

# **An Investigation into the lung function, health-related quality-of-life and functional capacity of a cured Pulmonary Tuberculosis population in the Breede Valley, South Africa: a pilot study**

by

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## Declaration

I, the undersigned, hereby declare that the entirety of the work contained herein is my own original work, that I am the authorship owner thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification at any university.

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## Abstract

### Background:

Pulmonary tuberculosis (PTB) remains a major concern worldwide. Although PTB is curable, both the disease and its treatment may have considerable medical, social and psychological consequences which may result in a decreased quality of life and functioning. Characterization of the functional capabilities of PTB patients post-treatment and the impact of PTB on their quality of life may identify a need for more holistic management of PTB treatment that extends beyond microbiological cure.

### Methods:

Firstly, an in-depth scoping review was conducted using the following key words: *Pulmonary tuberculosis (MESH term) and Health related quality of life (HRQoL)*, *Pulmonary tuberculosis (MESH term) and Spirometry and Pulmonary tuberculosis (MESH term) and Six minute walk test or 6MWT* to review the current literature reporting on the HRQoL, lung function measurements and exercise capacity of a PTB population (Chapter 2).

Secondly, a cross-sectional, quantitative, descriptive study was conducted. The study setting included five primary health care facilities (PHCF) in the Breede Valley sub-district of the Cape Winelands East District, Western Cape, South Africa. Adult patients diagnosed with PTB, 18 years and older and who were successfully managed through the Cape Winelands District Health Care system were considered for the study if they had least two negative sputum sample results and had completed at least five months of anti-tuberculosis treatment. Post treatment bronchodilator lung function tests, health related quality of life using the BOLD core questionnaire and six minute walk test distance (6MWD) was measured.

### Findings:

The comprehensive broad search of the literature yielded a total of 2446 articles. A total of 2422 articles were excluded since the title; abstract or full text article did not conform to the review question or were eliminated as duplicates across databases. Twenty-seven articles divided amongst the three subsections i.e. PTB and HRQoL (n=13), PTB and Spirometry (n=9) and PTB and exercise capacity (n=6), were included in the review.

In the cross-sectional study, 328 names were obtained from the TB registers of the five included PHCF of which 45 patients were included in the study (56% male; mean age,  $39.88 \pm 10.20$  years). The majority of patients (n= 206; 63%) were not contactable, and could not be recruited. Approximately half the total sample, (n=23; 52%) presented with normal lung function while n=11 (25%) presented with a restrictive pattern, n=9 (21%) presented with an obstructive pattern and only n=1 (2%) presented with a mixed pattern (defined as  $FEV_1 < 80\%$  predicted,  $FVC < 80\%$  predicted and  $FEV_1/FVC < 0.7$ ). The mean six minute walk distance (6MWD) was  $294.5m \pm 122.7m$ . Respondents scored poorly on all sub-domains of the SF-12v2 except vitality. Role emotional and role physical scored lowest with mean scores of 28.1 and 35.27 respectively, while vitality scored the highest with 52.78.

## **Conclusion**

The findings of this thesis suggest that even after microbiological cure, PTB patients may suffer from a decreased quality of life, impaired lung function and a decreased exercise capacity. Specific challenges to data collection in a rural region were identified; which included patient recruitment, field testing of exercise capacity (6MWD), and the generalizability of standardized questionnaires in rural regions. The findings of this pilot study serves to inform the planning of a larger observational study, in the rural Cape Winelands of the Western Cape, South Africa.

## Opsomming

### Agtergrond

Pulmonêre tuberkulose (PTB) wek wêreldwyd steeds groot kommer. Hoewel dit geneeslik is, kan die siekte sowel as die behandeling daarvan beduidende mediese, maatskaplike en sielkundige gevolge hê, wat lewensgehalte en funksionering kan knou. Die tipering van PTB-pasiënte se funksionele vermoëns ná behandeling sowel as die impak van PTB op hul lewensgehalte kan dalk dui op 'n behoefte aan die meer holistiese bestuur van PTB-behandeling, wat méér as blote mikrobiologiese genesing insluit.

### Metodes

Eerstens is 'n diepgaande bestekstudie aan die hand van die volgende trefwoorde onderneem: pulmonêre tuberkulose (MeSH-term) en gesondheidsverwante lewensgehalte (HRQoL), pulmonêre tuberkulose (MeSH-term) en spirometrie, en pulmonêre tuberkulose (MeSH-term) en die ses minute lange stapafstandtoets (6MWT). Na aanleiding daarvan is die huidige literatuur oor die HRQoL, longfunksiemetings en oefenvermoë van 'n PTB-populasie bestudeer (hoofstuk 2).

Tweedens is 'n kwantitatiewe, beskrywende deursneestudie onderneem. Die studie-omgewing het bestaan uit vyf fasiliteite vir primêre gesondheidsorg in die Breedevallei-subdistrik van die streek Kaapse Wynland-Oos, Wes-Kaap, Suid-Afrika. Volwasse pasiënte van 18 jaar en ouer wat met PTB gediagnoseer is en suksesvol deur die distriksgesondheidsorgstelsel van die Kaapse Wynland-streek bestuur word, is vir die studie oorweeg indien minstens twee van die pasiënt se sputummonsters TB-negatiewe resultate opgelewer het en die persoon reeds minstens vyf maande vir tuberkulose behandel is. Studiemetings het ingesluit brongodilator-longfunksietoetse ná behandeling, gesondheidsverwante beoordelings van lewensgehalte met behulp van die BOLD-vraelys, en die aflegging van 'n ses minute lange stapafstandtoets (6MWT).

### Bevindinge

Die omvattende breë soektog van die literatuur het 'n totaal van 2446 artikels opgelewer. 'n Totaal van 2422 artikels is uitgesluit, aangesien die titel; abstrakte of volledige teks artikel het nie voldoen aan die navorsings vraag, of is uitgeskakel as duplikate oor databasisse. Sewe en twintig artikels verdeel tussen die drie onderafdelings, naamlik PTB en HRQoL (n = 13), PTB en Spirometrie (n = 9) en PTB en oefening kapasiteit (n = 6), is ingesluit in die oorsig.

In die deursneestudie is 328 name uit die TB-registers van die vyf ondersoekpersele bekom. Altesaam 45 pasiënte (56% mans; gemiddelde ouderdom  $39.88 \pm 10.20$  jaar) is by die studie ingesluit. Die oorgrote meerderheid pasiënte (n = 206; 63%) kon nie bereik word nie, en dus ook nie gewerf word nie. Ongeveer die helfte van die algehele steekproef (n = 23; 52%) se longfunksie was normaal; n = 11 (25%) het 'n restriktiewe patroon getoon; n = 9 (21%) 'n obstruktiwe patroon, en slegs n = 1 (2%) 'n gemengde patroon (wat omskryf word as 'n FEV<sub>1</sub>-voorspellingswaarde van <80%, 'n FVC-voorspellingswaarde van <80%, en FEV<sub>1</sub>/FVC van <0.7). Die gemiddelde afstand wat in die ses minute lange staptoets afgelê is (6MWD), was  $294,5 \text{ m} \pm 122,7 \text{ m}$ . Respondente behaal swak

op al die sub-domein van die SF-12v2 behalwe vitaliteit. Rol emosionele en rol fisiese behaal laagste met die gemiddelde tellings van 28.1 en 35,27 onderskeidelik, terwyl vitaliteit behaal die hoogste met 52,78.

### **Gevolgtrekking**

Die bevindinge van hierdie tesis gee te kenne dat PTB-pasiënte selfs ná mikrobiologiese genesing dalk swakker lewensgehalte, verswakte longfunksie en 'n afname in oefenvermoë ondervind. Bepaalde uitdagings vir data-insameling in 'n landelike omgewing is uitgewys, onder meer pasiëntewerwing, veldtoetsing van oefenvermoë (6MWD) en die veralgemeenbaarheid van gestandaardiseerde vraelyste in landelike gebiede. Die bevindinge van hierdie proefstudie kan gebruik word om die beplanning van 'n groter waarnemingstudie in die landelike Kaapse Wynland-streek in die Wes-Kaap, Suid-Afrika, te rig.

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**Dedications:**

This Thesis is dedicated to my *mom, dad, brother, sister and sister-in-law*

Thank you for believing in me and supporting me amidst many a trying time

To my friends that stood by me through the good times and the bad

And finally

To a friend who was like a brother who will always be immortalized in my heart.

In loving memory of *Lester Williams 1976 - 2010*



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## Glossary of Terms

### List of Abbreviations

6MWT / 6MWD – Six Minute Walk Test / Distance

COPD – Chronic Obstructive Pulmonary Disease

DOTs – Directly Observed Shortcourse Therapy

FEV<sub>1</sub> – Forced Expiratory Volume in 1 second

FVC – Forced Vital Capacity

GOLD – Global Initiative for Chronic Obstructive Lung Disease

HRQoL – Health Related Quality of Life

MCS – Mental Component Score

MMP – Matrix Metalloproteinase

PCS – Physical Component Score

PTB – Pulmonary Tuberculosis

QOL – Quality of Life

SF-12 – Short Form 12

### Categorization and Definitions

#### GOLD categorization of obstruction

GOLD I(MILD)	FEV <sub>1</sub> /FVC < 0.70	FEV <sub>1</sub> ≥ 80% predicted
GOLD II(Moderate)	FEV <sub>1</sub> /FVC < 0.70	50% ≤ FEV <sub>1</sub> < 80% predicted
GOLD III(Severe)	FEV <sub>1</sub> /FVC < 0.70	30% ≤ FEV <sub>1</sub> < 50% predicted
GOLD IV(Very severe)	FEV <sub>1</sub> /FVC < 0.70	FEV <sub>1</sub> < 30% predicted or FEV <sub>1</sub> < 50% predicted plus chronic respiratory failure

#### Treatment outcomes as defined by the World Health Organisation

**Cure** – a patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear- or culture-negative in the last month of treatment and on at least one previous occasion

[http://www.who.int/tb/publications/tb\\_treatmentguidelines/en/index.html](http://www.who.int/tb/publications/tb_treatmentguidelines/en/index.html)

## Chapter 1: Introduction

The following thesis reports on the lung function, HRQoL and exercise capacity of a microbiologically cured PTB population in a rural setting in the Western Cape, South Africa. This thesis is intended to serve as a baseline to inform the planning of a larger study in the same region. The thesis is presented in four chapters. The final chapter contains appendices which are intended to support or provide more detail to the thesis.

## Background

Global efforts in the fight against PTB have yielded positive results. Since 2003 the worldwide incidence per capita has been falling with treatment success rates slowly rising<sup>1</sup>. South Africa is flagged as one of the 22 high burden countries, contributing approximately 8% of the total global burden of all TB cases<sup>2</sup>. South Africa has the seventh highest TB incidence in the world<sup>2</sup>. In accordance to world trends, South Africa's cure rates and treatment success rates have increased from 66% in 2000 to 70% in 2007<sup>2</sup>. This figure, however, is well below the stipulated figure set by the World Health Organisation (WHO) of 85%.

PTB has long been associated with chronic respiratory symptoms, dating back to 1846 when Hutchinson first tested the vital capacity of TB patients<sup>3</sup>. The idea received very little research attention possibly due to the success of treatment in the 1960's onwards in developed countries<sup>4</sup>. Increased efforts to measure the global burden of diseases and its impact on quality of life (QOL), has resurrected the interest in PTB and its sequelae<sup>4</sup>. Increased attention to chronic obstructive pulmonary disease (COPD) in both rich and poor countries could also be a major contributor to the spark of interest in PTB. A study by Snider et al.(1971) identified that heavy smoking and more severe TB independently increased the presence of airflow obstruction by approximately twofold, while the effect was additive but not synergistic in the presence of the two factors<sup>1,5</sup>. Thus, the focus of more recent studies has shifted more towards the non-tobacco related causes, of which PTB is now recognized as an important contributor to chronic airflow limitations in countries with high TB prevalence<sup>4</sup>.

PTB and COPD share similar pathophysiological characteristics. The subsequent development and progression of disease, seen in both PTB and COPD, result in characteristic destructive parenchymal changes to lung tissue<sup>6</sup>. Destruction of the extra-cellular matrix which comprises of collagen and elastic and is integral to the structure of the lung may be the common pathological link between the two diseases<sup>7</sup>. Normal lung function requires alveolar support by the extra-cellular matrix and in many pulmonary diseases, abnormal remodelling or destruction of the extra-cellular matrix is caused by the matrix metalloproteinase (MMP)<sup>7</sup>. MMP's are a family of zinc dependent protease enzymes capable of destroying the extra-cellular matrix<sup>6</sup>. MMP's have the ability to cause significant host damage and thus are tightly regulated. However, in diseases where there is altered or unregulated MMP activity damage to lung architecture is severe<sup>7</sup>. The antigenic wall component of mycobacterium tuberculosis stimulates the release of MMP-9 as well as up regulating genetic expression of MMP-1 and MMP-9<sup>6</sup>. Parenchymal lung damage central to the development of cavitation often complicating active PTB is the result commonly seen by clinicians<sup>6</sup>. Similarly, studies have found increased levels of MMP-8 and MMP-9 in tobacco related COPD<sup>6</sup>. It would thus be expected that



changes to the extra-cellular matrix would predominantly involve lung parenchyma rather than the airways in both PTB and COPD<sup>6</sup>.

Despite the known structural changes to lung tissue resulting in sequelae associated with PTB, no treatment programs currently exist which recognizes these physiological and clinical changes that take place in PTB. The focus of most governmental strategies to combat the PTB epidemic is on microbiologic markers and outcomes such as cure, mortality and treatment completed/failure<sup>8</sup>. The impact of COPD on patients' lung function and quality of life is well recognized by the literature, but little attention is given to the impact of PTB after microbiological cure.

Thus, the aim of this thesis is to describe the lung function, exercise capacity and HRQoL of a cured PTB population.

## Outline of Thesis

The following thesis will be presented in “**masters by publication**” format

Chapter 1 introduces the reader to the burden of disease caused by PTB, the link between PTB and chronic obstructive pulmonary disease (COPD), as well as the rationale for conducting the study.

Chapter 2 provides an in depth scoping review of the current literature pertaining to PTB and HRQoL, PTB and lung function and PTB and exercise capacity (specifically measured by the 6-minute walk test).

Chapter 3 is the main article chapter which is a cross sectional, observational study which aims to describe the lung function, exercise capacity and HRQoL of a cured PTB population in a rural setting entitled:

*An Investigation into the health related quality of life (HRQoL) and functional assessment of a cured Pulmonary Tuberculosis (PTB) population in the Breede Valley District, South Africa: a pilot study*

### Please Note:

Chapter 3 (Article) has been presented according to the requirements of the journal in which the authors are intending to publish (BMC Public Health)

The bibliography for the entire thesis is listed at the end of the thesis. Therefore, bibliographic information continues throughout the thesis. This will be amended before publication of the article (Chapter 3).

In Chapter 4, the findings of the thesis are critically reviewed and discussed. The limitations and challenges faced during the data collection phase are unpacked and further elaborated on with mention of suggestions for future research.

Lastly, Chapter 5 provides a list of appendices including data not represented in Chapter 3 as well as raw data

## **1.1 Significance of this study**

This study offered a unique opportunity to determine the burden of disease and health related quality of life (HRQOL) in a cured TB population. This study serves a base study for the further development of a multidisciplinary, strategic approach to the optimization of interventions in the rural community.

## Chapter 2: Literature Review

### 2.1 Introduction

The link between pulmonary tuberculosis (PTB) and chronic obstructive pulmonary disease (COPD) has recently re-surfaced as a point of interest amongst researchers <sup>9</sup>. Studies have shown that early and partially treated PTB can result in airflow limitation <sup>10</sup>. Studies with longer follow-up periods have shown that in many cases, patients who have completed PTB treatment, have evidence of permanent airflow obstruction or restrictive impairment <sup>10</sup>. PTB can lead to pulmonary scarring and a decline in lung function <sup>11</sup>. In the PLATINO (Proyecto Latinoamericano de Investigación Obstrucción Pulmanar)<sup>11</sup> and the PREPCOL (Prevalencia de EPOC en Columbia)<sup>11</sup> studies, which are population-based surveys to estimate the prevalence of COPD using spirometry, a report of previous PTB or previous PTB treatment was strongly associated with the development of COPD as defined by the Global initiative for Chronic Obstructive Lung Disease (GOLD) criteria <sup>11</sup>.

There are distinct differences in the epidemiology of PTB between developing countries and first world countries <sup>12</sup>. In developed countries, where strategies to control the disease has led to a decline in the incidence of PTB, the annual risk of infection is low with most new cases resulting from endogenous reactivation of remote infection acquired when the disease was more prevalent. The majority of new cases therefore occur in the elderly ( $\geq 65$  years) <sup>12</sup>. However, in countries where the standard of living is low, and health resources are scarce, the risk of new case infection is high and 80% of cases involve persons in their economically productive years (15-59 years) <sup>12</sup>.

In the Western Cape, one of nine provinces in South Africa, the incidence of TB is 909/100000 <sup>2</sup>, making it the province with the single highest incidence of TB in South Africa <sup>2</sup>. Approximately 90% of new smear positive cases falls within the economically active age group <sup>13</sup>. The emergence of multi-drug resistant strains of TB and co-infection with Human Immuno deficiency Virus (HIV) has greatly complicated the management and control of TB <sup>12</sup>. Co-infection with HIV is the strongest known risk factor for both immediate and delayed progression from infection to active TB <sup>12</sup>. The risk of progression to disease for co-infected persons is 5%-10% per year compared with a 5%-10% lifetime risk for HIV negative persons <sup>12</sup>. Fuelled by colliding disease epidemics, PTB notifications are now more prevalent between the ages of 20 and 40 years <sup>14</sup>.

South Africa is flagged as one of the 22 high burden countries, contributing approximately 8% to the total global burden of all PTB cases <sup>2</sup> and that PTB has long been associated chronic airflow limitations in countries with high tuberculosis prevalence <sup>9</sup>. However, few studies have analysed the impact of PTB on HRQoL, exercise capacity and lung function immediately after completion of PTB treatment.

Therefore, the aim of this scoping review is to search the literature for relevant studies pertaining to PTB and health-related quality-of-life (HRQoL), exercise capacity as measured by the six minute walk

test (6MWT) and lung function as measured by spirometry. This review is intended to provide an overview of the literature and possibly serve as a base to inform the planning of future studies. Following an initial scan of the literature and consultation with experts in the field, the initial broad research question was defined as follows: *How does PTB affect lung function, HRQoL and exercise capacity in a cured, post-PTB population?*

### **2.2.1 Methods of Review**

A scoping review was undertaken using the methodological framework originally outlined by Arksey and O'Malley from York University in the United Kingdom<sup>15</sup>. The “York framework” suggests five stages to performing this type of review. The five stages are: *Identification of the research question to be addressed; identification of the studies relevant to the research question; selection of studies to be included in the review; charting of the information and data within the included studies and collating, summarizing and reporting on the results of the review*. An optional sixth phase of this methodology type, *consultation with stakeholders*, was not undertaken in this review.

### **2.2.2 Search strategy**

A comprehensive search of PubMed, Cochrane Library, Cinahl, Biomed Central, Web of Science and Scopus was conducted using the following key words: *Pulmonary tuberculosis (MESH term), Health related quality of life or HRQoL, Pulmonary tuberculosis (MESH term) and Spirometry and Pulmonary tuberculosis (MESH term) and Six minute walk test or 6MWT*. Due to time limitations and a lack of resources, articles were limited to those published in English.

### **2.2.3 Article Selection**

In order to identify relevant articles, the search terms were divided into 3 sub-sections i.e. PTB and HRQoL, PTB and Spirometry and PTB and exercise capacity. Articles were screened for those specifically pertaining to PTB. Articles published in English, on an adult population (over 18 years old) diagnosed with either PTB or latent PTB and addressing either 1 or more of the above mentioned outcomes were included in the review. Cost-analysis studies, case reports and letters to the editor were amongst the articles which were excluded from this review. The principal reviewer assessed the titles and abstracts of the articles. When the titles or abstracts did not clearly indicate whether an article should be included or excluded, the full text was assessed and a second reviewer was consulted for opinion on whether the article should be included in this review.

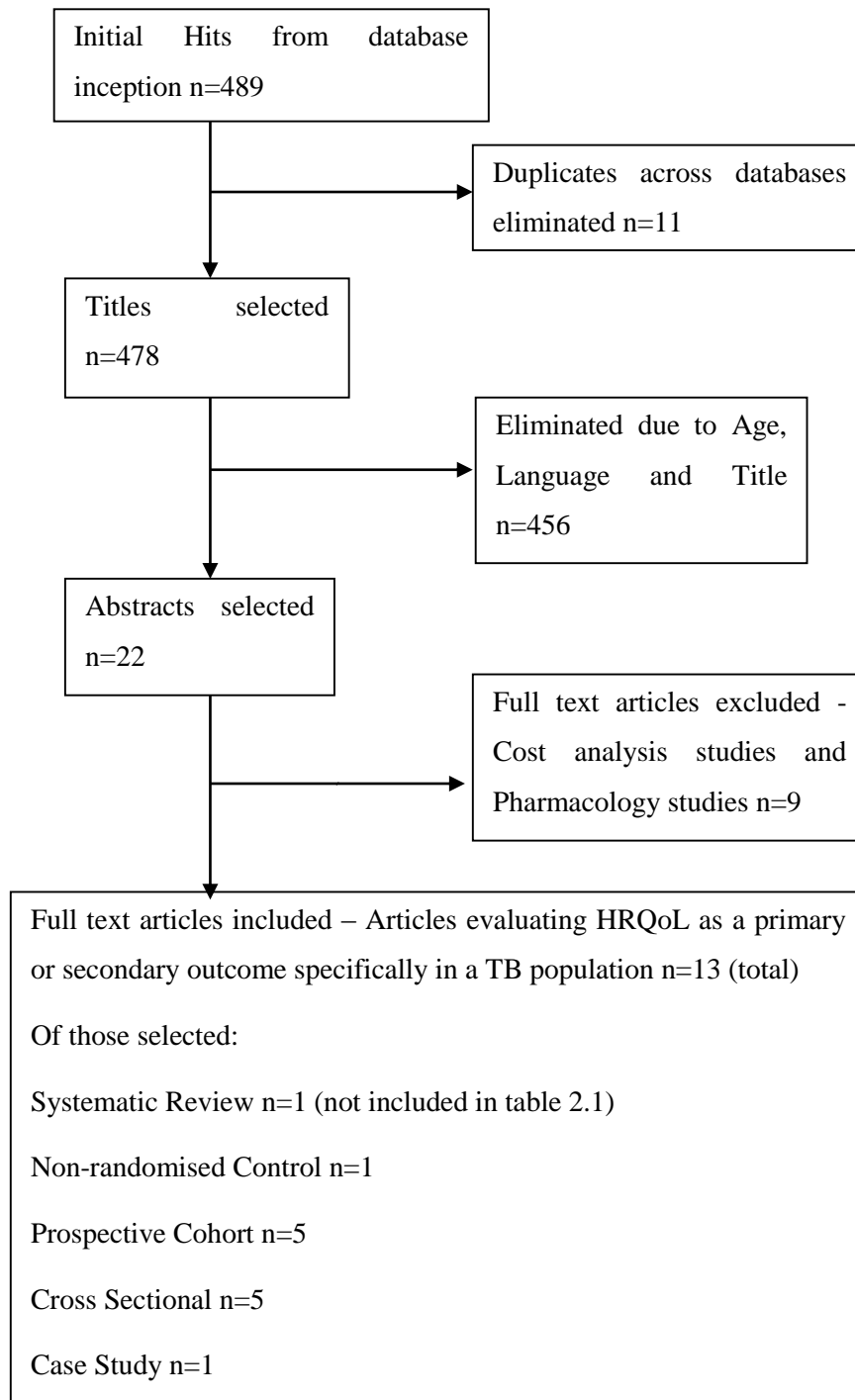
#### **2.2.4 Charting Process**

Descriptive data including general citation information, country of origin, type of study, clinical setting, primary objective, results of study and author's conclusion were extracted from the included articles and charted in a MS Excel spreadsheet to create a database. Information gathered from the articles will be discussed narratively and data are summarized in tables and figures where applicable.

#### **2.3 Results**

The comprehensive broad search yielded a total of 2446 articles. A total of 2422 articles were excluded since the title; abstract or full text article did not conform to the review question or were eliminated as duplicates across databases. Twenty-seven articles divided amongst the three subsections i.e. PTB and HRQoL (n=13), PTB and Spirometry (n=9) and PTB and exercise capacity (n=6), were included in the review.

Figure 2.1 depicts the flow diagram of articles included and excluded for the key words; PTB and health related quality of life or HRQoL. Table 2.1 summarizes the included articles for PTB and health related quality of life. Although 13 articles were included, 1 article was a systematic review and thus was not included in table 2.1. The findings of the systematic review were thus discussed narratively.



**Figure 2.1: Flow Chart of Pulmonary Tuberculosis AND Health Related Quality of Life or HRQoL**

**Table 2.1: Overview of Studies on PTB and HRQoL**

<b>Author</b>	<b>Year</b>	<b>Study Design</b>	<b>Country</b>	<b>Patients</b>	<b>Gender</b>	<b>HRQoL Tool</b>	<b>Standardised</b>	<b>Comparison</b>	<b>Conclusion</b>
Aggarwal et al	2013	Prospective	India	Pulmonary Tuberculosis	Male and Female	WHOQoL-BREF	✓	Category I treatment regimen or smear positive with Category III regimen	HRQoL is impaired in patients with PTB, and improves rapidly and significantly with program based treatment.
Ahmed Awaisu et al	2012	Non-Randomised	Malaysia	Pulmonary Tuberculosis	Male and Female	EQ-5D	✓	PTB on DOTS with PTB on DOTS and smoking cessation included	An integrated PTB-tobacco treatment strategy could potentially improve overall quality of life outcomes among PTB patients who are smokers
Atif M et al	2012	Case Study	Malaysia	Pulmonary Tuberculosis relapse due to DMII	Male	SF-36v2	✓	None	Relapse of PTB might be due to poor glyceamic control and malnutrition
Babikako et al	2010	Cross Sectional	Uganda	Pulmonary Tuberculosis and HIV	Male and Female	MOS	✓	None	Domains worst affected in patient category Start of Treatment, 2 Months on Treatment and Completed Perceived Health Bodily Pain Quality of Life
Chamla, D	2004	Prospective	China	Pulmonary Tuberculosis	Male and Female	MOS SF 36	✓	PTB with Control	SF-36 scores are low in PTB patients indicating a decline in HRQoL, however, scores increase over the course of treatment
Deribew, Amare et al	2009	Cross Sectional	Ethiopia	Pulmonary Tuberculosis and Latent Tuberculosis Infection	Male and Female	WHOQoL HIV and Kesler Scale	✓	None	Domains worst affected at time of Survey: Pain Anxiety Mobility
Godoy M.D. et al.	2012	Cross Sectional	Brazil	Multi-Drug Resistant Tuberculosis	Male and Female	Airways Questionnaire 20	✓	None	78% patients reported a decrease in their Quality of Life

<b>Author</b>	<b>Year</b>	<b>Study Design</b>	<b>Country</b>	<b>Patients</b>	<b>Gender</b>	<b>HRQoL Tool</b>	<b>Standardised</b>	<b>Comparison</b>	<b>Conclusion</b>
Kruijshaar, M.E. et al	2010	Prospective	England	Pulmonary Tuberculosis	Male and Female	HRQoL SF-36v2, EQ-5D, VAS  Anxiety STAI-6  Depression CES-D	✓	None	PTB patients suffer from significantly diminished HRQoL at diagnosis. Treatment improved pts health scores within 2 months, but this is still below the UK norms
Lemos et al	2012	Cross Sectional	Brazil	Pulmonary Tuberculosis and HIV	Male and Female	HAT-QoI	✓	None	Domains worst affected at time of Survey:  Sexual Activities Financial Concern Secrecy
Marra CA et al	2008	Prospective	Canada	Pulmonary Tuberculosis and Latent Tuberculosis Infection	Male and Female	SF-36v2 and DI(Back depression index)	✓	None	Active PTB patients had large improvements in most HRQoL domains by 6 months, however, when compared to LPTBI and US norms, HRQoL was still low at completion
Othman G.Q. et al	2011	Prospective	Yemen	Pulmonary Tuberculosis and Extra Pulmonary Tuberculosis	Male and Female	DR-12 Short Form	✓	PTB with EPTB	At the start of treatment, PTB patients have significantly lower HRQoL than those with extra PTB. Both groups of pts HRQoL improves after onset of treatment
Pasipanodya et al	2007	Cross Sectional	USA	Pulmonary Tuberculosis and Latent Tuberculosis Infection	Male and Female	St Georges Respiratory Questionnaire	✓		Domains Worst Affected at time of Survey: Symptoms Activities Impact

Key: ✓=Yes; EPTB=Extra Pulmonary Tuberculosis; LPTBI=Latent Pulmonary Tuberculosis Infection; PTB=Pulmonary Tuberculosis; HRQoL=Health Related Quality of Life



### **2.3.1 Pulmonary Tuberculosis and Health-Related Quality-of-Life**

Descriptive data were extracted from the 12 eligible studies on PTB and HRQoL, summarised and expressed in Tables 2.1 and 2.2. All included studies were published between 2004 and 2013. Five of the 12 studies incorporated a cross-sectional study design and five articles incorporated a prospective study design. The study by Awaisu et al (2012) was the only study to utilize a non-randomized control design<sup>16</sup>. Three studies were conducted at a public hospital, four studies at a clinic and one only 1 study used both public and private hospitals. The studies by Godoy et al (2012) and Aggarwal et al (2013) carried out the studies at the Laboratory of Respiratory Physiology, University of Rio de Janeiro and microscopy centres, patients' homes and multiple directly observed therapy short-course (DOTS) centres, respectively<sup>8,17</sup>. The total number of participants recruited for all studies were n=2123, with Aggarwal et al (2013) including a total of n=675 in a study conducted in India<sup>8</sup>. Participants of the studies were between 15 years and 70 years. Studies by Babikako et al (2010), Marra et al (2008), Awaisu et al (2012), Jotam et al (2007) and Godoy et al (2012) all reported age as a mean with standard deviation<sup>16-20</sup>. The study by Aggarwal et al (2013) was the only study not to mention age range or a mean with standard deviation<sup>8</sup>. Eight of the 12 studies were conducted in third world countries while the studies by Pasipanodya et al (2007), Marra et al (2008) and Kruijshaar et al (2010) were conducted in the USA, Canada and England respectively<sup>19-21</sup>.

### **2.3.2 Tools and Outcomes**

All of the included studies made use of standardized HRQoL tools and three of the twelve studies validated standardized HRQoL tools in their local population. All included studies evaluated HRQoL as either a primary or secondary outcome measure. The studies by Marra et al (2008) and Kruijshaar et al (2010) both added depression indexes as secondary outcome measures<sup>19,21</sup>. HRQoL tools and domain characteristics are tabled in Table 2.1.

### 2.3.3 Results of Pulmonary Tuberculosis and HRQoL

The average patient treatment time for tuberculosis across all of the included studies was 7.45 months. Godoy et al (2012) evaluated patients after an eighteen-month treatment regimen for multi-drug resistant tuberculosis and only evaluated patients who were sputum clear at the twelve month mark<sup>17</sup>. Six studies, including a case study by Atif et al (2012), evaluated patients at their initial diagnosis, after the intensive phase of treatment and again after treatment completion<sup>8, 16, 19, 21-23</sup>. Lemos et al (2012) and Pasipanodya et al (2007) only evaluated their subjects after completion of treatment<sup>20, 24</sup>. Both Othman et al (2011) and Kruijshaar et al (2010) evaluated their subjects HRQoL at initial diagnosis and at one month into treatment<sup>21, 25</sup>. However, Kruijshaar et al (2010) added an extra quality of life data collection point at the end of treatment<sup>21</sup>. Deribew et al (2009) was the only study to report on patients' quality of life after the intensive phase of their tuberculosis treatment alone<sup>26</sup>.

A wide variety of generic instruments were used to report on HRQoL. The SF-36 questionnaire was used most (n=4; 30% of included studies). The SF-36 is a short form questionnaire adapted from the longer Medical Outcomes Survey questionnaire. It comprises of 36 items which is divided into eight domain subscales including Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), Vitality (VT), General Health (GH), Social Functioning (SF), Role Emotional (RE) and Mental Health (MH). From these domains, a physical component summary (PCS) and mental component summary (MCS) score can be calculated. Kruijshaar et al (2010) used both the SF-36v2 and the European Quality of life (EQ-5D) in a United Kingdom population and validated these against the Visual Analogue Scale (VAS)<sup>21</sup>. Awaisu et al (2012) was the only other study to use a validated EQ-5D questionnaire in the Malaysian population<sup>16</sup>. Deribew et al (2009) and Aggarwal et al (2013) both used the World Health Organisation Quality of Life (WHOQoL) questionnaire, while Godoy et al (2012) and Lemos et al (2012) used the Airways Questionnaire 20 and the HIV/AIDS Targeted Quality of Life (HAT QoL), respectively<sup>8, 17, 24, 26</sup>. The long Medical Outcomes Survey was used by Babikako et al (2010), who validated it against the VAS in a local population<sup>18</sup>. The only study to use a disease specific tool was the study done by Othman et al (2011), who used the DR-12 short form<sup>25</sup>. The DR-12 short form is a PTB specific questionnaire developed and validated in an Indian population and first reported on in 2003<sup>27</sup>. The questionnaire comprises of 12 items and covers PTB symptoms, socio-psychologic factors and exercise adaptation.

All of the included studies reported a decrease in patients' HRQoL. Godoy et al (2012) reported that 78% of patients with multi-drug resistant PTB suffered from a decreased HRQoL<sup>17</sup>. Lemos et al (2012) and Awaisu et al (2012) both reported on a decrease in HRQoL in patients co-infected with both PTB and HIV when compared to PTB alone<sup>16, 24</sup>. Six of the twelve studies, who all recorded quality of life at multiple stages of tuberculosis treatment, reported that HRQoL was poor at the start of treatment, but improved as the tuberculosis treatment progressed. Characteristics of the domains that showed the most improvement during the course of tuberculosis treatment for the various HRQoL tools are presented in Table 2.2. In general, physical health and bodily pain/pain are the most frequently reported domains to

have improved across all HRQoL tools. A comparison of domains measured and domains best improved at follow-up are tabulated in table 2.2.

#### **2.3.4 Reviews**

Guo et al (2009) published a systematic review entitled: *Measuring health-related quality of life in tuberculosis: a systematic review*<sup>28</sup>. Six electronic databases were searched including MEDLINE, EMBASE, Cochrane Library, PsychInfo, CINAHL and HaPI using the keywords *tuberculosis, quality of life, quality adjusted life years, health utility, health status, life quality and well-being*. An initial literature search identified 2540 articles of which 12 were included in the review after inclusion and exclusion criteria. Marra et al (2008), Chamla et al (2004) and Pasipanodya (2007) were the only three studies that overlapped with this scoping review<sup>19, 20, and 23</sup>. This scoping review included 9 articles which were published after 2009. Keywords and databases searched also differed between the scoping review and the systematic review.

#### **2.3.5 Discussion and Conclusion of the effect of Pulmonary Tuberculosis on HRQoL**

Traditionally, medical outcomes were measured using objective clinical indicators such as physiological tests and disease status. However, a gradual shift in this philosophy has led to the inclusion of the patients' perspective in the evaluation of medical outcomes<sup>29</sup>. A need arose to assess health status beyond the traditional indicators of morbidity and mortality<sup>23</sup>. HRQoL measurements are important for assessing the impact of the chronic disease and its treatment on patients<sup>29</sup>.

The results of this scoping review on HRQoL agree with the findings of the systematic review by Guo et al (2009)<sup>28</sup>. Guo et al (2009) concluded that tuberculosis has substantial adverse impacts on patients' quality of life, even after they have been deemed cured<sup>28</sup>. The findings of this review suggest that patients perceived HRQoL is decreased in all patients diagnosed with PTB. The quality of life does improve as pharmacological treatment progresses. However, Marra et al (2008) concluded that even though there was an increase in reported HRQoL, these scores were still lower than the population normal or those patients with latent tuberculosis infection<sup>19</sup>. Kruijshaar et al (2010) also noted that HRQoL scores had increased by the two-month mark of pharmacological treatment but these too were decreased when compared with the population normal values<sup>21</sup>.

It appears that the domains worst affected from when patients are diagnosed, with TB, are physical health and bodily pain, but these were also the two domains that rapidly improved as treatment progressed. Mental and social domains seemed to not improve for a longer period time, sometimes even after the patient is deemed cured. Tuberculosis is however a disease that is associated with lower socio economic status and is more prevalent in middle to low income countries<sup>30</sup>. Therefore, reasons for the prolonged decrease in psychological and mental domains could be attributed to environmental and social factors such as the stigmatism associated with the disease.

Evident from this review is the wide variety of HRQoL tools used in the studies included. The systematic review by Guo et al (2009) suggested that a standardized HRQoL tool be developed for TB to assess changes in health status as the disease treatment progresses<sup>28</sup>. However, six of the 12 studies in this scoping review utilized the SF-36 or derivatives thereof, and were able to identify changes in TB patients' perceptions of health. This suggests that the SF-36 is sensitive enough to detect changes in HRQoL in a TB population. Othman et al (2011) used the DR-12 questionnaire which is a PTB specific questionnaire developed in India and first reported in 2003<sup>25</sup>. The questionnaire has however not been used in many other populations to date. Guo et al (2009) also noted that the DR-12's validation process was not conducted in a systematic fashion and the evidence for the validity of the questionnaire was not convincing<sup>28</sup>.

**Table 2.2: Comparisons of Domains best Improved of HRQoL before PTB treatment, intensive phase of PTB treatment and after PTB treatment**

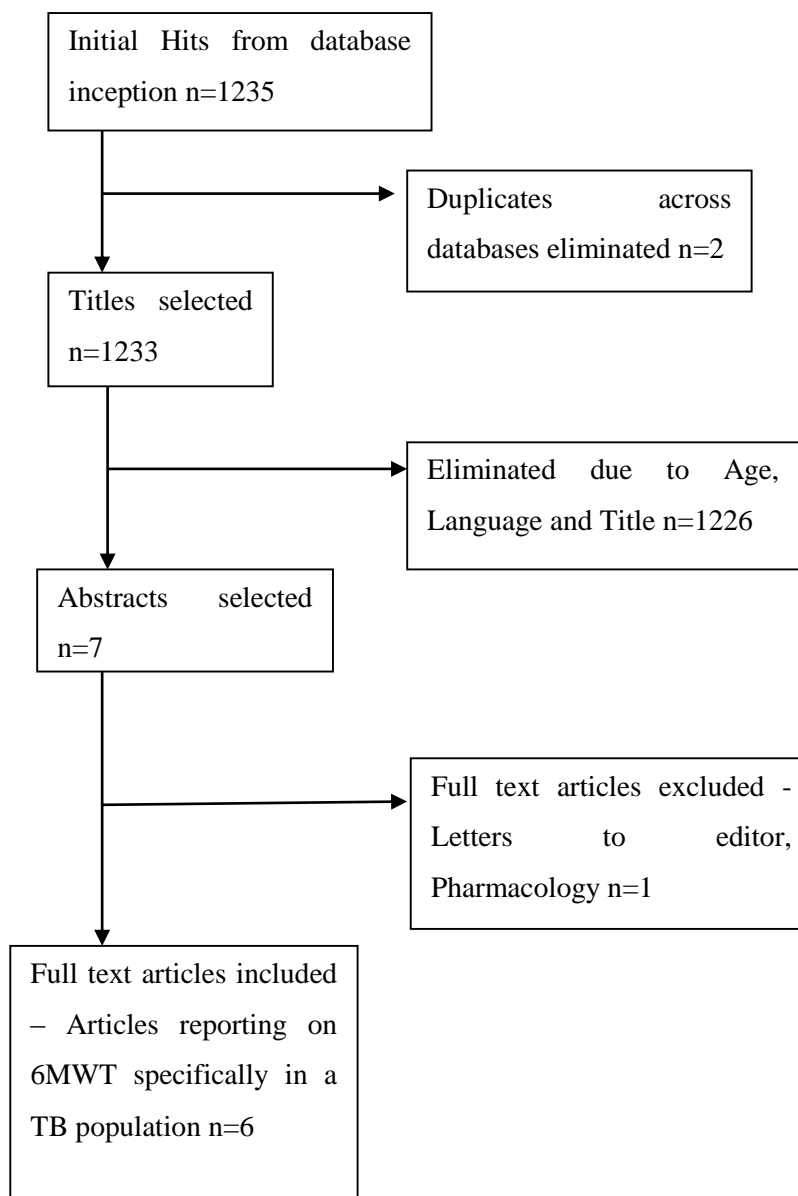
<b>Author</b>	<b>HRQoL Tool Used</b>	<b>Validity and Reliability</b>	<b>Standardised</b>	<b>Domain Measured at Initial Diagnosis</b>	<b>Domain Improvement After Intensive Phase/1<sup>st</sup> Follow-up</b>	<b>Domain Improvement at End of Treatment</b>	<b>Domains Best Improved</b>
Aggarwal A et al	WHOQoL-BREF	3 of 24 items had Spearman's $\rho$ coefficient >0.60 and 8 items >0.75 = good convergent validity  Cronbachs $\alpha$ >0.70	✓	Physical, Psychological, Social relationships Environment	Physical  Psychological  Social relationships Environment	Physical  Psychological  Social relationships Environment	Physical, Psychological,  However, these domains were significantly lower amongst sputum positive patients and among those on Category I treatment compared with Category III patients
Ahmed Awaisu et al	EQ-5D	Validated by EuroQoL group UK for use in Malaysian population	✓	Mobility Self care Usual activities Pain Anxiety	Mobility Self care Usual activities Pain Anxiety	Mobility Self care Usual activities Pain Anxiety	Pain, Anxiety, Mobility  Improvement in both DOTS group and smoking cessation DOTS group
Atif M et al	SF-36v2	n/a	✓	PF RF BP GH VT SF	PF RF BP GH VT SF	PF RF BP GH VT SF	Improvement in all domains however still under the Malaysian norms published by Azman et al. Quality of life of the Malaysian general

					RE	RE	✓	RE	✓	population: results from a postal survey using the SF-36v2. Medical Journal of Malaysia, 2003;58:694-711
					MH	MH	✓	MH	✓	
Chamla, D	MOS SF 36	SF-36 had item consistency ranging 0.56 to 0.86 for PTB and Control	✓	PF	PF	PF	✓	PF	✓	PF,BP, GH
		Reliability Coefficients by Cronbachs $\alpha$ ranged 0.88 to 0.97		RF	RF	RF	✓	RF	✓	All physical scales increased in PTB group significantly over course of treatment compared to Control
				RE	RE	RE	✗	RE	✓	
				BP	BP	BP	✗	BP	✓	
				VT	VT	VT	✓	VT	✗	
				SF	SF	SF	✗	SF	✓	
				MH	MH	MH	✓	MH	✗	
				GH	GH	GH	✓	GH	✓	
Kruijshaar, M.E. et al	HRQoL		✓	PF	PF	PF	✗	PF	n/a	EQ-5D =
	SF-36v2, EQ-5D, VAS	n/a		RF	RF	RF	✓	RF	n/a	Pain/Discomfort & Problems with self care
	Anxiety	Reliability in this n at Diagnosis		BP	BP	BP	✓	BP	n/a	Proportions of problems are larger than seen in UK norms
	STAI-6	Cronbachs $\alpha=0.887$		GH	GH	GH	✗	GH	n/a	
	Depression			VT	VT	VT	✓	VT	n/a	
	CES-D	Cronbachs $\alpha=0.894$		SF	SF	SF	✓	SF	n/a	SF-36v2 = RP, SF, MCS
				RE	RE	RE	✓	RE	n/a	
				MH	MH	MH	✓	MH	n/a	PCS & MCS significantly lower than UK norms at Diagnosis.

<b>Author</b>	<b>HRQoL Tool Used</b>	<b>Validity and Reliability</b>	<b>Standardised</b>	<b>Domain Measured at Initial Diagnosis</b>	<b>Domain Improvement After Intensive Phase/1<sup>st</sup> Follow-up</b>	<b>Domain Improvement at End of Treatment</b>	<b>Domains Best Improved</b>		
Marra CA et al	SF-36v2 and DI(Back depression index)	n/a	✓	PF RP BP GH VT SF RE MH	PF RP BP GH VT SF RE MH	✓ ✓ ✗ ✗ ✓ ✓ ✓ ✓	PF RP BP GH VT SF RE MH	✓ ✓ ✗ ✓ ✓ ✓ ✓ ✓	VT, PF, RF, SF, RE  Patients with active PTB had bigger HRQoL deficits than those with LPTBI when compared to US norms
Othman G.Q. et al	DR-12 Short Form	Reliability α=0.71  Validity after translated in Arabic by distribution among doctors nurses and social scientists for content relevance	✓	Symptoms Life activities Social activities	Symptoms Life activities Social activities	✓ ✓ ✓	Symptoms Life activities Social activities	n/a n/a n/a	Symptoms, Life activities  HRQoL improved significantly in PPTB and Extra PPTB groups

Key: ✓ =Yes; ✗ = No; PF=physical functioning; RP=role physical; BP=bodily pain; GH=general health; VT=vitality; SF=social functioning; RE=role emotional; MH=mental health

Figure 2.2 depicts the flow diagram of articles included and excluded for the key words; PTB and six minute walk test or 6MWT. Table 2.3 provides an overview of the included articles for PTB and exercise capacity.



*Figure 2.2: Flow Chart of Pulmonary Tuberculosis and Six-minute walk test (6MWT)*

#### **2.4 Pulmonary Tuberculosis and Exercise Capacity**

Descriptive data were extracted from the six included studies and summarised and expressed in Table 2.3. All of the included studies were published between 2003 and 2012. Five studies utilized an observational study design and one study including a prospective cohort<sup>17,31-34</sup>. Ando et al (2003) was the only study to utilize an intervention type design, reporting on 6MWT data at baseline and again



after an intervention<sup>35</sup>. Yoshida et al (2006) and Ando et al (2003) carried out their studies in Japan<sup>34</sup>.<sup>35</sup>. Miguire et al (2009) and Pontororing et al (2010) carried out their studies in Indonesia while Sivaranjini et al (2010) and Godoy et al (2012) carried out their studies in India and Brazil, respectively<sup>17, 31-33</sup>. Sivaranjini et al (2010) and Yoshida et al (2006) obtained their study sample from public hospitals where as Maguire et al (2009), Pontororing et al (2010) and Ando et al (2003) all used the clinic setting<sup>31-35</sup>. Yoshida et al (2006), Sivaranjini et al (2010) and Ando et al (2003) used a patient sample suffering from pulmonary tuberculosis sequelae (PTS). The total number of participants recruited for all the studies was n=365. The observational study by Pontororing et al (2010) yielded the most participants (n=164)<sup>32</sup>. Four of the six included studies evaluated either exercise tolerance/training as part of a pulmonary rehabilitation program as their primary outcome measure. The study by Pontororing et al (2010) compared current Indonesian management of TB with the standards set by the World Health Organisation (WHO) as their primary objective<sup>32</sup>.

**Table 2.3: Overview of PTB and Exercise Capacity**

<b>Author</b>	<b>Study Design</b>	<b>Year</b>	<b>Country</b>	<b>Setting</b>	<b>Sample Size</b>	<b>Comparison</b>	<b>6 Minute Walk Test Procedure</b>
Ando et al	Non Randomized Trial	2003	Japan	Clinic	n=64	PTB with COPD	As described by Steele et al 1996
Godoy et al	Observational	2012	Brazil	Laboratory of Respiratory Physiology, University of Rio de Janeiro	n=18	None	According to ATS Guidelines
Maguire et al	Prospective	2009	Indonesia	Clinic	n=69	None	According to ATS Guidelines
Pontororing et al	Observational	2010	Indonesia	Clinic	n=162	PTB with HIV and without HIV	According to ATS Guidelines
Sivaranjini et al	Observational	2010	India	Public Hospital	n=60	PTB with Normal Population	According to ATS Guidelines
Yoshida et al	Observational	2006	Japan	Public Hospital	n=10	None	As described by Steele et al 1996

Key: PTB=Pulmonary Tuberculosis; HIV=Human Immuno Deficiency Virus; COPD=Chronic Obstructive Pulmonary Disease

Table 2.4 summarizes the results of the 6 included articles on PTB and exercise capacity.

**Table 2.4: Results of PTB and Exercise Capacity**

<i>Author</i>	<i>Year</i>	<i>Population</i>	<i>Improvement in 6MWD or 6MWWD</i>	<i>Improvement in SPO2</i>	<i>Improvement in Heart Rate</i>	<i>Improvement in Dyspnoea Score</i>	<i>Improvement in Fatigue Score</i>
Ando et al	2003	Pulmonary Tuberculosis Sequelae and Chronic Obstructive Pulmonary Disease	✓	n/a	n/a	n/a	n/a
Godoy et al	2012	Multi-Drug Resistant Tuberculosis	n/a	n/a	n/a	n/a	n/a
Maguire et al	2009	Pulmonary Tuberculosis	✓	n/a	n/a	n/a	n/a
Pontororing et al	2010	Pulmonary Tuberculosis	n/a	n/a	n/a	n/a	n/a
Sivaranjini et al	2010	Pulmonary Tuberculosis Sequelae	n/a	n/a	n/a	n/a	n/a
Yoshida et al	2006	Pulmonary Tuberculosis Sequelae	✓	✗	✗	✓	✓

Key: ✓=Yes; ✗=No; 6MWD – 6-minute walk distance; 6MWWD – 6-minute walk weight distance

#### 2.4.1 Results of PTB and Exercise Capacity

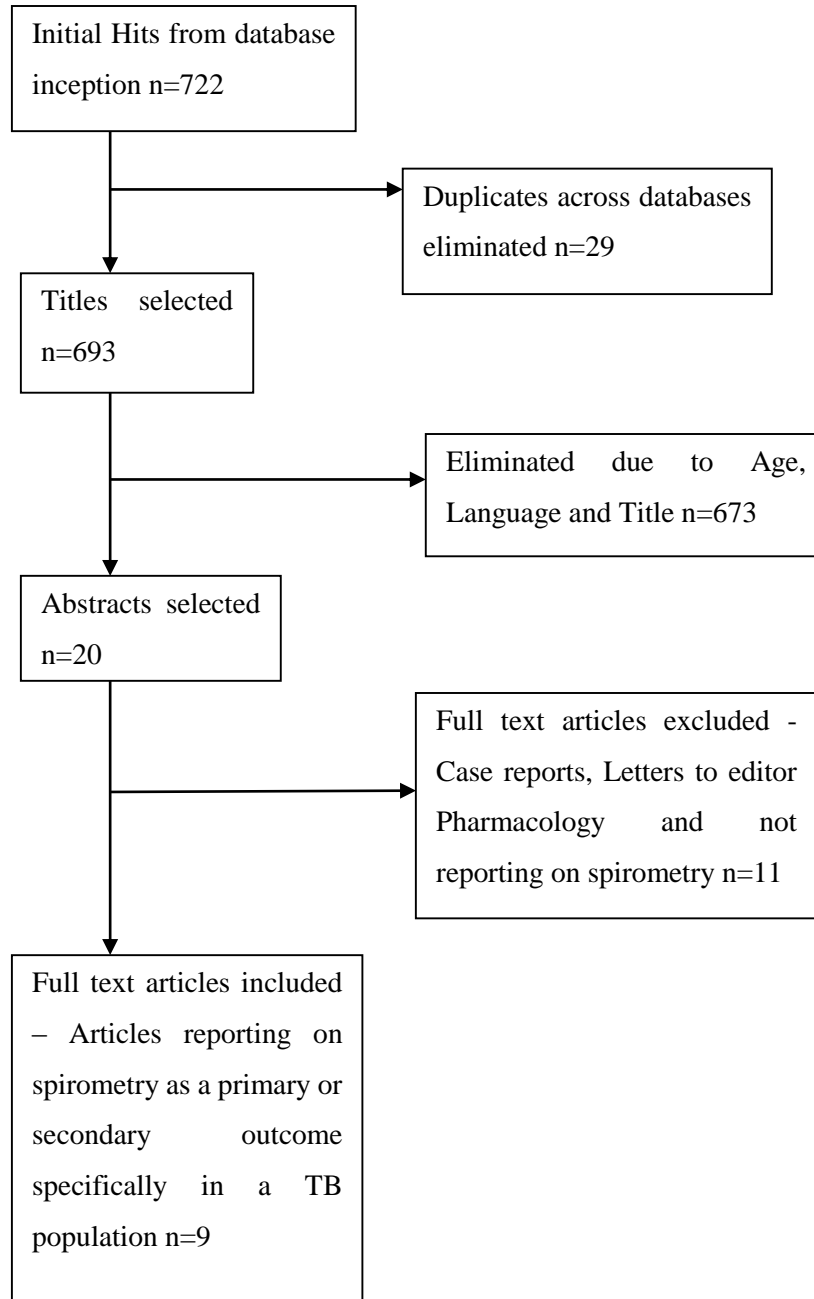
Studies by Maguire et al (2009), Sivaranjini et al (2010), Pontororing et al (2010) and Godoy et al (2012) all used a 6MWT procedure as recommended by the American Thoracic Society 2002<sup>31-33</sup>. Yoshida et al (2006) and Ando et al (2003) used the procedure for the 6MWT as described by Steele et al (1996), which does not vary to that described by the American Thoracic Society. All of the included studies assessed functional capacity either as a baseline measurement for patients diagnosed with PTB or as a comparison between PTB and HIV, COPD or population norms. Maguire et al (2009) reported on the six minute walk weight distance (6MWWD) at the start of treatment, two months into treatment and again at the end of treatment on newly diagnosed smear positive patients with no previous history of PTB<sup>31</sup>. Maguire et al (2009) saw a rise of 12.3% in 6MWWD from baseline to end of treatment<sup>31</sup>. Yoshida et al (2006) and Ando et al (2003) both reported an increase in six minute walk test distance (6MWD) after exercise<sup>34,35</sup>. The studies by Sivaranjini et al (2010) and Godoy et al (2012) both reported decreased 6MWD when compared to a normal group or the percentage predicted in their respective studies<sup>17,33</sup>. Yoshida et al (2006) was the only study to report on an increase in Modified Borg Scale dyspnoea and fatigue scores from baseline to after exercise intervention, while no improvement was seen in oxygen saturation and heart rate values<sup>34</sup>.

### **2.4.2 Discussion and Conclusion of PTB and Exercise Capacity**

The 6MWT is a simple, inexpensive and practical functional walk test that requires little technician training and basically only the ability to walk<sup>33</sup>. The test has traditionally been used in patients suffering from chronic cardiac or respiratory illness and could be used as either a once off generic measure of functional status, or as an outcome measure from a rehabilitation program<sup>33</sup>. All six of the included studies used a 30 meter, inside corridor.

The findings of this review indicate that overall, 6MWT distance is decreased in patients diagnosed with PTB when compared to normal walking distances. The impact of PTB on 6MWT distance varies depending on age and the severity of the disease. Sivaranjini et al (2010) concluded that PTB has a considerable impact on the functional capacity of older patients in India, while Ando et al (2003) noted that pulmonary rehabilitation is beneficial for patients with PTB, as in patients with COPD, if the severity of lung destruction in the diseases is similar<sup>33,35</sup>. The 6MWD should be considered as an adjunct measure to distance alone as it is shown to correlate well for VO<sub>2</sub>max as well as aerobic threshold<sup>31</sup>.

Figure 2.3 depicts the flow diagram of articles included and excluded for the key words; PTB and spirometry. Table 2.5 provides an overview of the included articles for PTB and spirometry.



*Figure 2.3: Flow Chart of Pulmonary Tuberculosis and Spirometry*

## 2.5 Pulmonary Tuberculosis and Spirometry

Descriptive data were extracted from the nine included studies and summarised in Table 2.5. All of the studies were published between 1996 and 2012. Godoy et al (2012) carried out their study in Brazil, while the two studies done in the United States were both carried out by Pasipanodya et al (2007) and Pasipanodya et al (2012)<sup>17,20,36</sup>. Menezes et al (2007) used five Latin American countries in a multi-centre study<sup>37</sup>. The remaining five studies were carried out in Spain, Canada, Korea, South Africa and Pakistan. Candela et al (1996) used a retrospective study design. Long et al (1998), de Villiers et al (2004) and Pasipanodya et al (2012) all used prospective study designs<sup>36,38-40</sup>. Menezes et al (2007) and Godoy et al (2012) both made use of cross-sectional study designs while Lee et al (2011) used a clustered, multi-stage cross-sectional design for a population based survey<sup>17,37,41</sup>. Pasipanodya et al (2007) was the only study to use a case-control design<sup>20</sup>. The total number of subjects tested for lung function across the studies was n=9889, with the population-based studies by Menezes et al (2007) and Lee et al (2011) yielding the highest number of patients at n=3687 and n=5571, respectively<sup>37,41</sup>. All of the studies included both male and female patients with an age ranging from <28yrs to >60yrs. Table 2.5 provides an overview of articles included on PTB and spirometry.

**Table 2.5 Overview of included studies on PTB and Spirometry**

<b>Author</b>	<b>Year</b>	<b>Study Design</b>	<b>Country</b>	<b>Population</b>	<b>Sample</b>
Baig et al	2010	Descriptive	Pakistan	Past PTB	n=47
Candela et al	1996	Retrospective	Spain	EPTB	n=81
de Villiers et al	2004	Prospective	South Africa	MDR PTB	n=33
Godoy et al	2012	Cross Sectional	Brazil	MDR PTB	n=18
Lee et al	2011	Clustered	Korea	Past PTB	n=3687
Long et al	1998	Prospective	Canada	PTB	n=25
Menezes et al	2007	Cross Sectional	Brazil, Uruguay, Mexico, Chile, Venezuela	Platino Sample	n=5571
Pasipanodya et al	2007	Case Control	USA	PTB & LPTBI	n=107
Pasipanodya et al	2012	Prospective	USA	PTB	n=320

Key: MDR=Multi-Drug Resistant; PTB=Pulmonary Tuberculosis; LPTBI= Latent Pulmonary Tuberculosis Infection; EPTB=Extra Pulmonary Tuberculosis

### 2.5.1 Results of Pulmonary Tuberculosis and Spirometry

Due to the heterogeneity of the included studies, the results of Long et al (1998), Lee et al (2011) and Menezes et al (2007) were not included in the table, but will rather be described in narrative form. Spirometry results for the other included studies are described in Table 2.6. For the purposes of this review, the pattern of lung impairment was described as obstructive, restrictive or mixed and reported as percentages of the total study population.

**Table 2.6: Results of PTB and Spirometry with Lung Function Classification**

<b>Author</b>	<b>Year</b>	<b>Obstructive Pattern</b>	<b>Restrictive Pattern</b>	<b>Mixed Pattern</b>	<b>Normal</b>	
Baig et al	2010	55.3%	29.9%	14.8%		
Candela et al	1996	3%	10%	not reported		
de Villiers et al	2004	12%	42%	39%	2%	
Godoy et al	2012	39%	22%	17%	22%	
Pasipanodya et al	2007	PTB	13%	31%	not reported	
		LPTBI	1%	15%	not reported	
Pasipanodya et al	2012	10.75%	73.25%	16%		

Key: PTB=Pulmonary Tuberculosis; LPTBI=Latent Pulmonary Tuberculosis Infection

The most predominant pattern of lung impairment across the studies is a restrictive pattern. However, Baig et al (2010) and Godoy et al (2012) both found the obstructive patterns to have higher population percentages in their studies<sup>17,42</sup>. Long et al (1998) reported on the relationship between lung structure (CT scan) and lung function (spirometry), with or without cavitation in a PTB population<sup>39</sup>. The results of the study by Lee et al (2011) are described in Table 2.7<sup>41</sup>.

**Table 2.7: Spirometry (Lee et al 2011) Airflow obstruction as defined FEV1/FVC <0.70**

<b>Total Sample n=3687</b>	<b>Percentage of Sample with Airflow Obstruction</b>
Previous PTB	27.9%
No Previous PTB	6.5%
Smoker	13.8%
Never Smoker	4.7%

Menezes et al (2007) extracted data for PTB from a much larger study looking at the burden of lung disease in Latin America called the PLATINO study<sup>37</sup>. In their multistage survey, they identified previous PTB as a risk factor for COPD.

A summary of the spirometry results are described in Table 2.8.

**Table 2.8: PTB and Spirometry (PLATINO)**

<b>Total Sample n=5571 of which 132 has medical diagnosis of PTB</b>		
	No Medical Diagnosis of PTB	Medical Diagnosis of PTB
Post Bronchodilator FEV1% of predicted	95.82+-17.4	91.43+-18.8
Post Bronchodilator FVC% of predicted	98.12+-15.52	96.13+-16.34
Post Bronchodilator FEV1/FVC% of predicted	97.85+-10.0	91.79+-13.27

Key: PTB=Pulmonary Tuberculosis; FEV1= Forced Expiratory Volume in 1 second; FVC=Forced Vital Capacity

The authors of the study found that the association of PTB with FEV1 values was stronger than that of FVC and as a result, the FEV1/FVC values showed a marked reduction, characteristic of an obstructive pattern.

### 2.5.2 Reviews

Two reviews were found during the literature search. The first was a systematic review entitled: *A systematic review of the association between pulmonary tuberculosis and the development of chronic airflow obstruction in adults*<sup>43</sup>. The authors performed a search of the PubMed/Medline database and articles were excluded if; they did not contain original research, they had insufficient details of either the methodology or results to assess the validity of the findings and if the patients were on active PTB treatment without post treatment follow-up. Nineteen studies with a variety of study designs were included in the review. Four of the studies in the current review overlap with the studies included in the systematic review. Reasons for the small overlap of studies could be attributable to databases searched, difference in search terms and the specific inclusion and exclusion criteria of the systematic review. The authors concluded that the association between chronic airway obstruction (COA) and a history of PTB is positive. “However, whether PTB-associated COA should be considered part of the COPD spectrum, a phenotype of COPD or an unrelated disease remains unclear.”<sup>43</sup>

The second review identified in the literature search was conducted by Ehrlich in 2011 entitled: *Chronic airflow obstruction and respiratory symptoms following tuberculosis: a review of South African studies*<sup>9</sup>. The authors aimed to review population-based and occupational based South African studies that provides estimates of association between PTB, chronic symptoms and loss of lung function. The authors concluded that the studies reviewed contributed to the evidence of a strong association between PTB, even if properly treated, and subsequent airflow obstruction as well as restrictive loss.

### 2.5.3 Discussion and Conclusion of PTB and Spirometry

The association between PTB and lung function impairment has been around for several years<sup>9</sup>. PTB has recently been identified as an independent risk factor for the development of COPD in major population based studies such as the PREPCOL and PLATINO studies<sup>37</sup>. Consequences of PTB include permanent scarring, bronchiectasis and pleural fibrosis<sup>43</sup>. During the treatment of active PTB, lung function impairment is usually restrictive in nature. This may persist or develop into an obstructive pattern<sup>43</sup>. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) identifies obstructive lung function impairment as FEV1/FVC <0.07. Despite the fact that PTB has been identified as a risk factor for the development of COPD through population based COPD screening studies, the spirometric values are often influenced by concurrent risk factor exposure such as smoking, biomass fuel exposure, dust and childhood respiratory illness; making it difficult to distinguish pure obstructive abnormalities from other lung structural abnormalities without full body pletysmography<sup>43</sup>.

The findings of this review suggest that lung function impairment is evident after PTB. The severity and pattern of the lung function impairment varies according to how long after the patient is deemed cured the spirometry is done, the amount of times the person has been diagnosed with PTB and even the severity of the PTB itself. The review also suggests that lung function measurements appear to be dynamic in nature, with patients tested immediately after anti-tuberculosis treatment showing more restrictive pattern, but patients who have been deemed cured over 10 years ago presenting with sequelae and respiratory symptoms show more obstructive patterns. The results of this review agree with the findings of the systematic review by Allwood et al (2013) who confirmed a positive association between a past history of PTB and the presence of airflow limitation<sup>43</sup>. In a high PTB burden area such as South Africa, PTB as a contributor to the development of COPD is important to health care providers and policy makers as it appears that microbiological cure is only the start of what should be a dynamic, holistic management of both the active disease as well the sequelae there of.



## **2.6 Conclusion**

This broad, scoping review of the literature indicates that PTB patients suffer from a decreased HRQoL, impaired lung function and a reduced exercise capacity. Spirometric values are also reduced when compared with normal population values or patients with latent PTB infection. Despite a wide variety of HRQoL tools used in various studies, patients perceptions of their physical health, specifically the domains of bodily pain and physical functioning (as scored by the SF-36 HRQoL instrument), showed good improvement with anti-tuberculosis therapy, however, these scores were also below population normal scores. Therefore, this review highlights a need for continued intervention after tuberculosis drug therapy and serves as a good foundation to inform the planning of future studies in this patient population

## Chapter 3

### **An Investigation into the health related quality of life (HRQoL) and functional assessment of a cured Pulmonary Tuberculosis (PTB) population in the Breede Valley District, South Africa: a pilot study**

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## Article Abstract

### Background:

Pulmonary tuberculosis (PTB) remains a major concern worldwide. Although PTB is curable, both the disease and its treatment may have considerable medical, social and psychological consequences which may result in a decreased quality of life and functioning. Characterization of the functional capabilities of PTB patients post-treatment and the impact of PTB on their quality of life may identify a need for more holistic management of PTB treatment that extends beyond microbiological cure.

### Methods:

A cross-sectional, quantitative, descriptive study was conducted. The study setting included five primary health care facilities (PHCF) in the Breede Valley sub-district of the Cape Winelands East District, Western Cape, South Africa. Adult patients diagnosed with PTB, 18 years and older and who were successfully managed through the Cape Winelands District Health Care system were considered for the study if they had least two negative sputum sample results and had completed at least five months of anti-tuberculosis treatment. Post treatment bronchodilator lung function tests, health related quality of life using the BOLD core questionnaire and six minute walk test distance (6MWD) was measured.

### Findings:

Of the 328 names obtained from the TB registers of the five included PHCF, 45 patients were included in the study (56% male; mean age,  $39.88 \pm 10.20$ ). The majority of patients ( $n=206$ ; 63%) were not contactable, and could not be recruited. Approximately half the total sample, ( $n=23$ ; 52%) presented with normal lung function while  $n=11$  (25%) presented with a restrictive pattern,  $n=9$  (21%) presented with an obstructive pattern and only  $n=1$  (2%) presented with a mixed pattern (defined as  $FEV_1 < 80\%$  predicted,  $FVC < 80\%$  predicted and  $FEV_1/FVC < 0.7$ ). The mean six minute walk distance (6MWD) was  $294.5m \pm 122.7m$ . Respondents scored poorly on all sub-domains of the SF-12v2 except vitality. Role emotional and role physical scored lowest with mean scores of 28.1 and 35.27 respectively, while vitality scored the highest with 52.78.

### Conclusion

The findings of this study suggest that even after microbiological cure, PTB patients may suffer from a decreased quality of life, impaired lung function and a decreased exercise capacity. Challenges faced during this pilot study such as patient recruitment, 6MWD and the generalizability of standardized questionnaires in rural regions are crucial in the development of a larger study. The findings of this pilot study serves to inform the planning of a larger observation study, with matched case controls, in the rural Cape Winelands of the Western Cape, South Africa.

## Background

Tuberculosis (TB) is described as a social disease because it is closely linked to the issues of overcrowding, poverty and unemployment<sup>13</sup>. South Africa is burdened with one of the worst TB epidemics in the world and in the Western Cape; one of nine provinces in South Africa, the incidence of TB is 909/100000<sup>13</sup>. Approximately 90% of new smear positive cases falls within the economically active age group<sup>13</sup>. Fuelled by interacting epidemics like HIV, TB notifications are now more prevalent between the ages of 20 and 40 years<sup>14</sup>.

Despite many advances in modern medicines fight against TB, TB remains a major cause of death worldwide, especially in low-middle income countries<sup>30</sup>. PTB has been identified as a risk factor for the development of chronic obstructive pulmonary disease (COPD)<sup>44</sup>. In the PLATINO

<sup>1</sup> and the PREPCOL<sup>211</sup> studies, reports of previous PTB or previous PTB treatment was strongly associated with the development of COPD as defined by the Global initiative for Chronic Obstructive Lung Disease (GOLD) criteria<sup>11</sup>. Pathophysiologically, PTB has been hypothesized to result in sequelae which could affect a patients' functional ability and impair lung function<sup>17</sup>. In high incidence countries such as South Africa, a significant number of COPD cases are likely to be due to PTB sequelae, however, epidemiological studies documenting the prevalence of post –TB COPD still need to be conducted<sup>45</sup>.

The World Health Organisation (WHO) defines health as “a state of complete physical, mental and social “well-being” and not only “the absence of disease or infirmity”<sup>46</sup>. Current government intervention strategies are focused on identification of new cases and bacteriological markers until outcomes such as cured, treatment completed or treatment failure/defaulted have been achieved<sup>8</sup>. Although PTB is curable, both the disease and its treatment may have considerable medical, social and psychological consequences which may result in a decreased quality of life and functioning<sup>21</sup>. Thus, the clinical burden of the disease may exist beyond the duration of the treatment of the infection<sup>8</sup>. Characterization of the functional capabilities of PTB patients post-treatment and the impact of PTB on their quality of life may identify a need for more holistic management of patients presenting with PTB that extends beyond microbiological cure.

Context: Baseline data is needed to plan the future physiotherapeutic management of PTB patients in the Overberg. Using a primary outcome of COPD prevalence a sample of 200 patients was deemed sufficient to detect a chronic obstructive pulmonary disease (COPD) prevalence of 15 % (95%CI 10%-20%). Sample size was calculated using FEV<sub>1</sub> and FEV<sub>1</sub>/FVC prevalence proportion ratios based on Western Cape BOLD data<sup>47</sup>. The BOLD study data identified a prevalence of obstructive airway disease in the Uitsig community (Cape Town, Western Cape) of 22% and found an association between

<sup>1</sup> PLATINO - Proyecto Latinoamericano de Investigación Obstrucción Pulmanar

<sup>2</sup> PREPCOL - Pravalencia de EPOC en Columbia

airway obstruction and a previous history of PTB. To inform the planning of a larger, observational study, a pilot study was undertaken. The primary objectives of this paper is to describe the demographics, respiratory symptoms, pulmonary airflow patterns (using spirometry) health related quality of life and exercise capacity (using the six minute walk test) of patients from one sub-district. A secondary objective is to report on recruitment strategies needed to optimize patient recruitment in the region.

## **Methods**

### **Ethical Considerations**

Ethical approval for the study was obtained from the Committee for Human Research at Stellenbosch University (S12/06/186). (Appendix A-4) Permission was obtained from the district Department of Health and all patients provided written informed consent prior to participating in the study. (Appendix A-1 and Appendix A-2)

Design: Cross-sectional, quantitative, descriptive study.

### **Sample Description**

Adult patients (18 years and older), diagnosed with PTB; and successfully followed up through the course of their treatment by the Cape Winelands District Health Care system, were considered for the study. Patients were included in the study if they had at least two negative sputum sample results and completed at least five months of anti-tuberculosis treatment. Patients were excluded if they presented with haemoptasis, pneumothorax, unstable cardiovascular status, aneurysms, recent eye surgery, recent abdominal or thoracic surgery or did not provide consent.

Setting: The Breede Valley is a sub-district of the Cape Winelands East District and has the town of Worcester at its centre. The Breed Valley District is a predominantly rural region about 112km from Cape Town central business district. Five primary health care facilities (PHCFs), (ie. Rawsonville Clinic, Worcester Clinic, Orchards Clinic, De Doorns Clinic and Touws River Clinic) were identified as sites for sputum sample collection in the region and were used for data collection.

### **Training**

The PI is a qualified physiotherapist with six years of clinical and teaching experience in the field of cardio pulmonary physiotherapy. Prior to commencement of this study, the PI was trained in the spirometry maneuver, by lung function technicians at Tygerberg Hospital. The manoeuvre was performed based on ATS guidelines<sup>48</sup>. Prior to data collection, the PI was responsible for the training of the research assistant (RA) for the collection of body mass index, height and weight data as well as the execution of the six minute walk test according to ATS guidelines<sup>49</sup>.

## Measurements and Procedures

### Lung Function

Post bronchodilator<sup>47</sup> lung function tests were performed using the SpiroBank II (MIR, Roma Italy) and analyzed using the Win Spiro v4.4 software. European Respiratory Society (Economic Community for Coal and Steel) normal reference values were applied and these were corrected for race (African descent). The Spirobank II (MIR, Roma Italy) is a battery operated handheld automatic calibrated spirometer<sup>50</sup> which uses a reusable turbine sensor to measure both volume and flow. (Appendix B-3) The Spirobank II office spirometer meets ATS (diagnostic devices) recommendations for accuracy and precision for measuring both FEV<sub>1</sub> and FVC<sup>51</sup>, and was found to be a practical, compact and valid when compared to the Jaeger MasterScope laboratory spirometer. For this study, calibration was checked at regular intervals using a 3l calibration pump and the deviation was not allowed to be more than 5% as per manufacturer recommendation. (Appendix C-7) The Spirobank II has been used in several studies<sup>50,52,53</sup>.

The device was piloted by the PI, prior to data collection, on a normal, student population (n=3) for standardization of manoeuvre procedure and reproducibility of lung function measurements according to ATS guideline standards. (Appendix C-6) Each student performed a minimum of three spirometry manoeuvres. The results of which were all reproducible with 150ml for FEV<sub>1</sub> and FVC.

### Health Related Quality of Life (The BOLD Core Questionnaire)

The BOLD Core questionnaire was created from existing, validated questionnaires<sup>47</sup>. The questionnaire has been validated in BOLD studies, following a standardized methodology, around the world, including Cape Town, South Africa<sup>47</sup>. The questionnaire also incorporates the SF-12v2 questionnaire, a shortened form of the SF-36v2, which is used to assess the patients HRQoL. The SF-12 has been validated in many studies and shows good correlation to the SF-36v2<sup>54</sup>. The 12 items reflect the following eight sub-domains: self-perceived general health (GH), bodily pain (BP), physical functioning (PF), role physical (RP), vitality (VT), role emotional (RE), mental health (MH) and social functioning (SF). A physical health component summary score (PCS) and a mental health component summary score (MCS) was generated for each patient using the Quality Metric software scoring algorithm. The scores were then normalized to be comparable with a mean population score of 50. The lower the physical health score (PCS) or mental health score (MCS), the more activity limitation the person has. The questionnaire has been translated into Afrikaans, and tested in one sample within the Cape Metropole<sup>47</sup>. The questionnaire includes information on respiratory symptoms (cough, sputum, wheezing, shortness of breath) occupation, respiratory diagnosis (asthma, emphysema, COPD, chronic bronchitis, TB, etc.), co-morbidities, health care utilization, medication use, activity limitation and health status. Permission to use the questionnaire was obtained from BOLD (Appendix A-1)

The questionnaire was piloted, by the PI, on the first n=2 patients during data collection to assess patient's general understanding of the questionnaire. Both patients understood the questionnaire and it was determined that the questionnaire would take 35-50 minutes to complete. The results were included and analysed with the study data.

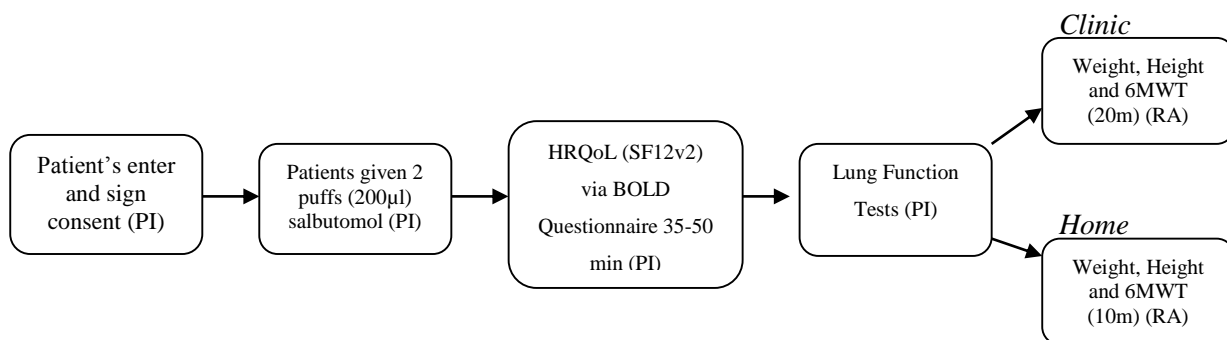
### Exercise Capacity - The Six Minute Walk Test (6MWT)

The 6MWT is a self-paced, submaximal measure of exercise capacity. During the 6MWT, patients choose their own intensity of exercise and are allowed to stop and rest during the test. The six-minute walk test (6MWT) is a valid, reliable, safe and cost-effective test to measure exercise capacity<sup>49</sup>. Several studies have used the 6MWT in a TB population<sup>17, 31,32,34,35</sup>.

The 6MWT was piloted, by the RA, on the first n=2 subjects during data collection to standardize the procedure according to ATS guideline standards<sup>49</sup>. The results were included and analysed with the main study data.

### Data Collection and Procedure

Data were collected between December 2012 and August 2013. Patient names and contact details were obtained from the tuberculosis registers at the five clinics by the PI. The RA was responsible for telephonically contacting patients and scheduling appointments. If patients were unable to attend the clinic, the research team would set up appointments for data collection at their homes. Figure 3.1 shows the procedure for data collection at clinics and at patients' homes.



**Figure 3.1: Procedure for data collection at clinics and patient homes**

Lung function data were collected by the PI using field spirometry. The spirometry maneuver was explained and fully demonstrated by the PI prior to execution by the patient. A minimum of three manoeuvre attempts were performed and attempts had to be reproducible within 150ml. Patients were given two minutes rest between manoeuvres or until their breathing rate returned to normal.

6MWT data were collected by the RA. Patients had to walk standardized distances which were marked by two cones. Baseline and post-test heart rate (HR) and oxygen saturation percentage (SPO<sub>2</sub>%) were measured using the Nellcor Oximax N-65 portable pulse oximeter (Covidien Colorado USA). Patients'

dyspnoea and fatigue were measured before and after the execution of the test using the Modified Borg Scale. (Appendix B-10).

The standardized 6MWT allows for a 30 meter track, however, due to space limitations within the community, distances had to be standardized to 20m at the clinics and further reduced to 10 m at patient's homes.

HRQoL data were collected by the PI using the BOLD core questionnaire. The questionnaire was administered by the PI in a private location.

### **Data Management and Quality Control**

All data were entered electronically by the PI and was stored on a password protected laptop. Spirometry data were downloaded via USB to a research laptop and patient information was coded.

Spirometry reports were checked by Prof. Irušen (Dept of Medicine, Stellenbosch University) for acceptability and reproducibility criteria According to ATS guidelines. The Spirobank II spirometer also has a built in instant quality report (on manoeuvre) with prompts as to what the patient is doing wrong. (eg. breathe all the air out of your lungs; breathe out faster etc.)

The RA used a quality control checklist (Appendix B-5) to ensure that the execution of the 6MWT was consistent. All encouraging commands to patients were uniform and spoken in a calm, monotone voice. Patients were informed of time intervals at 4 minutes, 2 minutes and at the end of the test.

### **Statistical Analysis**

Data were analyzed using Statistica v11. Descriptive statistics were used to describe basic features of the data. Means and standard deviations were reported for normally distributed data. Where data were skewed, medians and interquartile ranges were reported. T-test analysis was used to compare the distances of patients who walked the 20m course vs those who walked the 10m course. A p value of <0.05 was used to determine statistical significance, if any. Analysis of SF12v2 data were analysed using Quality Metric Health Outcomes Scoring Software v4.5. Patients' data were removed from analysis if they could not successfully complete an outcome according to the study criteria or stipulated guidelines.

### **Results**

A total 324 patient names were obtained from the folders at the five included clinics. Of these, 45 patients were contactable and successfully recruited for the study (Figure 3.2). The majority of patients n= 206 (63%) were not contactable, for a variety of reasons (Figure 3.2), and thus could not be recruited. Descriptive characteristics of the 45 included patients are shown in table 3.1.



**Table 3.1: Descriptive Characteristics of population**

<b>Demographics</b>	<b>Total n=45</b>
Gender (male) % (n)	56% (n=25)
Age (years)	39.88±10.20
Race	Coloured = 93% (n=42)      Black = 7% (n=3)
Weight (Kg)	55.60 ±11.21
Height (m) (mean & SD)	1.65 ±0.11
BMI (Kg/m <sup>2</sup> ) (mean & SD)	20.53±4.05
Years of Formal Schooling (years)	7.8 ±3.52
<b>Respiratory Conditions or Symptoms</b>	
Previously diagnosed with TB (%)	64.4% (n=29)
Number of times diagnosed with TB (mean & SD)	1.86±0.63
Diagnosed Emphysema (%)	0%
Diagnosed Asthma (%)	20% (n=9)
Diagnosed COPD (%)	6.6% (n=3)
Breathing problems interfered with ADL's (%)	35.5% (n=16)
Usually cough without a cold (%)	64.4% (n=29)
Usually cough up phlegm (%)	73.3% (n=33)
Have had wheezing in the last 12 months (%)	62.2% (n=28)
<b>Tobacco Use</b>	
Smoking History (%)	78% (n=35)
Cigarette Type (%)	Manufactured = 57.14% (n=20) Hand Rolled = 25.71% (n=9) Both = 17.14% (n=6)
<b>Occupational Exposure</b>	
Worked for longer than 1 year in a dusty job? (%)	78% (n=35)
Worked in a dusty job and cigarette smoker (%)	17.1% (n=6)
<b>Co-Morbidities</b>	
Heart Disease (%)	2% (n=1)
Hypertension (%)	8% (n=4)
Lung Cancer (%)	0%
Stroke (%)	6% (n=3)
<b>Spirometry</b>	
FEV1 % Predicted (Mean ± SD)	90.96±32.43
FVC % Predicted (Mean ± SD)	83.15±35.54
FEV1/FVC % Predicted (Mean ± SD)	93.71±14.64
Obstruction Pattern (%)	21% (n=9)
Restrictive Pattern (%)	25 % (n=11)
Mixed Pattern (%)	2% (n=1)
Normal Lung Function	52% (n=23)

The study sample comprised of 25 men and 20 women. The majority of the population classified themselves as coloured  $n=42$  (93%) and the average years formal schooling was  $7.8 \pm 3.52$  years. Almost two thirds of the population ( $n=29$ ; 64%) had previously been diagnosed with TB and  $n=4$  (8%) had been hospitalized for breathing problems before they were 10 years old. Co-morbidities such as heart disease ( $n=1$ ), hypertension ( $n=4$ ) and stroke ( $n=3$ ) were present in a total of eight patients. The mean BMI of  $20.53 \pm 4.73$  fell within normal range. Over three quarters of the population  $n=35$  (78%) had a smoking history or had been exposed to occupational dust while only a small proportion  $n=6$  (17%) were exposed to both. Only  $n=3$  (6.6%) patients were previously diagnosed with chronic obstructive pulmonary disease.

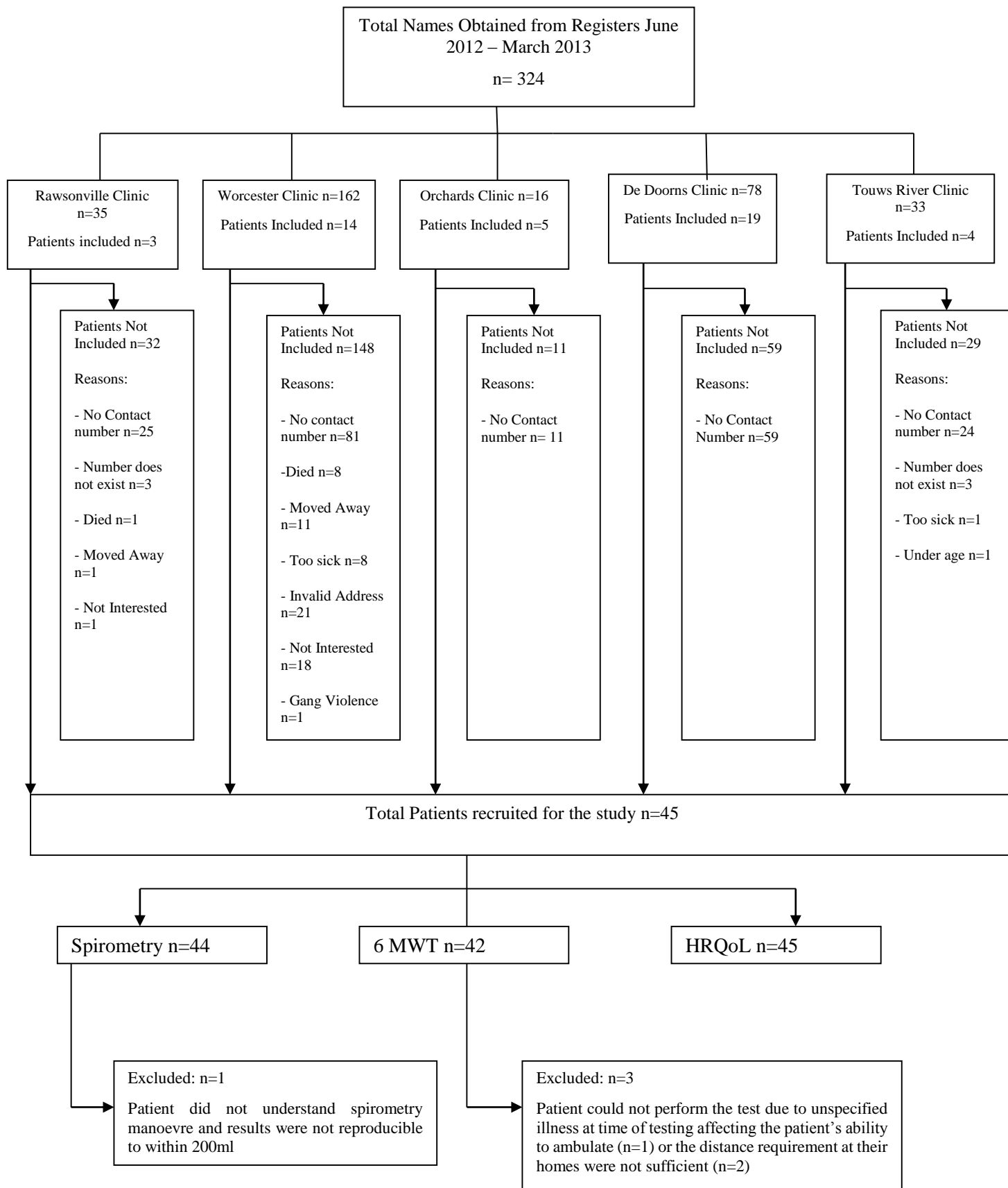
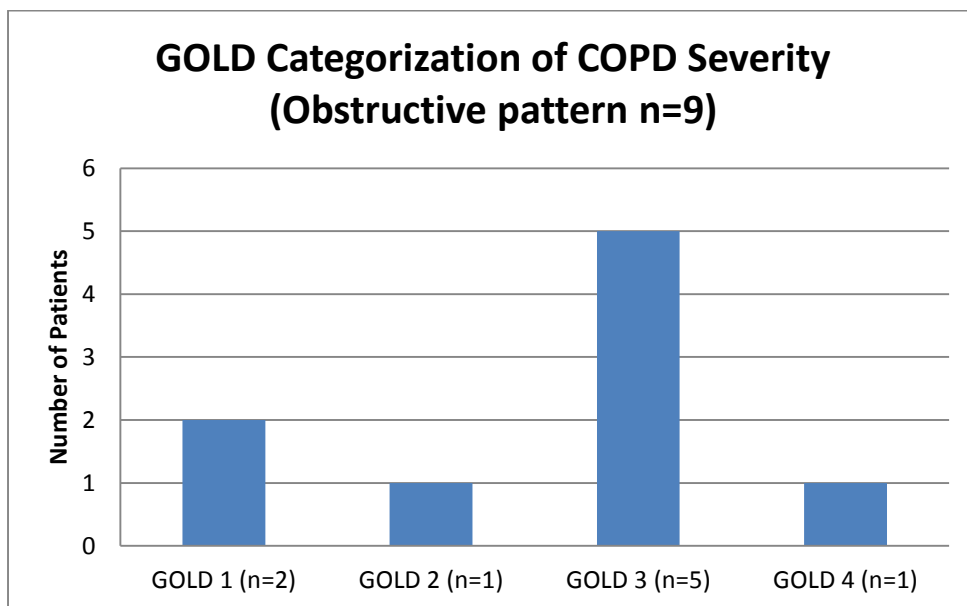


Figure 3.2: Flow diagram of Patients included and excluded from the study

## Lung Function

Of the 44 patients data analysed, just over half the sample, n=23 (52%) presented with normal lung function patterns, n=11 (25%) presented with a restrictive pattern, n=9 (21%) presented with an obstructive pattern and only n=1 (2%) presented with a mixed pattern (defined as  $FEV_1 < 80\%$  predicted,  $FVC < 80\%$  predicted and  $FEV_1/FVC < 0.7$ ). A summary of the spirometry values is shown in Table 3.1. No significant associations were identified between respiratory symptoms of cough and  $FEV_1$  or between smoking or occupational dust exposure and  $FEV_1$ . Spirometry results did not statistically differ between patients who identified themselves as smokers and those who did not. (Appendix C-1) Figure 3.3 summarizes the categorization of COPD severity according to GOLD criteria of the present population (n=9). Full spirometry results with GOLD classification are represented in Appendix C-5.



Key: GOLD 1:  $FEV_1 \geq 80\%$  predicted, GOLD 2:  $50\% \leq FEV_1 < 80\%$  predicted, GOLD 3:  $30\% \leq FEV_1 < 50\%$  predicted, GOLD 4:  $FEV_1 < 30\%$  predicted

**Figure 3.3: Categorization of Obstructive pattern according to GOLD criteria**

## Exercise Capacity

The mean ( $\pm$  SD) six minute walk distance (6MWD) for the 42 included patients (male n=24, 57.1%) was  $294.05m \pm 122.7m$ . The 6MWD was significantly shorter for patients who completed the 10m (n=27) course when compared to patients completing the 20m course (n=15) ( $p < 0.001$ ). While physiological measurements of oxygen saturation ( $SPO_2$ ) and heart rate remained constant from baseline to post-test measurements, patients perceptions of dyspnea ( $p < 0.001$ ) and fatigue ( $p < 0.001$ ) changed from baseline to post-test measurement (Table 3.2). The 6MWD was not associated with age ( $p = 0.279$ ;  $r = -0.167$ ) (Appendix C-4) or BMI ( $p = 0.461$ ;  $r = -0.113$ ) (Appendix C-4).

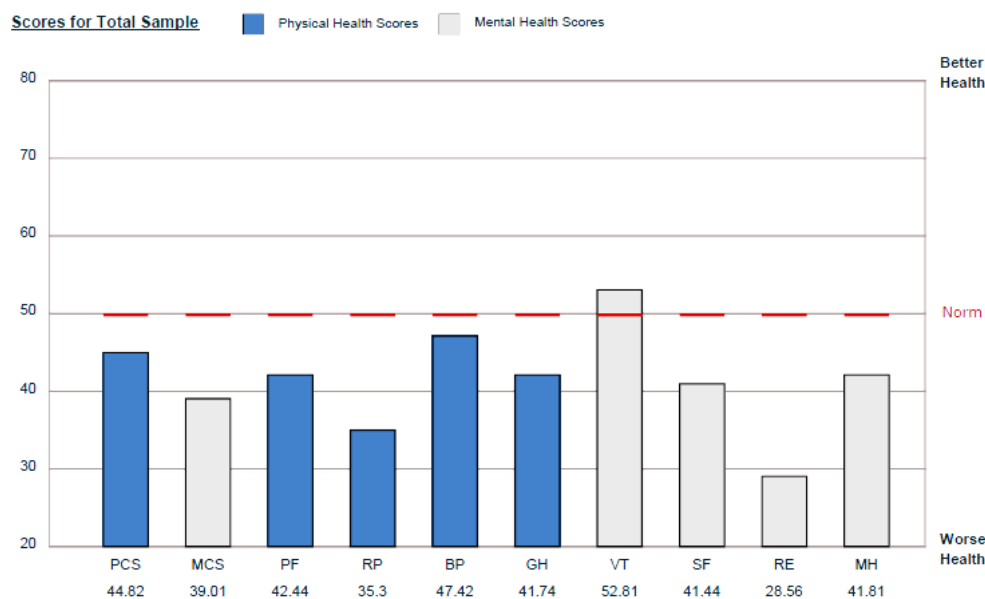
**Table 3.2: Results of 6MWT (Exercise Capacity)**

	<i>Baseline</i>	<i>Min Value</i>	<i>Max Value</i>	<i>End of Test</i>	<i>Min Value</i>	<i>Max Value</i>	<i>p Value</i>
<b>SPO<sub>2</sub>** (%)</b>	96.93±3.9	82	100	96.95±2.41	89	100	0.964
<b>Heart Rate** (BPM)</b>	91.06±18.01	49	129	92.88±19.19	53	143	0.235
<b>Dyspnoea** (Modified BORG)</b>	0.79±1.33	0.0	4.0	1.48±1.64	0.0	5.0	0.001
<b>Fatigue** (Modified BORG)</b>	0.98±1.53	0.0	5.0	1.70±1.73	0.0	6.0	0.001

Key: \* = mean ±SD; \*\* = mean ± SD and pValue; SPO<sub>2</sub>: Oxygen saturation

### Health Related Quality of Life

Respondents scored poorly on all sub-domains of the SF-12v2 except vitality. The mean summary scores obtained for both mental and physical health were lower than the population norm of 50. Role emotional and role physical scored lowest with mean scores of 28.1 and 35.27 respectively, while vitality scored the highest with 52.78. Both mental component score (MCS) and physical component score (PCS) were lower than the population norm. Patients' perception of their mental health was worse than their perception of their physical health. (See Figure 3.4).



**Figure 3.4: SF12v2 Domain Scores**

### Patient Recruitment Strategies

Despite the fact that the PI communicated with all of the PHCF managers on patient availability during the planning phase of the study, patient recruitment presented a major problem. Violence and unrest in the district, lack of transport, lack of patient motivation and understanding, migrant labour and incorrect

patient contact details were documented reasons why patients did not attend clinics. TB nurses relied on either community workers or word of mouth to communicate with patients. Therefore, the research team developed individual recruitment strategies for each of the clinics. (Appendix B-2) When patients with valid contact details were unable to attend the clinic, the research team went door-to-door setting up appointments and collecting data.

## **Discussion**

The findings of this pilot study suggest that patients who have completed anti-tuberculosis drug therapy and who are deemed cured may suffer from impaired lung function, a decreased exercise capacity and a decreased quality of life. However, the study also highlighted concerns with patient recruitment and the execution of outcomes measures in this rural environment. The information gathered in this pilot study will thus be valuable to inform the planning of future studies.

### **Lung Function and Tuberculosis**

A little under half of the population presented with either airflow obstruction or an obstruction/restriction pattern at the end of their PTB treatment. There seems to be very little agreement in the literature as to the dominant lung function pattern associated with the disease. Godoy et al (2012) found obstruction as the most prevalent pattern at 39%<sup>17</sup>. Snider et al (1971) found 23% of the population with an obstructive pattern and 19% with a mixed obstruction/restriction pattern<sup>5</sup>. PTB is associated with lung tissue scarring which could result in restrictive patterns<sup>55</sup>. However, field spirometry may mask certain lung function abnormalities and full body plethysmography is needed for accurate diagnosis.

### **Exercise Capacity and Tuberculosis**

6MWD was reduced in the present study. Studies by Sivaranjini et al (2010), Godoy et al (2012), Yoshida et al (2006) and Ando et al (2003) all reported reduced 6-minute walk test distances (6MWD) in PTB patients<sup>17, 33-35</sup>. Sivaranjini et al (2010) recorded a mean ( $\pm$ SD) 6MWD of 285.79 $\pm$ 79.81 meters in males and 245.5 $\pm$ 73.11 meters in females<sup>33</sup>.

The findings in the present study are similar to that of Sivaranjini et al (2010), and also found an overall reduced 6MWD in a cured PTB population. However, the aforementioned studies all used a 30m, indoor corridor to perform the 6MWT and distances varied between 245m and 415m<sup>33</sup>. Thus, it would appear that there is much variation in the distances achieved by patients post PTB treatment.

Despite the reduction in the 6MWD in the present study, patients still managed to achieve distances comparable to those found in other studies with more controlled environments.

Casanova et al (2011) recorded a mean 6MWD in 444 healthy patients of 571 $\pm$ 90m. This meant that on average, the patients had to turn 19 times during the test<sup>56</sup>. Patients in the present study turned an average of 19 times for those who walked 20m and 24 times for those who walked 10m. ATS guidelines recommend that the test should ideally be done indoors in a 30m straight corridor. Normative values have been established for this distance and distances usually exceeding 30m<sup>57</sup>. In the primary care

setting, this is often not possible and space limitations force clinicians and researchers to modify the course length<sup>57</sup>.

Beekman et al (2013) evaluated the impact of a course length of 30m versus a course length of 10m on 6MWD in COPD patients and found that a 10m course significantly shortens the distance that people with COPD achieve on the 6MWT<sup>57</sup>. Therefore, normative equations and predictors of morbidity and mortality of the 30m course cannot be assumed when using a 10m course<sup>57</sup>. Factors such as patients' poor health perception, understanding and lack of previous exposure to the 6MWT may have influenced the overall 6MWT results. A recent study by Bohannon et al (2014) concluded that based on completion rates, distances walked, reliability and high correlation between distances walked over 2 minutes and 6 minutes, the distance covered in the 2 minute walk test may be considered a viable alternative to the distances covered in the 6MWT in community-dwelling individuals<sup>58</sup>.

### **Health Related Quality of Life and Tuberculosis**

The results of the present study suggest that PTB does negatively impact on patients perceived HRQoL in both a physical and mental capacity. This result mirrors that of a systematic review which suggested that patients' perception of their physical health appeared to be more affected by the disease but improved quickly with treatment. Perceptions of mental health, however, tended to persist well after patients were deemed microbiologically "cured".

### **Clinical Implications**

The results of this pilot study should be interpreted with caution. Adaptations to the 6MWT course were necessary in the rural environment. While our findings are similar to the reported 6MWD in a PTB population, normal reference values cannot be assumed for a reduced course length. Researchers should develop suitable reference values for a reduced 6MWD for use in the rural setting.

Even though the researcher developed individual recruitment strategies for each of the PHCF's, we were only able to recruit 45 patients. Future research should build on the strategies of the present study to optimize patient recruitment in the rural setting.

### **Limitations to the Study**

There are limitations to the present study. Due to the small sample size, the results are not generalizable for the population. The BOLD Core Questionnaire had never been used on a rural population before. This could have presented bias when patients answered the questions. Due to space limitations at both the clinics and the homes of the patients, the 6MWT course length had to be reduced and therefore established reference equations cannot be applied in this population. This study was however done as a pilot field study and offers realistic and pragmatic insight into the study population.

**Conclusion**

The findings of this cross sectional pilot study suggest that patients who have completed anti-tuberculosis drug therapy and who are deemed cured may suffer from impaired lung function, a decreased exercise capacity and a decreased quality of life. Future studies should investigate whether or not these patients would benefit from pulmonary rehabilitation. The data reported in this pilot study can inform the planning of a larger observational study in the Overberg region.

**Conflicts of Interest**

The authors declare that there are no financial or personal associations that may have inappropriately influenced this study.

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**Author Contributions**

KD collected data, processed data and drafted the manuscript. SH and EI contributed to the development of the study concept, analysis and interpretation of the data and provided critical revision of the manuscript for important intellectual content. HP assisted in the planning of data collection and collected data. All authors read and approved the final manuscript.



## Chapter 4

### General Discussion

This thesis set out to review the current literature and describe the characteristics of a cured pulmonary tuberculosis (PTB) population in terms of lung function measurements, health related quality of life (HRQoL) and exercise capacity in a rural community in the Breede Valley District of the Western Cape, South Africa. To date, no South African study has described this population. Previous studies, including the BOLD study<sup>47</sup>; have focused on lower social economic communities in the Cape Metropole of the Western Cape, South Africa. The findings of this study suggest that patients who have completed anti-tuberculosis drug therapy and who are deemed cured may suffer from slightly impaired lung function, a decreased exercise capacity and a decreased quality of life. The results of this study therefore agree with a previous study by Godoy et al (2012) who described similar outcomes in a Brazilian population<sup>17</sup>.

#### 4.1 Tuberculosis and its impact on Quality of Life in South Africa

In South Africa, the directly observed tuberculosis short course (DOTS) is implemented for the diagnosis and treatment of PTB. Despite the fact that the program has been around since 1995, cure rates in South Africa remain well below the World Health Organisations (WHO) recommendation of 85%. DOTS is almost strictly applied from a biomedical perspective and therefore, current TB literature is almost entirely written from that viewpoint<sup>30</sup>. The program mainly focuses on bacteriological markers and outcomes such as cure, mortality and treatment defaulted/failure<sup>8</sup>. Unfortunately, PTB patients do not only have to deal with the physical symptoms of the disease, but with the physiological, financial and psychosocial issues associated with the disease as well<sup>8</sup>. In high burden areas like South Africa, stigmatisation and patients perceptions of the disease also contribute to the lack of successful management of the disease<sup>30</sup>. The symptoms and burden of disease therefore often extends to beyond chemotherapy or once a patient is deemed cured.

The findings of this study are in alignment with the findings of the scoping review (chapter 2) in that patients who have completed anti-TB chemotherapy and who are considered cured continue to present with a decreased quality of life. This study found that patient perceptions of mental health were lower than patient perceptions of physical health at the time of assessment. This is in contrast to a large population-based South African study by Louw et al (2012) who found that perceptions of physical health were lower than perceptions of mental health. This could be due to the fact that Louw et al (2012) measured patients' quality of life one month into their PTB treatment<sup>59</sup>. Other studies (Godoy et al 2012, Kruijshar et al 2010) who measured patients' quality of life at various stages throughout their PTB treatment, found that perceptions of physical health were lower at diagnosis, but rapidly improved as PTB treatment progressed<sup>17,21</sup>. However, perceptions of mental health continued to remain low even

after completion of PTB treatment<sup>60</sup>. Louw et al (2012) further identified predictors of good physical health as higher educational level, lower psychological stress, being diagnosed with less than three chronic illnesses and being HIV negative. Predictors of poor mental health were poverty, scoring low on the psychological distress scale and being HIV positive. In the present study, a small proportion of the population (16%) was diagnosed with co-morbidities but all had fewer than three, and the mean years of formal schooling was 7.8 years. These are all predictors of good physical health. However, poverty and unemployment was a huge issue in the present population and this could have contributed to their ongoing poor perception of their mental health status. The present study brings to light a global issue in the current approach to tuberculosis management. Although the WHO aims to eradicate the disease, the psycho-social issues that patients are left with remains a problem. A more holistic approach that provides patients with treatment options after microbiological cure is needed to truly deem a patient cured.

#### **4.2 Tuberculosis and Lung Function: Colliding Epidemics in a high burden setting**

A rise in the global burden of chronic obstructive pulmonary disease (COPD) has sparked recent research efforts to focus on the non-tobacco causes of COPD. Among these non-tobacco related causes, PTB has been marked as an independent risk factor for the development of COPD. Even though the aetiologies of the diseases are different, both result in pulmonary scarring which could lead to airflow limitations<sup>60</sup>. The results of this study found that just under half the population presented with lung function abnormalities. Pasipanodya et al (2007) found restriction to be the most predominant pattern five months into PTB treatment in a population in the United States<sup>20</sup>. There still seems to be much debate in the literature as to what the predominant lung function abnormality is related to PTB. However, there is definitely enough agreement to say that PTB patients do suffer from lung function abnormalities even once they have been deemed cured.

Although not measured in the current study, it may be worth mentioning that pulmonary function abnormalities tend to persist or change after completion of TB treatment<sup>43</sup>. In a study conducted on gold miners in South Africa, FEV<sub>1</sub> and FVC values were found to be worse six months after treatment but stabilized 13 to 18 months after treatment<sup>10</sup>. Chung et al (2011) identified smear-positive disease, extensive disease before treatment, prolonged treatment duration and less radiographic improvement after treatment as positive risk factors for the deterioration of lung function after treatment<sup>61</sup>. In the large population based studies (PREPCOL, PLATINO and BOLD Cape Town South Africa), a mainly 'self-reported' history of PTB was positively associated with the development of COPD. However, these studies fail to expose the dynamic progression of the pathology after treatment. The systematic review by Allwood et al (2013) however, confirms the association between a history of PTB and airflow obstruction, but whether PTB should be added to the list of recognized exposures for the future development of COPD is unclear<sup>43</sup>. Larger studies measuring the lung function of confirmed PTB patients followed up to 18 months after treatment will provide the evidence to confirm the causal nature

between PTB and airflow obstruction. However, the results of this study do not differ from smaller studies done on similar populations<sup>43</sup>.

### **4.3 Tuberculosis and its impact on Exercise Capacity**

The six-minute walk test (6MWT) is a valid, reliable, safe and cost-effective test to measure exercise capacity in COPD patients<sup>49</sup>. The 6MWT is also a widely-used and validated test of exercise capacity for cardiac and pulmonary disorders which could be used as a predictor of morbidity and mortality<sup>62</sup>. Health professionals may opt for the 6MWT above other exercise tests due to its close resemblance of activities of daily living, its simplicity and its broad applicability to a wide variety of patient groups<sup>57</sup>. Physiotherapy practices in the primary care setting often have to decrease the course length distance of the 6MWT due to limited available space and therefore opt to perform the test over 10m instead<sup>57</sup>.

The mean walking distance achieved in this study was 294.5m±122.7m. Due to space limitations at the clinics, the authors of this study had to reduce the course length, as measured at the clinics, to 20m. When engaging patients at their homes, the course length had to further be reduced to 10m as the properties of the homes were small. The impact of PTB on exercise capacity could therefore not be established in this population as reference values for the 6MWT are calculated using a distance of 30m or more<sup>57</sup>. However, the distance walked in the present study is comparable to other studies utilizing a 30m course length in a similar population. Previous studies recorded ranges that varied from 245m to 415m in PTB populations<sup>17,31-33,35</sup>. These distances are still well below the distance achieved by healthy individuals<sup>56</sup>

The 6MWT is often used as an outcome measure for pulmonary rehabilitation programs and has been well established in COPD and cardiac rehabilitation programs. There have been very few studies evaluating the impact of pulmonary rehabilitation programs on patients with tuberculosis<sup>63</sup>. Exercise training is an important part of pulmonary rehabilitation and has shown to improve activities of daily living and quality of life scores in patients with COPD<sup>63</sup>. It is generally believed that pulmonary rehabilitation can be beneficial in a variety of non-COPD lung disorders including cystic fibrosis, pulmonary fibrosis and restrictive thoracic disease<sup>35</sup>. A study by Ando et al (2003) compared a group of post-tuberculosis patients who had undergone thoracoplasty and presented with stable restrictive or mixed lung function patterns, with a group of stable COPD patients after a nine week pulmonary rehabilitation program using the 6MWT as a comparable outcome measure<sup>35</sup>. The authors of that study found that firstly, the degree of disability between groups are comparable if the FEV<sub>1</sub> is the same. Secondly, both groups benefitted from a nine week pulmonary rehabilitation program<sup>35</sup>. The six-minute walk distance (6MWD) had improved similarly in both groups and was maintained for up to six months after the program<sup>35</sup>. Another study by Yoshida et al (2006) evaluated the short-term effects of exercise training to improve exercise performance in patients with tuberculosis sequelae presenting with a higher proportion of restrictive ventilator deficit than obstructive deficit<sup>34</sup>. The authors found a 10% improvement in 6MWD after exercise training. Exercise training using the 6MWT as a comparable outcome was considered safe and effective in both of the above studies.

## 4.4 Challenges of Research in the Rural Setting

### 4.4.1 The Community

Worcester is a small town with a population of approximately 317 373<sup>2</sup>. It serves as a central hub for the Breede Valley District. The district extends from Rawsonville to Touws River, covering a distance of approximately 100km between the towns. Most of the surrounding area is privately-owned farmland. The majority of the population included in this study classified themselves as coloured, and if employed, worked on the farms. Many of the farmers in the district made use of migrant labourers who are employed during the harvesting season of the year. The area of De Doorns was plagued by violent protests during the start of the data collection period of the current study and the researchers were unable to access this community during the protests. The researchers could also only access certain local communities in the Worcester region between Tuesdays and Thursdays and between the times of 8am and 2pm. These areas were deemed as unsafe to access any other times.

### 4.4.2 The Clinics

The five included clinics in this study each service a dedicated area between Rawsonville and Touws River. Patients have access to a clinic depending on their residential location. Worcester CHC is the largest clinic in the district and generally handles the TB caseload of the town and its surrounding communities. TB patients are initially assessed at the clinic but receive their medication via DOTS provided by community workers. Most of the clinics in the district make use of volunteer community workers to provide care for the chronically ill who struggle to access the clinics. Community workers therefore monitor DOTS patients but are also responsible for patients with other chronic illness such as polio, diabetes and strokes. The clinics do not have an electronic database for TB diagnosis and monitoring in place. TB nurses therefore have to record all patient data manually in a TB register. At majority of the clinics, the researchers could not be accommodated inside the clinic due to limited space available. Data collection had to therefore be done outside.



**Figure 4.1: Spirometry and 6MWT at Rawsonville and Touws River Clinics**

#### ***4.4.3 The Reliability of Patients***

The researchers' initial plan was to recruit patients at their five month sputum follow-up appointments at the clinics. The researchers soon discovered that patients were not given a specific time and date for their follow-up appointments but rather a week within which they had to return for their sputum appointment. This made it difficult for the researchers to know when to be at which clinic. In the more rural areas, patients had to occasionally walk up to 30km to the nearest clinic. TB nurses at the larger clinics also struggle to communicate with patients as their contact details are seldom accurate. The TB nurses therefore send letters with community workers informing patients of an overdue appointment.

#### ***4.4.4 The BOLD Core Questionnaire***

The BOLD Core questionnaire is a questionnaire that was created mostly from existing, validated questionnaires<sup>47</sup>. The questionnaire has been validated in multi-national studies utilizing the BOLD methodology. It is intended to collect data on respiratory symptoms, exposure to risk factors, occupation, co-morbidities, health care utilization, activity limitations and health status<sup>47</sup>. Even though the questionnaire has been translated into Afrikaans and validated in the Uitsig community in Cape Town, patients in this population seemed to struggle understanding the level of questioning in the questionnaire. Patients from the more rural areas who generally had a lower level of education took much longer to complete the questionnaire than those with a higher level of education. It appeared to researchers that patients would answer the questions whether they understood the questions or not. On average, the questionnaire took between 30 and 40 minutes to complete. The questionnaire did not seem patient friendly for the study population. Allowing patients to speak freely about their experiences after PTB treatment rather than provide them with a set of preset answers may have resulted in more reliable responses in the present population.

#### **4.5 Limitations to the Study**

This study presented with a few limiting factors which may have influenced the validity of the results. External validity was mainly affected by population validity. Firstly, the small sample size means that the results cannot be generalized for the current population. Personological factors, such as patients not truly understanding the motivation behind why they were being subjected to the tests, as well as patients' poor perceptions of their health status may have impacted on their motivation to perform tests. The questionnaire used in the study presented patients with multiple choice options. This could have affected the measurement of the dependant variables of the questionnaire when compared to allowing patients to speak freely about their perceptions of the disease. Challenges (such as space limitations and environmental factors that were not ideal for data collection) may have impacted on the quality of measurement of outcome measures. The time period for data collection was limited and this had a huge impact on sample size and therefore generalizability of the results. Gaining permission from the local farmers to access the farms will ensure patients are present for data collection as for many patients, the

more time they spend away from work the less they are paid. Improved patient preparation and an explicit explanation of the study procedure will help patients better understand the reasons for the research and may improve patient motivation.

#### **4.6 Recommendations for future research and Clinical Relevance**

The information gathered in this pilot study should be used to inform researchers interested in executing larger observational studies in the Overberg region.

- **Recruitment Strategies:** To ensure a larger population, future researchers should understand the barriers associated with patient recruitment in the Overberg region. Despite planning and good communication with the PHCF managers of the included clinics, issues such as migrant labour, violence and patients unable to attend the clinics were major barriers. Each clinic in the present study had a different means of communicating with the patients and the researchers had to adapt and develop patient recruitment strategies for each clinic. Possibly including the farmers in the planning of future studies and intercepting patients at their place of work could ensure a more compliant patient sample as patients are paid for hours worked and missing work to attend clinics would mean less income.
- **The 6MWD:** The 6MWD had to be reduced to accommodate lack of space at the clinics and the small living area with rough rocky terrain and steep gradients at patients' homes. This is a common occurrence in rural research around the world<sup>57</sup>. Despite the modifications to the 6MWT in the present study, distances achieved were comparable to other studies executing the 6MWT in a similar population. The variability in the 6MWT distances achieved in the literature and modifications to accommodate lack of space in the rural setting means that established reference values and indicators for morbidity and mortality should not be used in this population. Researchers should consider the impact of these modifications and establish normal reference values for a reduced 6MWT distance and possibly include measurements of maximal oxygen consumption (VO<sub>2</sub>max) as an indicator of sub-maximal aerobic exercise capacity. The 2 minute walk test should also be considered as a viable alternative to the 6MWT in the community setting.
- **The BOLD Core Questionnaire:** While the questionnaire has been previously validated in a COPD population in the Cape Metropole of the Western Cape, the PI is of the opinion that some sections of the questionnaire may have been difficult for patients in the more rural farmlands to answer. Some patients took much longer to respond to questions than others. Stigmas associated with TB in the community may have also played a role in the way patients responded to questions, despite the fact that all patients were interviewed privately. The SF-12v2, however, was sensitive enough to reveal patients perceptions of their physical and mental health status, which were comparable to health perceptions in other PTB populations.
- Researchers should consider establishing reliable reference data values for a decreased course length in the 6MWT. This will aid in more reliable assessment of exercise capacity in this

study population. The 2 minute walk test should also be considered as an alternative to the 6MWT in the community where patient compliance and completion rates of the 6MWT are poor.

- Albeit that the researchers developed specific recruitment strategies for each of the included PHCF's, only a small number of patients were recruited. Future studies should further develop these strategies to optimize patient recruitment.
- The inclusion of a control group of normal people from the same region may provide future researchers with a baseline for comparison of HRQoL in the region.
- The authors suggest that cured PTB patients be monitored for up to 18 months after they have completed PTB treatment to establish whether there is progression of the pathology with relation to spirometry, HRQoL and exercise capacity

#### **4.7 Conclusion**

The findings of this observational study suggest that even after microbiological cure, PTB patients suffer from a decreased quality of life, impaired lung function and possibly, a decreased functional exercise capacity. Policies addressing a bio-psycho-social model should be implemented at primary care level which includes a holistic management of PTB patients, even after they have been deemed microbiologically cured. Physiotherapists at primary care institutions should continue monitoring patients after anti-TB treatment and consider including these patients in a regular pulmonary rehabilitation program as early as possible. This may have a positive impact on a patient's quality of life while simultaneously improving/maintaining the patient's lung function. This was a pilot study aimed at describing the functional health status and quality of life of a cured PTB population in the Breede Valley sub-district of the Overberg region in the Western Cape. The information gained and recruitment strategies developed in this pilot study is intended to inform the planning and development of a larger observational study in the region.

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## Appendix A-1: Permission to gain access to the clinics and to use the BOLD Core Questionnaire

Daniels, KJ, Mr <kurtd@sun.ac.za>

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**From:** Daniels, KJ, Mr <kurtd@sun.ac.za>  
**Sent:** 22 November 2012 01:02 PM  
**To:** 'shatitus@pgwc.gov.za'  
**Subject:** FW: Health research permission: Rural project 2012RP139

Dear Sr Titus

My project has finally been approved by PGWC and they have granted me access to the Worcester region (Please see email from Carmen Sisam below). I was wondering if I could perform a pilot trial run to orientate the research assistants as to how they need to collect data, at Worcester CHC on Monday 26<sup>th</sup> November? When we initially spoke, you mentioned that we could use the UKWANDA room at the clinic. The pilot will only be 3-5 patients and we basically want to see how long the whole procedure will take and if there are any hiccups with our process.

Thank You

Kurt Daniels  
Junior Lecturer / Marketing  
Division of Physiotherapy  
Faculty of Medicine and Allied Health Sciences  
Stellenbosch University  
Tygerberg Campus

Office Number: +2721 938 9017

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**From:** Carmen Lyn Sisam [mailto:CarmenLyn.Sisam@westerncape.gov.za]  
**Sent:** 22 November 2012 09:03 AM  
**To:** Beyers, N, Prof <nb@sun.ac.za>; Barsdorf, N, Dr <nbarsdorf@sun.ac.za>; Hanekom, SD, Dr <sdh@sun.ac.za>  
**Cc:** Irusen, EM, Prof <eirusen@sun.ac.za>; Daniels, KJ, Mr <kurtd@sun.ac.za>; Charlene Roderick  
**Subject:** RE: Health research permission: Rural project 2012RP139

Dear Susan

Access to Cape Winelands for this project has been approved.

You will receive your approval letter within the next week.

Kind regards  
Carmen sisam

---

**From:** Beyers, N, Prof <nb@sun.ac.za> [mailto:NB@sun.ac.za]  
**Sent:** 22 November 2012 08:51 AM  
**To:** Barsdorf, N, Dr <nbarsdorf@sun.ac.za>; Hanekom, SD, Dr <sdh@sun.ac.za>  
**Cc:** Irusen, EM, Prof <eirusen@sun.ac.za>; Daniels, KJ, Mr <kurtd@sun.ac.za>; Carmen Lyn Sisam  
**Subject:** RE: Health research permission: Rural project 2012RP139

Dear Susan

I handed the e-mail string to the PHRC secretariat yesterday and Carmen Sisam kindly offered to give feedback

Kind regards

Daniels, KJ, Mr <[kurtd@sun.ac.za](mailto:kurtd@sun.ac.za)>

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From: Burney, Peter G J [[p.burney@imperial.ac.uk](mailto:p.burney@imperial.ac.uk)]  
Sent: 06 June 2012 11:08 AM  
To: Daniels, KJ, Mr <[kurtd@sun.ac.za](mailto:kurtd@sun.ac.za)>  
Cc: BOLDCENTREUK  
Subject: RE: BOLD core questionnaire

Dear Mr Daniels,

Thank you very much for this clarification.  
There is no problem in you using the BOLD core questionnaires.  
I assume (maybe wrongly) that your predominantly farming community around Worcester will be predominantly Afrikaans speaking, and if that is so you ought probably to use the questionnaire translated by the BOLD programme in Cape Town. As some people at Tygerberg were involved with the Lung Health Survey - of which the BOLD survey was a part - including Emmarantia van Schalkwyk, I guess this would not be a problem. Would you like me to ask?

Best wishes,

-----Original Message-----

From: Daniels, KJ, Mr <[kurtd@sun.ac.za](mailto:kurtd@sun.ac.za)> [<mailto:kurtd@sun.ac.za>]  
Sent: 06 June 2012 09:02  
To: Burney, Peter G J  
Subject: RE: BOLD core questionnaire

Hello Dr Burney

I apologise for the late reply, I have been away from my desk. I am conducting this epidemiological study as a masters project.

I thought I would give you some background into what we are looking for. As you are probably well aware, South Africa has one of the highest burdens of Tuberculosis worldwide. While simultaneously presenting with an exponentially high burden of COPD, of which a large percentage are diagnosed with causes other than smoking. At primary health care level, these epidemics are colliding, and the TB patient that has successfully completed treatment and is classified as cured is still presenting with a decreased quality of life. The community we have chosen is a predominantly farming community in Worcester, about 112km from the CBD of Cape Town.

Therefore, the purpose of this study is to identify the prevalence of COPD in newly cured TB patients. The BOLD methodology is well structured and uniform throughout the world, and therefore, we thought of applying the structure to our project. So, unfortunately, the population does not represent that which the BOLD methodology requires. However, it does provide a sound infrastructure for the basis of this study. The plan is to eventually cover most of that district as many previous studies were conducted in the Cape Metropol.

I do not want to step on anyone's toes with regards to copyrighted information. Thus, would it be possible for us to use the questionnaire, but not be referred to as part of the BOLD studies?

If so, Prof Vollmer suggested that I ask you for the updated English version of the questionnaire?

The BOLD organisation will be acknowledged in the final thesis, but at this stage I would not want to classify myself as part of the BOLD team. (Hopefully one day :-)

I do realise that you are extremely busy. Thank you for taken the time to respond to me.



## **Appendix A-2: Consent Form English**

### **PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM**

#### **TITLE OF THE RESEARCH PROJECT:**

An Investigation into the lung function, health related quality of life (HRQoL) and functional capacity of a cured Pulmonary Tuberculosis (PTB) population in the Breede Valley: a pilot study

#### **PREFERENCE NUMBER:**

**PRINCIPAL INVESTIGATOR: Mr K.J. Daniels**

**ADDRESS: 30 The Vines West**

**Steenbok Street**

**Durbanville**

**Cape Town**

**CONTACT NUMBER: 0844477490**

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Committee for Human Research at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

The aim of this study is to try and identify problems that you might have in your everyday life after you have completed your TB treatment. TB does damage to the lung tissue and therefore could affect your breathing, work or the way that you do your everyday activities. Participants for this study are selected based on the local clinics database of patients who have been on TB treatment. Participants who test negative for TB at their 5 month clinic visit will be asked to participate in this study.

Participants will be asked to complete a questionnaire about their breathing, daily activities and lifestyle. They will then be asked to perform lung function tests which will be done by a trained professional. Lastly, they will be asked to participate in a test designed to assess how tired they get while doing normal activities.

Why have you been invited to participate?

Participants have been specifically invited to participate in this study because you have been diagnosed with TB, and are currently completing your TB treatment at your local clinic.

What will your responsibilities be?

As a participant in the study, you will be expected to complete a questionnaire, perform a test to assess how well your lungs work and perform a test to assess how tired you get while doing everyday activities.

Will you benefit from taking part in this research?

You do not stand to gain any financial benefit from the research. The results of this study will benefit patients in the future and help us identify how to effectively manage patients after they have completed their TB treatment.

Are there any risks involved in your taking part in this research?

The study procedures are designed to have minimal risks. Participants are advised to discontinue the tests if they feel heart or chest pains, severe shortness of breath, severe headaches and dizziness.

As a participant, will be expected to perform measurements to see how well your lungs work 20 minutes after the administration of a short acting bronchodilator (medication to help you breathe easier). Fainting in older people and participants with weak lungs are the primary risks associated with the manoeuvre. Tremors and an increase in heart rate are adverse effects associated with bronchodilator usage. (medication)

If you do not agree to take part, what alternatives do you have?

This study serves as a baseline study for future implementation. If you do not wish to participate, the management of your condition will continue as per normal.

Who will have access to your medical records?

All information gathered and used in the study will be treated as strictly confidential and protected. If the study is used in publications, the identity of the participant will remain anonymous. Only doctors, the researcher and specifically appointed research assistants will have access to the information.

Will you be paid to take part in this study and are there any costs involved?

**No, you will not be paid to take part in the study. There will be no costs involved for you, if you do take part. Your study appointments will coincide with your normal clinic appointment.**

Is there anything else that you should know or do?

**You should inform your family practitioner or usual doctor that you are taking part in a research study.**

**You can contact Mr Kurt Daniels at tel. 0844477490 if you have any further queries or encounter any problems.**

**You can contact the Committee for Human Research at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.**

**You will receive a copy of this information and consent form for your own records.**

Declaration by participant

By signing below, I ..... agree to take part in an inspiratory muscle training program research study entitled An Investigation into the lung function, health related quality of life (HRQoL) and functional capacity of a cured Pulmonary Tuberculosis (PTB) population in the Breede Valley: a pilot study

**I declare that:**

I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.

I have had a chance to ask questions and all my questions have been adequately answered.

I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.

I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) ..... on (*date*) ..... 2012

Signature of participant      Signature of witness

Declaration by investigator

I (*name*) ..... declare that:

I explained the information in this document to .....

I encouraged him/her to ask questions and took adequate time to answer them.

I am satisfied that he/she adequately understands all aspects of the research, as discussed above

I did/did not use a translator. (*If a translator is used then the translator must sign the declaration below.*)

Signed at (*place*) ..... on (*date*) ..... 2012

Signature of investigator      Signature of witness

Declaration by translator

I (*name*) ..... declare that:

I assisted the investigator (*name*) ..... to explain the information in this document to (*name of participant*) ..... using the language medium of Afrikaans/Xhosa.

We encouraged him/her to ask questions and took adequate time to answer them.

I conveyed a factually correct version of what was related to me.

I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*) ..... on (*date*) ..... 2012

Signature of translator    Signature of witness

### **Appendix A-3: Consent Form Afrikaans**

#### **DEELNEMERINLIGTINGSBLAD EN -TOESTEMMINGSVORM**

#### **TITEL VAN DIE NAVORSINGSPROJEK:**

An Investigation into the lung function, health related quality of life (HRQoL) and functional capacity of a cured Pulmonary Tuberculosis (PTB) population in the Breede Valley: a pilot study

#### **VERWYSINGSNOMMER:**

**HOOFNAVORSER: : Mr K.J. Daniels**

**ADRES: 30 The Vines West**

**Steenbok Street**

**Durbanville**

**Cape Town**

**KONTAKNOMMER: 0844477490**

U word genooi om deel te neem aan 'n navorsingsprojek. Lees asseblief hierdie inligtingsblad op u tyd deur aangesien die detail van die navorsingsprojek daarin verduidelik word. Indien daar enige deel van die navorsingsprojek is wat u nie ten volle verstaan nie, is u welkom om die navorsingspersoneel of dokter daarvoor uit te vra. Dit is baie belangrik dat u ten volle moet verstaan wat die navorsingsprojek behels en hoe u daarby betrokke kan wees. U deelname is ook **volkome vrywillig** en dit staan u vry om deelname te weier. U sal op geen wyse hoegenaamd negatief beïnvloed word indien u sou weier om deel te neem nie. U mag ook te eniger tyd aan die navorsingsprojek onttrek, selfs al het u ingestem om deel te neem.

Hierdie navorsingsprojek is deur die Komitee vir Mensnavorsing **van die Universiteit Stellenbosch** goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki en die Etiese Riglyne vir Navorsing van die Mediese Navorsingsraad (MNR).

#### **Wat behels hierdie navorsingsprojek?**

Die doel van die studie is om te identifiseer of jy probleme ondervind in jou daaglikse lewe nadat jy die TB behandeling voltooi het. TB veroorsaak skade aan die long weefsel en kan gevolglik 'n invloed he op jou asemhaling, werk en self op die wyse waarop jy alledaagse aktiwiteite uitvoer. Pasiënte vir die studie word gekies deur databasisse van die klinieke in hulle omgewing na te gaan en so te sien watter pasiënte op die 6 maande TB behandeling was. Pasiënte wie wat op TB behandeling was en na 5 maande by hulle kliniek besoek negatief toets, sal gevra word om aan die studie deel te neem. Wanneer die pasiënte dan terug keer na die kliniek vir hulle finale besoek op 6 maande, sal hulle dan gevra word om 'n vraelys in te vul oor hulle asemhaling, daaglikse aktiwiteite en leefstyl. Daarna sal gevra word dat hulle 'n longfunksie toets ondergaan, die toets sal deur 'n proffesionele persoon toegepas word. Laastens

sal hulle ook gevra word om deel te neem aan 'n toets wat spesifiek ontwerp is om te waar te neem hoe moeg die pasient raak terwyl hulle normale aktiwiteite uitvoer.

Waarom is u genooi om deel te neem?

U word spesifiek uitgenooi om deel te neem aan die studie aangesien u gediagnoseer was met TB en tans u TB behandeling by u naaste kliniek voltooi.

Wat sal u verantwoordelikhede wees?

As 'n deelnemer in die studies sal daar van u verwag word om 'n vraelys in te vul; 'n longfunksie toets te ondergaan en 'n toets te doen om sodoende u funksionele kapasiteit te bepaal.

Sal u voordeel trek deur deel te neem aan hierdie navorsingsprojek?

Deelnemers sal geen finansiële vergoeding ontvang vir die navorsing nie. Die uitslag van die studies sal al die deelnemers in die toekoms tot voordeel staan, dit sal ons help om pasiënte meer effektief te behandel nadat hulle hul TB behandeling voltooi het.

Is daar enige risiko's verbonde aan u deelname aan hierdie navorsingsprojek?

Die studie is ontwerp om minimale risiko's te dra. Deelnemer word aanbeveel om dadelik met die toets te stop indien hulle enige hart, borskaspyne, kortasem, erge kopseer of duisligheid ervaar.

Watter alternatiewe is daar indien u nie instem om deel te neem nie?

Die studie dien as 'n basis studie vir verdere implimentasie. Indien u sou besluit om nie aan die studie deel te neem nie sal u TB behandeling soos normal voortgaan.

Wie sal toegang hê tot u mediese rekords?

Al die versamelde inligting sal vertroulik en beskerm gehanteer word. Die deelnemer sal anoniem bly indien die resultate gebruik word vir 'n publikasie of tesis. Net die dokters en navorsings personeel sal toegang tot die inligting hê.

Sal u betaal word vir deelname aan die navorsingsprojek en is daar enige koste verbonde aan deelname?

U sal nie betaal word vir deelname aan die navorsingsprojek nie, maar u vervoer en etes ten opsigte van elke besoek vir die navorsingsprojek sal betaal word. Deelname aan die navorsingsprojek sal u niks kos nie.

Is daar enigiets anders wat u moet weet of doen?

U moet u huisarts of gereelde algemene praktisyn in kennis stel van u deelname aan die navorsingsprojek. (*sluit in indien van toepassing*)

U moet ook u mediese fonds in kennis stel van u deelname aan die navorsingsprojek. (*sluit in indien van toepassing*)

U kan Mr Kurt Daniels kontak by tel. 0844477490 indien u enige verdere vrae het of enige probleme ondervind.

U kan die Komitee vir Mensnavorsing kontak by 021-938 9207 indien u enige bekommernis of klagte het wat nie bevredigend deur u studiedokter hanteer is nie.

U sal 'n afskrif van hierdie inligtings- en toestemmingsvorm ontvang vir u eie rekords.

Verklaring deur deelnemer

**Met die ondertekening van hierdie dokument onderneem ek,**

....., **om deel te neem aan 'n navorsingsprojek getiteld An Investigation into the lung function, health related quality of life (HRQoL) and functional capacity of a cured Pulmonary Tuberculosis (PTB) population in the Breede Valley: a pilot study**

Ek verklaar dat:

Ek hierdie inligtings- en toestemmingsvorm gelees het of aan my laat voorlees het en dat dit in 'n taal geskryf is waarin ek vaardig en gemaklik mee is.

Ek geleentheid gehad het om vrae te stel en dat al my vrae bevredigend beantwoord is.

Ek verstaan dat deelname aan hierdie navorsingsprojek **vrywillig** is en dat daar geen druk op my geplaas is om deel te neem nie.

Ek te eniger tyd aan die navorsingsprojek mag onttrek en dat ek nie op enige wyse daardeur benadeel sal word nie.

Ek gevra mag word om van die navorsingsprojek te onttrek voordat dit afgehandel is indien die studiedokter of navorser van oordeel is dat dit in my beste belang is, of indien ek nie die ooreengekome navorsingsplan volg nie.

Geteken te (*plek*) ..... op (*datum*) ..... 2005.

Handtekening van deelnemer      Handtekening van getuie

Verklaring deur navorser

Ek (*naam*) ..... verklaar dat:

Ek      die      inligting      in      hierdie      dokument      verduidelik      het      aan  
.....

Ek hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.

Ek tevrede is dat hy/sy al die aspekte van die navorsingsprojek soos hierbo bespreek, voldoende verstaan.

Ek 'n tolk gebruik het/nie 'n tolk gebruik het nie. (*Indien 'n tolk gebruik is, moet die tolk die onderstaande verklaring teken.*)

Geteken te (*plek*) ..... op (*datum*) ..... 2005.

Handtekening van navorder      Handtekening van getuie

Verklaring deur tolk

Ek (*naam*) ..... verklaar dat:

Ek die navorser (*naam*) ..... bygestaan het om die inligting in hierdie dokument in Afrikaans/Xhosa aan (*naam van deelnemer*) ..... te verduidelik.

Ons hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.

Ek 'n feitelik korrekte weergawe oorgedra het van wat aan my vertel is.

Ek tevrede is dat die deelnemer die inhoud van hierdie dokument ten volle verstaan en dat al sy/haar vrae bevredigend beantwoord is.

Geteken te (*plek*) ..... op (*datum*) ..... 2005.

Handtekening van tolk      Handtekening van getuie



## Appendix A-4: Ethics Approval



UNIVERSITEIT·STELLENBOSCH·UNIVERSITY  
jou kennisvennoot • your knowledge partner

### Approval Notice New Application

21-Sep-2012  
Daniels, Kurt KJ

Ethics Reference #: S12/06/186

Title: An Investigation into the lung function, Health Related Quality of (HRQOL) and Functional Capacity of a cured pulmonary tuberculosis (PTB) population in the Breede Valley :a pilot study

Dear Mr. Kurt Daniels,

The New Application received on 18-Jul-2012, was reviewed by members of Health Research Ethics Committee 1 via Expedited review procedures on 20-Sep-2012 and was approved.

Please note the following information about your approved research protocol:

Protocol Approval Period: 20-Sep-2012 -20-Sep-2013

Please remember to use your protocol number (S12/06/186) on any documents or correspondence with the REC concerning your research protocol.

Please note that the REC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

#### After Ethical Review:

Please note a template of the progress report is obtainable on [www.sun.ac.za/rds](http://www.sun.ac.za/rds) and should be submitted to the Committee before the year has expired.

The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number projects may be selected randomly for an external audit.

Translation of the consent document in the language applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372

Institutional Review Board (IRB) Number: IRB0005239

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

#### **Provincial and City of Cape Town Approval**

Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western Cape Department of Health ([healthres@pgwc.gov.za](mailto:healthres@pgwc.gov.za) Tel: +27 21 483 9907) and Dr Helene Visser at City Health ([Helene.Visser@capetown.gov.za](mailto:Helene.Visser@capetown.gov.za) Tel: +27 21 400 3981). Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.

For standard REC forms and documents please visit: [www.sun.ac.za/rds](http://www.sun.ac.za/rds)

If you have any questions or need further help, please contact the REC office at 0219389657.

#### **Included Documents:**

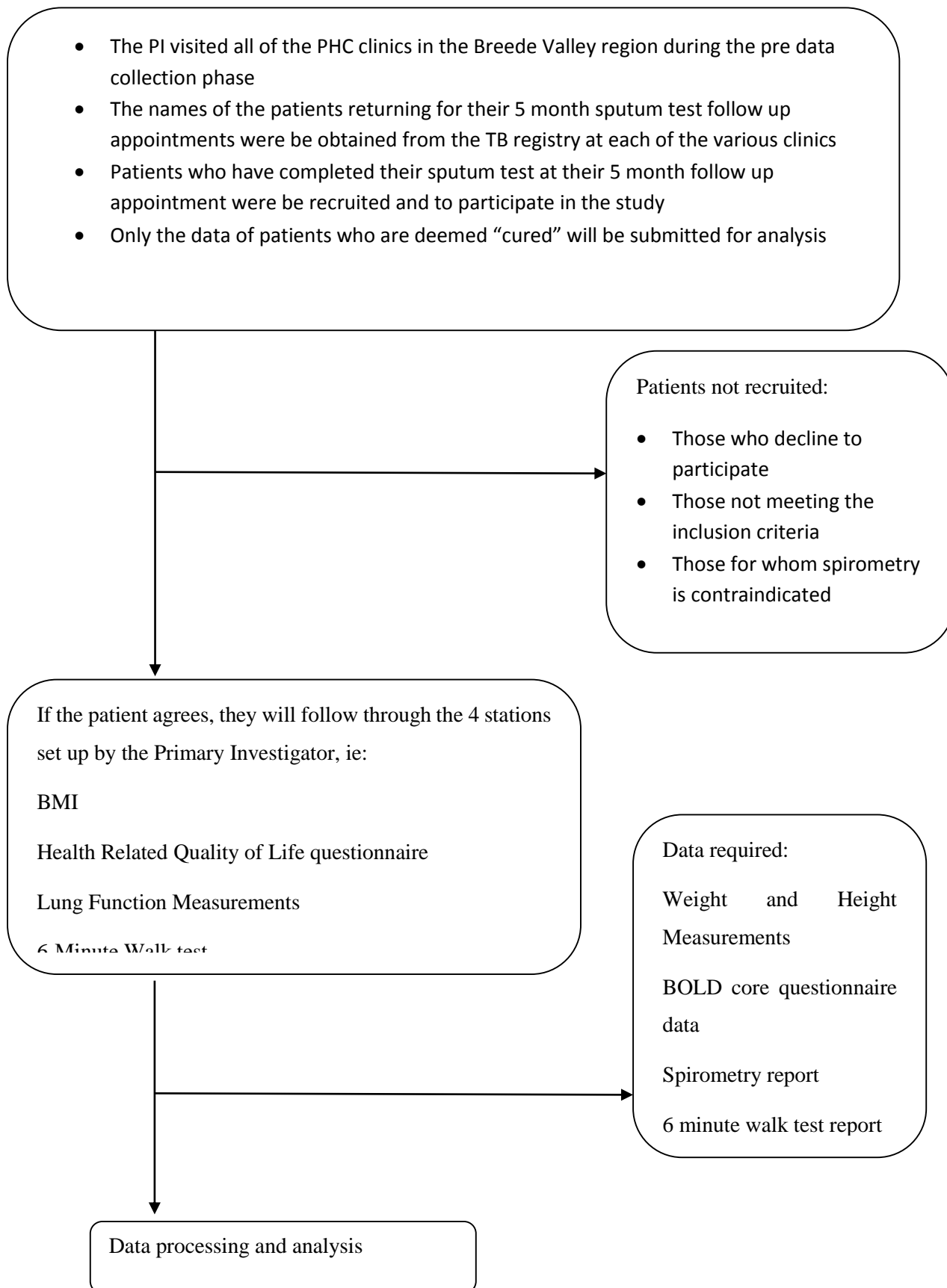
Protocol  
Checklist  
Application Form  
Investigators declaration  
Synopsis

Sincerely,

Franklin Weber  
REC Coordinator  
Health Research Ethics Committee 1

## Appendix B-1: Flow diagram of patient recruitment procedure

### Flow Diagram of Recruitment Procedure



## **Appendix B-2: Recruitment Strategies for individual clinics**

### Clinic Patient Recruitment Strategies

#### **Touws Rivier Clinic**

The researcher would travel to the clinic and set up a date that suited both him and the staff at the clinic. On the same day, the researcher would ask the TB nurse for a list of names of patients that have either completed, or are going to complete their TB treatment in that month. The nurse would then contact the patients and ask them to come through to the clinic on the date that was arranged.

This strategy worked well as the TB nurse knows the patients personally. She mentioned that she does community visits on a Friday and that is when she would convey the information to the patients. The only unreliable aspect was the patients themselves. Even though patients confirmed that they would come to the clinic on the set date, when the researcher arrived at the clinic, maybe 1 or 2 of the booked patients would pitch.

One way of eliminating the fact that the researcher is reliant on the patients to come to the clinic is possibly setting up a date when the research team could accompany the nurse on the home visits and recruit the patients at their home. My only concern with this is that the homes may not have the capacity to accommodate the 6MWT.

#### **Orchards Clinic**

Orchards clinic is a tiny clinic that mainly services the surrounding farming area. At this clinic, the researcher would once again set up an appointment date with clinic that suited everyone. The researcher would request a list of names of all the patients who have completed or who are completing their treatment in the month from the nursing. The nurse knows her patients well and would contact the patients (usually when they came to the clinic for their tablets) and ask the patients to report to the clinic on the arranged date.

This worked well as the clinic is small and does not have many TB patients. Due to the personal relationship and sense of community amongst the patients, as well as the clinic, patients tend to respect and respond to the Dr's and Nurses at the clinic. All of the patients that were requested or booked pitched up for their appointments.

The patient numbers at the clinic are small and the strategy at this clinic seems to work fine. The patients live on farms and there is no way of getting hold of them as most of them do not have contact numbers. So, the nurse relies on the patients to come to the clinic for any form of communication, because following up on these patients is a definite problem at the clinic.

#### **De Doorns Clinic**

De Doorns Clinic is a rather large clinic servicing the De Doorns area. Here too, the researcher would set up an appointment with the TB nurse for a date that would suit him when the research team could

return. The researcher was told that patients were booked at the clinic every day. The number of patients that are seen at the clinic per day is unknown. When arriving at the clinic for data collection, it seems that the nurse misunderstood the requirement for the study and recruitment had to be done by the research team in the waiting area.

According to the TB nurse, De Doorns clinic also makes use of community workers to carry out the DOTS program. Therefore, it is possible that only the patients who have changed their treatment regime as well as patients who have to provide sputum samples are the only patients that actually come in to the clinic.

One way to potentially optimize the amount of patients recruited for the study is to work with the community workers from the clinic. The community workers can provide a list of names and contact numbers of people who are potentially completing treatment and the research team could contact them to ask if they would like to participate in the study. They can then decide if the team will go to the people's houses or get everyone to a central point for data collection.

### **Rawsonville Clinic**

The researcher would follow the same procedure as for the previous clinics by arranging a date that the team could come in for data collection. The first round of data collection at Rawsonville clinic did not yield many patients. The researcher was told by the TB nurse that the DOTS program is carried out at the clinic and that there are no community workers working in the area. The nurse keeps good track of the patients that either need to provide sputum samples, or that are completing treatment. One of the biggest issues at the clinic is that most of the patients there do not have contact numbers. They are also mostly farm workers which means that time spent working is more money for them. Therefore, the reliability of the patients arriving at the clinic when they are scheduled to arrive cannot be guaranteed.

Therefore, in the first round of data collection, the researcher made an appointment to collect data at the clinic when more than 1 person was scheduled to provide 5 month sputum samples. All of the patients that were scheduled on that day arrived at the clinic.

For the second round of data collection, the researcher thought that to optimize the amount of patients included in the study, he would go to the clinic and compile a list of names of patients that were completing treatment in that month from the patients file. From a list of about 12 names: 2 were under age and still at school, 6 did not have contact numbers and 4 had contact numbers. Of the 4 with contact numbers, only 3 were reachable. All 3 patients arrived at the clinic on the day that was scheduled for data collection.

### **Worcester CHC**

Worcester CHC was used as home base for the data collection phase. Here, the researcher would communicate with the TB nurse as well as the desk clerk who performed all of the administrative tasks

of the TB clinic. The TB nurse said that it was extremely difficult for her to know in advance which patients were where in their treatment because of the patient numbers at the clinic. Basically, the patient collects his/her folder at the folder counter in the morning and would then report to the TB clinic. The patient waits in a waiting area until their name is called by the TB nurse. The nurse then looks at the patient file and determines the plan of action for the patient. The researchers thus decided to recruit patients in the waiting area and stationed a research assistant there to explain what the project is about and identify any patients who were eligible for the study. A drawback of this method of recruitment was that patients had to self identify if they matched the specified criteria. Patients were screened again once they arrived at the data collection stations. Most of the time, the patients folder was being held at pharmacy or by a doctor and many patients did not arrive at the data collection stations with their clinical folders.

The researcher decided that the appointment system would not work at this clinic as eligible patients for the study were unpredictable. Therefore, the research team decided to stay at the clinic for a week from 8am until 1pm and recruit as many patients as possible.

This method of recruitment did not yield many patients. Many patients who volunteered for the study were defaulters who had to have their drug regimen changed. Others were children and under age.

The clinic does make use of DOTS community workers. Each area in the Worcester region has between 2 and 3 community workers taking care of the chronically ill. One of the suggestions to overcome the poor patient numbers at Worcester CHC was to possibly work with the community workers and let them identify patients who are completing treatment in a particular month. The research team could then recruit all of those patients on one day and in one central area with the patients having to come to the clinic. The researcher suggested that the community workers identify the patients and hand them a letter, written up by the researcher, explaining the project and containing an appointment date when the research team will be collecting the data. Another suggestion to overcome the poor patient numbers was to use the TB registry and identify patients who have who have started their TB treatment in the last 6 months of 2012. The files of all of the patients for which there are final negative sputum results will be pulled. A list will be compiled with the patients contact number/details as received from the file. These patients will be contacted and asked to come to the clinic on a particular day.

## Appendix B-3: Spirobank II

### Turbine Yes Please! Why the MIR digital turbine does not require calibration

13 February 2014 at 18:49

The MIR range of spirometers use a digital turbine flow meter working on the infrared interruption principle. The turbine system is made up of the following elements:

- A turbine tube, made from a special polycarbonate material, which is permeable to infrared light,
- Two deflectors, one at each end of the tube (entry and exit) made from the same polycarbonate material, which serve to create the "swirl" effect of the air passing through the tube, and
- A moving part or rotor, consisting of a blade plus a metal axis.

Two sets of infrared transmitters (TX) and receivers (RX) detect the rotation of the rotor within the tube and generate digital impulses, the number of these impulses is directly proportional to the velocity of the air (inspired or expired) passing through the tube. This velocity is a function of the physical form of the two deflectors, and the form of the deflectors cannot change during normal use.

The maximum velocity of the rotor, for flows generated during normal spirometry testing, is around 1000 revolutions per second. The metal axis is made from a special alloy and it is supported at each end by a bearing made from a synthetic sapphire. This specification excludes the possibility of modifications in the response of the turbine due to wear in the turbine mechanism.

In addition, it is very important to underline that, unlike the other kinds of flow meter such as those based on pressure, the measurements made with this mechanical flow meter are NOT influenced in any way by the ambient conditions ie temperature, pressure, humidity and density (or viscosity) of the gas being measured.

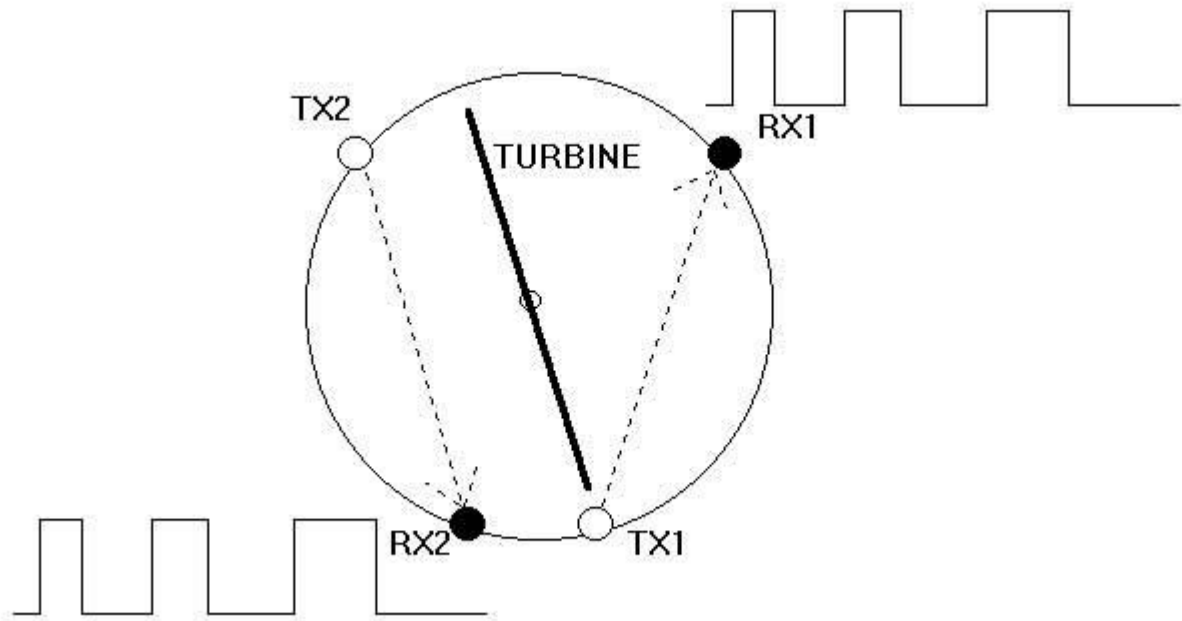
Given all of the above, it can be deduced that in normal conditions and with the flow meter undamaged, the measurement depends only and exclusively on the velocity of the air in transit through the turbine tube.

The only way in which the measurement can change would be by the presence of some kind of "foreign body" within the turbine tube, such as a hair, thread or sputum. This could create a kind of friction which could slow down or even stop the normal rotation of the rotor within the turbine tube.

In order to ensure the absence of such friction, MIR spirometers use a software algorithm which constantly analyses the movement of the rotor and within a certain range of very low flow the device gives a feedback of an acoustic signal "beep" when the flow is within this range, thus ensuring that the rotor is moving freely and without any such friction.

Thanks to this constant acoustic feedback before, during and after every spirometry test, the user is able to guarantee the correct functioning of the flow measurement system. Of course, the user is also able to use any normal system (pump, calibration syringe etc), to check the correct functioning of the system.

To conclude, it is possible to confirm that providing the turbine is kept clean and free from foreign bodies, then the response of the turbine set at the factory cannot be modified and thus the turbine does not require calibration.



**Appendix B-4: BOLD Core Questionnaire Used**

Kode van land: \_\_\_\_\_ 1

Kode van stad: \_\_\_\_\_ 2

ID: \_\_\_\_\_ 3

Datum: \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ 4-6  
d d m m j j j j**BOLD KERNVRAELYS**

## Demografiese besonderhede

1. *Wat is die geslag van die deelnemer?* Manlik  1 7Vroulik  22. *Wat is u ras?* \_\_\_\_\_ 83. *Wat is u geboortedatum?* \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ 9-11  
d d m m j j j j4. *Hoeveel jaar van formele onderwys het u voltooi?* \_\_\_\_\_125. *Wat is die hoogste vlak van formele onderwys wat u* Primêre skool  1 13*voltooi het?* Middelbare skool  2Hoërskool  3Kollege  4Technikon/Universiteit  5Geen  6Onbekend  76. *Wat is die hoogste vlak van formele onderwys wat* Primêre skool  1 14*u vader voltooi het?* Middelbare skool  2Hoërskool  3Kollege  4Technikon/Universiteit  5Geen  6Onbekend  7



## Respiratoriese simptome en siektetoestande

Die vrae het hoofsaaklik betrekking op u bors. Antwoord asseblief ja of nee, indien moontlik. Indien u twyfel of u antwoord ja of nee moet wees, sê dan asseblief nee.

## Hoes

7. Hoes u gewoonlik sonder dat u verkoue is? Ja  1 15  
Nee  2

[Indien **ja**, gaan asseblief voort met vraag 7A; indien **nee**, spring na vraag 8]

- 7A. Is daar maande wanneer u die meeste dae hoes? Ja  1 16  
Nee  2

[Indien **ja**, vra beide vraag 7B en 7C; indien **nee**, spring na vraag 8]

- 7B. Hoes u vir soveel as drie maande per jaar op die meeste dae? Ja   
1 17  
Nee  2

- 7C. Hoeveel jaar het u al die hoes? Minder as 2 jaar  1 18  
2-5 jaar  2  
Meer as 5 jaar

## Slym

8. Hoes u gewoonlik slym op uit u bors, of het u gewoonlik Ja  1 19  
slym op u bors wat moeilik uithoes wanneer u nie Nee  2  
verkoue is nie?

[Indien **ja**, gaan voort met vraag 8A; indien **nee**, spring na vraag 9]

- 8A. Is daar maande wanneer u op die meeste dae hierdie slym het? Ja  1 20  
Nee  2

[Indien **ja**, vra beide vraag 8B en 8C; indien **nee**, spring na vraag 9]

- 8B. Hoes u vir soveel as drie maande elke jaar  
die slym op die meeste dae uit? Ja  1 21  
Nee  2

- 8C. Hoeveel jaar het u reeds die slym? Minder as 2 jaar  1 22

- 2-5 jaar  2  
 Meer as 5 jaar  3

## Hyg/Fluit

9. Het u op enige tydstip die afgelope 12 maande 'n gehyg Ja  1 23  
 of gefluit in u bors gehad? Nee  2

*[Indien ja, vra beide vraag 9A en 9B; indien nee, spring na vraag 10]*

- 9A. In die afgelope 12 maande, het u die gehyg of gefluit net Ja  1 24  
 gehad terwyl u verkoue was? Nee  2

- 9B. In die afgelope 12 maande, het u ooit 'n hyg- of fluitaanval Ja  1 25  
 gehad wat u kortasem laat voel het? Nee  2

## Kortasemigheid

10. Ly u aan 'n toestand anders as kortasemigheid wat maak Ja  1 26  
 dat u nie kan loop nie? Nee  2

*[Indien ja, beskryf die toestand asseblief in die ruimte hieronder en spring dan na vraag 12. Indien nee, gaan direk aan met vraag 11.]*

## Aard van die toestand(e):

11. Het u las van kortasemigheid wanneer u vinnig loop op 'n gelykte, of Ja  1  
<sup>27</sup>  
 teen 'n effense opdraande uitloop? Nee  2

*[Indien ja, vra vraag 11A tot 11D; indien nee, spring na vraag 12]*

- 11A. Moet u op 'n gelykte stadiger loop as ander mense van Ja  1 28  
 u ouderdom omdat u kortasem raak? Nee  2  
 Nie van toepassing  3

- 11B. Is dit ooit vir u nodig om eers te gaan staan om u asem terug Ja  1 29  
 te kry wanneer u teen u eie pas op 'n gelykte loop? Nee  2  
 Nie van toepassing  3

- 11C. Moet u ooit eers gaan staan om u asem terug te kry nadat Ja  1 30  
 u op 'n gelykte sowat 100 tree geloop Nee  2

het (of na 'n paar minute)? Nie van toepassing  3

11D. Is u te kortasem om uit die huis uit te gaan of uitasem Ja  1 31

nadat u aan- of uitgetrek het? Nee  2

Nie van toepassing  3

12. Het 'n dokter of ander gesondheidsorgverskaffer al ooit Ja  1 32

vir u gesê dat u emfiseem het? Nee  2

13. Het 'n dokter of ander gesondheidsorgverskaffer al ooit vir u gesê Ja

1 33

dat u asma, asmatiese brongitis of allergiese brongitis het? Nee  2

*[Indien ja, vra vraag 13A. Indien nee, spring na vraag 14]*

13A. Het u nog steeds asma, asmatiese brongitis of Ja  1 34

allergiese brongitis? Nee  2

14. Het 'n dokter of ander gesondheidsorgverskaffer al ooit vir u gesê Ja

1 35

dat u chroniese brongitis het? Nee  2

*[Indien ja, vra vraag 14A. Indien nee, spring na vraag 15]*

14A. Het u steeds chroniese brongitis? Ja  1 36

Nee  2

15. Het 'n dokter of ander gesondheidsorgverskaffer al ooit vir u gesê Ja  1

37

dat u chronies obstruktiwe longsiekte het? Nee  2

### **Bestuur van toestand**

Nou gaan ek u vrae vra oor enige medisyne wat u dalk neem om u beter te laat asemhaal. Ek wil graag weet van medisyne wat u gereeld neem en van medisyne wat u moontlik net neem om simptome te verlig. Ek wil graag hê u moet my vertel van al die medisyne wat u neem, in watter vorm u dit neem, en hoe dikwels u dit elke maand neem.

16. In die afgelope 12 maande, het u enige medikasie geneem vir u asemhaling? Ja  1 38

Nee  2

16A. Medikasie: Naam ( <b>nie ingevoeg</b> )					
---	--	--	--	--	--

16B. Medikasie: Kode	_____ 39	_____ 44	_____ 49	_____ 54	_____	
16C. Formulering	Pille <input type="checkbox"/> 1 Inasemtoestel <input type="checkbox"/> 2 Fynsproeier <input type="checkbox"/> 3 Vloeistof <input type="checkbox"/> 4 Setpil <input type="checkbox"/> 5 Inspuiting <input type="checkbox"/> 6 Ander <input type="checkbox"/> 7	Pille <input type="checkbox"/> 1 Inasemtoestel <input type="checkbox"/> 2 Fynsproeier <input type="checkbox"/> 3 Vloeistof <input type="checkbox"/> 4 Setpil <input type="checkbox"/> 5 Inspuiting <input type="checkbox"/> 6 Ander <input type="checkbox"/> 7	Pille <input type="checkbox"/> 1 Inasemtoestel <input type="checkbox"/> 2 Fynsproeier <input type="checkbox"/> 3 Vloeistof <input type="checkbox"/> 4 Setpil <input type="checkbox"/> 5 Inspuiting <input type="checkbox"/> 6 Ander <input type="checkbox"/> 7	Pille <input type="checkbox"/> 1 Inasemtoestel <input type="checkbox"/> 2 Fynsproeier <input type="checkbox"/> 3 Vloeistof <input type="checkbox"/> 4 Setpil <input type="checkbox"/> 5 Inspuiting <input type="checkbox"/> 6 Ander <input type="checkbox"/> 7	Pille <input type="checkbox"/> 1 Inasemtoestel <input type="checkbox"/> 2 Fynsproeier <input type="checkbox"/> 3 Vloeistof <input type="checkbox"/> 4 Setpil <input type="checkbox"/> 5 Inspuiting <input type="checkbox"/> 6 Ander <input type="checkbox"/> 7	Pille <input type="checkbox"/> 1 Inasemtoestel <input type="checkbox"/> 2 Fynsproeier <input type="checkbox"/> 3 Vloeistof <input type="checkbox"/> 4 Setpil <input type="checkbox"/> 5 Inspuiting <input type="checkbox"/> 6 Ander <input type="checkbox"/> 7
<b>16D. Neem u die medikasie meeste dae, net wanneer u simptome het, of beide?</b> <i>(Indien 'meeste dae', vra V16E; indien 'simptome', vra V16F; indien 'beide', vra V16E en V16F.)</i>	Meeste dae <input type="checkbox"/> 1 Simptome <input type="checkbox"/> 2 Beide <input type="checkbox"/> 3	Meeste dae <input type="checkbox"/> 1 Simptome <input type="checkbox"/> 2 Beide <input type="checkbox"/> 3	Meeste dae <input type="checkbox"/> 1 Simptome <input type="checkbox"/> 2 Beide <input type="checkbox"/> 3	Meeste dae <input type="checkbox"/> 1 Simptome <input type="checkbox"/> 2 Beide <input type="checkbox"/> 3	Meeste dae <input type="checkbox"/> 1 Simptome <input type="checkbox"/> 2 Beide <input type="checkbox"/> 3	
16E. Wanneer u die medikasie neem, hoeveel dae per week neem u dit?	_____ dae 42	_____ dae 47	_____ dae 52	_____ dae 57	_____ dae	
16F. Terwyl u die medikasie moes neem, hoeveel maande uit die afgelope 12 maande het u dit geneem?	0-3 <input type="checkbox"/> 1 43 4-6 <input type="checkbox"/> 2 7-9 <input type="checkbox"/> 3 10-12 <input type="checkbox"/> 4	0-3 <input type="checkbox"/> 1 48 4-6 <input type="checkbox"/> 2 7-9 <input type="checkbox"/> 3 10-12 <input type="checkbox"/> 4	0-3 <input type="checkbox"/> 1 53 4-6 <input type="checkbox"/> 2 7-9 <input type="checkbox"/> 3 10-12 <input type="checkbox"/> 4	0-3 <input type="checkbox"/> 1 58 4-6 <input type="checkbox"/> 2 7-9 <input type="checkbox"/> 3 10-12 <input type="checkbox"/> 4	0-3 <input type="checkbox"/> 1 4-6 <input type="checkbox"/> 2 7-9 <input type="checkbox"/> 3 10-12 <input type="checkbox"/> 4	

Indien die deelnemer nie enige medikasie neem om met asemhaling te help nie, spring na vraag 17.

17. Vertel my asseblief van enige ander produkte wat u neem of dinge wat u doen om u asemhaling aan te help waarvan u my nog nie vertel het nie.

Medisyne of aktiwiteit	Kode
	_____ 74
	_____ 75
	_____ 76
	_____ 77

18. Het 'n dokter of ander gesondheidsorgverskaffer u al ooit  1 78  
in 'n toestel laat blaas om die lug in u longe te meet (d.w.s. 'n spirometer  2  
of belugtingsmeter)? Nee

*[Indien ja, vra vraag 18A. Indien nee, spring na vraag 19]*

18A. Het u die afgelope 12 maande so 'n toestel gebruik? Ja  1 79  
Nee  2

19. Het u al ooit so gesukkel met asemhalingsprobleme Ja  1 80  
dat dit met u gewone daaglikse aktiwiteite ingemeng het, Nee  2  
of gemaak het dat u nie kon werk nie?

*[Indien ja, vra vraag 19A. Indien nee, spring na vraag 20]*

19A. Hoeveel sulke episodes het u die afgelope \_\_\_\_\_ episodes 81  
12 maande beleef?

*[Indien 19A >0, vra vraag 19B en 19C, spring andersins na vraag 20]*

19B. Vir hoeveel van die episodes die afgelope \_\_\_\_\_ episodes 82  
12 maande was dit nodig om 'n dokter te sien?

19C. Vir hoeveel van die episodes die afgelope \_\_\_\_\_ episodes 83  
12 maande is u gehospitaliseer?

*[Indien 19C >0, vra vraag 19C1, spring andersins na vraag 20]*

19C1. Vir hoeveel volle dae is u die afgelope \_\_\_\_\_ days 84  
12 maande vir asemhalingsprobleme gehospitaliseer?

**Tabakrook**

Nou gaan ek u uitvra oor rook. Eers gaan ek oor sigarette vra.

20. Het u al ooit sigaret gerook? Ja  1 85  
Nee  2

(“Ja,” beteken meer as 20 pakkies sigarette in ’n leeftyd of ’n jaar lank meer as 1 sigaret elke dag)

[Indien ja, vra vraag 20A tot by 20D; spring andersins na vraag 22]

20A. Hoe oud was u toe die eerste keer gereeld \_\_\_\_\_ jaar oud 86  
sigaret begin rook het?

20B. Indien u ophou rook het, hoe oud was \_\_\_\_\_ jaar oud 87  
u toe u die laaste keer opgehou het?

20C. Gemiddeld hoeveel sigarette per dag \_\_\_\_\_ sigarette/dag 88  
rook u (het u gerook) oor die hele tydperk  
wat u rook (gerook het)?

20D. Gemiddeld oor die hele tydperk wat u Klaar vervaardig  1 89  
rook (gerook het), rook (het) u hoofsaaklik Handgerol  2  
klaar vervaardigde of handgerolde sigarette (gerook)?

[Indien die deelnemer tans sigaret rook (vraag 20B nie ingevul), vra dan vraag 21A en 21B. Spring andersins na vraag 22]

21A. Hoeveel keer die afgelope jaar het u vir \_\_\_\_\_ keer 90  
minstens 24 uur ophou rook?

21B. Oorweeg u dit ernstig om op te hou rook? Ja, binne die volgende 30 dae  1  
91  
Ja, binne die volgende 6 maande  2  
Nee, dink nie aan ophou nie  3

22. Het u al ooit pyp of sigare gerook? Ja  1 92  
Nee  2

[Indien ja, vra vraag 22A. Indien nee, gaan aan met vraag 23]

22A. Rook u tans pyp of sigare? Ja  1 93  
 Nee  2

*[Indien die respondent nog nooit gerook het nie (dus “nee” geantwoord het op beide vraag 20 en 22), spring dan na vraag 25. Gaan andersins aan met vraag 23]*

23. Het ’n dokter of ander gesondheidsorgverskaffer Ja  1 94  
 u al ooit aangeraai om op te hou rook? Nee  2

*[Indien ja, vra vraag 23A en 23B. Indien nee, spring na vraag 24]*

23A. Is u in die afgelope 12 maande aangeraai Ja  1 95  
 om op te hou rook? Nee  2

23B. Het u enige medikasie (op voorskrif of daarsonder) Ja  1 96  
 gebruik om u te help ophou rook? Nee  2

*[Indien ja, vra eers vraag 23B1 en dan vraag 24. Indien nee, spring na vraag 24]*

23B1. Watter soort medikasie het u geneem Nikotienvervanging  1 97  
 om u te help ophou rook? Bupropion  2  
 Tofranil  3  
 Ander  4

24. Het u enige iets anders gedoen Ja  1 98  
 om u te help om op te hou rook? Nee  2

*[Indien ja, vra vraag 24A, spring andersins na vraag 25]*

24A. Wat het u gebruik of gedoen? Hipnose  1 99  
 Akupunktuur  2  
 Bioterugvoering  3  
 Ander  4

Beroepsblootstelling

25. Het u al ooit ’n jaar of langer stowwerige werk gedoen? Ja  1 100  
 Nee  2

*[Indien ja, vra vraag 25A, spring andersins na vraag 26]*

25A. Hoeveel jaar lank het u op stowwerige plekke gewerk? \_\_\_\_\_ jaar 101

Bykomende siektetoestande

26. Het 'n dokter of ander gesondheidsorgverskaffer al ooit vir u gesê u het:

26A. 'n Hartkwaal Ja  1 102  
Nee  2

26B. Hipertensie Ja  1 103  
Nee  2

26C. Diabetes Ja  1 104  
Nee  2

26D. Longkanker Ja  1 105  
Nee  2

26E. Beroerte Ja  1 106  
Nee  2

26F. Tuberkulose Ja  1 107  
Nee  2

*[Indien ja op 26F, vra dan 26F1; spring andersins na vraag 27]*

26F1. Neem u tans medisyne vir tuberkulose? Ja  1 108  
Nee  2

*[Indien nee op 26F1, vra dan 26F2; spring andersins na vraag 27]*

26F2. Het u al ooit medisyne gebruik vir tuberkulose? Ja  1 109  
Nee  2

27. Het u al ooit 'n operasie op u borskas ondergaan waarin Ja  1 110  
'n deel van u long verwyder is? Nee  2

28. Is u as kind vir asemhalingsprobleme gehospitaliseer Ja  1 111  
voor u 10 jaar oud was? Nee  2



29. Het u die afgelope 12 maande 'n griepinspuiting gekry? Ja  1 112  
Nee  2
30. Het 'n dokter of ander gesondheidsorgkundige al vir u vader, Ja  1 113  
moeder, suster of broer gesê dat hulle met emfiseem, chroniese Nee  2  
brongitis of chronies obstruktiwe longsiekte gediagnoseer is?
31. Het enige iemand wat in u huis woon (behalwe uself) die afgelope Ja  1  
114  
twee weke 'n sigaret, pyp of sigaar in die huis gerook? Nee  2

**SF-12**

*Onderhoudvoerder: Lees die volgende instruksies voor aan die deelnemer.*

**INSTRUKSIES:** Dié opname wil weet wat u siening omtrent u gesondheid is. Die inligting help tred hou met hoe u voel en hoe goed u in staat is om u daaglikse aktiwiteite uit te voer. Beantwoord telkens die vraag deur die antwoord af te merk soos aangedui word. Antwoord asseblief so goed u kan as u nie seker is wat om te antwoord nie.

32. Sou u oor die algemeen sê u gesondheid is: (*Merk een af.*) Uitstekend  1  
115  
Baie goed  2  
Goed  3  
Redelik  4  
Swak  5

33. Die volgende items handel oor aktiwiteite wat u dalk op 'n tipiese dag sou uitvoer. Beperk u gesondheid u *tans* in die uitvoer daarvan? Indien wel, in watter mate?

- 33A. **Matige aktiwiteite**, soos om 'n tafel Ja, beperk my baie  1 116  
rond te skuif, 'n stofsuier te stoot, Ja, beperk my effens  2  
rolbal te speel, of gholf te speel Nee, beperk my glad nie  3

- 33B. Om **etlike** stelle trappe te klim Ja, beperk my baie  1 117  
Ja, beperk my effens  2  
Nee, beperk my glad nie  3

34. Het u die **afgelope 4 weke** enige van die volgende probleme ondervind met u werk of enige ander gereelde daaglikse aktiwiteit **as gevolg van u fisieke gesondheid**?

34A. **Minder bereik** as wat u sou wou Ja  1 118  
Nee  2

34B. Was beperk ten opsigte van **tipe** werk of ander aktiwiteite Ja  1  
119  
Nee  2

35. Het u die **afgelope 4 weke** enige van die volgende probleme ondervind met u werk of ander daaglikse aktiwiteite **as gevolg van enige emosionele probleem** (soos om depressief of angstig te voel)?

35A. **Minder bereik** as wat u sou wou Ja  1 120  
Nee  2

35B. Het die werk of ander aktiwiteit nie so **nougeset** as gewoonlik  
gedoen nie Ja  1 121  
Nee  2

36. In watter mate het pyn die **afgelope 4 weke** ingemeng met Glad nie  1  
122  
u gewone werk (dit sluit werk buite die huis sowel as huiswerk in)? Effens  2  
Redelik  3  
Taamlik baie  4  
Uitermatig baie  5

37. Hierdie vrae het te doen met hoe u gevoel het en hoe dit met u gesteld was die **afgelope 4 weke**. Gee vir elke vraag asseblief telkens die een antwoord wat die beste beskryf hoe u gevoel het.

Hoe dikwels die **afgelope 4 weke**...

37A. Het u kalm en rustig gevoel? Heeltyd  1 123  
Gewoonlik  2  
Dikwels  3  
Somtyds  4  
Selde  5  
Nooit  6

37B. Het u baie energiek gevoel? Heeltyd  1 124  
Gewoonlik  2  
Dikwels  3

- Somtyds  4  
 Selde  5  
 Nooit  6

- 37C. Het u mismoedig en terneergedruk gevoel? Heeltyd  1 125  
 Gewoonlik  2  
 Dikwels  3  
 Somtyds  4  
 Selde  5  
 Nooit  6

38. Hoe dikwels die *afgelope 4 weke* het u fisieke gesondheid Heeltyd  1  
 126  
 of emosionele probleme ingemeng met u sosiale Gewoonlik  2  
 aktiwiteite (soos om by vriende of familie Dikwels  3  
 te kuier, en so meer)? Somtyds  4  
 Selde  5  
 Nooit  6

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## EKONOMIESE IMPAK

### Verlore werksdae

Die volgende vrae gaan oor werk en tye wat u dalk weens u asemhalingsprobleme nie kon werk nie.

39. Het u in enige stadium die afgelope 12 maande gewerk vir 'n inkomste? Ja  1  
 127  
 Nee  2

[Indien *nee*, gaan voort met vraag 39A; indien *ja*, spring na vraag 40]

- 39A. Het u die afgelope 12 maande hoofsaaklik weens Ja  1 128  
 asemhalingsprobleme nooit vir 'n inkomste gewerk nie? Nee  2

39B. Het u die afgelope 12 maande nooit vir 'n inkomste gewerk nie Ja  1 129  
 omdat u 'n voltydse tuisteskepper of versorger was? Nee  2

*[Indien ja, gaan voort met vraag 39C, indien nee, spring na vraag 44]*

39C. Het gesondheidsprobleme u die afgelope 12 maande verhoed Ja  1 130  
 om die gewone pligte van 'n tuisteskepper/versorger uit te voer? Nee  2

*[Indien ja, gaan voort met vraag 39D en 39E, indien nee, spring na vraag 44]*

39D. Hoeveel **volle dae** die afgelope 12 maande was u weens \_\_\_\_\_ dae 131  
 gesondheidsprobleme nie in staat om u pligte as  
 tuisteskepper/versorger uit te voer nie?

39E. Hoeveel **volle dae** die afgelope 12 maande was u spesifiek \_\_\_\_\_ dae  
 132  
 weens asemhalingsprobleme nie in staat om u pligte as  
 tuisteskepper/versorger uit te voer nie?

*[Spring asseblief na vraag 44]*

40. Hoeveel maande uit die afgelope 12 maande \_\_\_\_\_ maande 133  
 het u vir 'n inkomste gewerk?

41. In die maande wat u gewerk het, hoeveel dae per week \_\_\_\_\_ dae 134  
 het u vir 'n inkomste gewerk?

42. Hoeveel uur per dag werk u gewoonlik vir 'n inkomste? \_\_\_\_\_ uur 135

43. Het u gesondheidsprobleme u die afgelope 12 maande daarvan Ja  1 136  
 weerhou om vir 'n inkomste te werk? Nee  2

*[Indien ja, gaan voort met vraag 43A en 43B, indien nee, spring na vraag 44]*

43A. Hoeveel **volle dae** was u die afgelope 12 maande weens u \_\_\_\_\_ dae  
 137  
 gesondheidsprobleme nie in staat om vir 'n inkomste te werk nie?

43B. Hoeveel **volle dae** was u die afgelope 12 maande spesifiek weens \_\_\_\_\_ dae  
 138  
 asemhalingsprobleme nie in staat om vir 'n inkomste te werk nie?

Niewerkaktiwiteite nie bygebring

Die volgende vrae handel oor tye wat u moontlik weens u asemhalingsprobleme nie u normale aktiwiteite kon bybring nie (soos om inkopies te doen, vriende/familie te besoek, kerk toe te gaan, of ander aktiwiteite).

44. Het u die afgelope 12 maande weens gesondheidsprobleme **nie** Ja  1 139  
 aan een of meer niewerkverwante aktiwiteit deelgeneem nie? Nee  2

[Indien **ja**, gaan voort met vraag 44A en 44B, indien **nee**, spring na vraag 45]

44A. Hoeveel **volle dae** het u die afgelope 12 maande \_\_\_\_\_ dae 140  
 weens u gesondheidsprobleme nie deelgeneem nie aan  
 aktiwiteite wat nie werkverwant is nie?

44B. Hoeveel **volle dae** het u die afgelope 12 maande \_\_\_\_\_ dae 141  
 spesifiek weens asemhalingsprobleme nie deelgeneem nie  
 aan aktiwiteite wat nie werkverwant is nie?

Respiratoriese simptome en siektetoestande

Die volgende vrae handel oor simptome wat met u asemhaling of u borskas verband hou. Die vrae klink dalk soos vorige vrae, maar antwoord asseblief so goed u kan. Indien u twyfel of u ja of nee moet sê, antwoord dan asseblief nee.

Hoes

45A. Het u die afgelope 12 maande gehoës Ja  1 142  
 terwyl u nie verkoue gehad het nie? Nee  2

45B. Het u die afgelope 12 maande vroegoggende gehoës of Ja  1 143  
 gehoës sodra u opgestaan het? Nee  2

[Indien **nee** op **BEIDE** vraag 45A en 45B, spring na vraag 46. Indien **ja** op 45A of 45B, antwoord die volgende:]

45C. Het u die afgelope 12 maande vir drie maande Ja  1 144

of langer dié hoes op die meeste dae gehad? Nee  2

45D. Hoeveel jaar lank het u al die hoes? \_\_\_\_\_ jaar 145

Slym

46A. Het u die afgelope 12 maande slym uit u bors Ja  1 146

opgehoes behalwe wanneer u verkoue was? Nee  2

46B. Het u die afgelope 12 maande vroegoggend of sodra u opgestaan het slym uit u bors opgehoes? Ja  1 147

Nee  2

[Indien **nee** op **BEIDE** 46A en 46B, spring na vraag 47. Indien **ja** op 46A of 46B, antwoord die volgende:]

46C. Het u die afgelope 12 maande vir drie maande of langer Ja  1 148

op die meeste dae slym uit u bors opgehoes? Nee  2

46D. Hoeveel jaar lank het u so slym uit u bors opgehoes? \_\_\_\_\_ years 149

Hoes- en slymepisodes

47A. Het u die afgelope 12 maande periodes of episodes beleef waarin Ja  1 150

u 'n hoes met slym gehad het wat 'n week of langer aangehou het? Nee  2

(Indien u hoes gewoonlik met slym gepaard gaan, moet u asseblief net periodes of episodes tel wat met 'n *groter* gehoes en *meer* slym gepaard gegaan het.)

[Indien **nee**, spring na **VOLTOOI DEUR** aan die einde van die vraelys. Indien **ja**, antwoord die volgende:]

47B. Nagenoeg hoeveel sulke episodes het u \_\_\_\_\_ episodes 151

die afgelope 12 maande gehad?

47C. Hoeveel jaar lank al het u minstens een \_\_\_\_\_jaar 152

so 'n episode per jaar?

Voltooi deur: \_\_\_\_\_ 153

**Appendix B-5: 6MWT Check List**

<b>6MWT Procedure Check list</b>	
<b>PATIENT INFORMATION</b>	
A light meal is acceptable before the test is conducted	
Patient should not have done any vigorous exercise 2 hours prior to the commencement of the test	
Document any medication used	
<b>SAFETY – Precautions and contraindications</b>	
Vascular compromise eg DVT	
Cardiac compromise: atrial fibrillation; tachycardia; unstable BP	
Pulmonary compromise: SATS < 92	
<b>PATIENT PREPARATION</b>	
Comfortable clothing should be worn	
Appropriate shoes for walking should be worn (Otherwise, bare foot)	
Patient should use their usual walking aids while performing the test (cane, walker etc)	
<b>PREPARATION</b>	
Mark out distance of 30 meters in a walkway or hall/gym in 5m increments using tape against the wall or on the floor	
Use cones to indicate starting and turning points	
Ensure 40% O2 mask is available	
Explain the Modified BORG Scale (measurements are taken before, immediately after and again 2 minutes after the test was performed)	
<b>MEASUREMENTS</b>	
Document time of 6MWT	
Position the patient in a chair near the starting point for at least 5 minutes before the test	
During this time	
Check for any cardiac or pulmonary instability which would compromise walking ability	
Check that the patient is suitably dressed (clothing and shoes) for test	
Measure pulse rate and breath rate at rest	
Patient then stands and is asked to rate their baseline dyspnoea and overall fatigue using the BORG Scale	
<b>TESTING PROCEDURE</b>	

Set the lap counter and timer to zero	
Assemble all necessary equipment (lap counter, timer, clipboard, Borg Scale) and move to starting point	
Position the patient at the starting line	
Instruct the patient about the testing procedure using the standardized script	
Do not talk to anyone during the test. Use an even tone of voice when using standardized encouragement phrases	
Each time the patient returns to the starting point, click the lap counter once and let the patient see you doing it	
Watch the patient at all times. Do not get distracted during the test	
Only use the scripted encouragement every minute using an even tone	
When timer rings or buzzes, say "STOP!" and walk to where the patient has stopped	
Take a chair to the patient if the patient seems exhausted	
Mark the spot where the patient has stopped by placing a piece of tape on the floor	
<b>POST TEST PROCEDURE</b>	
Record the post test BORG dyspnoea and fatigue levels. Remind the patient of the pre test scores and ask them to compare	
Ask the patient "What, if anything, kept you from walking further?"	
Record pulse rate and breath rate	
Document the laps from the lap counter. Measure the remaining distance (round up)	
Wait 2 mins and record the pulse rate and breath rate again	
<b>PROCEDURE IF PATIENT STOPS BEFORE 6 MINUTES</b>	
Mark the spot where the patient stopped by placing a piece of tape on the floor	
Do not stop the timer	
Use scripted words to instruct patient	
Place the patient in a chair	
Patient decided if/when they want to continue. Continue using the scripted text when counting down 6 minutes	
If patient is unable to continue (physiotherapists assessment) note on the worksheet the distance, the time stopped and the reason for stopping prematurely	
Also document pulse rate, breath rate and fatigue and dyspnoea (BORG scale) scores	



## Appendix B-6 &amp; B-7: 6MWT Instructions English and Afrikaans

**INSTRUCTION SCRIPT (Even tone)**

**INITIAL INSTRUCTION:** "The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall while resting, but resume walking as soon as you are able. You will be walking back and forth around the cones. I will be right behind you the entire time so that I can make sure you are safe. You should pivot briskly around the cones and continue back the other way without hesitation. Now I'm going to show you. Please watch the way I turn without hesitation." *Demonstrate by walking one lap yourself. Walk and pivot around a cone briskly.* **CONTINUE:** "Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. Start now, or whenever you are ready

**AFTER THE FIRST MINUTE:** "You are doing well. You have 5 minutes to go."

**4 MINUTES REMAINING:** "Keep up the good work. You have 4 minutes to go."

**3 MINUTES REMAINING:** "You are doing well. You are halfway done."

**2 MINUTES REMAINING:** Keep up the good work. You have only 2 minutes left."

**1 MINUTE REMAINING:** "You are doing well. You have only 1 minute to go."

**15 SECONDS FROM COMPLETION:** "In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will bring you a chair."

**IF THE PATIENT STOPS WALKING DURING THE TEST:** "You can lean against the wall if you would like; then continue walking whenever you feel able. If you like I can also bring you a chair to sit on while you rest"

## INSTRUKSIE TEKS (Gebruik 'n egalige toon)

**AANVANKLIKE INSTRUKSIE:** "Die doel van hierdie toets is om so ver as moontlik te stap vir 6 minute. Jy gaan op en af loop in die gang. Ses minute is 'n lang tyd so jy gaan hoë vereistes stel aan jou liggaam. Jy sal waarskynlik moeg en uitasem word. Jy mag enige tyd stadiger loop, of heeltemal stop en rus as dit nodig is. Jy kan teen die muur leun om te rus maar begin weer loop sodra jy kan. Jy gaan heen en weer om die twee bakens loop. Ek gaan die hele tyd agter jou loop om seker te maak dat jy veilig is. Loop flink om elke baken en keer dan terug sonder om te huiwer. Nou gaan ek jou wys. Kyk asb na die manier waarop ek draai sonder om te huiwer.

***Demontreer aan die pasient deur een rondte te stap. Veral die draai om die bakens is belangrik. GAAN VOORT*** "Is jy gereed om dit te doen? Ek gaan hierdie horlosie gebruik om die rondtes te tel wat jy voltooi. Ek gaan hierdie knoppie druk elke keer as jy om die eerste baken gaan. Onthou die doel is om so ver as moontlik vir 6 minute te loop, maar moenie begin draf of hardloop nie. Jy kan begin sodra jy gereed is.

**NA DIE EERSTE MINUUT:** "Jy doen goed. Jy het 5 minute om te gaan."

**4 MINUTE OOR:** Hou aan met die goeie werk. Jy het 4 minute om te gaan.

**3 MINUTE OOR:** "Wel gedaan. Jy is nou halfpad daar

**2 MINUTE OOR:** Hou aan met die goeie werk. Jy het net 2 minute om te gaan.

**1 MINUTE OOR:** "Jy doen goed. Net een minuut om te gaan

**15 SEKONDES VOOR DIE EINDE:** "Binne enkele oomblikke gaan ek jou vra om te stop. Wanneer ek dit doen wil ek he jy moet onmiddelik stop net waar jy is. Ek sal dan vir jou 'n stoel bring

**INDIEN DIE PATIENT OPHOU OM TE STAP:** "Jy kan teen die muur leun as jy wil; en begin dan maar net weer loop sodra jy voel jy kan. Ek kan ook vir jou 'n stoel bring om op te sit as jy wil.

**Appendix B-8: 6MWT Data Collection Sheet**

## 6MWT Data Collection Sheet

Measurements	Baseline	End of Test	2 min after Test
Time			
Heart Rate			
Breath Rate			
Dyspnoea (BORG Scale)			
Fatigue (Borg Scale)			
Lap Counter: Number of laps x60 meters completed			
Partial laps completed (Total rounded up)			
Total			

Patient stopped before 6 minutes?

YES / NO

Reason:

Chest Pain

Intolerable Dyspnoea

Leg Cramps

Staggering

Diaphoresis

What prevented you from walking further?

-----  
-----  
-----  
-----  
-----

Symptoms at the end of exercise?

YES / NO

Angina

Dizziness

Hip/Leg/Calf Pain

### Appendix B-9: BMI Data collection sheet

#### BMI DATA COLLECTION SHEET AND MEDICATION ADMINISTRATION SHEET

Patient Reference Number

.....

Gender:                      Male                                            Female                     

Age: .....

Weight (kg): .....

Height (cm): .....

Body Mass Index (kg/m<sup>2</sup>): .....

Medication:

Time Administered: .....

Dosage: 2 Puffs of MDI                     

Side Effects experienced:                       Yes                       No

If                      yes,                      describe                      side                      effects:

.....

.....

.....

.....

**Appendix B-10: Modified BORG Scale**

<b>DIE BORG SKAAL</b>	
0	Hoegenaamd niks
0,5	Baie, baie min (net-net merkbaar)
1	Baie gering
2	Effens (lig)
3	Gematigd
4	Effens straf
5	Straf (swaar)
6	
7	Baie straf
8	
9	
10	Baie, baie straf

*Vertaal deur SU Taallab. Oktober 2008*

*Nota aan kliënt: Ek het hierdie vertaling gedoen met die aanname dat die skaal die vlak van inspanning wanneer oefening gedoen word (level of exertion), beskryf.*

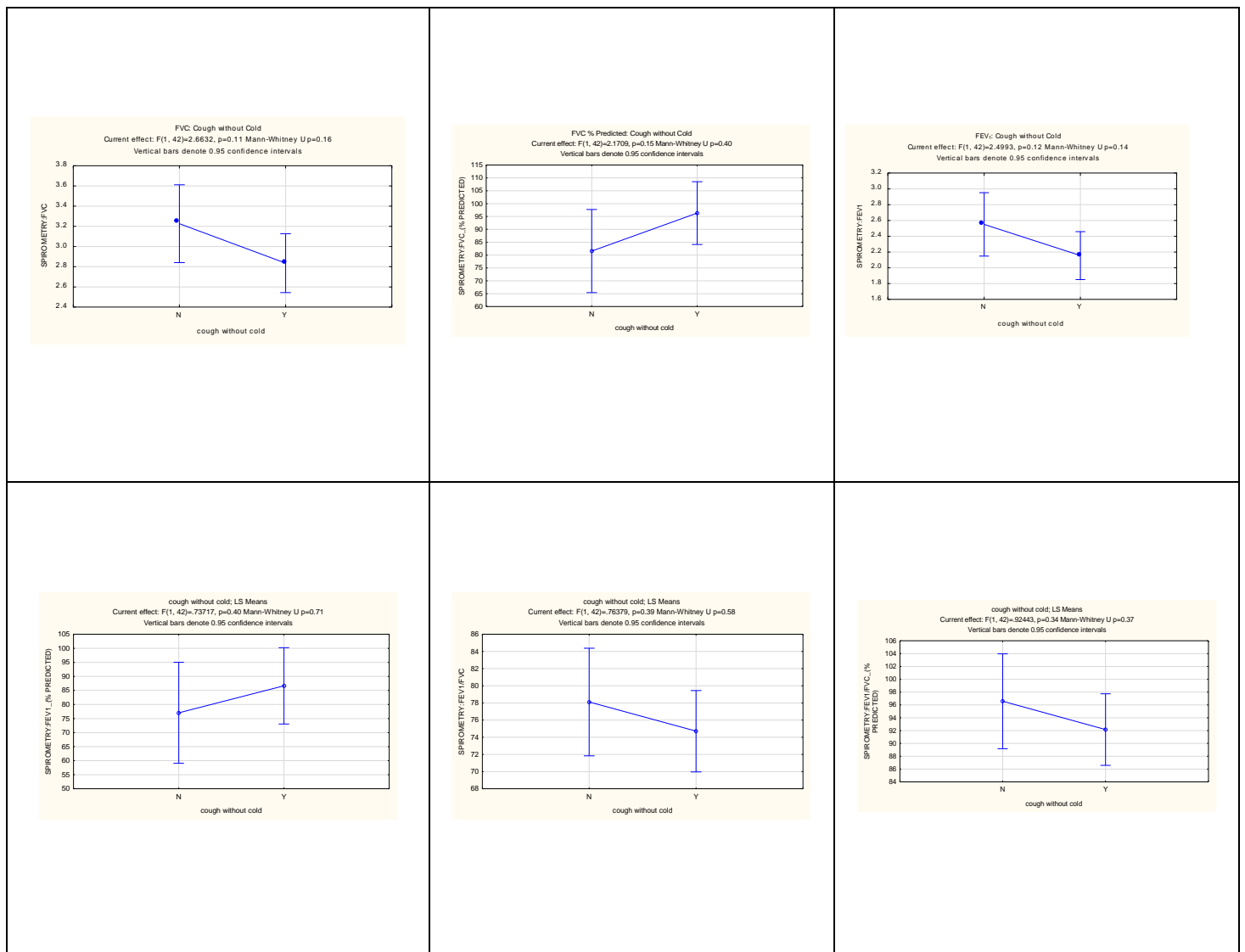
## THE BORG SCALE

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe (heavy)
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

## Appendix C-1: Associations between spirometry and symptoms of cough

The study sample were categorized into respondents who answered ‘yes’ and respondents who answered ‘no’ to the questions of: “Cough without having a cold”, “Cough for longer than 3 months”, “Current Smoker” and “Worked in a dusty job”. These 4 categories were compared with the FVC, FVC (%Pred), FEV<sub>1</sub>, FEV<sub>1</sub> (%Pred), FEV<sub>1</sub>/FVC and FEV<sub>1</sub>/FVC (%Pred). ANOVA was used to analyse data and detect any differences between ‘yes’ and ‘no’ groups.

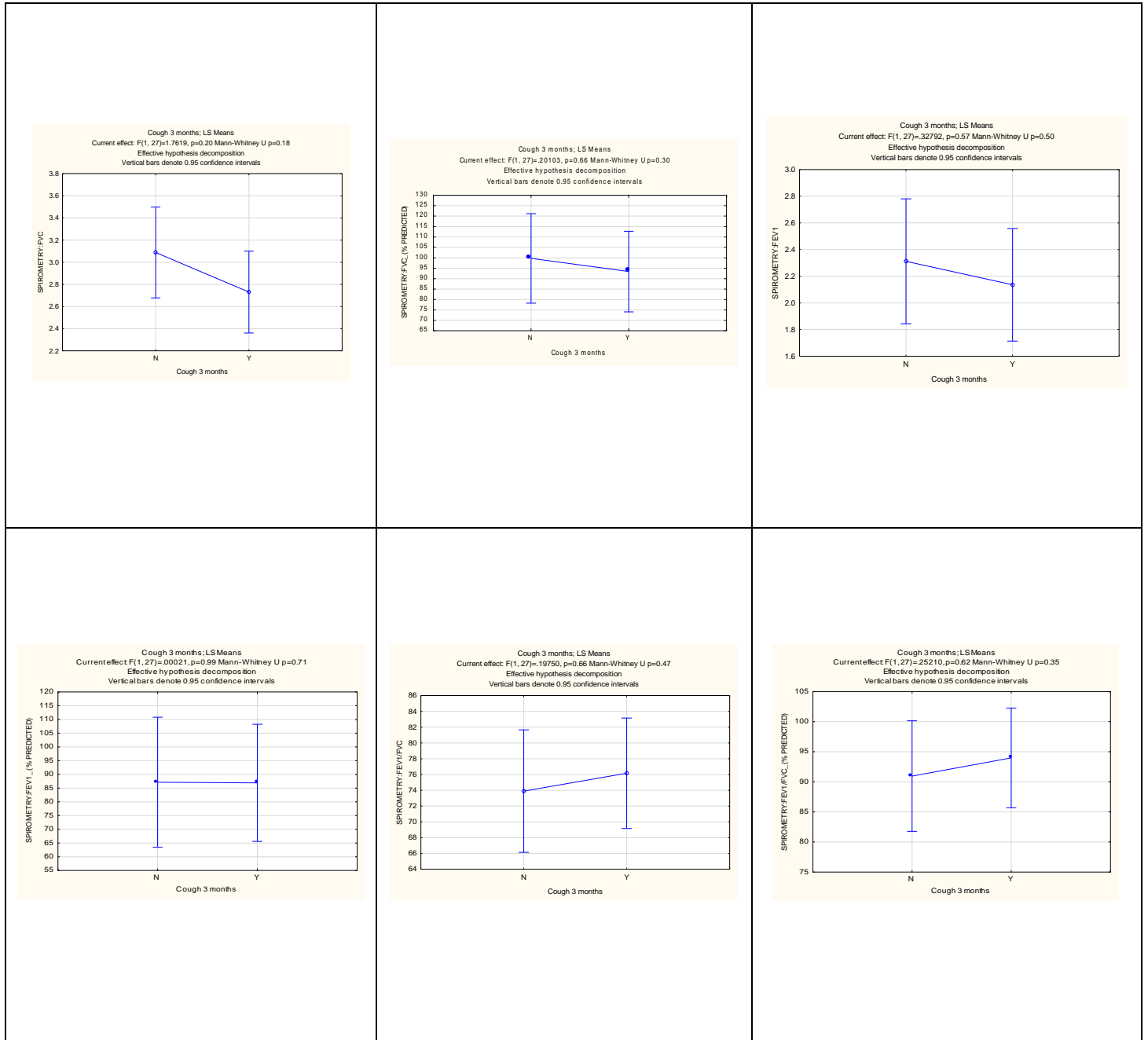
### Cough without having a cold



There was no significant difference between the groups with regards to spirometry results. Patients who coughed without having a cold did however show a decrease in FVC ( $F(1;42)=2.66;p=0.11$ ), a decrease in FEV<sub>1</sub> ( $F(1;42)=2.49;p=0.12$ ) and a decrease in FEV<sub>1</sub>/FVC ( $F(1;41)=0.76;p=0.39$ ).

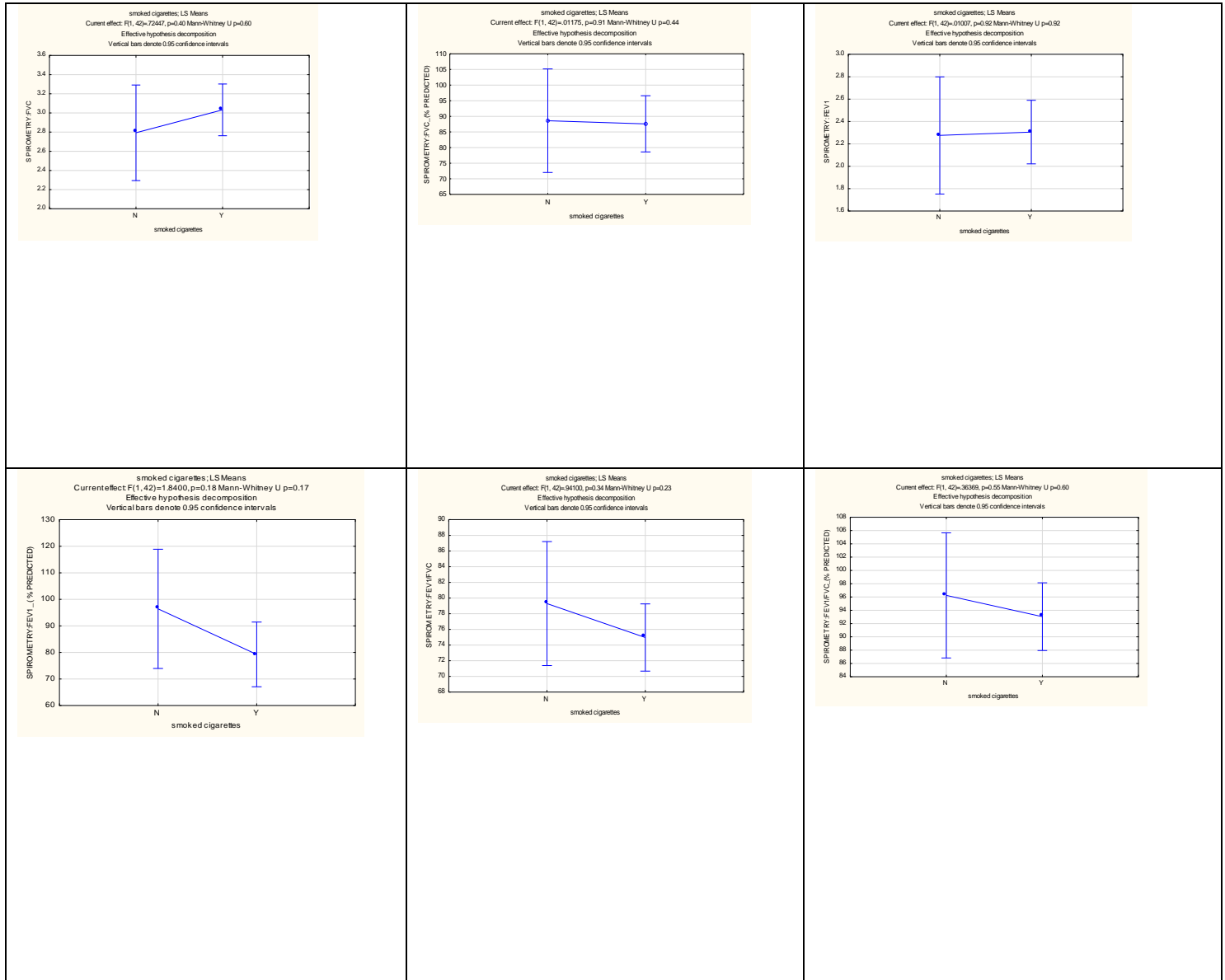


### Cough for longer than 3 months



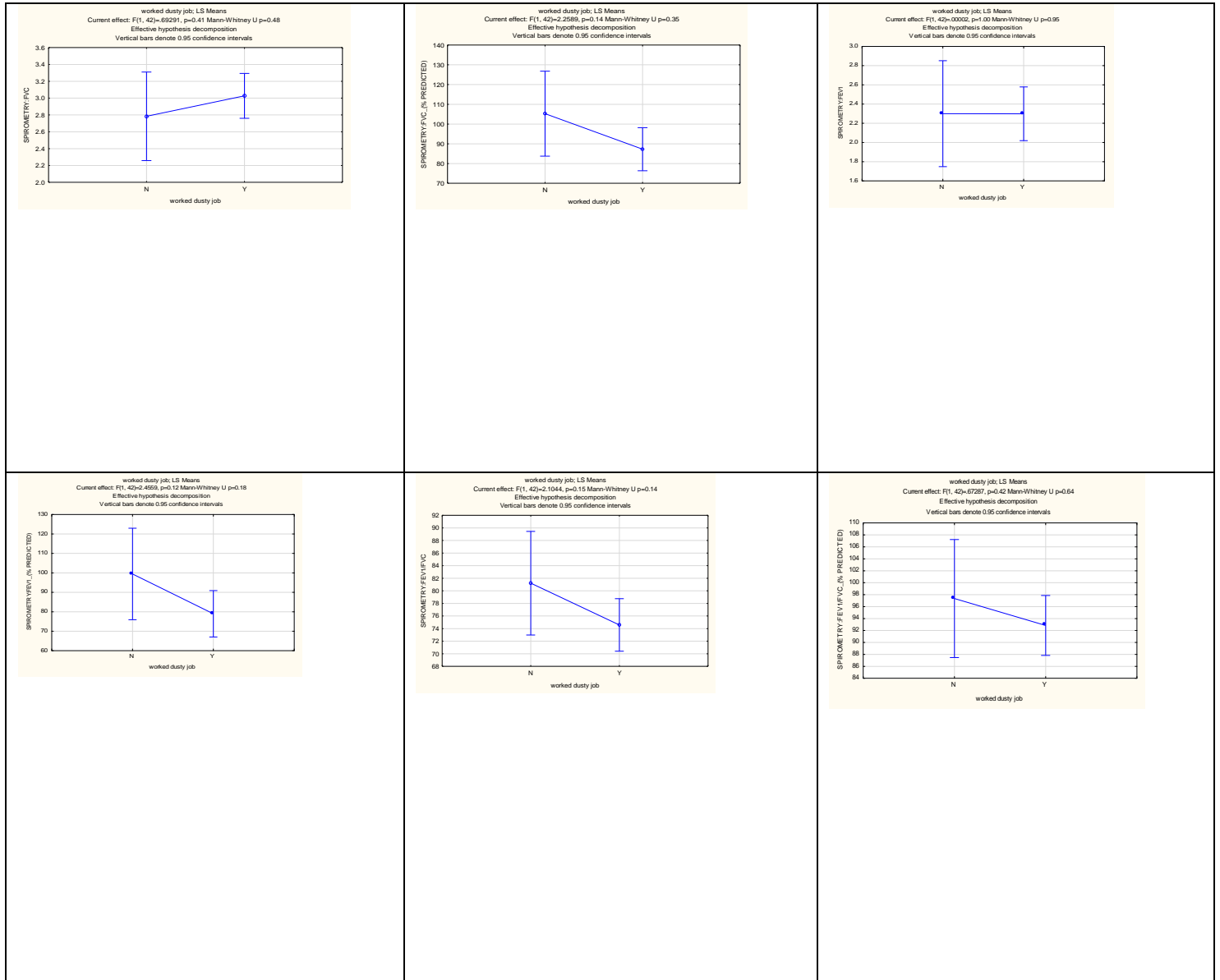
For patients who coughed longer than three months, there was also no significant difference between the groups. However, those who coughed for more than three months showed a decrease in FVC ( $F(1;27)=1.76;p=0.20$ ) as well as a decrease in  $FEV_1$  ( $F(1;27)=0.33;p=0.57$ ).

## Smoked Cigarettes



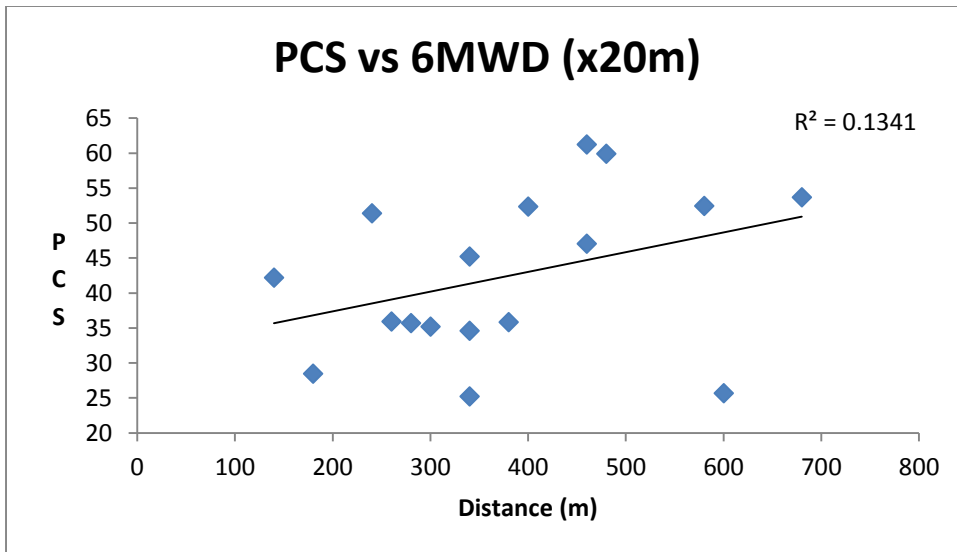
No significant difference was found between smokers and non smokers. However, smokers showed a decrease in FEV1 (%Pred) ( $F(1;42)=1.84;p=0.18$ ) as well as FEV1/FVC (% Pred) ( $F(1;42)=0.36;p=0.55$ )

## Occupational Dust Exposure

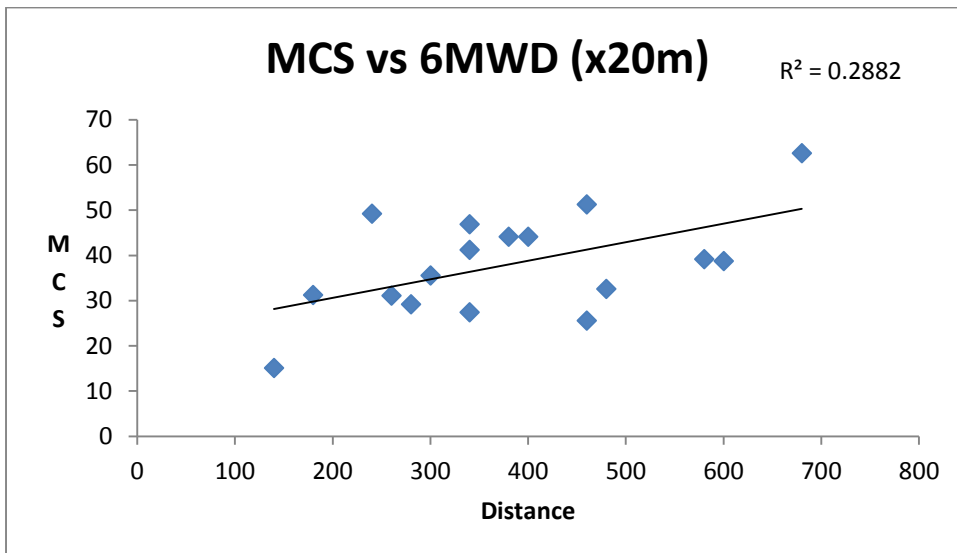


Once again, there were no significant differences between those who worked in a dusty job for longer than 1 year versus those who did not. However, those who were exposed to occupational dust showed a decrease in FEV1 (%Pred) ( $F(1;42)=2.45;p=0.12$ ), a decrease in FEV1/FVC and FEV1/FVC (%Pred) ( $F(1;42)=2.10;p=0.15$  and  $F(1;42)=0.67;p=0.42$ ) respectively.

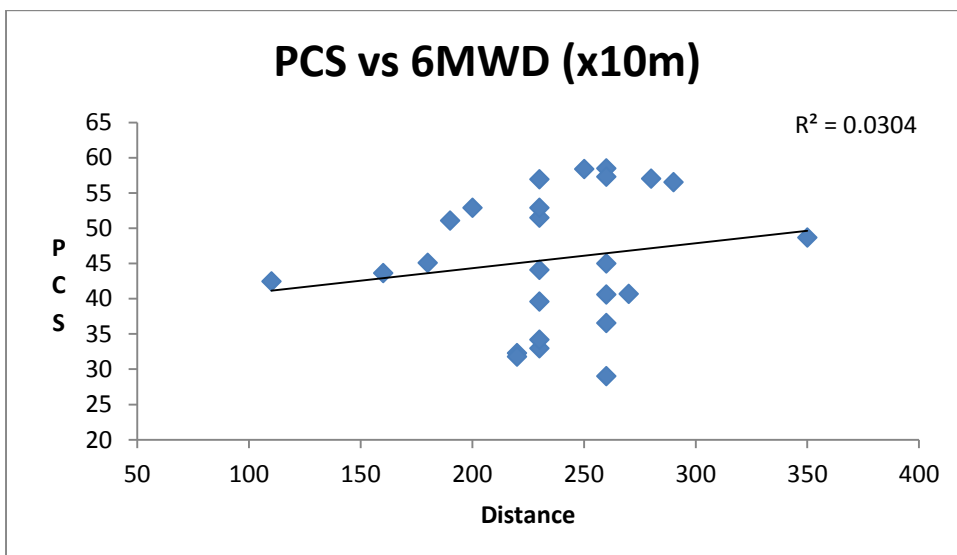
**Appendix C-2: Associations of PCS and MCS with 6MWD**



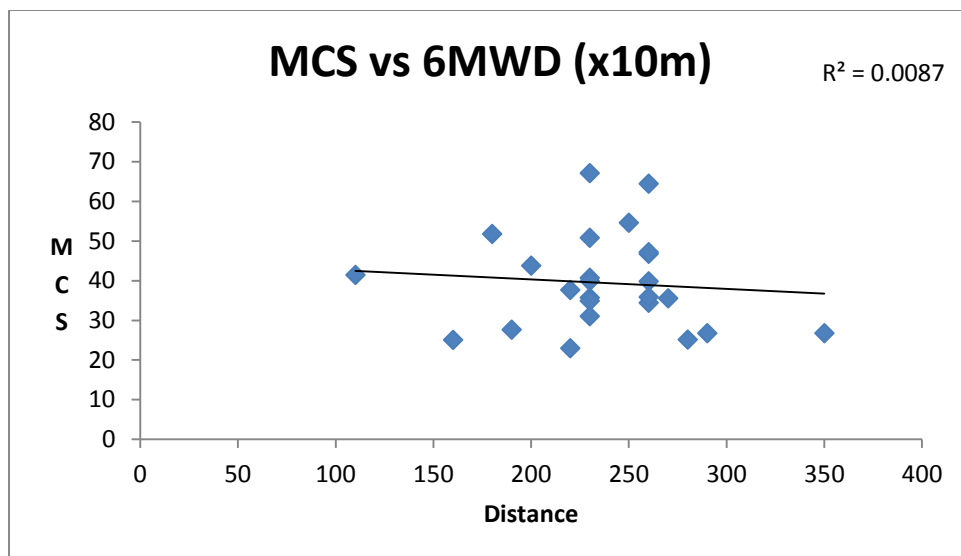
Pearsons Corr 6MWD x20m vs PCS =0.366



Pearsons Corr 6MWD x20m vs MCS = 0.537



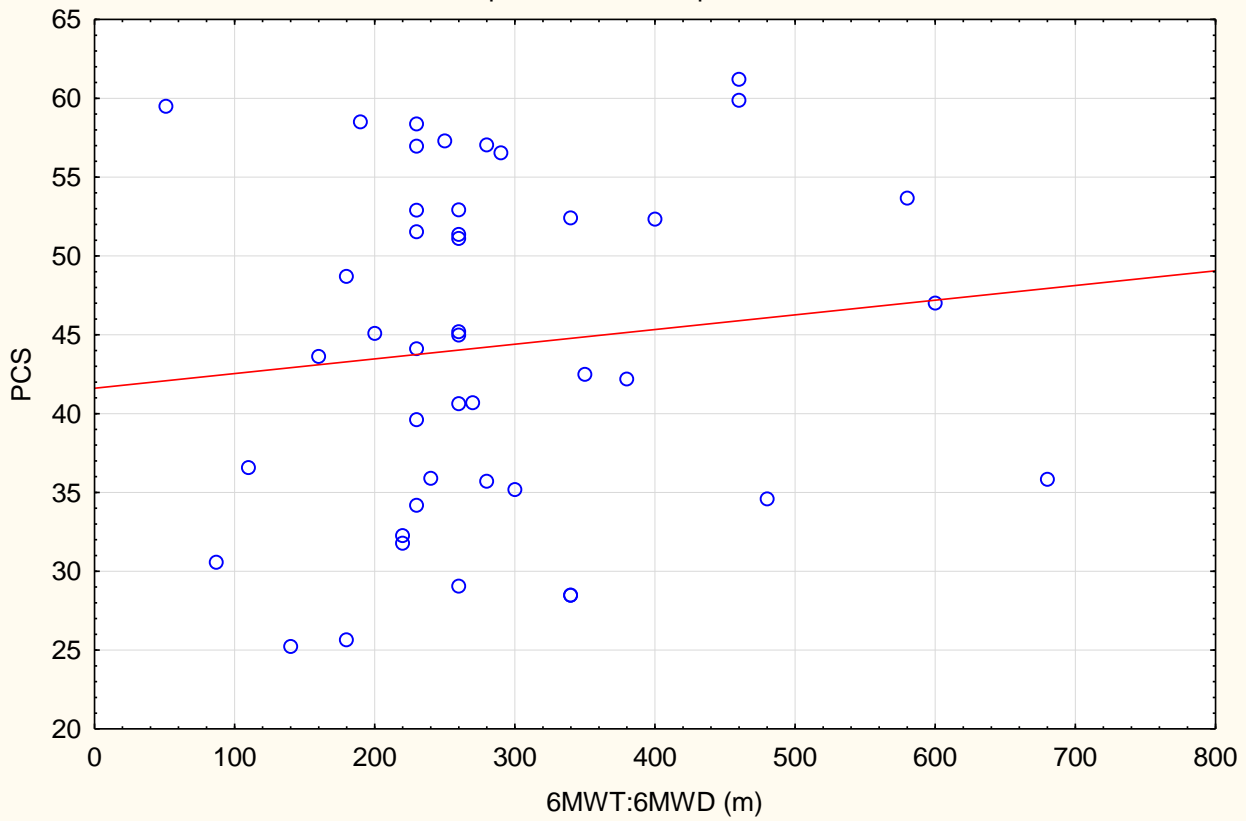
Pearsons Corr 6MWD x10m vs PCS = 0.174

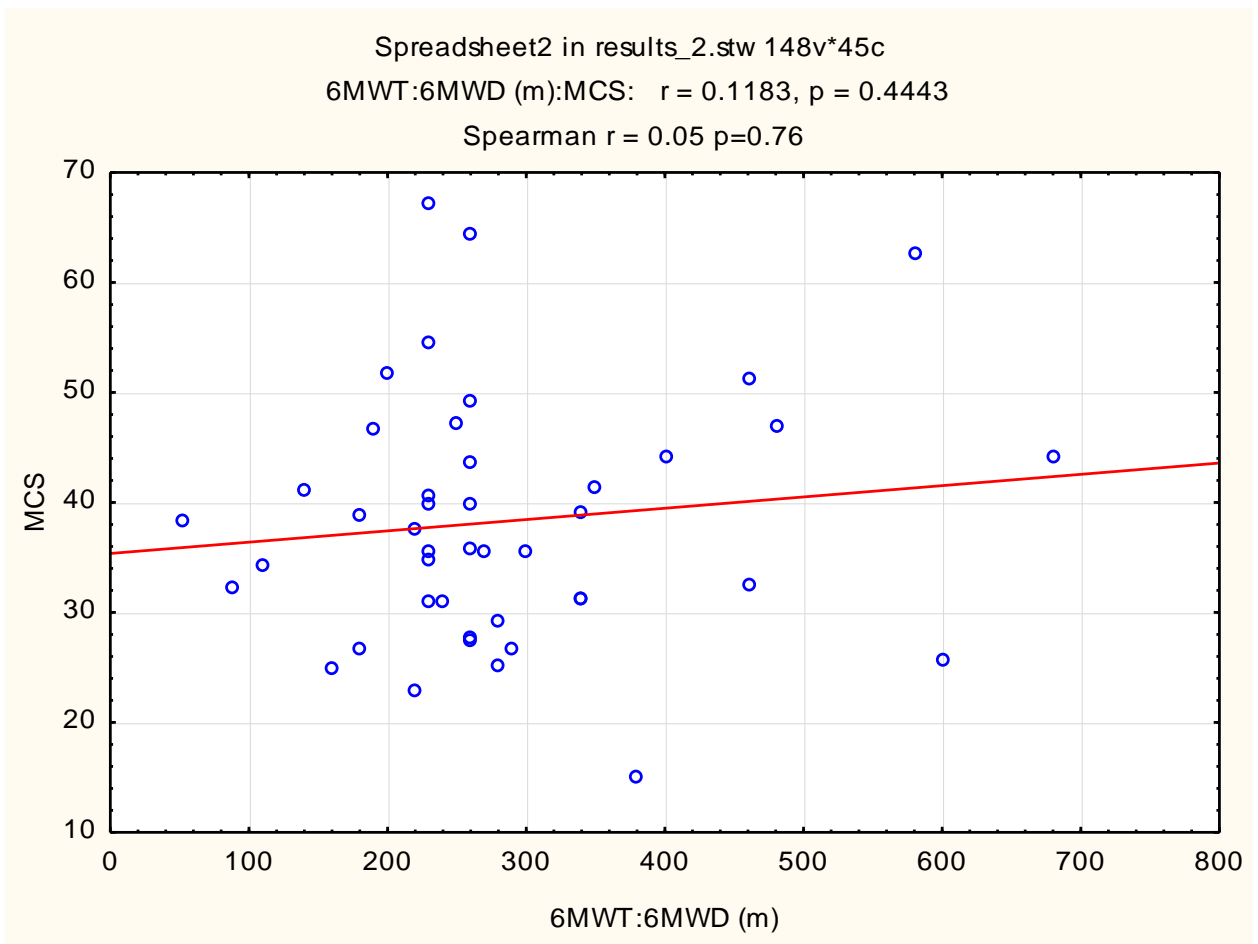


Pearsons Corr 6MWD x10m vs MCS = -0.093

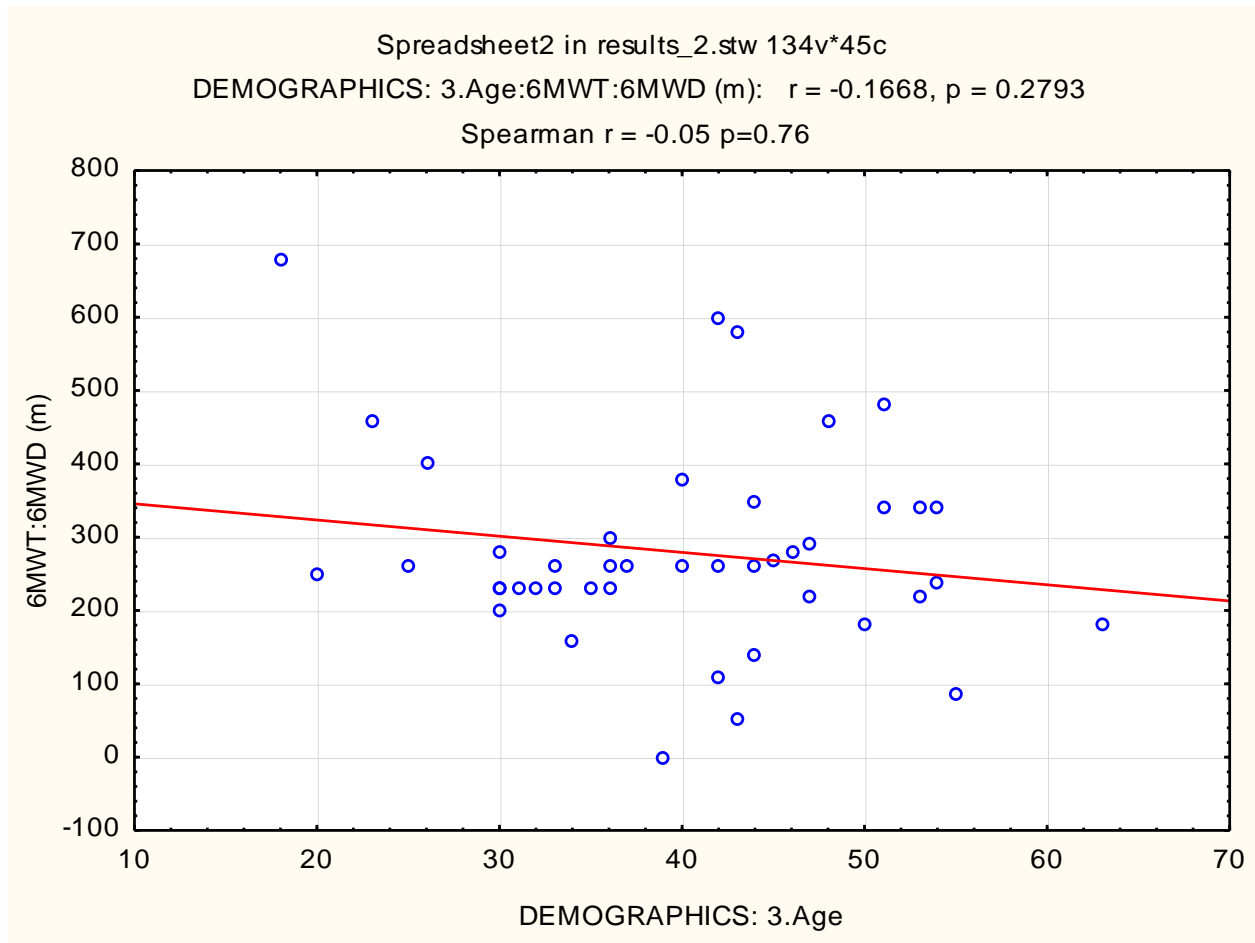
### Appendix C-3: PCS and MCS association with 6MWD

Spreadsheet2 in results\_2.stw 148v\*45c  
6MWT:6MWD (m):PCS:  $r = 0.1125$ ,  $p = 0.4673$   
Spearman  $r = 0.13$   $p=0.40$



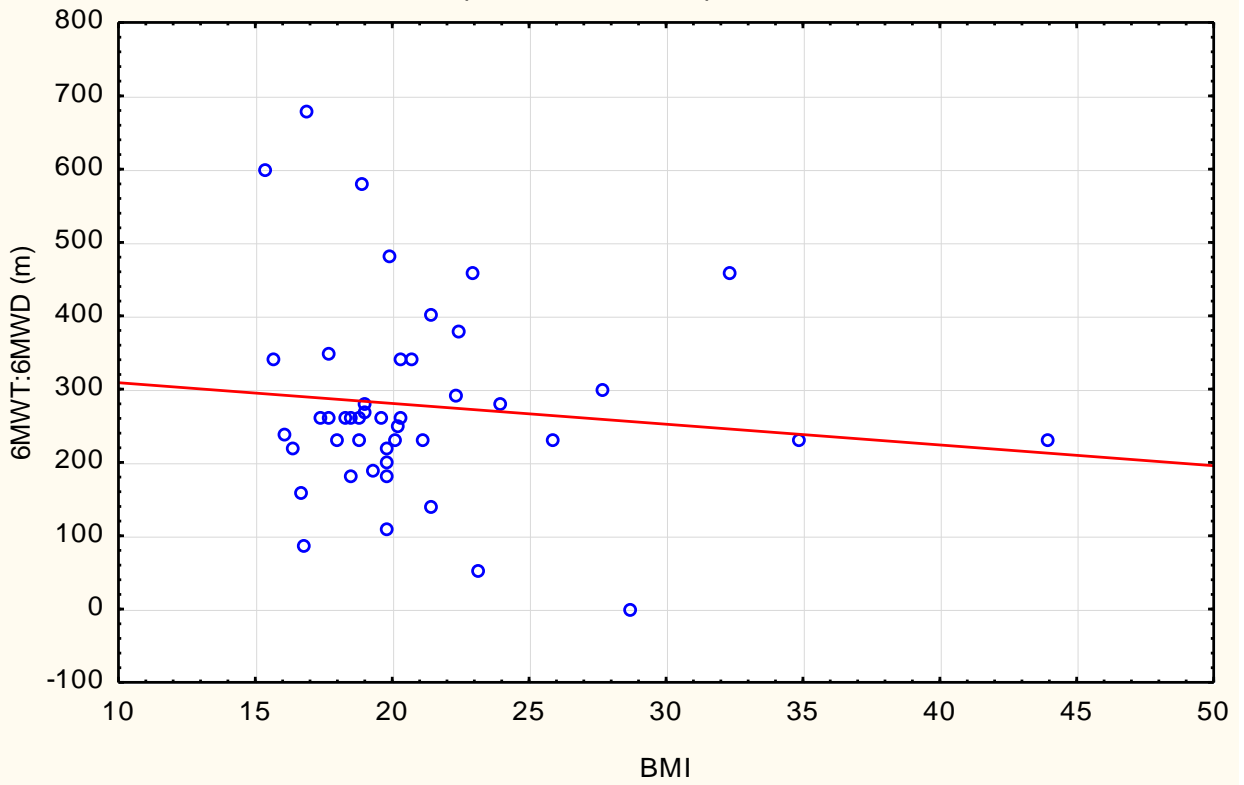


### Appendix C-4: Age and BMI association with 6MWD





Spreadsheet2 in results\_2.stw 134v\*45c  
BMI:6MWT:6MWD (m):  $r = -0.1125$ ,  $p = 0.4617$   
Spearman  $r = -0.02$   $p=0.92$



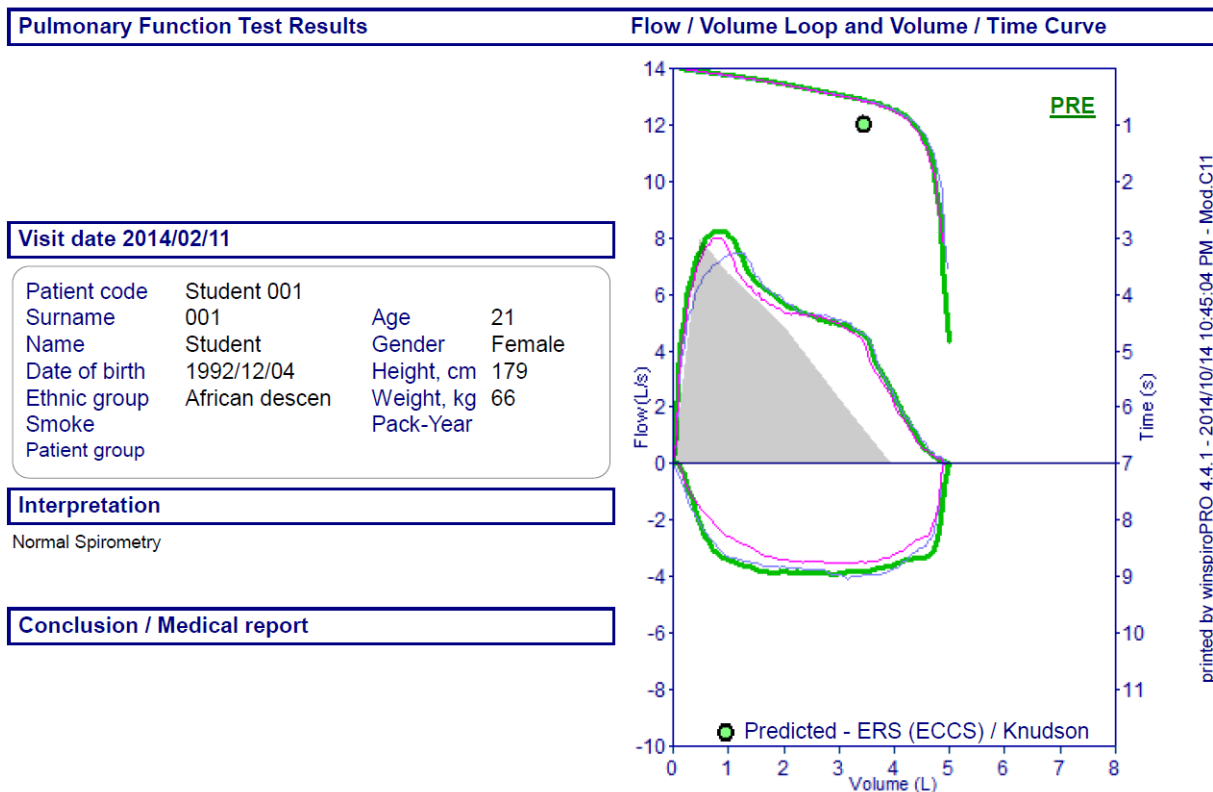
**Appendix C-5: Full Spirometry with GOLD Classification**

Reference	SPIROMETRY:FVC	SPIROMETRY:FVC_PRED	SPIROMETRY:FVC_PREDICTED	SPIROMETRY:FEV1	SPIROMETRY:FEV1_PRED	SPIROMETRY:FEV1_PREDICTED	SPIROMETRY:FEV1/FVC	SPIROMETRY:FEV1/FVC_PRED	SPIROMETRY:FEV1/FVC_PREDICTED	GOLD Stage Classification
**1	3.66	3.61	101.385	3.25	3.15	103.174	90.3	84.16	107.295	
**2	4.45	4.74	93.881	3.89	4	97.25	87.4	82.71	105.670	
12*1	2.35	2.7	87.037	1.8	2.32	77.586	76.6	82.26	93.119	
12*2	2.17	2.84	76.408	1.89	2.46	76.829	87.1	83.4	104.436	
12*3	2.73	4.29	63.636	1.94	3.34	58.083	71.1	76.05	93.491	
12*4	3.39	3.09	109.708	2.53	2.62	96.564	74.6	79.65	93.659	
12*5	2.9	3.64	79.670	1.35	3.07	43.973	46.6	79.83	58.374	Stage 3
12*6	3.99	2.84	140.492	3.54	2.54	139.370	88.7	91.77	96.654	
12*7	3.74	2.15	173.953	3.31	1.82	181.868	88.5	80.74	109.611	
12*8	2.96	2.53	116.996	2.08	2.17	95.852	65	78.93	82.351	Stage 1
12*9	2.13	3.06	69.607	1.6	2.53	63.241	75.1	78.21	96.023	
12*10	1.98	2.28	86.842	1.53	1.94	78.865	77.2	80.17	96.295	
12*11	2.48	2.8	88.571	1.31	2.4	54.583	52.8	81.12	65.088	Stage 2
12*12	1.63	2.39	68.200	0.98	2.03	48.275	60.1	79.79	75.322	Stage 3
12*13	2.44	3.32	73.493	2.07	2.74	75.547	84.8	78.03	108.676	
12*14	2.07	2.44	84.836	1.55	2.09	74.162	74.9	81.5	91.901	
12*15	2.45	3.28	74.695	1.78	2.66	66.917	72.7	77.49	93.818	
12*16	2.97	4.39	67.653	2.14	3.67	58.310	72.1	81.27	88.716	

12*1 7	3.13	3.35	93.432	2.1	2.82	74.468	67.1	79.65	84.243	Stage 1
12*1 8	3.17	3.67	86.376	2.76	3.11	88.745	87.1	80.91	107.650	
12*1 9	1.98	2.54	77.952	1.79	2.18	82.110	90.4	81.31	111.179	
12*2 0	3.89	4.74	82.067	2.98	3.87	77.002	76.6	79.47	96.388	
12*2 1	1.63	3.2	50.937	0.95	2.53	37.549	58.3	76.05	76.660	Stage 3
12*2 2	2.74	3.38	81.065	2.18	2.94	74.149	79.6	83.59	95.226	
12*2 3	2.88	3.62	79.558	2.53	3	84.333	87.8	79.29	110.732	
12*2 4	3.14	3.15	99.682	2.75	2.75	100	87.6	84.35	103.852	
12*2 5	3.85	4.29	89.743	3.55	3.59	98.885	92.2	81.27	113.448	
12*2 6	2.82	4.58	61.572	2.22	3.79	58.575	78.7	80.73	97.485	
12*2 7	2.05	2.74	74.817	1.1	2.37	46.413	55.6	82.64	67.279	Stage 3
12*2 8	3.11	4.06	76.600	2.53	3.24	78.086	81.4	77.49	105.045	
12*3 0	2.01	4.06	49.507	0.94	3.32	28.313	46.8	79.11	59.158	Stage 4
12*3 1	3.92	4.27	91.803	2.78	3.46	80.346	70.9	78.75	90.031	
12*3 2	3.45	4.32	79.861	3.15	3.59	87.743	91.3	80.73	113.093	
12*3 3	3.19	5.05	63.168	1.84	4.23	43.498	57.7	82.71	69.761	Stage 3

12*3										
4	2.62	2.98	87.919	1.96	2.56	76.562	74.8	80.36	93.081	
12*3										
5	2.53	3.24	78.086	2.02	2.81	71.886	79.8	82.45	96.785	
12*3										
6	2.93	3.34	87.724	2.52	2.9	86.896	86	82.64	104.065	
12*3										
7	3.47	5.06	68.577	2.69	4.19	64.200	77.5	81.63	94.940	
12*3										
8	3.56	3.14	113.375	2.97	2.77	107.220	83.8	81.99	102.207	
12*3										
9	2.71	2.81	96.441	2.34	2.42	96.694	86.3	81.88	105.398	
12*4										
0	5.2	4.65	111.827	4.43	3.88	114.175	85.1	81.63	104.250	
12*4										
1	2.94	3.61	81.440	2.24	3.15	71.111	76.2	83.21	91.575	
12*4										
2	2.67	3.24	82.407	2.08	2.79	74.551	77.9	80.17	97.168	
12*4										
3	2.27	3.84	59.114	1.33	3.2	41.562	58.6	80.19	73.076	Stage 3

### Appendix C-6: Pilot Study Data (Lung Function)



PRE Trial date 2014/02/11 12:39:12 PM										
Parameters	BTPS 1,092 25°C - 77°F	Pred	PRE	%Pred	POST	%Pred	%Chg	PRE#1	PRE#2	PRE#3
Best values from all loops										
<b>FVC</b>	L	3.95	5.00	127				5.00	4.96	4.88
<b>FEV1</b>	L	3.46	4.44	128				4.44	4.43	4.34
<b>FEV1/FVC</b>	%	84.4	88.8	105				88.8	89.3	88.9
<b>PEF</b>	L/s	7.99	8.30	104				8.30	7.54	8.03
Values from best loop										
<b>FEF2575</b>	L/s	4.31	5.39	125				5.39	5.51	5.25
<b>FEF25</b>	L/s	6.74	7.25	108				7.25	7.49	6.58
<b>FEF50</b>	L/s	4.92	5.22	106				5.22	5.30	5.28
<b>FEF75</b>	L/s	2.36	3.19	135				3.19	3.22	3.16
<b>FEV3</b>	L	3.75	4.90	131				4.90	4.92	4.85
<b>FET</b>	s	6.00	4.83	81				4.83	3.56	3.10
<b>FIVC</b>	L	3.95	4.83	122				4.83	4.89	4.68
<b>FIV1</b>	L	3.46	4.12	119				4.12	4.08	4.68
<b>FIV1/FIVC</b>	%	84.4	85.3	101				85.3	83.4	100.0
<b>PIF</b>	L/s	7.99	3.98	50				3.98	4.08	3.57
<b>ELA</b>	Years	21	0					0	0	0
<b>VC</b>	L									
<b>IVC</b>	L									
<b>FEV1/VC</b>	%									
<b>ERV</b>	L									
<b>IC</b>	L									
<b>EVol</b>	mL		130							

<b>Quality Report</b>	<b>A</b>
Repeatable FVC, Repeatable FEV1, Repeatable PEF	

Signature

Instrument used  
Spirobank II S/N 004126



**Pulmonary Function Test Results**

**Flow / Volume Loop and Volume / Time Curve**

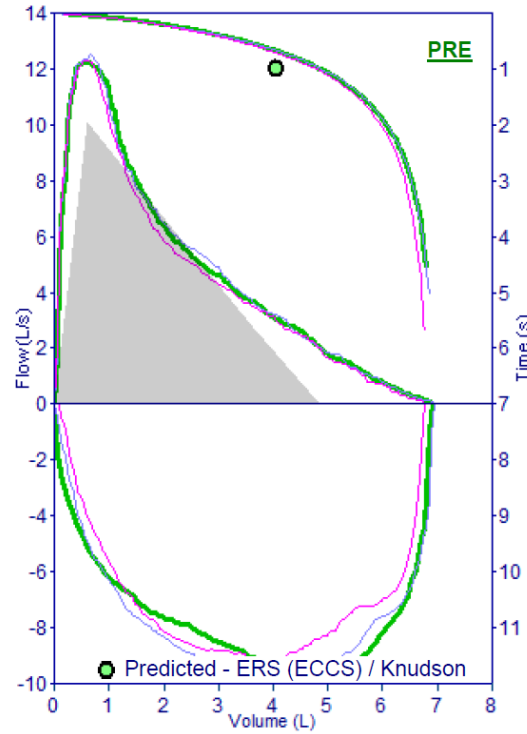
**Visit date 2014/04/08**

Patient code	Student 007	Age	22
Surname	007	Gender	Male
Name	Student	Height, cm	180
Date of birth	1992/03/23	Weight, kg	99
Ethnic group	African descen	Pack-Year	
Smoke			
Patient group			

**Interpretation**

Normal Spirometry

**Conclusion / Medical report**



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**PRE Trial date 2014/04/08 01:00:59 PM**

Parameters	BTPS 1.097 24°C - 75.2°F	Pred	PRE	%Pred	POST	%Pred	%Chg	PRE#1	PRE#2	PRE#3
Best values from all loops										
FVC	L	4.84	6.94	143				6.91	6.94	6.78
FEV1	L	4.07	4.94	121				4.94	4.91	4.82
FEV1/FVC	%	82.7	71.2	86				71.5	70.7	71.1
PEF	L/s	10.13	12.54	124				12.31	12.54	12.34
Values from best loop										
FEF2575	L/s	5.12	3.64	71				3.64	3.59	3.54
FEF25	L/s	8.63	7.12	82				7.12	7.09	6.73
FEF50	L/s	5.70	3.84	67				3.84	3.93	3.74
FEF75	L/s	2.71	1.65	61				1.65	1.78	1.56
FEV3	L	4.60	6.59	143				6.59	6.56	6.42
FET	s	6.00	5.20	87				5.20	5.47	5.69
FIVC	L	4.84	6.93	143				6.93	6.90	6.65
FIV1	L	4.07	6.93	170				6.93	6.90	6.65
FIV1/FIVC	%	82.7	100.0	121				100.0	100.0	100.0
PIF	L/s	10.13	9.60	95				9.60	10.00	9.18
ELA	Years	22	0					0	0	0
VC	L									
IVC	L									
FEV1/VC	%									
ERV	L									
IC	L									
EVOL	mL		140							

**Quality Report** **A**  
 Repeatable FVC, Repeatable  
 FEV1, Repeatable PEF

Signature

Instrument used  
 Spirobank II S/N 004126

1 / 1



**Pulmonary Function Test Results** **Flow / Volume Loop and Volume / Time Curve**

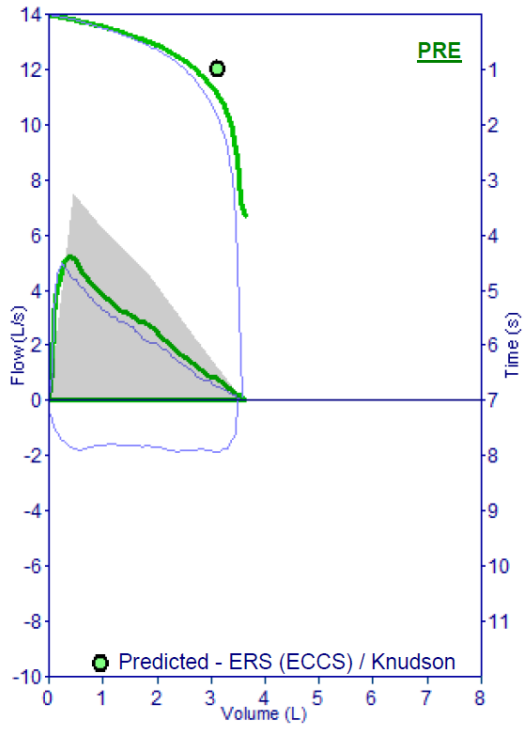
**Visit date 2012/10/10**

Patient code	Student 3	Age	21
Surname	MacKenzie	Gender	Female
Name	Jacqui	Height, cm	170
Date of birth	1991/04/22	Weight, kg	56
Ethnic group	African descen	Pack-Year	
Smoke			
Patient group			

**Interpretation**

Normal Spirometry

**Conclusion / Medical report**



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**PRE Trial date 2012/10/10 02:59:23 PM**

Parameters	BTPS 1.12 19°C - 66.2°F	Pred	PRE	%Pred	POST	%Pred	%Chg	PRE#1	PRE#2	PRE#3
Best values from all loops										
FVC	L	3.59	3.64	101				3.64	3.58	
FEV1	L	3.14	2.79	89				2.79	2.60	
FEV1/FVC	%	84.4	76.6	91				76.6	72.6	
PEF	L/s	7.49	5.23	70				5.23	4.97	
Values from best loop										
FEF2575	L/s	4.20	2.52	60				2.52	2.14	
FEF25	L/s	6.45	3.93	61				3.93	3.47	
FEF50	L/s	4.70	2.77	59				2.77	2.16	
FEF75	L/s	2.27	1.15	51				1.15	1.00	
FEV3	L	3.41	3.57	105				3.57	3.47	
FET	s	6.00	3.66	61				3.66	6.95	
FIVC	L	3.59								
FIV1	L	3.14								
FIV1/FIVC	%	84.4	0.0	0				0.0	100.0	
PIF	L/s	7.49								
ELA	Years	21	0					0	0	
VC	L									
IVC	L									
FEV1/VC	%									
ERV	L									
IC	L									
EVol	mL		0							

**Quality Report** **C**

Repeatable FVC, Repeatable PEF

Signature

Instrument used  
Spirobank II S/N 004126



## Appendix C-7: Spirometer Calibration

### Spirometer Calibration Report

Reusable (dark plastic)



Calibration test **SUCCESSFULLY COMPLETED**. The Device is now using the following correction values:  
(Expiration: 1.15% ,Inspiration: 1.25%)

Date 2012/10/08

Time 16:32

#### Device

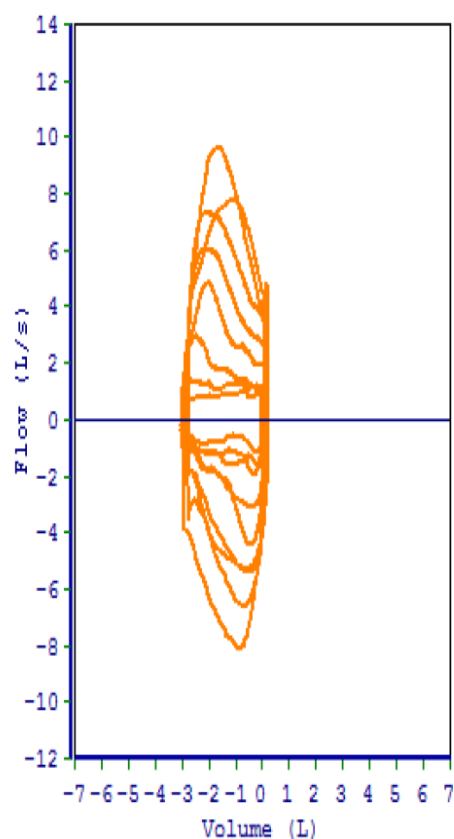
**Spirobank II**  
Serial Number 004126  
Version 3.6  
Turbine Reusable

#### Calibration Test Results

BTPS 1.115  
Test Target 3 L

Expiration Correction 1.15%

Inspiration Correction 1.25%



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#### Calibration Test Details

Expiration (L)	3.03	3.04	3.07	3.07	3.06	3.04	3.01	2.98		
Inspiration (L)	3.00	3.04	2.99	3.02	2.96	3.02	3.02	3.05	3.11	

\* Volume Out Of Range (Excluded from Calibration)



**Spirometer Calibration Report**

Reusable (dark plastic)



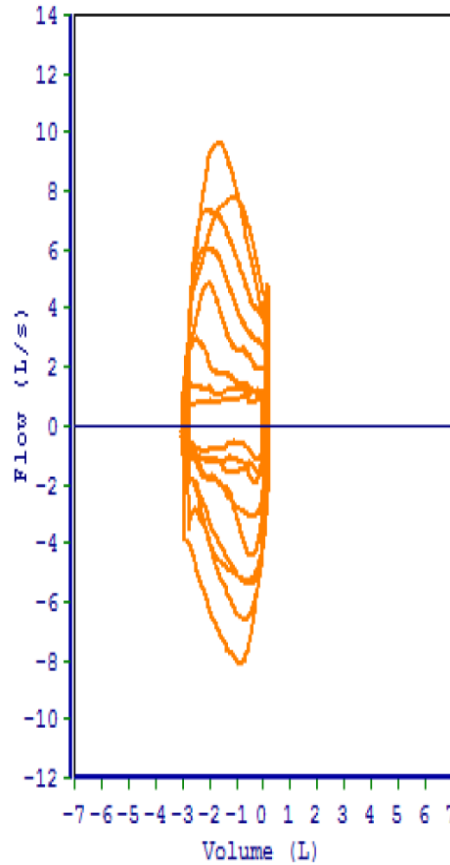
The device calibration correction has been reset to the following default values: Expiration 0%, Inspiration 0% (factory settings)

Date 2012/10/10

Time 14:36

Device	
<b>Spirobank II</b>	
Serial Number	004126
Version	3.6
Turbine	Reusable

Calibration Test Results	
BTPS	1.12
Test Target	3 L
Expiration Correction	0 %
Inspiration Correction	0 %



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**Calibration Test Details**

Expiration (L)	3.03	3.04	3.07	3.07	3.06	3.04	3.01	2.98		
Inspiration (L)	3.00	3.04	2.99	3.02	2.96	3.02	3.02	3.05	3.11	

\* Volume Out Of Range (Excluded from Calibration)

**Spirometer Calibration Report**

Reusable (dark plastic)



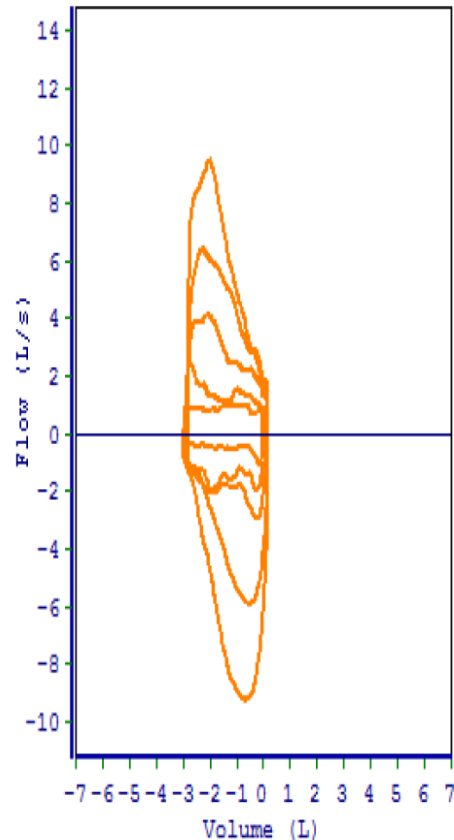
Calibration test **SUCCESSFULLY COMPLETED**. The Device is now using the following correction values:  
(Expiration: 1.43% ,Inspiration: 0.75%)

Date ----- 2012/12/20

Time ----- 21:39

Device	
<b>Spirobank II</b>	
Serial Number	004126
Version	3.6
Turbine	<b>Reusable</b>

Calibration Test Results	
BTPS	1.087
Test Target	3 L
<b>Expiration Correction</b>	<b>1.43 %</b>
<b>Inspiration Correction</b>	<b>0.75 %</b>



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**Calibration Test Details**

Expiration (L)	3.00	3.07	3.06	3.06	3.04	3.04	3.01	2.98		
Inspiration (L)	2.97	2.95	2.99	3.05	3.08	3.02	3.02	3.05	3.11	

\* Volume Out Of Range (Excluded from Calibration)

**Spirometer Calibration Report**

Reusable (dark plastic)



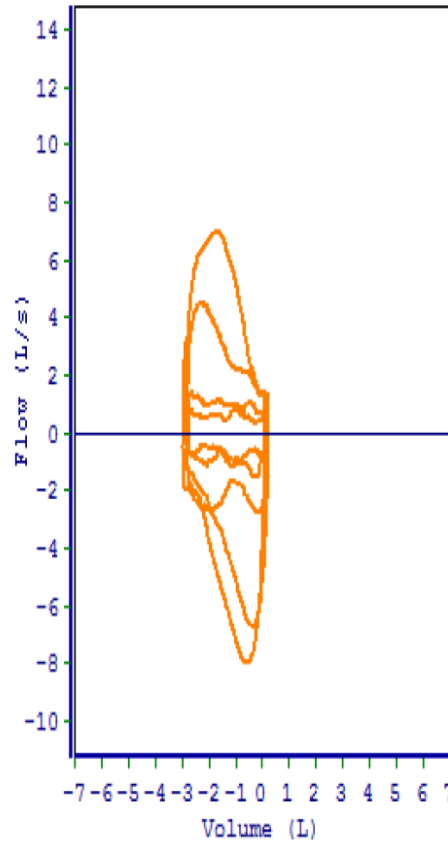
Calibration test **SUCCESSFULLY COMPLETED**. The Device is now using the following correction values:  
 (Expiration: 0.25% ,Inspiration: 0.94%)

Date 2013/02/11

Time 13:11

Device	
<b>Spirobank II</b>	
Serial Number	004126
Version	3.6
<b>Turbine</b>	<b>Reusable</b>

Calibration Test Results	
BTPS	1.097
Test Target	3 L
<b>Expiration Correction</b>	<b>0.25 %</b>
<b>Inspiration Correction</b>	<b>0.94 %</b>



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**Calibration Test Details**

Expiration (L)	2.97	3.03	3.06	2.98	3.04	3.04	3.01	2.98		
Inspiration (L)	2.78	2.99	3.03	3.09	3.11	3.02	3.02	3.05	3.11	

\* Volume Out Of Range (Excluded from Calibration)