unable to attend the clinic. However, due to safety concerns, clinic visits were considered more appropriate.

5.7 Conclusion

Participants in this research study demonstrated substantial palliative care needs regardless of where on the DR-TB trajectory they were placed. Higher symptom burden scores correlated with a greater need for palliative care referral. In the context of the southern sub-district of Cape Town, these patients also had significant pre-existing socio-economic hardships and day-to-day concerns that needed to be addressed in order for improvement in all aspects of quality of life.

The next chapter discusses the contextual and realistic aspects of providing palliative care to DR-TB patients in response to the needs expressed.

CHAPTER 6

Conclusion

6.1 Introduction

Drug-resistant TB is a life-threatening infection - with a significant mortality rate. It poses an increasing problem globally, nationally and locally – particularly in vulnerable communities disadvantaged by socio-economic injustices. Recognising this, the WHO identified DR-TB patients as requiring palliative care. (45) This need for palliative care has also been re-iterated in the End-TB strategies(59), the South African National MDR-TB guidelines(19) and the Hospice Palliative Care Association (HPCA) of South Africa's Guidelines for providing palliative care to patients with tuberculosis.(58)

A "needs-based" model of palliative care, rather than a "prognosis-based" model is promoted by the WHO. (52) However, the literature proved scanty regarding what those palliative care needs of DR-TB patients might be. What is more, the literature did not identify a reliable, validated means of assessing these palliative care needs – particularly in a low-to middle-income setting.

Therefore, this study aimed to assess the palliative care needs of patients with DR-TB infection within the southern sub-district of Cape Town by means of a researcher-designed questionnaire. This cross-sectional study included twenty-eight patients at different stages of their disease trajectory. Their needs were documented in Chapter 4 and discussed further in Chapter 5.

6.2 The findings of this research study

Each respondent proved to have been impacted by DR-TB – with all respondents displaying at least one palliative care need (see Figure 9). A score of greater or equal to 10 in the palliative care need index of the questionnaire correlated with the necessity for referral for further management. The absence of pain did not exclude a need for palliative care in these DR-TB patients. Notably, the majority of those requiring referral were HIV co-infected and/or in the 35-49 year age category. Individuals were affected physically, psychologically, emotionally, socially, economically and spiritually- oftentimes leading to vulnerability and further suffering. A range of significant palliative care needs was identified with respect to patients' quality of life, functional capacity, symptom burden and preservation of dignity.

Respondents' quality of life was affected by their high symptom burden, impaired functional performance status, large pill-burden and anti-tuberculosis drug side effects. Unemployment, financial

insecurity and worry impacted their quality of life. The findings revealed that respiratory and gastrointestinal issues were inadequately controlled and visual loss often went unreported to HCPs. Financial worries and concerns regarding familial responsibility were prominent. Holistic care was absent in the accounts of DR-TB patients interviewed during this study. Respondents expressed a desire for a more rewarding therapeutic relationship, having been affected by stigma and lacking a sense of self-worth and empowerment.

The researcher found literature to support the hypothesis that the higher the symptom burden and the lower the quality of life, the greater and more urgent the need for palliative care provision. However, the sample size of 28 was insufficient to validate the hypothesis statistically.

6.3 The optimal timing for integrating a palliative care needs assessment in the DR-TB disease trajectory

The WHO definition of Palliative care(49) stated that it should be initiated early in the illness trajectory, along with curative therapies that were intended to prolong life. Many patients experienced distressing symptoms at the time of DR-TB diagnosis and as a consequence of TB medication side effects. The disease trajectory of DR-TB appeared chequered (as Figure 21 illustrated) resulting in the impossibility of predicting treatment outcomes or when the patient was nearing the end of life.

Thus, all DR-TB patients should be assessed for their palliative care needs at the time of diagnosis and at regular intervals during their illness journey - regardless of whether the end result is cure, treatment failure or ultimately death. Regular palliative care needs assessment would ensure that a palliative care approach was adopted throughout the disease trajectory. Continuing palliative care needs assessment is imperative during routine care and particularly in those whose treatment had failed and had been discharged back into the community.

6.4 Response to DR-TB patients' palliative care needs –ethically and realistically

HCPs treating DR-TB patients need to be informed of the benefits of providing palliative care. The provision of palliative care to DR-TB patients is a "fundamental ethical obligation" (50) and should be appropriate to the expressed and anticipated needs along their disease journey. The needs discovered in this study are significant and the requisite response should be proportional - without compromising curative therapy. The global, national and local willingness to respond to these needs exposes human rights and justice issues. (104) Palliative care must form part of standard, holistic, patient-centred DR-TB care at the local, national and global level.

Furthermore, the determination of palliative care amongst DR-TB patients should be standardised – and thus an assessment tool is required. The questionnaire used in this research study is a modest beginning.

Realistically, those DR-TB patients with fewer, simpler needs qualify for general palliative care delivered by their regular HCP practising a palliative care approach and patient-centred care. However, more complicated, multi-dimensional needs require the services of a specialist, inter-disciplinary palliative care team.

All DR-TB patients should be treated with dignity according to "The Patients' Charter for Tuberculosis Care." (57) Thus their needs and human rights ought to be respected and the obligations and responsibilities of HCPs and governments recognised. Identifying needs and understanding DR-TB patients' quality of life and burden of disease allows the response of the DR-TB management team to be culturally competent and patient-centred; it also directs cost-effective allocation of resources towards treatment, adherence and symptom management for the holistic care of patients within their community.

Responding to patients' palliative care needs also requires a public health approach. Focus should be placed on improving patients' health literacy, empowering patients and addressing stigma. Patients' co-morbidities also need to be attended to – such as substance abuse, HIV co-infection and Diabetes.

6.5 Implications of this research study's findings

The findings of this research contribute to the knowledge of DR-TB patients' lived experience and their palliative care needs in a setting such as the southern sub-district of Cape Town. All DR-TB patients require palliative care.

Figure 21 dispelled the idea that a palliative care approach was only relevant in the last few weeks of life and emphasised that it should be integrated actively alongside curative treatment (113) to provide relevant, "culturally sensitive" (20) and anticipatory support.

6.6 Recommended further studies

Further research is required to validate the DR-TB palliative care needs assessment tool used in this study. A longitudinal study design to determine the evolution of palliative care needs during the DR-TB disease trajectory might be more clinically relevant. This study's questionnaire could also be adapted to be used prospectively. Valuable research would be to evaluate the effect of palliative care intervention on quality of life and symptom burden in DR-TB patients and to document patient-reported outcomes.(52)

More work needs to be done to identify those patients at risk of deteriorating clinically during treatment(67) and recognising unmet palliative care needs. Validating the proposed DR-TB disease trajectory would be useful for patients, caregivers, educators, HCPs and DR-TB strategists.

6.7 Further challenges of providing palliative care to DR-TB patients

The over-burdened health care system currently does not allow lengthy consultations with patients and their families. A utilitarian approach predominates – often at the expense of the patients' dignity and personhood.(47)

Patients, their families and HCPs need to be educated regarding the intentions and benefits of palliative care so that the necessary paradigm shift occurs: palliative care should no longer be thought to be nihilistic and contrary to prescribed medical management. A generalised, patient-centred approach needs to be reinforced by means of continuing education and practical strategies such as incorporating assessment tools and questionnaires into the care process to improve the recognition of symptoms and care needs.(52)

Another challenge at national and local level would be the provision of culturally compassionate, end-of-life care for DR-TB patients (15,120) – both in the community and in dedicated palliative care facilities. These budgetary provisions require political determination.

However, the provision of community-based palliative care is hindered by feared and actual criminal violence. Violence limits patients' access to health care and health care providers' access to patients. This lack of physical safety in the disadvantaged communities of Cape Town should be prioritized on the national, regional and local political agendas.

Lastly, palliative care cannot occur if fastidious infection control is not practised and this imposes further challenges on budget, personal risk and health care worker willingness to undertake their work of caring.

6.8 Conclusion

The effects of the "White Plague" still pervade society. The experiences and histories of DR-TB patients within the southern sub-district of Cape Town have provided a detailed picture of the suffering that results from this infection. To alleviate this suffering and address this growing epidemic, palliative care services are urgently required to fulfil the ethical obligations of treating patients with dignity and respect throughout their disease trajectory.

6.9 Plan for dissemination of findings:

The research findings will be reported back to the local TB clinic staff via email as well as information pamphlets made available for distribution to DR-TB patients in their respective clinics. The Department of Health, the City of Cape Town, HPCA, D.P.Marais and Brooklyn Chest hospitals will be emailed a copy of the thesis – welcoming discussion regarding the results. Findings will be shared with other palliative care colleagues who might be interested in continuing research in this area. It is also planned to publish the research findings in a peer-reviewed journal and to submit the study's abstract to the 49th Union World Conference on Lung Health.

*

"Measures of suffering have been absent, and so the need for palliative care and pain relief services has been easy to miss. That excuse no longer holds." (121)

REFERENCES

(1) Kim C. Born there: A poem. Online Journal of Health Ethics 2011;7(2):01.02.2017.
(2) Migliori G, Loddenkemper R, Blasi F, Raviglione M. 125 years after Robert Koch's discovery of the tubercle bacillus: the new XDR-TB threat. Is "science" enough to tackle the epidemic? Eur Resp J 2007;29(3):423-427.
(3) Ryan F. The Forgotten Plague. How the Battle against Tuberculosis was won-and lost. First Paperback edition ed. New York: Back Bay Books. Little, Brown and Company; 1992.
(4) Statistics South Africa. Mortality and causes of death in South Africa, 2015: Findings from death notification. STATS SA 2017;STATISTICAL RELEASE(P0309.3):1-140.
(5) The World Health Organization. The Global Tuberculosis Report 2016. 2016; Available at: www.who.int/tb/publicatuibs/global_report/en/. Accessed Nov/8, 2016.
(6) WHO Global TB Report. Will we ever eliminate tuberculosis, the voiceless disease? Lancet Respiratory 2017(March):5.
(7) Shabi K. Matroyshka Nesting Dolls: Meaning of Russian Wooden Stacking doll. 2015; Available at: http://legomenon.com/russian-matryoshka-nesting-dolls-meaning.html. Accessed May/7, 2016.
(8) Department of Health Republic of South Africa. National Tuberculosis Management Guidelines 2014. 2014; Available at: www.tbonline.info/media/uploads/documents/ntcp_adult_tb-guidelines-27.5.2014.pdf. Accessed December/5, 2017.
(9) Loveday M, Padayatchi N, Voce A, Brust J, Wallengren K. The treatment journey of a patient with multi-drug-resistant tuberculosis in South Africa: is it patient-centred? Int J Tuberc Lung Dis 2013;17(10):S56-S59.
(10) Calver A, Falmer A, Murray M, et al. Emergence of increased resistance and extensively drug-resistant tuberculosis despite treatment adherence, South Africa. Emerg Infect Dis 2010;16:264-271.
(11) Seear M. The need for coordinated action against falsified and substandard medicines. Int J Tuberc Lung Dis 2013;17:1.
(12) Eldholm V, Monteserin J, Rieux A, Lopez B, Sobkowiak B, Ritacco V, et al. Four decades of transmission of a multidrug-resistant *Mycobacterium tuberculosis* outbreak strain. Nat Commun 2015;6(7119).
(13) Dheda K, Shean K, Zumla A, et al. Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study. Lancet 2010;375:1798-1807.
(14) Dheda K, Gumbo T, Maartens G, Dooley K, McNerney R, Murray M, et al. The epidemiology, pathogenesis, transmission, diagnosis, and management of multi-drug-resistant, extensively drug-resistant, and incurable tuberculosis. Lancet Respiratory 2017(March):7-76.
(15) Dheda K, Gumbo T, Gandhi N, Murray M, Theron G, Udwadia Z, et al. Global control of tuberculosis: from extensively drug-resistant to untreatable tuberculosis. Lancet Respiratory 2014;2(4):321-338.
(16) Cox H, Dickson-Hall L, Jassat W, Moshabela M, Kielmann K, et al. Drug-resistant tuberculosis in South Africa: history, progress and opportunities for achieving universal access to diagnosis and effective treatment. In: Padarath A, Barron P, editors, editors. South African Health Review 2017. 20th ed. Durban: Health Systems Trust; 2017. p. 157-168.
(17) Reves R, Blakey D, Snider D, Farer L. Transmission of multiple drug-resistant tuberculosis: report of a school and community outbreak. Am J Epidem 1981;113:423-435.
(18) World Health Organization. Global Tuberculosis Report 2015. 2015; Available at: http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf. Accessed March/1, 2016.
(19) Department of Health, Republic of South Africa. Management of Drug-Resistant Tuberculosis, Policy Guidelines (Updated- January 2013). 2013; Available at: http://www.health-e.org.za/wp-content/uploads/2014/06/MDR-TB-Clinical-Guidelines-Updated-Jan-2013.pdf. Accessed February/6, 2016.
(20) Venkatraju B, Prasad S. Psychosocial trauma of diagnosis: A Qualitative study on rural TB patients' experiences in Nalgonda District, Andhra Pradesh. Indian J Tuberc 2013;60:162-167.
(21) Harding R, Foley KM, Connor SR, Jaramillo E. Palliative and end-of-life care in the global response to multidrug-resistant tuberculosis. Lancet Infect Dis 2012 08;12(8):643-646.

(22) Thomas BE, Shanmugam P, Malaisamy M, Ovung S, Suresh C, Subbaraman R, et al. Psycho-Socio-Economic Issues Challenging Multidrug Resistant Tuberculosis Patients: A Systematic Review. PLoS One 2016 01/25;11(1):e0147397-e0147397.
(23) Abubakar I, Zignol M, Falzon D, Raviglione M, Ditiu L, Masham S, et al. Drug-resistant tuberculosis: time for visionary political leadership. Lancet Infect Dis 2013 6;13(6):529-539.
(24) Bauer M, Leavens A, Schwartzman K. A systematic review and meta-analysis of the impact of tuberculosis on health-related quality of life. Qual Life Res 2013;22(8):2213-2235.
(25) Bateman C. Defusing the new drug-resistant TB time bomb. SAMJ 2014;104(8):528-529.
(26) Centers for Disease Cotrol and Prevention. Emergence of *Mycobacterium tuberculosis* with extensive resistance to second-line drugs-worldwide. MMWR 2006;55:301-305.
(27) World Health Organization. Global TB Facts 2015. 2015; Available at: http://www.who.int/tb/Global_TB_Facts.pdf?ua=1. Accessed Aprl/28, 2016.
(28) World Health Organization. Tuberculosis profile: South Africa. 2014; Available at: https://extranet.who.int/sree/Reports?op=Replet&name=%2FWHO_HQ_Reports%2FG2%2FPROD%2FEXT%2FTBCountryProfile&ISO2=ZA&LAN=EN&outtype=pdf. Accessed March/20, 2016.
(29) Global Tuberculosis Report 2015. 2015; Available at: http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf. Accessed February/10, 2016.
(30) WHO. Global Tuberculosis Report 2017. 2017; Available at: http://www.who.int/tb/publications/global_report/en/. Accessed February/5, 2018.
(31) Kanabus A. Information about Tuberculosis: Drug resistant TB in South Africa- Hospitalization & statistics. 2017; Available at: http://www.tbfacts.org/drug-resistant-tb-south-africa/. Accessed May/10, 2017.
(32) Klopper M, Warren R, Hayes C, Gey van Pittius N, Streicher E, Müller B, et al. Emergence and Spread of Extensively and Totally Drug-Resistant Tuberculosis, South Africa. Emerg Infect Dis 2013;19(3):449-455.
(33) Pietersen E, Ignatius E, Streicher E, Mastrapa B, Padanilam X, Pooran A, et al. Long-term outcomes of patients with extensively drug-resistant tuberculosis in South Africa: a cohort study. Lancet 2014;383(9924):1230-1239.
(34) Dheda K, Limberis J, Pietersen E, Phelan J, Esmail A, Lesosky M, et al. Outcomes, infectiousness, and transmission dynamics of patients with extensively drug-resistant tuberculosis and home-discharged patients with programmatically incurable tuberculosis: a prospective cohort study. Lancet Respiratory 2017;5(4):269-281.
(35) Senthilingam M, Pietersen E, McNerney R, Riele J, Sedres P, Wilson R, et al. Lifestyle, attitudes and needs of uncured XDR- TB patients living in the communities of South Africa: a qualitative study. Trop Med Int Health 2015;20(9):1155-1161.
(36) Collins F. TB Sufferers sent home to die, and perhaps to kill. Sunday Times News 2016(04.12.2016).
(37) Connor S, Foley K, Harding R, Jaramillo E. Declaration on palliative care and MDR/XDR-TB. Int J Tuberc Lung Dis 2012;16(6):712-713.
(38) World Health Organization, USAID, Department of Health South Africa. Report of the Evaluation of South Africa Drug-Resistant TB Programme and its implementation of the Policy Framework on Decentralized and Deinstitutionalised Management of Multidrug Resistant TB - Main Report. (14 February 2016):1-104.
(39) Western Cape Provincial AIDS council. Annual Progress Report 2014/15 - Provincial Strategic Plan 2012-2016. SANAC 2016:1-38.
(40) Upshur R, Singh J, Ford N. Apocalypse or redemption: responding to extensively drug-resistant tuberculosis. Bull World Health Organ 2009;87(6):481-483.
(41) World Health Organization. WHO treatment guidelines for drug-resistant tuberculosis 2016 update. 2016.
(42) Pooran A, Pieterson E, Davids M, Theron G, Dheda K. What is the cost of diagnosis and management of drug-resistant tuberculosis in South Africa? PloS one 2013;8:c54587.
(43) Sotgiu G, Migliori G. Effect of the short-course regimen on the global epidemic of multidrug-resistant tuberculosis. The Lancet 2017;5(3):159-160.
(44) Kendall E, Fojo A, Dowdy D. Expected effects of adopting a 9 month regimen for multidrug-resistant tuberculosis: a population modelling analysis. Lancet Respiratory 2016 Jan 5, 2017;5(2):05.02.2017.

(45) World Health Organization. The WHO Global Atlas on Palliative Care at the End of life; Chapter 6: Methodology for estimating the number of people in need of palliative care. 2014; Available at: http://www.thewhpca.org/resources/global-atlas-on-end-of-life-care. Accessed February/21, 2017.
(46) Isaakidis P, Rangan S, Pradhan A, Ladomirska J, Reid T, Kielmann K. 'I cry every day': experiences of patients co-infected with HIV and multidrug-resistant tuberculosis. Trop Med Int Health 2013 09;18(9):1128-1133.
(47) Lopez C, Bertram-Farough A, Heywood D, Dawson L, Dillon m, Chochinov M, et al. Knowing about you: eliciting dimensions of personhood within tuberculosis care. Int J Tuberc Lung Dis 2017;21(2):149-153.
(48) Oxford University Press. English Oxford Living Dictionaries. 2017; Available at: https://en.oxforddictionaries.com/definition/humane. Accessed May/10, 2017.
(49) World Health Organization. WHO Definition of Palliative Care. 2012; Available at: http://www.who.int/cancer/palliative/definition/en/. Accessed April/28, 2016.
(50) World Health Organization. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. 2014; Available at: http://apps.who.int/iris/bitstream/10665/130918/1/9789241548809_eng.pdf. Accessed March/2, 2016.
(51) Temel J, Greer J, Muzikansky A, Gallagher E, Admane S, Jackson V, et al. Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer. N Engl J Med 2010;363(8):733-742.
(52) Beernaert K, Pardon K, Van dB, Devroey D, De Laat M, Geboes K, et al. Palliative care needs at different phases in the illness trajectory: a survey study in patients with cancer. Eur J Cancer Care 2016;25(4):534-543.
(53) Mason PH, Roy A, Spillane J, Singh P. Social, Historical and Cultural Dimensions of Tuberculosis. J Biosoc Sci 2016;48(2):206-232.
(54) de Souza F, Villa T, Cavalcante S, Netto A, Lopes L, Conde M. Peculiarities of tuberculosis control in a scenario of urban violence in a disadvantaged community in Rio de Janeiro, Brazil. J Bras Pneumol 2007;33(3):318-322.
(55) Brown J, Capocci S, Smith C, Morris S, Abubakar I, Lipman M. Health status and quality of life in tuberculosis. Int J Inf Dis 2015 3;32:68-75.
(56) Girgis A, Waller A. Palliative care needs assessment tools. In: Cherney N, Fallon M, Kaasa S, editors. Oxford Textbook of Palliative Medicine Oxford: Oxford University Press; 2015. p. 363-375.
(57) The Patients' Charter for Tuberculosis Care. 2006; Available at: http://www.who.int/tb/publications/2006/patients_charter.pdf. Accessed March/14, 2016.
(58) Hospice Palliative Care Association of South Africa. Guidelines for providing Palliative Care to patients with Tuberculosis. 2011; Available at: http://www.hpca.co.za/category/tb.html. Accessed February/28, 2016.
(59) World Health Organization. The WHO End TB Strategy. 2015; Available at: http://www.who.int/tb/End_TB_brochure.pdf?ua=1. Accessed March/2, 2016.
(60) Ismail N, Mvusi L, Nanoo A, Dreyer A, Omar S, Ihekweazu C, et al. Drug Resistant Tuberculosis in South Africa: findings from a nationwide survery, 2012-2014. Communicable Diseases Surveillance Bulletin 2016;14(4):1-125.
(61) The Lancet Respiratory Medicine Commission: Drug-resistant Tuberculosis. The Lancet Respiratory medicine 2017(March):1-76.
(62) Morden E, Groenewald P, Zinyakatira N, Neethling I, Msemburi W, Daniels J, et al. Western Cape Mortality Profile 2013. South African Medical Research Council 2016(ISBN: 978-0-621-44356-1).
(63) Chang B, Wu AW, Hansel NN, Diette GB. Quality of life in tuberculosis: a review of the English language literature. Qual Life Res 2004;13(10):1633-1642.
(64) Ahmad N, Javaid A, Syed Sulaiman S, Basit, A., Afridi, AK., Jaber A, Khan A. Effects of Multidrug Resistant Tuberculosis Treatment on Patients' Health Related Quality of Life: Results from a Follow Up Study. PloS one 2016;11(7):e0159560.
(65) Godoy MDP, Mello FCQ, Lopes AJ, Costa W, Guimarães FS, Pacheco AGF, et al. The functional assessment of patients with pulmonary multidrug-resistant tuberculosis. Respir Care 2012;57(11):1949-1954.
(66) Harding R, Defilippi K, Cameron D. What palliative care-related problems do patients with drug-resistant or drug-susceptible tuberculosis experience on admission to hospital? A cross-sectional self-report study. Palliat Med 2016 10;30(9):862-868.

(67) van der Walt M, Lancaster J, Shean K. Tuberculosis Case Fatality and Other Causes of Death among Multidrug-Resistant Tuberculosis Patients in a High HIV Prevalence Setting, 2000-2008, South Africa. PloS one 2016;11(3):February 28, 2017.
(68) de Vallière S, Barker RD. Poor performance status is associated with early death in patients with pulmonary tuberculosis. Trans R Soc Trop Med Hygiene 2006;100(7):681-686.
(69) Brown J, Capocci S, Smith C, Morris S, Abubakar I, Lipman M. Health status and quality of life in tuberculosis. Int J Inf Dis 2015;32:68-75.
(70) Sharma R, Yadav R, Sharma M, Saini V, Koushal V. Quality of life of multi drug resistant tuberculosis patients: A study of North India. Acta Med Iran 2014;52(6):448-453.
(71) Leidy N, Revicki D, Geneste B. Recommendations for evaluating the validity of quality of life claims for labelling and promotion. Value in Health 1999;2(2):113-127.
(72) Aydin I, Ulasahin A. Depression, Anxiety comorbidity, and disability in tuberculosis and chronic obstructive pulmonary disease patients: Applicability of GHQ-12. Gen Hosp Psychiatry 2001;23(2):77-83.
(73) Von Elm E, et al. The STROBE Initiative: The strengthening of reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. J Clin Epidemiol 2008;61(4):344-349.
(74) Dhingra V, Rajpal S. Health related quality of life (HRQL) scoring in tuberculosis. Parameters 2003;1(2):3.
(75) Guo N, Marra F. Measuring health-related quality of life in tuberculosis: a systematic review. Health and Quality of Life Outcomes 2009;7(14):1-10.
(76) Das M, Isaakidis P, van den Bergh R, Kumar A, Nagaraja S, Valikayath A, et al. HIV, multidrug-resistant TB and depressive symptoms: when three conditions collide. Global Health Action 2014;7(24912):1-5.
(77) Morris MD, Quezada L, Bhat P, Moser K, Smith J, Perez H, et al. Social, economic, and psychological impacts of MDR-TB treatment in Tijuana, Mexico: a patient's perspective. Int J Tuberc Lung Dis 2013 07;17(7):954-960.
(78) Kleinman A. Patients and Healers in the contect of culture. London: University of California Press; 1980.
(79) Epner D, Baile W. Patient-centered care: the key to cultural competence. Ann Onc 2012;23(3):33-42.
(80) Papadopoulos I, Shea S, Taylor G, Pezzella A, Foley L. Developing tools to promote culturally competent compassion, courage, and intercultural communication in healthcare. J Compassionate Care 2016;3(2).
(81) Osman M, Seddon J, Dunbar R, Draper H, Lombard C, Beyers N. The complex relationship between human immunodeficiency virus infection and death in adults being treated for tuberculosis in Cape Town, South Africa. BMC public health 2015;15(556).
(82) Waitt C, Squire S. A systematic review of risk factors for death in adults during and after tuberculosis treatment. Int J Tuberc Lung Dis 2011;5(7):871-875.
(83) Chui YY, Kuan HY, Fu ICY, Liu RKY, Sham MK, Lau KS. Factors associated with lower quality of life among patients receiving palliative care. J Adv Nurs 2009 09;65(9):1860-1871.
(84) Justice A, Holmes W, Gifford A, Rabeneck L, Zackin R, Sinclair G, et al. Development and validation of a self-completed HIV symptom index. J Clin Epidemiol 2001;54(12, Supplement 1):S77-S90.
(85) Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5:649-655. Am J Clin Oncol 1982;5:649-655.
(86) Highet G, Crawford D, Murray S, Boyd K. Development and evaluation of the Supportive and Palliative Care Indicators Tool (SPICT): a mixed-methods study. BMJ Supportive & Palliative Care 2013 July 25.
(87) Gestsdottir B, Hjaltadottir I, Gudmannsdottir G, Jonsson P, Gunnarsdottir S, Sigurdardottir V. Symptoms and functional status of palliative care patients in Iceland. Br J Nurs 2015;24(9):478-483.
(88) Harding R, Selman L, Agupio G, Dinat N, Downing J, Gwyther L, et al. Validation of a core outcome measure for palliative care in Africa: the APCA African Palliative Outcome Scale. Health and Quality of Life Outcomes 2010;8(1):1.
(89) African Palliative Care Association. Guidelines for the Use of the APCA African Palliative Outcome Scale. 2011; Available at: https://aidsfree.usaid.gov/sites/default/files/pos_guidelines.pdf. Accessed March/1, 2016.

(90) Dix O. Impact of the APCA African Palliative Outcome Scale (POS) on care and practice. 2012; Available at: www.pos_pal.org/doca/Impact_of_APCA_POS.pdf. Accessed March/2, 2016.
(91) Kelly AM, Smith B, Luo Z, Given T, Wehrwein I, Farley JE. Discordance between patient and clinician reports of adverse reactions to MDR-TB treatment. Int J Tuberc Lung Dis 2016;20(4):442-447.
(92) Kelly AM, Smith B, Luo Z, Given B, Wehrwein T, Master I, et al. Discordance between patient and clinician reports of adverse reactions to MDR-TB treatment. Int J Tuberc Lung Dis 2016;20(4):442-447.
(93) Vaghela JF, Kapoor SK, Kumar A, Dass RT, Khanna A, Bhatnagar AK. Home based care to multi-drug resistant tuberculosis patients: A pilot study. Indian J Tuberc 2015 04;62(2):91-96.
(94) Chochinov H, McClement S, Hack T, Thompson G, Dufault B, Marlos M. Eliciting personhood within clinical practice: effects on patients, families, and health care providers. J Pain Symptom Manage 2014;11:291.
(95) The Gold Standards Framework. The GSF Prognostic Indicator Guidance. 2011; Available at: www.goldstandardsframework.org.uk. Accessed February/13, 2018.
(96) Stangroom J. Social Science Statistics - Mann-Whitney U calculator. 2017; Available at: http://www.socscistatistics.com/tests/mannwhitney/Default.aspx. Accessed September/12, 2017.
(97) Stangroom J. Spearman's (Rho) Correlation calculator. 2017; Available at: http://www.socscistatistics.com/tests/spearman/Default.aspx. Accessed September/13, 2017.
(98) Bland J, Altman D. Statistics notes: Cronbach's alpha. BMJ 1997;314:275.
(99) Banerji D, Anderson S. A social study of awareness of symptoms among persons with pulmonary tuberculosis. Bull World Health Organ 1963;29:665-683.
(100) Hongthiamthong P, Subhannachart P, Raintawan P, Fuangtong P. Clinical aspects and treatment outcome in HIV-associated pulmonary tuberculosis: An experience from a Thai referral centre. J Med Assoc Thai 1994;77(10):520-524.
(101) COTEC., IFMSA., European forum for primary care., WFOT., EPHA., WHPCA., et al. Statement on Refugee and Migrant Health. 2017; Available at: ifmsa.ord/wp-content/uploads. Accessed November/17, 2017.
(102) Martinez R, Fernandez A. The Social and Economic Impact of Illiteracy. 2010; Available at: www.unesco.org/santiago. Accessed November/18, 2017.
(103) Statistics for the City of Cape Town- 2012 - Overview. Compiled by Strategic Development Information and Knowledge Management Department, City of Cape Town, using 2011 Census data supplied by Statistics South Africa. 2012; Available at: http://www.capetown.gov.za/Family%20and%20home/education-and-research-materials/data-statistics-and-research/cape-town-census. Accessed September/10, 2017.
(104) Upshur R, Singh J, Ford N. Apocalypse or redemption: responding to extensively drug-resistant tuberculosis. Bull World Health Organ 2009;87:481-483.
(105) Lowther K, Simms V, Selman L, Sherr L, Gwyther L, Karluki H, et al. Treatment outcomes in palliative care: the TOPCare study. A mixed methods phase III randomised controlled trial to assess the effectiveness of a nurse-led palliative care intervention for HIV positive patients on antiretroviral therapy. BMC infectious diseases 2012;12(28):19 November 2017.
(106) Avong Y, et al. Doing No Harm? Adverse Events in a Nation-Wide Cohort of Patients with Multidrug-Resistant Tuberculosis in Nigeria. PLos ONE 2015;10(3):e0120262.
(107) Sagwa E, Mantel-Teeuwisse A, Ruswa N. Occurrence and clinical management of moderate-to-severe adverse events during drug-resistant tuberculosis treatment: a restrospective cohort study. J Pharm Policy Practice 2014;7(14).
(108) Gebremariam M, Bjune G, Frich J. Barriers and facilitators of adherence to TB treatment in patients on concomitant TB and HIV treatment: a qualitative study. BMC Public Health 2010 2010;10(651).
(109) Daftary A, Padayatchi N, O'Donnell M. Preferential adherence to antiretroviral therapy over tuberculosis treatment: A qualitative study of drug-resistant TB/HIV co-infected patients in South Africa. Global Public Health 2014 10/21;9(9):1107-1116.
(110) DiMatteo M, Lepper H, Croghan T. Depression is a risk factor for noncompliance with medical treatment: a meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 2000;160:2101-2107.
(111) Morris MD, Quezada L, Bhat P, Moser K, Smith J, Perez H, et al. Social, economic, and psychological impacts of MDR-TB treatment in Tijuana, Mexico: a patient's perspective. Int J Tuberc Lung Dis 2013 07;17(7):954-960.

(112) Cleeland C. Symptom burden: multiple symptoms and their impact as patient-reported outcomes. J Natl Cancer Inst Monogr 2007;37:16.
(113) Murray S, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. BMJ 2005;330:1007-1011.
(114) Sagwa E, Ruswa N, Mavhunga F, Rennie T, Leufkens H, & Mantel-Teeuwisse A. Adverse events and patients' perceived health-related quality of life at the end of multidrug-resistant tuberculosis treatment in Namibia. Patient Preference and Adherence 2016;10:2369-2377.
(115) Atif M, Syed Sulaiman S, Shafie A, et al. Impact of tuberculosis treatment on health-related quality of life of pulmonary tuberculosis patients: a follow-up study. Health and Quality of Life Outcomes 2014;12(19).
(116) Post S, Puchalski C, Larson D. Physicians and Patient Spirituality: Professional Boundaries, Competency, and Ethics. Ann Intern Med 2000;132(7):578-583.
(117) Vega P, Sweetland A, Acha J, Castillo H, Guerra D, Smith Fawzi M, et al. Psychiatric issues in the management of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2004;8(6):749-759.
(118) Abrahams N, Jewkes R. Managing and resisting stigma: a qualitative study among people living with HIV in South Africa. J Int AIDS Soc 2012;15(2):17330.
(119) Moya S. South Africa Unemployment Rate. 2017; Available at: www.tradingeconomics.com. Accessed November/14, 2017.
(120) Dheda K, Migliori G. The global rise of extensively drug-resistant tuberculosis: is the time to bring back sanatoria now overdue? Lancet 2012;379:773-775.
(121) Knaul F, et al. Alleviating the access abyss in palliative care and pain relief - an imperative of universal health coverage: The Lancet Commission Report. Lancet 2017 12 October 2017;0(0):12 February 2018-http://dx.doi.org/10.1016/S0140-6736(17)32513-8.
(122) WHO. End TB brochure. 2018; Available at: http://www.who/tb/post2015_strategy/en. Accessed February/1, 2018.

APPENDICES

APPENDIX 1

Declaration on Palliative Care and MDR/XDR-TB(37)

Geneva, Switzerland, 19 November 2010

As a group of experts in palliative care and MDR/XDR-TB, we declare:

1. That access to palliative care for individuals (adults and children) with MDR/XDR-TB is a human right and promotes dignity.
2. That palliative care is an essential component of the provision of care for individuals (adults and children) with MDR/XDR-TB, wherever in the world that they are receiving care
3. That palliative care should be strengthened where being provided, and integrated alongside the prevention and treatment of MDR/XDR-TB
4. That palliative care in the context of MDR/XDR-TB should be integrated into the management of MDR/XDR-TB from the time of diagnosis until the patient reaches cure or end of life. The problems faced by MDR/XDR-TB patients and families span multiple physical, psychological, social and spiritual dimensions. We believe that the existing WHO definition of palliative care is highly appropriate for patients with drug-resistant TB.
5. That palliative care strengthens the Stop TB strategy.
6. That, as experts on MDR/XDR-TB and palliative care, we are keen to learn from each other.
7. That we are committed to developing the agenda on palliative care in MDR/XDR-TB, and improving access to care, medications, training and capacity building, and collaborating to improve the knowledge base through research.

Palliative Care and MDR/XDR-TB Integration Meeting, November 18-19, 2010
Open Society Foundations – Worldwide Palliative Care Alliance – WHO Stop TB

APPENDIX 2

Summary of the End TB Strategy (30,122)

Aim: To end the global TB epidemic

For the period 2016-2035

Key principles:

i. Adaptation of the strategy and targets at country level, with global collaboration
ii. Protecting and promoting human rights, ethics and equity
iii. Building a strong coalition with civil society and communities
iv. Government stewardship and accountability, with monitoring and evaluation

Pillars:

i. Integrated, patient-centred care and prevention. Key components: early diagnosis of TB, treatment of all people with TB, collaborative TB/HIV activities, preventive treatment
ii. Bold policies and supportive systems. Key components: political commitment, engagement of communities, universal health coverage, social protection
iii. Intensified research and innovation. Key components: Discovery, development and rapid uptake of new tools, interventions and strategies; research

Targets:

For 2035: 95% reduction in TB deaths and an 89% reduction in TB incidence, compared with 2015
For 2030: 90% reduction in TB deaths and an 80% reduction in TB incidence, compared with 2015
For 2020: 35% reduction in TB deaths and an 20% reduction in TB incidence, compared with 2015

For 2020 and thereafter: 0% of TB-affected households that experience catastrophic costs as a result of TB disease

APPENDIX 3

Visual aid of Likert-type scale used for African APCA-POS questions

APCA-POS (28-34)

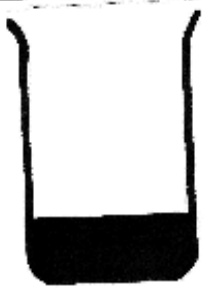
0	
1	
2	
3	
4	
5	

APPENDIX 4

Visual aid used for Likert-type scale for Symptom burden questions

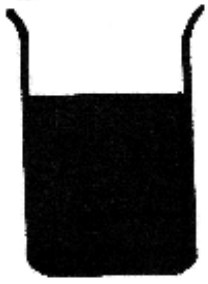
SYMPTOM BURDEN/ SIMPTOOM-LAS/ INGABA ZIYA KU KHATHAZA IMPHAWU ZESISI GULO: (35-60)

0. I *do not have this symptom*
   Ek *het nie die simptoom nie*
   Andinazo imphawu *kodwa azindi khathazi*

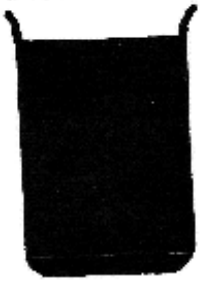


1. I have this symptom, *it doesn't bother me*
   Ek het die simptoom, *maar dit pla my nie*
   Ndinazo ezi impawu, *kodwa azindi khathazi*

2. I have this symptom, *it bothers me a little*
   Ek het die simptoom, *dit pla my 'n bietjie*
   Ndinazo ezi impawu, *ziyandi khathaza ka ncinci*



3. I have this symptom, *it bothers me*
   Ek het die simptoom, *dit pla my*
   Ndinazo ezi impawu, *ziyandi khathaza*



4. I have this symptom, *it bothers me a lot*
   Ek het die simptoom, *dit pla my baie*
   Ndinazo ezi impawu, *ziyandi khathaza ka khulu*

APPENDIX 5

Questionnaire (English translation)

A study to determine the Palliative Care Needs of Patients with Drug Resistant Tuberculosis in the Southern sub-district of Cape Town

Researcher: Dr Shannon Odell, shannonodell@yahoo.com, 084 556 2778

Expected time required for completion: 20 minutes

Introduce yourself to patient in a non-threatening manner: ☐

Language communicated in: Afrikaans: ☐ English: ☐ isiXhosa: ☐ Other: ☐

Information sheet given: ☐

Written consent form signed: ☐

	Date: DD /MM / YY Time:
1. Age (years):	2. Male: ☐ Female: ☐
3. Citizenship: South African: ☐	Non-South African: ☐
4. First language: Afrikaans: ☐ English: ☐ Xhosa: ☐ Other: ☐	
5. Marital status: Single: ☐ Married: ☐ Partnership/cohabitating: ☐ Divorced: ☐ widowed: ☐ ☐ Other: ☐	
6. Highest education level: primary school: ☐ secondary school: ☐ tertiary education: ☐ none: ☐ ☐	
7. Setting of interview: Clinic: ☐ Household: ☐	
8. Participant's dwelling: brick house: ☐ informal settlement: ☐	
9. Number of windows in dwelling:	
10. Suburb where participant currently resides:	
11. Number of people residing in household (including participant):	
12. Are there other people at your home with TB?: Yes: ☐ No: ☐	
13. Previously diagnosed with TB: Yes : ☐ No: ☐ Uncertain: ☐	
14. When DR-TB was diagnosed: 2017: ☐ 2016: ☐ 2015: ☐ 2014: ☐ 2013: ☐ 2012: ☐ before: ☐	
15. When was anti-tuberculosis medication started? 2017: ☐ 2016: ☐ 2015: ☐ 2014: ☐ 2013: ☐ 2012: ☐ before 2012: ☐	
16. Are you currently taking anti-tuberculosis medication? Yes: ☐ No: ☐	
17. DR-TB status: defaulter: ☐ treatment failure: ☐ culture converted: ☐ Sputum culture positive: ☐	
18. What is your HIV status? Not willing to disclose: ☐ Positive: ☐ Negative: ☐ Unknown: ☐ ☐	
19. Are you also on anti-retroviral medication?: Yes: ☐ No: ☐	
20. How many tablets/pills do you have to take each day? <10 ☐; 10-19 ☐; >20 ☐	
21. Do you have problems taking so many tablets? Yes: ☐ No: ☐	
22. Do you smoke cigarettes? Yes: ☐ No: ☐	
23. Do you use other drugs such as tik, dagga, heroine, cocaine? Yes: ☐ No: ☐	

24. Have you been hospitalized during the last year? Yes: ☐ No: ☐
25. Do you receive help from home-based carers? Yes: ☐ No: ☐
26. Has having TB affected your ability to work? Yes: ☐ No: ☐

27. Functional status/ECOG status:

Fully active: able to carry on all activities without restriction	0
Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature	1
Ambulatory and capable of self-care but unable to carry out any work activities. Up and about more than 50% of waking hours	2
Capable of only limited self-care: confined to bed or chair 50% or more of waking hours	3
Completely disabled: cannot carry on any self-care: totally confined to bed or chair	4
(Dead	5)

APCA POS:

Ask the patient:

28. Please rate your pain during the last week:	no pain at all	0
	Slight pain	1
	Moderate pain	2
	Severe pain (interferes with activities of daily life)	3
	Very severe pain	4
	Worst/overwhelming pain	5
29. Have any other symptoms (eg nausea, coughing or constipation) been affecting how you feel in the last week?	No symptoms at all	0
	Slight symptoms	1
	Moderate symptoms	2
	Severe symptoms (interferes with activities of daily living)	3
	Very severe symptoms	4
	Overwhelming. The worst symptoms imaginable	5
30. Have you been feeling worried about your illness in the past week?	Not at all worried	0
	Worried very occasionally	1
	Worried some time	2
	Worried a lot of the time	3
	Worried most of the time	4
	Worried all of the time	5
31. Over the past week, have you been able to share how you are feeling with your family and friends?	Not at all	0
	Only once	1
	Occasionally	2

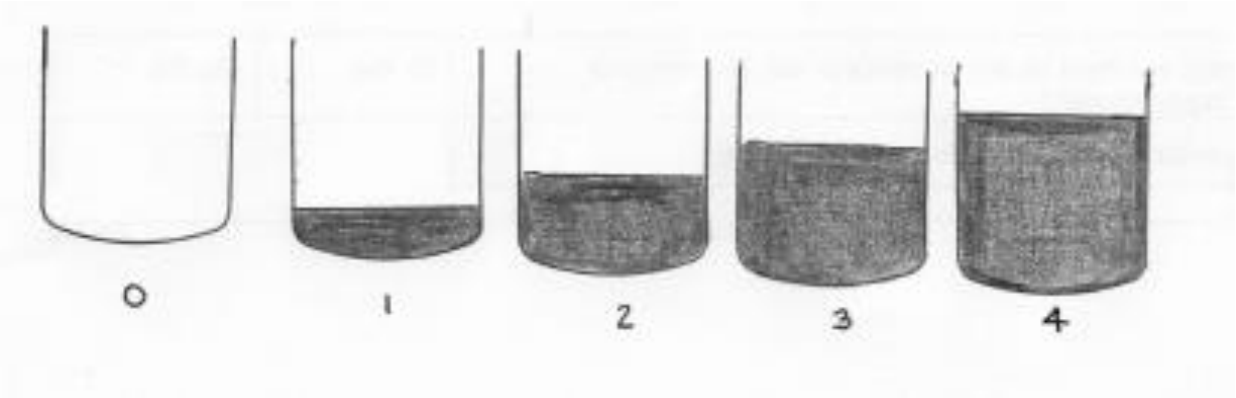
	Fairly frequently	3
	Often	4
	Yes, I've talked freely	5
32. Over the past week have you felt that life was worthwhile?	Not at all	0
	Not very often	1
	Occasionally	2
	Some of the time	3
	Most of the time	4
	Yes, all of the time	5
33. Over the past week, have you felt at peace?	Not at all	0
	Not very often	1
	Occasionally	2
	Some of the time	3
	Most of the time	4
	Yes, all the time	5
34. Have you had enough help and advice for your family to plan for the future?	None	0
	Very little	1
	For a few things	2
	For several things	3
	For most things	4
	As much as wanted	5

Ask the family member: (Not applicable)

How much information have you and your family been given?	None	0
	Very little	1
	Some	2
	Quite a lot	3
	A great deal	4
	As much as wanted	5
How confident does the family feel caring for _____?	Not at all	0
	Not confident about many things	1
	Confident about a few things	2
	Confident about some things	3
	Confident about most things	4
	Very confident	5
Has the family been feeling worried about the patient over the last week?	Not at all worried	0
	Worried very occasionally	1
	Worried some of the time	2
	Worried a lot of the time	3
	Worried most of the time	4
	Worried all of the time	5

Symptom burden:
The following questions ask about symptoms in the last week. Please rate how you were bothered by each symptom. (Mark with an X)

0= I *do not have this symptom*
1= I have this symptom, *it doesn't bother me*
2= I have this symptom, *it bothers me a little*
3= I have this symptom, *it bothers me*
4= I have this symptom, *it bothers me a lot*



	0	1	2	3	4
35. difficulty falling or staying asleep					
36. feeling dizzy or light-headed					
37. fatigue or loss of energy					
38. pain, numbness or tingling in the hands or feet					
39. nausea or vomiting					
40. diarrhoea					
41. loss of appetite					
42. shortness of breath					
43. coughing up blood					
44. skin problems, such as rash, dryness or itching					
45. ringing in your ears or loss of hearing					
46. joint pains					
47. ongoing pain at injection sites					
48. confusion or trouble remembering					
49. tremors, shaking or fits					
50. feeling sad, down or depressed					
51. feeling suicidal					
52. feeling hopeless					
53. feeling anxious or scared					
54. having remorse or regret					
55. feeling like you're not coping					
56. feeling stigmatized by family, relationships are limited					
57. feeling stigmatized by community or discriminated against					
58. feeling stigmatized by health care professionals, abandoned					
59. feeling isolated and lonely					

60. worried about finances/money					

61. Please tell me more about what troubles you the most.

_____

_____

_____

62. What else do I need to know about you to be able to provide good care?

_____

_____

_____

63. Distress protocol required: ☐ Because:_____
Patient referred to: _____

Reassure participant that information given will remain confidential: ☐

Enquire whether the participant has any further questions or comments relating to the research: ☐

Thank the participant for their time and input: ☐

Time taken to complete survey:_____ mins

APPENDIX 6

Questionnaire (Afrikaans translation)

‘n Studie om die Palliatiewe Versorgingsbehoeftes van Pasiënte met Medikasie Weerstandige-Tuberkulose (DR-TB) in die Suidelike subdistrik van Kaapstad te bepaal.

Dr Shannon Odell; shannonodell@yahoo.com; 0845562778

Verwagte tyd wat nodig is vir die voltooiing: 20 minute

Stel jouself aan die pasiënt bekend op ‘n nie-bedreigende manier: ☐

Taal waarin daar gekommunikeer is: Afrikaans: ☐ Engels: ☐ isiXhosa: ☐ Ander: ☐

Inligtingsbladsy gegee: ☐

Ingeligte toestemmingsdokument geteken: ☐

	Datum: DD/MM/JJ Tyd:
1. Ouderdom (jare):	2. Manlik: ☐ Vroulik: ☐
3. Burgerskap: Suid-Afrikaans: ☐ Nie-Suid-Afrikaans: ☐	
4. Eerste taal: Afrikaans: ☐ Engels: ☐ isiXhosa: ☐ Ander: ☐	
5. Huweliksstatus: Enkel: ☐ Getroud: ☐ Vennootskap/woon saam: ☐ Geskei: ☐ Weduwee/wewenaar: ☐ Ander: ☐	
6. Hoogste onderwysvlak: laerskool: ☐ hoërskool: ☐ tersiëre onderwys: ☐ geen: ☐	
7. Omgewing van onderhoud: Kliniek: ☐ Tuis: ☐	
8. Deelnemer se behuising: baksteenhuis: ☐ informele behuising: ☐	
9. Hoeveel vensters in die huis?	
10. Woongebied waarin die deelnemer tans woon:	
11. Aantal mense inwonend in die huishouding:	
12. Is daar mense in die huishouding wat tans geïnfekteer is met TB:	
13. Voorheen gediagnoseer met TB: Ja: ☐ Nee: ☐ Onseker: ☐	
14.Wanneer is DR-TB gediagnoseer? 2017: ☐ 2016: ☐ 2015: ☐ 2014: ☐ 2013: ☐ 2012: ☐ vroeër: ☐	
15. Wanneer is U met TB medikasie begin? 2017: ☐ 2016: ☐ 2015: ☐ 2014: ☐ 2013: ☐ 2012: ☐ voor 2012: ☐	
16. Gebruik u tans TB (anti-tuberkulose) medikasie? Ja: ☐ Nee: ☐	
17. DR-TB status: droster (defaulter): ☐ nalatigheid in verband met medikasie to neem (treatment failure): ☐ kulturele oortuigings : ☐ sputum culture positive: ☐	
18. Wat is u HIV status? Nie bereid om saam te deel nie: ☐ Positief: ☐ Negatief: ☐ Onbekend: ☐	
19. Gebruik u tans ook ARVs (anti-retrovirale medikasie)?: Ja: ☐ Nee: ☐	
20. Hoeveel pille (tablette) moet u elke dag neem? <10 ☐; 10-19 ☐; >20 ☐	

21. Vind u dit moeilik om al die pille (tablette) te neem? Ja: ☐ Nee: ☐
22. Rook u sigarette? Ja: ☐ Nee: ☐
23. Gebruik u ander dwelms soos tik, dagga, heroine of kokaiene? Ja: ☐ Nee: ☐
24. Is u gehospitaliseer gedurende die afgelope jaar? Ja: ☐ Nee: ☐
25. Ontvang u hulp van tuisversorgers?: Ja: ☐ Nee: ☐
26. Vandat jy TB het, is daar enige probleme om jou werk te doen? Ja: ☐ Nee: ☐

27. Funksionele status/ ECOG status:

Ten volle aktief: in staat om alle aktiwiteite, sonder beperkings uit te voer.	0
Beperk ten opsigte van uitpeuttende, fisiese aktiwiteite, maar kan loop/is beweeglik en is in staat om ligte werk of werk van ‘n sittende aard te doen.	1
Kan loop/beweeglik en in staat tot selfversorging, maar nie in staat om enige werksaktiwiteite uit te voer nie. Op en aan die gang vir meer as 50% van die dag.	2
Slegs in staat tot beperkte selfversorging: 50% of meer van tyd bedlêend of beperk tot ‘n stoel	3
Heeltemal gestremd; nie in staat tot enige selfversorging nie; heeltemal bedlêend of beperk tot ‘n Stoel	4
(Oorlede	5)

APCA African POS:

28. Evalueer asb u pyn gedurende die afgelope week:	Geen pyn	0
	Effense pyn	1
	Matige pyn	2
	Ernstige pyn (beperk alledaagse aktiwiteite)	3
	Baie ernstige pyn	4
	Die ergste/oorweldigende pyn	5
29. Het enige ander simptome (bv naarheid, gehoes of hardlywigheid) u gemoedstoestand beïnvloed die afgelope week?	Geen simptome	0
	Ligte simptome	1
	Matige simptome	2
	Ernstige simptome (beperk alledaagse aktiwiteite)	3
	Baie ernstige simptome	4
	Oorweldigend. Die ergste simptome denkbaar	5
30. Was u die afgelope week bekommerd oor u siekte?	Glad nie bekommerd nie	0
	So nou en dan bekommerd	1
	Soms bekommerd	2

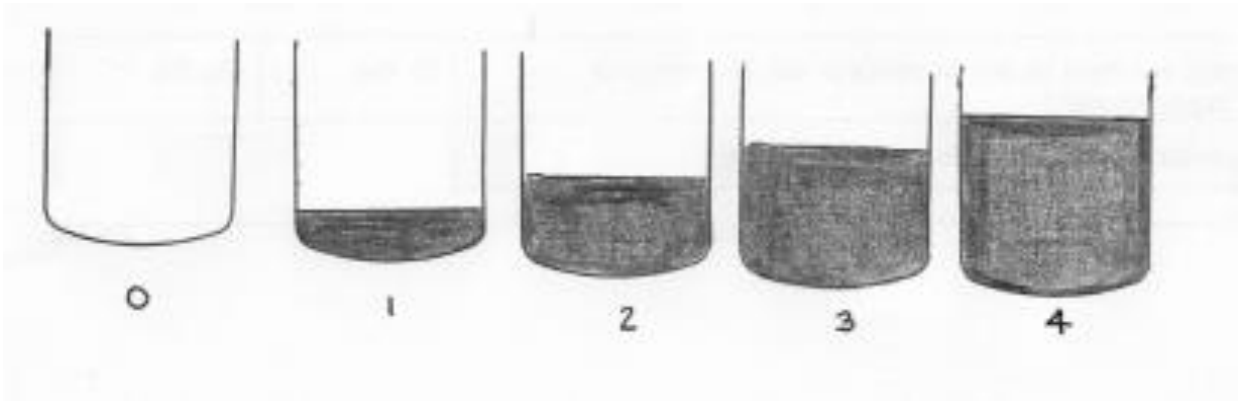
	Dikwels bekommerd	3
	Meeste van die tyd bekommerd	4
	Die heeltyd bekommerd	5
31. Was jy die afgelope week in staat om jou gevoelens met jou familie en vriende saam to deel?	Glad nie	0
	Slegs een keer	1
	So nou en dan	2
	Redelik gereeld	3
	Dikwels	4
	Ja, ek het vrymoediglik gepraat	5
32. Het jy die afgelope week ervaar dat die lewe die moeite werd is?	Glad nie	0
	Nie baie dikwels nie	1
	So af en toe	2
	Somtyds	3
	Meeste van die tyd	4
	Ja, die heeltyd	5
33. Het jy die afgelope week vrede in jou gemoed ervaar?	Glad nie	0
	Nie baie dikwels nie	1
	Af en toe	2
	Somtyds	3
	Meeste van die tyd	4
	Ja, die heeltyd	5
34. Het jy voldoende hulp en advies ontvang, sodat jou familie vir die toekoms kan beplan?	Geen	0
	Baie min	1
	Met ‘n paar goed/items	2
	Met verskeie goed/items	3
	Met meeste goed/items	4
	Genoegsame informasie	5

Van hoeveel inligting is jy en jou familie voorsien?	Geen	0
	Baie min	1
	Sommige	2
	Nogal baie	3
	Besonder baie	4
	So veel as nodig	5
Hoe seker voel jou familie oor die versorging van _____	Glad nie	0
	Nie seker oor baie goed nie	1

	Seker oor ‘n paar goed/dinge	2
	Seker oor sommige goed/dinge	3
	Seker oor meeste goed/dinge	4
	Baie seker	5
Was die familie bekommerd oor die pasiënt gedurende die laaste week?	Glad nie bekommerd nie	0
	So nou en dan bekommerd	1
	Soms bekommerd	2
	Dikwels bekommerd	3
	Meestal bekommerd	4
	Die heeltyd bekommerd	5

Simptoom-las:
Die volgende vrae gaan oor simptome oor die afgelope 7 dae (een week). Evalueer asb hoeveel elke betrokke simptoom jou gepla het. (Merk met ‘n X)

0= Ek het nie die simptoom nie.
1= Ek het die simptoom, (maar) dit pla my nie.
2= Ek het die simptoom; dit pla my ‘n bietjie.
3= Ek het die simptoom; dit pla my.
4= Ek het die simptoom; dit pla my baie.



	0	1	2	3	4
35. Raak moeilik aan die slaap of bly nie aan die slaap nie					
36. Voel duiselig of lighoofdig					
37. Moegheid of gebrek aan energie					
38. Pyn, gevoelloosheid of ervaar prikkelgevoel in hande of voete					
39. Naarheid of gooi op					
40. Diaree					
41. Geen eetlus					
42. Kortasem					
43. Hoes bloed					
44. Velprobleme soos uitslag, droogheid of gejeuk					
45. Gesuis/gefluit in ore of gehoorverlies					
46. Gewrigspyne					
47. Voortdurende pyn in areas wat ingespuit is					
48. Verwarring of sukkel om te onthou					

49. Bewerasie of stuiptrekkings					
50. Voel hartseer, af of depressief					
51. Selfmoord neigings					
52. Voel hulpeloos/sonder hoop					
53. Voel angstig of bang					
54. Ervaar selfverwyt of spyt					
55. Voel of jy nie in beheer is nie.					
56. Voel verstoot deur familie; verhoudings is beperk					
57. Voel verstoot deur gemeenskap of word teen gediskrimineer					
58. Voel verstoot deur professionele gesondheidssorg persone					
59. Voel geïsoleerd en eensaam					
60. Voel bekommerd oor finansies/geld					

61. Sê vir my wat pla jou die meeste?

_____

_____

_____

62. Wat anders van jouself kan jy vir my sê, te sorg dat jy die beste behandeling kan kry?

_____

_____

_____

63. Nood protokol benodig: ☐ Omdat:_____

Pasiënt is verwys na: _____

Verseker deelnemer weereens dat gegewe inligting vertroulik sal bly: ☐

Doen navraag of die deelnemer enige verdere vrae of opmerkings het, wat verband hou met die navorsing.: ☐

Bedank die deelnemer vir sy/haar tyd en insette: ☐

Tyd geneem om die opname te voltooi: _____ minute

APPENDIX 7

Questionnaire (isiXhosa translation)

U phando ngokufuna u kwazi nge zidingo zesigulane e sine Drug Resistant Tuberculosis eSouthern sub-district of Cape Town

Ophandayo Qgirha u Shannon Odell, shannonodell@yahoo.com, 084 556 2778

Ixesha e lilinganiselweyo loku qhiba: 20 minute

Zazise kusigulane nge ndlela engamothusiyo: ☐

U lwimi lwa sekhaya: Afrikaans: ☐ English: ☐ isiXhosa: ☐ Other: ☐

Iphepha lolwazi nge sazi si vumelwano: ☐

Um thathi ngxaxheba u xelelwe nge sazi si vemelwano : ☐

	Date: DD /MM / YY Time:
1. Age (years)/iminyaka yakhe:	2. indoda (M) : ☐ Intombi (F): ☐
3. Ungumi waphi: South African/ungumi walapha: ☐ Non-South African/ ungumi wanga phandle: ☐	
4. ulwimi lwenkobe: isibhulu: ☐ Isingesi: ☐ Xhosa: ☐ ezinye: ☐	
5. Marital status: andi tshatanga: ☐ nditshatile: ☐ Ndiyahlalisana: ☐ ndo hlukene nomlingani wam: ☐ Umhlolo/umhlolokazi ☐ ezinye: ☐	
6. I banga eli phezuli owali phumelelayo esi kolweni: Isikolo samabanga aphantsi: ☐ Isikolo samabanga a phezulu: ☐ nDyunivesiti: ☐ zange ndalibeka esikolweni: ☐	
7. Lwe nzelwa phi oludliwano ndlebe Clinic: ☐ endlini: ☐	
8. Umthathi nxaxheba uhlala endlini enjani: indlu yesi tena ☐ ityotyombhe: ☐	
9. Zingaphi ifestile endlwini:	
10. Isi xeko apho umthathi ngxaxheba ehlala khona:	
11. Banga phi abantu abahlala nom thathi mgxaxheba:	
12. Banga phi abantu abahlala nom thathi mgxaxheba abanale ithsolongwane ye TB:	
13. wakhe wa nayo ngaphambili I TB: Ewe ☐ hayi: ☐ andi qhinisekanga: ☐	
14. I qale nini ukuku phatha le ntsholongwane ye DR-TB: 2017: ☐ 2016: ☐ 2015: ☐ 2014: ☐ 2013: ☐ 2012: ☐ Ngaphambili: ☐	
15. wa qala nini uku sebenzisa ama pilisi e anti-tuberculosis? 2017: ☐ 2016: ☐ 2015: ☐ 2014: ☐ 2013: ☐ 2012: ☐ Nga phambili: ☐	
16. Ingaba u thatha ipilisi ze anti-tuberculosis? Ewe: ☐ Hayi: ☐	
17. Si yintoni is simo sakho se DR-TB: oyeke unyango phambi kwe thuba: ☐ ukupheza konyango: ☐ ukuphela kwentsholongwane: ☐	
18. Si yintoni isimo sakho se HIV? Siyifihlo yam: ☐ ndinayo: ☐ andinayo: ☐ andisazi: ☐	
19. Ingaba u thatha ipili I anti-retroviral? Ewe: ☐ Hayi: ☐	
20. Zingaphi I pillisi ozithathayo nge mini? <10 ☐ 10-19 ☐ >20 ☐	
21. Ingaba ufumana ubunzima Ngo ku thatha I pillisi ezinintsi ka ngaka? Ewe: ☐ Hayi: ☐	
22. Ingaba uyatshaya icuba? Ewe: ☐ Hayi: ☐	

23. Ingaba usebenzisa iziyobisi? I tiki, intsango, heroine okanye I cocaine? Ewe: ☐ Hayi: ☐
24. Ubukhe wa lala esibhedlela kulo nyaka uqhithileyo? Ewe: ☐ Hayi: ☐
25. Ingaba uyalifumana uncedo kubantu aba zisa uncedo ezidlini? Ewe: ☐ Hayi: ☐
26. Ingaba unayona ingxeki yokusebenza kube unesisisfo sephepha? Ewe: ☐ Hayi: ☐

27. Izinga lokwazi ukuzenzela

Uyakwazi ukuzenzela	0
Uyanzinyelwa ngumsebenzi ofuna amandla kodwa u ya kwazi uku hambha, no kwenza Imisebenzi enga funi mandla	1
uya kwazi ukuzihambela, kwaye uya kwazi ukuzonga uthi elapha abe engaphaya I xesha elingange 50% emini	2
uyazama kekodwa ukuzonga kodwa uyo yisakala.uhleli esebhedini okanye ehleli esitulweni I xesha elingange 50% emini	3
Akakwazi tu ukuzihambela: akakwazi tu ukuzonga:ubophelelekile e bhedini okanye esitulweni	4
(uswelekile	5)

APCA African POS:

28. ndicela undi xelele ngobu ngaka nani bentlungu zakho kule veki /nyaka uphelileyo	akukho zinhlungu	0
	zikhona kancinci	1
	Ziya vakala wethu	2
	Zibuhlungu kwaye zindi sebenzisa Kabuhlungu	3
	Zibuhlungu kakhulu	4
	Ziyandongamela intlungu	5
29. Ingaba ezinye ze zi mphawu beziku phatha, kulonyanka/veki uqhithileyo? (ukukhonyuluka,khohlela okanye ukuqhinwa kwe sisu?	Hayi andinazo ezi mphawu	0
	Zikhona,kodwa hayi ngamandla	1
	Zikhona kodwa ziya nyamezeleka	2
	Zikhona ngamandla ezimphawu, andikwazi uku sebenza kakuhle	3
	Ziyandihlupha ka khulu ezimphawu	4
	Ziya ndonga mela	5
30. Ingaba ubuziva ukhathazekile ngesi gulo sakho kulo nyaka uqhithileyo?	Hayi bendinga khatha zekanga	0
	Be ndikhatha zeke kancinci	1
	Be ndikhe ndikhathazeke ngamanye ama xesha	2
	Be ndikhathazeke kakhulu amaxesha amaninzi	3

	Be ndikhathazeke kakhulu amaxesha amaninzi	4
	Be ndikhatha zekile ngawo wonke ama xesha	5
31. Kulonyaka uqhithileyo,ubukhe wakwazi u ku xelela usapho lwakho ngendlala oziva ngayo nge si gulo sakho?	Hayi	0
	ndaba xelela kakanye	1
	ndakhe ndaba xelela	2
	ndi ya ba xelela	3
	ndi ba xelela oko oko	4
	Ewe, ndi thetha ngo ku khulilekileyo Nabo	5
32. kwezi veki zigqithileyo ubukhe wabubona ubomi bumyoli/ bumnandi?	Hayi	0
	hayi kakhulu	1
	Nga manye amaxesha	2
	Nga manye amaxesha	3
	Ngama xesha amaninzi	4
	Ewe, ngawo wonke amaxesha	5
33. kule veki I phelileyo,ingaba ubuziva u no xolo empheulweni wakho	Hayi	0
	Hayi ngama xesha amaninzi	1
	Nga manye ama xesha	2
	Nga manye ama xesha	3
	Ngama xesha ama ninzi	4
	Ewe ,ngawo wonke ama xesha	5
34. Lungaka nani uncedo,ne ngcebiso enizi fumaneyo, wena no sapho lwakho,ezizakuni nceda nge qhubakela phambili?	Ayikho	0
	Incinci	1
	Zi khona endinazo	2
	ndi nazo eziza ku nceda kwi zinto ezimbalwana	3
	ndi nazo,ezizakundinceda kwi zinto ezininzi	4
	Si nazo kangangoko sizi funa	5

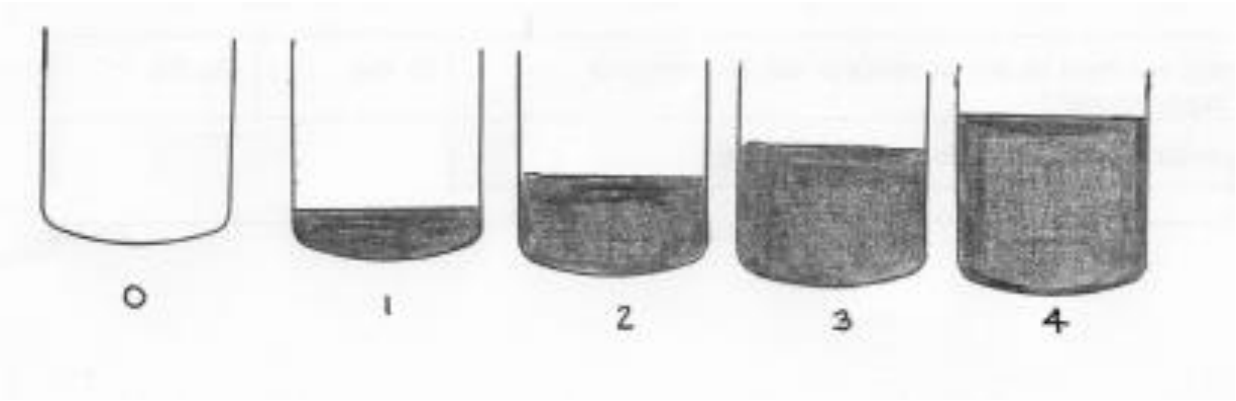
Not applicable

Lungaka nani u lwazi ,eluninikiwe wena no sapho Lwakho?	Alukho	0
	Lu ncinci ka khulu	1
	Lukhonanya	2
	Luninzana	3
	Luninzi	4
	Kanga ngoku sili funa	5
Lu zi thembhe ka ngaka nani u sapho lwakho, ngo konga wena?	Aluzi thembhanga tu	0
	aluzi thembhanga nge zinto ezininzi	1
	Luzi thembhe ngezinto ezimbalwa	2
	Luzi thembile ngezinye zezinto	3
	Luzi thembile ngezinto ezininzi	4
	Luzithembhe ka khulu	5

Ingaba usapho lwakho ,be lukhathazekile kule veki iphelileyo ngawe?	Bebenga khathazekanga tu	0
	bebe khathazeke nje	1
	bebe khathazekile ngamanye ama xesha	2
	bebe khathazekile ngama xesha amaninzi	3
	bebe khathazekile ngama xesha amaninzi	4
	bebe khathazekile ngama xesha wonke	5

Ingaba ziya ku khathaza imphawu zesisi gulo

Le mibuzo I landelayo ,I buza nge mphawu zakule nyanga I qhithileyo. Ndicela u bonise ukuba be zi ku khathaza kangaka nani na I mpawu zesisi gulo



0= *Andinazo imphawu*

1= *ndinazo ezi impawu kodwa azindi khathazi*

2= *ndinazo ezi impawu, ziyandi khathaza ka ncinci*

3= *Ndinazo ezi impawu, ziyandi khathaza*

4= *Ndinazo ezi impawu, ziyandi khathaza ka khulu*

	0	1	2	3	4
35. awu kwazi ku lala okanye ukunga lali					
36. uphathwa sisi yezi okanye u kujikelezwela yi ntloko					
37. uku dinwa okanye uku phelelwa nga mandla					
38. intlungu,ukuba ndindisholo kwezandla okanye inyawo					
39. uku khonyuluka okanye ukugabha					
40. ingaba uhanjiswa sisusu					
41. ukungabi namandla					
42. uku phelelwa ngu moya okanye uku phefumla nzima					
43. khohle la I gazi					
44. ingxaki no lusu,I rwayibhane,uku xweba kolusu,uku rhawuzelela ko lusu					
45. uku ngeva kakuhle					
46. Intlungu zemi phakathi					
47. intlungu kule ndawo u jove kuyo					

48. u ku dideka okanye uku libala					
49. ukungcangcazela,uku xhuzula					
50. uziva umoya wakho ungonwabanga/udangele/uphantshi					
51. I ngaba vzuva ufuna ukuzi bulala ngamanye ama xesha?					
52. uziva uphelelwe li thembha					
53. Uziva wothukile okanye u so yika					
54. Uziva u zi so la					
55. Uziva ingathi aku nyamezeleki					
56. Uziva uhlelelekile lu sapho lwakho,awunaba lingani					
57. Uziva u hlelelekile kwi lokisi yakho					
58. Uziva u hlelelekile ngabantu bakwezempilo					
59. Uziva u wedwa,					
60. Ingaba ukhathazekile nge mali					

61. Ndixelele banzi ngengxaki onazo ezikuhluphayo?

_____

_____

_____

62. Loluphi uhlobo endinganceda ngalo ukusiza kakuhle?

_____

_____

_____

63. ingaba iyamcaphukisa imibuzo: ☐ kuba: _____

isiguli sithunwe ngu:_____

Mthembise umthathi ngxaxheba ukuba,oluphando luzakuba yifihlo: ☐

Buza u kuba umthathi ngxaxheba akanazo na yena eyakhe imibuzo okanye into afuna uku yithetha ehambhelana nolu phandolwazi? ☐

Bulela umthathi nxaxheba nge xesha lakhe nange ngalelo lakhe: ☐

I xesha elisetyenzisiweyo ukuze kuqhitywe olu dliwano ndlebe _____imizuzu

APPENDIX 8

Information sheet for trial participants (English translation)

A study to determine the Palliative Care Needs of Patients with Drug Resistant Tuberculosis in the Southern sub-district of Cape Town

Thank you for thinking about taking part in this research study.

This information sheet will give you an idea of what it will involve, so please read it carefully. It is available in English, Afrikaans and isiXhosa, and the interviewers will read it to you if you so wish.

Feel free to ask the interviewer any questions if you're unsure about anything. Please don't feel pressurized to agree straight away, rather be sure you understand fully what will be asked of you, and take time to discuss with a friend or family member if you need to. The interview could then be arranged at another, more suitable time.

Your taking part in this research is completely voluntary and unconditional, which means that if you'd rather not answer the questions or wish to stop during the interview, that is your choice, and it will not be held against you or affect the care you will receive by the doctors, nurses or counselors involved in your current and future management. **This gives you the opportunity to be completely honest in your answers. Very importantly, should you prefer not to participate, your ongoing care will not be affected.**

Who is doing this research?
Dr Shannon Odell, who is a medical doctor, studying palliative medicine. She, along with the help of a volunteer or counselor/s will be conducting this research- speaking to patients and asking the questionnaire. The volunteer or counselor may be known to you already, and have been involved in your care and follow-up before. **This relationship will not change by your participating or not participating in this research, however you may find that your relationship with the volunteer or counselor is strengthened.**

Why is this research being done?
This study wants to understand how DR-TB affects you-the symptoms that are difficult for you and the quality of life you are challenged with.

Why is this research important?
This research is important because little is known of what it feels like to have DR-TB in this community of Cape Town. It is important to find out how many patients are struggling with similar symptoms, and how severely these impact on the quality of your lives. This knowledge is vital in the planning of better health service provision and support for those affected by DR-TB.

What information is being collected?
Questions regarding your quality of life and the physical, psychological, social, financial and spiritual symptoms you experience will be asked from a questionnaire and completed by the interviewer.

What will happen to the results of this questionnaire?
All the answers from the questionnaires will be collected, kept safe and confidential and then analysed. Your name will not appear on this analysis, and all your answers will remain confidential. That means that **no matter what you say, it will not point back at you, and your honest answers will not affect your current care or future management.** The final results and analysis will be presented to the Department of Health, the Western Cape Government, the City of Cape Town and other interested parties or possible donors. By sharing this information I hope to highlight the need for providing better care for all DR-TB patients in the community and urge for more funding to be available to deliver this care.

How long will this information be kept?

Your answers will be stored until all questionnaires have been collected, studied and the results have been summarized and written into a thesis document. After the presentation of the findings all the answers will be deleted.

With whom will these results be shared?
Dr Odell and the volunteer/counselors involved in asking the questionnaire will share information if there are any problems experienced in the process of collecting the information. This information will be confidential, with **the focus on what is reported and not who reported the information**. This information will also be discussed with Dr Odell's supervisor and the assistant helping with the analysis. The final results will be submitted as part of the Master of Philosophy thesis to the University of Cape Town in the last quarter of 2017. Further sharing of information is planned with the Department of Health, the Western Cape Government, the City of Cape Town and other interested parties or possible donors. Results will also be available at the local clinic for any DR-TB patients in the community whether they have participated in the questionnaire or not.

What will it mean for you?
The questionnaire will take approximately 20-30 minutes of your time, and there will be no payment.

What if the questions are too upsetting?
You may stop the interview at any time and change your mind about carrying on. **Your taking part is voluntary and you will not be discriminated against if you find it too upsetting to continue**. The person interviewing you might then suggest referring you to the clinic for further help or care.

What does "informed consent" mean?
Before giving your permission to be included in this study, it is very important to be aware of what that means. The aim of the consent form is to give you further information on the study, that you understand what will be asked of you and to make sure you can make your own decision based on correct, honest information, without feeling forced to do so.

If you have any further queries about this research study, please contact:
Dr Shannon Odell
084 556 2778
shannonodell@yahoo.com

Should you have any queries regarding your rights and welfare participating in this research, please contact the UCT Research Ethics Committee:
Mrs Lamees Emjedi
Research Ethics Committee Administration Supervisor
E52 Room 24, Old Main Building, Groote Schuur Hospital, Observatory
021 406 6338

Please keep this information sheet in a safe place should you need to refer to it at a later stage.

APPENDIX 9

Information sheet for trial participants (Afrikaans translation)

'n Studie om die Palliatiewe Versorgingsbehoeftes van Pasiënte met DR-TB in die

Suidelike sub-distrik van Kaapstad te bepaal

Dankie vir u gewilligheid om deel te neem aan hierdie navorsingsstudie.

Hierdie inligtingsbladsy sal u ‘n aanduiding gee wat die studie behels. Lees dit asb sorgvuldig deur. Dit is beskikbaar in Engels, Afrikaans en isiXhosa en die onderhoudvoerders kan dit vir u lees, indien u dit verkies. Rig gerus enige vrae aan die onderhoudvoerder, as u onseker is oor enigiets. Moet asb nie verplig voel om dadelik in te stem nie. Indien nodig, maak eerder seker u verstaan wat van u verwag word en neem tyd om dit met ‘n vriend of familielid te bespreek. Die onderhoud kan dan gereël word op ‘n meer geleë tyd.

U deelname aan hierdie navorsing is heeltemal vrywillig en onvoorwaardelik, wat beteken dat as u liewer nie die vrae wil beantwoord nie en verkies om te onttrek tydens die onderhoud, dit nie teen u gehou sal word of die behandeling beïnvloed wat u tans deur die dokters, verpleegsters of beraders wat betrokke is by u huidige of toekomstige behandeling ontvang nie. Dit gee u die geleentheid om heeltemal eerlik te wees met u antwoorde. Dis belangrik om te onthou dat indien u verkies om nie deel te neem nie, u voortdurende versorging nie geraak sal word nie.

Wie doen hierdie navorsing?
Dr Shannon Odell, ‘n mediese dokter, wat tans in palliatiewe medisyne studeer. Sal met behulp van ‘n vrywilliges of berader/s die navorsing behartig, met die pasiënte gesels en die vraelys hanteer. Die vrywilliges en berader mag reeds aan u bekend wees en was dalk vroeër betrokke by u versorging en opvolg. Hierdie verhouding sal nie verander deur u deelname/nie-deelname aan hierdie navorsing nie. U mag selfs vind dat U verhouding met die betrokke berader sterker word.

Waarom word hierdie navorsing gedoen?
Hierdie studie probeer bepaal hoe DR-TB u affekteer, die simptome wat vir u moeilik is (om te hanteer) en die uitdagings wat die kwaliteit van U lewe beïnvloed.

Hoekom is hierdie navorsing belangrik?
Hierdie navorsing is belangrik omdat baie min bekend is van hoe dit voel om DR-TB te hê in die gemeenskap van Kaapstad. Dit is belangrik om uit te vind hoeveel pasiënte met dieselfde simptome sukkel en hoe ernstig die impak is op u lewenskwaliteit. Hierdie kennis is baie belangrik in die beplanning en voorsiening van beter gesondheidsdienste vir diegene met DR-TB.

Watter tipe inligting word versamel?
Vrae sal op die vraelys gevra word oor u lewenskwaliteit, sowel as die fisiese simptome, emosiönele, sosiale, finansiële en geestelike behoeftes wat u ervaar en dan voltooi word deur die onderhoudvoerder.

Wat gaan gebeur met die uitslae van die vraelys?
Al die antwoorde op die vraelys sal versamel word, veilig en vertroulik bewaar word en dan geanaliseer word. U naam sal nie op die analise verskyn nie en al u antwoorde sal vertroulik bly. Dit beteken dit maak nie saak wat u antwoord nie, dit sal nie na u terugverwys word nie en u earlike antwoorde sal nie u huidige of toekomstige versorging en hantering beïnvloed nie. Die finale uitslae en analise sal aan die Departement van Gesondheid, die Wes-Kaapse en Kaapstad Regering en ander belangstellende of moontlike skenkers aangebied word. Deur die deel van hierdie inligting, hoop ek om die nood/behoefte vir beter versorging aan alle DR-TB pasiënte in die gemeenskap uit te lig en te pleit vir groter befondsing om hierdie diens te lewer.

Hoe lank sal die inligting bewaar word?
U antwoorde sal gebêre word totdat al die vraelyste ingesamel, bestudeer en die uitslae opgesom en in ‘n tesis opgeteken is. Na die aanbieding van die bevindinge sal al die antwoorde uitgewis word.

Met wie gaan hierdie uitslae gedeel word?
Dr Odell en die vrywilliges/beraders betrokke in die vrae van die vraelys sal inligting deel indien daar enige probleme ervaar word tydens die insameling van inligting. Hierdie inligting is vertroulik, met die fokus op wat gerapporteer is en nie wie die inligting gerapporteer het nie. Hierdie inligting sal ook bespreek word met Dr Odell se toesighouer en die wat help met die analise. Die finale uitslae sal aangebied word as deel van die Meesters in Filosofie tesis aan die Universiteit van Kaapstad, tydens die laaste kwartaal van 2017. Verdere deel van inligting word beplan met die Departement van Gesondheid, die Wes-Kaapse regering, die stad, Kaapstad en ander belangstellende partye of moontlike skenkers. Uitslae sal ook beskikbaar wees by die plaaslike kliniek vir enige DR-TB pasiënte in die gemeenskap, of hul deelgeneem het of nie.

Wat sal dit vir u beteken?
Die vraelys sal ongeveer 20-30 minute van u tyd in beslag neem en daar is geen vergoeding nie.

Wat gebeur indien die vrae te ontstellend is?
U mag die onderhoud enige tyd staak en van besluit verander om voort te gaan. U deelname is vrywillig en daar sal nie teen u gediskrimineer word, indien U dit te ontstellend vind om voort te gaan nie. Die onderhoudvoerder mag voorstel om u na die kliniek te verwys vir verdere hulp of ondersteuning.

Wat beteken "ingeligte toestemming"?
Voordat u toestemming gee om ingesluit te word in hierdie studie, is dit baie belangrik om bewus te wees oor wat dit beteken. Die doel van die toestemmingsvorm is om aan u verdere inligting te gee oor die studie, sodat u verstaan wat van U gevra sal word en om seker te maak dat u, u eie besluit kan maak, gebasseer op korrekte, earlike inligting, sonder om verplig te voel om dit te doen.

Indien u enige verdere navrae oor hierdie navorsingsstudie het, kontak asb:
Dr Shannon Odell
084 556 2778
shannonodell@yahoo.com

Indien u enige navrae oor u regte en welvaart het, terwyl u deelneem aan hierdie navorsing, kontak asb:
Die UK Navorsings – Etiese – Komitee
Mev Lamees Emjedi
Navorsing(s) Etiese Komitee Administratiewe Toesighoer
E52 Kamer 24, Ou Hoofgebou, Groote Schuur Hospitaal, Observatory
021 406 6338

Bêre asb hierdie inligtingsbladsy op 'n veilige plek, indien u later daarna wil terugverwys.

APPENDIX 10

Information sheet for trial participants (isiXhosa translation)

I phepha lolwazi ngom thathi nxaxeba kolu phandulwazi

U phando ngokufuna u kwazi nge zidingo zesigulane e sine Drug Resistant Southern sub-district of Cape Town

Enkosi ngoku cinga uku thatha inxaxheba kolu phandolwazi. Eli phepha lolwazi lizakunika incazelo malunga nga le mibuzo ozo kuyi buzwa, nceda uyifunde nge ndlela e cacileyo, Le mibuzo ikho nge lwimi lwe si Ngisi,Afrikaans nange si Xhosa, cela umbuzi mibuzo akafundela xa ufuna. Khululeka umbuze umbuzi mibuzo nawuphi na umbuza xa kukho into ongayi qondiyo.ungazivi unyanzelekile uku phendula, Qala ngo ku fundisisa lemibuzo kugala. Kwaye u thathe ixesha lakho, ukhe u thethathethane nomhlobo okanye umdeni wakho malunga nalemibuzo. **Oludliwano ndlebe lunge nzeka ngelinye ixesha, I xesha ela nelisa wena. Yazi ukuba awu nyanzeliswa ukuba u thathe ingxagxe ba kolu phando lwazi, isi qhibo so. Ukuba uqhibe ekubeni unga thathi inxaxheba, yazi ukuba u longiwo lwakho aluzuku phazamiseka, luzaku qhubeka njenge siqhelo. Eli lithuba lokuba uphendule ngokunyanisekileyo, kubalulekile ukuba wazi ukuba xa uziva ungathandi ukuvakalisa izimvo zakho, oko akunakuchaphazeleka ubudlelwane bakho nobethu.**

Ngu bani lo wenza o lu phandulwazi?
U qhira Shannon Odell,No mncedisi wakho/izakube ingabo aba qhuba olu thetho thethwano malunga no lu phando lwazi.U mncedisi izakuba ngumtu osele umqhelile,obesebenzisana nawe encedisana nawe esigulweni sakho. U budlelwana benu abusoze butshintshe ngexa yakuba uthathe inxaxheba okanye ugqibe ekubeni ungayi thathi inxaxheba.

Lwe nzelwa ntoni olu phandu lwazi?
Lincedisa eku caciseni ezinye zemphawu zesisi gulo no kwazi ibanga le mpilo elinga philwa ngum guli.

Kutheni lubalulekile alu phando lwazi?
Olu phandolwazi lubaluleke ngoba luncinci ulwazi olwaziwayo malunga nesisi gulo I DR-TB kule ndawo esikuyo apha e Kapa. Ku balulekile ukwazi ukuba zinga phina izigulani ezikhathazwe zimphawu ezifanayo zesisi gulo,kwaye zilwenza lube njani uzinga lwabo lo kuphila ne sisi gulo. Olulwazi lubalulekile xana umzi wezempilo ehlela indlela yoku jonga izigulane Ze DR-TB.

lo luphi o lu lwazi lufunwayo?
Kolu dliwano ndlebe u zaku buzwa malunga nobunjani be mpilo oyiphilayo nesisi gulo, si kuphatha njani emzimbheni,emoyeni, ubudlelwane bakho nabanye abantu bu caphazelekenjani, nase malini kwakunye nemphawu ezikuphathayo zesisi gulo.

Yintoni ezakwenzeka kwizi phumo zoludliwano ndlebe?
Zonke iziphumo ziza ku gcinwa, kwindawo ekhuselekileyo. I gama lakho liza kuhlala liyi mfihlo, ne mphendulo zakho ziza ku khuselwa. Lento ke I thatha ukuthi, imphendulo zakho azisoze zaziwe ukuba zezakho, ukunyaniseka kwakho ekuphenduleni lemibuzo akusoze ku phazamise indlela ohoyeke ngayo. E pheleleyo incukaca izakunikwa, iDepartment of Health. Sibabonise ukuba bazazi ifuno zazi gulane, banduleke ukuncedisa ngoncedo oluzakunceda izigulane.

Lu za Ku thatha I xesha elingakanani olu lwazilugciniwe?
Imphedulo zakho zoludliwanondlebe zizakugcinwa kuze kufumaneke zonke imphedulo. Xa sezi ncwangci siwe zonke, ulwazi ne ngcazelo ifumanekile, imphendulo zakho ziza ku cinwa ke.

Ziza ku boniswa bani ezizi phumo?
Nge li xesha zi qhokelelwa zonke ezi ncukanca, Dr Odell kwa kunye nomncedisi wakhe bazaku lencukaca izaphindwa I bonwe ngum phathi ka Dr Odell, xa e ncedisa ekuhloleni yonke incukaca ethe yafumaneka. E pheleleyo incukaca izakunikwa, I University of Cape Town, phakathi kulo nyaka uzayo 2017. Banalo igunya loku bona iziphumo zolu phandulwazi, I ziphumo zolu phandulwazi zi za

kuumaneka kwi clinic Ye DR-TB nabantu aba gula yi MDR-TB baza kwazi ukuzi bona iziphumo xabezi funa.

Zakunceda ngantoni wena yonke lento
Oludliwano ndlebe luzaku thatha imizuzu e yi 20-30minute.Awuzuku bhatalwa ngoku_thatha kwakho inxagxeba.

Wenza njani xa lemibuzo I khathaza umthathi ngxaxeba?
Lumise u dliwano ndlebe,ungamphathisi tyala umthathi ngxaxheba. U vumelekile,u kungaqhubekeki umthathi nxaxheba xa engasa ziva mnandi e moyeni.

Yintoni isazi mvumelwano?
Phambi kokuba u vume u ku thatha ingxagxeba ko lu phando lwazi. Injongo yolutyikityo sivumelwano kukunika olunye ulwazi ngolu phando,nokukhusela. Iimfihlo zakho kunye namandla akho okuzigqibela, Nokugcina uxanduva kulo ophandayo. Lento ke yenza ukuba lo ophandayo enze ngoku the gca nangokunyaniseka, nokuthi nabo abathatha inxaxheba kolu phando babopheleleke ekuthetheni inyaniso kangangoko banako.

Ukuba unayo eminye imibuzo malunga nolu phado lwazi ,nceda u thethe no
Dr Shannon Odell
084 556 2778
shannonodell@yahoo.com

Ukuba ufuna ulwazi ngelungelo lwakho nangoku khuseleka kwakho njengomthathi ngxaxheba ko lu phandu lwazi, nceda u thethe ne : contact the UCT Research Ethics Committee
Mrs Lamees Emjedi
Research Ethics Committee Administration Supervisor
E52 Room 24, Old Main Building, Groote Schuur Hospital, Observatory
021 406 6338

Nceda u ligcine kwindawo ekhuselekileyo e li phepha le ngcaciso, ukuze uzokwazi ukulifumana mhla uli funa.

APPENDIX 11

Informed consent document- English (to be kept by researcher):

A study to determine the Palliative Care Needs of Patients with Drug Resistant Tuberculosis in the Southern sub-district of Cape Town

Ask potential participant to recall the: day of the week: ☐ month: ☐ year: ☐ suburb: ☐ country: ☐

Questions asked by the potential participant regarding the research study and participation:

_____

_____

_____

Researcher's affidavit:

The participant has been provided with the information sheet regarding this research study and has been given the opportunity to ask questions to clarify any issues or concerns about the study. The participant seems to understand what their involvement will involve. To the best of my knowledge, the participant has not been hindered by a communication barrier in their understanding and consenting to their involvement in this questionnaire, and has been assessed as being competent to give informed consent and continue.

Researcher's name: _____

Researcher's signature: _____

Date: _____

Participant's consent:

By signing this consent form, I have understood what this research will involve, the time it will take and that my answers will not affect my relationship with the counselor/ volunteer or affect my current or future care and management. I have been given the opportunity to ask questions where I might have been unclear on an issue. I realize that I am allowed to stop the questionnaire at any time if it becomes too upsetting for me.

I would like to continue with the questionnaire and give my permission voluntarily to take part.

Participant's name: _____

Participant's signature: _____

Date: _____

Witness's name: _____

Witness's signature: _____

Date: _____

APPENDIX 12

Ingeligte toestemmingsdokument – Afrikaans (moet deur navorser bewaar word)

'n Studie om die Palliatiewe Versorgingsbehoeftes van Pasiënte met DR-TB in die Suidelike sub-distrik van Kaapstad te bepaal.

Ask potential participant to recall the: dag van die week: ☐ maand: ☐ jaar: ☐ woongebied: ☐ land: ☐

Vrae met betrekking tot die inligtingsbladsy en opname:

_____

_____

_____

Navorser se verklaring:

Die deelnemer is voorsien van die inligtingsbladsy met betrekking tot die navorsingsstudie en is die geleentheid gegun om vrae te vra oor enige sake of voorbehoude oor die studie. Dit lyk of die deelnemer verstaan wat hul betrokkenheid sal behels. Na die beste van my wete, is die deelnemer nie verhinder deur gebrekkige kommunikasie om te verstaan wat die gee van sy/haar toestemming in die aflê van die vraelys behels nie en is gevind om in staat te wees om ingeligte toestemmimg te gee en voort te gaan met die studie.

Navorse se naam: _____

Navorser se handtekening: _____

Datum: _____

Deelnemer se toestemming:

Deur die teken van hierdie toestemmingsbrief/vorm, verstaan ek wat hierdie navorsing behels, die tyd wat dit in beslag sal neem en dat my antwoorde nie my verhouding met die berader/vrywilliges of my huidige of toekomstige versorging en behandeling sal beïnvloed nie. Ek is die geleentheid gegee om vrae te vra, waar ek onseker was oor 'n saak. Ek besef dat ek die vraelys enige tyd mag staak, indien dit my te erg ontstel. Ek wil graag voortgaan met die vraelys en gee vrywilliglik my toestemming om deel te neem.

Deelnemer se naam: _____

Deelnemer se handtekening: _____

Datum: _____

Getuie se naam: _____

Getuie se handtekening: _____

Datum: _____

APPENDIX 13

Informed consent document (to be kept by researcher)- isiXhosa translation

Esisazi sivumelwano sigcinwe ngum phandi lwazi .

U phando ngokufuna u kwazi nge zidingo zesigulane e sine Drug Resistant Southern sub-district of Cape Town

Uyakwazi ukukhumbhula :I nstuku ze veki: ☐ Inyanga: ☐ U nyaka: ☐ I lokisi yakho: ☐ I lizwe lwakho: ☐

Imibuzo mayelana ne phepha lo lwazi nge sazi si vumelwano:

_____

_____

_____

I sithembhiso somphandulwazi:

Umthathi nxaxheba ulinikiwe I phaphe elimnika ulwazi nengcazelo malunga nolu phando lwazi, kweye ulinikiwe nethuba loku buza yonke imi buzo Anayo, kwakunye nezinto angazivamcam ngolu phando. Umthathi nxaxheba ujongeka ecacelwe yindima azakuyidlala Malunga nolu phandolwazi. Ngoku qonda kwam. Umthathi nxaxheba uye wacaciselwa ngolwimi lwakhe lwenkobe Malunga nendima yakhe azakuyidlala kolu phando lwazi, kwaye uhloleke ekwi simo esifanelekileyo ukuba angakwazi ukuphedua lemi buzo.

Igama lomphandi lwazi _____

utyikityo yom phandi lwazi _____

Umhla: _____

I sazi sivumelwano nomthathi ngxaxheba:

Ngoku vuma uku thatha ingxaxheba ko lu phando lwazi, lonto I thetha ukuba wazi ngcono nge xesha elizo ku funeka ukuze imibuzo iphenduleke yonke, kwaye u cacelwa ukuba ekuthatheni kwakho inxaxheba kulu phando lwazi, lonto ayi zo ku phazamise uncedo lwakho e clinic.ucacelwa ukuba ungali misa nangeliphi na ixesha oludliwano ndlebe xana ungaziva mnandi .

I gama lomthathi nxaxheba: _____

utyikityo yomthathi nxaxheba: _____

Umhla: _____

Igama le igqina: _____

Utyikityo le ingqina: _____

Umhla: _____

APPENDIX 14

Referral Note to Healthcare facility if Distress protocol required

Date: _____

Dear _____

at _____ facility.

Many thanks for seeing _____

who, whilst participating in a research study: **"A study to determine the Palliative Care Needs of Patients with Drug Resistant Tuberculosis in the Southern sub-district of Cape Town" (HREC number 416/2016)** has required referral due to:

_____

_____

_____

It would be greatly appreciated if you could address this issue and provide further management.

Kind Regards

_____(signature)_____(Name)

_____(Contact details)_____(Designation)

Should you require further information pertaining to this study, please contact: Dr Shannon Odell, shannonodell@yahoo.com, 0845562778

APPENDIX 15

HPCA Research Ethics Committee approval letter

HPCA care & support
Hospice Palliative Care Association of South Africa

2nd Floor,
DMB Building
Golf Park
Raapenberg Road, Mowbray.
Tel: 021 531 0277
Fax: 021 531 1706
Email: info@hpca.co.za
www.hpca.co.za

15th December 2016

Dr Shannon Odell
shannonodell@yahoo.com

c.c. Dr Rene Krause
Faculty of Health Sciences, UCT
rene.krause@uct.ac.za

Dear Dr Odell

PROTOCOL 04/16 : A Study to Determine the Palliative Care Needs of Patients with Multi-Drug Resistant Tuberculosis in the Southern Sub-District of Cape Town." S Odell, Living Hope Hospice, Fish Hoek.

The above protocol was reviewed by the HPCA Research Ethics Committee at its meeting held on 29 November 2016. Queries raised on the protocol have been appropriately addressed and the protocol is given full ethics approval.

Please note the following :

- An original signed copy of the amended protocol and supporting documentation (as approved) must be submitted to the HPCA offices in Cape Town;
- Ethics approval is valid for one year only;
- Application for recertification of the protocol should be submitted a couple of months prior to the 29th November 2017 to ensure continuous approval;
- ANY changes to an approved protocol must be reviewed by the Research Ethics Committee.

It would also be appreciated if, once the study has been completed, the End of Study Report be completed and submitted to the Research Ethics Committee together with a summary of the results for inclusion on the HPCA web-site.

I would like to take this opportunity to wish you well with your research.

Yours sincerely

PROFESSOR A DHAI
Chair : Hospice Palliative Care Research Ethics Committee
Reg. No. : REC-250408-005

APPENDIX 16

Western Cape Department of Health research request approval letter

Western Cape Government
Health

STRATEGY & HEALTH SUPPORT
Health.Research@westerncape.gov.za
tel: +27 21 483 6857: fax: +27 21 483 9895
5th Floor, Norton Rose House,, 8 Riebeek Street, Cape Town, 8001
www.capegateway.gov.za)

REFERENCE: WC_2016RP2_500
ENQUIRIES: Ms Charlene Roderick

University of Cape Town

Anzio Road

Observatory

Cape Town

7925

For attention: Dr Shannon Odell

Re: A study to determine the Palliative care needs of patients with Multi-drug resistant Tuberculosis in the southern sub-district of Cape Town.

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research.

Please contact following people to assist you with any further enquiries in accessing the following sites:

Hout Bay Harboour CDC	**Toni Ahjam**	**021 790 1050**
Lotus River CDC	**Gaironessa Jones**	**021 703 3131**
Retreat CHC	**Henry Lemmetjies**	**021 713 9741**

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.

2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final feedback (**annexure 9**) within six months of completion of research. This can be submitted to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).

3. In the event where the research project goes beyond the *estimated completion* date which was submitted, researchers are expected to complete and submit a progress report (**Annexure 8**) to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).

4. The reference number above should be quoted in all future correspondence.

Yours sincerely

DR A HAWKRIDGE

DIRECTOR: HEALTH IMPACT ASSESSMENT

DATE: 16/11/2016.

CC: **K GRAMMER** **DIRECTOR: SOUTHERN/ WESTERN**

APPENDIX 17

City of Cape Town Health Department research request approval letter

CITY OF CAPE TOWN
ISIXEKO SASEKAPA
STAD KAAPSTAD

CITY HEALTH

Dr Hélène Visser
Manager: Specialised Health

T: 021 400 3981 **F:** 021 421 4894 **M:** 083 298 8718
E: Helene.Visser@capetown.gov.za

2016-11-08

Re: Research Request: A study to determine the Palliative care needs of patients with Multi-Drug Resistant Tuberculosis in the Southern sub-district of Cape Town (7743)

Dear Dr Odell,

Your research request has been approved, but space cannot be guaranteed. Please liaise with the Sub District office regarding access to list of DR TB clients. Clients must give permission for researcher to do a home visit **before** a home visit is conducted.

Southern Sub District:
Contact People

Dr M Osman (Sub District Manager)
Tel: (021) 444-3258/ 083 556 9838
Mrs K Shuping (Head: PHC & Programmes)
Tel: (021) 444-3260 / 082 728 4531

Please note the following:

1. All individual patient information obtained must be kept confidential.
2. Access to the clinics and its patients must be arranged with the relevant Managers such that normal activities are not disrupted.
3. A copy of the final report must be sent to the City Health Head Office, P O Box 2815 Cape Town 8001, within 6 months of its completion and feedback must also be given to the clinics involved.
4. Your project has been given an ID Number (7743) Please use this in any future correspondence with us.

Thank you for your co-operation and please contact me if you require any further information or assistance.

Yours sincerely

DR G H VISSER
MANAGER: SPECIALISED HEALTH

cc. Dr Osman & Mrs K Shuping
Dr Jennings
Ms Caldwell

APPENDIX 18

UCT HREC Approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.arendien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

12 October 2016

HREC REF: 416/2016

Dr R Krause
Division of Palliative Medicine
School of Public Health & Family Medicine
Entrance 5, Level 2
Falmouth Building -FHS

Dear Dr Krause

PROJECT TITLE: A STUDY TO DETERMINE THE PALLIATIVE CARE NEEDS OF PATIENTS WITH MULTI-DRUG RESISTANT TUBERCULOSIS IN THE SOUTHERN SUB-DISTRICT OF CAPE TOWN (MPhil candidate-Dr S Odeli)

Thank you for your response letter dated 13 September 2016, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 October 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

We acknowledge that the student; Dr S Odeli will also be involved in this study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC 416/2016

APPENDIX 19

UCT Research Ethics Committee Final Approval Letter

HUMAN RESEARCH ETHICS COMMITTEE
-6 MAR 2017
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS006: Protocol Amendment

HREC office use only (FWA00001637; IRB00001938)		
☒ Approved	☐ Type of review: Expedited	☐ Full committee
This serves as notification that all changes and documentation described below are approved.		
Signature Chairperson of the HREC		Date 8/3/2017

Note: All major amendments must include a local **PI Synopsis** justifying the changes for the amendment. Please note that incomplete amendment submissions will not be reviewed.

Comments from the HREC to the Principal Investigator:
Note: The approval of this protocol amendment does not grant annual approval. Please complete the FHS016 / FHS017 form for annual approval at least one month before study expiration.

Principal Investigator to complete the following:

1. Protocol Information

Date (when submitting this form)	27.02.2017
HREC REF Number	416/2016
Protocol title	A study to determine the palliative care needs of patients with drug-resistant tuberculosis in the southern sub-district of Cape Town
Protocol number (if applicable)	N/A
Principal Investigator	Dr Rene Krause
Department / Office Internal Mail Address	**Division of Palliative Medicine** **School of Public Health and Family Medicine** **Entrance 5, Level 2** Falmouth Building

1.1 Is this a major or a minor amendment? (see FHS008hlp) Major (tick box) Minor (tick box)	☒ Major	☐ Minor
1.2 Does this protocol receive US Federal funding?	☐ Yes	x☐ No
1.3 If the amendment is a major amendment and receives US Federal Funding, does the amendment require full committee approval?	☐ Yes	X☐ No

APPENDIX 20

Distress Protocol

If, whilst administering the questionnaire, the trial participant displays or expresses severe physical, emotional or existential distress then he/she will be offered the opportunity to halt the questioning and the distress protocol will be implemented:

i. Try to ascertain the reason for the distress and remain calm
ii. Acknowledge how the line of questioning might be distressing
iii. Give the trial participant the opportunity to stop the interview temporarily or withdraw from the study entirely
iv. Reaffirm that withdrawing will not jeopardize further management or care
v. Recommend referral be made to appropriate health care professional at the nearest clinic for management of specific distress.
vi. If patient consents to referral, make the necessary arrangements
vii. If the trial participant wishes to continue the questioning when more comfortable, proceed
viii. Offer further counseling
ix. Apologize for this line of questioning causing distress
x. Thank the trial participant for their time
xi. Contact clinic at a later stage to ensure patient is receiving the necessary management

Similarly, should the interviewer feel that his/her physical safety be in jeopardy or that infection control be insufficient, then the questionnaire is to be stopped, and the following procedure followed:

i. Apologize for having to stop the research questioning
ii. Explain your concern for safety or infection control
iii. Enquire whether another time or place could be arranged to continue completing the questionnaire
iv. If yes, then reschedule an interview at a more appropriate location or time, without the validity of the answers being affected. Ensure that adequate corrective measures are instituted.
v. If no, thank them for their time and **reassure them that there would not be any negative consequences to their future and ongoing management**

In either situation, ensure that it is documented on the questionnaire, by marking the relevant check box that the distress protocol was required.

APPENDIX 21

Indications for DR-TB Treatment Withdrawal

According to the Department of Health Policy Guidelines on the Management of Drug-Resistant Tuberculosis(19):

Treatment withdrawal is considered when:

- No further drugs or surgery are available
- The patient no longer consents to treatment
- Where treatment has a negligible chance of success and is considered futile eg chronic defaulters or causing additional suffering eg in advanced terminal disease. In these instances continuing treatment might result in amplification of resistance.

APPENDIX 22

Anti-tuberculosis Drug abbreviations

(Am): Amikacin

(Amx/Clv): Amoxicillin/clavulanate

(Azr): Azithromycin

(Cm): Capreomycin

(Clr): Clarithromycin

(Cfz): Clofazimine

(Cs): Cycloserine

(E): Ethambutol

(Eto): Ethionamide

(Gfx): Gatifloxacin

(Im): Imipenem

(H)/(INH): Isoniazid

(Km): Kanamycin

(Lvx): Levofloxacin

(Lzd): Linezolid

(Mfx): Moxifloxacin

(Ofx): Ofloxacin

(PAS): Para-Aminosalicyclic acid

(Pto): Prothionamide

(Z): Pyrazinamide

(R): Rifampicin

(S): Streptomycin

(Trd): Terizidone

(Th): Thioacetazone

(Vm): Viomycin