Exploring demand and supply constraints on early TB detection in South Africa

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Declaration

By submitting this dissertation electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously – in its entirety or in part – submitted it for obtaining any qualification.

This dissertation includes two original papers published in peer-reviewed journals (Paper One (Chapter 2) published in *BMC Health Services Research*: doi: 10.1186/s12913-019-3992-6 and Paper Two (Chapter 3) published in *International Journal of Environmental Research and Public Health*: doi: 10.3390/ijerph15040729) and one original unpublished paper (Paper Three (Chapter 4)). The development and writing of the papers (published and unpublished) were the principal responsibility of myself and, for each of the cases where this is not the case, a declaration is included in the thesis indicating the nature and extent of the contributions of co-authors.

Declaration by the candidate:

With regard to Chapter Two, the nature and scope of my contribution were as follows:

Nature of contribution	**Extent of contribution (%)**
Conceived and designed the study; analysed and interpreted the data; wrote the paper; read, edited and approved the paper.	80%

The following co-authors have contributed to Chapter Two:

Name	**e-mail address**	**Nature of contribution**	**Extent of contribution (%)**
Cobus Burger	[redacted]	Provided technical inputs; read, edited and approved the paper.	6%
Mareli Claassens	[redacted]	Participated in data acquisition; provided clinical inputs; read, edited and approved the paper.	4%
Virginia Bond	[redacted]	Participated in data acquisition; provided anthropological inputs; read, edited and approved the paper.	4%
Ronelle Burger	[redacted]	Conceived and designed the study; read, edited and approved the paper.	6%

Declaration with signature in possession of candidate and supervisor.

With regard to Chapter Three, the nature and scope of my contribution were as follows:

Nature of contribution	Extent of contribution (%)
Conceived and designed the study; managed the data collection; analysed and interpreted the data; wrote the paper; read, edited and reviewed and edited the paper.	80%

The following co-authors have contributed to Chapter Three:

Name	e-mail address	Nature of contribution	Extent of contribution (%)
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Dumisani Hompashe	[redacted]	Managed the data collection; proofread the paper.	4%
Anja Smith	[redacted]	Conceived and designed the study; managed the data collection; proofread the paper.	5%
Ronelle Burger	[redacted]	Conceived and designed the study; managed the data collection; reviewed, proofread and edited the paper.	6%

Declaration with signatures in possession of candidate and supervisor.

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It is done. To God be the glory.

Dedications

This body of work is dedicated to all people affected by tuberculosis in South Africa. My hope is that these findings will contribute to policies that will make a meaningful and positive difference to the patient's TB care journey.

Abstract

The infectious nature of tuberculosis (TB) makes early TB detection an important public health objective. In the South African context, where the high TB burden remains concentrated among the poor and is exacerbated by the human immunodeficiency virus epidemic, TB control is a high priority for the National Department of Health. However, without an adequate grasp of the supply and demand issues underlying delays in TB detection, policies intended to improve detection, and ultimately TB outcomes, are unlikely to succeed.

The overarching aim of the three chapters in this thesis is to consider the role of crucial demand- and supply-side constraints on early TB detection in South Africa. In this regard, three key factors are considered: The health-seeking behaviour of TB-symptomatic persons, the quality of TB care at the primary healthcare level and the role of nurse workloads in TB-detection protocol compliance.

Early TB detection advances access to treatment, thereby preventing further transmission, in other words, demand prevention. Of great importance in determining whether a TB-symptomatic person seeks healthcare or not are the individual's social and economic circumstances, as well as other generally unobservable factors such as TB stigma.

Findings from Chapter 2 indicate that most persons with a chronic cough did not seek care for it. This is a perturbing finding considering that data were collected in high TB burden communities. Findings also provide evidence that in these communities, TB-control interventions may benefit from focusing on youth, those with lower levels of education, smokers and higher socioeconomic status sub-groups. Although no role for stigma in health-seeking behaviour was found, this finding underscores the need to improve methods to measure stigma.

On the supply side, access to affordable, quality healthcare services with adequate capacity and the willingness to identify presumptive TB patients are essential prerequisites for the timely detection of TB. Chapters 3 and 4 explore supply-side weaknesses that place critical constraints on the effectiveness of TB detection at the primary healthcare level.

Chapter 3 uses the unannounced Standardised Patient (SP) method to measure the quality of TB screening at primary healthcare facilities in urban South Africa. Findings from this chapter highlight the disconnect between the prescribed TB protocols and its implementation. Even though gaps and missed opportunities for early TB detection are identified (i.e. there is room for improvement), some findings are positive. These positive findings imply that there is a stronger than expected responsiveness to TB detection in South Africa than the current literature would suggest, although it is clear that weaknesses remain. Chapter 4 uses an SP fixed effects model to estimate primary healthcare facility correlates of TB-detection protocol compliance. The chapter provides evidence that human resource constraints at primary healthcare facilities are associated with suboptimal quality of TB detection. This chapter also recommends further investigation regarding the role of management in quality of care.

The findings of this thesis contribute to the small but growing literature on the economics of infectious diseases and are intended to inform, guide and further enhance TB policies in South Africa. It also provides quantitative evidence for future quality-improvement research in this area.

Opsomming

Die aansteeklike aard van tuberkulose (TB) maak die vroeë opsporing van gevalle 'n belangrike doel van openbare gesondsheidsbeleid. In Suid-Afrika, waar die hoë TB-las onder armes gekonsentreerd bly en vererger word deur die menslike immuniteidsgebreksvirus epidemie, is die beheer van TB 'n groot prioriteit vir die Nasionale Departement van Gesondheid. Maar sonder 'n voldoende begrip van die vraag- en aanbodfaktore wat die opsporing van TB gevalle vertraag sal beleid moeilik kan slaag.

Die oorkoepelende doel van die drie hoofstukke in hierdie proefskrif is om die rol van vraag- en aanbodbeperkings op die vroeë opsporing van TB gevalle in Suid-Afrika te beskou. In hierdie verband word drie faktore ondersoek: Die gesondheidsoekende optrede van TB-simptomatiese persone, die gehalte van TB sorg op primêre gesondheidsvlak, en die rol van die werklading van verpleegsters in die toepassing van die protokol vir die opsporing van TB gevalle.

Vroeë opsporing van TB gevalle verbeter toegang tot behandeling, waardeur verdere oordrag verhinder word, d.w.s. dit verhinder die groei van die vraag na sorg. Iemand met TB simptome se sosiale en ekonomiese omstandighede, sowel as faktore soos stigma (wat moeilik waargeneem word), beïnvloed tot 'n belangrike mate of die persoon stappe neem om gesondheidsorg te bekom.

Bevindinge uit Hoofstuk 2 dui daarop dat die meeste mense met 'n kroniese hoes nie gesondheidsorg bekom het nie. Dit is 'n onrusbarende bevinding, gegewe dat die data afkomstig is uit gemeenskappe met hoë TB-voorkoms. Die bevindinge dui ook daarop dat ingrypings om TB beter te beheer in sulke gebiede liefs moet konsentreer op die jeug, mense met laer opvoedingsvlakke, rokers en hoë sosio-ekonomiese statusgroepe. Al kon daar geen statistiese aanduidings gevind word dat stigma die soeke na gesondheidsorg beïnvloed nie, is dit tog noodsaaklik om die rol van beter meting van stigma te beklemtoon.

Aan die aanbodkant is toegang tot bekostigbare gesondheidsdienste van gehalte met voldoende kapasiteit en die bereidheid om moontlike TB pasiënte te identifiseer 'n belangrike voorvereiste vir die tydige opsporing van TB gevalle. Hoofstukke 3 en 4 verken aanbodkant-gebreke wat belangrike beperkings plaas op die effektiewe opsporing van TB op primêre gesondheidsvlak.

Hoofstuk 3 gebruik die onaangekondigde "Standaard-pasiënt"-(SP) metode om die gehalte van TB diagnose by primêre gesondheidsfasiliteite in stedelike Suid-Afrikaanse gebiede te meet. Bevindinge van hierdie hoofstuk beklemtoon die groot verskil tussen voorgeskrewe TB-riglyne en hulle implementering. Ten spyte van die identifikasie van gapings en verspilde geleenthede vir vroeë opsporing van TB, is van die bevindinge positief. Die positiewe bevindinge impliseer dat daar beter as verwagte TB identifikasie in Suid-Afrika bestaan as wat die bestaande literatuur voorstel, alhoewel dit duidelik is dat daar steeds tekortominge bestaan. Hoofstuk 4 gebruik 'n SP vaste-effek model om die korrelasies tussen primêre gesondheidsfasiliteite en korrekte toepassing van TB-riglyne te beraam. Die hoofstuk toon dat beperkte menslike hulpbronne by primêre gesondheidsfasiliteite verband hou met sub-optimale opsporing van TB. In hierdie hoofstuk ord daar ook aanbevelings gemaak oor die nodgiheid van verdere ondersoek in rol van bestuur in kwaliteit van gesondheidsorg.

Die bevindinge van hierdie proefskrif dra by tot die beperkte maar groeiende literatuur oor die ekonomie van aansteeklike siektes en is bedoel om as inligting en as gids vir die versterking van TB-beleid in Suid-Afrika te dien. Die kwantitatiewe bevindinge dien as 'n kennis basis vir toekomstige navorsing oor gehalte-verbetering op hierdie gebied.

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List of Abbreviations

AIDS	acquired immune deficiency syndrome
CHW	community health worker
DHIS	District Health Information System
DOTS	directly observed treatment short course
GDP	gross domestic product
HBC	high-burden country
HIV	human immunodeficiency virus
LMIC	low- and middle-income country
MCA	multiple correspondence analysis
MIC	middle-income country
PACK	Practical Approach to Care Kit
PCA	principle component analysis
PHC	primary healthcare
REC	Research Ethics Committee
RESET	regression-error specification test
SANTMG	South African National TB Management Guidelines
SES	socio-economic status
SINJANI	Standard Information Jointly Assembled by Networked Infrastructure
SOCS	Secondary Outcomes Cohort Study
SP	standardised patient
TB	tuberculosis
WHO	World Health Organisation
ZAMSTAR	Zambia and South Africa TB and AIDS Reduction

Chapter 1

Introduction

The tuberculosis (TB) crisis is a longstanding one in South Africa. The opening section of the thesis provides an overview of this crisis, focusing primarily on the post-apartheid era. This section is followed by a discussion of the motivation behind the selection of research questions related to TB detection, underpinned by the most relevant theories on the economics of infectious diseases. The research questions selected, which are all related to the demand and supply constraints on early TB detection in South Africa, are then specified, and a cursory overview of the main findings given. The essential yet undervalued contribution of policy-relevant descriptive studies is discussed, with an analysis of the contribution that the thesis makes to this field. The final sub-section of this chapter also includes an outline of the conceptual framework that is later used (in Chapter 5) to contextualise and rearticulate the findings of the thesis to recommend future policy in South Africa.

1.1. TB in the South African Context

Because of the historical legacy of apartheid, healthcare in South Africa is characterised by persistent inequalities across healthcare systems and in other health-related areas. These have translated into chronic inequity in health outcomes between races, genders, cultures, socio-economic statuses, and geographic locations [1]. Despite some recent progress[1], the country's health outcomes remain poor and most of the country's quadruple burden of disease – divided into communicable,[2] non-communicable, perinatal and maternal, and injury-related disorders –

[1] Infant mortality rates have fallen considerably from 1997 to 2017 [2] and the adult life span has increased to 63 years [3].
[2] Infectious.

still falls mostly on the previously disadvantaged [4]. It is in this context that TB – one of the two leading communicable diseases in South Africa[3] [5] – is still regarded as a disease of the poor [6].

Although TB is preventable and curable, it is nevertheless a pandemic [7] and the leading cause of infectious disease mortality worldwide [8]. Developing countries in sub-Saharan Africa and Asia account for approximately 80% of the global TB burden [9] and are therefore classified as TB high-burden countries (HBCs). South Africa, one of the 22[4] countries identified in 1998 as TB HBCs, continues to struggle with this disease, which is the primary driver of morbidity and mortality [8] and the leading cause of death [10] in South Africa.

According to the latest World Health Organisation (WHO) estimate, South Africa had an incidence of 322 000 new cases of active TB in 2017 [11]. This translated into an incidence rate of 567 active TB cases per 100 000 population in that year [11]. Due to the high co-infection[5] rate in South Africa, TB mortality estimates are reported separately for cases excluding human immunodeficiency virus (HIV)-positive TB and cases of HIV-positive TB. This separation allows one to get an unbiased picture of TB mortality trends that is not skewed by the convergent HIV epidemic of recent decades. In 2017, South Africa reported a figure of 22 000 deaths from TB for individuals who were not co-infected, and 56 000 deaths from TB for co-infected individuals [11], highlighting the severe impact of HIV and acquired immune deficiency syndrome (AIDS) on TB [5]. TB is also the leading cause of death in South Africa, albeit with a declining share (the death rate from TB dropped from 8.3% in 2014 to 6.5% in 2016) [10]. Also, the chronic poor control of TB has led to the development of drug-resistant TB, which is more laborious and more costly to treat than drug-sensitive TB [12]. The depth and magnitude of the

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[3] HIV/AIDS being the other.
[4] The 22 HBCs listed since 1998: Afghanistan, Bangladesh, Brazil, Cambodia, China, Democratic Republic of Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, Philippines, Russian Federation, South Africa, Tanzania, Thailand, Uganda, Vietnam, Zimbabwe.
[5] Infected with both TB and HIV.

impact of TB described here point to a public health crisis that warrants an urgent response from the South African government.

Even though the global incidence of TB is falling at approximately 2% per year, this figure needs at least to double annually by 2020 in order to reach the milestones of WHO's End TB Strategy[6] [13]. This global TB crisis, therefore, still needs political will and government commitment to TB control in affected countries. One of South Africa's key TB targets for 2022 – as described in the National Strategic Plan – is to diagnose 90% of all cases of TB [14]. The South African government has prioritised early case detection in TB-control policies and guidelines in order to achieve the National Strategic Plan TB targets. These policies and guidelines have incorporated, to greater or lesser degrees, urgent calls for the following [15]:

- Testing for TB in every symptomatic patient presenting at primary healthcare (PHC) facilities;
- Provider-initiated TB case finding in all HIV-infected individuals treated at PHC facilities;
- Active screening of household contacts of infectious TB patients;
- Identification of high TB prevalence communities in order to implement appropriately targeted programmes that increase the identification of individuals with pulmonary symptoms (e.g. chronic coughing) for TB testing.

As a WHO member affected by the TB pandemic, South Africa has pledged to allocate substantial resources to decreasing TB-related deaths and the incidence of active TB [16]. In 2018, South Africa's National Department of Health allocated US$271 million towards financing its National TB Programme [11]. To place this figure in context, the HIV and TB budget allocation as a share of national consolidated health allocation has increased from 8.3% in

[6] The WHO's End TB Strategy milestones set for 2020 are (i) to reduce deaths from TB by 95%, (ii) to reduce new TB cases by 90%, and (iii) to reduce to zero catastrophic expenses caused by TB.

2014/15 to 9.5% in 2017/18, with an expectation that this percentage will rise to double digits over the medium term [17]. Although public policy efforts such as the National Department of Health's world-class policies to eradicate TB [14], its prioritisation of the National TB Programme, and significant fiscal shifts towards PHC – where the majority of TB cases are diagnosed and treated – may be showing some effect, South Africa is far from achieving its 2022 TB targets. In this regard, South Africa's TB crisis continues.

The success of TB-control activities is highly dependent on a well-functioning healthcare system that ensures affordable, universal access to quality healthcare services [12,15,18–20]. The first democratically-elected South African government of 1994 prioritised healthcare reform and implemented progressive policies – such as the expansion of the healthcare facility network and the gradual abolition of user fees for PHC services – to promote accessible and affordable healthcare for the most vulnerable [21–23]. However, even though physical access to PHC services has increased in post-apartheid South Africa [19,21], the health system is still overburdened and poorly managed [12,24,25]. The result is that TB care at a PHC level is predominantly of a suboptimal quality [20,26].

'Quality of care' in this context refers to the degree to which the healthcare services provided increase the likelihood of the desired health outcomes being achieved, and also the degree to which they are aligned to current professional knowledge [27]. Key descriptors of this broad definition of quality of care include terms such as safe, timely, effective, equitable, efficient, and patient-centred [28,29]. In South Africa, as in other low- and middle-income countries (LMICs), the measurement of healthcare quality is uncertain, and information on it is scarce [30]. The lack of robust and easily accessible healthcare quality metrics can be a barrier to the designing of appropriate quality-improvement interventions that could lead to better health outcomes.

The current supply dynamics in the South African health system are exacerbated by the many social and economic burdens that exist on the demand side [31], including the indirect and opportunity costs of seeking TB care [32]. The result is an inconsistently implemented National TB Programme that struggles to achieve the TB outcomes it aims at. This thesis reveals some of the weaknesses of South Africa's healthcare system in the face of a high TB caseload (and of its direct impact on mortality and share of deaths), TB's concentration among the poor, and the high priority it requires within the National Department of Health. The thesis also contributes to the small but growing health economics literature on TB and provides quantitative evidence to inform and guide relevant policymakers who are designing policy interventions.

1.2. Why the Focus on TB Detection?

Infectious[7] diseases like TB have a unique feature: unlike non-communicable, perinatal and maternal, and injury-related disorders, infectious diseases are transmitted from person to person. For TB, this happens specifically via droplet infection [33]. Given this characteristic, the impact and associated costs of TB are not only borne by the individual, but by society at large. Understanding human behaviour – especially decision-making related to health-seeking behaviour – and externalities are thus core considerations in TB research. Also, the communicable nature of TB makes it challenging to analyse empirically. Despite this, the need for TB research is significant [34] and pressing, as the implications for public health when a TB contagion is not controlled can be severe.

The infectious nature of TB makes early TB detection, which includes testing, particularly important. TB detection advances access to treatment, thereby preventing infectious persons from continuing transmission; in other words, they provide demand prevention. However, from

[7] Communicable.

the individual's perspective, there is not much incentive to test for TB in the absence of affordable treatment.

If the private cost of seeking healthcare for TB outweighs the private benefit, it is conceivable that a potentially infectious person will decide not to seek healthcare. This scenario may seem surprising given that for most diseases, the standard model of economic behaviour predicts that the private benefits of seeking healthcare would greatly outweigh the private costs when the future is discounted at a constant rate [35]. However, the infectious individual studied in this thesis is only mildly symptomatic (i.e. mainly suffers from a persistent cough) as opposed to being gravely ill. The relative mildness of the present symptoms may result in an individual preference change that lowers the discount rate in the long-run when compared to the short-run [36]. Under this condition, the returns to health-seeking for this individual is only realised far into the future and the so-called present bias – an example of time inconsistency – may explain the delay in health-seeking behaviour for 'trivial' symptoms [35].

Furthermore, in the South African context of poverty, high income inequality and widespread unemployment – where indirect and opportunity costs for seeking healthcare are nontrivial [21] – the scenario of delayed health-seeking described above may be plausible even though TB testing and treatment are fully subsidised by the government, i.e. the direct costs are zero. Another important yet underrecognized factor when considering the private costs of seeking TB care is usage costs, i.e. the nontrivial side-effects of anti-TB drugs. Drawing on economic insights from a deworming intervention in Kenya [37], it is likely that through social learning individuals may become aware of the high usage costs of TB treatment – its severe side-effects – which further reduce the anticipated private returns from seeking healthcare.

In addition, classical economic utility theory assumes that individuals would not factor the social benefits of TB testing and treatment into their utility function, even though the social returns to such behaviour would far exceed the private returns. This translates into a gap between the marginal private and marginal social benefit – the public health externality – which explains why demand prevention will be suboptimal (Q_0 in Figure 1.1) if provision is left solely to the market. Under these conditions, public health interventions are required to internalise the marginal external benefit so that demand prevention may be increased (Q_1 in Figure 1.1) [38].

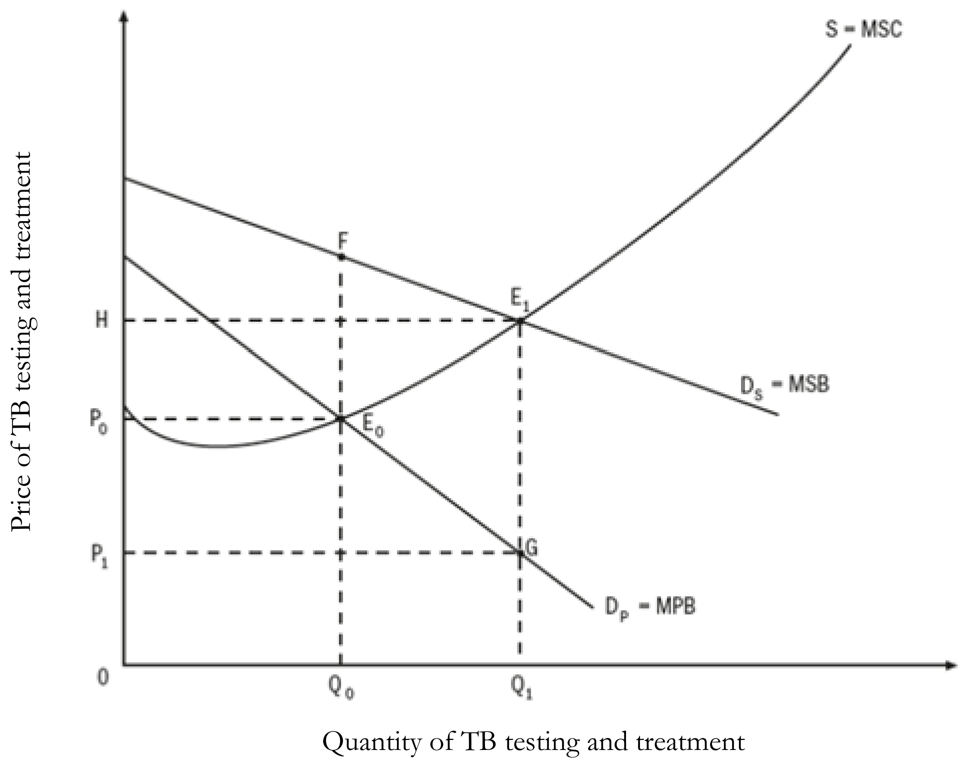

Figure 1.1: The external benefits of TB testing and treatment
S = supply; MSC = marginal social cost; D_S = social demand; MSB = marginal social benefit; D_P = private demand; MPB = marginal private benefit. Source: Figure adapted from Black & Siebriets **[39]**

Public health interventions that promote early TB detection may, to some extent, be motivated by an assumption that individuals are altruistic [34]. Considering the full costs and benefits, infectious individuals bear the cost of their (at minimum) 6-month TB treatment journey even when the (greater) benefit accrues to society [34]. In some cases the magnitudes of the individual costs and social benefits may be such that altruism (the weight the individual places on the social benefit), may be crucial for determining the decision taken. The empirical analysis of altruism amongst infectious individuals is therefore of interest, although rarely studied in economics [40] because quantifying the externality is challenging and highly dependent on the nature of the disease and the proposed intervention [41]. At present, the few empirical studies on altruism amongst infectious individuals are confined to vaccinations for influenza [42], and thus there is currently no empirical evidence to support the altruism argument to justify early TB detection interventions.

As previously mentioned, the spread of TB and its consequences can be more effectively mitigated through early TB detection (and subsequent appropriate treatment) [43]. In addition to the private and social benefits of early TB detection, amplifying TB detection interventions is essential in order to enhance the efficiency and impact of new diagnostic tools [20]. At least one modelling study has demonstrated that the impact of cure rates on TB control is significantly amplified when combined with early case detection [44]. For all these reasons, TB detection remains one of the cornerstones of TB control [15].

Unfortunately, individuals with active TB often remain undetected for too long, resulting in disease progression and suffering for the TB carrier, associated health-related costs, and the further spread of the disease to vulnerable persons in both the immediate and non-immediate environments [15,20]. This thesis therefore focuses on TB case detection, in particular detection arising from actions taken by the patient, referred to as the 'patient-initiated pathway' [45].

The patient-initiated pathway is regarded as the most important route to TB detection [45]. This process, also referred to as passive case finding, involves a person with TB symptoms actively seeking care for his or her symptoms. Whether the person does so will depend mainly on demand-side factors, such as sufficient awareness and knowledge about when, where and how to seek care. This highlights the important role of *information* in health-seeking behaviour [35,46,47]. The failure to recognise TB symptoms blocks the patient-initiated pathway at an early stage

(Figure 1.2). If the patient does reach the point in the pathway of recognizing the symptoms, he or she then needs to progress to accessing healthcare. However, symptom recognition alone does not guarantee health-seeking at this stage in the pathway.

Without access to information on the benefits of early TB detection, a person who recognises their symptoms may still underinvest in healthcare. In the developing country context of high TB burden countries, where *imperfect information* is exacerbated by weak penetration of public health communication and low education levels, it is conceivable that some TB carriers may still fail to access healthcare [35]. The complementarity between *education and information* warrants a mention here given the dire state of South Africa's education system [48]. In seminal work by Schultz, he argues that schooling enhances information acquisition and processing [49]. This implies that without education, it may be challenging for individuals to process and internalise the health information at their disposal, and therefore individuals with lower levels of education may be disadvantaged in this regard [50,51].

However, even if an individual has free access to information and this information was readily processed, one cannot assume that a TB-symptomatic person will automatically progress to accessing healthcare. The recent and growing literature on *active information avoidance* may be useful to explain why patient delay and access delay occurs along the patient-initiated pathway [52,53].

Active information avoidance (referred to as information avoidance from this point) occurs when people avoid information under the dual criteria that (1) there is an awareness that the information exists and (2) the information is costless to obtain. In the South African context, neither of these conditions may hold for all members of its society. It is highly likely that for the majority of vulnerable South Africans there exist nontrivial indirect and opportunity costs to accessing information. However, it remains worthwhile considering that information avoidance, specifically avoidance caused by *risk, loss and disappointment aversion* [54,55] and *anxiety* [56,57], may account for some of the patient and access delays encountered along the patient-intiatied pathway.

The *social, demographic and economic circumstances* of the individual can have a strong influence on whether the symptomatic person seeks healthcare or not [35], along with other generally unobservable factors such as *anticipated TB stigma* [58]. These factors, which may pose barriers to accessing healthcare (Figure 1.2), are further investigated in Paper One (Chapter 2).

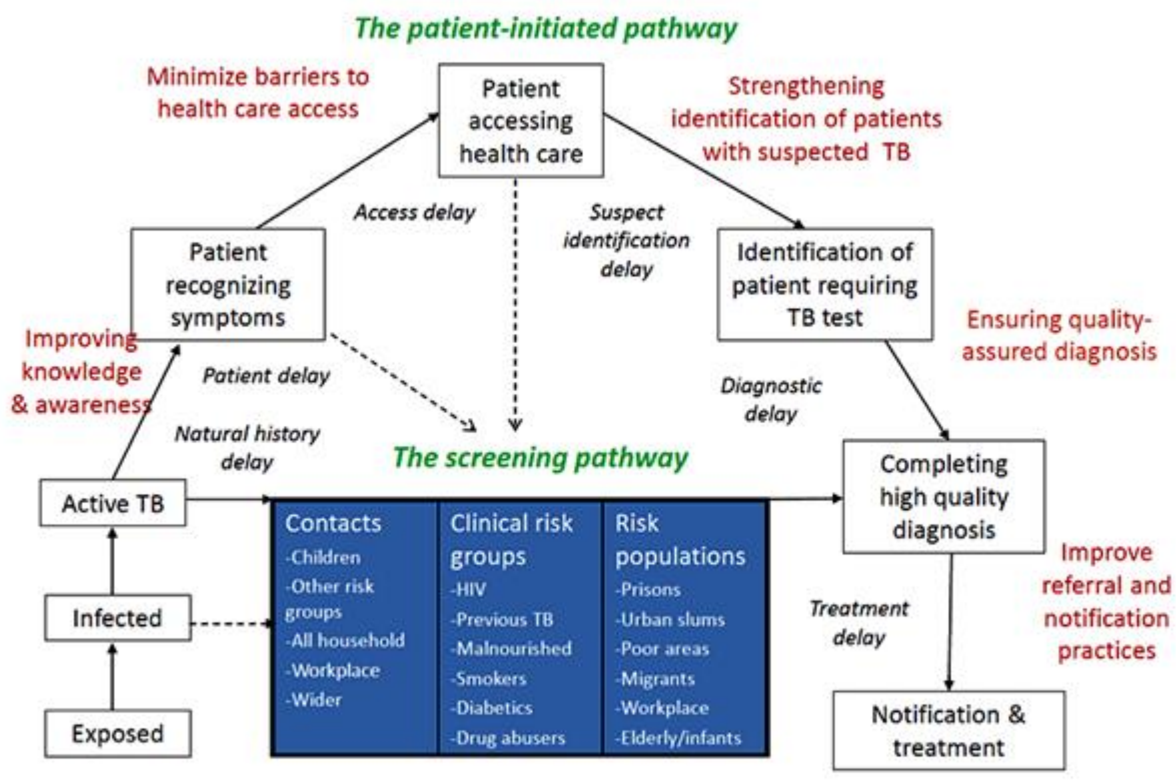

Figure 1.2: The patient-initiated pathway and the screening pathway to TB case detection
Source: World Health Organisation [45]

Supply factors are also relevant to the patient-initiated pathway, from the first accessing of healthcare to the final stages of notification and treatment. Access to affordable, *quality* healthcare services with both an adequate capacity and a willingness to identify presumptive TB patients, accurate diagnostic services, and a functioning referral and notification system are all necessary for the successful completion of the patient-initiated pathway (Figure 1.2). If any of these elements are lacking, delays to detection may arise at any stage in the pathway.

As one of the published research papers (Paper Two, Chapter 3) in this thesis shows, poor follow-up and communication practices – evidence of *weak information flows* from the provider to the patient – also posed critical constraints to timely TB detection for patients who sought help for a cough at a PHC facility. Patient follow-up and communication practices may be implicit in the WHO's process of notification and treatment, but, given both their importance and the neglect they have received, there may be benefits in making this explicit (Figure 1.2). Other supply constraints to quality TB detection at PHCs in South Africa are also considered in Paper Three (Chapter 4).

The pervasive *information asymmetries* at play within healthcare – between patient and healthcare provider, healthcare provider and public health officials, and public health officials and patients – create high levels of uncertainty that undermine trust [46]. In the absence of well-developed and credible regulatory frameworks and enforceable minimum standards (both examples of institutional arrangements), the patient-provider interaction cannot be mediated, and consequently the quality of care received may be inadequate [59–62]. Poor quality of care may partly explain why demand for public healthcare services in developing countries is suboptimal [21,35,63–65].

Furthermore, patients may rely on soft proxies for quality – such as patient-centred features like staff friendliness – due to information asymmetries. This means that even in cases where the clinical quality of care is good, if patient-centredness is lacking the quality of the care may still be perceived as poor by the patient. When trust in the healthcare system is compromised, potentially infectious persons may delay seeking care for mild symptoms (e.g. a chronic cough) because they anticipate that the indirect and opportunity costs incurred when seeking care are unlikely to result in quality service provision.

The complementary approach of systematic screening using the screening pathway,[8] as illustrated in Figure 1.2, may be considered in contexts where significant efforts to reduce constraints to the patient-initiated pathway have already been made. This active approach to case-finding involves the targeted identification of persons with presumptive TB among those who do not actively seek care for their TB symptoms, remaining undiagnosed or being diagnosed too late. The screening pathway also includes active identification of presumptive TB among persons who start but fail to complete the patient-initiated pathway [45]. If focused on high-risk groups and executed correctly – using an approach suitable to the local health system, resources, and the epidemiological context – systematic screening may reduce morbidity and mortality. Nevertheless, given the risks and costs associated with systematic screening, its potential benefits need to be carefully assessed before undertaking it. Poorly-targeted systematic mass screening should be avoided, as there is a high risk of wasting scarce resources and the potential to cause more harm than good [66–69].

It is useful to consider the documented gaps and weaknesses at the primary stages in the TB pathway of care to better understand TB detection in a more localised context [70]. The primary stages of TB care overlap with the access, identification, and diagnostic milestones in the patient-initiated pathway of care. The few empirical South African studies centred on these stages in the case-detection process show poor management of persons presenting with classic TB symptoms [20]. One study found that between 63% and 79% of TB-related symptoms were missed when patients were seen at PHC facilities in South Africa [71]. This finding echoes that of another PHC study, which found that only 23% of TB-symptomatic persons were asked to provide

[8] Also referred to as active case finding.

sputum for a TB test [72]. An empirical study estimating losses along the TB-care pathway found that 5% of individuals who engaged with the public health system in South Africa were unable to access TB tests [19]. In addition, the study showed that deviations from diagnostic guidelines might partially contribute to the 13% of TB cases lost between TB testing and diagnosis. Such missed opportunities are further exacerbated when one considers that the quality of care received by persons who manage to continue along the TB-care pathway is not guaranteed, but that goes beyond the scope of this thesis.

The empirical studies described above underscore the critical role of supply-side factors in determining the success of TB detection, and therefore of TB control. It is vital to remember that these studies only investigate cases where the person has sought healthcare. Multiple demand-side factors may prevent an individual from seeking care, but there is a dearth of studies investigating this phenomenon [73,74]. Without an adequate grasp of the supply and demand issues underlying delays in TB detection, policies intended to improve detection are unlikely to succeed.

A recently-published article, which considered the status of economic research on infectious diseases over the last two decades, described how there is a lack of both theoretical and empirical economic research on human behaviour in infectious diseases [34]. In particular, the few papers in traditional economics journals that investigate prevention strategies for infectious diseases do not cover TB but instead focus on diseases like HIV/AIDS, sexually transmitted infections, malaria and influenza [34,35]. Perhaps this is understandable given the aetiology of TB, its treatment duration (a minimum of 6 months) and that its preventative measures are not as explicit as those for other infectious diseases, e.g. condom use (HIV/AIDS and sexually transmitted infections), insecticide-treated bednets (malaria), and vaccinations (influenza). This gap in economic research on TB is worrying when one considers that human behaviour may be the single most crucial factor impacting the spread of TB and the success of public health interventions [75].

Economists are trained to use various theories and empirical methods to explain the behaviour of individuals and groups and are therefore well-positioned to make meaningful research contributions in the field of TB. However, the unique characteristics of TB as an infectious disease and the idiosyncratic complexities of the health systems where TB is prevalent, make it imperative for economists to adopt an interdisciplinary approach when doing TB research in high TB burden countries. An interdisciplinary approach requires economists to integrate perspectives from anthropology, sociology, psychology, implementation science, epidemiology and clinical medicine. This thesis is a product of extensive multi-disciplinary and multi-stakeholder engagement with the aforementioned disciplines and relevant government stakeholders, and therefore draws on a range of concepts and approaches not usually considered the scope of traditional economics. The thesis should be read from this perspective.

In the dynamic context of TB in South Africa, an ongoing supply of empirical evidence is needed to give the information necessary to guide and enhance public health policies. A research focus on TB case detection is fully justified by this need for empirical evidence. In particular, there is an urgent need to measure the extent to which TB policies and protocols are implemented. The research outputs from this thesis are thus aimed at helping policymakers in South Africa to make optimal choices that strengthen health systems and ensure the effective delivery of quality healthcare.

1.3. Research Questions

The focus of this thesis, which is a compilation of three studies undertaken by the author in the course of studying for a PhD, is on South Africa's ongoing battle against TB in the context of an ailing primary healthcare system. The overarching purpose of the three papers is to consider the role of relevant demand- and supply-side constraints to early TB detection in South Africa. The three factors examined are health-seeking behaviour (demand-side), the quality of TB screening at PHC facilities (supply-side), and PHC nurse workloads (supply-side):

(i) *What are the key demand-side factors associated with impediments to health-seeking for persons with presumptive TB in the Western Cape?*

(ii) *What is the quality of TB screening at PHC facilities in urban South Africa?*

(iii) *What is the relationship between TB-detection protocol compliance and nurse workload?*

The three research questions cited above – (i), (ii) and (iii) – are mapped out according to corresponding objectives – 1, 2, 3 – below:

Objective 1: *To estimate demand-side characteristics correlated with the health-seeking behaviour of persons with presumptive TB in the Western Cape.*

Objective 2: *To measure empirically the quality of TB screening at PHC facilities in urban South Africa, using a Standardised Patient (SP) analysis.*

Objective 3: *To estimate the PHC facility correlates of TB-detection protocol compliance in South Africa.*

Paper One (Chapter 2) investigates demand-side correlates of health-seeking behaviour for persons coughing for more than two weeks in order to understand this vulnerable population better. The study analyses data from a cohort study (SOCS - Secondary Outcome Cohort Study) embedded in a community randomised trial ZAMSTAR (Zambia and South Africa TB and AIDS Reduction Study) in eight high-burden TB communities in the Western Cape, South Africa. Uni- and multivariate logistic regressions are used to estimate the odds ratios of consulting for a cough (of more than two weeks duration) for a range of relevant patient predictors.

Paper Two (Chapter 3) measures the quality of TB screening at PHC facilities in South Africa using SP analysis. This is the first multi-district SP study conducted in South Africa. The SP method involves sending a covert fieldworker (the SP) to a healthcare facility where he or she presents with pre-determined TB symptoms that should predictably map to a set of clinical questions, examinations and tests. This method allows researchers to observe how healthcare providers identify, test and advise presumptive TB patients, and whether this aligns with clinical protocols and best practice.

Paper Three (Chapter 4) explores PHC facility correlates of TB-detection protocol compliance in South Africa. Nurses are considered the primary input for service delivery at PHC facilities in South Africa. It is therefore hypothesised that constraints on nurse workloads may be correlated with lower TB-detection protocol compliance. Data on essential TB-screening checks – collected using the SP approach – are used to measure protocol compliance while data on PHC facility characteristics are sourced from the District Health Information System, Census, and a PHC facility survey. An SP fixed effects model is used to determine the PHC facility correlates of TB-detection protocol compliance.

1.4. The Contribution of Policy-Relevant Descriptive Studies

In his 1980s paper *Description as Choice,* Sen argued that methodological research in economics tended to concentrate on predictive and prescriptive concerns at the expense of other motivations for research [76]. This apparent bias has meant that descriptive studies in economics have been less favoured than studies using sophisticated econometric techniques. Not much has changed since Sen made these observations. In his 2018 paper, *Sins of Omission and the Practice of*

Economics, Akerlof argued that the discipline of economics favours and rewards 'hard'[9] economics at the expense of 'soft' economics [79].

Like Sen, Akerlof believes that such bias encourages economic research to avoid relevant research questions that are difficult to answer using 'hard' methods (the 'sins of omission' referred to in the article's title). In this context, a hierarchy has developed within economics: quantitative work is regarded as superior to qualitative work. From there, causal empirical studies are regarded as superior to ones that study correlations, with 'hard' identification studies only being outranked by 'harder' theoretical studies underpinned by elegant mathematical models (and not words) [79]. Akerlof uses a simple model to describe how academic economists make trade-offs between the 'hardness' and the importance of a topic when deciding on research topics. He argues that, for academic economists, socially suboptimal topic choices are made in order to maximise private utility. The resultant trade-off of topic importance for topic hardness is underpinned by what he refers to as a 'hardness' bias. Akerlof makes an explicit call for economics as a discipline to reassess the current criteria for publication and promotion. He also argues for 'greatly increased tolerance' in publication and promotion norms in order to reduce hidebound methodological biases.

A recent online debate [80] that engaged leading development economists globally also questioned the overemphasis on identification studies and whether these have crowded out descriptive studies in development economics. The argument was put forward that the current trend left researchers feeling pressured to turn what would be otherwise good descriptive studies into bad causal studies, and asserted that it is often harder to do a descriptive study because of the stronger persuasion it requires. The debate resulted in a thought piece [81] that reviewed

[9] Based on Comte's theory on the hierarchy of science [77] where sciences are classified from 'hard' to 'soft', with physics being the 'hardest' and history, sociology and anthropology regarded as the 'softest' [78].

examples of descriptive studies over the last decade and examined what the features were that led to their publication.

One of the key features identified was that published descriptive studies answer economic questions which focused on one country in a developing context, specifically a relatively large country of international interest. Studies from India and China that describe aspects of the development process appear to generate the most attention in this regard [82–88].

The second feature of published descriptive studies is the use of innovative data collection methods. A study describing the quality of healthcare in rural India using audit studies [82] combined both of these features: it focused on a large country (India) and used a novel data collection technique. The use of clinical vignettes and of standardised (or simulated) patients to collect data in Indian-based development studies are further examples of innovative data collection [87,89]. Given the effort and cost that goes into the data collection process of development studies such as these, there is room for more useful descriptive papers to be generated from them [90].

This thesis combines the key features of a published descriptive study: focus on a large, developing country of international interest (South Africa) and the use of an innovative data collection technique (the Standardised Patient method). In addition to this thesis meeting the academic goal of being publishable, and in part already published (Papers One and Two), the information gathered for this thesis can be used to inform public policy. To achieve the goal of informing public policy, the importance of context to policy decisions must be seriously considered. For this reason, the findings of the three papers that make up the body of the thesis are rearticulated in Chapter 5 (5.2.1 to 5.2.6) to highlight their policy implications.

As a guide to help clarify the relationship between context and the translation of knowledge into policy, I use a recently developed conceptual framework that was designed using knowledge systematisation work, literature reviews, and in-depth interviews with 48 experts and policymakers (mostly in developing countries) [91]. The framework is made up of six dimensions of context and aims to assist researchers in identifying gaps where efforts can be concentrated more effectively in order to enhance interaction between knowledge and policy. These six framework dimensions will be used to structure the discussions on knowledge and policy in relation to the thesis's findings and current TB policies in South Africa. The discussion, which translates newly-generated knowledge into policy advice, will be laid out in Chapter 5.

The six analytical dimensions of context are: (1) macro-context, (2) intra- and inter-relationships with state (public) and non-state (non-public) agents, (3) culture, (4) organisational capacity, (5) management and processes, and (6) core resources. A description of each dimension is presented below [91]. Sub-dimensions of particular relevance to this thesis are expanded on in Chapter 5 as well.

1) Macro-context: This dimension captures the overarching national factors that create the 'big picture' within which policy is developed. The knowledge regime is an essential structural sub-dimension of the macro-context from a researcher's perspective. This regime is defined as the organisational and institutional framework that generates data, research, policy recommendations, and ideas that stimulate public debate and policymaking [92]. Key aspects to consider in a knowledge regime are the availability of public data and information, the funding of the knowledge sector, scarce skills in the labour market, critical thinking, the capacity to conduct policy-relevant research, and the social valuation of science. Most of these aspects have directly impacted on the development of this thesis, which generated knowledge related to TB policy in the macro-context of a relatively constrained knowledge regime. In this broader context, the findings on the supply constraints on early TB detection (Paper Two and Paper Three

(Chapter 3 and Chapter 4) of this thesis, respectively) will be discussed to highlight the apparent disconnect between the prescribed TB protocols and their implementation at a PHC level. On the demand side, evidence from Paper One (Chapter 2), detailing the health-seeking behaviour of presumptive TB patients, will be contextualised to highlight how much scope remains within the health system for a greater focus on preventative strategies. Of the other macro-context factors possible, crises and transitions are relevant sub-dimension given South Africa's persistent TB crisis and ailing health system.

2) Intra- and inter-relationships with public and non-public agents: While this dimension forms part of the macro-context, it is discussed separately due to the importance of internal relationships between stakeholders and public institutions (including related government agencies) for how knowledge is translated (or not) into policy. In the context of early TB detection, the principal demand-side agent that policymakers need to consider is the presumptive TB patient. The characteristics of presumptive TB patients and their health-seeking behaviour are investigated in Paper One (Chapter 2) and discussed in their contextual framework in Chapter 5. Potential barriers to the relationship between patients and providers, drawn from findings in Paper Two (Chapter 3), are also discussed. Evidence from Paper Two (Chapter 3) and Paper Three (Chapter 4) highlights the latent gap between demand and supply agents in the South African health system. Furthermore, pertinent findings from Paper Two (Chapter 3) and Paper Three (Chapter 4) are reoriented in the context of the hierarchical relational structure within which demand and supply agents need to operate.

   Relevant sub-dimensions here include support from public agencies that produce data and research, and formal channels of interaction with researchers and research institutions. These contextual factors were also important during the secondary data collection phase of Paper One (Chapter 2) and the study design and primary data collection phases of Paper Two (Chapter 3).

3) Culture: This framework draws on earlier work [93] that defines culture as a collection of shared assumptions learned by a group. The role of incentives in culture is a useful sub-dimension for researchers to understand whether and how research is used to shape policy. Findings from Paper One (Chapter 2) reveal how relevant demand-side factors interact with the health system to create a culture that may impact health-seeking behaviour. On the supply side, incentives that are of critical importance at a PHC level – where the bulk of TB policies are implemented – include promoting an institutional culture of learning from mistakes and performance management. However, the prevailing institutional culture of the South African public health sector has been described as strongly hierarchical, dominated by command- and control-type decision-making [94]. Paper Three (Chapter 4) offers useful evidence as a base from which to explore potential strategies to alleviate this weakness in the healthcare system. Expectations of how the findings of this thesis might be translated into policy are also briefly discussed in the context of culture.

4) Organisational capacity: This dimension is defined as how well an organisation uses its resources (both human and legal) to perform its duties. Even though organisational capacity is not explored explicitly in this thesis, considering it within South Africa's public health sector helps to contextualise the supply-side findings in Paper Two (Chapter 3) and Paper 3 (Chapter 4). The relevance of human resources organisational capacity in the South African context is also considered insofar as it relates to the presumptive TB patient's experience of healthcare services and how this, in turn, may impact health-seeking and health demand (this is related to Paper One (Chapter 2)).

5) Management and processes: Organisations are underpinned by continuous processes and policies, and how day-to-day decisions are made. Management and process mechanisms include planning, communication, decision-making, problem-solving, monitoring and evaluation [95]. The importance of effective communication among agents within the health system cannot be overemphasised, given the high degree of information asymmetry in the field of health and healthcare. Evidence from Paper Two (Chapter 3) points to bottlenecks in information flows from the provider to the patient. These findings are explored, and their consequences for the National TB Programme and health demand (related to Paper One (Chapter 2)) are discussed. Findings from Paper Two (Chapter 3) are discussed to assess the usefulness of the SP method as a potential monitoring and evaluation tool.
6) Resources: This dimension focuses on the budget committed to research, time, knowledge infrastructure, and technology. Technology and knowledge infrastructure are inter-related resource sub-dimensions that are critical for the production and flow of policy-relevant knowledge [91]. Issues relating to knowledge infrastructure are further explored in relation to Paper Two (Chapter 3), where knowledge was generated using a gold-standard but expensive and time-intensive method (the SP method).

Chapter 2

Paper One: Patient predictors of health-seeking behaviour for persons coughing for more than two weeks in high-burden tuberculosis communities - the case of the Western Cape, South Africa

This study aimed to analyse the patient predictors of health-seeking behaviour for persons coughing for more than two weeks to better understand this vulnerable and important population. The study analysed data from a cohort study (SOCS - Secondary Outcome Cohort Study) embedded in a community randomised trial ZAMSTAR (Zambia and South Africa TB and AIDS Reduction Study) in eight high-burden TB communities in the Western Cape, South Africa. These datasets are unique as they contain TB-related data as well as data on health, health-seeking behaviour, lifestyle choices, employment, socio-economic status, education and stigma. We use uni- and multivariate logistic regressions to estimate the odds ratios of consulting for a cough (of more than two weeks duration) for a range of relevant patient predictors. Three hundred and forty persons consulted someone about their cough and this represents 37% of the 922 participants who reported coughing for more than two weeks. In the multivariate analysis, respondents of black ethnic origin (OR 1.99, 95% CI 1.28-3.12, $p<0.01$), those with higher levels of education (OR 1.05 per year of education, 95% CI 1.00-1.10, $p=0.05$), and older respondents (OR 1.02 per year, 95% CI 1.01-1.04, $p<0.01$) had a higher likelihood of consulting for their chronic cough. Individuals who smoked (OR 0.63, 95% CI 0.45-0.88, $p<0.01$) and those with higher levels of socio-economic status (OR 0.81, 95% CI 0.71-0.92, $p<0.01$) were less likely to consult. We find no evidence of stigma playing a role in health-seeking decisions, but caution that this may be due to the difficulty of accurately and reliably capturing stigma due to, amongst other factors, social desirability bias. The low levels of consultation for a cough of more than two weeks suggest that there are opportunities to improve case-finding. These findings on health-seeking behaviour can assist policymakers in designing TB screening and active case-finding interventions that are targeted to the characteristics of those with a chronic cough who do not seek care.

2.1. Background

TB transmission is amplified in the context of the prevailing HIV pandemic in the WHO (World Health Organization) African region, where 31% of all new TB cases in adults are attributable to HIV infection [5]. In this context where transmissions occur more readily, delays to seeking healthcare have a higher mortality and morbidity cost [8,96]. This translates into high health and socio-economic costs (due to loss of or decreased employment), which inevitably places a higher burden on scarce public resources [97,98].

Delays in seeking healthcare for a cough may arise from the patient or the healthcare system, or, most likely, both. The focus of this study is on understanding how individual characteristics are correlated with the health-seeking decisions of symptomatic cases.

Very few studies comprehensively investigate health-seeking behaviours from the patient perspective exclusively [73,74]. More often, studies focus on delays in diagnosis to explore both demand and supply dynamics. However, often such approaches do not allow for a detailed exploration of patient considerations.

The most recent systematic review of delays in TB diagnosis found that evidence describing the potential risk factors for delay are heterogeneous [58]. A risk factor in one setting may cause an increased delay while in another setting, a decreased delay. For example, a Zambian study found that HIV has a positive association with the risk of diagnostic delay [99], while studies in Ghana, Spain and Thailand showed a negative association for the same risk factor [100–102]. In addition, some predictors were identified extensively in many studies (namely older age, poverty, low levels of education and lack of TB awareness) while others may only appear in one study (for example, stigma). Based on the systematic review, the following prominent patient correlates were identified, amongst others: health status, socio-economic status, stigma, age, gender, education, TB knowledge levels, smoking and drinking.

Responding to the global call to address stigma in the fight against TB [103,104], this study is (as far as we know) the first to include a quantitative measure of TB stigma in modelling health-seeking behaviour. Our uniquely comprehensive data set allows us to address this gap in patient-focused analysis of health-seeking decisions. Such findings information can assist policymakers in designing more targeted TB screening and active case-finding interventions.

2.2. Method

2.2.1. Study Design and Setting

This cross-sectional study uses SOCS and other ZAMSTAR data to estimate the odds ratios of consulting for a cough (of more than two weeks) for relevant patient predictors.

ZAMSTAR was a community-randomised trial that aimed to reduce TB and AIDS in South Africa and Zambia, two countries with amongst the highest TB incidence rates globally (in 2010 TB incidence in Zambia was 495/100 000 people and 948/100 000 for South Africa [105]), using multiple interventions [68]. Study outcomes were measured in 2010 using prevalence surveys in communities that had TB notification rates of more than 400/100 000. In addition to objective health outcomes, the prevalence surveys collected individual-level data on health-seeking behaviour (Question Q41_CAC in ZAMSTAR prevalence survey reads: 'Did you consult anybody for this cough?), socio-economic status, demographics, self-reported health status and lifestyle choices. This secondary analysis study used data from the eight ZAMSTAR communities in the Western Cape, South Africa. Respondents were aged 18 years and older.

The aim of the SOCS was to recruit TB-affected households in each of the ZAMSTAR communities in order to collect stigma-related data from confirmed TB patients and their family members [106]. This study used the TB-stigma data derived from the first and second round of the SOCS (2008 to 2009) since it was the closest in time to the ZAMSTAR prevalence survey data (2010) and therefore captured the most recent degree of TB stigma.

These datasets – ZAMSTAR and SOCS - are unique given that they contain TB-related data as well as data on health, health-seeking behaviour, lifestyle choices, employment, socio-economic status, education and stigma. There is currently no other TB-related dataset of this size (n=30 017) in South Africa that provides such a comprehensive range of variables at an individual, household and community level.

2.2.2. Sample of Interest

The sample of interest was restricted to individuals who reported coughing for more than two weeks. According to TB-screening guidelines, all persons who report coughing for more than two weeks should be screened for TB [107].

2.2.3. Variables of Interest

The outcome variable used to capture health-seeking behaviour was a consulting dichotomised variable.

Age, education and an asset index (SES proxy) were included as continuous covariates.

The asset index was derived from household asset ownership indicators using Multiple Correspondence Analysis (MCA) (see *Multiple Correspondence Analysis and Related Methods* [108] for a detailed discussion of the methodology of MCA) to derive the weights. This multidimensional approach to measuring SES is based on seminal work in the development economics literature [109] and is increasingly used in welfare analysis and poverty targeting studies [110]. The initial validation study of the asset index (using data from developing countries Indonesia, Nepal and Pakistan) [109] produced internally coherent results which showed distinct separations across different SES households (poor, middle and rich) for each asset. The index was also robust to the assets included and was comparable with output and poverty levels across countries.

The index was composed of the following SES domains: semi-durable assets (television, refrigeration, motor vehicle, mobile phone), access to electricity, dwelling type (including formal and informal structures), domestic assistance, main type of toilet (including flush toilet and bucket system), main source of drinking water (including piped sources and wells), fuel access for keeping warm (including electricity and wood) and reliance on food relief (Table S1.B.2.3).

When regressing the components of the asset index on the asset index, the signs and size of the coefficients were as expected given that ownership of or access to more (or superior) assets indicate a higher SES (Table S1.B.2.4).

The model also contained dummy variables for gender, employment status, and ethnicity (only two ethnicities were observed in the sample of interest: Individuals of Cape coloured ethnic origin and individuals of black ethnic origin). A proxy for HIV was included as a dichotomous health-status covariate (see Text S1.C.2.1 for a description of how this proxy was created).

Lifestyle-choice binary variables related to smoking and drinking (alcohol) were included. These covariates were the only lifestyle-choice variables available in the ZAMSTAR dataset.

Respondents of the SOCS survey were presented with questions or statements linked to seven TB-stigma domains: unnecessary fears of transmission, blame, the experience of social exclusion, the experience of being made fun of, the experience of health-setting stigma, internal stigma and disclosure (Table S1.B.2.5). The first two TB-stigma domains pertain to household members of the confirmed TB patient; the remaining five pertain to the confirmed TB patient.

Only six of the seven stigma domains were used to create the stigma index: We regarded the disclosure of one's TB status as an outcome rather than a feature of stigma. This presented an endogeneity challenge and therefore we omitted the disclosure domain from our stigma index.

After summing the selected six stigma dummies, the composite variable was transformed into an index using the weighted arithmetic mean. For ease of interpretation, this stigma index was standardised using the z-score[10].

We calculated a mean stigma index per community, gender and age (Figure S1.A.2.2) (in the SOCS dataset). These mean values were used to create a stigma index for each ZAMSTAR respondent weighted according to their gender, age and the community in which they lived (see Text S1.C.2.2 for a more detailed description of the methodology used here).

2.2.4. Data Analysis and Processing

Descriptive statistics of the covariates were calculated for the sample of interest, as well as the subgroup that consulted and the subgroup that did not. A two-sample t-test with equal variances (for continuous covariates) and a chi-square test (for dichotomous covariates) were used to test for significant differences between the two sub-groups.

A logistic regression was used for uni- and multivariate analyses. In the model, the dependent variable captures health-seeking behaviour and relevant independent variables include socio-economic status, demographic, health status, lifestyle choice and stigma.

In line with best practice [111], a regression-error specification test (RESET) was conducted. The model passed the test and is well-specified since the RESET result was insignificant (chi-squared=1.82; p=0.18)[11]. Empirical analyses were performed using STATA (version 14.02, StataCorp LLC, College Station, TX, USA).

[10] A stigma index created using multiple correspondence analysis was highly correlated (correlation coefficient of 0.91, p<0.1) with the stigma index used in this study. Based on the high and statistically significant correlation between the indices, we opted to use the simpler derivation of the stigma index.

[11] In addition, the results of the multivariate model held up to robustness checks. See Table S1.B.2.6, Table S1.B.2.7 and Table S1.B.2.8 in the supplementary section for more details in this regard.

2.3. Results

2.3.1. Summary of Health-Seeking Outcomes

Three per cent of the full ZAMSTAR sample (922 out of 30 017 persons) reported coughing for more than two weeks. These 922 observations constitute the sample of interest. Thirty-seven per cent (340 persons) of this sample consulted someone about their cough, while the majority - 63 per cent (582 persons) - did not.

2.3.2. Characteristics of Persons Coughing for More than Two Weeks

The summary statistics of the sample characteristics are described in Table 2.1.

Table 2.1: Summary statistics of sample characteristics, 2010

Continuous covariates	**Sample mean** (n=922) [a]	**Std. Dev.**	**'Consult' mean** (n=340)	**Std. Dev.**	**'Did not consult' mean** (n=582) [b]	**Std. Dev.**
Stigma Index	-0.06	0.88	-0.12	0.90	-0.03	0.87
Age	40.25	14.82	42.29	14.84	39.05	14.68
Education [c]	7.64	3.63	7.66	3.68	7.63	3.60
Asset Index	-0.08	1.07	-0.19	1.15	-0.02	1.02
Dichotomous covariates	**Sample proportions** (n=922)	**Std. Dev.**	**'Consult' proportions** (n=340)	**Std. Dev.**	**'Did not consult' proportions** (n=582)	**Std. Dev.**
Men**	0.42	0.50	0.39	0.49	0.45	0.50
Black ethnicity***	0.84	0.37	0.91	0.29	0.80	0.40
Employed	0.29	0.45	0.26	0.44	0.30	0.46
HIV positive*	0.19	0.39	0.22	0.42	0.17	0.38
Drinks daily	0.06	0.24	0.07	0.25	0.06	0.24
Smoked***	0.46	0.50	0.36	0.48	0.52	0.50

[a] n = 921 for age variable, [b] n = 581 for age variable, [c] Education = years of education, *** $p<0.01$, ** $p<0.05$, * $p<0.1$ (derived from two-sample t-test with equal variances (continuous covariates) and chi-square test (dichotomous covariates)). Source: Own calculations, ZAMSTAR (2010)

2.3.2.1. SES and Demographic Characteristics

The mean age of those who consulted for their two-week cough was slightly higher; 42 years compared to those who did not consult (39 years). The mean highest level of education for those who consulted and those who did not was the same – namely Grade 8 (eight years of education).

The asset index ranged from -3.08 to 1.20 with a larger index representing a higher level of SES. The negative relationship between the probability of consulting and SES (Figure 2.1) means that individuals with higher levels of SES were less likely to consult.

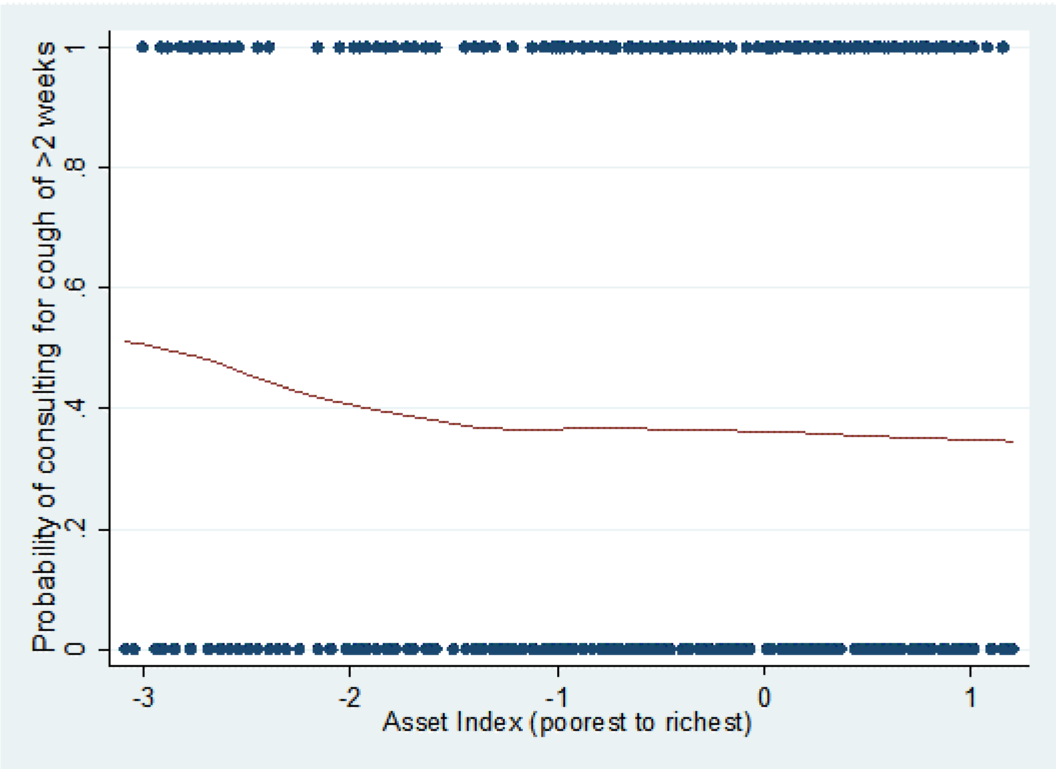

Figure 2.1: Probability of consulting by SES, 2010

Scatter plot and curve of best fit showing the relationship between the probability of coughing (for more than two weeks) and the asset index. Source: Own calculations, ZAMSTAR (2010)

Men were significantly less likely to consult than women, with 39% of those consulting being men. The employed were less likely to consult than the unemployed, while individuals of black ethnic origin were significantly more likely to consult than individuals of Cape coloured ethnic origin.

2.3.2.2. Clinical and Lifestyle Characteristics

Twenty-two per cent of those who consulted were HIV positive, while 17 per cent of those who did not consult were HIV positive (p=0.063).

Daily drinking ranged between six and seven per cent, with no significant differences between those who consulted and those who did not consult. The proportion of respondents who had ever smoked was significantly higher amongst those who did not consult (52%) than amongst those who did consult (36%).

2.3.2.3. Stigma

The stigma index ranged from -1.73 (minimum) to 1.78 (maximum) with a larger index representing a higher level of stigma. For those who consulted, the mean stigma level[12] was lower (-0.12) compared to those who did not (-0.03), although the difference in means between the two groups was not statistically significant.

2.3.3. Predictors of Health-Seeking Behaviour

Results for the univariate and multivariate logistic regressions (Table 2.2) are reported in brackets as follows: ORs, 95% CIs and p-values for the univariate regression are described first, followed by the results for the multivariate regression.

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[12] As described in section 2.2.3 and in more detail in Text S1.C.2.2, each individual in the ZAMSTAR dataset is assigned a stigma score based on the expected value of stigma (derived from SOCS dataset) for those from the same age, gender and community group.

Table 2.2: Univariate and multivariate logistic regression analysis for consulting for a cough (when coughing for more than two weeks), 2010

	Univariate (*n*=922) [a]		**Multivariate (*n*=921) [b]**	
VARIABLES	OR[c] (95% CI[d])	*p* value	OR (95% CI)	*p* value
Stigma index	0.88 (0.76-1.03)	0.13	1.05 (0.89-1.24)	0.58
Age[e]	1.01 (1.01-1.02)	<0.01	1.02 (1.01-1.04)	<0.01
Men	0.76 (0.57- 0.99)	0.04	0.88 (0.63-1.22)	0.44
Black ethnicity	2.42 (1.60-3.67)	<0.01	1.99 (1.28-3.12)	<0.01
Education[f]	1.00 (0.97-1.04)	0.87	1.05 (1.00-1.10)	0.05
Employed	0.85 (0.63-1.15)	0.29	0.92 (0.67-1.27)	0.63
Asset index	0.87 (0.77-0.98)	0.03	0.81 (0.71-0.92)	<0.01
HIV positive	1.37 (0.98-1.91)	0.06	1.30 (0.91-1.85)	0.15
Drinks daily	1.13 (0.66-1.95)	0.65	1.43 (0.80-2.54)	0.23
Smoked	0.53 (0.40-0.69)	<0.01	0.63 (0.45-0.88)	<0.01

[a] n = 921 for age variable, [b] Due to one missing age variable, [c] OR = odds ratio, [d] CI = confidence interval, [e] per year, [f] per year of education. Reference categories for dichotomous variables: Women, Cape coloured ethnicity, Not employed during last year, HIV negative/did not disclose HIV status, Never/occasional/used to drink, Never smoked. All other independent variables are continuous. Source: Own calculations, ZAMSTAR (2010)

Stigma has a statistically insignificant relationship with the probability of seeking healthcare for a cough of more than two weeks (OR 0.88, 95% CI 0.76-1.03, *p*=0.13; OR 1.05, 95% CI 0.89-1.24, *p*=0.58). The stigma result remained insignificant (OR 0.96, 95% CI 0.82-1.12, *p*=0.59) even when the multivariate regression was rerun without the variables for SES and ethnicity (Additional robustness checks are included in Table S1.B.2.6, Table S1.B.2.7 and Table S1.B.2.8 of the supplementary section).

The odds ratio of men consulting is less than one in the univariate regression (OR 0.76, 95% CI 0.57- 0.99, *p*=0.04) but this becomes statistically insignificant in the multivariate regression (OR 0.88, 95% CI 0.63-1.22, *p*=0.44). Employment does not show any significant relationship with the likelihood of consulting though the likelihood of the employed consulting is consistently less than the not employed (OR 0.85, 95% CI 0.63-1.15, *p*=0.29; OR 0.92, 95% CI 0.67-1.27, *p*=0.63). Being of black ethnic origin and a year older is associated with a higher likelihood of consulting (OR 2.42, 95% CI 1.60-3.67, *p*<0.01; OR 1.99, 95% CI 1.28-3.12, *p*<0.01 and OR 1.01, 95% CI 1.01-1.02, *p*<0.01; OR 1.02, 95%CI 1.01-1.04, *p*<0.01, respectively). In the case of respondents of black ethnic origin, the reference case is respondents of Cape coloured ethnic origin.

The odds ratio of consulting for each standard deviation increase in the asset index was less than one (OR 0.87, 95% CI 0.77-0.98, *p*=0.03; OR 0.81, 95% CI 0.71-0.92, *p*<0.01). For each additional year of education, the odds of consulting was 1.05 times more likely in the multivariate results (OR 1.00, 95% CI 0.97-1.04, *p*=0.87; OR 1.05, 95% CI 1.00-1.10, *p*=0.05).

HIV-positive individuals were more likely to consult than their HIV-negative counterparts or those who did not disclose their HIV status (OR 1.37, 95% CI 0.98-1.91, *p*=0.06; OR 1.30, 95% CI 0.91-1.85, *p*=0.15) but these findings are not statistically significant in the multivariate regression. There was no significant increased likelihood of consulting for drinking daily (OR

1.13, 95% CI 0.66-1.95, $p=0.65$; OR 1.43, 95% CI 0.80-2.54, $p=0.23$). Persons having smoked were significantly less likely to consult (OR 0.53, 95% CI 0.40-0.69, $p<0.01$; OR 0.63, 95% CI 0.45-0.88, $p<0.01$).

2.4. Discussion

Only thirty-seven per cent of respondents had consulted someone when coughing for more than two weeks. Respondents of black ethnic origin (OR 1.99, 95% CI 1.28-3.12, $p<0.01$), those with higher levels of education (OR 1.05 per year of education, 95% CI 1.00-1.10, $p=0.05$), and older respondents (OR 1.02 per year, 95% CI 1.01-1.04, $p<0.01$) had a higher likelihood of consulting for a chronic cough. The opposite held for those who smoked (OR 0.63, 95% CI 0.45-0.88, $p<0.01$) and those with higher levels of socio-economic status (OR 0.81, 95% CI 0.71-0.92, $p<0.01$).

2.4.1. Limitations

The nature of cross-sectional analysis restricts the scope for proving causality. No data were available for one of the more prominent predictors of health-seeking behaviour in the TB literature: TB knowledge levels.

Our data is derived from communities where there is a high prevalence of TB. It is plausible that a gap would exist between stigma scores of TB positive households and non-TB positive households in these communities. However, most important is the relative stigma scores and that it is comparable across communities.

2.4.2. Interpretation

Compared to similar studies in developing countries, the proportion of respondents who consulted for a chronic cough is relatively low [112,113]. This is a worrying finding considering that data were collected in high-burden communities with TB notification rates of more than 400/100 000.

Using the multivariate analysis approach we find no evidence of a role for stigma in health-seeking behaviour amongst persons coughing for more than two weeks, but caution against assuming that this means stigma does not present an important constraint to health-seeking behaviour. Given the strong qualitative evidence of a role for stigma in health-seeking [114], one explanation for the lack of quantitative evidence may be that it is not measured well given the challenges of truthfully extracting information on prejudice and bias against TB sufferers. The insignificance of our stigma variable alongside others may thus be partly attributable to the difficulty in accurately capturing stigma via self-reported measures due to social desirability bias and partly to not triangulating this finding with other data sources, including qualitative data. These findings add impetus to the global call for improved tools for measuring stigma and evaluating stigma interventions [115]. (See Text S1.C.2.3 for an additional discussion on the null stigma results.)

Contrary to some studies on health-seeking behaviour [96,116–118], gender and employment status do not seem to be significantly associated with the probability of seeking healthcare in the multivariate analysis. However, the models consistently show that men are less likely to consult than women, which is in keeping [58,113,119–122] with health-seeking literature.

The employed and those with higher levels of SES are consistently less likely to consult. This negative association is supported by most SES and health-seeking findings [73,123–125]. It is conceivable that below a certain household income threshold, the opportunity cost of working would be relatively higher when compared to those above the threshold. This may explain the negative relationship between these SES variables and health-seeking behaviour.

Cultural dynamics not fully captured in the stigma variable may explain the relatively large, statistically significant differential in the relationship between ethnicity and health-seeking behaviour. Confirming previous findings in the health-seeking literature [58], we find that the educated were significantly more likely to consult. Older individuals were also more likely to consult. We accounted for the possibility of a non-linear relationship between age and health-seeking behaviour (see Table S1.B.2.6) in the multivariate analysis (OR 1.00, p=0.17) and found that at older ages this relationship persists, which is in contrast with the health-seeking literature [58,74].

The positive association between HIV and consulting is not significant, but this may be due to an under-reporting of HIV positive cases.

Having smoked is the only significant lifestyle choice variable, with those having smoked being less likely to consult. It is possible that those who have smoked attribute their symptoms to smoking rather than TB [126]. This relationship may be driven by the harmful consequences smoking has on the lungs and immune system. It is also plausible that having 'ever smoked' captures unobservable characteristics which may influence one's likelihood of consulting.

2.4.3. Generalizability

External validity is limited to high TB-prevalence communities in South Africa but given South Africa's high TB prevalence and incidence, these findings are still of international interest. Finding no role for stigma in health-seeking behaviour is important because it highlights the need to triangulate methods and debate how stigma measures interact with other factors in multivariate analyses.

2.5. Conclusion

Most persons coughing for more than two weeks did not seek consultation about their chronic cough. Respondents of black ethnic origin, those with higher levels of education and older respondents had a greater likelihood of consulting. Smokers and those with higher SES were less likely to consult.

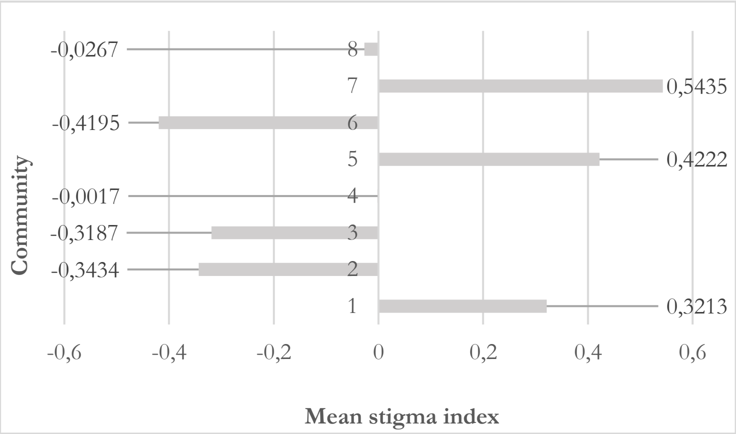
TB-control programmes should be more cognisant of the patient characteristics of presumptive TB patients who do not seek care. This information can assist policymakers in designing more targeted TB screening and active case-finding interventions. In the high TB burden communities of South Africa, such interventions may benefit from focusing on youth, those with lower levels of education, smokers, higher SES subgroups and also the population of Cape coloured ethnic origin. These findings add to the meagre body of literature analysing the health-seeking behaviour of this vulnerable and important population.

Our study responds to the global call to address stigma in the fight against TB by being the first (as far as we know) to include a quantitative measure of TB stigma in modelling health-seeking behaviour. Our uniquely comprehensive data set allows us to address this gap in patient-focused analysis of health-seeking decisions. Although we find no role for stigma in health-seeking behaviour, it is important because it highlights the need to triangulate methods and debate how stigma measures interact with other factors.

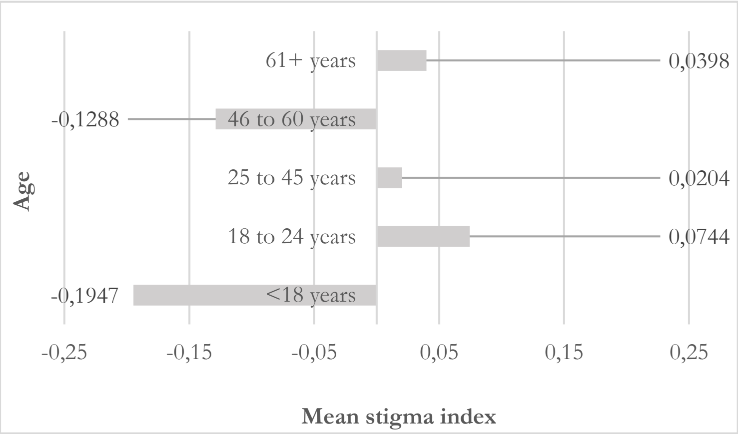
Supplementary Materials 1

Supplementary Materials 1.A: Figures

(a)



(b)



(c)

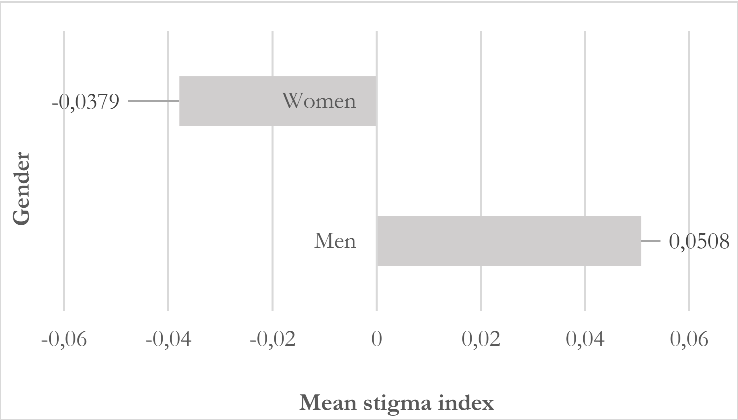


Figure S1.A.2.2.: Stigma level by community (a), age (b) and gender (c), 2008-2009

Figures (a-c) showing mean stigma index levels (standardised using z-score) for each community (1-8), for each age category (<18 years, 18-24 years, 25-45 years, 46-60 years, 61+ years) and for each gender (women and men).

Source: own calculations, SOCS of ZAMSTAR (2008/2009)

Supplementary Materials 1.B: Tables

Table S1.B.2.3: SES indicator set.

Table showing SES components collected in ZAMSTAR study that was used to create an asset index for this study.

Domain	Items	Indicator coding
Semi-durable household assets	Television	1 = yes 0 = no
	Refrigeration	1 = yes 0 = no
	Motor vehicle	1 = yes 0 = no
	Mobile phone	1 = yes 0 = no
Household access to electricity	Electricity in the household	1 = yes 0 = no
Dwelling type	1. House (single unit) 2. House (multi-unit) 3. Traditional dwelling 4. Flat 5. Room in backyard 6. Informal dwelling in backyard 7. Informal dwelling not in backyard 8. Caravan 9. Worker hostel 10. Other (incl. 6 and 7)	Appropriate category selected by respondent
Household domestic assistance (not related to household head)	Household employment of a domestic worker	1 = yes 0 = no
Main type of household toilet	1. Private flush toilet 2. Shared flush toilet 3. Pit latrine 4. VIP Latrine 5. Bush/field 6. Bucket system 7. Chemical 8. Other	Appropriate category selected by respondent
Main source of household drinking water	1. Piped to residence 2. Piped to yard 3. Public tap 4. Protected well 6. Traditional well 7. Borehole 8. River 9. Other (incl. 7 and 8)	Appropriate category selected by respondent
Fuel access for keeping household warm	0. Nothing 1. Electricity 2. Petroleum gas 3. Kerosene 4. Charcoal 5. Wood	Appropriate category selected by respondent
Household reliance on food relief	Household reliance on food relief during the past 18 months	1 = yes 0 = no

Source: ZAMSTAR (2010)

Table S1.B.2.4: Correlation between components of asset index and asset index.

Table showing correlation between components of asset index and asset index.

Items	Coefficients (n= 30 017)
Television	0.568***
Refrigeration	0.471***
Motor vehicle	0.233***
Mobile phone	0.137***
Electricity in the household	0.758***
House (single unit)	0.401***
House (multi-unit)	0.280***
Traditional dwelling	-0.067***
Flat	0.350***
Room in backyard	-0.269***
Worker hostel	0.081***
Other (incl. informal dwellings in backyard & not in backyard)	0.027***
Household employment of a domestic worker	0.203***
Private flush toilet	0.666***
Shared flush toilet	0.240***
Pit latrine	-0.126***
VIP Latrine/chemical	-0.523***
Bush/field	-0.249***
Bucket system	0.013***
Piped to residence	0.189***
Piped to yard	0.004***
Public tap	-0.426***
Protected well	0.068***
Other (incl. borehole, river, traditional well)	-0.333***
Nothing	0.027***
Electricity	0.225***
Petroleum gas	0.172***
Kerosene	0.070***
Charcoal	-0.074***
Wood	-0.167***
Household reliance on food relief during the past 18 months	-0.089***

*** $p<0.01$, ** $p<0.05$, * $p<0.1$; Caravan (n=2) and other types of toilets (n=19) omitted due to collinearity. Source: Own calculations, ZAMSTAR (2010)

Table S1.B.2.5: TB-stigma indicator set.

Table showing TB-stigma indicator set used in the SOCS study.

Population group	Domain	Indicator coding [a]
Household members of confirmed TB patient	Transmission myths (3 items)	1 = agreed to any one of the three transmission myths 0 = disagreed with all
Household members of confirmed TB patient	Blame	1 = agreed that TB is a punishment for being bad 0 = disagreed
Confirmed TB patient	The experience of social exclusion (4 items)	1 = agreed to any one of the four examples of social exclusion 0 = disagreed with all
Confirmed TB patient	The experience of being made fun of (3 items)	1 = agreed to any one of the three examples of being made fun of 0 = disagreed with all
Confirmed TB patient	The experience of health-setting stigma	1 = yes 0 = no
Confirmed TB patient	Internalised stigma	1 = yes 0 = no
Confirmed TB patient	Disclosure[b]	1= yes 0= no

[a] Answers signalling stigma were coded '1' while no stigma were coded '0'. [b] Disclosure domain excluded from stigma index. Source: SOCS of ZAMSTAR (2008/2009)

Table S1.B.2.6: Additional multivariate logistic regressions for consulting for a cough (when coughing for more than two weeks), 2010.

	Multivariate logistic regressions (*n*=921) [a]					
	(1)		(2)		(3)	
VARIABLES	OR[b] (95% CI[c])	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Stigma index	1.05 (0.89-1.24)	0.58	1.06 (0.90-1.25)	0.51	1.05 (0.89-1.24)	0.57
Age[d]	1.02 (1.01-1.04)	<0.01	1.06 (1.01-1.04)	0.02	1.02 (1.01-1.04)	<0.01
Age squared			1.00 (0.99-1.00)	0.17		
Men	0.88 (0.63-1.22)	0.44	0.88 (0.63-1.22)	0.43	0.88 (0.63-1.22)	0.43
Black ethnicity	1.99 (1.28-3.12)	<0.01	2.03 (1.30-3.18)	<0.01	2.00 (1.28-3.14)	<0.01
Education[e]	1.00 (1.00-1.10)	0.05	1.05 (1.00-1.10)	0.05	1.05 (1.00-1.10)	0.05
Employed	0.92 (0.67-1.27)	0.63	0.89 (0.65-1.23)	0.50	0.92 (0.67-1.27)	0.63
Asset index	0.81 (0.71-0.92)	<0.01	0.81 (0.71-0.93)	<0.01	0.80 (0.64-0.99)	0.04
Asset index squared					0.99 (0.88-1.11)	0.87
HIV positive	1.30 (0.91-1.85)	0.15	1.26 (0.88-1.81)	0.21	1.30 (0.91-1.86)	0.15
Drinks daily	1.43 (0.80-2.54)	0.23	1.36 (0.80-2.54)	0.30	1.43 (0.80-2.54)	0.23
Smoked	0.63 (0.45-0.88)	<0.01	0.62 (0.45-0.87)	<0.01	0.63 (0.45-0.88)	<0.01

[a] n = 921 for age variable, [b] OR = odds ratio, [c] CI = confidence interval, [d] per year, [e] per year of education. Reference categories for dichotomous variables: Women, Cape coloured ethnicity, Not employed during last year, HIV negative/did not disclose HIV status, Never/occasional/used to drink, Never smoked. All other independent variables are continuous. The second model (2) includes an age squared variable and the third model (3) includes an asset index squared variable. These models are contrasted with the original multivariate model (1) discussed in the paper (see Table 2.2). Source: Own calculations, ZAMSTAR (2010)

To account for the possibility of a non-linear relationship between age and health-seeking, a variable for age squared (age*age) was created and added to the multivariate logistic regression (model 2 in Table S1.B.2.6). The results of the original multivariate logistic regression (model 1, taken from Table 2.2) remained robust to the inclusion of the age squared variable (model 2), and an asset index squared variable (model 3) as demonstrated in Table S1.B.2.6.

Table S1.B.2.7: Multivariate logistic regression for consulting for a cough (when coughing for more than two weeks) using an MCA-derived stigma index, 2010.

	(*n*=921) [a]			
	(1)		(2)	
VARIABLES	OR[b] (95% CI[c])	*p* value	OR (95% CI)	*p* value
Stigma index	1.05 (0.89-1.24)	0.58		
Stigma index (MCA[d])			0.99 (0.57-1.72)	0.99
Age[e]	1.02 (1.01-1.04)	<0.01	1.02 (1.01-1.03)	<0.01
Men	0.88 (0.63-1.22)	0.44	0.89 (0.64-1.23)	0.48
Black ethnicity	1.99 (1.28-3.12)	<0.01	1.97 (1.26-3.07)	<0.01
Education[f]	1.00 (1.00-1.10)	0.05	1.05 (1.00-1.10)	0.06
Employed	0.92 (0.67-1.27)	0.63	0.93 (0.68-1.28)	0.65
Asset index	0.81 (0.71-0.92)	<0.01	0.81 (0.71-0.93)	<0.01
HIV positive	1.30 (0.91-1.85)	0.15	1.30 (0.91-1.86)	0.15
Drinks daily	1.43 (0.80-2.54)	0.23	1.40 (0.79-2.49)	0.25
Smoked	0.63 (0.45-0.88)	<0.01	0.63 (0.45-0.88)	<0.01

[a] n = 921 for age variable, [b] OR = odds ratio, [c] CI = confidence interval, [d] multiple correspondence analysis, [e] per year, [f] per year of education. Reference categories for dichotomous variables: Women, Cape coloured ethnicity, Not employed during last year, HIV negative/did not disclose HIV status, Never/occasional/used to drink, Never smoked. All other independent variables are continuous. The second model (2) uses an MCA-derived stigma index. This model is contrasted with the original multivariate model (1) discussed in the paper (see Table 2.2). Source: Own calculations, ZAMSTAR (2010)

Table S1.B.2.7 shows that the results of the original multivariate logistic regression (model 1, taken from Table 2.2) remained robust when changing the stigma index to one derived using multiple correspondence analysis (model 2).

Table S1.B.2.8: Linear probability model (1) and multivariate logistic regression (2) for consulting for a cough (when coughing for more than two weeks), 2010.

	(*n*=921) [a]			
	(1)		(2)	
VARIABLES	OR[b] (95% CI[c])	*p* value	Coefficient	*p* value
Stigma index	1.05 (0.89-1.24)	0.58	0.010	0.606
Age[d]	1.02 (1.01-1.04)	<0.01	0.005	<0.01
Men	0.88 (0.63-1.22)	0.44	-0.029	0.431
Black ethnicity	1.99 (1.28-3.12)	<0.01	0.135	<0.01
Education[e]	1.00 (1.00-1.10)	0.05	0.010	0.053
Employed	0.92 (0.67-1.27)	0.63	-0.018	0.616
Asset index	0.81 (0.71-0.92)	<0.01	-0.048	<0.01
HIV positive	1.30 (0.91-1.85)	0.15	0.058	0.154
Drinks daily	1.43 (0.80-2.54)	0.23	0.075	0.253
Smoked	0.63 (0.45-0.88)	<0.01	-0.102	<0.01

[a] n = 921 for age variable, [b] OR = odds ratio, [c] CI = confidence interval, [d] per year, [e] per year of education. Reference categories for dichotomous variables: Women, Cape coloured ethnicity, Not employed during last year, HIV negative/did not disclose HIV status, Never/occasional/used to drink, Never smoked. All other independent variables are continuous. Source: Own calculations, ZAMSTAR (2010)

As shown in Table S1.B.2.8, the results of the original multivariate logistic regression (model 1, taken from Table 2.2) remained robust when changing the econometric model to a linear probability model (model 2).

Supplementary Materials 1.C: Texts

Text S1.C.2.1: Description of how the HIV proxy was created.

The dichotomous variable for HIV was derived from a combination of confirmed HIV-serology results as well as self-reported HIV-status results due to the large proportion of missing values in the self-reported HIV variable (26% of the combined HIV variable was supplemented by the HIV-serology results). The combination of the serology and self-reported results captures the largest possible number of observations for HIV status.

Text S1.C.2.2: Methodology used to assign stigma scores to individuals in ZAMSTAR dataset.

For this study, there were no individual-level data on stigma for the ZAMSTAR sample. In lieu of individual-level stigma data for the ZAMSTAR sample, the next-best option was to exploit the three[13] available demographic and geographic data that were common to both the SOCS and ZAMSTAR datasets and use it to derive a stigma proxy for the ZAMSTAR sample.

The expected value of stigma – based on age, gender and community characteristics in the SOCS data – is then assigned to the expected stigma value of each group characteristic to individuals in the ZAMSTAR dataset. We expect E(u_ individual) to be equal to zero, and therefore expect E(StigmaSOCS|Age, Gender, Community) to be unbiased.

$$E(StigmaSOCS|Age, Gender, Community)=E(StigmaZAMSTAR|Age, Gender, Community)\ldots[1]$$

However, we concede that measuring expected values for stigma as opposed to individual-level stigma is less informative and likely to bias the results downwards due to aggregation bias.

Furthermore, we acknowledge that the approach taken is also constrained by the few characteristics (only three: age, gender and community) we were able to account for when calculating the expected stigma values (see equation [1] above). This limits the variation of the

[13] The SOCS dataset was parsimonious. Besides stigma data, the only other data available were demographic and geographic data for age, gender and community.

expected stigma values and may contribute to the null results obtained for stigma in this study.

Text S1.C.2.3: Additional discussion on null stigma results.

The null stigma results may also be partly attributable to the relatively low level of healthcare seeking in the study population (63 per cent did not consult for a cough), with stigma exerting no additional deterring effect. Also, with the incidence of TB being high (TB notification rates of more than 400/100 000), TB is likely to be less stigmatised especially since it is contracted involuntarily. These factors may result in TB stigma being too low to detect a measurable effect.

We concede that the combination of low variation in both the dependent (consulting for a cough) and independent variable (stigma) may be the reason for the null result - and not because the relationship is truly zero. Study samples with more variation in both variables of interest – health-seeking and stigma – may likely reveal a different result.

Appendix 1

Appendix 1.A: Acknowledgments

Academic support from ReSEP (Research on Socio-Economic Policy) is acknowledged. The authors thank the participants and communities who participated in ZAMSTAR SOCS. We would like to thank the ZAMSTAR PIs, Nulda Beyers, Helen Ayles, Peter Godfrey-Faussett, and the CREATE Consortium, under the leadership of Richard Chaisson, for allowing us to use the data.

Appendix 1.B: Author Contributions

Ronelle Burger and Carmen Christian conceived and designed the study; Mareli Claassens and Virginia Bond participated in data acquisition; Carmen Christian analysed and interpreted the data; Cobus Burger provided technical inputs; Mareli Claassens provided clinical inputs; Virginia Bond provided anthropological inputs; Carmen Christian wrote the paper; Carmen Christian, Mareli Claassens, Cobus Burger, Virginia Bond and Ronelle Burger reviewed, proofread and edited the manuscript.

Appendix 1.C: Competing Interests

The authors declare no conflict of interest.

Appendix 1.D: Ethical Approval and Consent to Participate

We have permission from the ZAMSTAR principal investigators to use the ZAMSTAR and SOCS data in this secondary analysis. Ethics approval for the ZAMSTAR and SOCS studies were obtained from the Biomedical Ethics Committee at the University of Zambia, Lusaka, Zambia; the Stellenbosch Health Research Ethics Committee, Tygerberg, South Africa; and the London School of Hygiene & Tropical Medicine, London, UK. Individual written consent was obtained from all participants included in the ZAMSTAR SOCS cohort. Ethics approval for this study was obtained from the Research Ethics Committee: Human Research (Humanities) at Stellenbosch University, Stellenbosch, South Africa (project number SU-HSD-004732).

Appendix 1.E: Funding

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Chapter 3

Paper Two: Measuring Quality Gaps in TB Screening in South Africa Using Standardised Patient Analysis

This is the first multi-district Standardised Patient (SP) study in South Africa. It measures the quality of TB screening at primary healthcare (PHC) facilities. We hypothesise that TB-screening protocols and best practices are poorly adhered to at the PHC level. The SP method allows researchers to observe how healthcare providers identify, test and advise presumptive TB patients, and whether this aligns with clinical protocols and best practice. The study was conducted at PHC facilities in two provinces and 143 interactions at 39 facilities were analysed. Only 43% of interactions resulted in SPs receiving a TB sputum test and being offered an HIV test. TB sputum tests were conducted routinely (84%) while HIV tests were offered less frequently (47%). Nurses frequently neglected to ask SPs whether their household contacts had confirmed TB (54%). Antibiotics were prescribed without taking temperatures in 8% of cases. The importance of returning to the facility to receive TB test results was only explained in 28% of cases. The SP method has highlighted gaps in clinical practice, signalling missed opportunities. Early detection of sub-optimal TB care is instrumental in decreasing TB-related morbidity and mortality. The findings provide the rationale for further quality improvement work in TB management.

3.1. Introduction

Developing countries in sub-Saharan Africa and Asia account for close to 80% of the global TB burden [9]. It is therefore unsurprising that South Africa, a high-burden TB country, struggles with this pandemic which remains the main driver of morbidity and mortality [8]. Within this context, local and international research highlighting gaps and weaknesses in TB protocol implementation [26,127–131] and a global call for shifts towards quality improvement [25,132,133] motivated us to consider the quality of TB screening in South Africa.

There is a growing consensus that increasing healthcare coverage is unlikely to improve health outcomes if the quality of care is lagging [63,89,134,135]. There are few studies on the quality of TB diagnosis and treatment [133]. Some of these use novel approaches yet still find that there are significant gaps in the quality of TB care in high-burden countries [26]. Our study adds to the literature in the quality of care space.

Measuring quality of care comes with challenges [136,137]. The available measurement tools have strengths and weaknesses. At a facility level, few reliable measures exist that can be easily implemented and used to flag problems with the quality of care. Patient acceptability and satisfaction indicators can capture some aspects of quality. However, while easy to compile and reasonably affordable, they are subjective in nature [138], suffer from recall constraints [139] and are limited by the difficulty with clinical assessments [136]. Clinical vignettes are useful for measuring provider knowledge, but this is not a good indicator of provider effort since evidence suggests that knowledge and practice diverge [138–141]. Direct provider observation—while simple to execute—is subject to the Hawthorne effect [136]. Clinical audits of patient files have their own shortcomings and are often reliant on small samples [142–144]. Routinely captured health outputs—such as TB success and cure rates—are influenced by both demand and supply factors which make it difficult to interpret facility-level changes in such indicators.

The Standardised Patient (SP) method is an attempt to seek a more accurate and reliable measurement of the clinical aspect of a healthcare interaction [89,145–149]. Although this method is regarded as a gold standard for measuring quality of care [150] it also suffers from weaknesses such as only being feasible for easily simulated conditions; the possibility of exposing SPs to hazardous environments; its limitation to contexts where 'walk-ins' are acceptable; and, the general dislike of the method by healthcare providers [136]. However, used alongside existing indicators, data derived from the SP method can offer a more comprehensive understanding of the quality of care compared to alternative methods.

The purpose of this study is to objectively measure the quality of TB screening at metro-district primary healthcare (PHC) facilities in South Africa using the SP method. This is the first multi-district SP study in South Africa. The method allows researchers to observe how PHC providers identify, test and advise presumptive TB patients, and whether this aligns with clinical protocols and best practice.

3.2. Methods

3.2.1. Sampling and Setting

The study was conducted at 43% of PHC facilities in the Cape Town metropolitan district (Western Cape Province) and 26% of Buffalo City (Eastern Cape Province) in South Africa[14]. It was assumed that urban facilities in the rest of the country would be similar. Furthermore, PHC expenditure per capita (uninsured) was similar in the districts for the 2015/2016 financial year—

[14] The study conducted a random sampling of 20 metropolitan facilities within each province (Eastern and Western Cape). Due to the very high cost of the study, the sample size and location were mainly dictated by the study's budget constraints.

R1203 in Buffalo City and R1117 in Cape Town[15] [151]. In total, 39 PHC facilities were covered, 19 in Cape Town (one facility was excluded due to access issues) and 20 in Buffalo City.

The 2015 TB (all types) incidence rates for both study districts exceeded the national average of 520 cases per 100,000, with Cape Town reporting a rate of 596 and Buffalo City a slightly higher rate of 743 [152]. For the same year, the known TB/HIV co-infection rate was 44.6% in Cape Town and 45.7% in Buffalo City [151].

Both Cape Town and Buffalo City PHC facilities implemented TB-screening protocols that complied—at the very minimum—with the South African National TB Management Guidelines (SANTMG) of 2014 [152]. These guidelines formed the basis of the TB instruments (discussed in more detail below under Section 3.2.3).

3.2.2. The SP Method[16]

The SP approach involved sending a covert fieldworker (SP) to a healthcare facility where he/she presented with an opening statement describing a set of pre-determined symptoms (TB symptoms in this case) that would predictably map to a set of clinical questions, examinations and tests. Closely approximating a real-life patient required rigorous training and precise instructions to the SP. The eight recruited SPs—four from each province—were trained according to a script with standard questions likely to be asked at a TB screening. Their responses were standardised and designed to avoid invasive examinations. The SPs were trained to only supply information in response to questions asked by the healthcare worker, with explicit instructions not to voluntarily disclose any additional information. The SPs presented using their own identities to reduce the likelihood of being detected.

[15] The 2015/2016 PHC expenditure per capita (uninsured) for all metropolitan (urban) facilities were above the national average of R993, with Ekurhuleni the highest-spending metro at R1 222 per capita and Tshwane the lowest at R1 012.

[16] A supplementary methods section has been added to expand on the development of the SP instruments (Text S2.D.3.1), SP recruitment and training (Text S2.D.3.2) and field work procedure and management (Text S2.D.3.3).

Healthcare providers were unaware that the SP was not a real patient. This provided an opportunity to observe the healthcare worker's actions in a natural environment. After the interaction, the SP captured details about the facility visit on a score sheet (discussed in more detail under Section 3.2.3). High-reliability recall of SPs was demonstrated in a validation study that compared data collected through exit interviews with SPs post interaction with data collected through voice recordings of the SP-provider interaction [89]. While the validation study provides confirmation about the reliability of the method, we acknowledge that this would vary from case to case, similar to standard surveys and fieldwork. Due to ethical issues with recording nurse interactions with patients, it is not feasible to use voice recordings to validate SP recall in each SP study. In lieu of voice recordings, we employed quality control mechanisms and scrutinised SP motivation and recall prior to recruitment (see Text S2.D.3.2).

Comparing the clinical treatment received by the SP to clinical practice and protocols enabled researchers to measure clinical quality at the facility level. The rationale was to understand whether the healthcare worker asked the correct questions and conducted the required examinations and tests, measured according to standardised protocols and practice.

SP work in India [145] has shown that it provides reliable quality findings that do not necessarily correlate with and follow patterns of alternative facility-level measures such as patient satisfaction or clinical knowledge. The method has also been validated in other low- and middle-income settings including Kenya and China [145,147,153,154].

In TB research, SP studies are increasingly recognised as helping to identify and monitor deficiencies in health systems such as provider behaviour that may compromise the diagnostic evaluation [26,133].

3.2.3. Instruments and Data Collection

3.2.3.1. TB-Screening Instruments

The SP's interaction with the healthcare provider was guided by a carefully developed script and documented using a comprehensive score sheet. Scripts (Tool S2.C.3.1) and score sheets (Tool S2.C.3.2) were developed based on publicly available instruments from an international SP manual [155], local TB-screening guidelines (Tool S2.C.3.1, Tool S2.C.3.2, the SANTMG [152], Primary Care 101 [156], Practical Approach to Care Kit (PACK) Adult [157]) and best practices. The score sheet made provision for capturing the most essential clinical components of the interaction first to minimise recall bias.

The TB-screening instruments were reviewed by various external stakeholders in the respective study districts: clinical experts, PHC providers, public health specialists and programme managers (Table S2.B.3.1). They were then piloted at five PHC facilities in Cape Town in 2015 ($n = 14$). Pilot findings assisted us with refinement of the instruments which were sent out to relevant external stakeholders for a second round of review (see Text S2.D.3.1).

3.2.3.2. Data Collection

The full roll-out of the project commenced at various stages during 2016 and early 2017, taking six months to complete. A sample size of 156 patient-facility interactions was anticipated (Figure S2.A.3.1) given that a total of 39 facilities would be visited by four SPs. Each SP visited study facilities in his or her province. A breakdown of SP characteristics can be found in Table S2.B.3.2.

All SPs were provided with official letters which they could use in the event of being exposed as a covert fieldworker. The letter explained that the SP was part of a study endorsed by the respective departments of health. None of the SPs were detected during the study.

TB score sheets were completed by the SP in privacy immediately after leaving the facility to minimise recall lapses and biases. To monitor data capturing quality and reliability, a fieldwork manager conducted bi-weekly debriefing sessions with SPs where TB score sheets were audited.

After taking failed visits and 'home facilities' into account, the sample size was reduced to 143 interactions (Figure S2.A.3.1). To maintain the study integrity and the privacy of the SP, SPs were not allowed to visit any of the facilities they used regularly (also known as 'home facility'). Failed SP visits were defined as an SP not entering the facility or being turned away from the facility at any point before being seen by a healthcare worker.

The study collected and aggregated anonymised data. Where serious facility-level problems were detected, provincial health authorities were alerted.

3.2.4. Statistical Analysis

Clinical data derived from the TB instrument are presented as binary variables. We focus on variables that are included in TB-screening protocols and best practices, and use uni- and bivariate analysis of these variables to describe the levels of the quality of TB screening. Data analyses were conducted at the facility visit level (and not at the individual healthcare provider level). Statistical analyses were performed using STATA (version 14.02, StataCorp LLC, College Station, TX, USA) software.

3.2.5. Ethical Considerations and Approval

Ethical concerns for the SP method include the risks that the SP is exposed to as well as the issue of concealment. Risks to the SP were minimised during training and preparation, as well as by intentionally designing scenarios that did not involve invasive examinations (such as TB screening). Scripts also included excuses that the SP could use to prevent further examination should they need to exit an interaction.

The concealment involved in the SP method differentiates this work from traditional surveys. Concealed research—also referred to as covert research—is regarded as permissible under certain circumstances if it is integral to the nature of the research being conducted, i.e., non-concealment will undermine the purpose of the research [158]. This study was granted ethical clearance from the Research Ethics Committee for Human Research (Humanities) at Stellenbosch University, South Africa (HS1096/2014-REC).

3.3. Results

Summary statistics for the variables of interest were generated (Table S2.B.3.3). Results are reported as a percentage, followed by the absolute value and 95% confidence interval in brackets. Variables of interest were stratified by SP, facility (Table S2.B.3.4), gender and age (Table S2.B.3.5). No consistent pattern of significant variation in means emerged, except across SPs—and to a lesser degree—across facilities.

3.3.1. Case Description and Management

The case description for each SP was presumed TB with more than two weeks of coughing, fever and weight loss. Having the SPs present in this manner allowed us to observe how PHC providers identify, test and advise presumptive TB patients.

The failed visit rate captures the proportion of unsuccessful facility visits where the SP left the facility without consulting a provider. This rate makes provision for excluding cases where the SP could not visit a facility because it was their local or 'home facility'. Overall, the failed visit rate was 6% or nine out of a potential 152 patient-provider interactions (Table S2.B.3.6).

For the 143 analysable interactions SPs presented with the following opening statement: 'I have been coughing a lot recently'. Programme managers and clinicians advised against adding 'for two weeks' because this could appear contrived or rehearsed and not aligned with how patients who are concerned about their cough would normally present at facilities. If they were not triaged or identified for TB screening, SPs were trained to add: 'I think I may have TB'. We required SPs to track whether they mentioned TB explicitly in their opening statement. More than 90% (91%; 124; 0.85–0.95) of SPs were triaged for TB screening without the need to mention TB.

3.3.2. Adequate Case Management

Based on a review of guidelines and protocols, and consultations with clinical experts and programme managers, we defined a minimum level of case management for TB screening as a sputum test and an offer of an HIV test. Applying this definition, we find that 43% (61; 0.35–0.51) of SPs were correctly managed. This result is driven mainly by a low rate of HIV tests offered, since sputum tests were conducted at 84% (120; 0.77–0.89) of visits while HIV tests were offered at only 47% (67; 0.39–0.55). SPs were asked about household TB contacts in 54% (77; 0.46–0.62) of cases.

Using the SANTMG benchmark of checking for four essential TB symptoms: coughing for more than two weeks, weight loss, night sweats, and fever for more than two weeks, the overall finding shows that just over half (55%) of the essential history checklist questions were asked. The prevalence of the questions asked was: cough duration (80%; 114; 0.73–0.86), night sweats (59%; 84; 0.50–0.67) weight loss (55%; 78; 0.46–0.63) and duration of fever (25%; 36; 0.19–0.33).

3.3.3. Medical Examinations

Blood pressure and weight measurements were performed most frequently (43% (61; 0.35–0.52) and 38% (54; 0.31–0.47), respectively) at SP TB screenings. Pulses were checked the least frequently at 13% (18; 0.08–0.20) of interactions. Temperatures were taken at 16% (22; 0.10–0.27) of interactions overall and in 22% (8; 0.11–0.39) of cases where the SPs were asked whether they had a fever (the standardised response was yes).

3.3.4. Dispensing of Antibiotics

For interactions where no temperatures were taken, antibiotics were prescribed 8% (10; 0.05–0.15) of the time (10 out of 119 cases). Amoxycillin was prescribed for most of these cases (eight), while penicillin was prescribed for one case and a trimethoprim and sulfamethoxazole combination antibiotic for another.

3.3.5. Access to Surgical Masks

SPs had access to surgical masks in 48% (69; 0.40–0.57) of cases.

3.3.6. Follow-up

Fifteen per cent (15; 0.09–0.23) of SPs did not receive any verbal or written communication about returning to collect their TB test results. Only 28% (33; 0.20–0.37) reported that nurses explained the importance of returning for their TB test results.

3.4. Discussion

To be considered of acceptable quality, TB care needs to comply with (international) standards [26]. For South Africa, TB-screening protocols used at a PHC level comply with the SANTMG which is derived from the World Health Organization's TB guidelines. The discussion highlights some of the missed opportunities in the current implementation of TB-screening protocols which were identified using the SP method.

While an overall failed visit rate of 6% may seem low at first glance, this translated into nine of the SPs not having the opportunity to be screened for TB (Table S2.B.3.6). This represents a loss of presumptive TB patients from the TB care cascade at the earliest point. In this study, SPs were not given a waiting time in terms of how long they should wait before leaving, i.e. SPs could only leave the facility when instructed to do so by staff at the facility. Often no reason was provided when SPs were told to leave the facility, other times they were informed it was due to staff constraints, e.g., a nurse being on sick leave. Patients who have experienced failed visits at a

PHC facility may also become discouraged and could be reluctant to return. Systems need to be developed to ensure that presumptive TB patients are prioritised, even when facilities are short-staffed.

Given the prioritisation of HIV and TB care in South Africa over the past two decades through additional funding and training, it is disappointing to see that in only 43% of cases did the public healthcare system meet the minimum threshold for adequate case management. This was driven mainly by a lower than expected rate of offering HIV tests (47% of cases) which is concerning given the high TB/HIV co-infection rate in South Africa (57% in 2015 [151]) and the resources that have been invested in training, awareness and fighting stigma. It is also worrisome because the level of sensitivity of TB test results using Xpert®, the recommended TB diagnostic tool in South Africa, is influenced by HIV status [159]. False-negative TB test results carry costs for the individual and perpetuate the spread of infectious TB. Even though sputum tests were conducted often (84% of visits), there is room for improvement.

Besides people who are HIV positive, the SANTMG recommends that a high index of suspicion is required for patients who have been in contact with a person with confirmed TB. From this perspective, enquiring whether anyone in the household had confirmed TB was viewed as important by TB-control programme managers. Despite this, SPs were asked about household TB contacts in only 54% of cases.

There are many potential reasons for deviations from protocols including inadequate training, lack of knowledge, deficiencies in monitoring and evaluation [160,161] and, more broadly, a lack of clinical governance [162–165]. Unfortunately, due to our limited sample, we cannot test the plausibility of rival explanations for poor protocol compliance.

Checking for the four main symptoms of pulmonary TB is essential in a clinical interaction since every patient with a positive TB symptom should be tested for TB, according to the SANTMG.

The overall finding shows that just over half of the essential history checklist questions were asked. Similarly, physical examinations linked to TB screening were conducted at less than 50% of SP interactions. Cough duration emerged as the most frequently asked essential history checklist question, which implies that healthcare providers relied almost exclusively on this symptom when determining whether the patient requires a sputum test or not.

In less than 10% of the interactions, SPs had to provide the additional statement of 'I think I may have TB' before being triaged or identified for TB screening. This reinforces a hypothesis that persistent coughing, the opening statement of the SP, is top of mind as a TB symptom and elicits the appropriate referral within the facility.

A worrisome finding emerged: 8% of SP interactions where no temperatures were taken resulted in the prescription of antibiotics. Considering the local antibiotic algorithm and TB-screening protocol, there was no indication for antibiotics to be administered. Practices such as this may lead to an increase in drug-resistant bacteria in South Africa. Further research is needed to understand why this practice occurs. It may be a form of empirical antibiotic treatment that is practised in certain countries [89], though the South African TB protocol does not allow for empirical antibiotic treatment unless the patient has a temperature greater than, or equal to, 38 degrees Celsius [156]. Irrespective of the rationale, the risks associated with this practice are high and, at this preliminary stage, should be considered unsafe.

Providing surgical masks has been deemed a best practice by clinical experts and programme managers and is considered an infection-control measure. SPs had access to a surgical mask at less than half of interactions (48%). Making surgical masks more readily available to all patients entering facilities is a simple and pragmatic way of reducing the risk of droplet infection [166,167].

Lack of information-sharing, particularly in terms of continuity of care, emerged during the interactions: approximately two out of ten SPs were not informed about returning to the facility for their TB test results. Even when cases were managed correctly, very little effort was made to explain the importance of returning for TB test results. This was explained at less than a third of interactions (28%). The overall pattern suggests low effort exerted in communicating valuable information to the patient regarding the dangers of untreated TB and the need to start treatment as soon as possible.

This suggests that a diagnostic gap exists with some presumptive TB patients leaving facilities without being tested for TB; others leaving the facility without knowing that they need to return for results and why; and, some TB test results may come back as a false-negative. These findings about deficiencies in diagnostic protocol compliance add to the literature analysing the weaknesses in the health system and can provide useful feedback to national and provincial governments.

We argue, based on this study and the relevant studies cited, that the care provided for TB screening in South Africa is not as effective as it could be given its resources. The multiple gaps in protocol adherence are a concern that needs to be acknowledged and addressed because they contribute to TB deaths and disappointing TB outcomes. Protocols and best practices may need to be interrogated to ensure that their most important elements are prioritised, allowing for more pragmatic implementation in high-burden settings. Ensuring that basic and important steps in the TB-screening protocol are adhered to may prevent the loss of presumptive TB patients in the healthcare system.

The increasing popularity of the SP method in measuring the quality of healthcare is supported by the findings of this study which was able to identify deficiencies in the health system, specifically provider behaviour that compromised the diagnostic evaluation of TB patients. The method has been used as a complementary but ad hoc monitoring tool in other countries [148].

3.5. Conclusions

Use of the SP method to measure the quality of TB screening—the first endeavour of its kind in South Africa—shows evidence of gaps in clinical practice, signalling missed opportunities for diagnosis. Early and reliable detection of sub-optimal quality of TB care is instrumental in decreasing TB-related morbidity and mortality, highlighting the usefulness of the SP method. The study findings provide the foundation for further quality and quality improvement in the management of TB, particularly in high-burden countries such as South Africa.

Supplementary Materials 2

Supplementary Materials 2.A: Figures

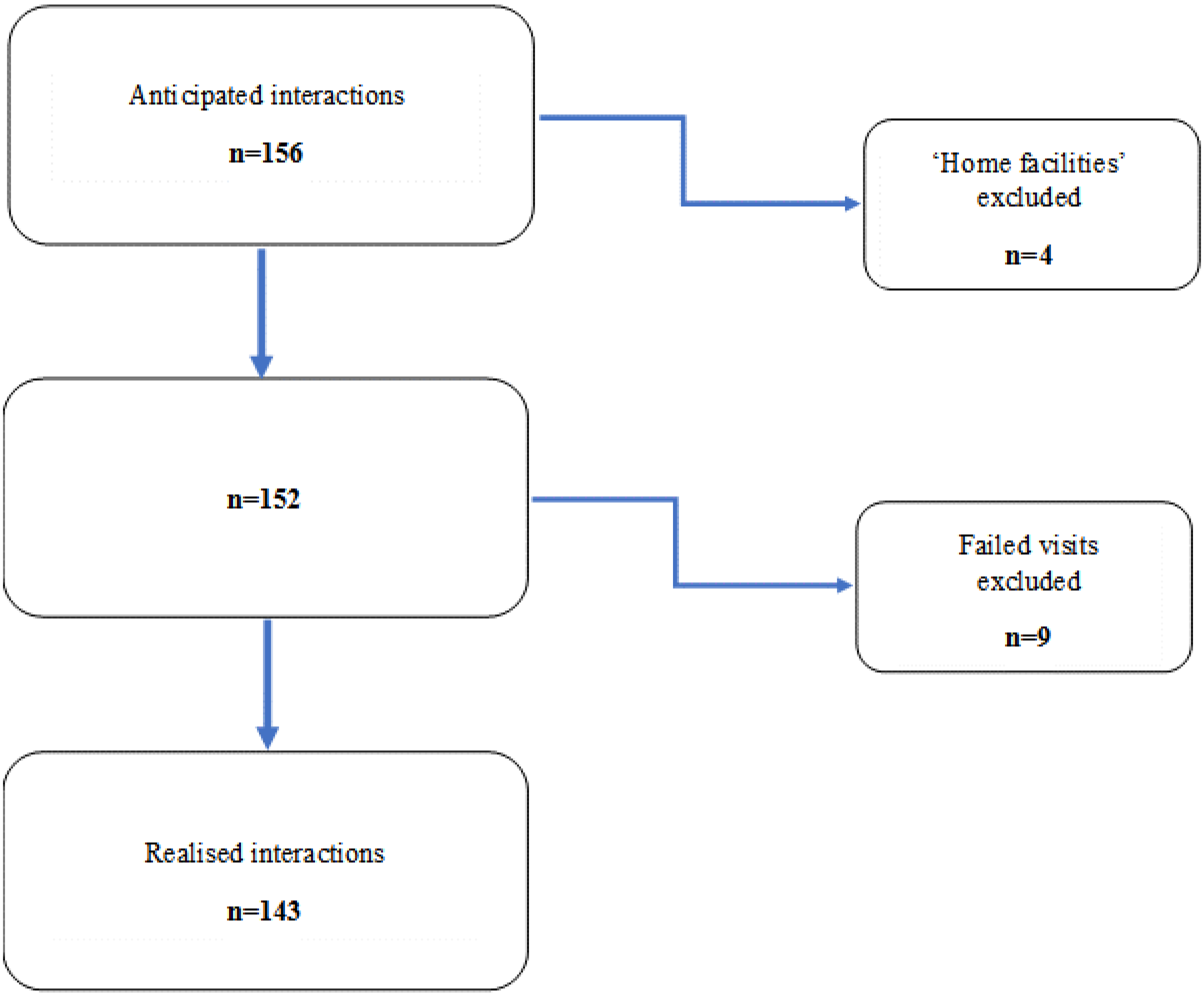

Figure S2.A.3.1: Exclusions from standardised patient-facility interactions
'Home facility' refers to a primary healthcare facility that the SP used regularly. Failed visits were defined as an SP not entering the facility or being turned away from the facility at any point before being seen by a healthcare worker.

Supplementary Materials 2.B: Tables

Table S2.B.3.1: List of external reviewers of TB-screening instruments

Department, Institution	Job Title	Inputs
Health Impact Assessment Unit, Department of Health, Western Cape Government	Public Health Specialist (1)	Provided referrals to relevant stakeholders for review of instruments.
	Public Health Specialist (2)	Provided the relevant TB guidelines. Reviewed early versions of the instruments.
Desmond Tutu TB Centre, Stellenbosch University	Research Clinician (1)	Provided clinical expertise when drafting instruments. Reviewed instruments.
	Research Clinician (2)	Provided clinical expertise when drafting instruments. Reviewed instruments.
Facility-based Programmes, Department of Health, Western Cape Government	Programme Manager	Provided insights about integrated approach to primary healthcare assessment. Ensured that instruments contained integrated clinical questions.
HAST (HIV & AIDS, STI and TB) Directorate: TB Prevention and Management, Department of Health, Western Cape Government	Deputy Director	Provided insights about the current management of presumed TB patients at primary healthcare facilities. Reviewed instruments and provided inputs.
	Assistant Deputy Director	Provided insights about the current management of presumed TB patients at primary healthcare facilities. Reviewed instruments.
Integrated Strategic Management, Eastern Cape Government Department of Health	Chief Director	Provided referrals to relevant stakeholders for review of instruments.
TB Directorate, Department of Health, Eastern Cape Government	Provincial Programme Manager	Provided insights about the current management of presumed TB patients at primary healthcare facilities. Reviewed instruments and provided inputs.

Instruments include both the TB-screening script and score sheet.

Table S2.B.3.2: Standardised patient characteristics (*n*=8)

Characteristic		n (%)
Gender	Male	4 (50)
	Female	4 (50)
Age	<30 years	4 (50)
	≥30 years	4 (50)
Race	Black	6 (75)
	Coloured	2 (25)
Education	< Matric	1 (12.5)
	Matric	3 (37.5)
	> Matric	4 (50)

Matric is the final year of secondary schooling, i.e. 12 years of education completed and passed. In South Africa there are four main racial classifications – Black, Coloured, White and Indian.

Table S2.B.3.3: Summary statistics of variables of interest

Variable	Observations	Mean	Std. Dev.	Min	Max
Adequately managed	143	.4265734	.4963176	0	1
TB test conducted	143	.8391608	.3686739	0	1
HIV test offered	143	.4685315	.5007627	0	1
Asked about household TB contacts	143	.5384615	.5002708	0	1
Opening statement only 'coughing a lot'	136	.9117647	.2846854	0	1
Asked about cough duration	142	.8028169	.3992801	0	1
Asked about night sweats	143	.5874126	.4940302	0	1
Asked about weight loss	143	.5454545	.4996798	0	1
Asked about fever duration	143	.2517483	.4355429	0	1
Blood pressure measured	141	.4326241	.4972060	0	1
Weight measured	141	.3829787	.4878462	0	1
Pulse checked	140	.1285714	.3359269	0	1
Temperature taken	141	.1560284	.3641759	0	1
Temperature taken if asked about fever duration	36	.2222222	.421637	0	1
Antibiotics prescribed without taking temperature	119	.0840336	.2786113	0	1
Access to surgical mask	143	.4825175	.5014507	0	1
Return for TB test results communicated	103	.8543689	.3544608	0	1
Explained importance of returning for TB test results	119	.2773109	.4495642	0	1

Table S2.B.3.4: One-way ANOVA of variables of interest by standardised patient and facility

Variable	Between standardised patients			Between facilities		
	Lowest mean	Highest mean	Prob > F	Lowest mean	Highest mean	Prob > F
Adequately managed	.05263158	1	0.0000	0	1	0.0000
TB test conducted	.36842105	1	0.0000	.5	1	0.5284
HIV test offered	.05263158	1	0.0001	0	1	0.0000
Asked about household TB contacts	0	.89473684	0.0002	0	1	0.5665
Opening statement only 'coughing a lot'	.68421053	1	0.0004	.5	1	0.7803
Asked about cough duration	.47368421	1	0.0020	.33333333	1	0.5941
Asked about night sweats	.10526316	1	0.0000	.25	1	0.3508
Asked about weight loss	.31578947	1	0.0558	0	1	0.1764
Asked about fever duration	0	.52631579	0.0004	0	1	0.1751
Blood pressure measured	0	.8	0.0524	0	1	0.0040
Weight measured	0	.52631579	0.7884	0	1	0.0000
Pulse checked	0	.53333333	0.0000	0	.5	0.8192
Temperature taken	0	.33333333	0.3495	0	.75	0.0004
Temperature taken if asked about fever duration	0	.66666667	0.3638	0	1	0.7215
Antibiotics prescribed without taking temperature	0	.47058824	0.0000	0	.66666667	0.6943
Access to surgical mask	.6875	1	0.0018	0	1	0.0005
Return for TB test results communicated	.5625	1	0.0059	0	1	0.0691
Explained importance of returning for TB test results	0	.69230769	0.0030	0	1	0.0031

Standardised patient: *n*=8; Facility: *n*=39

Table S2.B.3.5: One-way ANOVA of variables of interest by gender and age

Variable	Between genders			Between age categories		
	Men mean	Women mean	Prob > F	≤ 30 years mean	> 30 years mean	Prob > F
Adequately managed	.43478261	.41891892	0.8493	.375	.50909091	0.1163
TB test conducted	.92753623	.75675676	0.0052	.80681818	.89090909	0.1855
HIV test offered	.44927536	.48648649	0.6586	.40909091	.56363636	0.0725
Asked about household TB contacts	.71014493	.37837838	0.0000	.67045455	.32727273	0.0000
Opening statement only 'coughing a lot'	.92424242	.9	0.6215	.87058824	.98039216	0.0289
Asked about cough duration	.82608696	.78082192	0.5015	.86363636	.7037037	0.0200
Asked about night sweats	.68115942	.5	0.0279	.70454545	.4	0.0003
Asked about weight loss	.66666667	.43243243	0.0047	.59090909	.47272727	0.1697
Asked about fever duration	.23188406	.27027027	0.6002	.29545455	.18181818	0.1295
Blood pressure measured	.46376812	.40277778	0.4685	.47727273	.35849057	0.1703
Weight measured	.36231884	.40277778	0.6242	.35227273	.43396226	0.3373
Pulse checked	.15942029	.09859155	0.2857	.18181818	.03846154	0.0142
Temperature taken	.17391304	.13888889	0.5699	.15909091	.1509434	0.8982
Temperature taken if asked about fever duration	.25	.2	0.7292	.19230769	.3	0.5004
Antibiotics prescribed without taking temperature	.03508772	.12903226	0.0659	.13513514	0	0.0097
Access to surgical mask	.52173913	.44594595	0.3683	.5	.45454545	0.5997
Return for TB test results communicated	.8852459	.80952381	0.2889	.88235294	.8	0.2661
Explained importance of returning for TB test results	.21875	.34545455	0.1258	.21126761	.375	0.0509

Men: *n*=4; Women: *n*=4; ≤ 30 years: *n*=5; > 30 years: *n*=3

Table S2.B.3.6: Failed visit rate of standardised patients

	Total (*n*)
Anticipated SP Interactions	156
Facility Not Visited Since SP's 'Home Facility'	4
Failed Visits	9
Realised SP Interactions	143
Failed Visit Rate	0.06

'Home facility' refers to a primary healthcare facility that the SP used regularly. Failed visits were defined as an SP not entering the facility or being turned away from the facility at any point before being seen by a healthcare worker. The denominator used when calculating the failed visit rate is 152 since it excludes the 4 'home facility' interactions from the anticipated SP interactions (*n*=156).

Supplementary Materials 2.C: Tools

Tool S2.C.3.1: SP TB scenario script

SCRIPT: Tuberculosis

INSTRUCTIONS TO FIELD WORKERS:

ACCURACY: To ensure accuracy we recommend that you use your mobile phone to capture times and make notes while you wait on how full the waiting room was. Do not at any time make notes on the actual score sheet at the clinic.

SAFETY: In the unlikely event that a health worker is suspicious and confronts you, please present the letter from the Department of Health. It is vital that you always travel with your letter. Thus far we have had almost 200 interactions (this number includes other clinical scenarios) and no confrontations, but it is important to know what to do in such a case. The first option would be to end the interaction with an excuse and leave, but if this does not work you will need to present the letter.

BASIC INFECTION CONTROL MEASURES: If you find yourself in a clinic where there are no open windows and no adequate ventilation, try to walk outside for 10 minutes after every hour. You may need to ask someone to keep your place in the queue for you.

ASSESSING TESTS: Nurses may not always tell you what tests they are doing. However, after the role-play you should know when your temperature, blood pressure, pulse rate, height and weight are being taken. You have also been shown what chest percussions, chest auscultations and feeling for lymph nodes look like, in case this is also performed.

PRESCRIBED MEDICINES: If any medicines are prescribed, do not collect it. Rather attach the prescription to the questionnaire. If medicines are dispensed by the nurse, bring them along.

Medical setting: Local facility

Patient clothing: What you usually wear, but your dress style should remain consistent throughout the study.

Patient presentation and emotional tone: You are very tired and coughing intermittently. When talking to the nurse you will use non-medical terminology, but you have a general understanding of the body. Speak in English if the nurse is English speaking. Otherwise, speak in your home language, isiXhosa.

1. ***Opening statement (volunteered):***

   a) Good afternoon sister. I have been coughing a lot recently.

   If you are not triaged and fast-tracked to the TB clinic, volunteer the following additional information.

   b) Sister, I think I may have tuberculosis.

2. ***History of present illness (question-and-answer format)***

   Q: How old are you?
   A: *I'm …. years old. (Your real age)*

   Q: How long have you been coughing?
   A: I have been coughing for more than 2 weeks.

   Q Do you have a dry cough or a wet cough? (May not be asked if nurse is observing your cough)
   A: In the morning the cough is wet, but I always spit out the phlegm. After that my cough is drier.

   Q: Is there sputum in the cough? If yes, what colour is the sputum?
   A: Yes, there is sister, especially when I wake up. It is brownish in colour.

   Q: Is there blood in the sputum?
   A: No sister, there is no blood.

   Q: Do you have pains in your chest when you breathe?
   A: Not really sister, only when I cough hard in the morning.

   Q: Did you lose weight?
   A: I cannot be sure but my clothes are a little looser though.

   Q: Describe your appetite?
   A: I haven't been eating much, I don't feel like food.

   Q: Do you have night sweats?
   Yes sister, I have night sweats.

   Q: Describe the night sweats?
   The clothes I sleep in get wet.

   Q: Do you feel tired?
   A: Yes I feel very very tired sister.

   Q: Are you ever short of breath? (May not be asked if the nurse is observing your breathing)
   A: Sometimes when I move sister.

   Q: Have you been having fever? If yes, for how long?
   A: Yes, sister. I started getting fevers since last weekend.

Q: What is the severity of your fever?
A: My fevers are not severe.

Q: Do you have a flu or cold?
A: I don't think so.

Q: Do you have any body aches or headache?
A: No sister, I do not.

Q: Does anyone in your household have tuberculosis? Have you been in contact with anyone who has TB?
A: No sister.

Q: Has this cough happened to anyone else in the household?
Yes sister, my….[a family member]. (S)he is still coughing but he doesn't want to come to the clinic, says it's just a cough, nothing serious.

Q: Is anyone in the household under 5 years or older than 60 years?
No, sister

Q: Did you take any medication for these symptoms yet?
A: Yes sister, cough syrup from the pharmacy. And Panado.

Q: Have you ever taken medicine for tuberculosis?
A: No sister, I have not had TB before and have never taken medicine for it.

Q: Do you smoke? Do you drink alcohol?
A: No sister, I'm not allowed to do that.

Q: When last have you been tested for HIV? What is your status?
A: I tested for HIV again a few weeks ago. I am HIV…. [Produce proof if sister insists on having it].

Q: Are you diabetic?
A: No sister.

Q: Have you ever worked in a mine?
A: No sister.

3. Review of systems, social history, family history, allergies

Housing conditions (assuming that this is important for TB):
- Small house in the township.
- Poor construction, walls are very damp due to water infiltration.
- Windows kept closed during winter.
- Access to running water and toilet inside the house.

Review of system:
- Recently noticed a persistent cough, especially when waking up.
- Worried, since you know coughing is associated with TB.
- Your clothes are getting loose.

Family history:

- A family member is also coughing, but is not worried about it.
- Nobody in the household is under 5 years or older than 60 years.

4. ***Relevant physical exam components***
   - A full physical examination: height, weight, temperature, pulse rate, blood pressure.
   - The following are clinical examinations which may be performed if transferred to a doctor or senior practitioner: chest inspection, chest percussion, examination of mouth/throat, chest auscultation.

5. ***Other relevant examinations***
   - 1 x TB sputum spot tests.
   - You are offered an HIV test after being counselled.

6. ***Possible treatments, including educational measures and referral if necessary***
   - Nurse explains the importance of cough etiquette i.e. cover mouth with toilet paper or handkerchief when coughing. You are also advised to wash your hands as soon you are done coughing.
   - You may be offered a course of oral antibiotics, for instance amoxycillin, to be completed over 5-7 days, oxygen (probably not), and referral to hospital if sister believes signs and symptoms warrant it (probably not).

7. ***Questions to ask the sister, if prompted:***
   - None

8. ***Particular items to note:***
   - Did the nurse ask enough questions about your current condition?
   - Did the nurse ask whether you have any questions?
   - Did the nurse ask whether anyone in the household has TB? Or whether you were in contact with anyone with TB?
   - Did the nurse adequately explain medical terms, or advice given to you, regarding TB?
   - Did the nurse explain basic infection control measures in the household? E.g. the nurse must explain about good ventilation in the house, about cough etiquette, etc.
   - Did the nurse observe you when you provided your sputum? Did she explain how you should cough up the sputum? Where did this take place?
   - Did the nurse tell you to return to the clinic to collect your results? If so, after how many days? Did she write this down? Did she explain the importance of returning to the clinic to get the results?
   - How was the also nurse's attitude towards you? Was she friendly, respectful, irritated, etc.?

Tool S2.C.3.2: SP TB score sheet

SCORE SHEET: Tuberculosis

Score Sheet Information:

Name MP	
Facility Visited	
Folder Number	
Date of Visit	

Notes by Supervisor:

Full payment?	Yes	Partly	No
If Partly or No, why?			
Other			

Section 1	General questions	Number	
1.1	How many patients were waiting when you reached the clinic?	☐	
1.2	How many patients were in the clinic when you left?	☐	
1.3	Time entered facility	:	
1.4	Time sputum test taken	:	
1.5	Time exited facility	:	
1.6	Language treated in: isiXhosa ☐	Afrikaans ☐	English ☐
1.7	Opening statement:	Coughing a lot ☐	Think I have TB ☐

Key summary questions:		
A1 – You had access to a surgical mask at the facility	Yes	No
A2 – The health care worker asked whether you had been in contact with someone with TB	Yes	No
B1 – The health care worker asked about TB symptoms (coughing for > 2 weeks, weight loss, fever, night sweats)	Yes Somewhat Yes	No Somewhat No
B2 – The health care worker asked whether you were diabetic	Yes	No
C – The health care worker offered you an HIV test	Yes	No
D1 – The health care worker asked you to return to the clinic for your TB test results after two days	Yes	No
D2 – The health care worker explained the importance of returning to the clinic to get your results	Yes	No
E – All medical terms were clearly explained and clear language was used	Yes	No
F – The health care worker was friendly, open, compassionate and non-judgemental	Yes Somewhat Yes	No Somewhat No

Section 2: MEDICAL HISTORY

No.	**Question**	**Asked?**	**Notes**
2.1	Age	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.2	Duration of cough?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.3	Wet or dry?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.4a	Sputum in cough?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.4b	What is the colour of the sputum?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.5	Blood in cough?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.6	Chest pain?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.7	Weight loss?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.8	Describe your appetite	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.9	Night sweats	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.10	Are you tired?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.11	Shortness of breath?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.12a	Fever?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.12b	Duration of fever?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	

2.13	Severity of fever?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.14a	Do you have a cold/flu?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.14b	Do you have diabetes?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.15a	Body aches?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.15b	Headache?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.16a	Does anyone in the household have TB?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.16b	Have you been in contact with anyone with TB?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.17	Is anyone in the household coughing?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.18	Are you taking medication?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.19	Have you ever taken TB meds?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.20	Do you smoke?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.21	Do you drink?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.22	Were you asked when last you were tested for HIV?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.23	Were you asked to disclose your HIV status?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.24	Was it explained to you why it was necessary for the health care worker to know your HIV status?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.25a	Did you have access to a mask at the facility?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.25b	Did the health care worker wear an N95 respirator?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	

SOCIAL HISTORY AND FAMILY

No.	Question	Asked?	Notes
2.26a	Any questions about community/family background?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.26b	Were you asked whether you work or have ever worked in the mines?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	
2.27	Is anyone in the household under 5 years or older than 60 years?	Yes ☐ No ☐ Unsure ☐ Self-given ☐	

PHYSICAL EXAMINATION			
2.28	Height	Yes ☐ No ☐	
2.29	Weight	Yes ☐ No ☐	
2.30	Temperature	Yes ☐ No ☐	
2.31	Pulse rate	Yes ☐ No ☐	
2.32	Blood pressure	Yes ☐ No ☐	
2.33	Examination of mouth/throat	Yes ☐ No ☐	
2.34	Chest percussions (tapping your chest)	Yes ☐ No ☐	
2.35	Chest auscultation (using a stethoscope)	Yes ☐ No ☐	
2.36	Feeling for lymph nodes (glands in neck)	Yes ☐ No ☐	
Section 3: TESTS			
3.1a	TB test (provided 1 x sputum containers)	Yes ☐ No ☐	
3.2b	Were you supervised/observed when providing your sputum sample?	Yes ☐ No ☐	
3.2c	Was your sputum collected in a separate room/area?	Yes ☐ No ☐	
3.2	HIV test offered	Yes ☐ No ☐	
3.3	HIV test conducted	Yes ☐ No ☐	

Section 4: TREATMENT				**Notes**
4.1	Medicines dispensed?	Yes ☐ No ☐		
	If yes, details:			
	Name:	Dose:	Duration:	
4.2	Counselling on cough etiquette?	Yes ☐ No ☐		
4.3	Counselling on hand washing?	Yes ☐ No ☐		
4.4	Counselling on infection control measures **at home** e.g. open windows and curtains, ensure adequate ventilation?	Yes ☐ No ☐		

Section 5: DIAGNOSIS			
5.1	Did the health care worker discuss a possible diagnosis?	Yes ☐ No ☐	
5.2	If yes, what was it?	N/A ☐	
Section 6: FOLLOW UP QUESTIONS			
6.1a	Did the health care worker give you an appointment card with a specific date to return to the clinic for results?	Yes ☐ No ☐	
6.1b	Did the health care worker write down a specific date in your folder book to return to the clinic for results?	Yes ☐ No ☐	
6.1c	Did the health care worker tell you to return to the clinic for your TB results?	Yes ☐ No ☐	
6.2	If yes, after how many days were you requested to return to the clinic for your TB results?	N/A ☐	
6.3	Did the health care worker explain the importance of returning to the clinic for results?	Yes ☐ No ☐	
6.4	Did the health care worker ask you to return to the clinic if your symptoms got worse?	Yes ☐ No ☐	
Section 7: FEES			
7.1	Fee charged by healthcare worker	R.	
7.2	**TOTAL FEE**	**R.**	

Tool S2.C.3.3: TB-screening tool for presumptive TB and TB contacts, Cape Town metropolitan district

Nov-15

SCREENING TOOL FOR PRESUMPTIVE TB & TB CONTACTS
For TB-suspects, contacts, prophylaxis in HIV. To be used as part of PACK 101 based screening.

History
(This section can be completed by administrative support staff)

PATIENT PERSONAL DETAILS (add patient sticker)	Name		Folder number	
	Surname		Clinic	
	Address		Date of Birth	
			Contact No	

TB HISTORY	Previous TB	Y	N	Year		Clinic	
	Previous treatment outcome	Cure		Complete	Default	Failure	Transfer
	Previous MDR-TB	Y	N	Outcome	Default	Failure	Cure

HISTORY OF CONTACT	Known contact with confirmed TB patient	Y		N				
	MDR/XDR contact	Y	N		Clinic			
	MDR/XDR contact resistance pattern							

EXPOSURE RISK	Health worker	Y	N	Mines / Quarry / Sandblasting...	Y	N
	Prisoner	Y	N	Other	Y	N

TB SYMPTOMS	Adults			Children < 8 years		
	Cough > 2 weeks	Y	N	Cough/wheeze > 2 weeks	Y	N
	Drenching night sweats	Y	N	Fatigue (child does not play)	Y	N
	Blood stained sputum	Y	N	Fever ≥ 2 weeks	Y	N
	Weight loss	Y	N	Weight loss	Y	N
	Fever ≥ 2 weeks	Y	N	Not gaining weight (failure to thrive)	Y	N
	Chest pain on breathing	Y	N			

Action
(This section to be completed by clinician - PN or MO)

HCT	HIV	Pos	Neg	Refused	CD4 result	
	ART	Y	N	ARV Start Date		

OBSERVATIONS	Weight		kg	Failure to thrive (check growth curve in RTH Card)	Y	N
	Temperature		C	Neck stiffness	Y	N
	Respiratory rate		/min	Visible masses neck/axilla/groin	Y	N
	BP		mmHg			
	Pulse		/min			

TB SKIN TEST	Mantoux	Date		Date read		Result		

SPUTUM	Specimen	Test	Date	Lab no	Result	DST	
						Rif (S/R)	INH (S/R)
	1						
	2						
	3						
	4						
	5						

ANTIBIOTIC	Name antibiotic	Y	N	Date	

NURSE-BASED DIAGNOSIS AND ACTION	Adult NO TB: Prophylaxis not required		Unconfirmed TB & still symptomatic: Refer to Medical Officer	
	Child < 5 years and/or HIV +ve NO TB: drug sensitive TB prophylaxis required		Confirmed TB (Notify & treat for TB	
			Confirmed DR-TB refer to Medical Officer	
			Child contact of confirmed adult DR-TB – refer to medical officer	

NAME SIGNATURE (PN/MO)		Date		Follow up	Date	
					Date	

Source: Provincial Department of Health, Western Cape Government (scan of hard copy)

Tool S2.C.3.4: TB symptom screening tool for adults and children, Buffalo City

EASTERN CAPE — TB SYMPTOM SCREENING TOOL FOR ADULTS AND CHILDREN

ECDOH

PATIENT DETAILS

Surname: ______ First Name:

Physical Address: ______ Age: ______

Telephone Number: ______ Patient folder Number: ______

MEDICAL HISTORY

Close contact of a person with infectious TB:	Yes	No	Unknown	(Tick √)
Type of index patient:	DS-TB	Rif Resistant TB	MDR-TB or XDR-TB	
Diabetic:	Yes	No	Unknown	
HIV Status:	Positive	Negative	Unknown	

Other: (Specify) ______

TB SYMPTOM SCREEN

1. ADULTS

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more OR of any duration if HIV positive		
Persistent fever of more than two weeks		
Unexplained weight loss >1.5kg in a month		
Drenching night sweats		

2. CHILDREN

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more which is not improving on treatment		
Persistent fever of more than two weeks		
Documented weight loss/ failure to thrive (check Road to Health Card)		
Fatigue (less playful/ always tired)		

If "Yes" to one or more of these questions, consider TB.
If the patient is coughing, collect sputum specimen and send it for Xpert testing.
If the patient is not coughing but has the other symptoms, clinically assess the patient or refer for further investigation.

Date of last TB test: ______

Patient referred for assessment and investigation: Yes / No

Date of referral: ______ Facility name:

Name: ______ Date: ___/___/___

Source: Provincial Department of Health, Eastern Cape Government (scan of redacted hard copy)

Supplementary Materials 2.D: Texts

Text S2.D.3.1: Development of the SP instruments

The SP's interaction with the healthcare provider was guided by a carefully developed script of a clinical scenario and documented using a comprehensive score sheet. The TB script (Tool S2.C.3.1) and score sheet (Tool S2.C.3.2) were based on publicly available instruments from an international SP manual [155], local TB-screening guidelines (Tool S2.C.3.1, Tool S2.C.3.2, the SANTMG [152], Primary Care 101 [156], Practical Approach to Care Kit (PACK) Adult [157]) and further developed in close collaboration with clinical experts, PHC providers, public health specialists and programme managers (Table S2.B.3.1) from the respective study districts.

The primary considerations when developing the SP instruments are discussed below:

Clinical scenario

The TB scenario depicted had to be clinically sound and convincing. Furthermore, the presenting symptoms had to be obvious enough to elicit TB screening at the PHC facility but not too severe to warrant intrusive management or referral to a district hospital. In this regard, all instrument collaborators agreed that a chronic cough – expressed as 'I have been coughing a lot recently' – would be a clinically sound and believable criterion to trigger awareness and subsequent management of a potential TB case. Also, the TB symptoms included in the SP script were purposefully selected to mimic the early stages of TB. A presentation of early TB symptoms should trigger routine TB screening which does not entail intrusive investigations. For example, the TB symptom of haemoptysis (coughing up blood) was excluded because this would signal an advanced stage of TB and may have resulted in the SP being referred and admitted to a district hospital.

SP characteristics

When developing the TB script, we deviated from the international SP manual [155] in that the

SP's personal characteristics were not constructed according to a particular personality type or appearance, i.e. SPs presented at facilities using their own identities. Our deviation was justified on two grounds: First, presenting with one's own identity eliminated the need for SPs to recall a predetermined character. This enhanced the standardisation and authenticity of SP interactions. Second, all individuals who responded to the SP recruitment advert matched the socioeconomic status (unemployed or underemployed at the time) and race (non-white) profile of a typical, South African public healthcare user. From this perspective, all recruits came across as believable public healthcare users in the South African context. The SPs brought with them an inherent understanding of local norms and behaviour related to South Africa's public healthcare system.

Guidelines and best practices

In addition to local TB-screening guidelines, best practices were also considered when developing the TB score sheet. PHC providers, public health specialists and programme managers argued that the study would benefit from measuring relevant best practices — such as access to surgical masks and communication about follow-up — because it would provide them with meaningful information that they could not access through routine monitoring and evaluation processes.

Minimising recall bias

The score sheet was designed so that the most essential clinical components of the interaction were placed first on the score sheet. This was done in order to minimise recall bias. SPs also presented with their own identities (described in more detail under *SP Characteristics* in this supplementary text), thereby further reducing recall bias.

Piloting of instruments

The first drafts of TB instruments were piloted at 5 PHC facilities in Cape Town in 2015 (n = 14 SP interactions). Four of the 5 pilot facilities were also contained in the main study. However, the SPs used to pilot the TB instruments were not the same SPs used when conducting the main study. There was, therefore, no possibility that the SPs used for the TB scenario in the main study may have been recognised by PHC facility staff because of the pilot study.

Pilot findings assisted with further refinement of the instruments. The revised instruments were reviewed by instrument collaborators before it was finalised. Due to further refinements of the instruments post-pilot, data from the pilot study were not included in the main study.

Text S2.D.3.2: SP recruitment and training

The piloting of SP instruments in 2015 provided an opportunity to refine SP screening and training methods for the main study. In order to conduct the pilot, the study team needed to recruit SPs. This exercise, based on materials from an international SP manual [155] and facilitated by a PHC professional nurse, took place over three days. Twelve fieldworkers were trained, but only eight were recruited for the pilot (three of whom piloted the TB instruments). As mentioned in Text S2.D.3.1, none of SPs used to pilot the TB instruments were reused for the TB scenario in the main study.

At the start of the pilot training, the study team explained the rationale of the SP project to SP candidates. This helped them to understand that an essential consideration for SP recruitment and training was their ability to present TB symptoms and recall the scripted answers to questions healthcare workers may ask during an interaction.

Lessons from the pilot training highlighted recall and credibility as key criteria to consider when evaluating SP candidates.

Credibility

The professional nurse who facilitated the pilot training provided valuable insights regarding the SP presentation and realistic depiction of the cases. The credibility of SP presentations was observed and reviewed during individual SP scenario role-playing. The role-play was a simulated patient-nurse interaction with the professional nurse (training facilitator) playing the role of the PHC nurse.

After each role-play, the SP candidate received feedback about the credibility of their presentation from the nurse, the study team and other SP candidates. This was an interactive process that allowed SP candidates to learn from their mistakes (and that of others) and the study team to observe who the most credible SP candidates were.

During the pilot, some SP candidates revealed a tendency to prompt the nurse (about what to ask next) during the role-play. Although it was made explicit in training that prompting the nurse defeats the purpose of the study, some candidates had a strong tendency to do so. SPs were trained to err on the side of caution and only supply information in response to questions asked by the healthcare worker, with explicit instructions not to voluntarily disclose any additional information.

In addition to prompting, some candidates had a tendency to overact. This characteristic was highlighted by the professional nurse who facilitated the training. For example, some SP candidates would act out grossly exaggerated coughing spells during role-play. Prompting and overacting – two characteristics that diminished the SP's credibility – were critical findings that emerged during the pilot training. These characteristics were used as disqualifiers for SP recruitment during both the pilot and main study.

Recall

The memorisation of the standardised script and accurate recall of the questions asked and examinations completed during an SP interaction were crucial characteristics of an ideal SP candidate. Recall was tested during role-play when the study team and fellow SP candidates would score the SP interaction using the applicable clinical score sheet. Once the SP candidate had completed role-playing, he/she would immediately complete the score sheet too (this is what would be expected from them in the field). Upon completion of the score sheet, the SP candidate would share his/her answers with the observers, who in turn would confirm whether the patient-nurse interaction was accurately captured or not. This intense process became an essential tool for evaluating SP recall. Candidates who demonstrated poor or inconsistent recall were not recruited as SPs during both the pilot and main study.

For the main study, 20 potential SPs were screened and trained in each province over five days. The SP training methods that were refined during the pilot were used once more during SP training and recruitment for the main study. The recall and credibility of SP candidates were reviewed by the study team through repetitive role-playing and scoring of the interactions. Candidates who performed well in both recall and credibility were recruited into the final pool of SPs.

SP screening and training were combined in order to allow for sufficient opportunities to adequately assess potential SPs. From each group of 20, only 12 SPs were recruited: 4 SPs for the TB scenario, while the remaining eight were used for other SP clinical scenarios (contraception and hypertension). This meant that ultimately 8 SPs were recruited for the TB scenario—4 from each province.

As previously mentioned, SP responses were standardised and designed to avoid invasive examinations. Routine TB screening does not entail intrusive management or referral, and in this regard, SPs were protected as long as they followed the script (see discussion in Text S2.D.3.1). In the unlikely event that an SP interaction led to intrusive management or referral, SPs were trained to fake a family emergency (receiving the news via their cell phones) and leave the facility immediately.

The SP training also contained a briefing session on safety. Furthermore, SPs were advised not to ask for directions while in a new community (so as not to identify themselves as new to the area).

Text S2.D.3.3: Field work procedure and management

Each SP in each province (4 SPs per province) was scheduled to visit each study facility (19 in Western Cape and 20 in Eastern Cape) only once. There were zero repeat or follow-up visits in the study design for the TB scenario.

The fieldwork manager drafted a roster to inform each SP which PHC facility they had to visit on each day of the week. The nature of accessing public healthcare in South Africa (arriving at the facility before opening time) meant that SPs could only visit one PHC facility per day. Furthermore, the roster was drawn up to ensure that only one SP would present with the TB case scenario at a study facility on any given day. This aspect of field work planning was included to minimise the likelihood of SP detection.

In addition, this study did not require informed consent from PHC facility staff, and therefore staff were not primed to expect a fake patient. The SP training and script development were also focused on SP scenarios and presentations being as credible as possible (see Text S2.D.3.1 and Text S2.D.3.2). Despite the above-mentioned reasons for a low likelihood of SP detection, SPs were still provided with an official letter in the event of SP detection. The letter explained that the SP was part of a study endorsed by the respective departments of health.

The roster enabled the fieldwork manager to conduct random audits of whether SPs visited their allocated study facility on the specified date. SPs were instructed to send their GPS locations to the fieldwork manager (via Whatsapp pings) once they arrived at and left their designated facility. SPs travelled to facilities using public transport as most public healthcare users would do so.

SPs were instructed to complete the TB score sheets in privacy immediately after leaving the facility to minimise recall lapses and biases. To monitor data capturing quality and reliability, the fieldwork manager conducted bi-weekly debriefing sessions with SPs where TB score sheets were audited. The debriefing sessions were also used to identify any gross ethical or clinical violations that may have occurred during SP interactions at facilities. Any incident of this nature would immediately be reported to the provincial health authorities. No such incidents were reported for any TB interactions.

Upon finalisation of the data collection process, all medical records generated through the study was removed or deleted. This ensured that SPs maintained a pure clinical profile of their own true health visits in the system. It also ensured that the provincial health authorities were protected from potential medico-legal cases that may be based on 'fake' clinical interactions. In this regard, the field work schedule and personal details of all SPs were provided to provincial authorities. In terms of data protection and confidentiality agreements, all data collected were aggregated and anonymised.

Appendix 2

Appendix 2.A: Acknowledgments

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Appendix 2.B: Author Contributions

Ronelle Burger, Ulf-G. Gerdtham, Carmen S. Christian and Anja Smith conceived and designed the study; Carmen S. Christian, Anja Smith, Dumisani Hompashe and Ronelle Burger managed the data collection; Carmen S. Christian analysed the data; Carmen S. Christian wrote the paper; Carmen S. Christian, Ulf-G. Gerdtham and Ronelle Burger reviewed and edited the manuscript.

Carmen S. Christian, Ulf-G. Gerdtham, Anja Smith, Dumisani Hompashe and Ronelle Burger proofread the manuscript.

Appendix 1.C: Conflicts of Interest

The authors declare no conflict of interest

Chapter 4

Paper Three: Facility-level determinants of TB-Detection Protocol Compliance at Primary Healthcare Facilities in Urban South Africa

This paper investigates primary healthcare (PHC) facility correlates of TB-detection protocol compliance in urban South Africa. It is hypothesised that constraints on nurse workload may be correlated with lower TB-detection protocol compliance. Data on protocol compliance were sourced from an unannounced Standardised Patient (SP) study (n=143). TB-detection protocol compliance was measured using essential TB-screening checks. Additional secondary data on facility characteristics were sourced from the District Health Information System, Census, and a PHC facility survey. The correlates of protocol compliance are estimated using an SP fixed effects model. The findings suggest a consistently negative, albeit relatively small, correlation between nurse workload and protocol compliance. This result is highly significant for taking temperatures (p<0.01), where a ten-patient increase in the daily nurse workload would decrease the likelihood of a TB tester's temperature being taken by 7.61%. These findings suggest that facilities with very high nurse workloads may be associated with suboptimal quality of TB care. It also provides quantitative evidence for future quality-improvement research.

4.1. Introduction

Tuberculosis (TB) remains one of the top ten causes of death – worldwide – and the leading cause of infectious diseases [168]. South Africa, a high TB-burden country, had an incidence of more than 500 new TB cases per 100 000 in 2017 [168]. There is an international consensus that increasing health access without a concomitant improvement in the quality of care will not result in the desired health outcomes [63,134,169,170]. Furthermore, evidence suggests that, in developing countries, the quality of care is low, mainly because of poor adherence to clinical protocols [141,171]. Yet few quantitative studies investigate factors associated with the quality of TB care, including the quality of TB detection [133]. In other words, there is a gap in the empirical literature when it comes to explaining the determinants of TB care quality, specifically, TB detection quality. This motivates an investigation of facility-associated correlates of TB-detection protocol compliance in South Africa.

Research focusing on the quality of TB care highlights weaknesses in compliance with TB protocols [26,127–131]. Clinical protocols, no matter how clinically valid, are only as useful as the extent to which they are implemented by healthcare providers. The extent to which healthcare providers implement clinical protocols may be explained by information asymmetries. Information asymmetries are pervasive within healthcare – between patient and healthcare provider, and healthcare provider and facility manager, examples relevant to this study – and this creates high levels of uncertainty [46]. These market failures may be overcome by government intervention in the form of well-designed and credible accountability frameworks and enforceable minimum standards, like clinical protocols [59–62]. However, if government fails in this regard, the patient-provider interaction cannot be mediated and thus the quality of service delivered may be poor [59–62,172,173].

In this case of a weak institutional relationship between the patient and the provider, revealed through poor quality of care, one important aspect to consider and understand is what some of the supply constraints are that result in this suboptimal outcome. Since primary healthcare (PHC) – and therefore TB detection – is nurse-driven in South Africa, nurses are considered the primary input for service delivery [174], and so it becomes important to ensure that the incentives of nurses are aligned with the well-being of patients [172]. Nurses, however, have their own constraints and preferences, making it imperative to first explore these constraints and preferences *before* designing appropriate incentives for nurses to fulfil their duties optimally [172]. This argument – to prioritise an investigation of PHC nurse constraints – provides the theoretical rationale for this study. Exploring nurse constraints in the context of suboptimal TB care at the PHC-level in South Africa underpins the study's hypothesis that constraints on nurse workload may be associated with lower TB-detection protocol compliance. This hypothesis is also informed by the empirical literature on nurse workload and quality of care in South Africa.

Findings from a 2018 qualitative study that assessed barriers to implementation of the National TB Programme in South Africa found that increased workloads had a negative effect on the quality of care rendered to TB patients [175]. Study participants asserted that the pressures of the work environment were exacerbated by other responsibilities, in addition to the core responsibility of managing TB patients. These findings were echoed in another South African study, which found that the daily integration of multiple PHC services, including new programmes being introduced, placed an increased workload on nurses at PHC facilities [176].

Because the literature on the relationship between nurse workload and quality of care in South Africa is parsimonious at a PHC level [175,176], some evidence in this regard is reviewed at a hospital level. A qualitative study that investigated nurse-reported[17] quality of care at hospitals in South Africa found that higher nurse workloads were significantly associated with poor quality of care at public tertiary hospitals [181]. These findings mirror the evidence found in similar hospital-level studies conducted internationally [178,182–187] although South Africa's findings

[17] International studies validate that nurse-reported quality care closely track independent data on patient outcomes ([177–180].

are significantly worse when compared to European and US[18] hospitals in a comparative study [178].

For this study, TB-detection protocol compliance is measured using key TB-screening indicators – conducting a TB test, offering an HIV test, taking a temperature, and explaining the importance of returning to the facility – drawing on data collected from a study that used the Standardised Patient (SP) approach. Patient acceptability and satisfaction indicators, clinical case vignettes, direct provider observation, clinical audits of patient files, and routinely captured health outputs are alternative tools used to measure the quality of care, and each is characterised by strengths and weaknesses [136,139–144,188]. However, the covert nature of the SP approach – sending a fake patient to interact with and observe a healthcare professional's clinical behaviour – offers a more granular and reliable understanding of quality [89,146–149,188–190]. The data on nurse workloads and other facility and feeder community characteristics were obtained from the District Health Information System, a PHC facility survey and Census.

The findings of this cross-sectional study suggest a a consistently negative, albeit relatively small, correlation between nurse workload and protocol compliance. This result is highly significant for taking temperatures ($p<0.01$), where a ten-patient increase in the daily nurse workload would decrease the likelihood of a TB tester's temperature being taken by 7.61%. These findings add to the limited literature available on protocol compliance amongst nurses: most available studies on compliance focus on doctors [191]. It also provides quantitative evidence for future quality-improvement research in this area.

[18] United States.

4.2. Data and Methods

4.2.1. Setting

This cross-sectional study uses data from various sources to estimate facility-level determinants of TB-detection protocol compliance at PHC facilities in urban South Africa. The study is therefore set at the PHC level in South Africa. It focuses on facilities in the Cape Town metropolitan district (Western Cape Province) and Buffalo City (Eastern Cape Province). All study facilities are run by the Provincial Department of Health in each province.

In both districts, PHC expenditure per capita (for the uninsured) was comparable for the 2015/2016 financial year—R1203 in Buffalo City and R1117 in Cape Town [151]. In 2015, the TB (all types) incidence rates for both the Cape Town metropolitan district and Buffalo City exceeded the national average of 520 cases per 100 000: a rate of 596 and 743, respectively. The 2015 TB/HIV co-infection rate for the study districts were similar: 44.6% for Cape Town and 45.7% for Buffalo City [151].

Facilities in both Cape Town and Buffalo City subscribe to TB-screening protocols that comply with the South African National TB Management Guidelines 2014 (SANTMG 2014) [152]. These guidelines form the basis of the SP scripts and score sheets used to collect the data on TB-screening quality (discussed in more detail in section 4.2.2.1).

4.2.2. Data Sources

Data on TB-screening quality were sourced from a study that used the SP approach and data on facility and feeder community[19] characteristics were obtained from the District Health Information System (DHIS), a PHC facility survey and Census.

[19] Primary healthcare facilities provide services to the population from feeder (surrounding) communities.

4.2.2.1. Data sourced from the SP study

The PhD candidate formed part of the research team that collected data using the SP approach and was therefore able to access and use the data for this study. With the SP approach, eight covert field workers (SPs) were sent to the PHC facilities[20] where they presented with a standardised opening statement – 'I have been coughing a lot recently'. This opening sentence is indicative of a chronic cough which should trigger TB screening in order to detect (identify and diagnose) a potential TB patient. SPs received rigorous training so that they could memorise a script with standard questions most likely to be asked at the TB screening. It was emphasized that SPs should only supply pre-determined answers in response to questions asked by the healthcare worker, i.e. they could not voluntarily disclose any information.

Healthcare workers at the PHC facilities were not aware that the SP was a fake patient. This type of concealment allows researchers – via the SP – to capture the healthcare worker's behaviour in a day-to-day setting. After the facility interaction, the SP would record relevant details about the facility visit on a score sheet.

Both TB-screening instruments, the script and the score sheet, were designed on the basis of publicly available documents from an international SP manual [136], the local TB-screening guidelines (the SANTMG [152], Primary Care 101 [156], Practical Approach to Care Kit (PACK) Adult [157], and best practices.

The data were collected over six months, mainly during the latter half of 2016. A total of 39 facilities were covered – 19 in Cape Town (with one facility excluded because of access issues) and 20 in Buffalo City – with each facility visited by four SPs. A sample size of 156 patient-

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[20] 4 SPs in each province visited each study facility in each province (19 facilities in Cape Town and 20 in Buffalo City) once, i.e. a single visit, no repeat visits or follow-ups.

facility interactions was therefore anticipated. After accounting for failed visits[21] and 'home' facilities[22], 143 patient-facility observations were available for analysis. All collected data were anonymised.

An in-depth description of the data sourced from the SP study has been published and may be referred to for more details [190].

4.2.2.2. Data sourced from the DHIS, Census and a PHC facility survey

Data for the 39 facilities were sourced from the South African DHIS. An application for the data was submitted to the Chief Director for Health Information Management, Monitoring and Evaluation in 2015.

A few DHIS indicators were missing for some Western Cape facilities. These missing data may be attributed to local differences in the data capturing systems: the Western Cape captures data via SINJANI (Standard Information Jointly Assembled by Networked Infrastructure) before it is exported to the DHIS, which may increase the likelihood of missing data.

Data capturing the socio-economic status (SES) of the feeder communities in which the facilities are located were sourced from South Africa's Census 2011. This data is publicly available from Statistics South Africa.

A researcher[23] working on a PHC management study returned to all 39 SP study facilities (early in 2017) and collected data related to the non-clinical characteristics of the facility. One of the items observed (in the facility manager's office) was whether the facility manager used a

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[21] Failed visits rate were defined as unsuccessful facility visits when the SP left the facility without consulting a healthcare worker.
[22] For ethical reasons, SPs were not permitted to visit their local or 'home' facilities.
[23] The researcher referred to here was not the PhD candidate but a research assisitant – Lisanne Koomen – working on a different study.

computer. This data point proxied technology and is used in the analysis with permission from the principal investigator[24] of the PHC management study.

4.2.3. Econometric Analysis

The relationship between nurse workload and TB-detection protocol compliance is estimated using an SP fixed effects (SPFE) model with feeder community SES and technology controls. Given the available data, this approach gets one as close as possible to dealing with sources of endogeneity which may bias naive estimates.

An SPFE approach eliminates SP-specific attributes – such as physical appearance and personality – which are assumed to be constant throughout data collection. In the short-to-medium term, the structural nature of public health diminishes the likelihood of bi-directional causality, where nurse workload may be directly affected by protocol compliance.

Observable factors that may be correlated with both protocol compliance and nurse workload are also controlled for. Some unobservable factors correlated with the variables of interest may remain, such as nurse motivation, knowledge and skills.

The model below (equation 4.1) illustrates the relationship between TB-detection protocol compliance (Q) and nurse workload (NW) for SP interaction i and facility f, with a residual ε. X is a vector of control variables and α denotes the unobserved systematic differences between the SPs.

$$Q_{if} = NW_f \beta + X_{if} \gamma + \alpha_i + \varepsilon_{if} \qquad (4.1)$$

TB-detection protocol compliance (Q) is described using dichotomous outcome variables to express the following: TB test conducted, HIV test offered, temperature taken, and healthcare

[24] Professor Ronelle Burger.

worker explained the importance of returning to the facility for follow-up.[25] These variables were deemed to be the most important proxies of TB-detection protocol compliance based on guidelines and best practice.

In addition, a TB-detection protocol compliance index was created by summing the four TB-screening indicators. The index was transformed so that it ranged from zero to 100, with a score of 100 indicating the highest possible level of protocol compliance. As a robustness check, a composite protocol compliance index using Multiple Correspondence Analysis (MCA) is also created. The MCA-derived protocol compliance index was highly correlated to the additive protocol compliance index (0.9827, $p<0.01$). Based on this correlation, the additive index was used in the analysis, as it lends itself to an intuitive interpretation of results.

NW is proxied using a continuous indicator for nurse workload sourced from the DHIS data. In the South African context, PHC is nurse-driven. Workload is therefore proxied by the DHIS indicator for PHC professional nurse clinical workload, defined as the average number of clients seen per professional nurse per clinical work day (see Table S3.B.4.8 in the supplementary materials section for more details about DHIS indicator).

X is a vector of the following control variables:

1) SES, proxied by SES (described below) of feeder communities;
2) Technology, proxied by facility manager using a computer.

The SES of the feeder communities of each facility was created using Principal Component Analysis (PCA) of SES variables,[26] which was sourced from Census data. The dichotomous covariate capturing a facility manager using a computer was sourced from the PHC facility survey data. The inclusion of this technology covariate is supported by evidence in a systematic

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[25] Regardless of whether a TB test was conducted or not.

[26] Geographical means for per capita income, the employment rate, access to piped water, access to potable water, access to refuse removal, access to a toilet, access to electricity, matriculation rate, and urban status.

review of studies that highlight the role of communication technology in health services quality [192].

Given the relatively small sample size (n=143), the model was kept as parsimonious as possible. Various specifications of an SPFE model are constructed. All models were estimated using robust standard errors.

4.2.4. Ethical Considerations and Approval

The research team that collected the SP data was granted ethical clearance from the Research Ethics Committee for Human Research (Humanities) at Stellenbosch University, South Africa (HS1096/2014-REC).

A data user's agreement between the South African National Department of Health and the research team was entered into before receiving limited indicators from the DHIS dataset. The South African government remains the owner of this DHIS data. Census data are publicly available and therefore no permission was required to use it. Data on technology at PHC facilities were obtained from the principal investigator of the PHC management study with permission to use it for secondary analysis.

4.3. Results

A comprehensive breakdown of the descriptive statistics for all variables can be found in the supplementary materials section (Table S3.B.4.9). Where applicable, descriptive results are reported in the following order: percentage, absolute value, and 95% confidence interval in brackets. Results from the multivariate analyses are reported in terms of the coefficient. Where results are statistically significant, this will be indicated before the closed bracket.

4.3.1. Descriptive statistics

4.3.1.1. TB-Detection Protocol Compliance

TB sputum tests were conducted at 84% of interactions (120; 95% CI 0.77-0.89), HIV tests were offered at 47% of interactions (67; 95% CI 0.39-0.55), and SP's temperatures were taken at 16% of interactions (22; 95% CI 0.10-0.27) [190] (Figure 4.1). Explaining the importance of returning to the PHC facility was conducted at 25% of interactions (35; 95% CI 0.18-0.32) (Figure 4.1).

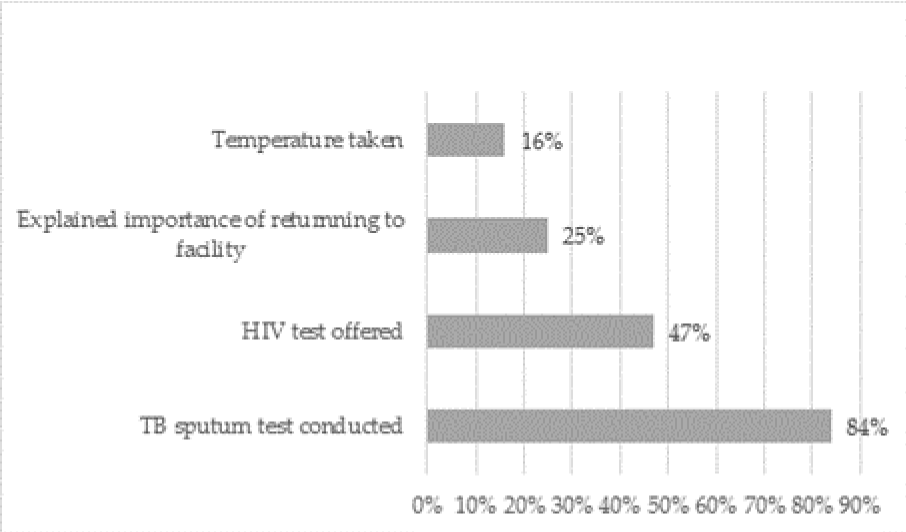

Figure 4.1: Proportions of TB-screening indicators

Source: Own calculations, SP data (2016/2017)

The TB-screening protocol compliance index has a mean value of 42.5. Figure S3.A.4.3 in the supplementary materials section shows that the distribution is skewed to the right.

When interpreting the covariate coefficients of the protocol compliance index in later analysis, it is useful to contextualise the index relative to its components (TB-screening indicators). A meaningful way of expressing the compliance index in relation to the TB-screening indicators is achieved by regressing each of the indicators on the protocol compliance index itself. There is evidence from the size of the coefficients (Table 4.1) that a ten-point increase in the compliance index (which ranges from zero to 100) is equivalent to a larger increase in the likelihood of offering an HIV test (15.1%) and of explaining the importance of returning (11%) relative to the likelihood of conducting a TB test (7.6%) and taking a temperature (6.3%).

Table 4.1: OLS regressions of protocol compliance on TB-screening indicators

VARIABLES	(1) TB test conducted	(2) HIV test offered	(3) Temperature taken	(4) Explained importance of returning
Protocol Compliance Index	0.00760***	0.0151***	0.00632***	0.0110***
	(0.00101)	(0.00102)	(0.00107)	(0.00104)
Constant	0.520***	-0.179***	-0.111**	-0.230***
	(0.0502)	(0.0508)	(0.0533)	(0.0519)
Observations	140	140	140	140
R-squared	0.291	0.614	0.201	0.444

Standard errors in parentheses, *** $p<0.01$, ** $p<0.05$, * $p<0.1$. Source: Own calculations, SP data (2016/2017) and DHIS data (2016)

Variation in the means of the variables of interest is noted across facilities (see one-way ANOVA output in Table S3.B.4.10).

4.3.1.2. Nurse workload and Protocol Compliance

Nurses saw an average of 25 clients per clinical day (std. dev. 10.35) at study facilities, with the workload distribution only slightly skewed to the right (median 23.5) as seen in Figure 4.2.

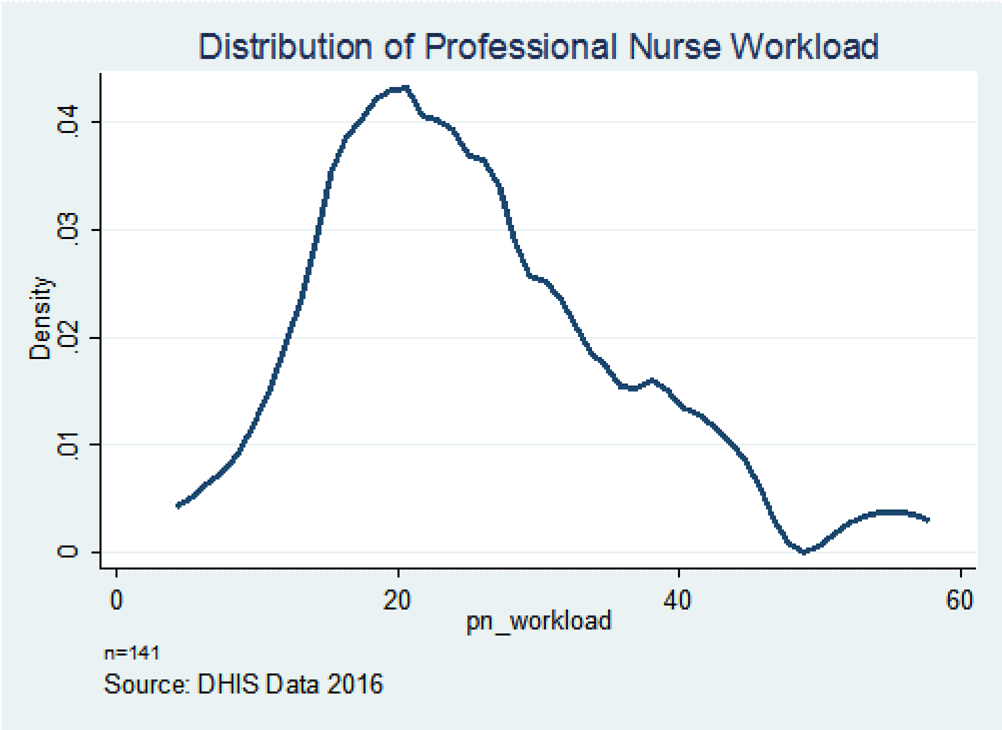

Figure 4.2: Distribution of professional nurse workload

Source: Source: DHIS (2016) data

A preliminary regression of nurse workload on TB-detection protocol compliance (composite protocol compliance index) are shown in Table 4.2.

Table 4.2: OLS regression of nurse workload on protocol compliance and TB-screening indicators

VARIABLES	(1) Protocol Compliance Index	(2) TB test conducted	(3) HIV test offered	(4) Temperature taken	(5) Explained importance of returning
Nurse workload	-0.898***	-0.00639**	-0.0138***	-0.00875***	-0.00799**
	(0.201)	(0.00299)	(0.00393)	(0.00293)	(0.00346)
Constant	65.13***	0.997***	0.821***	0.379***	0.442***
	(5.466)	(0.0808)	(0.106)	(0.0797)	(0.0936)
Observations	138	141	141	139	140
R-squared	0.128	0.032	0.082	0.061	0.037

Standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1. Source: Own calculations, SP data (2016/2017) and DHIS data (2016)

The nurse workload coefficient is economically moderate, negative, and statistically significant (-0.898, $p<0.01$). At this stage of the analysis, it appears that a higher nurse workload is correlated to a lower protocol compliance index.

The same negative and statistically significant correlation with nurse workload is observed for all individual components of the protocol compliance index, i.e. TB test conducted, HIV test offered, temperature taken, and importance of returning explained (Table 4.2). A comparison of the findings for TB-screening indicators shows that the negative association between nurse workload and TB screening was the weakest for conducting a TB test when compared to the rest of the TB-screening indicators. Most notably, the negative association between nurse workload and TB screening is more than twice as strong for offering an HIV test than doing a TB test.

4.3.1.3. SES of Feeder Community and Protocol Compliance

The SES index ranged from -3.14 to 2.48, with a larger index representing a higher level of SES. The SES coefficient is positive and statistically significant (Table 4.3, column 1: 7.799, $p<0.01$). At this stage of the analysis, it appears that a higher SES is positively correlated with protocol compliance. The positive relationship means that facilities located in feeder communities with higher levels of SES were more likely to score higher for protocol compliance.

Table 4.3: OLS regressions of SES on protocol compliance and TB-screening indicators

VARIABLES	(1) Protocol Compliance Index	(2) TB test conducted	(3) HIV test offered	(4) Temperature taken	(5) Explained importance of returning
SES index	7.799***	0.0324	0.154***	0.0488**	0.0648**
	(1.574)	(0.0237)	(0.0297)	(0.0236)	(0.0275)
Constant	44.01***	0.845***	0.498***	0.166***	0.258***
	(2.049)	(0.0311)	(0.0389)	(0.0307)	(0.0361)
Observations	140	143	143	141	142
R-squared	0.151	0.013	0.161	0.030	0.038

Standard errors in parentheses, *** $p<0.01$, ** $p<0.05$, * $p<0.1$. Source: Own calculations, SP data (2016/2017) and DHIS data (2016)

The same positive relationship between SES and protocol compliance is observed for all the individual components of the protocol compliance index (Table 4.3), although the relationship was not statistically significant for the likelihood of conducting a TB test.

4.3.1.4. Technology and Protocol Compliance

Facility managers used computers at approximately half (53%) of facilities. The positive relationship between protocol compliance and technology may imply that facilities where managers used computers were more likely to be compliant with TB-detection protocols (Table 4.4).

Table 4.4: OLS regressions of technology on protocol compliance

VARIABLES	Protocol Compliance Index
Facility manager uses computer	29.84***
	(3.729)
Constant	27.31***
	(2.685)
Observations	135
R-squared	0.325

Standard errors in parentheses, *** $p<0.01$, ** $p<0.05$, * $p<0.1$. Source: Own calculations, SP data (2016/2017) and DHIS data (2016)

The relationship between the use of computers by facility managers and protocol compliance is further explored by decomposing the analysis for each TB-screening indicator. The same large, positive and statistically significant correlation between computer use and compliance is observed for all individual components of the protocol compliance index (Table 4.5).

Table 4.5: OLS regressions of technology on TB-screening indicators

VARIABLES	(1) TB test conducted	(2) HIV test offered	(3) Temperature taken	(4) Explained importance of returning
Facility manager uses computer	0.145**	0.568***	0.167***	0.326***
	(0.0628)	(0.0706)	(0.0620)	(0.0690)
Constant	0.758***	0.182***	0.0758*	0.0769
	(0.0453)	(0.0510)	(0.0445)	(0.0500)
Observations	138	138	136	137
R-squared	0.038	0.323	0.051	0.142

Standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1. Source: Own calculations, SP data (2016/2017) and DHIS data (2016)

A comparison of the findings for TB-screening indicators shows that the positive association between facility manager use of technology and TB screening was the strongest for offering an HIV test when compared to the rest of the TB-screening indicators. This finding is almost twice as strong when compared to explaining the importance of returning, which in turn is approximately twofold the strength of the association for doing a TB test and taking a temperature.

4.3.2. Multivariate Analysis

Table 4.6 displays the results of the multivariate analysis estimating the relationship between the protocol compliance index and the independent variables.

Table 4.6: Multivariate analyses of protocol compliance index and covariates including SPFE

VARIABLES	(1) Protocol Compliance Index	(2) Protocol Compliance Index	(3) Protocol Compliance Index
Nurse workload [a]	-0.439	-0.388	-0.360
	(0.338)	(0.308)	(0.224)
SES of feeder community		2.781	1.768*
		(1.530)	(1.818)
Facility manager uses computer			18.24**
			(5.739)
Constant	53.59***	52.89***	42.95***
	(8.489)	(7.978)	(6.118)
Observations	138	138	135
R-squared	0.128	0.202	0.355

[a] average number of clients seen per professional nurse per professional nurse clinical work day, [b] proportion TB clients who were identified as HIV positive while on TB treatment; SPFE are included in all models, Robust standard errors in parentheses, *** p<0.01, ** p<0.05, * p<0.1

Column 1 shows the SPFE estimates for the relationships between protocol compliance and nurse workload. In column 2, the feeder community SES variable is added to the model. The final column (3) presents the coefficients of the fully specified model, which also controls for technology (use of computer by facility manager).

The results of the first SPFE model indicate that for every ten additional patients seen by a nurse per clinical day, the protocol compliance index would decrease by 4.39 points (-0.439, p=0.236). This negative relationship between nurse workload and protocol compliance remains constant when the feeder community SES control is added (column 2: -0.388, p=0.248), as well as in the fully specified model (column 3: -0.360, p=0.153), resulting in a compliance index decrease of 3.8 and 3.6 points respectively for every ten additional patients seen. The statistical insignificance of these nurse workload findings implies that we cannot rule out with any confidence that an increase in nurse workload would have no effect on the protocol compliance index.

To contextualise these results (see 4.3.1.1. TB-Detection Protocol Compliance for discussion on context), the finding in the final model suggests that for every ten additional patients seen by a nurse per clinical day, the likelihood of conducting a TB test, taking a temperature, offering an HIV test, and explaining the importance of returning to the facility would decrease by less than 6%.

Facilities in feeder communities with higher SES were slightly more likely to comply with protocols. On average, the protocol compliance score would increase by between 2.781 (p=0.112) and 1.768 (p<0.1) for every standard deviation increase in the SES index.

The results of the fully specified model indicate that at facilities where managers use a computer, the protocol compliance index would increase by 18.24 points (p<0.05). To contextualise this result (see 4.3.1.1. TB-Detection Protocol Compliance for discussion on context) the finding suggests that for facilities where managers use computers, the likelihood of conducting a TB test, taking a temperature, offering an HIV test, and explaining the importance of returning to the facility could increase by at least 11%.

Table 4.7 displays the fully-specified SPFE models that estimate the relationship for each TB-screening indicator and the independent variables.

Table 4.7: Multivariate analyses of TB-screening indicators and covariates including SPFE

VARIABLES	(1) TB test conducted	(2) HIV test offered	(3) Temperature taken	(4) Explained importance of returning
Nurse workload [a]	-0.00301	-0.00226	-0.00761***	-0.00195
	(0.00398)	(0.00476)	(0.00210)	(0.00301)
SES of feeder community	-0.0212	0.0703**	0.0183	-0.0164
	(0.0236)	(0.0251)	(0.0372)	(0.0349)
Facility manager uses computer	0.0551	0.445**	0.0657	0.184
	(0.0826)	(0.127)	(0.0719)	(0.130)
Constant	0.876***	0.321**	0.327***	0.197**
	(0.108)	(0.104)	(0.0647)	(0.0760)
Observations	138	138	136	137
R-squared	0.035	0.343	0.093	0.139

[a] average number of clients seen per professional nurse per professional nurse clinical work day, [b] Facility manager uses a computer, [c] proportion TB clients who were identified as HIV positive while on TB treatment; SPFE are included in all models, Robust standard errors in parentheses, *** $p<0.01$, ** $p<0.05$, * $p<0.1$

The findings suggest a consistently negative, albeit relatively small, relationship between nurse workload and the TB-screening outcome variables. This result is highly significant for taking temperatures ($p<0.01$), where a ten-patient increase in the daily nurse workload would decrease the likelihood of a TB tester's temperature being taken by 7.61%.

To test for a non-linear relationship between nurse workload and quality, a local polynomial is constructed for each TB-screening indicator (Figure S3.A.4.4). Overall, the local polynomials show that for large portions of the nurse workload distribution, the relationship between workload and quality are negative and mostly linear. This is most clearly seen for the TB-screening indicator for taking a patient's temperature.

In terms of technology, the findings indicate a consistently positive relationship between manager use of a computer and the outcome variables. The only statistically significant relationship was observed in the relationship between computer use and offering an HIV test, with it being a strongly positive relationship: at facilities where managers used computers, the likelihood of an HIV test being offered would increase by 45% ($p<0.01$).

4.4. Discussion

4.4.1. Limitations

The multivariate analysis is limited in its capability to address all potential sources of endogeneity. Even though multiple datasets (SP study, DHIS, PHC facility survey, Census) were used in order to obtain as many relevant variables as possible, the final dataset remains limited. A more comprehensive model would include correlates such as nurse motivation and characteristics of facility management. Future quality-improvement studies may find it helpful to collect data of this nature, as it is not collected in general household surveys.

Without controlling for knowledge, this study assumes that all professional nurses have the same level of TB-protocol knowledge. Although studies in other LMICs find that what health workers do differs from what they know (the so-called 'know do' gap) [89,141,146,193], we cannot assume that this is also the case in South Africa. Further exploratory research could use clinical case TB vignettes to measure nurse knowledge in the South African context. This type of research may provide evidence that excludes nurse knowledge as a constraint on TB-protocol adherence.

4.4.2. Interpretation

4.4.2.1. Nurse Workload and TB-Detection Protocol Compliance

From the perspective of the existing pool of literature on the relationship between nurse workload and quality of care, the findings add to the evidence that heavier nurse workloads are associated with a poorer quality of healthcare [169,175,176,194–196]. This outcome may occur in the short term as a consequence of having less face-to-face time with a patient [197], or through the cumulative medium- to long-term effects of decreased motivation, burnout, and labour-related issues such absenteeism or high staff turnover [175,198–201].

In working environments characterised by high nurse workloads, the marginal benefits of clinical protocols should be weighed against their marginal costs. Clinical guidelines that are too cumbersome, complicated and time-consuming are criticised by their implementers [200,202] for the additional workload they add in contexts that cannot accommodate it. Since social and organisational factors – major contributors to nurses' adoption of clinical protocols – present barriers to protocol compliance [191], some consideration needs to be given to designing protocols that are appropriate for the context.

If programme managers accept that protocol compliance is low in work environments at risk of high workloads, then pre-emptive and proactive interventions may ensure that patients receive at least a basic level of care. Such interventions may require the adoption of streamlined versions of protocols that allow nurses to see as many patients as possible while still providing an acceptable level of clinical care. A compromise of this nature will at least ensure that nurses are not left to make their own, random, decisions regarding which elements of protocols they adhere to when under pressure of time. However, this type of intervention should be regarded as selective. It should not apply to every nurse at every facility, but rather only be instituted at facilities where nurse workload exceeds an evidence-based cut-off. More research is necessary to determine the cut-off points for nurse workloads in order to ensure that the suggested recommendation is not abused and used in appropriate contexts.

In a developing country context, the burden of disease rests mainly on nurses who engage in task-shifting and task-sharing in order to cover service delivery gaps created by a shortage in other health personnel [203,204]. While this is a matter of pragmatism, policymakers should be mindful that trade-offs in protocol compliance may accompany the inevitable increase in nurse workload. This trade-off in protocol compliance may manifest as nurses prioritising certain aspects of protocols above others. In this study, for example, evidence points to increased nurse workload having the largest negative effect on the probability of taking the temperature of a presumptive TB patient.

For reasons not explored in this study, nurses may regard temperature-taking as less critical or more time-consuming than other TB-screening tasks. In the South African context, where there is increasing antibiotic resistance and antibiotics are dispensed to presumptive TB patients without first taking the patient's temperature [190], the relationship between nurse workload and taking temperature is an important finding of this paper and urgently warrants further research.

Recommendations such as selective protocol streamlining and task-shifting are not fail-proof and may result in unintended consequences on the demand-side. Permitting nurses to see more patients but for shorter periods may compromise the patients' experience of care. If patients perceive that they are not taken seriously at a facility visit, this may feed into future curtailment of health-seeking behaviour.

4.4.2.2. Emerging Considerations: Use of Technology

The findings indicate a consistently positive relationship between manager use of a computer and the outcome variables, which is statistically significant for offering an HIV test: nurses were 45% ($p<0.05$ in Table 4.7) more likely to offer presumptive TB patients an HIV test at facilities where managers used computers.

Beyond the functional importance of technology in the delivery of health services, the use of computers by facility managers could also be a proxy for various unmeasured characteristics of the facility that are positively correlated with quality of care. These unmeasured characteristics may include characteristics of the facility manager. This interpretation is suggestive of a more indirect transmission mechanism between technology and quality of care. It may be the case that good facility management, proxied by computer use, allows the facility to escape the trap of high workloads that lead to low quality. In this scenario, computer use only serves as a signal of management, not the tool itself.

Based on these findings, further exploration of the relationship between facility management and quality of care is therefore recommended.

4.4.3. Generalizability

The external validity of the results is limited to PHC facilities in urban settings in a developing country context.

4.5. Conclusion

The findings of this study provide quantitative evidence for future quality-improvement research in TB care, specifically on the role of nurse workload and facility management in determining the quality of TB detection.

Failure to address suboptimal TB-detection protocol compliance will ensure that poor TB outcomes persist and that South Africa will struggle to meet its National Strategic Plan's 90-90-90 targets.

Supplementary Materials 3

Supplementary Materials 3.A: Figures

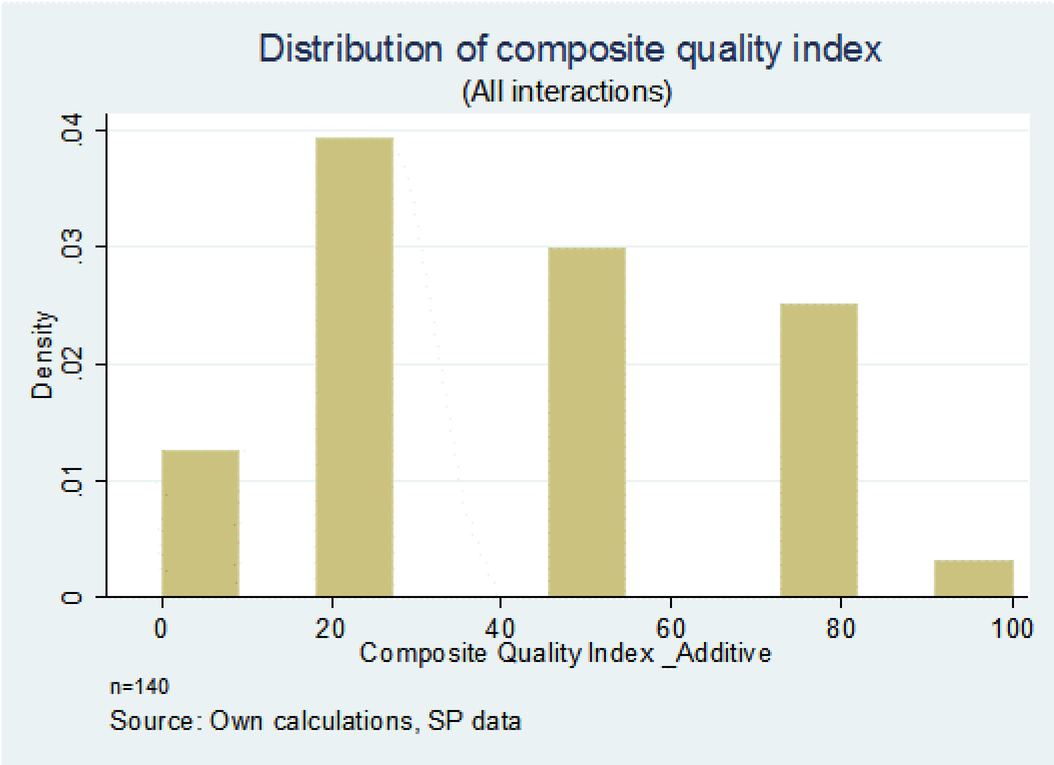

Figure S3.A.4.3: Distribution of TB-screening composite index

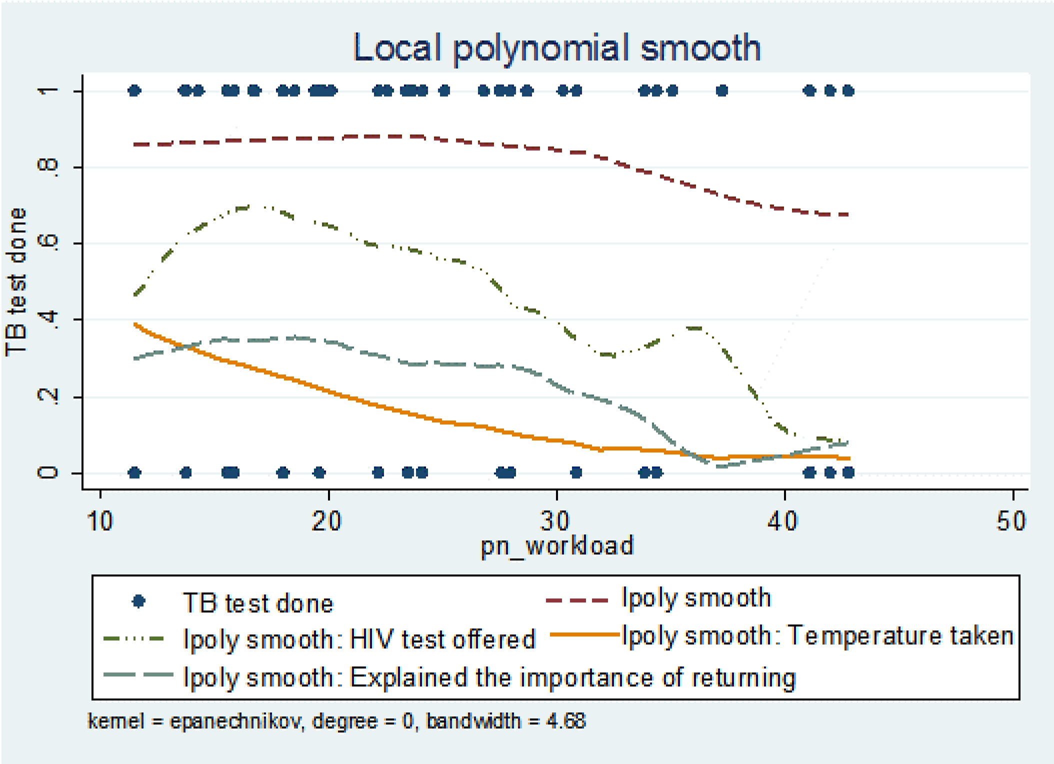

Figure S3.A.4.4: Smoothed polynomial showing the relationships between nurse workload and TB-screening indicators

To test for a non-linear relationship between nurse workload and quality, a local polynomial is constructed for each TB-screening indicator (TB test done, HIV test offered, temperature taken and explained the importance of returning) in Figure S3.A.4.4. The following outliers were excluded: 2 PHC facilities with a nurse workload of less than 10 patients per day, and 2 PHC facilities where the nurse workload was more than 43 patients per day.

There appears to be no discernible relationship between nurse workload and conducting a TB test (short dash, maroon line) until a nurse has seen approximately 25 patients per day. After the 25th patient, the association between nurse workload and conducting a TB test becomes negative until the end of the distribution.

For HIV tests offered (dash and three dots, green line), the association with nurse workload is positive until workload reaches about 16 patients per day, after which the probability of offering an HIV test decreases until about the 32nd patient. After the 32nd patient, the positive relationship reappears until the 35th patient, after which the negative relationship returns until the end of the distribution.

For temperature taken (solid, orange line), the association with nurse workload appears to be negative throughout the distribution. As nurse workload increases, the probability of taking a temperature decreases, albeit at a decreasing rate towards the end of the distribution.

For explaining the importance of returning (long dash, teal line), it appears that a negative relationship with nurse workload takes effect from the 18th patient until a workload of 38 patients per day. After the 38th patient, the probability of explaining the importance of returning becomes positive until the end of the distribution.

Supplementary Materials 3.B: Tables

Table S3.B.4.8: Description of DHIS indicator used for facility-level variable

Indicator name	Numerator	Denominator	Definition	Use and context	Month, Year
PHC[a] professional nurse clinical workload	PHC clients seen by professional nurse	PHC professional nurse clinical work days	Average number of clients seen per professional nurse per professional nurse clinical work day.	Monitors staff allocation/management and provide indirect indication of quality of care. Low work load may be due to inefficient staff utilisation, and very high workload indicates too little time spent per client. Do not include delivery service time in numerator or denominator.	Jan-May 2016 (5-month average)

[a] Primary healthcare. Source: DHIS Metadata

Table S3.B.4.9: Summary statistics of variables

Variable	Observations	Mean	Std. Dev.	Min	Max
TB test conducted at interaction	143	0.84	0.37	0	1
HIV test offered at interaction	143	0.47	0.50	0	1
Temperature taken at interaction	141	0.16	0.36	0	1
Explained importance of returning to the facility at interaction	142	0.25	0.43	0	1
TB-screening protocol compliance index at interaction	140	42.50	25.92	0	100
Nurse workload at facility	141	25.02	10.38	6.90	55.10
Feeder community socio-economic status	143	-0.19	1.30	-3.14	2.48
Facility manager uses a computer	139	0.53	0.50	0	1
Facility has a telephone	139	0.97	0.17	0	1

Table S3.B.4.10: One-way ANOVA of variables of interest by facility

Variable	Between facilities		
	Lowest mean	Highest mean	Prob > F
TB test conducted (*n*=39)	0.50	1	0.53
HIV test offered (*n*=39)	0	1	0.00
Temperature taken (*n*=39)	0	0 .75	0.00
Explained importance of returning to facility (*n*=39)	0	1	0.00
TB-screening protocol compliance index (*n*=39)	12.50	93.75	0.00
Nurse workload at facility (*n*=38)	6.90	55.10	0.00

Appendix 3

Appendix 3.A: Acknowledgments

This work is based on the research supported in part by the National Research Foundation of South Africa (Grant Numbers: RCA13102556861, CPRR150722129596, SFP150803134521 and SDG160531166953). We received generous institutional support, policy inputs and advice from numerous individuals at the Eastern Cape and Western Cape Departments of Health, specifically the respective Health Impact Assessment and Research Units, the TB-control Programmes and District Management teams. The guidance and support of Lyn Horn—medical practitioner, bio-ethicist and chair of REC (Research and Ethics Committee): Humanities at Stellenbosch University—helped us to navigate the ethical challenges intrinsic to this study. We thank Karel Haal for his dedicated efforts as field work manager.

Chapter 5

Conclusion

This final chapter of this thesis begins by summarising each paper's main findings and contributions to the current pool of descriptive economic studies on early TB detection. The findings are then repositioned and interpreted through the six lenses of the conceptual framework described in Chapter 1 (1.4. The Contribution of Policy-Relevant Descriptive Studies). The intent of this is to translate the newly-generated knowledge into policy implications and recommendations. In so doing, this exercise highlights – based on the thesis's findings – gaps and weaknesses in the South African health system and how they relate to the National TB Programme. The chapter ends with a discussion of the limitations of the thesis, remaining research gaps, and suggested proposals for future research.

5.1. Summary of Paper Findings

The spread of TB and its consequences can be mitigated more quickly and effectively through early TB detection. This group of thesis papers focused on TB case detection, in particular, detection arising from the patient-initiated pathway. Individual social, demographic and economic circumstances are of great importance in determining whether a TB-symptomatic person seeks healthcare or not, as are other generally unobservable factors such as anticipated TB stigma [58]. The nature of these factors, which may pose barriers to accessing healthcare (Figure 1.2) were investigated in Paper One (Chapter 2).

Paper One (Chapter 2) responds to the global call to address stigma in the fight against TB and is the first study (as far as we know) to include a quantitative measure of TB stigma when modelling health-seeking behaviour. Access to a uniquely comprehensive data set made it possible to address this gap in the patient-focused analysis of health-seeking decisions. Although

Paper One (Chapter 2) found no evidence that stigma played a part in health-seeking behaviour, the research is relevant because it highlights the need to triangulate methods and to debate how stigma measures interact with other factors.

Paper One (Chapter 2) also showed that most persons coughing for more than two weeks did not consult someone about their chronic coughs. It is at this point that the role of *information* in health-seeking becomes evident [35,46,47]. Without access to information on the benefits of early TB detection, a person who recognises their symptoms may still underinvest in healthcare. In the developing country context of high TB burden countries, where *imperfect information* is exacerbated by weak penetration of public health communication and low education levels, it is conceivable that some TB carriers may still fail to access healthcare [35].

Findings from Paper One (Chapter 2) show that in high TB burden communities in the Western Cape, respondents of black ethnic origin, those with higher levels of education and older respondents were more likely to consult. The complementarity between *education and information,* especially in the South African context [48] is revealed with these findings. Because education enhances information acquisition and processing [49], less educated individuals may find it challenging to internalise the health information at their disposal, and therefore individuals with lower levels of education may be less likely to consult [50,51]. Findings from Paper One (Chapter 2) show that smokers and those with higher SES were less likely to consult. These findings are important because the literature analysing the health-seeking behaviour of this vulnerable group is sparse.

Supply factors were also involved in the patient-initiated pathway of TB detection, from accessing healthcare to the final stage of notification and treatment. In Paper Two (Chapter 3) the use of the SP method to measure the quality of TB screening – the first time this has been done in South Africa – has revealed evidence of gaps in clinical practice, signalling missed opportunities for TB detection. The study also revealed a few positive findings too. The early and reliable detection of suboptimal quality of TB care is instrumental in decreasing TB-related morbidity and mortality, and the SP method is particularly useful for this. The paper's findings – summarised below – add to the literature analysing the weaknesses and strengths in South Africa's health system and provide useful feedback to national and provincial governments for further improvement in the quality of TB management (this is further explored in sections 5.2.1 to 5.2.6).

Paper Two (Chapter 3) revealed a failed visit rate of 6% (Table S2.B.3.6). The failure of the public health system to screen TB-symptomatic persons at their first facility visit represents a loss of presumptive TB patients from the patient-initiated pathway of TB detection at an early point. In addition to not receiving the care sought, patients who seek healthcare but are not able to obtain it may become discouraged and reluctant to return. This evidence illustrates how supply-side barriers to early TB detection also feed into demand-side barriers.

The high rate (more than 90%) of referral for TB testing as a result of the SP's opening statement 'I have been coughing a lot recently' is a positive finding. This evidence reinforces a hypothesis that persistent coughing and the opening statement of the SP are most influential in whether symptoms are considered to indicate TB and the appropriate referral within the facility is made. Also, TB tests were conducted at 84% of SP visits. Such findings highlight that in some regards, the health system performs better than anticipated.

A concerning finding from Paper Two (Chapter 3) is that in only 43% of the SP cases did the public healthcare system meet the minimum threshold for adequate case management. This outcome was mainly caused by HIV tests being offered less often than expected (47% of cases). It raises a red flag given the high TB/HIV co-infection rate in South Africa (57% in 2015 [151]) and the resources that have been invested in training, awareness, and fighting stigma. It is also worrying because the level of sensitivity of TB test results using Xpert®, the recommended TB diagnostic tool in South Africa, is influenced by HIV status[27] [159].

The SANTMG recommends that a high index of suspicion is required for patients who have been in contact with a person with confirmed TB. Despite this, SPs were asked about household TB contacts in only 54% of cases. This finding represents yet another missed opportunity for TB detection.

A disturbing finding also emerged that in 8% of SP interactions where no temperatures were taken, antibiotics were prescribed. Neither the local antibiotic algorithm nor the TB-screening guideline would recommend the administration of antibiotics in such circumstances. Practices such as this could lead to an increase in drug-resistant bacteria in South Africa. Further research is needed to understand why this practice occurs.

Paper Two (Chapter 3) highlighted practices that exacerbate *information asymmetry* in healthcare. Poor follow-up and communication practices – evidence of *weak information flows* from the provider to the patient – were found to pose critical constraints on timely detection of TB for patients who sought help for a cough at a PHC facility. Even when cases were managed correctly, minimal effort was made to explain the importance of returning for TB test results: this was explained at fewer than a third of SP interactions (28%). This finding is indicative of a diagnostic gap, with some presumptive TB patients leaving facilities without being tested for TB, and others leaving the facility without knowing that they needed to return for results and why.

Even though gaps and missed opportunities for early TB detection are identified in Paper 2 (Chapter 3) (i.e. there is room for improvement), some findings are positive. These positive

[27] Xpert® is less sensitive to detecting TB in HIV-positive patients than in HIV-negative patients. For this reason, sputum samples from HIV-positive patients undergo additional TB diagnostic tests. In the case where a sputum sample is not accompanied by an HIV status, the current laboratory practice is that the patient is assumed to be HIV-negative. This assumption may result in a false-negative TB test.

findings imply that there is a stronger than expected responsiveness to TB detection in South Africa than the current literature would suggest, although it is clear that weaknesses remain.

Other supply constraints on early TB detection at PHCs in South Africa are considered in Paper Three (Chapter 4). Ultimately, the successful implementation of a clinical protocol depends – in part – on the acceptance of it by those who are to implement it; in the South African TB context, this would be nurses (see section 5.2. below for a further discussion of this policy-relevant concern). The extent to which nurses implement clinical protocols may be explained by *information assymetries*. Information asymmetries are pervasive within healthcare – between patient and healthcare provider, and healthcare provider and facility manager, examples relevant to Paper Three (Chapter 4) – and this creates high levels of uncertainty [46]. It therefore becomes important to ensure that the incentives of nurses are aligned with the well-being of patients [172]. Nurses, however, have their own constraints and preferences, making it imperative to first explore these constraints and preferences *before* designing appropriate incentives for nurses to fulfil their duties optimally [172]. Paper Three's (Chapter 4) hypothesis is that constraints in nurse workload at PHC facilities may be associated with lower TB-detection protocol compliance.

Paper Three (Chapter 4) revealed a consistently negative, but relatively weak, relationship between nurse workload and TB-detection protocol compliance. This result was highly significant for taking temperatures ($p<0.01$): an increase in the daily nurse workload of 10 patients led to a 7.61% decrease in the likelihood of the patient's temperature being taken. These findings add to the existing literature on the relationship between nurse workload and quality of care and suggest that heavier nurse workloads are one of the things that are associated with poorer quality of TB care. The paper offers some insight into one of the many reasons for deficiencies in protocol compliance, adding further to the literature analysing South Africa's health system. The relationship between these findings and gaps in the South African health system is further explored in sections 5.2.1 to 5.2.6.

Paper Three (Chapter 4) also shows that there was a consistently positive relationship between manager use of a computer and the outcome variables. In particular, there was a strongly positive relationship between technology and offering HIV tests: at facilities where managers used computers, the likelihood of an HIV test being offered increased by 45% ($p<0.01$). The use of computers by facility managers is most likely a proxy for various unmeasured characteristics of the facility that are positively correlated with quality of care. These unmeasured characteristics may include characteristics of the facility manager. This suggests a more indirect transmission mechanism between technology and quality of care. As such, computer use may serves as a proxy of management, not the tool itself. Paper Three (Chapter 4) provides quantitative evidence for future quality-improvement research, specifically on the effect of nurse workload and management quality on the quality of TB detection.

The findings noted in this subsection, and the strengths and weaknesses they reveal, make a useful contribution to the small but growing health economics literature on TB and its management.

5.2. Implications for Policy

5.2.1. Macro-context

The success of any national TB programme and its activities are embedded in and therefore highly dependent on a well-functioning healthcare system that ensures affordable, universal access to quality healthcare services. The South African health system, however, is overburdened and poorly managed, with a resultant suboptimal quality of TB care at a PHC level. Research focusing on the quality of TB care has highlighted weaknesses in TB-protocol compliance as a contributor to poor TB outcomes. At the same time, it must be appreciated that clinical protocols, no matter how clinically valid, are only useful to the extent to which they are implemented. Based on the findings in Papers Two and Three (Chapter 3 and Chapter 4), in some regards, there is a divide between the prescribed TB protocols and their implementation at a PHC level in the South African context.

Public health policymakers in South Africa should not ignore the fact that service delivery at a PHC level is nurse-driven, and it is, therefore, the nurse who makes the final decision about how to implement any prescribed protocol. In PHC environments characterised by high nurse workloads, it is plausible that the individual nurse will make an implicit decision based on weighing the marginal benefits of clinical protocols against the marginal costs. If clinical protocols are too cumbersome, too complicated and too time-consuming, nurses may prioritise certain aspects of protocols over others. Based on the findings in Paper Two (Chapter 3), it is encouraging to see that referral for a TB test is top of mind when a patient reports that they have been coughing a lot (more than 90%), and TB tests were conducted at 84% of SP visits. In these cases, the majority of nurses made the correct call despite the constraints of the given day.

However, some thesis findings show that weaknesses remain in the system. Policymakers should therefore be conscious of context-specific trade-offs that may result in unintended, suboptimal outcomes when devising protocols. Consideration should be given to whether current protocols are feasible in resource-constrained high-pressure contexts. In Paper Three (Chapter 4), for example, the evidence points to an increased nurse workload having the greatest negative effect on the probability of taking the temperature of a presumptive TB patient. Nurses may have reasons, not explored in this thesis, for regarding temperature-taking as less critical than other TB-screening tasks. In the broader context of increasing antibiotic resistance in South Africa and the discovery that antibiotics are being dispensed to persons with presumed TB without a temperature being taken, the findings of Paper Two (Chapter 3) are of great concern and warrant further investigation by the National Department of Health.

Since social and organisational factors are contributors to nurses' adoption of clinical protocols, are slow-changing by nature, and currently present barriers to protocol compliance [191], policymakers may consider the shorter-term option of designing protocols that are appropriate for the current context. Acknowledging and accepting these factors may require policymakers to endorse streamlined versions of cumbersome protocols at overburdened facilities so that nurses can see as many as patients as possible and still provide an acceptable level of clinical care. If programme managers accept that protocol compliance is low in specific work environments where workloads are likely to be high, then pre-emptive and proactive interventions of this nature may safeguard that patients receive at least a basic level of care. This type of compromise will ensure that nurses are not left to make their own, random, decisions as to which elements of protocols they will adhere to when pressed for time. However, it must be stressed that the suggested intervention should be selective – i.e. only be instituted at facilities where nurse workload exceeds an evidence-based cut-off.

Overall, the South African TB guidelines and best practices need to be reviewed to ensure that their most essential elements are prioritised, allowing for more practical implementation in high-burden settings. This approach could be considered 'Back to Basics'. Ensuring that basic and important steps in the TB-screening protocol are adhered to may reduce the missed opportunities to detect TB – a problem highlighted in Paper Two (Chapter 3) – and prevent the loss of presumptive TB patients by the healthcare system.

Given the TB crisis in South Africa, curative policies which are implemented at the PHC level (such as TB protocols) outweigh preventative policies which should be implemented within communities. However, there is still scope for the health system to focus more strongly on preventative strategies such as health promotion. The demand-side findings from Paper One (Chapter 2) showed that the health-seeking behaviour of presumptive TB patients remains a barrier to early TB detection. Besides TB knowledge, other factors omitted from the study that may explain health-seeking behaviour include soft proxies of poor healthcare supply such as long waiting times, insufficient medication and rude staff. If this were the case, it is plausible that supply-side constraints may determine low demand for services. Future studies should investigate the impact of 'softer' supply-side constraints on health-seeking behaviour (and thus demand).

Paper One (Chapter 2) also described the typical characteristics of presumptive TB patients who do not seek care. This information could assist National TB Programmes in designing more targeted TB screening and active case-finding interventions within communities. In the high TB-burden communities of South Africa, such interventions may benefit from focusing on youth, those with lower levels of education, smokers, and higher SES subgroups.

Although some progress has been made in the fight against TB, HIV and AIDS – both of which are closely associated with TB[28] – continue to overshadow TB in terms of political support, advocacy and funding [206]. In the past, the TB crisis in South Africa – and high TB-burden countries globally – had to compete for resources with the HIV crisis. More recently, the TB crisis has been overshadowed by HIV's successes, notably the widespread roll-out of antiretroviral treatment [207]. While these successes in the management of HIV are laudable, concomitant attention to the TB crisis is important.

Because of the link between function and funding, there will inevitably be functional imbalances when the allocation of funds to two deeply intertwined infectious diseases is skewed. Even though international and local health authorities acknowledge that the management of TB and HIV cannot be separated and advocate policies geared towards the *integration* of its services, this acknowledgement does not always translate into optimally distributed funding – and consequently health services – between the two diseases. For example, Paper Two (Chapter 3)

[28] HIV-positive persons are at least 16 times more likely to develop TB than HIV-negative persons. TB is the most common infectious illness among HIV-positive persons, even those on antiretroviral treatment. TB also remains the major cause of HIV-related deaths. [205]

found that the public healthcare system met the minimum threshold for adequate case management in fewer than 50% of SP cases, mainly because HIV tests were offered less often than expected (47% of cases only). This is a clear illustration of the *suboptimal integration* of TB and HIV programmes at a PHC level, and this imbalance in function must be noted in relation to the imbalanced funding context in which it is embedded.

To date, the largest donor funder for TB, the Global Fund to Fight AIDS, Tuberculosis, and Malaria, has committed only 16% of its funding to TB, compared to the 48% that is allocated to HIV/AIDS (the largest single share). This disparity in funding extends to TB research too. Total TB research and development expenditures for 2017 ($767.8 million) [208] remain over $1 billion short of the $2 billion per annum that is needed to be spent on ending the TB epidemic by 2030 [209].

5.2.2. Intra- and Inter-relationship with Public and Non-public Agents

In the context of early TB detection, the primary agent that policymakers need to consider on the demand side is the presumptive TB patient. This assertion would be in keeping with the redefined notion of a high-quality health system which puts patients at the centre of policies [169]. Understanding the socio-economic and demographic context of the presumptive TB patient and his or her reasons for delayed health-seeking – as described for the Western Cape context in Paper One (Chapter 2) – may strengthen the quality of engagement between patients and healthcare providers. Should patients and healthcare providers strengthen the quality of their relationship, it follows that information asymmetries characteristic of health and healthcare (and exacerbated by the poor communication practices revealed in Paper Two (Chapter 3)) will be ameliorated.

The reality in South Africa is that the health system is overburdened and healthcare providers are not easily accessed by patients. There are several reasons for this – see 1.1. TB in the South African Context, Paper Two (Chapter 3) and Paper Three (Chapter 4) – but the latent gap between demand and supply agents may be bridged by community health workers (CHWs). CHWs are embedded in the community and best placed to support the health system through active health promotion strategies relevant to TB. However, a successful CHW programme is highly dependent on these health workers being recognised as an integral part of the community health system [210] and incorporated into any interventions aimed at strengthening it.

On the supply side of public healthcare, the health system operates mainly through agents employed across the three levels of government: national, provincial and municipal. TB protocols are often drawn up by national or provincial programme managers but are expected to be implemented by agents such as nurses at the municipal level of government. The hierarchical structure of the relationship between agents at the various levels may help to explain the disconnect, in some contexts, between the prescribed TB protocols and their implementation at a PHC level (Paper Two (Chapter 3) and Paper Three (Chapter 4). Both TB policy formulation and implementation could be improved by the facilitation of timely, bidirectional information flows between all relevant agents and across all three spheres of government regarding the context and quality of TB care

The interdisciplinary nature of this thesis topic has necessitated multidisciplinary and multi-sector engagement from the initial conceptualisation of the knowledge generation process to the final submission of individual papers or the present thesis. Despite the consensus that policy and programme solutions benefit from an interdisciplinary approach, the institutionalisation of siloed, single-disciplinary approaches to problem-solving persists and exacerbates the challenges experienced when doing interdisciplinary research. Within this context, the interaction between agents from various disciplines and sectors presented both challenges and benefits. Specialised training and varied backgrounds at times led to difficulties in communicating ideas, because of discipline-specific terminology. However, considering different (and sometimes opposing) ideas ensured that the research process was rigorous and constructed so that its outputs were more likely to be useful to policymakers.

Contextual factors linked to relationships with agents, both public and non-public, also became relevant during the secondary data collection phase of Paper One (Chapter 2) and Paper Three (Chapter 4), and the study design and primary data collection phase of Paper Two (Chapter 3). The researcher-policymaker relationship was relevant when collecting primary data for this thesis because the process required the research team[29] to work with policymakers from the provincial departments of health. For the researcher, a lack of information about bureaucratic processes and power dynamics at the provincial departments of health occasionally led to strained researcher-policymaker interactions and subsequent delays in the research process. However, commitment to the research and trust between the public agents and the research team were established after the investment of substantial time and resources by both sides. Based on the experience gained during this thesis, it is recommended that researchers develop and build meaningful working relationships with relevant policymakers before starting collaborative projects. Adequate investments in such social capital will help to build greater trust between researchers and policymakers and may improve synergetic collaboration in future projects.

As agreed in advance, a confidential report of the SP research findings was shared with health authorities before academic submissions and publishing, in order that critical issues could be dealt with appropriately. This agreement was deemed to be reasonable and ethical as there is generally a substantial delay between the submission and publication of an academic article. Critical findings from the SP research, specifically those that related to early TB detection, could not be held back from the health authorities, given the current TB crisis in South Africa.

[29] The research team collected primary data across three clinical domains – TB, hypertension and family planning – using the SP approach.

Accessing secondary data from public and non-public agents proved to be challenging and time-consuming. Numerous emails, phone calls (and sometimes Skype sessions) were required before data transfer was possible. The strength of relationships established with public and non-public custodians of the data requested played a role in determining how quickly data was released. On average, it took approximately one year to access the secondary data required for this thesis. However, through the process of procuring secondary data, inter- and intra- relationships between agents – the researchers and the custodians of the data – were strengthened, and private systems were developed to simplify future procurement of secondary data.

5.2.3. Culture

Another useful sub-dimension with which to examine the research findings is the role of cultural incentives in determining individual behaviour. Policymakers need to be aware of demand-side incentives that could interfere with early TB detection. For example, evidence from Paper One (Chapter 2) showed that, of persons coughing for more than two weeks, those who had a higher SES were less likely to seek care for their coughs. At first appearance, this finding may seem counterintuitive in the context of South Africa's high unemployment rate. However, it could be argued that individuals who are employed may consider the opportunity cost of seeking healthcare too high. Similarly, even though Paper One (Chapter 2) found no quantitative evidence that stigma was a factor in health-seeking behaviour, TB programme managers need to be aware of the potential impact of anticipated stigma on health-seeking behaviour and investigate other research methods in order to understand better how stigma interacts with relevant factors in the health system.

Incentives that are of critical importance at a PHC level, where most TB policies are implemented, include promoting an institutional culture of learning from mistakes and performance management. In the high-pressure, constrained environment of a local PHC, a culture of learning may be difficult to develop without facility-level information on the quality of care. PHC facility managers may not have the time to audit the numerous TB-related paper-based documents and registers in order to track performance. Also, time constraints and confidentiality may make it impossible to observe closed interactions between staff and patients directly.

As previously mentioned, the prevailing institutional culture of the South African public health system is strongly hierarchical. Furthermore, the system is dominated by command- and control-type decision-making where management is regarded as an administrative function rather than a process that enables learning. In such a culture, the introduction of new policies that challenge the status quo is likely to be resisted. It should, therefore, be expected that research findings that recommend policy changes – such as those of this thesis – are likely to be slow to gain acceptance and will require intense and recurring engagement with strategic agents in the South African health system.

Of relevance here is the question of how the SP method will be viewed by a highly unionised nursing workforce, characterised by solidarity, and a strong medical fraternity characterised by agency. When research findings from this SP study were fed back to agents working in the TB programme, the research method was generally regarded with hostility and suspicion. This response is rational when the incentives of these agents are considered. Policymakers, however, need to understand that the pervasive culture in South Africa's public health sector may pose a challenge to the scalability of interventions using the SP method. It is therefore recommended that agents be accustomed gradually to the idea of using the SP method as a potential monitoring and evaluation tool.

Based on multiple interactions with public agents, it became evident that a lack of transparency prevails within government departments. This was best illustrated through the challenging process of accessing secondary healthcare data from public custodians of data (discussed in section 5.2.2. Intra- and Inter-relationship with Public and Non-public Agents). Recognising this lack of transparency and its adverse effects – delayed analysis of the available data, fewer evidence-based policies and poorer data quality – may motivate senior public agents to invest in strategies that reward a culture of transparency.

5.2.4. Organisational Capacity

The organisational capacity of human resources has been identified as a relevant lens through which to interpret the nurse-related findings in Paper Two (Chapter 3) and Paper 3 (Chapter 4). The National TB Programme in South Africa, which is nurse-driven, is characterised by task-orientated nursing practice. Task-orientated nursing can be defined as an organisational practice that is geared towards the completion of discrete tasks [211]. An unintended consequence of this organisational practice is that focus is placed on the task at hand rather than on the patient, who often experiences medical care as depersonalised [212]. In recognition of the negative implications of task-orientated organisational approaches, and with the broader goal of improving the quality of care, the National Department of Health introduced the 'Ideal Clinic' programme in 2013 to integrate health services in a patient-centred approach [213]. However, changes in organisational capacity are hard to achieve and maintain [214], and therefore, in practice, the task-oriented approach persists in South Africa [211].

Findings from Paper Two (Chapter 3) reinforce a hypothesis that persistent coughing is most recognised as a TB symptom by nurses and elicits the appropriate referral within the facility. This finding is a quintessential example of how a task-oriented approach can elicit an efficient and effective clinical response. However, other evidence from Paper Two (Chapter 3) and Paper 3 (Chapter 4) points to deviations from TB-detection protocols, in particular, when nurse workload is increased. Despite the pervasive task-oriented organisational capacity amongst nurses, this does not necessarily translate into high clinical quality services based on strict adherence to prescribed tasks. If this were the case, a depersonalised service might have been more acceptable as an unintended consequence of a task-oriented approach. Instead, it would appear that this 'friendliness' trade-off is not necessarily accompanied by a higher quality of care. The inevitable result is that the end-user – a presumptive TB patient in this case – may leave a PHC facility with both suboptimal clinical care *and* a 'cold' experience. This type of service delivery is neither effective nor patient-centred and can therefore not be considered a good quality of care. Such deficits in the soft features of service delivery (a supply constraint) may feed into a low demand for seeking care when ill.

While this thesis focused on the clinical tasks associated with TB detection protocols (Chapter 3 and Chapter 4) – and this is an essential component of quality care – the patient's experience at PHC facilities are equally important since these contribute to the health-seeking behaviour and ultimately the health demand of presumptive TB patients. It is therefore recommended that future research on demand constraints on TB detection include a more in-depth exploration of patients' perceptions of their experiences at PHC facilities.

5.2.5. Management and Processes

The term 'management and processes' covers contextual matters related to planning, communication, decision-making, problem-solving, and monitoring and evaluation. These concepts are closely related to the many possible reasons for deviations from protocols, including deficiencies in monitoring and evaluation and, more broadly, a lack of clinical governance. The findings of this thesis help inform policies in this regard.

Paper Two (Chapter 3) shows the SP method's high degree of specificity in picking up problems with protocol implementation at a PHC level. This specificity makes the method potentially very useful as a monitoring and evaluation tool. The financial cost of the SP method, relative to other monitoring and evaluation tools (discussed further in 5.3. Limitations, Remaining Gaps and Future Research), may preclude it being used regularly. However, the SP method may still be suitable and warranted for intermittent use (for example, every two to three years) or at specific PHC facilities that have been flagged as having problems with service delivery.

The importance of effective communication between agents within the health system cannot be overemphasized, given the high degree of information asymmetry in the health and healthcare systems. Results from Paper Two (Chapter 3) highlight poor follow-up and poor communication as critical constraints on efficient TB detection for patients who sought help for a cough at a PHC facility. The mismanagement of information by the healthcare provider translates into an information deficit for the patient, which inevitably leads to suboptimal patient decision-making and health-seeking behaviour (related to Paper One (Chapter 2)). The findings on poor information flows provide useful feedback to the National TB Programme.

5.2.6. Resources

Technology and knowledge infrastructure are inter-related resource sub-dimensions that are critical for the production and flow of policy-relevant knowledge [91]. Although the SP method is regarded as the gold standard for assessing the quality of care, the relatively high cost of the method and the time required to generate knowledge through it means that it is not necessarily scalable. A recently published paper aims to develop and validate a more cost-effective alternative to the SP method using smart-phone based virtual patients[30] [215]. This method may overcome the financial difficulties of scaling up the SP method. However, it is acknowledged that smart-phone based virtual patients would still be subject to the Hawthorne effect and selection bias, with the extent of these effects yet to be determined.

5.3. Limitations, Remaining Gaps and Future Research

While the contributions of this thesis's findings to the economics of TB literature are meaningful, especially from a policy perspective, they do come with some critical limitations that have to be acknowledged. Recognizing these will also help to identify the remaining research

[30] Smartphone virtual patients (VPs) are an extension of computerised vignettes which are interactive and can realistically represent the complexity of a clinical encounter. Smartphone VPs, as a further improvement on computerised vignettes, create visualised and interactive simulations that replicate clinical complexity. Healthcare workers will use their smartphones to assess the VPs, and are therefore aware that they are being monitored. The awareness that they are being monitored may alter their behaviour in terms of how they respond to the vignette questions (Hawthorne effect).

gaps in the field of TB detection, providing in turn justification for further research that may extend the findings from this thesis.

Although Paper One (Chapter 2) found no quantitative evidence of a role for stigma in health-seeking behaviour, this does not mean that stigma is not an important constraint on health-seeking behaviour. Given the strong qualitative evidence of a role for stigma in health-seeking, one explanation for the lack of quantitative evidence may be the difficulty obtaining and measuring truthful information about prejudice and bias against TB sufferers. Stigma, like all socially-sensitive variables, is hard to measure accurately using self-reported measures because respondents will try to give a socially-desirable answer. There is therefore still a gap in the research on the quantitative estimation of stigma's role in health-seeking. Future research in this area should be aimed at developing improved tools and novel methods, such as, for example, an implicit attitude test, for measuring stigma.

Another limitation of Paper One (Chapter 2) is that no data were available to analyse how patients' knowledge of TB influenced their health-seeking behaviour. Furthermore, of the demand constraints on early TB detection not covered in this thesis, the patient's experience of care at PHC facilities emerges as a potential factor in the patient's likelihood of delaying health-seeking or avoiding return visits. Future research on the quality of TB care would benefit from an exploration of patient experiences at TB clinics and patients' levels of knowledge about TB in order to understand better how these two factors feed into health-seeking behaviour and ultimately into the demand for TB care.

As there are currently few valid measurement tools and little information on healthcare quality, the findings from Papers Two and Three (Chapter 3 and Chapter 4) are extremely meaningful in the South African health context. This study is the first time in South Africa that the SP method has been used to measure the quality of TB detection. Nevertheless, despite its usefulness and the information it generates, the SP method may be too expensive to use at scale, or regularly in LMICs like South Africa. Future research could explore the use of smart-phone based unannounced virtual patients, a method soon to be piloted in China.

As antibiotic resistance increases both locally and globally, the unindicated antibiotic prescriptions at the PHC level discovered during the study (see Paper Two (Chapter 3)) are of concern. However, the SP instrument used in this study did not go into specific detail regarding antibiotic information. When the SP instrument for this study was designed, trade-offs were made in terms of content in order to prioritise the most important questions but avoid an overly cumbersome instrument. Future SP research focusing on deviations from TB antibiotic algorithms is therefore recommended to understand some of these troubling prescription practices better.

There are many possible reasons for deviations from protocols that emerge from Paper Two (Chapter 3). These include inadequate training, lack of knowledge, low motivation, deficiencies in monitoring and evaluation and, more broadly, a lack of clinical governance. Unfortunately, due to the limited data sample and variables in Paper Three (Chapter 4), the plausibility of rival explanations for poor protocol compliance could not be tested. One of the most pertinent of these rival explanations is the level of knowledge of TB protocols that nurses have. There is still a research gap on this question. Further exploratory research could use clinical case TB vignettes to measure nurse knowledge in the South African context. Findings from such research may provide evidence that excludes nurse knowledge as a constraint on TB protocol adherence.

The limitations described above provide meaningful insights into the research gaps in early TB detection and offer a clear indication of where future research is needed in this area.

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