Economic support to improve TB treatment outcomes in South Africa: a pragmatic cluster randomized controlled trial

By

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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.

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Abstract

This thesis focused on the provision of economic support to improve the outcomes of patients on TB treatment. Although the association between poverty and tuberculosis is generally acknowledged, there is little evidence to guide the use of economic interventions to improve tuberculosis control. In South Africa, a high burden country with extensive poverty, such evidence is particularly important.

The first part of this thesis is a Cochrane systematic review of evidence from randomized controlled trials regarding the effectiveness of economic support among patients with tuberculosis. Eleven trials were included: ten conducted among marginalised groups in the United States on economic support for people on prophylactic treatment for latent TB; and one from Timor-Leste on economic support for patients with active TB. The review found that the use of economic interventions in patients with latent TB may increase the return rate for reading tuberculin skin test results, probably improves clinic re-attendance for initiation or continuation of prophylaxis and may improve completion of prophylaxis, compared to normal care. However, it is uncertain if economic support improves treatment completion in patients with active TB (low quality evidence).

The second part of the thesis reports the findings of a pragmatic, cluster randomized controlled trial to evaluate the feasibility and effectiveness of delivering economic support to patients on treatment for active TB in South Africa. Patients with drug sensitive pulmonary TB were offered a monthly voucher valued at ZAR120 until completion of treatment or a maximum of eight months. Patients in control clinics received usual TB care. A parallel process evaluation provided contextual information to explain the trial findings. The qualitative component of this evaluation consisted of in-depth interviews with a sample of trial participants, including patients, nurses and health managers, to assess responses to the voucher and its administration. The quantitative component included a survey of patients' household expenditure to assess patients' levels of poverty and the effects of the voucher on these, and an analysis of the goods on which patients spent their vouchers.

4091 patients were included in the trial: 1984 in the control arm (10 clinics) and 2107 in the intervention arm (10 clinics). Intention to treat analysis showed a small but non-significant improvement in treatment success rates in intervention clinics (intervention 76.2%; control 70.7%; risk difference 5.6% (-1.2; 12.3%), p = 0.107). Fidelity to the intervention was low, partly because nurses preferred to issue vouchers based on perceived financial need, rather than on eligibility. Logistical difficulties in delivering vouchers to clinics also undermined fidelity. The vouchers did not significantly increase patients' household expenditure, but were experienced by patients as helpful, especially in providing more food with which to take their tablets.

Factors related to the administration of economic support may undermine its effectiveness in improving TB treatment outcomes. Further research is needed to explore how best to deliver such economic support to those eligible to receive it, particularly in low and middle income countries where the burden of tuberculosis is highest.

Opsomming

Hierdie tesis was toegespits op die verlening van ekonomiese steun om die uitkomste van pasiënte op tuberkulose- (TB-) behandeling te verbeter. Hoewel die verband tussen armoede en TB in die algemeen erken word, is daar nie veel bewyse om die gebruik van ekonomiese intervensies ter verbetering van TB-beheer te staaf nie. In Suid-Afrika – ’n land met ’n hoë TB-las en wydverspreide armoede – is sulke bewyse veral belangrik.

Die eerste deel van hierdie tesis behels ’n sistematiese Cochrane-oorweging van bewysmateriaal afkomstig van verewekansigde, gekontroleerde proewe oor die doeltreffendheid van ekonomiese steun aan pasiënte met tuberkulose.

Altesame 11 proewe is ingesluit: Tien is gedoen onder gemarginaliseerde groepe in die Verenigde State met die fokus op ekonomiese ondersteuning aan mense wat profilaktiese behandeling vir latente TB ontvang het. Een, van Timor-Leste, was gefokus op ekonomiese ondersteuning aan pasiënte met aktiewe tuberkulose. Die ondersoek het aan die lig gebring dat, vergeleke met normale sorg, die gebruik van ekonomiese intervensies by pasiënte met latente tuberkulose tog die omdraaikoers vir die lees van tuberkulien-veltoetsresultate kan verhoog, waarskynlik hertoelating tot klinieke vir die inisiëring of voortsetting van profilakse verbeter, en die voltooiing van profilakse kan verbeter.

Die tweede gedeelte van die tesis behels ’n verslag oor die bevindings van ’n pragmatiese, trosverewekansigde gekontroleerde proef, om te bepaal hoe doenlik en doeltreffend dit sou wees om ekonomiese steun te verleen aan pasiënte wat in Suid-Afrika vir aktiewe tuberkulose behandel word. Pasiënte met middelsensitiewe pulmonêre tuberkulose het tot en met die voltooiing van hul behandeling, of tot ’n maksimum van agt maande, ’n maandelikse koopbewys ter waarde van ZAR120 ontvang. Pasiënte in kontroleklinieke het die gewone TB-sorg ontvang. ’n Parallelle prosesevaluering het kontekstuele inligting voorsien ter verklaring van die bevindinge van die proef. Die kwalitatiewe komponent van hierdie evaluering het bestaan uit diepte-onderhoude met ’n steekproef van alle deelnemers aan die proefneming, insluitend pasiënte, verpleegpersoneel en gesondheidsbestuurders, om hul reaksies te bepaal op die koopbewys self sowel as op die administrasie daarvan. Die kwantitatiewe komponent het ’n opname oor pasiënte se huishoudelike besteding ingesluit, ter vasstelling van hul armoedevlak en die moontlike uitwerking van die koopbewys daarop, asook ’n ontleding van die goedere waarop pasiënte hul koopbewyse bestee het.

Altesame 4 091 pasiënte is by die proef ingesluit – 1 984 in die kontrole-afdeling (10 klinieke) en 2 107 in die intervensie-afdeling (10 klinieke). ’n Voorneme-om-te-behandel- (ITT-) ontleding toon ’n klein dog nie-betekenisvolle verbetering in behandelingsuksessyfers in intervensieklinieke (intervensie 76,2%; kontrole 70,7%; risikoverskil 5,6% (-1,2; 12,3%), p = 0.107). Getrouheid aan die intervensie was laag – deels omdat verpleegkundiges verkies het om die koopbewyse op grond van veronderstelde finansiële behoeftigheid eerder as volgens die studiekriteria uit te deel. Die koopbewyse het nie pasiënte se

huishoudelike besteding beduidend verhoog nie, maar pasiënte het dit wél as nuttig ervaar, veral omdat hulle daarmee meer kos kon koop om saam met hul pille in te neem.

Faktore wat verband hou met die administrasie van ekonomiese ondersteuning kan die doeltreffendheid van sodanige steun in die verbetering van TB-behandelingsuitkomste ondermyn. Verdere navorsing word vereis om te verken wat die beste manier sou wees om sodanige ekonomiese steun te bied aan diegene wat daarvoor in aanmerking kom, veral in lae- en middel-inkomstelande, waar die TB-las die hoogste is.

This work is dedicated to my darlings

Isabella, Christina and Georgina,

Who make my heart sing

It is also for Damian,

Who has been a brick from the beginning

And in memory of my parents,

Who gave me wings.

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AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Treatment
CCT	Conditional cash transfer
CDC	Centres for Disease Control and Prevention
DOTS	Directly Observed Treatment, Short Course
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HIV	Human Immunodeficiency Virus
INH	Isoniazid (drug used as preventive therapy for patients with latent TB)
RCT	Randomised controlled trial
TB	Tuberculosis
WHO	World Health Organisation

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Definition of terms

Absolute poverty: The lack of the minimum level of material goods (food, shelter etc) that are necessary to sustain life in the purely biological sense (Alcock 2006: 64)

Active tuberculosis: "a disease that is caused by Mycobacterium tuberculosis or other members of the Mycobacterium tuberculosis complex family in any part of the body and that is in an active state as determined by either:

1) A smear or culture taken from any source in the person's body tests positive for tuberculosis and the person has not completed the appropriate prescribed course of medication for active tuberculosis disease.

2) Radiographic, current clinical, or laboratory evidence is sufficient to support a medical diagnosis of tuberculosis for which treatment is indicated." (CDC 2011)

Adherence: The extent to which patients follow the instructions they are given for taking their prescribed medications (Haynes et al 2008)

Catastrophic health expenditure: "… when a household must reduce its basic expenditure over a period of time to cope with health costs" with reductions of between 5% and 20% being used as illustration in various studies (Xu et al 2003)

Chronic poverty: "when an individual experiences significant capability deprivations for a period of five years or more" (Hulme and Shepherd 2003)

Conditional cash transfers: “regular, predictable amounts of money given to households and individuals by governmental or non-governmental agencies” (Forde et al 2011).

Deprivation: “the effects of poverty on one’s life”, similar in meaning to the term “multi-dimensional poverty” which acknowledges the multi-faceted nature of poverty as being more than lack of material goods (Friedman and Bhengu 2008: 201)

DOTS supporters (Directly Observed Treatment Supporters): community-based lay health workers who assist the TB Control Programme in various ways; most importantly in the context of this trial, DOTS supporters observed treatment taking and verified patients’ adherence (Dick et al 2005)

DOTS Strategy: The Directly Observed Treatment, Short Course Strategy is the strategy recommended by the World Health Organisation internationally for TB control. It consists of five components: Sustained political and financial commitment; Diagnosis by quality ensured sputum-smear microscopy; Standardized short-course anti-TB treatment (SCC) given under direct and supportive observation (DOT); A regular, uninterrupted supply of high quality anti-TB drugs; and Standardized recording and reporting. (WHO 2006)

Economic incentive (see also material incentive): An incentive that makes a positive economic impact on the patient’s life, and that can be quantified in monetary terms; for example, cash, vouchers or food. Economic incentives can be direct, such as the former examples, or indirect, such as the provision of a service for free, for which the patient would otherwise have had to pay.

Economic shock: A “sudden and substantial decline in the level of economic activity” (Weeks and Drengacz 1982)

Enabler: Financial or material assistance to help patients overcome barriers to accessing and completing treatment (Lutge et al 2012)

Food security: “access to food, adequate in quantity and quality, to fulfill all nutritional requirements for all household members throughout the year” (Jonsson and Toole 1991).

Household: “a person or group of persons who usually live and eat together, sharing the same housing unit, facilities and food” (Nzimande 2010: 13).

Incentive: “any financial or material reward that patients and/or providers receive, conditional on their explicitly measured performance or behaviour” (Beith et al 2007).

Latent tuberculosis: “the presence of Mycobacterium tuberculosis bacteria in the body as evidenced by a significant reaction to a Mantoux tuberculin skin test or positive interferon gamma release assay. A person with latent TB infection does not have an illness nor is he or she infectious” (CDC 2011)

Material incentive (see also economic incentive): a physical incentive that has monetary value and can be quantified in economic terms.

Poverty alleviation: Bringing people closer to the poverty line (Booysen 2004)

Poverty eradication: Lifting people out of poverty (Booysen 2004)

Poverty gap: "… the difference between each poor household's income and the poverty line. Thus, it measures the depth of poverty of each poor household. The aggregate poverty gap is calculated by summing the poverty gaps of each poor household. Therefore, it is equivalent to the total amount by which the incomes of poor households need to be raised each year to bring all households up to the poverty line and, hence, out of poverty" (SARPN 2004)

Poverty headcount ratio: The "proportion of the poor in the total population" (Subramanian 2005)

Poverty line: a level of income or expenditure below which people are considered poor (Bhorat et al 2011).

Poverty rate: The percentage of people who lived in poverty in one calendar year (US Census Bureau 2012).

Pragmatic trial: "A trial that aims to test a treatment policy in a 'real life' situation, when many people may not receive all of the treatment, and may use other treatments as well. This is as opposed to an explanatory trial, which is done under ideal conditions and is trying to determine whether a therapy has the ability to make a difference at all (i.e. testing its efficacy)" (MRC 2012)

Relative poverty: When "individuals, families and groups….lack the resources to obtain the types of diet, participate in the activities and have the living conditions and amenities which are customary…in the societies to which they belong" (Alcock 2006: 64).

Results-based financing: “the transfer of money or material goods conditional on taking a measurable action or achieving a predetermined performance target”. Also known as “pay-for-performance, performance-based funding, and output-based aid.” (Oxman and Fretheim 2009)

Social protection: “the public actions taken in response to levels of vulnerability, risk and deprivation which are deemed socially unacceptable within a given polity or society” (Norton et al 2001)

Unemployment, strict (official, narrow) definition: “those people within the economically active population who: did not work during the seven days prior to the interview; want to work and are available to start work within two weeks of the interview; and have taken active steps to look for work or to start some form of self-employment in the four weeks prior to the interview”. (Lehohla 2004)

Unemployment, expanded definition: “those people within the economically active population who: did not work during the seven days prior to the interview; want to work and are available to start work within two weeks of the interview” but have given up on looking for work. (Lehohla 2004).

Chapter 1:
Background to and rationale for this thesis

Introduction

In this chapter, the background to and rationale for this thesis are described and discussed. Firstly, the evidence for the relationship between poverty and TB, which forms the foundation for this thesis, is presented. This evidence describes the possible "causal pathways" for the effect of poverty on the development of TB disease and on the outcomes of patients on TB treatment. In light of the strong association between TB and HIV, and the high co-infection rate in South Africa, I also discuss the effects of poverty on HIV epidemiology and clinical outcomes, and how this might relate to TB. The models for our intervention are described, and the use of similar interventions in South Africa (in the form of social grants) is discussed. Finally, the structure of the thesis and the contents of the succeeding chapters are outlined.

Background

It is generally accepted that poverty and ill health are closely related. Much of the literature converges on a consensus opinion that income poverty, with its multiple dimensions, is detrimental to health (Biggs *et al* 2008, Harris 2004, Benzeval and Judge 2001, Fulton 1980). Indeed, the World Health Organisation's Commission on the Socio-Economic Determinants of

Health found that there is sufficient evidence supporting this relationship to justify action (WHO 2008: Note from the Chair).

Tuberculosis (TB) is one of the diseases whose relationship with poverty seems to be particularly strong (Hargreaves *et al* 2011, Lonnroth *et al* 2010, Lancet 2005). There is a large body of work, dating back over a century, that emphasizes the close relationship between poverty and TB (Farmer 2001). Indeed, Robert Koch himself described the disease as "the outcome of social misery" (quoted in Farmer 2001: 202). Rene and Jean Dubois, in their seminal book "the White Plague: Tuberculosis, Man and Society" called tuberculosis "a social disease", which emphasizes the importance of social context in the development and course of TB (Dubos and Dubos: xv).

The way in which poverty impacts on TB has been outlined in various "causal pathways". Food insecurity, with consequent under-nutrition, is one of the fundamental features of poverty (ASSAF 2007), and poor nutrition is a powerful determinant of TB disease (Cegielski *et al* 2012, ASSAF 2007, Van Lettow *et al* 2004, Tverdal 1986, Edwards *et al* 1971). Under-nutrition undermines the functioning of the immune system, even leading to secondary immunodeficiency, which in turn increases the risk of developing disease from new and latent TB infections (Gupta *et al* 2009). Protein appears to play an important role (Bates *et al* 2004), with low consumption of dietary protein (Strachan *et al* 1995) and low albumin levels (Cegielski *et al* 2012) both increasing the risk of TB. Similarly, under-nutrition increases the risk of death in patients on treatment for TB (Zachariah *et al* 2002). Although a recent systematic review of trials found insufficient evidence to judge the effectiveness of nutritional supplements in

improving the outcomes of patients on treatment for tuberculosis (Sinclair *et al* 2011), other studies suggest that various micronutrients are important in the pathophysiology of TB. Low plasma ferritin is an independent risk factor for treatment failure in patients with pulmonary TB (Isanaka *et al* 2012), and low levels of vitamin A are associated with increasing severity of the disease (Pakasi *et al* 2009). Vitamin D, an important immunonodulator, may also play a role in the development and prognosis of TB disease (Battersby *et al* 2012). Other micronutrients which may influence the risk and course of TB are zinc, vitamins C and E, selenium and copper (Gupta *et al* 2009). Other conditions of poverty, such as overcrowding and poor ventilation, are also important in the spread of the infection (Baker *et al* 2008, Bates *et al* 2004) but fall outside the scope of this thesis.

The prevalence of TB is higher in poorer countries (Ploubidis *et al* 2012) and among poorer communities in wealthy countries (Bates *et al* 2004). Indeed, in South Africa, a country of profound income inequality (Coovadia *et al* 2009), TB has been called a "barometer of poverty" (Andersson 1990).

Tuberculosis and poverty in South Africa

Tuberculosis has a long history in South Africa and like many other diseases in this country, its distribution is highly racialised (Coovadia *et al* 2009). Little is known of the prevalence of the disease or its effect on mortality prior to the eighteenth century, and the experience of African populations of tuberculosis before the advent of Europeans is debatable (Van Rensburg *et al* 2005: 12, Packard 1990: 25). It is likely though that it was not an important cause of morbidity and mortality because the conditions that favour the spread of the disease were largely absent

(Van Rensburg *et al* 2005: 12). Initially, tuberculosis was spread from early European colonists in the late eighteenth and early nineteenth centuries and the disease was concentrated in the more highly colonised Cape (Van Rensburg et al 2005: 12). However, the deliberate engineering of poverty among indigenous people to generate labour for South Africa's growing economy (Terreblanche 2002: 6) and in particular the use of migrant labour in the mines, with their overcrowded living conditions, poor wages and inadequate diets, resulted in a massive increase in the incidence of TB and the mortality due to the disease in African miners (Coovadia *et al* 2009, Packard 1990: 3).[1] These miners facilitated the spread of TB to rural populations, by frequent return to their homes in rural areas; indeed, miners who were ill were often forcibly repatriated because they were less productive (Packard 1990: 11). The impoverishment of rural people due to the imposition of taxes and the erosion of traditional diets increased their susceptibility to the disease (ibid). Rapid urbanization of Africans in the 1920s and 1930s and their squalid living conditions in peri-urban settlements further fuelled the disease in this group, where rates of TB remained much higher than in the white population which enjoyed far better living conditions (Packard 1990: 16). Apartheid and its defining policies of segregation and exploitation further exacerbated rates of disease and death in African populations (Coovadia *et al* 2009), including from tuberculosis (Packard 1990: 17). The continued impoverishment of black and rural populations, the fragmented and highly inequitable health care system and the emphasis on hospital-based and doctor-driven health care were all characteristics of the Apartheid era that facilitated the spread of TB and undermined its control (van Rensburg *et al* 2005: 22).

[1] Because the living and working conditions of white miners were superior, rates of TB were much lower in this group (Packard 1990: 5).

Since the advent of democracy in 1994, the inequalities in income and health that existed between race groups in South Africa have persisted and income inequality within race groups has increased (SARPN 2004).[2] Although there has been some debate on whether or not poverty in the country has decreased since 1994 (Aguero *et al* 2007, du Toit 2005), there is general consensus that income inequality has increased (Coovadia *et al* 2009, Aguero *et al* 2007, SARPN 2004). This inequality in income is reflected in inequalities in health across the country, both within and between provinces (Coovadia *et al* 2009), including in tuberculosis prevalence and outcomes. The prevalence of tuberculosis is highest in KwaZulu-Natal, which is also one of the poorest provinces in the country (Barron *et al* 2007), and the average TB cure rate in the most deprived districts of South Africa is 55.3% , whilst in the least deprived it is 71.4% (Day *et al* 2009:10).

The effect of poverty on tuberculosis epidemiology and clinical outcomes

The association between poverty and TB exists over the entire course of the disease, from initial infection to final outcome (Hargreaves *et al* 2011). Although effective treatment is available for drug-susceptible TB, and this is provided free of charge in public sector clinics in South Africa, there is a wealth of research that shows that the effect of poverty on TB outcomes is due, at least in part, to the costs of accessing and adhering to treatment (Ukwaja *et al* 2012, Munro *et al* 2007a, Zhang *et al* 2007, Rowe *et al* 2005, Yach 1988).

[2] The racial classification of South Africans into “Africans”, “Coloureds”, “Indians” and “Whites” was central to the Apartheid system and was legalized in the Population Registration Act of 1950 (Posel 2001). Because the racialised inequality of the country remains prevalent today, the terms are still used to describe population groups.

Poverty may cause delays in accessing initial treatment for TB, thus delaying the detection and treatment of TB and its complications. Even after the initiation of treatment, the limitations that poverty imposes on access to treatment may also reduce the likelihood of treatment success (Bates *et al* 2004). In South Africa, deprivation is an important determinant of the use of primary health care services (the level at which most TB care is delivered). The primary health care utilization rate is lowest (between 2.0 and 2.1 visits per person per year) in the most deprived districts of the country and highest (3 visits per person per year) in the least deprived (Day *et al* 2009: 8). Interestingly, some of the lowest primary health care utilization rates occur in South Africa's biggest cities, contradicting the assumption that access to health care in South Africa is worse in rural than in urban areas (ibid).

Having made the initial clinic visit for diagnosis and treatment, ongoing clinic access is further undermined by conditions of poverty. The costs of transport to the clinic, and of forgoing a day of economic activity, may be difficult if not impossible for patients to meet (Munro *et al* 2007a). It has been shown in several countries, that patients may have to sell assets or take out loans to pay for their treatment (Bates *et al* 2004); even in settings of general poverty, poorer patients are more severely affected than those who are less poor. For example, in Malawi, the costs of TB treatment for patients who were most poor amounted to 248% of their monthly expenditure, whereas for those who were less poor, it accounted for 124% of monthly expenditure (Bates *et al* 2004). In Tajikstan, the costs incurred during an episode of TB were two and a half times greater than the per capita GDP (Aye 2010) and in Swaziland, patients themselves identified two aspects of poverty as highly important in undermining adherence to

TB treatment: insufficient funds to attend the clinic for ongoing treatment, and lack of food whilst on TB treatment (Escott and Newell 2007).

In South Africa, financial constraints have been found to be major obstacles to the completion of TB treatment (Lutge *et al* 2009, Naidoo *et al* 2009, Yach 1988) and TB preventive therapy (Rowe *et al* 2005). In Rowe's qualitative study, financial limitations were universally reported by patients as general barriers to adherence, and cited again as preventing access to the clinic because of the expense of transport. In a survey of TB patients in KwaZulu-Natal, which served as a foundation for the work done in this thesis, it was shown that financial constraints were important factors in a patient's failure to complete TB treatment, even in populations where knowledge of TB was generally good (Lutge *et al* 2009). The majority (two thirds) of patients interviewed in this foundational work said it was "very expensive" to get to the clinic, with most (75%) using taxis as their main form of transport to the clinic. These expenses were incurred against a backdrop of high unemployment. Over half of all patients surveyed felt that the costs of accessing TB treatment over the course of the disease had had an important negative effect on their household finances (ibid). In addition, food security amongst these TB patients was low, with 42% of patients cutting the size of their meals and 31% cutting the size of their children's meals due to lack of food in the six months prior to the study (ibid).

The effect of poverty on HIV epidemiology and outcomes on treatment

It is crucial to include HIV in any discussion of TB in South Africa. The co-infection rate of these diseases is as high as 80% in some clinics in KwaZulu-Natal, and both the incidence and the geographical distribution of TB in the country have been profoundly affected by HIV.

Importantly, under-nutrition, TB and HIV also seem to act synergistically, thus creating the "perfect storm" for rampant epidemics in South Africa (ASSAF 2007). In addition, there has been "unparalleled" (Hargreaves *et al* 2011) research on the association between poverty and HIV, both globally and in South Africa, which is important both because of the influence of HIV on the epidemiology of TB, but also because it informs the relationship between poverty and TB, which has been less intensively researched.

The prevalence of HIV in South Africa is highest among Africans (13·3%), whilst Whites and Indians have very low prevalences of the disease (0·6% and 1·9%, respectively) (Coovadia *et al* 2009). Also, like TB, the prevalence of HIV in KwaZulu-Natal (one of the poorest provinces) is the highest in the country (Day *et al* 2012: 89; UNAIDS 2008). However, the role of income poverty in the transmission of HIV is controversial, with some studies showing that risk of infection increases with wealth (Barninghausen *et al* 2007), and others showing the opposite (Shisana and Simbayi 2002, quoted in Booysen 2004). What is clear though is that households affected by HIV are likely to be impoverished as a result of HIV and AIDS, both in terms of loss of income (Collins and Leibbrandt 2007, Booysen 2004) and in terms of increased expenses due to the illness. Burying a member who has died of HIV is an important cost for families. The majority (61%) of households in South Africa do not have insurance to cover funeral costs, which may cost up to seven months of income for poor households (Collins and Leibbrandt 2007). Since TB is the most important cause of death in patients with HIV in Africa (WHO 2012), these findings may also apply to families affected by TB.

As in TB, under-nutrition has been associated with poor prognosis in HIV infection (ASSAF 2007). Food insecurity has been associated with increased HIV transmission (Anema *et al* 2009) and is an important reason for non-adherence to anti-retroviral treatment. Patients who are food insecure are less likely to adhere to treatment, have lower baseline CD4 counts, incomplete virological suppression and are less likely to survive (Anema *et al* 2009, Weiser *et al* 2009). The side effects of antiretroviral drugs (ARVs) are exacerbated by the absence of food, and because these drugs can increase appetite, patients may experience "intolerable hunger in the absence of food" (Weiser *et al* 2009). Lack of food may therefore lead patients to skip doses if they cannot afford to eat (Yoder *et al* 2009: 50). The choice of either eating or getting their medicines, if money is limited, may lead some patients to choose food over accessing clinics in order to get their treatment (Weiser 2010). In addition, dietary diversity in HIV infected children in South Africa is significantly lower than in uninfected children living in the same areas, and this may be an important contributor to poor outcomes of infected children, even those on anti-retroviral treatment (Mpontshane *et al* 2008).

Anti-retroviral treatment programmes in sub-Saharan Africa retain an average of 60% of their patients, with a range of 46-85% (Rosen *et al* 2007). Although rates of adherence to ARVs have been shown to be as high or higher among patients in South Africa compared to those in high income countries (Orrell *et al* 2003), these high rates come at a cost. Patients have been shown to make "impossible choices" in order to obtain and take their treatment, such as borrowing, begging and doing without other necessities of life (Ware *et al* 2009). Money for transport to the clinic is considered an important factor in patients' inability to attend the clinic for their

appointments and to collect their medicines, with missed appointments leading to missed doses (Tuller *et al* 2010).

Rationale for this trial

South Africa has one of the highest burdens of tuberculosis in the world (Abdool Karrim *et al* 2009) and the outcomes of patients on TB treatment remain below the targets set by the World Health Organisation. In the context of 40% smear positivity, the national cure rate around the time of the trial was 67.5%, the treatment completion rate was 76.5% and the default rate was 7.5% (Day and Gray 2010). Although these outcomes represent improvements over the last decade, the transmission rate of TB has increased dramatically over this time and it has been suggested that the current national strategy for TB control, based on the DOTS Strategy, is insufficient to control the epidemic (Wood *et al* 2010).

Although the association between poverty and TB is well documented, there are very few programmes which directly address this relationship with economic interventions, and even fewer research studies which evaluate them (Hargreaves *et al* 2011). This is in part because such research is difficult to do. Because of the scale on which poverty occurs, and because of the complex relationship between different aspects of poverty and disease, such studies may be difficult to design and enormously costly to conduct. In the words of the Commission on the Socio-economic Determinants of Health, "Countries do not lend themselves to randomization. Interventions such as the development and implementation of laws ..... cannot be randomized across countries" (WHO 2008: 42). However, the Commission also states that, in spite of the growing body of evidence to support action in this field, "there is a pressing need to invest in a

great deal more research, bringing together different disciplines and areas of expertise, to work out how social determinants create health inequity, and how action on these determinants can produce better, fairer health" (WHO 2008: 27). Indeed, the third principle of action of the Commission is to "Measure the problem, evaluate action, expand the knowledge base" (WHO 2008: 2).

This call for research in the field has been echoed by some recent reviews (Lutge *et al* 2012, Boccia *et al* 2011, Lagarde *et al* 2009). In addition, a recent expert consultation on Social Protection for TB control, held at Chatham House in London in February 2012, concluded that "a) despite the indirect evidence gathered in a recent review...[ ]..., the actual impact of social protection on TB indicators (e.g. incidence, mortality, case finding, TB treatment adherence) remains unknown; b) it is unclear how social protection initiatives may be best integrated with current TB control activities and which forms of social protection are most likely to be successful, depending on the objectives posed".

Given the complexity of poverty as a phenomenon, and the depth and extent of poverty in South Africa, it is very difficult for small studies to investigate the effect of its alleviation on disease. Indeed, although "social Injustice is killing people on a grand scale", (WHO 2008: Executive summary), the scale is too vast for small intervention studies to meaningfully interrogate the multiplicity of interventions to alleviate poverty and the effects of these on health. It is, however, important to view the research around the eradication of such social injustice in a similar way to the injustice itself. As Amartya Sen says in "The Idea of Justice"

(2009:ii), "What moves us, reasonably enough, is not the realisation that the world falls short of being completely just, which few of us expect, but that there are clearly remediable injustices around us which we want to eliminate". Just as it is important to address these "clearly remediable injustices" instead of being weighed down by their enormity, it is important in research to start somewhere, by focussing on one or two links in the chain binding poverty and disease and testing interventions that weaken these links.

Models for our intervention: conditional cash transfers and economic incentives

Improving health by enabling or rewarding healthy behaviour is an area of increasing interest worldwide (Hargreaves *et al* 2011), and the idea can be encapsulated in the umbrella terms "results-based financing" or "pay-for-performance, performance-based funding, and output-based aid" (Oxman & Fretheim 2009). These terms include the two specific types of interventions of interest in this thesis: conditional cash transfers and economic incentives. Although the emphases of conditional cash transfers and economic incentives are different, they share many common features, and when incentives are used in low and middle income countries (which is where the largest conditional cash transfer programmes are run), the distinctions between them may become blurred. The major features of each, and the commonalities between them, are discussed further below.

Conditional cash transfers

The reduction of poverty and the improvement of access to health care are among the explicit aims of conditional cash transfer programmes. Such transfers are intended to increase household income and in so doing, improve household food security and overcome the barriers that poverty imposes on access to health care (Lagarde *et al* 2009). They compensate households for the indirect or opportunity costs associated with accessing health care (ibid) and protect them from the economic shocks that may be associated with illness. In addition, they serve to re-distribute wealth in society and because of their broader educational and developmental goals, also try to break inter-generational cycles of poverty (ibid). Conditional cash transfers have demonstrated potential in improving health outcomes by improving household economies (Boccia *et al* 2011; Lagarde *et al* 2009; United Nations 2009: 139). The best known examples of cash transfer programmes are those implemented in Latin America during the 1980s and onwards (Lagarde *et al* 2009). These cash transfers are conditional on certain behaviours on the part of recipients (ibid). Thus not only do conditional cash transfers help households cope with the costs of accessing health care (such as transport and treatment costs), and compensate participants for income lost when attending the health facility, they also create a demand for health services because of the need to meet the conditions of the transfer (Lagarde *et al* 2009). Patients and households are “rewarded” for practicing healthy behaviour and in this sense, conditional cash transfers can be seen to have an incentivising function, as well as a more developmental one. Many cash transfer programmes have indeed been shown to improve household economic well-being, household food security and access to health care (Boccia *et al* 2011), as well as health outcomes in terms of improved nutritional

status, fewer episodes of diarrhoea and reduction in the probability of illness in children of various age groups (Lagarde *et al* 2009). However, these findings are not uniform across all transfer programmes nor do they occur across all age groups (ibid). Of note, there are currently no studies of cash transfer programmes that have explicitly addressed tuberculosis (Boccia *et al* 2011).

Economic incentives

Economic or material incentives to encourage adherence to TB treatment are similar to conditional cash transfers in that the provision of the incentive also depends on a patient's compliance with a prescribed behaviour. However, the scope of the incentive is much more limited than that of the conditional cash transfer: where the cash transfer aims to address household poverty and factors associated with it (such as lack of access to education), the incentive focuses exclusively on a single health outcome, such as to reduce substance misuse (Burton *et al* 2010), encourage smoking cessation (Cahill and Perera 2011), promote adherence to the hepatitis B vaccination schedule (Seal *et al* 2003) and increasingly, to prevent HIV infection (World Bank 2011).

Although not specifically used to overcome barriers of poverty in accessing health care and adhering to treatment, economic incentives have been used among patients with tuberculosis to encourage adherence to treatment (Lutge *et al* 2012, reported in Chapter 2). It is possible that incentives may be more effective among patients in low and middle income countries, because they represent larger proportions of patients' generally low incomes (Oxman and Fretheim 2009). In such contexts, it might be more appropriate to refer to economic incentives

as "enablers" since, although their effect on poverty is lower than that of conditional cash transfers, they do assist patients in overcoming the obstacles to health care and health that are imposed by poverty. Thus in this thesis, the terms "incentive" and "enabler" are used together to emphasise the dual and often indistinguishable effect of economic interventions in the improvement of TB outcomes. For the sake of simplicity, and in order to capture both meanings in one word, the term "economic support" is most often used in this thesis.[3]

To date, there is very little evidence available to inform a decision on whether to use economic incentives or enablers among patients with active TB in low and middle income countries (Lutge *et al* 2012, reported in Chapter 2).

Difficulties in the delivery of conditional cash transfers and economic incentives

Although the conditionalities inherent in both conditional cash transfers and economic incentives have clear potential benefits, they also have potential drawbacks. Conditional cash transfers have been criticised as being paternalistic in their imposition on households of priorities for expenditure (Forde *et al* 2011). They may also be difficult to monitor and enforce, with many low income countries lacking the administrative capacity to do so (United Nations 2009: 140). The enforcement of conditions may also generate corruption, with the possibility that officials may be offered bribes to certify that conditions are being met (ibid) or recipients may report changes in behaviour but not actually practice them (Oxman and Fretheim 2009). Transfers or incentives may also be stolen or forged (ibid). They may have a perverse incentive

[3] The title of this thesis has been changed to replace the term "economic incentives" with which this PhD was first registered in 2009, with the term "economic support". The change reflects the evolution of ideas around the interventions that are the subject of this thesis and was accepted by both the Postgraduate and Health Research Ethics Committees of the University of Stellenbosch.

effect, with patients behaving in a way opposite to that intended by the programme in order to continue receiving the transfer or incentive. For example, women may increase their fertility because pregnant women are the targets of a particular transfer (ibid). They may also generate dependence on the transfer or incentive (ibid). Very poor families may struggle to meet the conditions in spite of the transfer, and so be excluded from the programme, resulting in a failure to assist those most in need (United Nations 2009: 140). Finally, targeting of certain households may generate conflict in communities where some are excluded from the programme (ibid). In spite of all these potential drawbacks, the conditionalities associated with cash transfers have been cited by some as the sole reason for their success in improving health and other outcomes (Forde *et al* 2011).

Both conditional cash transfers and economic incentives are possible to implement on a small (sub-national) scale, which makes them amenable to small-scale research projects, and both are attractive options for exploring ways to intervene in the cycle of poverty and TB.

Cash transfer programmes in South Africa

South Africa has an extensive programme of social protection for poor and vulnerable groups, in the form of cash transfers (known in this country as social grants). These grants have been shown to have a positive impact on the depth of poverty in the country (Armstrong 2008) and in terms of government expenditure, are the largest form of assistance to poor households in South Africa. The grants available in South Africa include: the old age pension (also known as the older person's grant), child support grant, disability grant, care dependency grant and foster care grant. The old age pension and the child support grant have the greatest coverage of all

these grants, and have increased dramatically in value since democracy (Booysen 2004). In addition, the number of beneficiaries of these grants has increased since 1994, with the age cut-off for the old age pension decreasing steadily, and the age cut off for the child support grant increasing steadily since then (Friedman and Bhengu 2008: 108).

Like conditional cash transfer programmes, the two most common social grants in South Africa (the old age pension and the child support grant) have important developmental effects. The old age pension has been shown to dramatically improve household finances and, in so doing, also improve the family's food security, and children's school enrollment (Case and Menendez 2007). In addition, in households where there is a recipient of an old age pension, it is easier for younger adults in the household to leave the area to find work elsewhere, and further improve the financial status of the household (Ardington *et al* 2009). Similarly, the Child Support Grant has reduced the number of children living in extreme poverty (Rispel 2009). Like the old age pension, the child support grant confers a measure of financial stability on the household that allows members to look for work "more intensively, extensively, and successfully than workers in comparable households without social grants" (ibid). Children living in households where the child support grant is received are also more likely to attend school, and have better nutritional status, than in households where no grants are received (ibid).

The only cash transfer programme in South Africa that is specifically related to an illness is the disability grant for TB or HIV. Patients with TB and/or HIV in South Africa may qualify for this grant if they are judged to meet certain criteria by attending doctors. The disability grant is an income replacement grant and, in the case of TB, is given for the duration of treatment. The

grant is generous and at the time of the trial, was valued at R1080.00 per month (the same value as the old age pension and about four times higher than the Child Support Grant). Although the disability grants for TB or HIV are not conditional on any behaviour on the part of the patient, they have been deemed to be very important, especially for patients with HIV, in order to integrate issues of food security with antiretroviral treatment programmes (Weiser 2010, Anema 2009). However, the determination of eligibility for these grants in South Africa is neither clear nor standardised and varies both between and within provinces (Whitworth *et al* 2006). In KwaZulu-Natal, the administrative processes required to access the grants are onerous and lengthy (personal experience of the principal investigator). Perhaps in part because of this, the grants have been shown to have relatively low coverage. In a study conducted in the Eastern Cape, only 35% of patients infected with HIV were receiving the disability grant, and a further 13% had previously received the grant but it had been stopped (Peltzer and Phaswana-Mafuya 2008). In the survey conducted in KwaZulu-Natal that informed this trial, only 21% of TB patients received a disability grant for either TB or HIV (Lutge *et al* 2009).

The possibility that the disability grant for TB or HIV may act as a disincentive for the completion of treatment must be kept in mind (Oxman and Fretheim 2009). In a qualitative study investigating adherence to anti-retroviral treatment in KwaZulu-Natal, patients with HIV reported that the disability grants were very helpful, attributing the improvement in their health to the food they were able to buy with the grant money (Yoder *et al* 2009: 44). However, termination of the grant (done when a patient's CD4 count returns to a certain level) was seen as problematic for patients (Yoder *et al* 2009: 61). Some of the patients cited in this report said

that they had stopped taking treatment because their grants had been stopped. For example, one had stopped treatment when his grant was terminated, but had returned to the clinic when his CD4 count was low enough to warrant a grant again (Yoder *et al* 2009: 62).

In addition to a disability grant, patients with TB in South Africa may be eligible to receive nutritional support from the clinic (Department of Health 2009). This may take the form of food supplements, such as powders that are re-constituted with milk or water, or food such as packets of beans, rice or porridge. However, in the research that informed this trial, it was shown that the supply of food parcels to the clinics has decreased over time, and for TB patients the provision can be erratic (Lutge *et al* 2009). Nurses may not be able to provide nutritional support to all patients who need it, and may have to ration it. In addition, the storage of such foodstuffs at clinics can be problematic as space is often limited and the foods attract rats and cockroaches.

In South Africa, all cash transfer programmes are unconditional. Neither the disability grants for patients with TB or HIV nor the nutritional support is tied to any conditions on the part of the patient. Although unconditional cash transfers are easier to administer (del Ninno 2005), it may be that if a transfer is intended to improve health outcomes, for example by improving a specific health behaviour, a conditional transfer would be more effective.

Development of our intervention

We reasoned that an economic transfer to patients with TB in South Africa could improve household economic well-being, and in so doing increase access to health care, improve household food security, improve patient adherence and thus improve outcomes on TB

treatment. We felt that research investigating the feasibility of delivering such a transfer and its effect on TB outcomes would be acceptable in the South African setting because:

- Cash transfer programmes are already well established in South Africa, and have demonstrated important effects in alleviating poverty
- Such transfers are already available to patients with TB (although their distribution is suboptimal)
- Conditional cash transfers have demonstrated improvements in access to health care, nutrition and certain health outcomes in other settings.

In developing the protocol for this research, we spoke to many stakeholders in the field of TB management and policy development in South Africa, including TB programme managers at all levels (district, provincial and national), local traditional leaders and local political representatives. We wanted to make sure that these stakeholders would support this research and, if our intervention was found to be effective, would be amenable to rolling it out on a large scale. In the course of these discussions, and as a result of the inputs we received, we decided to offer a voucher for foodstuffs instead of cash. This was preferred by the majority of stakeholders for the following reasons:

- It was a security risk to hold large sums of cash at clinics in KwaZulu-Natal
- If the cash were stolen from patients it would be impossible to verify the theft or replace the cash
- Most patients at public sector clinics did not have bank accounts, thus making electronic transfers difficult

- Cash could be spent on any items, and patients may have chosen to spend it on unhealthy or damaging items such as cigarettes or alcohol
- The expenditure of vouchers could be more easily monitored.

Managers in the TB programme were also concerned about potential adverse effects, such as generating dependence on the voucher, and a perverse incentive effect. To avoid this (and to remain within the limited budget of the trial), we decided to offer an amount significantly smaller than the disability grant for TB, but which we hoped would be enough to meaningfully assist poor patients. The R120.00 per month at which the voucher was valued was less than the food poverty line of R226.00 at the time of the study (Oosthuizen 2008), and was about a fifth of the value of the median per capita monthly income in KwaZulu-Natal around the time of the trial (Hall *et al* 2010). However, it was hoped that the voucher would allow households to increase expenditure on food stuffs. The amount offered in the voucher was sufficient to purchase a number of food stuffs commonly used in South African households (Table 1), which we hoped would improve household food security and the nutritional status of the index patient.

Table 1: Prices of selected food stuffs in January 2010 (mid-way through trial)

Commodity	**Rural price in ZAR**	**Urban price in ZAR**
Full cream long life milk 1 litre	10.28	9.72
Loaf of brown bread 700g	7.00	6.97
Loaf of white bread 700g	7.56	7.83
Maize meal 5kg	29.09	22.93
Margarine 500g	14.61	12.88
Peanut butter 400g	16.59	15.48
Rice 2kg	28.58	23.14
Sunflower oil 750ml	17.20	12.81
Ceylon/black tea 62.5g	7.06	7.02
White sugar 2.5kg	19.73	18.15

Source: Food Price Monitor 2011; available at http://www.namc.co.za/dnn/LinkClick.aspx?fileticket=r7dfjbWctLg%3D&tab. Accessed on 14th February 2013.

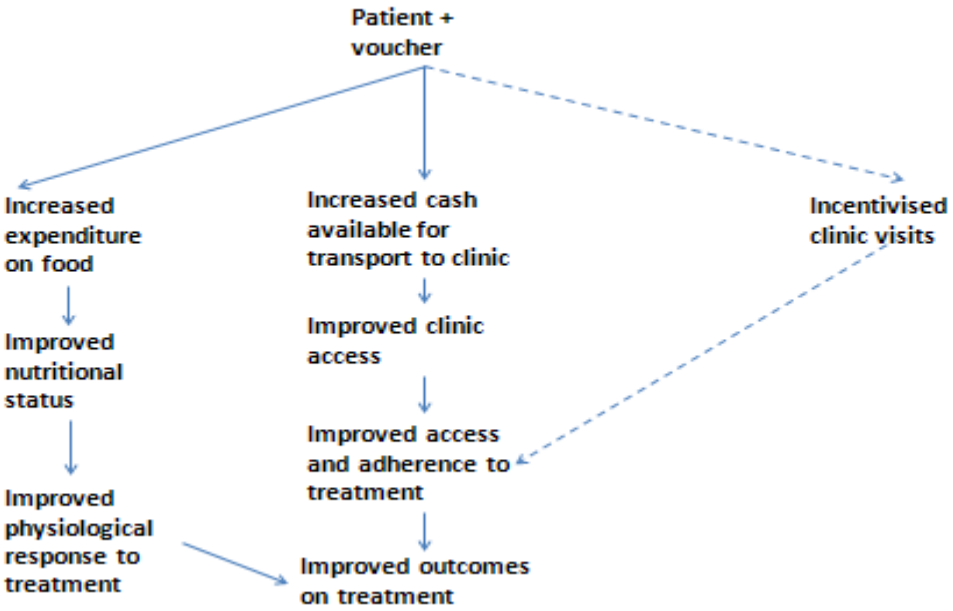
We also hoped that the voucher would free up money spent on food stuffs to meet other essential expenditure, such as transport to the clinic. In the research that informed this trial, patients in KwaZulu-Natal reported spending an average of R16.64 on transport to the clinic (with a range of R0 for those who walked, to R140.00) (Lutge *et al* 2009). We reasoned that the amount provided in the voucher could free up sufficient funds to facilitate clinic access.

Although it has been suggested that a once-off voucher on completion of TB treatment might be a stronger incentive for patients in South Africa to adhere to their treatment (Abdool Karrim *et al* 2009), and although we did expect that our voucher would have some incentivising effect,

our rationale for providing support was more to enable adherence than to reward it. We therefore decided to give the voucher on a monthly basis to assist patients with food and other expenditures during their treatment.

A simple logic model describing the postulated mechanisms of action of the voucher is illustrated in Figure 1 below (Anderson *et al* 2011).

Figure 1: Postulated mechanisms of action of the voucher



In addition to investigating whether the voucher would improve TB patients' outcomes on treatment, an important question to be answered in this trial was the feasibility of administering this voucher at public sector clinics in the province. A process evaluation was conducted alongside the trial, in order to best answer questions of feasibility, and to

interrogate the extent to which the mechanism of action of the voucher corresponded to our hypothetical model. As discussed above, it has been noted in previous research that the disability grant for patients with TB is seldom received and entails a lengthy and difficult application process (Lutge *et al* 2009, Whitworth *et al* 2006). The provision of food parcels to patients with TB is uneven because of an erratic supply (Lutge *et al* 2009). The feasibility of administration of material or economic support to TB patients is thus an important area of research. Even if an economic intervention were found to be effective in improving the outcomes of patients with TB, its impact would be limited if it were not feasible to administer it. Given the administrative difficulties demonstrated in the provision of other forms of economic support to TB patients in South Africa, it was important that this trial provide evidence that could be used by policy makers in the real-world South African setting (Treweek and Zwarenstein 2009). Our trial therefore had a "pragmatic attitude" (ibid) and tended towards the pragmatic domains of the Pragmatic-Explanatory Continuum Indicator Summary (PRECIS) tool (Thorpe *et al* 2009) which are described in more detail in Chapter 3.

Accordingly the pragmatic trial forming the central component of this thesis aimed to investigate the following:

- The feasibility of delivering a voucher to TB patients in KwaZulu-Natal and of integrating this with routine TB treatment
- The effectiveness of this voucher in improving the outcomes of patients on TB treatment
- The effect of the voucher on the patients' household expenditure.

Structure of the thesis

The structure of this thesis is as follows:

- Chapter 1: A discussion of the rationale for the thesis and the models on which we based our intervention
- Chapter 2: A report of the findings of a Cochrane systematic review, collating the existing evidence around the use of economic incentives and enablers in patients with TB (the Cochrane review was published in the Cochrane library in February 2012 (Lutge *et al* 2012))
- Chapter 3: A report of the conduct and findings of the pragmatic, cluster randomized controlled trial of economic support to improve TB treatment outcomes in South Africa (an abridged version of this report was published in the journal "Trials" in June 2013 (Lutge *et al* 2013)).
- Chapter 4: Part one of the process evaluation of the trial, reporting on the responses of nurses, managers, patients and shop keepers to the voucher
- Chapter 5: Part two of the process evaluation of the trial, reporting on the effect of the voucher on patients' household expenditure, and the goods on which the vouchers were spent
- Chapter 6: A summary of evidence that informed the trial, the findings of the trial and their implications
- Chapter 7: Suggested questions for further research in the field of economic interventions for the improvement of TB outcomes, and the ethical rationale for pursuing this research.

Cochrane systematic review: Material incentives and enablers in the management of tuberculosis

Introduction

This chapter describes a Cochrane systematic review which aimed to assess the evidence for the use of material incentives and enablers in the management of TB. This review complements the evidence available for the use of other forms of economic support, specifically conditional cash transfers, for improving patients' outcomes on TB treatment. This review was lead by me and was published in the Cochrane library in February 2012 (Lutge *et al* 2012). The review as presented in this thesis largely follows the format for Cochrane reviews of effects, conforming to requirements for the structure and content of these reviews. However, to improve the flow of this thesis, the format of the review has been altered slightly (primarily by excluding the abstract, and moving explanatory tables and figures to the appendices for this chapter).

Background

Description of the condition

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* which spreads from person to person by inhalation of respiratory droplets. The burden of disease is highest in low- and middle-income countries where it is associated with poverty,

overcrowding, and lowered immunity (due to poor nutrition or infection with the human immunodeficiency virus (HIV)) (WHO 2009a).

Following the initial infection, most people do not develop symptoms as the bacterium is completely controlled by the immune system, and lies dormant in a state known as "latent TB". Active TB, where the bacterium is no longer controlled by the immune system, can occur at any time following infection and most commonly affects the lungs, causing a chronic cough (which acts to spread the disease), loss of weight, loss of appetite, and general malaise (Harries 2006).

The most widely used method of diagnosing latent TB is the tuberculin test (also known as the Mantoux test), which involves injecting a small amount of a purified *M. tuberculosis* protein under the skin, usually of the forearm. If the person has previously been exposed to TB, a small swelling occurs due to a localised immune response, and the size of this response is measured 48 to 72 hours later (CDC 2010). Treatment of latent TB, often called TB prophylaxis, aims to prevent the later development of active disease, and reduce transmission.

Effective treatment for both active and latent TB requires regular medication to be taken for six to twelve months; non-adherence to this difficult and prolonged schedule is the most common cause of treatment failure (Narayanan 2003; Volmink 2000) and one of the most important obstacles to TB control globally. Non-adherence, with prolonged infectiousness, constitutes a health risk to close family and community contacts, and can lead to the development of drug resistant organisms which are more difficult and more expensive to treat (Lam 2002).

Adherence is not the sole responsibility of the patient, nor of the health system, but some combination of the two (Garner 2007), and consequently interventions aimed at reducing non-

adherence may need to target both. These interventions may be classified as: technical (making the medications simpler to take, such as reducing doses and personalising packaging); behavioural (establishing a pattern of behaviour through stimuli or positive reinforcement); educational (improving patients' capacity to manage their diseases, often through a cognitive didactic approach); structural (improving the accessibility and acceptability of TB programmes); or complex (a combination of these) (Haynes 2008; Munro 2007b; van Dulmen 2007; WHO 2003c). A review of direct observation has been completed indicating little added effect of direct observation (Volmink 2007), and a review of patient reminders and prompts is also available showing mixed effects (Liu 2008). A further review on patient education has recently been completed, showing potential benefits of educational interventions (M'Imunya 2012).

Description of the intervention

Incentives and enablers are interventions targeted at the patient which seek to either promote or assist improved adherence (WHO 2003a; WHO 2003b; WHO 2003c). They may be given directly as cash or vouchers (for example for groceries), or indirectly as the provision of a service for which the patient would otherwise have had to pay (for example transport to and from the clinic).

A recent overview of reviews found that material incentives improved adherence and outcomes for a number of health problems, and also increased the utilisation of health services for prevention programmes (Sutherland 2008). Conditional cash transfers, used primarily in Latin America, can be regarded as economic incentives used on a large scale to promote healthy behaviour in poor families and individuals (Lagarde 2007). They have been particularly

successful in promoting the use of health services and in improving nutritional and anthropometric outcomes in certain groups (Lagarde 2007).

How the intervention might work

Incentives are based on behavioural theories of reward for "good" behaviour (van Dulmen 2007), and may be defined as "any financial or material reward that patients and/or providers receive, conditional on their explicitly measured performance or behaviour" (Beith 2007). Alternatively, "enablers" assist patients to adhere by overcoming the financial barriers to treatment. In a recent qualitative review, economic constraints due to absences from work to attend appointments, or the direct and indirect costs of accessing treatment, were commonly cited by patients as important barriers to completing TB treatment (Munro 2007a).

As well as potential benefits, the use of material incentives may also have unintentional negative consequences. Patients who receive incentives to adhere to one health behaviour may be reluctant to adhere to others if they are not also accompanied by incentives (Malotte 1999). This might be especially important where incentives are offered in one of several possible stages in a multi-stage treatment process such as screening for and treating TB. Further possible negative effects include: resentment in patients who do not receive the incentive (Malotte 2001); fraud and corruption, with patients manipulating the incentive system to gain more; the creation of "ghost" patients allowing health staff to steal incentives from the system (White 1998); or the "perverse incentive" effect, where the incentive induces exactly the opposite behaviour to that intended; for example, patients who want to continue receiving the

incentive may deliberately not take medications in order to remain ill (Department of Social Development 2006).

Why it is important to do this review

In light of the increased risk of TB posed by HIV infection (Stop TB Partnership 2010), and the development of epidemics of drug-resistant forms of TB (Yang 2011; Wells 2007), efforts to help patients complete therapy are of paramount importance. If material incentives and enablers improve adherence rates amongst patients with TB, they should be used far more widely than they are currently.

Objectives

To evaluate the effects of material incentives or enablers given to patients undergoing diagnostic testing for TB, or receiving drug therapy to prevent or cure TB.

Methods

Criteria for considering studies for this review

Types of studies

Randomized controlled trials, where the unit of allocation was either an individual or cluster.

Types of participants

People receiving curative treatment for TB

This included smear positive cases, smear negative cases, new cases, and re-treatment cases.

People receiving preventive therapy for TB

This included patients at risk of developing active TB and taking anti-TB chemoprophylaxis (i.e. isoniazid preventive therapy).

People suspected of TB undergoing, and collecting the results of, diagnostic tests

Diagnosis of TB infection (using tuberculin skin tests) and disease (using sputum microscopy and culture) often requires the patient to return to the health facility a few days after the test is performed to receive the results. Incentives have been used to encourage patients to do this.

Children, adolescents and adults

Although it was originally intended to include only studies focusing on adults of 16 years and over, we decided to drop this age limitation as a few trials were found that investigated children or adolescents.

Types of interventions

Interventions included any form of material inducement to return for TB test results, or adhere to or complete anti-TB preventive or curative treatment. These may have been direct such as cash or vouchers, or indirect such as the provision of a service for which the patient would otherwise have had to pay (for example transport to and from the clinic). Non-material incentives, such as praise from a health worker, were not considered in this review, because their economic value is difficult to quantify and the form of the incentive is difficult to standardise.

In those trials where incentives were combined with other interventions, studies were only eligible for inclusion in a meta-analysis if disaggregation of the effect of the incentive was

possible. Other interventions that could be combined with incentives include health information and education, and increased access to health workers through home visits, or additional appointments.

Trials were only included if the standard TB curative or preventive treatment were the same across the control and treatment arms.

Control groups

Controls were those patients receiving standard TB treatment or preventive treatment, or undergoing testing for suspected TB, who had no incentive or an alternative incentive or intervention.

Types of outcome measures

Primary:

For treatment of active TB

Cure and/or completion of treatment, using the following World Health Organization (WHO) definitions (WHO 2009b):

Cured: A patient who was initially smear-positive and who was smear negative in the last month of treatment and on at least one previous occasion.

Successfully treated: A patient who was cured or who completed treatment.

For prophylaxis

Cases of TB.

For diagnostics

Number returning to collect test results within the appropriate time frame for that test.

Secondary:

Percentage of treatment completed, appointment keeping, presence of urinary markers, and certification by direct observation of treatment.

Adverse effects

Adverse events reported in trials, such as expenditure of cash or vouchers on unhealthy items. The latter were defined as commodities that undermine the patient's chance of cure, such as tobacco products or alcohol.

Costs

Cost effectiveness of the intervention; where costs include the direct and indirect costs incurred by patients, and costs to the health system of providing and administering the incentives/enablers.

Search methods for identification of studies

We attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress).

Databases

We searched the following databases using the search terms and strategy described in Appendix 2A: Cochrane Infectious Diseases Group Specialized Register (22 June 2011); Cochrane Central Register of Controlled Trials (CENTRAL: 22 June 2011); MEDLINE (1966 to 22

June 2011); EMBASE (1974 to 22 June 2011); LILACS (1982 to 22 June 2011); and Science Citation Index (EXPANDED) and Social Sciences Citation index (SSCI) (1956 to 22 June 2011).

We also searched the metaRegister of Controlled Trials (mRCT) using 'tuberculosis', 'incentive', 'cash transfer', 'adherence', 'compliance', and 'concordance' as search terms (1998 to 22 June 2011). In addition, we searched the WHO International Clinical Trials Registry Platform (http://www.who.int/ictrp/search/en/) for ongoing trials (22 June 2011). The detailed search strategies are presented in Appendix 2A.

Researchers and organizations

We contacted researchers and other experts in the field of TB and adherence research, for unpublished and ongoing trials.

Reference lists

We checked the reference lists of related reviews (Garner 2007; Haynes 2008; Lagarde 2007; Sutherland 2008; Volmink 2000) and all full-text articles reviewed for inclusion in this review.

Data collection and analysis

Selection of studies

Elizabeth Lutge (EL) and Stephen Knight (SK) independently screened all citations and abstracts identified by the search strategy for potentially eligible studies. The full text articles of potentially relevant studies were independently assessed by the two authors using the pre-specified trial inclusion criteria. Disagreements were resolved by discussion and consensus. When a disagreement could not be resolved we sought arbitration from a third author (Charles

Shey Wiysonge (CSW) or Jimmy Volmink (JV)). We excluded studies that did not meet the inclusion criteria and documented the reasons for exclusion in the table of "Characteristics of excluded studies".

Data extraction and management

Using a pre-designed data extraction form, EL and CSW independently extracted information from the selected trial reports on study methods used, participant characteristics, interventions, and outcomes. For all outcomes, we extracted the number of participants randomized and the number analysed. The trials identified and included in this review all randomized individual participants and reported only dichotomous outcomes. For each study, we extracted the number of participants with an outcome of interest in each group as well as the number of participants randomized to each group, and the number analysed.

Disagreements were resolved through discussion and consensus between EL and CSW initially, and with SK or JV if the disagreement was not resolved.

Assessment of risk of bias in included studies

EL and CSW independently assessed the risk of bias in each included study using the The Cochrane Collaboration's tool for this purpose (Higgins and Green 2011). The authors followed the guidance to assess whether adequate steps were taken to reduce the risk of bias across six specific domains, namely, random sequence generation; allocation concealment; blinding of participants, personnel and outcome assessment; incomplete outcome data; selective outcome reporting; and "other issues". For each included study, the two authors independently described what the trial authors reported that they did for each domain and then made a

decision relating to the risk of bias for that domain by assigning a judgement of "Low risk" of bias, "High risk" of bias, or "Unclear risk" of bias. The authors compared the results of their independent assessments of risk of bias and resolved any discrepancies by discussion and consensus. Any differences in opinion between the two authors was resolved by discussion and consensus, with arbitration by a third author (JV).

Assessment of reporting biases

If at least 10 studies were included in the meta-analysis for any outcome, we would have evaluated the likelihood of publication bias and other sources of bias by examining the degree of asymmetry of funnel plots. We chose this number because it has been shown that when there are fewer than 10 studies in a meta-analysis the power of funnel plot asymmetry tests is too low to distinguish chance from real asymmetry (Higgins and Green 2011).

Data synthesis

We analysed data using Review Manager 5. We analysed trial participants in the groups to which they were randomized, regardless of how much of the intended intervention they actually received.

All studies reported only dichotomous data, so we have expressed study results as the risk ratio (RR) with its 95% confidence interval (CI) for each outcome. We used the fixed-effect model for the primary analysis. When significant statistical heterogeneity was present and it was appropriate to combine the data, we used the random-effects model. We stratified analyses according to the type of incentive and control intervention, i.e. incentive versus routine care,

immediate versus deferred incentive, cash versus non-cash incentive, and incentive versus any other intervention.

In addition, we used the GRADE approach to summarise the quality of the evidence on the effects of material incentives or enablers on each outcome (Guyatt 2008). In the GRADE system, randomized trials without important limitations constitute high quality evidence. However, the system considers five factors that can lower the quality of the evidence, i.e. study limitations, inconsistent results across studies, indirectness of the evidence, imprecision, and publication bias. Overall, the GRADE system classifies research evidence into four categories ie high, moderate, low, or very low quality. High quality evidence implies that we "are very confident that the true effect lies close to that of the estimate of the effect", while very low quality evidence implies that the "true effect is likely to be substantially different from the estimate of effect" found in the review (Balshem *et al* 2011).

Subgroup analysis and investigation of heterogeneity

The presence of statistical heterogeneity across trials was determined by visually inspecting the forest plots to check for overlapping confidence intervals and by means of the chi^2 test for heterogeneity with a P value of < 0.10 indicating statistical significance. Further, the I^2 statistic was used to quantify the amount of heterogeneity as low (I^2 value of 25% or less), moderate (I^2 value between 25% and 75%), or high (I^2 value of 75% or more). If we had at least 10 studies in any meta-analysis that showed significant statistical heterogeneity, we would have explored the possible sources of heterogeneity by performing subgroup analyses; with subgroups defined by age, gender, socioeconomic status, and risk of bias (ie low versus high/unclear).

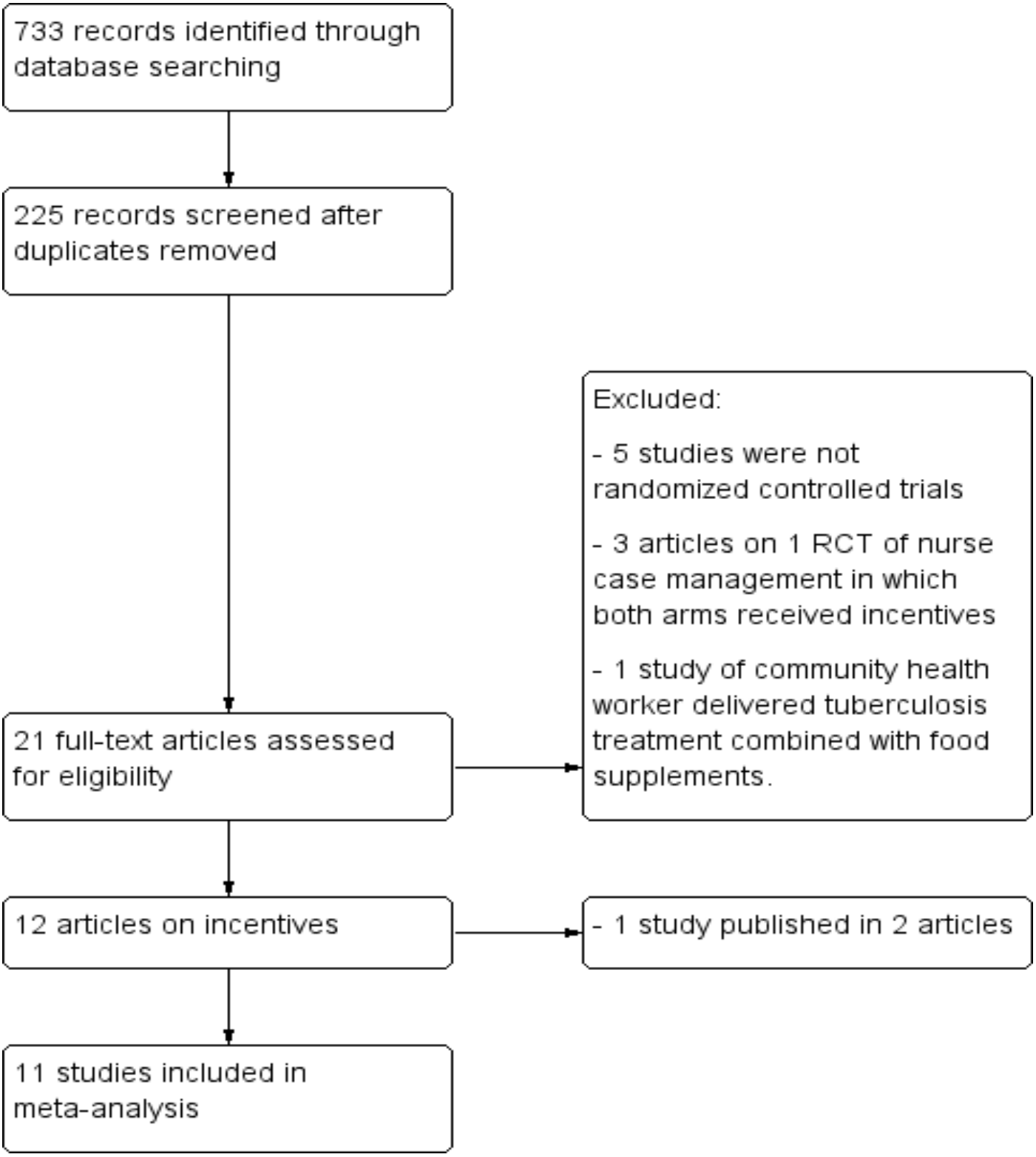
Results[4]

Description of studies

We obtained 733 titles and abstracts from the electronic search of databases, and no additional articles from contacting researchers or screening reference lists. After removal of duplicates, 225 records remained. Following discussion and consensus, we obtained 21 potentially eligible articles. Five of these articles were not randomized controlled trials (Cheng 1997; Filho 2009; FitzGerald 1999; Morisky 1990; Yao 2008), three were published reports of a trial of nurse case-management of latent TB in which both study arms received the same material incentive (Nyamathi 2006), and one was a trial of community health worker delivered TB treatment combined with food supplements (Jahnavi 2010). All these articles were excluded. Eleven randomized controlled trials met our inclusion criteria (Chaisson 2001; Malotte 1998; Malotte 1999; Malotte 2001; Martins 2009; Morisky 2001; Pilote 1996; Tulsky 2000; Tulsky 2004; White 1998; White 2002), and were included in the review. The final article (Kominski 2007) was a cost-effectiveness analysis of an included study (Morisky 2001). The search and selection of studies is shown Figure 1 below.

[4] Additional tables, figures and summaries are presented as appendices for this chapter at the end of the thesis.

Figure 1: PRISMA diagram showing the search for and selection of studies



Included studies

Ten of the 11 included trials were conducted in the USA, and only one was from a low- or middle-income country (Martins 2009: Timor-Leste).

Studies varied in size from 79 to 1078, with a mean of 430 participants, and most studies focused on very specific patient subgroups. Four studies were conducted among injection drug or cocaine users (Malotte 1998; Malotte 1999; Chaisson 2001; Malotte 2001), three on homeless or marginally housed adults (Pilote 1996; Tulsky 2000; Tulsky 2004), two studies on prisoners (White 1998; White 2002), and one assessed incentives given to adolescents aged 11 to 19 years (Morisky 2001). Only one study involved members of the general adult population with TB, and this focused on malnourished men living close to the study clinics (Martins 2009).

The studies assessed adherence to different stages of TB management. Some investigated the use of incentives in improving return for reading of tuberculin skin test results (Malotte 1998; Malotte 1999) while others focused on improving attendance at the clinic for initiation of treatment (Pilote 1996), adherence to preventive TB treatment (White 1998; Tulsky 2000; Chaisson 2001; Malotte 2001; Morisky 2001; White 2002; Tulsky 2004) and just one looked at adherence to treatment for active TB (Martins 2009).

The trials investigated various types of incentives, and several trials had multiple study arms receiving different forms of both material and non-material incentives. Eight studies included a study arm given cash in values of US $5 or US $10 (Pilote 1996, Malotte 1998, White 1998, Malotte 1999, Tulsky 2000, Chaisson 2001, Malotte 2001, Tulsky 2004). Three studies gave vouchers which could be redeemed for groceries, food, transport, meals at fast food outlets or

phone calls (Malotte 1999, White 2002, Tulsky 2004), and one study gave food as a hot daily meal (Martins 2009). In one study, adolescent patients negotiated the incentive they received from their parents (Morisky 2001). Common choices included special meals at home, going to a movie or renting a video.

These material incentives were compared with routine care, and in multi-arm trials also with motivational education (Malotte 1998; Malotte 1999), peer counselling (Morisky 2001; Pilote 1996; Tulsky 2000), and standardised education sessions (White 1998; White 2002). In addition, one study compared different levels of incentive (Malotte 1998), one study compared an immediate incentive, given monthly throughout treatment, with a lump sum given on completion (Chaisson 2001), and two studies compared different forms of incentive (Malotte 1999; Tulsky 2004).

Characteristics of included studies with their risk of bias tables are presented in Appendix 2C.

Excluded studies

One study was excluded because in both arms of the trial, patients were given the same incentive (Nyamathi 2006). Two other trials were excluded from this review because they were quasi-randomized; in one, randomization was done by day of the week (Cheng 1997) and in the other it was done by the last digits in the participants' clinic record numbers (Morisky 1990). Three trials were excluded because they were cross sectional studies where one group was given the incentive and the other was not (Filho 2009, FitzGerald 1999, Yao 2008), and another was excluded because the main intervention was community health-worker delivered TB treatment combined with food supplements (Jahnavi 2010).

Characteristics of excluded studies are presented in Appendix 2D.

Risk of bias in included studies

Our judgements about the risk of bias in each included study are summarised in Appendices 2E (Risk of Bias Graph) and 2F (Risk of Bias Summary).

Allocation (selection bias)

The generation of the randomization sequence was judged to be adequate in eight trials (Pilote 1996; White 1998; Tulsky 2000; Chaisson 2001; Malotte 2001; White 2002; Tulsky 2004, Martins 2009) and unclear risk in the remainder (Malotte 1998; Malotte 1999; Morisky 2001). The allocation concealment was judged to be adequate in four trials (White 1998; Malotte 2001; White 2002, Martins 2009) and unclear risk in the rest.

Blinding (performance bias and detection bias)

The blinding of outcome assessors was adequate in three trials (White 1998; White 2002; Tulsky 2004) and unclear in the rest.

Incomplete outcome data (attrition bias)

All the included trials addressed incomplete outcome data adequately.

Selective reporting (reporting bias)

It was unclear to us if any of the included studies were free of selective outcome reporting, since the study protocols were not available and there was no earlier methods paper listing the pre-specified outcomes for any of the studies.

Other potential sources of bias

Our assessment indicated that studies were free of other biases, except Tulsky 2004. This trial compared the effects of cash and non-cash incentives among homeless adults on adherence to

treatment for latent TB infection as well as the length of time needed to look for participants who missed their dose of medications. Although the participants were described as homeless, the study groups were not the same with respect to their primary housing in the year prior to the study. In the cash incentive arm, 23% had lived in a shelter or on the street, whilst 41% of the non-cash incentive arm had done so (Tulsky 2004). This baseline difference had the potential to introduce systematic differences in study outcomes.

Effects of interventions

Analyses for each comparison are presented in Appendix 2G, and forest plots for each analysis in Appendix 2H. However, because of its importance for this thesis, the forest plot illustrating the effect of incentives in patients on treatment for active TB is presented below.

Incentives versus routine care

Return to clinic for tuberculin skin test reading

Two studies in drug users from the USA compared material incentives ($5-$10) with routine care alone (Malotte 1998; Malotte 1999).

Material incentives significantly increased the proportion of people who returned for reading of the tuberculin skin test (two trials, 1371 participants: RR 2.16, 95% CI 1.41 to 3.29; Analysis 1.1). Although there was significant heterogeneity between these studies (I^2 = 86%), the heterogeneity relates to the magnitude of the observed effect, and not the direction or significance of the result. Both studies demonstrated a clinically important benefit.

Return to clinic for initiation or continuation of TB prophylaxis

Three studies from the USA compared material incentives with routine care alone (Pilote 1996; White 1998; White 2002). Pilote 1996 gave $5 to homeless people on return to a clinic after a positive tuberculin skin test, White 1998 gave $5 when recently released prisoners attended a community clinic for continuation of TB prophylaxis, and White 2002 gave recently released prisoners food or transportation vouchers worth $25 upon presentation at a TB clinic.

Incentives significantly increased clinic attendance for initiation or continuation of treatment for latent TB infection (three trials, 595 participants: RR 1.58, 95% CI 1.27 to 1.96; Analysis 1.2). Although heterogeneity between the relative effects was low (I^2 = 0%), there was a wide variation in the absolute benefit achieved with incentives. In the two trials in prisoners, attendance at clinic remained lower than 25% even in the intervention groups.

Completion of TB prophylaxis

Three studies, again from the USA, examined the effect of incentives on completion of TB prophylaxis. Malotte 2001 gave a $5 cash incentive to drug users on attendance for twice weekly directly observed treatment, White 2002 gave recently released prisoners transportation vouchers worth $25 upon first presentation at a TB clinic, and Morisky 2001 established an incentive agreement between adolescents aged 11 to 19 years and their parents, where parents provided cash or treats at various stages in the treatment process.

Incentives had no statistically significant effect on the completion of TB prophylaxis (three trials, 869 participants: RR 1.79, 95% CI 0.70 to 4.58, Analysis 1.3). However, there was significant heterogeneity in these results (I^2 = 90%). Malotte 2001 found a statistically

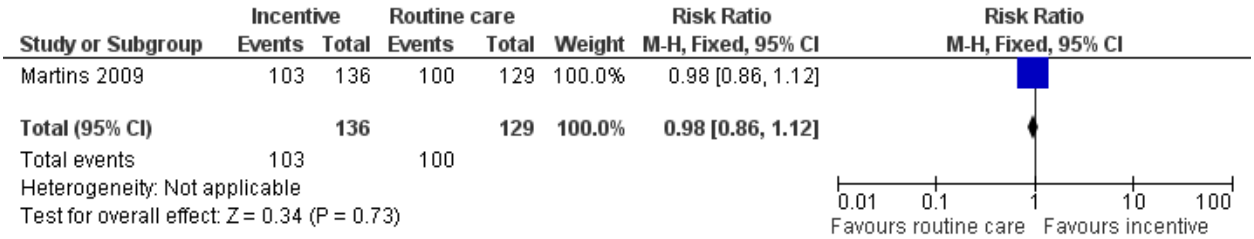
significant benefit with incentives (RR 14.53, 95% CI 3.64 to 57.98), but adherence in the control group was extremely low (3.6%). In Morisky 2001 completion of treatment was reasonable in the control group (77.8%), and did not significantly change with the incentive (76.4%), while in White 2002 completion remained low in both groups despite the intervention (13.8% control vs 14.1% intervention).

Completion of treatment for active TB

One trial compared incentives given as food (in the form of hot meals at the clinic during the intensive phase of treatment followed by monthly food parcels) to nutritional advice alone (Martins 2009). Both arms received usual TB care.

There was no significant difference in treatment completion rates between participants given nutritional supplements and those receiving nutritional advice alone (one trial, 265 participants, RR 0.98, 95% CI 0.86 to 1.12, Analysis 1.4). Treatment completion was below 80% in both the control (77.5%), and intervention groups (75.7%).

Figure 2: Completion of treatment for active TB



Immediate versus deferred incentive

Completion of TB prophylaxis

One study, (Chaisson 2001) compared the effects of an immediate incentive ($10 for each monthly appointment attended) with the promise of a deferred lump sum ($10 for each appointment attended) on completion of TB prophylaxis.

The participants who received the immediate incentives completed treatment more often than those whose incentives were deferred (83% vs 75%), but the difference was not statistically significant (one trial, 300 participants: RR 1.11, 95% CI 0.98 to 1.24; Analysis 2.1).

Cash versus non-cash incentives

Return to clinic for tuberculin skin test reading

One study amongst injection drug and crack cocaine users (Malotte 1999), directly compared a cash incentive ($10) with non-cash incentives (grocery store coupons, bus tokens and fast food coupons equivalent in value to $10).

The cash incentive was significantly more effective at increasing return for reading of tuberculin skin tests than any of the non-cash incentives (one trial, 651 participants: RR 1.13, 95% CI 1.07 to 1.19; Analysis 3.1).

Completion of TB prophylaxis

One study among homeless and marginally housed adults with latent TB infection (Tulsky 2004) compared a cash incentive ($5), with non-cash incentives (patients could choose between fast food or grocery store coupons, phone cards or bus tokens equivalent to $5).

Again, the cash incentive was significantly more effective than the non-cash incentives (one trial, 141 participants: RR 1.26, 95% CI 1.02 to 1.56; Analysis 3.2).

Different values of cash incentive

Return to clinic for tuberculin skin test reading

One trial (Malotte 1998), also compared different values of cash incentive ($10 versus $5).

The $10 incentive significantly increased the proportion of patients returning to the clinic to collect their diagnostic TB test result compared to the $5 incentive (one trial, 404 participants: RR 1.08, 95% CI 1.01 to 1.16; Analysis 4.1).

Incentives versus any other intervention

Return to clinic for tuberculin skin test reading

The two trials among drug users in the USA (Malotte 1998; Malotte 1999), also had a treatment arm which received 5 to 10 minutes of motivational education. The material incentives ($5 to $10) significantly increased the rate of return for tuberculin skin test reading compared to motivational education alone (two trials, 1366 participants:RR 2.16, 95% CI 1.56 to 3.00; Analysis 5.1).

Return to clinic for initiation or continuation of TB prophylaxis

Two trials assessing return to clinic for TB prophylaxis compared material incentives with education or counselling. Both were from the USA; Pilote 1996 used peer counsellors to encourage homeless men and women to attend clinic after a positive test result, and White 2002 gave education sessions every two weeks to prison inmates to encourage attendance at a community clinic upon release.

There was no significant difference between material incentives and education or peer counselling (two trials, 535 participants: RR 1.10, 95% CI 0.92 to 1.31; Analysis 5.2).

Completion of TB prophylaxis

Three trials also used peer counselling or education sessions to promote completion of TB prophylaxis: one among prison inmates (White 2002), one amongst homeless adults (Tulsky 2000), and one among adolescents (Morisky 2001).

The results were mixed. In adolescents, completion rates were high in both groups and with no significant difference between groups (one trial, 387 participants: RR 0.95, 95% CI 0.86 to 1.06). Among the homeless, the cash incentive appeared more effective than counselling but completion remained low in both groups (one trial, 80 participants: RR 2.34, 95% CI 1.11 to 4.93), and among prison inmates the trend was towards a benefit with counselling (one trial, 370 participants: RR 0.58, 95% CI 0.31 to 1.09).

Potential effect modifiers

The only potential effect modifier to be reported was educational status. Six trials assessed this and no effect on outcomes was noted (Pilote 1996; Malotte 1998; Malotte 1999; Malotte 2001; White 2002; Tulsky 2004).

None of the studies reported their results subgrouped by HIV status. In three studies it was noted that HIV positive patients were included (Malotte 1998; Malotte 1999; Malotte 2001), in one study it was noted that the population from which the study sample was drawn had a generally low prevalence of HIV (Martins 2009), and in a further three trials HIV positive patients were actively excluded (Tulsky 2000; White 2002; Tulsky 2004).

Adverse events

Although adverse events due to the anti-TB drugs administered (such as isoniazid) were noted, adverse effects of the incentives/enablers themselves were not. No study documented what patients chose to purchase with the cash or vouchers, and no study recorded incidents of theft, fraud or a perverse incentive effect.

Cost effectiveness

We found one paper reporting a cost analysis (Kominski 2007), which related to an included trial (Morisky 2001). This trial involved the administration of an incentive to adolescents with latent TB (in the form of a "contingency contract" with their parents).

As this trial failed to demonstrate any clinical benefit with the use of incentives, any further appraisal of the cost component was not considered useful.

Discussion

Summary of main results

When given as cash, incentives/enablers may increase the return rate for reading of tuberculin skin test results compared to normal care (*low quality evidence*), and will probably improve clinic re-attendance for initiation or continuation of anti-TB prophylaxis (*moderate quality evidence*).

Cash incentives may also be more effective than non-cash incentives (*low quality evidence*), and higher amounts of cash may be more effective than lower amounts (*low quality evidence*).

We currently don't know if material incentives/enablers can improve long-term adherence and completion of anti-TB treatment for active disease. Only one trial has assessed this and the incentive, given as a daily hot meal, was not well received by the population due to the inconvenience of attending the clinic at midday (*very low quality evidence*).

Material incentives/enablers may be more effective than motivational education at improving return tuberculin skin test results (*low quality evidence*), but may be no more effective than peer counselling, or structured education at improving continuation or completion of prophylaxis (*low quality evidence*).

Overall completeness and applicability of evidence

In line with Cochrane methodology, the evidence reviewed for this chapter consisted only of randomised controlled trials. Whilst such studies are considered to provide the highest quality evidence on the effectiveness of interventions, it is important also to consider other study types which may also provide insight into other questions, such as the acceptability of an

intervention. Such studies are discussed in more detail in the discussion section of Chapter 3, and in the final review of evidence presented in Chapter 6.

All but one of the studies included in this review were conducted in the USA, and in all but one the participants belonged to special groups (injecting drug users, homeless people, prison inmates, and adolescents). The applicability of these results to the broader adult population, especially in low- and middle-income countries where the burden of TB is highest, is therefore questionable. It is possible that these subpopulations have different relationships with material incentives than the general population, and a greater potential for misuse.

Another important consideration in extrapolating these results to other populations is HIV. It is possible that HIV co-infection may affect adherence to anti-TB medications, either positively (for example through adherence education received in the HIV programme), or negatively (for example because illness prevents patients from attending the clinic, or because patients are already taking a number of medications for HIV). However, HIV was not considered in most of these studies. Since the risk of developing TB among patients with HIV is far higher than in those who are HIV negative (WHO 2009a), future studies on incentives/enablers for TB should specifically investigate the effect of HIV status on outcomes.

In some settings, health workers and managers may be concerned about giving cash to patients. Indeed, this was the rationale for the inclusion of non-cash incentives in one of the trials in this review (Malotte 1999). The reason for this concern was not described in the trial, but could be related to the expenditure of cash on unhealthy purchases. Vouchers for specified goods cannot be spent on such items and in fact were demonstrated by this trial to have a

beneficial effect on return for tuberculin skin testing. None of the studies however investigated what purchases were made with cash or vouchers.

A further objection to the use of incentives/enablers may be to the rationale of “paying the patient” to behave in a healthy way (when it is considered the patients' responsibility to do so). However, in poor settings, it may be difficult, if not impossible, for the patient to access the clinic or pay for medicines (McIntyre 2006). This acknowledgement underlies conditional cash transfer programmes in Latin America, where patients are assisted financially in return for behaviours that will promote the health of families (Lagarde 2007). In these programmes, the economic transfer may act more to enable, than to incentivise, a certain health behavious. Such programmes have been shown to have benefits in a poor population (Lagarde 2007), as well as in groups of vulnerable patients in wealthier settings (such as homeless people in the USA) (Pilote 1996). However, the ethics of "paying patients" who are not poor or vulnerable is beyond the scope of this review.

Quality of the evidence

The quality of evidence provided by this review has been assessed using the GRADE approach, and is presented in five summary of findings tables (Appendix 2I). The evidence is generally considered to be of low or very low quality which indicates that further research is very likely to change these estimates of effect.

The main reason for downgrading quality was the indirectness of the evidence, with only one trial recruiting from the general adult population in low and middle income countries.

Potential biases in the review process

We minimised potential biases in the review process by adhering to the guidelines of the Cochrane Collaboration (Higgins and Green 2011). We conducted comprehensive searches of both peer-reviewed and grey literature, without limiting the searches to a specific language. Two independent authors assessed study eligibility, extracted data, and assessed the risk of bias in each included study.

Agreements and disagreements with other studies or reviews

Consistent with the findings of relevant previous reviews (Lagarde 2007; Haynes 2008; Sutherland 2008), we found that material incentives/enablers may promote the uptake of health services in certain settings, although the evidence is of low to very low quality. To the best of our knowledge, our review is the most comprehensive synthesis of existing evidence on the effects of material incentives/enablers in patients undergoing diagnostic testing for TB or receiving drug therapy to prevent or cure TB.

Authors' conclusions

Implications for practice

There is some evidence to support the use of material incentives/enablers to improve return rates for TB diagnostic test results and adherence to anti-TB preventive therapy. The data is currently limited to trials among predominantly male drug users, homeless, and prisoner subpopulations in the USA, and therefore the results are not easily generalised to the wider adult population, or to low- and middle-income countries, where the burden of TB is highest.

Implications for research

Further high-quality studies are needed to assess the effects and costs of incentives/enablers to improve adherence to the long-term treatment of active TB.

Future studies should specifically investigate the role of HIV and socioeconomic status in modifying the effects of incentives/enablers for TB treatment. The possible adverse effects of incentives/enablers such as misuse, fraudulent practices, the effect of incentives/enablers on non-recipients, and the perverse incentive effect, should also be considered.

Chapter 3

Does economic support improve TB treatment outcomes in South Africa? Findings from the randomised controlled trial

Introduction

This trial centred on two related questions, namely whether it was feasible to deliver economic support in the form of a voucher to patients with TB in public sector clinics in South Africa, and whether this support was effective in improving the treatment outcomes of those patients.

This chapter reports primarily on the effectiveness findings of the trial. The question of whether it is feasible to deliver this form of economic support in South Africa is answered primarily in Chapter 4 (process evaluation); however, elements related to the feasibility of distributing our voucher impacted on our findings of its effectiveness, and so are introduced in this chapter.

The report of the conduct and findings of this trial was published in the journal "Trials" in June 2013 (Lutge et al 2013).

Background

The randomised controlled trial is generally accepted to be the gold standard for generating evidence regarding the effectiveness or otherwise of an intervention. This is because

randomisation ensures that comparison groups are very similar in terms of known and unknown factors that are related to trial outcomes. Any effect demonstrated in a randomised controlled trial is more likely to be due to the intervention rather than to any confounding factor (Kirkwood 1988: 184). This was thus the design chosen to test our voucher.

Because we felt it would be logistically easier for nurses to administer the voucher to all of their patients with pulmonary TB (as opposed to certain patients within the clinic who were randomised to receive the voucher) (Weijer *et al* 2011), and because we hoped to avoid creating resentment among patients who did not receive the voucher, we decided to use a cluster rather than an individually randomised design. The cluster design allowed nurses to deliver the voucher to all eligible patients in the same way that they would do if this were a routine programme of the Department of Health. This trial design was therefore considered not only the most appropriate for answering the question of effectiveness, but also for assessing the feasibility of voucher administration in public sector clinics in South Africa.

Although the cluster design of this trial was the best way of achieving the trial's aims, the design is more demanding than that of an individually randomised trial, both in terms of the sample size (which needs to be larger than in individually randomised trials because of the correlation between participants within clusters), and the statistical analysis (Campbell *et al* 2004). In addition, issues of informed consent are more complex for cluster than for individually randomised controlled trials.

For a trial where the unit of randomisation is the cluster, but the intervention is applied at the individual level (like this one), the description "individual-cluster" trial is used and consent for

participation can be taken at both the cluster and the individual level (Edwards *et al* 1999). At a cluster level, consent for participation can be given by a "guardian" (someone who has the authority to act on behalf of a cluster, and who will have the best interests of the cluster at heart) (Edwards *et al* 1999). Such a person may be democratically elected, or may occupy this position by virtue of their employment or position in society. At an individual level, patients within a cluster can, and some argue should, give their informed consent for participation (Weijer *et al* 2011). However, in cases where the research is very low risk, and/or obtaining informed consent from each individual might make the project unfeasible, individual-level consent in an individual-cluster trial may be waived (Weijer *et al* 2011).

In order to test whether the administration of the voucher was feasible in the real world setting of public sector clinics in South Africa, this trial was pragmatic in design (Treweek and Zwarenstein 2009). The description of trials as pragmatic or explanatory was first made by Schwartz and Lellouch in 1967 (Schwartz and Lellouch 1967). Where pragmatic trials measure effectiveness ("the benefit the treatment produces in routine clinical practice"), explanatory trials measure efficacy ("the benefit a treatment produces under ideal conditions") (Eldridge 2010). Pragmatic trials are said to "help users choose between options for care" and explanatory trials, to "test causal hypotheses" (Thorpe *et al* 2009). Often, trials are not either "purely" pragmatic or explanatory but exist on a continuum where elements of both may be present (Thorpe *et al* 2009). The pragmatic-explanatory continuum indicator summary (PRECIS) tool describes 10 dimensions or domains which are building blocks in the design of a trial and which can sit anywhere along the pragmatic-explanatory continuum (Chaldikou *et al* 2012). These factors are:

- "Participant eligibility criteria
- Amount of flexibility with which the experimental intervention is applied
- Level of expertise practitioners have in using the experimental intervention
- Selection of the comparison arm and the amount of flexibility with which it is applied
- Level of expertise practitioners have in using the control intervention
- Intensity of follow up
- The nature of the primary trial outcome
- Use of strategies to maintain compliance among participants and the measurement of patient compliance
- Use of strategies to maintain compliance among practitioners and the measurement of practitioner compliance
- Type of analysis used to evaluate the data" (Chaldikou *et al* 2012).

These domains help to situate the trial on the pragmatic-explanatory continuum both in the design phase and once the trial has been completed (Chaldikou *et al* 2012). The Consolidated Standards for Reporting Trials (CONSORT) Statement guides the reporting of pragmatic trials (Zwarenstein *et al* 2008). The PRECIS tool is used to describe this trial (see Appendix 3A) and both the PRECIS tool and the CONSORT statement are used to discuss the trial and its findings.

Aim of the trial

To evaluate the feasibility and effectiveness of economic support for improving treatment outcomes in patients with pulmonary TB in a province of South Africa

Objectives of the trial

- To design and conduct a pragmatic, cluster randomised controlled trial in public sector clinics in KwaZulu-Natal in consultation with managers of the national and provincial TB Control Programme
- To develop a voucher which was recognised as legal trade by all stakeholders
- To minimise potential misuse of the voucher by features of its design and administration
- To train nurses in the delivery of the vouchers
- To establish contracts with local shops for the redemption of the vouchers
- To identify potential problems in the delivery of the vouchers as a routine part of the TB Control Programme of the Department of Health
- To identify problems in the redemption of the vouchers at participating shops
- To collect data on the outcomes on TB treatment of all participating patients, using routine Department of Health reporting systems
- To compare the outcomes of patients in intervention clinics with those of patients in control clinics.

The specific objectives of the process evaluation accompanying the trial are outlined in Chapters 4 and 5.

Study setting

This study was conducted in KwaZulu-Natal, one of South Africa's poorest and most populous provinces. The province has the second highest population and the second highest population density of the country, including the highest number of children under the age of one year (Day *et al* 2012: 202). Development indicators for the province remain poor, with 11.8% of adults over the age of 20 having had no schooling at all and a further 17.4% having had only some primary school education (Nzimande 2010: 22). The unemployment rate in the province (strict definition) is 29.2% (Gow *et al* 2007: 7) with over 50% of the unemployed having been without work for over three years (Gow *et al* 2007: 6).

KwaZulu-Natal has the highest incidence of TB in the country (1142 per 100 000) (Day *et al* 2012: 89) as well as the highest HIV prevalence rate (39.5%) (Day *et al* 2012: 203; UNAIDS 2008). Probably due to its high burden of HIV (Day *et al* 2012: 90), the province has for several years had the dubious honour of having the highest number of TB patients in the country (120 421 cases of all types of TB in 2010) (Day *et al* 2012: 202). Tuberculosis is the most important cause of death in the province, causing 16.2% of all deaths in 2009 (Statistics South Africa 2011: 81).

At the request of a senior TB programme manager, our trial included one urban district (eThekwini, also known as the city of Durban) and one rural district (Uthungulu). Uthungulu has

the fifth highest and eThekwini the sixth highest TB incidence of the 52 districts in the country (Day *et al* 2012: 90). Cure rates in these districts are low, however; both fall below the national average, with eThekwini ranked 41st, and Uthungulu 36th out of 52 districts (where first is best and 52nd is worst) (Day *et al* 2009: 101). In both eThekwini and Uthungulu, TB is the most important cause of death, causing 14.9% and 17.4% of all deaths in these districts in 2009 respectively (Statistics South Africa 2011: 94). At 46.4%, Uthungulu has the highest prevalence of HIV in the country, as measured by the annual Antenatal HIV Prevalence Survey (Day *et al* 2012: 203).

The poverty rate amongst individuals in KwaZulu-Natal is the second highest in the country, at 58.5%, and just over a quarter (25.5%) of all poor individuals in the country live in the province (Armstrong *et al* 2008). In a deprivation ranking of all South African districts, eThekwini lies within socio-economic quintile 4, and Uthungulu in socio-economic quintile 2 (where quintile 5 is least deprived, and quintile 1 is most deprived) (Day *et al* 2009: 2). Within eThekwini however, are large areas of deep poverty, such as informal settlements and former townships. It is in these areas of the city that the study was conducted.

Figure 1: Map of KwaZulu-Natal

(Source: GIS Unit, KwaZulu-Natal Provincial Department of Health, August 2012).

Methods

Trial design

This was a pragmatic, open, two-arm cluster randomized controlled trial, using primary health care clinics as clusters.

Nested within the controlled trial was a process evaluation, which consisted of two parts: an assessment of how participants responded to the vouchers (reported in Chapter 4), and an assessment of the impact of the voucher on patients' household economies (reported in Chapter 5).

Study setting and participants

Clinics

Public sector (government-funded) primary care clinics were chosen for this study, since these treat the majority of patients with TB in South Africa. These clinics are managed by professional nurses, and staffed by nurses of all grades.

Clinics with cure rates of between 40% and 70% for the year preceding the trial were eligible for inclusion in the study. The upper limit was set because demonstrating a clinically meaningful effect in clinics with cure rates higher than 70% would have required a very large sample size. The lower limit was set to reduce between-clinic variability and to exclude clinics where poor service provision and systemic weaknesses may have contributed to poor treatment success rates. In addition, only clinics seeing between 20 and 150 new smear positive TB patients per year were eligible for inclusion. The lower limit was set in order to meet the sample size

requirements of the trial, and the upper limit was set because implementing the intervention in very large clinics would have exceeded the limited budget of this trial.

Patients

All patients diagnosed with pulmonary TB that was considered to be sensitive to routine TB treatment, and attending intervention clinics within the period 01/07/2009 to 31/03/2010 were recruited into the trial; however, only patients who started TB treatment within this recruitment period were eligible for analysis. Patients were followed up to the end of their treatment (which is a maximum of six months in new cases and eight months in re-treatment cases). Both adults and children were included in the analysis because, as a high burden country, there are a significant number of children receiving treatment for TB in South Africa (Marais *et al* 2006).

Intervention

A voucher, valued at ZAR 120 (approximately $US 14.60 at the start of the trial) was offered to patients by nurses every month on collection of their treatment, to a maximum of eight months. A copy of a voucher is presented in Appendix 3B.

The vouchers were redeemable at specific general stores, chosen by the nurses at each participating clinic on the basis of their proximity to the clinic and the relative costs of their goods. At the request of TB programme managers, patients were advised by clinic nurses to spend the vouchers on healthy foodstuffs; however, nurses did not monitor their expenditure

and the stores were asked to allow patients to purchase any goods up to the value of the voucher.

Patients at control clinics received usual TB care.

Pilot study

The voucher and its administration were piloted in two clinics (one rural, one urban) prior to the trial. On the basis of the pilot study, minor modifications to the trial methodology were made. Specifically, since it was found during the pilot that many patients did not possess identity documents (ID books), the recording of a patient's identify number on the voucher was no longer mandatory in the main trial. However, the presentation of a patient's clinic book[5] was made mandatory, to confirm the patient's identify and eligibility for receipt of the voucher.

Support from study team for voucher delivery

Prior to the inception of the trial, the principal investigator and her assistant showed the TB nurses at each intervention clinic how to administer the voucher. Each nurse was given a study information sheet containing this information (see Appendix 3C). If nurses were replaced, outgoing nurses explained the process to new nurses and this was reinforced by an additional visit from the principal investigator. Nurses were able to telephone the principal investigator at any time to discuss queries about the voucher or its delivery. The principal investigator and her

[5] The patient's clinic book is a patient-held document that lists his or her diagnosis, treatment, clinic visits and, in the case of TB, number of doses of medication taken as verified by a DOTS supporter (a community-based lay health worker who supports TB treatment adherence).

assistant visited each intervention clinic every four to six weeks to collect the voucher receipts from the TB nurses and to discuss any problems that might have arisen in the trial.

Similarly, managers of participating shops were shown how the voucher was to be used at the outset of the study. Managers were responsible for training cashiers in the use of the voucher. Shops were visited by the principal investigator and her assistant every four to six weeks and at these visits, any problems with the administration of the voucher were discussed.

Logistics of voucher delivery

Nurses at intervention clinics were supplied with voucher books consisting of 100 vouchers each. In order to receive a voucher, patients were required to come to the clinic on the dates stipulated by the nurses, and also to present their clinic books with verification of adherence by their DOTS supporters. Pill counts were done by nurses if adherence was in doubt.

Each voucher had a unique number and consisted of three copies (pink, yellow and green). The vouchers were carbonised so that the information entered by the nurse onto the top copy would appear on two other copies below. The nurse entered the patient's name, gender, ID number and clinic number on the voucher, signed it and stamped the top copy with the clinic stamp. A unique sticker was placed on each voucher, without which it could not be redeemed, to minimise the risk of fraudulent copies of vouchers being made and used. The nurse gave the patient the top two copies of the voucher and kept the third copy at the clinic.

The patient took the two copies of the voucher to the designated shop and exchanged these for goods. Both copies of the voucher were retained by the shop. Every four to six weeks, the

principal investigator collected one copy of the vouchers from the shop, and used these to calculate the amount owed to the shop for goods purchased. This amount was deposited into the shop's bank account by electronic transfer. The shops kept one voucher copy for their own records.

In order to prevent "leakage" of vouchers to patients who were not eligible to receive them (Lagarde *et al* 2009), patients were asked to present their ID books, if available, and clinic books on redemption of the vouchers; these were presented on the patients' behalf if relatives or friends redeemed vouchers for very sick patients. Vouchers had to be redeemed within one month of acquisition, and could not be exchanged for cash. No change was given by the shops if the full amount was not spent, although patients could supplement the vouchers with their own cash. The till slips, or written lists, indicating the purchases made and their prices, were attached by cashiers to the redeemed vouchers and collected with the vouchers by the principal investigator. The vouchers collected from the shops were tallied with those collected from the clinics. Each voucher received from the clinics and redeemed from the shops was linked with individual patient data, so that for each patient the number of vouchers received and redeemed was ascertained.

The data on patient purchases was analysed and is reported in Chapter 5.

Ethics and consent

Ethical approval for the trial and its process evaluation was received from the Committee for Human Research at the University of Stellenbosch (reference N07/10/245) (see Appendix 3D). Permission to conduct the trial was received from the KwaZulu-Natal Provincial Department of

Health, the eThekwini and Uthungulu District Offices, the Health and Safety Sub-Committee of elected City Counsellors and the Research Committee of the eThekwini Municipality, the traditional leaders of the *isigodi* (wards) where rural clinics were situated, and the sisters in charge at individual intervention clinics. Although all participants in the main trial were informed verbally and in writing of the study, individual written consent from patients in intervention clinics was not sought, as acceptance of the voucher was interpreted as consent. Waiver of written informed consent from patients in intervention clinics was sought from and approved by the Committee for Human Research at the University of Stellenbosch before the trial started.

Individual written informed consent was obtained for all participants in the process evaluation sub-studies of the trial, in the language of their choice (either isiZulu or English) (see English versions in Appendices 3E and F).

Registration

This trial is registered with Current Controlled Trials (reference ISRCTN50689131), the South African Clinical Trials Registry (reference DOH-27-0409-2791), the Wellcome Trust Register of Clinical Trials (reference 083619), and the Pan African Clinical Trials Registry (reference PACTR2010010001275437).

The trial protocol is presented in Appendix 3G.

Outcomes

The primary outcome was TB treatment success, defined as the sum of those patients cured and those completing treatment. Secondary outcomes were default and treatment failure rates. Data on other routine TB treatment outcomes were also collected, as described below. The World Health Organisation definitions for these outcomes, which are used in South African clinics and were used for the purposes of this study, are as follows:

TREATMENT SUCCESS: "A patient who was cured or who completed treatment" (WHO 2009b)

CURED: "A patient who was initially smear-positive and who was smear negative in the last month of treatment and on at least one previous occasion" (WHO 2009b)

COMPLETED TREATMENT: "A patient who completed treatment but did not meet the criteria for cure or failure". This definition applies to pulmonary smear-positive and smear-negative patients and to patients with extra-pulmonary disease (WHO 2009b)

TREATMENT INTERRUPTION: "Cessation of treatment for less than two months" (WHO 2007)

TREATMENT FAILURE: "A patient who was initially smear-positive and who remained smear-positive at month 5 or later during treatment" (WHO 2009b)

DEFAULTED: "A patient whose treatment was interrupted for 2 consecutive months or more" (WHO 2009b)

DIED: "A patient who died from any cause during treatment" (WHO 2009b)

TRANSFERRED OUT: "A patient who transferred to another reporting unit and for whom the treatment outcome is not known" (WHO 2009b)

MDR TB: Infection with bacilli resistant to at least rifampicin and isonizid treatment (WHO 2007b).

TB treatment outcomes were ascertained by participating clinics using their usual procedures. In smear positive patients, this was done through sputum microscopy and culture after six or eight months of treatment (in the cases of new and re-treatment patients respectively). In smear negative patients, where initial diagnosis is based on chest x-rays and clinical signs, cure cannot be determined and treatment completion is the outcome used (Department of Health 2009). In keeping with its pragmatic nature, no additional clinical investigations were performed for the purposes of this trial.

Data on factors that have been shown to impact on adherence to treatment (Kipp *et al* 2011, Munro *et al* 2007a) were also collected. These factors were age, gender, employment status, type of TB and HIV status (determined by PCR or ELISA tests).

Clinic TB registers and individual patient files (held at the clinics) were the main sources for all these data. Patient files are completed by the consulting nurse, and clinic registers are completed in many cases by a clerk attached to the TB programme in the clinic. The latter are checked by the nurse or sister in charge of TB at the clinic. In a few small clinics, where clerks are not available, this record keeping is done by the nurse working in TB. In this study, the clinic register was the primary source of data. Patient files were used to fill in missing data for any patients whose information in the clinic registers was incomplete. Data obtained from clinic registers was checked for accuracy by comparing the outcomes obtained with those in a sample

of individual patient files. A ten percent random sample of data from the total trial population was checked. This was done by randomly identifying a starting point on the trial database, and retrieving every tenth patient file for those patients from the clinic.

Statistical methods

Sample size

At the time of the study, there were a total of 144 clinics in the urban, and 68 clinics in the rural district, providing TB care. A list of those clinics meeting the inclusion criteria was constituted. Twenty one clinics in the urban and five in the rural district were eligible for inclusion.

An intra-cluster correlation co-efficient (ICC) of 0.03 was calculated based on pre-trial data from the clinics. To detect a 15% difference in treatment success rates (which we felt would be the minimum required to influence policy), based on a power of 90%, at a significance level of 5% (two sided test) and an average cluster size of 100, 18 clinics were necessary. Twenty clinics were however included in the sample, to allow for clinic drop out during the trial.

Randomisation

The 20 study clinics were randomly selected from the 26 eligible clinics stratified by district (21 in eThekwini and 5 in Uthungulu). Sixteen study clinics were selected in the urban and 4 in the rural district. Within the two districts the study clinics were randomly assigned in a 1:1 ratio, using a randomisation list generated by the study statistician.

Clinics were allocated to intervention or control groups by the study statistician and no changes were made to this allocation. Staff in all clinics were aware that they were part of a trial to test the effectiveness of a voucher.

Clinics were enrolled by the principal investigator, and participants within the clinics were enrolled by the nurses in charge of TB care at each clinic.

Blinding

Because of the nature of the intervention, no blinding was possible in this study. Data extractors were not blinded as it was considered neither practical nor feasible to conceal from them the intervention status of the clinics from which they collected data.

Analysis

Analysis was by intention to treat (ITT) and patient level data was used for this purpose.

For the binary study outcome (treatment success achieved, not achieved) a generalised linear model (GLM) was used to evaluate the intervention effect with adjustment for the stratification of clinics at randomisation. The clustering effect of clinics was taken into account through cluster robust variance estimation.

An exploratory analysis was also done for the primary outcome, in order to assess the effect of the voucher on patients in intervention clinics who actually received it. This analysis was based on a “per protocol” analysis. Although in a strict per protocol analysis, only patients who received a voucher every month in their treatment period would be included, in this

exploratory analysis we included all patients in the intervention group who had received at least one voucher. The control group remained unchanged.

As an ancillary analysis of the ITT study population, a multiple regression model (GLM) was used to investigate the impact of adjusting for selected covariates on the estimated intervention effect. The covariates included in this model were employment status, whether the participant was a minor, whether the TB type was smear positive or diagnosed clinically or on x ray, and gender. The model was evaluated for interaction effects between the intervention and any of the covariates.

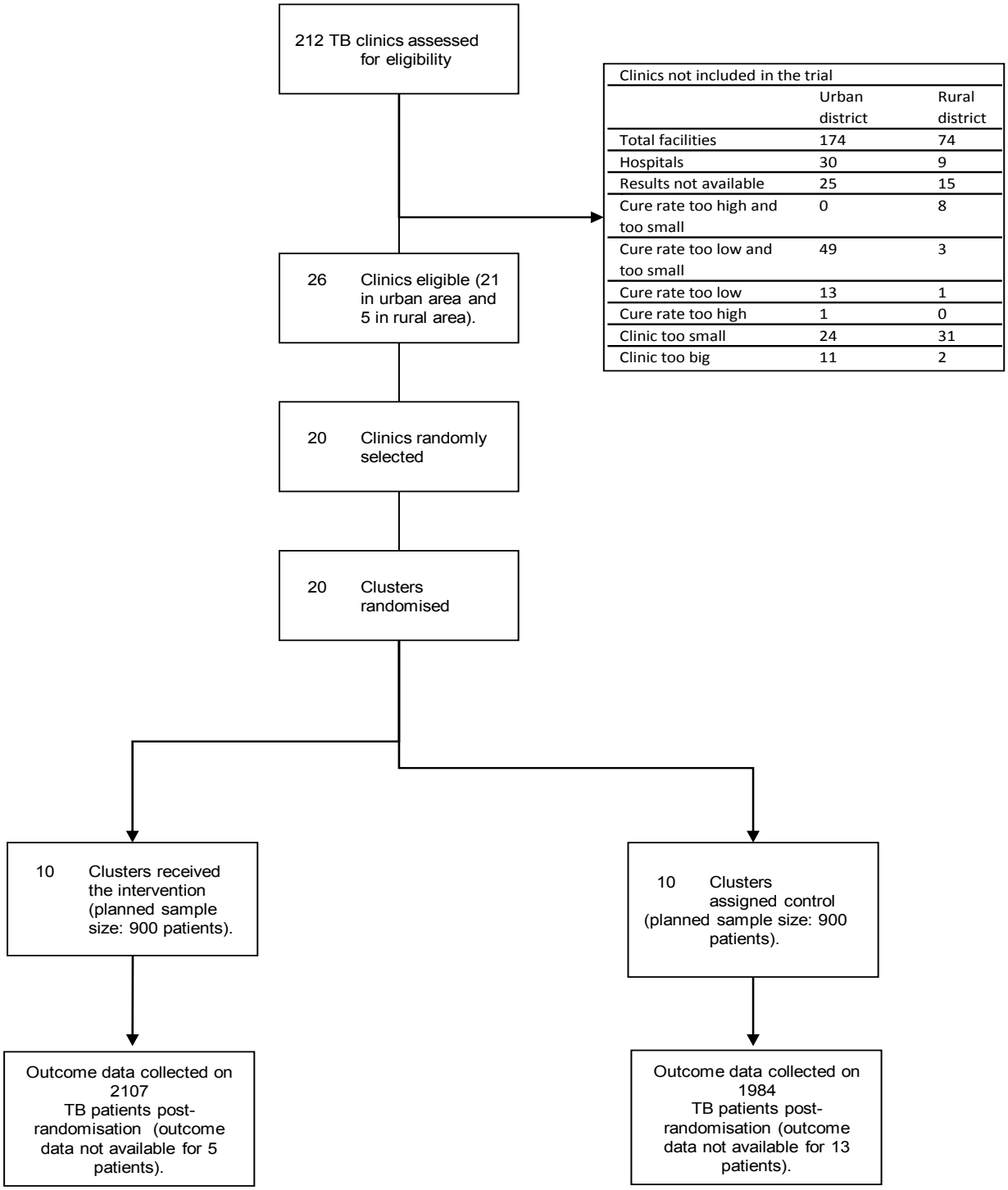
A further secondary analysis was done to test for a dose-response effect in the intervention arm. The study outcome was evaluated against the number of months the participant had received a voucher. The GLM approach was used for this purpose (McCullagh and Nelder 1989).

Results

Participant flow

As seen in the following flow chart, there was no loss of clinics in the trial, and all eligible patients in each clinic were included in the analysis. Loss to follow up was small, with outcome data unavailable on 0.2% of patients in intervention clinics and 0.7% of patients in control clinics.

Figure 2: Participant flow diagram



Clinics not included in the trial

	Urban district	Rural district
Total facilities	174	74
Hospitals	30	9
Results not available	25	15
Cure rate too high and too small	0	8
Cure rate too low and too small	49	3
Cure rate too low	13	1
Cure rate too high	1	0
Clinic too small	24	31
Clinic too big	11	2

Recruitment

Recruitment of patients took place over eight months (July 2009 to March 2010 inclusive). Patients who started treatment during this period were followed up to the end of their treatment. The trial ended on 30/09/2010, when the last recruited patients completed their full course of treatment.

Numbers analysed

A total of 4091 patients were included in this study, 1 984 in the control arm and 2 107 in the intervention arm. The number of patients enrolled by clinics varied between 68 and 335.

Baseline data

The baseline characteristics of the two groups are presented in a comparative table (Table 1).

Table 1: Baseline characteristics of trial cohorts*

	Intervention clinics	**Control clinics**
Total number of trial participants	2 107	1 984
Minimum number of participants per clinic	122	68
Maximum number of participants per clinic	335	335
Mean age of participants	29 years	32 years
Number (percentage) of male participants	1058 (50.2%)	1069 (53.9%)
Number (percentage) of participants in rural district	266 (12.6%)	167 (8.4%)
Number (percentage) of HIV positive participants	910 (68.0%) (1338 patients for whom a record of HIV testing was available)	1106 (73.0%) (1515 for whom a record of HIV testing was available)
Number (percentage) of unemployed participants	1 081 (60.2%)	1 228 (66.2%)
Number (percentage) of child participants (less than 13 years)	386 (21.5%)	251 (13.5%)
Number (percentage) of smear positive participants	903 (42.9%)	882 (44.5%)

* Data on HIV status and employment were not available for all patients.

Primary Outcomes

Intention to treat analysis showed a small and non-significant improvement in treatment success rates in the group receiving the vouchers. Exploratory analysis[6] however showed a significant improvement in treatment success rates in the intervention arm (Table 2).

Table 2: Primary outcome (treatment success) – intention to treat and exploratory analyses

Outcome	**Intervention group (%)**	**Control group (%)**	**Risk difference (%) (95% confidence interval) ‡**	**p-value**
Treatment success: Intention to treat analysis	1 606/2107 (76.2)	1 402/1984 (70.7)	5.6% (-1.2; 12.3%)	0.107
Treatment success: Exploratory analysis	1 051/1294 (81.2)	1 402/1984 (70.7)	10.6% (3.7; 17.5%)	0.003

† The estimated ICC for our study for the primary outcome was .033. This is very close to the ICC assumed in the sample size calculation (.03).

‡ Estimate from GLM model.

There was greater variability in the outcomes of clinics in the control arm compared to the intervention arm. There were four clinics in the intervention arm with treatment success rates of more than 80%, compared to only two in the control arm, and three clinics in the control arm with treatment success rates of less than 65% compared to none in the intervention arm (Table 3).

[6] The exploratory analysis was a modified per protocol analysis, where all patients who received at least one voucher were compared to the control group.

Table 3: Treatment success per clinic for intervention and control clinics (intention to treat analysis)

Intervention clinics			**Control clinics**		
Clinic	*Treatment success (%)*	*Other TB outcome (%)*	*Clinic*	*Treatment success (%)*	*Other TB outcome (%)*
1	202 (80.16)	50 (19.84)	1	88 (89.80)	10 (10.20)
2	238 (78.55)	65 (21.45)	2	99 (52.66)	89 (47.34)
3	198 (68.99)	89 (31.01)	3	112 (58.03)	81 (41.97)
4	198 (68.99)	89 (31.01)	4	240 (71.64)	95 (28.36)
5	83 (68.03)	39 (31.97)	5	204 (73.81)	72 (26.09)
6	274 (81.79)	61 (18.21)	6	159 (68.24)	74 (31.76)
7	82 (66.67)	41 (33.33)	7	140 (72.16)	54 (27.84)
8	183 (81.33)	42 (18.67)	8	233 (77.67)	67 (22.33)
9	106 (83.46)	21 (16.54)	9	85 (85.86)	14 (14.14)
10	104 (74.82)	35 (25.18)	10	41 (60.29)	27 (39.71)

Secondary outcomes

The treatment completion rates of patients in the intervention arm were almost ten percent higher than those in the control arm; however, the cure rates of patients in the intervention arm were slightly lower than those in the control. Default, treatment interruption and treatment failure rates were all lower in the intervention arm (Table 4).[7]

Table 4: TB treatment outcomes for patients in intervention and control clinics

Treatment outcome	**Intervention group (%) (n=2107)**	**Control group (%) (n=1984)**	**Total (%)**
Treatment completed	911 (43.2)	694 (35.0)	1605 (39.2)
Cured	695 (33.0)	708 (35.7)	1403 (34.3)
Defaulted	158 (7.5)	202 (10.2)	360 (8.8)
Treatment interrupted	0 (0.0)	15 (0.8)	15 (0.4)
Treatment failure	79 (3.8)	113 (5.7)	192 (4.7)
MDR TB	1 (0.1)	3 (0.2)	4 (0.1)
Died	151 (7.2)	137 (7.0)	288 (7.0)
Moved/transferred	107 (5.1)	99 (5.0)	206 (5.1)
No outcome data available	5 (0.2)	13 (0.7)	18 (0.4)

[7] Because most data were extracted from clinic registers, the reasons for default and the causes of death were not available.

Ancillary analysis

All patients were included in this analysis, although data on HIV status were missing for 1252 patients.

The intervention effect shown (4.2%) is slightly smaller than in the unadjusted intention to treat analysis (of 5.6%). Thus about 1.5% of the intervention effect in the unadjusted analysis can be explained by differences in the intervention and control clinics.

Patients who were unemployed had significantly lower treatment success rates than those who were employed. Children under the age of 13 had significantly better treatment success rates than those over 13 years, and women had better rates than men. Patients with smear positive TB had significantly better treatment success rates than those with smear negative TB, whilst patients on re-treatment (after default, completion or failure) had significantly lower treatment success rates than new patients. HIV positive patients had significantly lower treatment success rates compared to those who were HIV negative. No significant interactions between any of these sub-groups were found (Table 5).

Table 5: Regression model showing patient characteristics associated with treatment success (GLM model)

Patient characteristic	Number	Risk difference	95% confidence interval	P-value
Intervention group indicator	4091	0.042	-0.024; 0.109	0.211
Unemployed	3650	-0.052	-0.094; -0.009	0.017
Child	3650	0.058	0.008; 0.107	0.024
Smear positive TB	3614	0.043	0.01; 0.076	0.011
Re-treatment (versus new cases)	4084	-0.110	-0.16; -0.076	<0.001
HIV positive (versus HIV negative)	2839	-0.052	-0.083; -0.021	<0.001
Female	4076	0.043	0.023; 0.063	<0.001
Intercept*		0.718		

*The intercept represents the outcome in the control arm when all other covariates = 0.

Adherence to the intervention

Of all 2076 patients who were eligible to receive a voucher for the six to eight months of their treatment, 813 (36.2%) did not receive a voucher at all, and 671 (32.3%) received a voucher for between one and three months. The remainder received a voucher for four to eight months of treatment. In many cases, nurses in intervention clinics gave vouchers to those patients they considered more needy (process evaluation, reported in Chapter 4). This preference for giving vouchers to patients who were relatively more deprived is illustrated in an analysis of eligible patients who received at least one voucher, compared to eligible patients who didn't receive any vouchers at all (Table 6). There were significantly more unemployed patients in the group

that received vouchers (p = 0.04), whilst there were significantly fewer children in the group that received vouchers (p = 0.03). In addition, women were more likely to receive vouchers than men (p = 0.026).

Table 6: Comparison of eligible patients who received vouchers with eligible patients who did not[8]

Received at least one voucher	**Employed (%)**	**Children (%)**	**Pensioner (%)**	**Student (%)**	**Unemployed (%)**	**Total (%)**
No	117 (17.06)	178 (25.95)	12 (1.75)	2 (0.29)	377 (54.96)	686 (100)
Yes	172 (15.82)	202 (18.58)	16 (1.47)	6 0.55	691 (63.57)	1,087 (100.00)

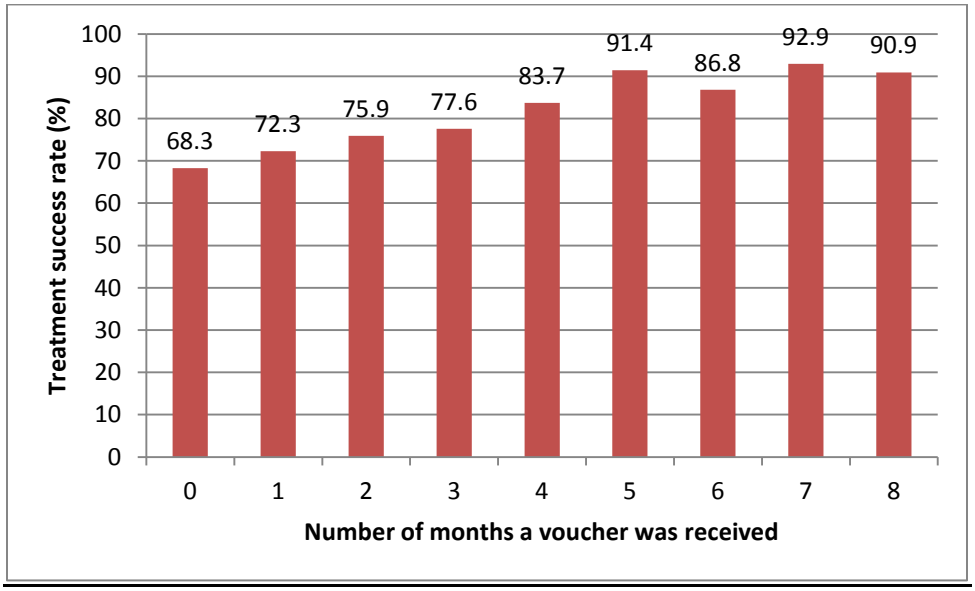
Another reason for the failure of eligible patients to receive a voucher every month may have been that nurses did not always give patients vouchers on the days that they came to collect their TB tablets. In some cases, this was because new voucher books had not yet been delivered to the clinics by the investigators, and in other cases it was because nurses preferred to give all vouchers out at month end (process evaluation, reported in Chapter 4).

[8] The patients analysed in this table represent the sub-set of trial patients for whom data on employment status was available.

Dose-response analysis

There was a strong dose-response effect (p<0.001) (Figure 2). The treatment success rate of patients who did not receive any vouchers was 68.3%, compared to a rate of more than 90% in patients who received a voucher for five months or more.

Figure 3: Effect of increasing frequency of vouchers on treatment success rate



Adverse events

The adverse events investigated in this study were those related to the voucher, and not to the clinical consequences of TB or its treatment. Specifically, there were very few reports of patients spending the vouchers on alcohol or cigarettes (assessment of expenditure of vouchers, reported in Chapter 5), very few reports of leakage of vouchers, and no reports of coercion of staff by patients to give them a voucher (process evaluation, reported in Chapter 4).

Other adverse events are discussed in more detail in the first part of the process evaluation (reported in Chapter 4) but are outlined briefly here. Some patients reported in interviews that when relatives or friends had redeemed vouchers on their behalf, the relatives had not given them (the patients) the goods. Finally, those patients who did not receive the vouchers (that is, those with extra-pulmonary TB) expressed varying degrees of anger about this, both to clinic nurses and to the principal investigator (process evaluation, reported in Chapter 4).

Discussion

This was the first trial in Africa to investigate the effect of economic support (a monthly voucher) on TB outcomes. The trial found a 5.6% improvement in treatment success rates among patients who received the voucher, meaning that for every 1000 patients who received the voucher, an additional 56 would have achieved treatment success. This was lower than the 15% difference that the study was powered to detect, which explains in part, the failure of the trial to achieve a significant result. This failure may be further explained by low fidelity to the intervention, which is discussed further in the process evaluation described in Chapter 4. The exploratory analysis, which compared patients who had received at least one voucher in intervention clinics to the control group, showed significantly higher treatment success rates in intervention compared to control clinics. A powerful dose-response effect was also demonstrated, with patients who received vouchers more frequently being more likely to complete treatment. These analyses are discussed further below.

Although we expected that the voucher would incentivise patients' clinic visits, our main aim in providing it was to make adherence easier by ameliorating two features of poverty which are

commonly associated with TB: under-nutrition and limited access to health care (Hargreaves *et al* 2011). We hypothesised that the voucher (if used for purchasing food) could have improved patients' food security and released household funds for use elsewhere, such as for transport to the clinic (Munro *et al* 2007a). In 2008, 71% of the households in KwaZulu-Natal lived on less than 40% of the median per capita income of R569.00 per month (Hall 2010). Thus, like conditional cash transfers, it would have served both as an incentive and as an enabler to access TB care.

Some randomised controlled trials have tested the effects of economic incentives in the context of TB. However, in the Cochrane review reported in Chapter 2, only one included trial focused on participants with active TB. In that study (conducted in a low income country), nutritional (food) support to patients on TB treatment had no effect on treatment completion rates (Martins *et al* 2009). Other non-randomised studies investigating the use of financial incentives in patients with active TB have had varying results. One such project in China where both patients and providers received cash incentives, showed no impact on TB outcomes (Yao *et al* 2008). A second project in Cambodia, where patients with TB received nutritional supplementation and participated in a microfinance programme, showed improved cure rates in the intervention group (Thim *et al* 2004). Although several large conditional cash transfer programmes show positive effects on household food security and access to health care, their effect on TB outcomes has not been measured (Boccia *et al* 2011). To our knowledge, no studies have tested the impact of economic support on TB outcomes in Africa, where the burden of TB is among the highest in the world and where poverty is extensive.

Social and economic interventions to strengthen TB control are rare (Hargreaves *et al* 2011). In South Africa, patients with TB may be given food parcels when they collect their treatment, and may also be eligible to receive a disability grant. Although data on receipt of food parcels and disability grants are not recorded in the TB registers at South African clinics, and were therefore not collected in this trial, we expect that, due to randomisation, the proportions of patients receiving them would be the same across intervention and control clinics.

In our study, the lack of a statistically significant effect in the intention to treat analysis may be due in part to the low fidelity to the intervention. It is likely that eligible patients who did not receive any vouchers at all were considered by nurses not to need them. Nurses in the trial, who are used to rationing food supplements to those patients whom they consider most needy, tended to give vouchers out in the same way (process evaluation, reported in Chapter 4). This is supported by the finding that unemployed patients in intervention clinics were more likely to receive vouchers than patients who were employed. Interestingly, eligible children were less likely to receive vouchers than adults, and although this seems surprising, it must be noted that the majority of these children would have been in receipt of a child support grant. One of the criteria reported by nurses for not giving vouchers to eligible patients was their receipt of other forms of state grants (process evaluation, reported in Chapter 4).

Eligible patients who received the vouchers only sometimes (as opposed to every month of treatment) may have been asked to make an additional visit to the clinic to collect the vouchers, either because the new voucher books had not yet arrived at the clinics, or because nurses preferred to give vouchers out at the end of the month (process evaluation, reported in

Chapter 4). This may have been difficult for some patients, either because they were too sick or too busy to travel or could not afford to travel. More rigorous monitoring of our intervention may have improved fidelity, and made it easier for a trial of this size to detect a significant effect (Oxman *et al* 2009). However, an important aim of this pragmatic trial was to assess the feasibility of administering such vouchers under normal public sector clinic conditions (process evaluation, reported in Chapter 4) (Zwarenstein *et al* 2008).

In a similar way to a per protocol analysis, the exploratory analysis attempted to estimate what effect the voucher might have had, if it had been administered closer to the way in which it was intended (Thorpe *et al* 2009). The patients in intervention clinics who received a voucher at least once were likely to be systematically different from the patients in intervention clinics who received no vouchers, and so not only is the potential bias in this exploratory analysis acknowledged, it can also to a certain extent be described (Zwarenstein *et al* 2008). The patients who received the vouchers were more likely to be unemployed and more deprived, than those who did not, because of the nurses' sense that it was unjust to give the vouchers to patients who needed them less (process evaluation, reported in Chapter 4). The analysis suggests that, in patients who received them, the vouchers did have a significant effect on treatment outcomes. Although the intention to treat analysis is presented as the main and most important finding of this trial, the exploratory analysis is included because it adds possible explanatory detail to the trial, and because it raises questions for further research. These questions, and others arising from this trial, are discussed in Chapter 6.

The findings of the dose response analysis support those of the exploratory analysis by suggesting that these vouchers have the potential to significantly improve outcomes on TB treatment. The fact that the sub-groups of patients who received the vouchers more frequently achieved significantly better TB outcomes than those who received it less frequently, implies that higher fidelity to the intervention, with delivery of the voucher to all eligible patients, may produce a significant benefit. In addition, the dose-response analysis argues against a perverse incentive effect of the voucher. If patients did try to remain ill in order to continue receiving the voucher, treatment success rates would have fallen with frequency and duration of receipt. This is an important finding, given the local and global concern about this unintended consequence of conditional cash transfers, economic incentives and results-based financing (Oxman and Fretheim 2009). However, a caveat to the interpretation of this dose reponse analysis is that it is possible that patients who attended clinics more regularly were more likely to receive vouchers, making it difficult to differentiate cause and effect. The possibility of reverse causality cannot be ruled out here and should be investigated in further trials in this field.

In this study, the conditionality (of adhering to TB treatment) appeared not to be difficult to enforce. Nurses were able to confirm that patients were indeed taking their tablets (and not just collecting them) by checking their clinic books, which DOTS supporters notated every time patients took their tablets. Although this method is not fool-proof, the data on TB outcomes support the idea that the conditionality of the trial was adhered to. This finding is an important contribution to the debate around the provision of social grants in South Africa. Concerns have been raised that the child support grant encourages teenage girls to fall pregnant in order to receive the grant (Makiwane *et al* 2006), and that the disability grant for HIV leads patients to

try to remain ill in order to continue receiving the grant (Yoder *et al* 2009). Such behaviour was not seen in this study. Although other studies of incentives programmes in health care have shown a range of adverse events (Oxman & Fretheim 2009), many of these were not found in this study (process evaluation, reported in Chapter 4).

Sub-group analysis showed that treatment success rates were better in women, patients who were employed, children under 13 years of age, and smear positive patients. Although such results are not found in all settings, they do reflect the findings of many other studies in Africa and elsewhere. In the African (Mature *et al* 2011) and South African contexts (Brust *et al* 2010), women have been shown to have better adherence to TB treatment than men. However, women in some settings may need to seek permission to attend clinics and may therefore have poorer adherence than men (Munro *et al* 2007a). In our study, employed patients were better off financially than those who were unemployed (assessment of patient poverty, reported in Chapter 5). The poorer outcomes of unemployed patients are reflected in the findings of several studies in Africa and elsewhere, where low income has been shown to be associated with poorer adherence to TB treatment (Munro *et al* 2007a, Muture *et al* 2011). In our study, children younger than 13 years had better outcomes on treatment than those older than 13. Although in some contexts adherence of children to TB treatment is low (Alperstein *et al* 1998, Guwatudde *et al* 2003), in South Africa, adherence of children has been shown to be high (van Zyl *et al* 2006). Finally, smear positive TB was associated in our study with better outcomes on treatment. A possible explanation for this is that these patients are less likely to be infected with HIV, which has been identified as an independent risk factor for default from TB treatment (Muture *et al* 2011, Brust *et al* 2010).

Limitations of the trial

This was a pragmatic trial, and so adherence to the intervention was not rigorously controlled. This resulted in approximately one third of eligible patients not receiving a voucher at all. An important limitation of the trial is that the contribution of various factors to this low fidelity was not quantified. These factors included the preference of nurses to give vouchers to patients who were more deprived, as well as the logistical issues involved in giving eligible patients their vouchers on their clinic appointment days. It was important for this trial to have a pragmatic nature because it answered questions relating to the feasibility of implementing economic support for patients with TB in South Africe. However, future research should investigate the extent to which different variables impact on the delivery of such support, and quantify their individual impact.

Adherence to treatment in this trial was measured by public sector clinics in their usual manner. Although DOT supporters indicated on patients' clinic books each time tablets were taken, no intermediate objective measures of adherence were made by the investigators, with the result that it is not known whether patients actually took their tablets as prescribed. However, given that the primary outcomes of the trial were dependent on adherence to treatment during the trial, additional measures of adherence are unlikely to have added much value to the findings.

At the time of the trial, TB and HIV services were run in separate parts of the clinic and significant numbers of TB patients were either not tested for HIV or their test results were not recorded in the TB register. Since a high proportion of TB patients in this trial and in KwaZulu-

Natal are also infected with HIV (Corbett et al 2003), and since the effects of poverty on adherence may be compounded by HIV (Weiser et al 2010, Anema et al 2009), this was an important limitation of the study.

We are not sure of the mechanism of action of the voucher in improving patient outcomes. Analysis of the impact of the voucher on patients' household expenditure (reported in Chapter 5) suggests that it did not significantly improve the economic well-being of patients' households. However, qualitative analysis (reported in Chapter 4) suggests that it did enable patients to buy more food with which to take their tablets, which many described as very helpful. An additional limitation of the trial however, is that the nutritional status of patients, and the effect of the voucher on this, were not assessed.

Most clinics and patients in the trial were situated in urban areas because relatively few rural clinics met the trial's inclusion criteria. Thus the extent to which the results of this trial can be generalised to rural areas may be limited.

Conclusions

This pragmatic cluster randomised trial which compared economic support for TB patients against usual care and was conducted in the real world setting of public sector clinics in South Africa, found no significant difference in treatment success rates between intervention and control clinics. Our findings suggest that factors related to the administration of such support may undermine its effectiveness. The low fidelity to the delivery of this voucher meant that only a third of all eligible patients received it for four months or more. However, among patients in intervention clinics who received the voucher at least once, treatment success rates

were significantly improved compared with rates in the control group. Further, in the intervention arm the more frequently the vouchers were received by patients, the higher their probability of treatment success. Further operational research is needed to explore how best to ensure the consistent and appropriate delivery of such support to those eligible to receive it, and to investigate whether, under conditions of higher fidelity, the extent of the benefit on treatment outcomes found in this study can be increased.

Chapter 4

Process evaluation (part one): A qualitative analysis of participants' responses to the voucher and its administration

Introduction

This chapter presents the findings of the first part of the process evaluation of this trial. It reports on the conduct and analysis of qualitative, in-depth interviews with all groups of participants in the trial: patients, nurses at intervention clinics, shop personnel, and managers of the TB programme at district, provincial and national level. This chapter is central to the assessment of the feasibility of delivering economic support to patients with active TB in public sector clinics in South Africa, and provides important information that helps to explain the findings of the main trial.

Background

Although randomised controlled trials provide high quality evidence for the efficacy or effectiveness of an intervention, they do not provide contextual information that might explain the findings of the trial. Such information is particularly important in pragmatic trials, where the real world settings in which interventions are delivered may have a profound impact on the conduct and the findings of the trial. This information may be provided by qualitative research

conducted alongside trials of such interventions (Lewin *et al* 2009). Such research can provide insight into issues which are not amenable to quantitative investigations, and which may be important for the replicability of trials, or for the large-scale implementation of the interventions tested therein (ibid). However, in spite of the recognition of the value that qualitative research adds to the conduct of a trial (Oakley *et al* 2006), such research is seldom conducted. In a recent review, it was found that less than a third of recently completed trials in the Cochrane Effective Practice and Organisation of Care register had a qualitative component, and all of those that did had been conducted in high income countries (Lewin *et al* 2009).

The importance of investigating the complexities of the context within which interventions are implemented is also reflected in the discipline of policy analysis. A linear or "top-down" approach to the assessment of the implementation of a policy or intervention views the process of delivery as a rational one influenced only by a set of centrally determined conditions (Sabatier and Mazmanien 1979, quoted in Walker and Gilson 2004). However, the "bottom-up" perspective sees such implementation as a dynamic and complex process which is directly and significantly affected by those who are required to implement the policy (Walker and Gilson 2004). Indeed, the bottom up approach sees the gap between the policy as planned and the policy as implemented not so much as policy failure but as a demonstration of how policy is "recreated through the process of implementation" (Hill 1997, quoted in Walker and Gilson 2004).

Process evaluations attempt to view the implementation and receipt of an intervention from the perspective of the implementers and the recipients, and use both qualitative and

quantitative methods to analyse the contributions of a variety of factors to the effectiveness, or otherwise, of an intervention (Oakley *et al* 2006). Importantly, where an intervention is not effective, process evaluations can help to ascertain whether it is the intervention itself that is inherently flawed, or whether the way in which it was delivered undermined its effectiveness (Rychetnik *et al* 2002). The following two chapters of this thesis (Chapters 4 and 5) constitute a process evaluation of the delivery and receipt of the voucher. The current chapter is a qualitative analysis of interviews conducted with a sample of participants in the trial, including patients, nurses, managers of the TB programme and shop personnel. Chapter 5 is an analysis of the economic status of patients' households and the effect of the vouchers on their expenditures.

As various models show, health behaviours such as adherence are complex phenomena, particularly for chronic conditions, and are dependent on both individual and contextual factors (Munro *et al* 2007b). Changing health behaviour by offering economic incentives or enablers is not necessarily a linear process, even in patients who are poor (Adato *et al* 2011). The responses of patients to economic support is affected by a multiplicity of social, cultural, political and economic factors and may not conform to theories of rational economic behavior (ibid). For example, although conditional cash transfers have had positive effects on health seeking behaviour and some aspects of health itself (Boccia *et al* 2011, Lagarde *et al* 2009) these effects have not been uniform and in some communities, uptake of certain health services remain poor in spite of the transfers. Qualitative research aims to explain why this may be so (Adato *et al* 2011).

The provision of economic support or incentives to promote health is controversial. In South Africa, where our trial was carried out, there is some opposition to social assistance in general, and in particular to social assistance for those who are ill, because of the fear that such grants will lead to a "culture of dependency" (Surender *et al* 2010). Concerns have also been expressed over recipients' use of social grant monies; many of the politicians and TB managers who were consulted in the planning phases of this trial felt that individuals might spend their vouchers on frivolous or even damaging items, such as alcohol or cigarettes. A final concern is that economic support for vulnerable people may constitute a perverse incentive; that is, it may encourage people to behave in ways that ensure the continuation of such support (Oxman and Fretheim 2009). Where concerns about an intervention are so prevalent, it is crucial that these are explored in studies that extend beyond assessments of effectiveness, to include assessments of how an intervention is implemented and used, and factors that impact on this.

As discussed in Chapter 3, the results of this trial were not significant. It is important to explore the reasons for this, because the level of effectiveness we found may have been influenced at least in part, by the context in which the intervention was delivered (Hawe *et al* 2004) and by the process of implementation itself. Factors that may have affected the implementation of our voucher include levels of programme support, and the prevailing beliefs and attitudes of health care providers and recipients.

Aim:

To explore the views and experiences of stakeholders regarding the voucher system and to examine contextual factors affecting its implementation.

Objectives:

- To investigate the administrative processes involved in delivering the vouchers
- To investigate the opinions of participants on the possible positive and negative aspects of the vouchers
- To investigate which contextual factors affected the implementation of the vouchers
- To investigate whether the vouchers assisted some patients to adhere better to treatment, and if so, how.

Methods

Study design

This was a qualitative study which used in-depth interviews as a tool to gather data.

Qualitative research aims to interpret or understand the world "from the point of view of participants in it" rather than to explain an objective "reality" (Green and Thorogood 2004: 13). It is based on the premise that the external "reality" that governs human behaviour is to a large extent socially constructed (ibid), so that the context in which people live and work affects and is affected by, their attitudes, beliefs and perceptions. Qualitative research is a vital tool for understanding how health is achieved (or not achieved) through, among others, healthy behaviours and the implementation of health systems.

These interviews describe, from the perspective of participants in the trial, the "reality" in which the trial took place and explain, at least in part, how this context influenced its conduct. They enable an understanding of how the participants in the trial perceived and experienced

the voucher, and its role in poverty alleviation and TB control, and explain to some extent how these perceptions and experiences affected their responses to the voucher and so influenced the results of the trial itself.

In this study, semi-structured in-depth interviews were conducted with patients who had received vouchers; nurses who had administered vouchers at intervention clinics; shop owners, managers and cashiers at the shops where vouchers were redeemed; and managers of the TB Control Programme at district, provincial and national level who had been involved in or were well informed about the trial. The research process was iterative, in that follow up interviews were conducted with selected participants to clarify issues raised in the initial interviews, or to discuss new issues that arose during implementation of the voucher system.

Population and sampling

Interviews were conducted with patients and nurses at intervention clinics. Clinics were selected purposefully to represent the range of settings in the trial, so that large and small and urban and rural clinics were included. Nurses in charge of the TB programme at seven out of ten participating clinics were interviewed. At the same clinics, patients were approached to be interviewed if they were receiving the voucher, and if they were attending one of the seven selected clinics on the day on which interviewers were present. Two fieldworkers stayed at the clinics all day, and each interviewed one or two patients every day. A month was spent at clinics conducting patient interviews. Interviews with patients were conducted until thematic saturation was reached.

Seven out of eight shops were included in this sub-study. This ensured that the range of stores participating in the trial, which included large chain stores as well as small owner managed shops, from both urban and rural areas, were represented. Personnel in management positions, who had been involved in the administration of the vouchers, were invited to participate. Four administration managers, one general manager, one owner and one cashier were interviewed.

Three senior TB managers from the two districts and one from the province in which the trial was conducted were interviewed, as well as one senior TB manager from the national level. These managers were selected because of their role in the running of the TB Control Programme, their awareness of the study from its inception, and because they were involved in policy formulation for TB management.

No participants refused to be interviewed.

Table 1: Participant demographic information

Group (number interviewed)	**% urban**	**% female**	**Median age**	**Median level of education**
Patients (29)	62	76	35	Grade 10
Nurses (7)	71	71	40	All professional nurses
Managers in the TB Control Programme (5)		60	49	Data not collected
Shop personnel (7)	71	71	30	Data not collected

All nurses interviewed were professional nurses, with a median nursing experience of 15 years. Patients' median level of education was Grade 10. Sixty nine percent of patients were unemployed, 14% worked in the informal sector, 3% in the formal sector and 14% were too young to work.

Data collection

Interviews with nurses, TB Control Programme managers and shop personnel were conducted face to face, between one researcher and one interviewee. Interviews with patients, which were also face-to-face, were conducted by one research assistant and attended by a second research assistant who managed the audio recorder and took additional notes. Interviews with patients were conducted in their first language, which was isiZulu for all patients participating

in this study. Interviews were audio recorded, transcribed verbatim and translated into English, with the translation checked by the second person who attended the interview. Interviews with nurses, shop personnel and TB managers were conducted in English (the language of training and reporting in KwaZulu-Natal), audio recorded and transcribed verbatim.

Interviews with managers of the TB Control Programme were conducted by the principal investigator, whilst interviews with nurses, shop personnel and patients were conducted by research assistants. This was because it was felt that the latter group of interviewees might feel obliged to give the principal investigator positive responses about the voucher and its system of implementation, given her involvement in the project. Although such constraints were possible in the interviews conducted with managers, they were less likely since TB managers held more senior positions in the health services and so would be on a more equal footing with the principal investigator.

Interviews with patients took place in the clinic grounds, away from the clinic building, or else in an unused room within the clinic, to preserve patient privacy. Interviews with nurses took place in unused consulting rooms or offices at the clinics, whilst those with shop owners, managers and cashiers took place in the administration offices of the shops. Interviews with TB programme managers took place in their offices or at a designated public meeting place.

Research assistants introduced themselves as such to all participants, emphasising that they were from an independent research organisation and not affiliated to the health services. Research assistants transcribed and translated (where necessary) the interviews they had conducted, and assisted in the analysis by providing their impressions of issues that were

important to interviewees and by applying these impressions in the identification of important codes and themes.

The subjects covered in the interviews are summarised in Table 2 below. Full interview guides are presented in Appendices 4A - D.

Table 2: Summaries of main questions put to participants

Patients were asked mainly about their adherence to TB treatment, and what factors (specifically those related to poverty) made adherence more difficult. They were also asked about their experiences of the voucher, and how it had helped them, if at all. Nurses were asked about the administration of the voucher, and what if any problems they encountered in this regard. They were asked whether they thought the voucher had impacted on patient adherence, and whether they thought that financial support in general was an acceptable and viable way of improving patients' outcomes on TB treatment. Shopkeepers were primarily asked about the administration of the voucher, and its impact on their workload and cash flow. Managers in the TB Control Programme were asked about the administration of the voucher, potential benefits and challenges of its delivery, and about their perceptions of financial support for health outcomes.

Data Analysis

Interviews were analysed thematically. Transcripts were coded manually, and from these codes, themes were built up, both within the groups of interviewees (patients, nurses, TB managers and shop personnel) and across these groups. Both similarities and differences between interviewees' responses were noted and discrepant views were described (these were views that did not fit with the general trend of the findings, but that needed to be considered and accounted for in the final explanation) (Green and Thorogood 2004: 177). Transcripts of interviews were read and re-read so that recurring ideas (meaning units) could be identified.

Abstractions (codes) of these meaning units were developed, and categories of codes built up into sub-themes and themes (Green and Thorogood 2004: 177-180). For each key analytic theme, data extracts were identified on the basis of being representative and/or interesting illustrations of an emerging issue. The process of data analysis is illustrated in Table 3. Analysis was undertaken by the principal investigator and one of the co-investigators, with contributions from the research assistants who were involved in data collection.

Analysis was informed by the principal investigator's knowledge of the setting and of TB care. However, no formal theoretical stance was taken. This qualitative aspect of the process evaluation focused on how people experienced the voucher and the trial, and so was informed by a set of specific research questions, which in turn shaped the interview guides and the analysis.

Table 3: Example of analytic process

Meaning unit	Code	Sub-theme	Theme
"It helps me as I say that when I receive the voucher I am able to buy food and take my tablets on the right time; I have to eat before I swallow my tablets that is how the voucher is helping me"	Voucher helps with buying food with which to take tablets	Important role of voucher is to prevent having to take tablets on empty stomach	Role of voucher in improving aherence
"... you know that you can only get the voucher while you are on treatment. The minute you are out, it's back to square one, and those needs that were catered for by those vouchers are now left hanging and the patient might be tempted to default treatment so that to continue getting these vouchers".	Patients may want to remain ill in order to continue receiving voucher	The voucher may act as a perverse incentive	Negative effects of voucher

Ethical considerations

Written informed consent was obtained from all participants in all interviews in the language of their choice (either isiZulu or English) (see Appendix 3E). Patients were assured that non-participation in these interviews would not impact on the treatment they received from the clinic, nor on their continued participation in the trial. All participants were assured of confidentiality, and no participants were paid for taking part in these interviews.

The hard copies of interviews and participants' consent forms were stored by the principal investigator, in locked drawers. Electronic copies of interviews were stored on the computer of the principal investigator which is password protected.

Results

These results explain both the implementation of the voucher (with implications for its operational feasibility and its effectiveness) and the views of trial participants regarding the voucher, including their opinions on the principle of social assistance for people who are ill. Specifically, the results cover the issues of the operational feasibility of implementing the voucher system, the leakage and misuse of vouchers, the fidelity to the prescribed process of voucher implementation, the perceived effects of the voucher on adherence to treatment and on household poverty, and views on the continuation of the voucher scheme.

Operational feasibility of voucher

The perceptions of participants were that it was operationally feasible to administer the voucher to patients as a routine part of the TB Control Programme. Both nurses and shop personnel who were responsible for administering the voucher, said that it was simple to do. For example, clinic nurses noted that:

"In administering we had no problems…" (Nurse, Clinic 8 page 2).

"…on my side it was easy to issue the voucher… It was getting more easier because I was used to issuing the voucher and it was just an ID number or date of birth, my signature and a stamp of the clinic. It was more easier as the time goes on – I was used to issuing it" (Nurse, Clinic 9 page 1).

The manager of a shop expressed a similar view:

"Easy … The whole control of it, the way it's being controlled it's very easy to actually do …" (Manager, Shop 6 page 1).

In addition, managers suggested that there were no significant additional costs or increases in workload incurred by the shops as a result of the administration of the voucher.

"No, there was no cost on my side and it wasn't time consuming at all so there was no problem on my side" (Manager, Shop 1 page 2).

Patients also found the process of receiving the voucher from the clinics and redeeming it at the shops to be problem-free.

"There is nothing that I can say is bad, it is all good…Yes it is easy… There (are) no problems" (Patient, Clinic 4 page 2).

"It's easy, there is no problem" (Patient, Clinic 7 page 6).

However, in spite of the general sense that the vouchers were not difficult to administer, two important administrative problems did occur and are discussed in the section "Logistical problems that impacted on fidelity to trial procedures" below.

Leakage and misuse of the vouchers

The terms "leakage" and "misuse" of vouchers are used variably by studies investigating the use of vouchers to incentivise behaviour change (Hanson *et al* 2008). In this thesis, the term "leakage" refers specifically to the receipt of the voucher by groups not eligible to receive it, whilst "misuse" is a broader term which encapsulates the concept of leakage and includes the

theft or fraudulent acquisition of a voucher, as well as the inappropriate expenditure of the vouchers.

Issues relating to the "leakage" of vouchers (to those for whom they were not intended) were closely monitored in this study. The investigators were able to correlate all vouchers issued by the clinics with those redeemed from the shops. Other cases of misuse of vouchers were not reported during the trial and did not impact on its conduct. Nevertheless, cases of "leakage" were described by interviewees and are reported here.

Generally, patients, nurses and shop personnel were happy that, on some occasions, relatives or friends of voucher recipients redeemed the vouchers on their behalf. However, there were three reports from interviewees of cases where patients were not given their vouchers, or the goods redeemed with their vouchers, by the people who had collected them.

"… we have the Nompilo's (lay DOT supporters) … there is a lot of cruelty going on, they act like they are coming to get it (the voucher) for you when they take it themselves and you will feel bad, so it's better to come and get it yourself" (Patient, Clinic 7 page 6).

"only exceptional … case where I discovered that one patient complained that some of the family members were taking the food … but only one patient … we could rectify that mistake" (Nurse, Clinic 9 page 1).

One shop owner said that a stolen voucher had been brought in to be redeemed.

"One case happened when a voucher was stolen but we managed to sort that one out ….I can't remember clearly what happened but the story from the cashiers was that someone came even

before the voucher was redeemed and said his voucher has been stolen and told them his name. When the person who stole the voucher came through he was asked his name and proof of that name and he left the voucher there and never came back" (Owner, Shop 5, page 2).

These were the only such incidents reported however, in over 2 000 patients who received vouchers over the study period. There were no occasions where the theft or loss of a voucher had to be investigated, or where the issuing of vouchers had to be stopped due to such problems.

Fidelity to trial procedures for implementation of the voucher system

In spite of their overall satisfaction with the administration of the voucher, patients, nurses and shop personnel discussed problems with the principle of giving vouchers only to patients who met the trial's eligibility criteria.

Some nurses expressed their belief that vouchers should not be given to patients who were relatively better off financially. This impacted on the proportion of eligible patients who received the voucher, as outlined in Chapter 3. At most clinics, nurses appear to have given vouchers to patients whom they considered more deprived. Nurses noted that it seemed unfair not to give vouchers to patients who were more deprived, even if they did not meet the clinical eligibility criteria, and equally unfair to give to those who, for example, were employed or in receipt of a social grant but did met the eligibility criteria. Nurses commented that:

"The malnourished patients I would give even though it's not PTB (pulmonary TB), sometimes I would use my discretion" (Nurse, Clinic 8 page 2).

"I would decide by looking at who is needy, considering their social problems, then I will give (to) extra pulmonary (patients);[9] *like if they do tell me they can't take pills on an empty stomach then I will give considering their background…but those who are working I wouldn't give … "* (Nurse, Clinic 7 page 3).

Nurses felt that it was not difficult to assess the patients' levels of need:

"It's easy (to decide who is needy)… By history taking I can ask them, how many members of the family, who is a breadwinner, who is working, then I can assess from there" (Nurse, Clinic 8 page 4).

The patients themselves felt that this was fair – if they were doing well financially that month, it was better that someone else received the voucher that they might have taken:

"When I am here I get it if I ask for it" (Patient, Clinic 5 page 4).

"Sometimes I do not ask for it, if I see that I do have something" (Patient, Clinic 5 page 2).

The nurses also felt that asking for the voucher meant that the patient needed it, and so were justified in receiving it:

"As I told you the ones who are working they don't even ask for anything, it's for those who are not working" (Nurse, Clinic 4 page 2).

[9] Nurses did not record the distribution of vouchers to patients with extra-pulmonary TB in the TB registers, thus it was not possible to verify statements such as these.

Furthermore, patients, nurses and shop personnel were concerned that only certain patients (i.e. those with pulmonary TB) were eligible to receive the voucher. They felt that this was unfair, given the depth of deprivation experienced by some patients.

"I do hear them saying that the voucher is given to those with PTB only … They are complaining - you know people they also want to get the voucher, they are not happy that some people are receiving it while others don't" (Mother of 5 year old patient, Clinic 7 page 4).

Even one cashier was distressed by this exclusivity:

"If you could also try and help the others not just the TB patients. We also have people sick besides (those) diagnosed with TB" (Cashier, Shop 4 page 5).

Managers of the TB programme also perceived this as a problem, not for the reasons of equity cited by patients and nurses, but because they feared that it would act as a perverse incentive.

"If you target for example the TB patients, then people see that TB patients have better or get things for just being TB patients. So now everyone will want to have TB to get those things especially if they are in need, like food and all those things" (TB Manager page 4).

"... you know that you can only get the voucher while you are on treatment. The minute you are out, it's back to square one, and those needs that were catered for by those vouchers are now left hanging and the patient might be tempted to default treatment so that to continue getting these vouchers" (TB manager, page 2).

It was clear from the interviews that all participants found the exclusivity of giving vouchers only to a select group of patients to be problematic. Nurses' further objections to this

exclusivity are raised under the section "The impact of the voucher on the nurse-patient relationship" below. The targeting of economic support to certain groups to the exclusion of others, is discussed further in the discussion section of this chapter, and in Chapter 6.

Logistical problems that impacted on fidelity to trial procedures

Administrative reasons for patients not receiving vouchers every month were that the vouchers were either not available (because they had not been delivered timeously to the clinic by investigators) or because nurses only gave them out at the end of the month.

Although the investigators visited clinics every four to six weeks, clinics would sometimes run out of vouchers before these visits. Sometimes nurses would only notify the investigators of this problem on the day that the vouchers ran out, and it was not always possible to deliver voucher books to clinics quickly enough to prevent some patients from leaving the clinic without vouchers. Patients commented that:

"Sometimes it happens that you come for the voucher and find there are no vouchers. They say come on the following or the third day" (Patient, Clinic 7 page 3)

Some nurses preferred to issue all vouchers in one batch at the end of the month, because they found it logistically easier to do this "in bulk". Patients were required to return to the clinic at the end of the month to get their vouchers.

"They tell us that we get them when it is month end" (Patient, Clinic 5 pg 2).

Travelling to the clinic on another day to collect their vouchers would have imposed additional costs on patients, and very poor patients may not have been able to afford this additional trip.

Similarly, patients who were working may not have been able to take time off work for an additional clinic visit, and patients who were very ill may not have been able to visit the clinic a second time in a month. Although the proportion of patients affected by these factors was not quantified in the trial, this qualitative part of the process evaluation suggests that at least some patients were affected by them.

Perceived effects of the voucher on adherence to treatment

Both nurses and patients felt that the voucher had improved adherence to treatment, as the following data extracts suggest:

"The adherence was excellent! Even if you check their files they were coming monthly now, there was no need to keep on phoning them to come forward for more treatment, they come monthly because they knew that they will get the voucher …" (Nurse, Clinic 9 page 1).

"I saw that it was bringing back the patients, because patients were informing others about the voucher and the defaulters were coming back to the clinic…Adherence has increased even on the strepto (streptomycin) patients, knowing that they'll get the voucher every month…. Since the voucher we haven't had a case where someone (was) stopping treatment and then coming back. We haven't had patients defaulting" (Nurse, Clinic 8 pages 1 and 2).

Patients also said that the voucher enabled better adherence to treatment, through addressing barriers to adherence that were related to poverty:

"Yes, having no money can have an effect (on adherence). Since in the clinic we are given a specific date to collect our treatment, if one does not have money on that day that will be the

problem…(Also) If you have TB you must take nutritious food and (if) you don't have money you can't take that kind of food" (Patient, Clinic 3 page 1).

The voucher alleviated some of these problems, as the following data extracts show:

"Yes it has made it better for me to take my pills, we were so happy about receiving it, food is a problem" (Patient, Clinic 7 page 5).

"It's very important and needed. Some times at home I don't have food so I am able to use the voucher for that. It helps a lot" (Patient, Clinic 8 page 2).

"It truly made it easier. I get motivated to take my treatment and I can't wait for my date to go to the clinic for my treatment." (Patient, Clinic 8 page 1).

How the voucher may have affected links between poverty and TB treatment outcomes

Many patients, nurses and shop personnel noted that the value of the voucher was small:

"It does help me for the time being. I think food for R120 is too small, but I appreciate what they are giving me … the vouchers are small, the voucher is for us to eat for few days, and it's finished" (Patient, Clinic 5 pages 1 and 5).

From the perspective of patients, the main value of the voucher lay in providing food with which to take their TB medication. A major theme that emerged from patient interviews was that it was very difficult to take TB tablets on an empty stomach. Doing so made many patients feel very hungry and it made others feel ill. For others, eating before taking their tablets increased the efficacy of the treatment.

"… most of the time the tablets are making you hungry you need to get food right away" (Patient, Clinic 7 page 8)

"Just imagine as I have said how difficult it is to take them on an empty stomach. In fact it seems as if they are not helping you here but they are killing you!" (Patient, Clinic 7 page 6).

"If you take the tablet without eating anything that tablet will not work - where is it going to stay? It's better if you got something to eat first" (Mother of 5 year old patient, Clinic 7 page 4).

The voucher enabled patients to buy food so that they could take their tablets on a full stomach.

"It helps me as I say that when I receive the voucher I am able to buy food and take my tablets on the right time; I have to eat before I swallow my tablets that is how the voucher is helping me" (Patient, Clinic 4 page 7).

In many cases, patients shared the food purchased with their vouchers with their families, as it was considered to be against the norms of family behaviour to eat it alone:

"Yes I have to share with them I cannot be able to eat alone … We are a family I cannot be able to eat by myself, I wasn't taught like not to share" (Patient, Clinic 7 page 4).

However in some cases, especially in the case of children or the elderly, the food was reserved for the index patient alone.

"It's for the child … This money is hers, the voucher belongs to her as she is taking the treatment" (Mother of 5 year old patient, Clinic 7 page 5).

In other cases, members of the household protected the index patient's superior claim to the food.

"What I can say is that at home I stay with people who knows the rules of a sick person. That is why they say I must not share it" (Patient, Clinic 5 page 3).

The fact that the voucher enabled patients to buy more food with which to take their tablets was a powerful one, echoed by many patients. However, the practice of sharing this food may have impacted on the benefit that the index patient could derive from it. If the economic support intended for one patient only is shared with family or community members, the

efficacy of that support may be diluted. The targeting and sharing of economic support for TB patients is discussed further in the discussion section of this chapter and in Chapter 6.

The impact of the voucher on the nurse-patient relationship

Although this was not specifically asked about in any participant interviews, many nurses noted spontaneously that the voucher had improved their relationships with patients. This, they suggested, was because nurses were doing something active and out of the ordinary for patients by giving out the vouchers, and the patients appreciated this.

"Otherwise our relationship with the patients has improved and patients are always asking for Sister .... (me)" (Nurse, Clinic 8 page 2).

"The relationship has grown very much… between us sisters and patients because they come here and get helped" (Nurse, Clinic 3 page 2).

An improved relationship with nurses was not raised by patients in their interviews, which suggests that they either did not experience this at all, or that it was not important enough for them to raise.

Conversely, the relationship between nurses and patients who were not eligible for the voucher suffered some strain as a result of this trial because nurses had to justify to them why some patients were allowed to receive vouchers and they were not.

"… it should be given to all the patients (at this clinic) not just some because people think that it's our own agenda that some people are given while others are not" (Nurse, Clinic 10 page 5).

"Now as a sister I have to explain why the other patient got the voucher and why the vouchers don't go to everyone who is sick…. you find that they are neighbours - the other neighbour got it and the other one did not and they now don't like each other" (Nurse, Clinic 3 page 4).

Continuing the voucher scheme: addressing poverty or creating dependency?

As opposed to managers in the TB Programme, who saw both benefits and drawbacks to the voucher, patients, nurses and shop personnel expressed almost universal support for its continuation.

"What I can say is that it does help because there are people who got real problem and bigger than my problem. You find that they really do not have food to eat - some end up not taking their pills because they do not have food to eat. At least this voucher is helping … they help, they do help a lot" (Patient, Clinic 7 page 4)

"I wish the vouchers can continue because it helps the patient very much and that most of the times TB patients don't work - they don't know where to get food because they don't have jobs and we give them porridge but nobody can survive with porridge only. With the voucher the patient can get real food after the porridge" (Nurse, Clinic 3 page 4).

Shop personnel were interested in participating in further trials of programmes involving similar voucher schemes, because their turnover and profit had increased without a commensurate increase in workload or costs.

In addition to its practical benefit, nurses did not see as problematic the principle of "paying patients" to behave in a healthy way. In the context of widespread poverty, the vouchers were not seen in this light.

"It's like we are supporting them (the patients) and it's a good thing because people don't have jobs so I don't see it as paying them, rather as supporting needy people" (Nurse, Clinic 8 page 3).

Managers of the TB programme had a rather more complex approach to the continuation of the voucher. On the one hand. they were supportive in principle of the idea of financial support for TB patients and also felt that it was important to address poverty in patients with TB.

"If we just leave those patients (i.e. don't materially support them) chances are we will get them coming back again with the disease… I think if we address poverty, if we improve the living conditions of people, then we will go a long way towards addressing TB" (Senior TB Manager page 2).

However, on the other hand, they were concerned about creating dependency on the vouchers and providing a perverse incentive to remain ill.

"We have had cases where patients will sell their sputum… Ja, we've had cases where they will sell their TB counts and cards and move into other clinics so that they can be considered to be on treatment and then, so that they can get (the disability) grant. So it does create dependence and there are loops within the system that make it vulnerable to misuse…" (Senior TB Manager page 3).

Although it did not seem to detract from her support of the continuation of the voucher, one nurse echoed this fear. *"The way people are depending on the money, some want to be sick"* (Nurse, Clinic 8 page 3).

A related concern of one senior TB manager was that receipt of the voucher would make it unnecessary for patients to work.

"The reason why people go for those grants is to get something to support their families….. So I see it as perpetuating the culture of not working because they're relying on the grant maybe… we don't want to create a situation where people are dependent on some monetary incentive somewhere" (Senior TB Manager page 2).

These complex views reflect both the perceptions of the widespread and deep poverty which prevails in KwaZulu-Natal and the effect of poverty on illness, as well as ideas on how poverty should be addressed. These views echo age-old debates over social support for the poor and are further discussed in the discussion section of this chapter, and in Chapter 6.

Discussion

This qualitative analysis provides contextual and process information which goes beyond the trial design and methodology to explain *why* our results were achieved (Rychetnik *et al* 2002). This type of information is important in all studies, but may be particularly so in trials with negative or inconclusive results like ours, because it helps to differentiate between interventions that failed because they were inherently flawed, and those that failed because they were poorly delivered (Rychetnik *et al* 2002). Placing trial findings in context also helps to gauge the transferability of interventions, and their possible effects in different settings (ibid).

Summary of findings

In this qualitative study, participants noted that it was operationally feasible to deliver the voucher to patients as an integrated part of the TB Control Programme in public sector clinics in KwaZulu-Natal. However, the study also found that there were two important factors which prevented the delivery of the voucher to all eligible patients, for every month of their treatment. Firstly, many nurses felt that the vouchers should be withheld from eligible patients who were better off financially; this meant that approximately one third of eligible patients did not receive a voucher at all (Lutge *et al* 2013, reported in Chapter 3). Secondly, the logistical issues involved in delivering a supply of vouchers to all intervention clinics before they ran out, and the preference of some nurses to give vouchers out in one batch at the end of the month, meant that vouchers were sometimes not given to eligible patients on their clinic appointment dates. Patients who were unable to make return trips to the clinics to collect their vouchers may have missed out on vouchers for some months of their treatment. This poor fidelity to the

guidance for implementation of the voucher explains in part the non-significant findings of the intention to treat analysis (Lutge *et al* 2013, reported in Chapter 3).

This study found further that there were few cases of "leakage" or misuse of vouchers, and that both nurses and patients felt that the voucher had helped to improve adherence to treatment. Specifically, patients appreciated the voucher because it enabled them to buy food with which to take their tablets. Although most participants felt that the value of the voucher was very small, patients, nurses and shop personnel generally felt that the voucher system should be continued. Managers in TB Control Programme, however, were ambivalent about this; although they acknowledged the importance of addressing poverty in order to improve TB control, they were also concerned about creating dependency on the voucher, and that the voucher might become a perverse incentive for patients to remain ill.

Feasibility of implementing the voucher system

Nurses, shop personnel and patients found that the voucher was generally easy to administer and use. This is contrary to administration of the disability grant for TB which sometimes involves a waiting period of a few months before it is disbursed, and additional visits to clinics and government offices to fill in and drop off forms. However, the low fidelity to the intervention meant that only one third of eligible patients received the vouchers for most months of their treatment. This low fidelity occurred for reasons of both principle (equity and social justice) and process (logistics of administration).

Nurses felt that giving vouchers to patients who were financially better off was unfair, and tended to exclude such patients even if they were eligible to receive the vouchers in terms of

the trial protocol. This approach impacted on the delivery of the vouchers, and reaffirms the importance of the "street level bureaucrat" as implementer (Walker and Gilson 2004). The term "street level bureaucrat" was first coined by Michael Lipsky (Lipsky 1980) and refers to public service workers who have important roles in delivering government services, have constant interaction with members of the public and are able to use their own discretion in carrying out their activities (ibid). Lipsky suggests that the implementer of a policy or intervention is not a passive medium, through which the policy or intervention passes from the designers to the recipients. On the contrary, implementers can be seen as active in interpreting and, if considered necessary, modifying that policy or intervention, to the extent that they can represent a level of policy-making themselves (ibid).

The nurses in our trial modified the delivery of these vouchers in a few ways, but perhaps most importantly for this trial, they rejected the eligibility criteria as being unjust. Working in a context of widespread and deep poverty, it seemed unfair to them to give vouchers only to those who met the eligibility criteria, when some of those who met the criteria needed the voucher less, and some who didn't meet the criteria needed it more. Nurses are confronted with similar issues in the distribution of food parcels at clinics (Lutge *et al* 2009). Because there are usually not enough food parcels for all those who need them, nurses must give to those who need them more. They seemed to use similar principles in the allocation of vouchers in this trial. Nurses' reluctance to adhere to the eligibility criteria of the trial can be explained by the complexity of the ways in which service providers make decisions and implement new policies (Walker and Gilson 2004), based on the social, cultural and historical contexts in which they

operate (Adato *et al* 2010). Although the eligibility criteria for receipt of a voucher (which did not include socio-economic status) were clearly outlined to nurses at the start of the trial, the imperative to ration the vouchers was stronger.

Many nurses expressed the wish that they could give the vouchers to all patients at their clinics. Their reasoning was not based on a fear of stigmatising people by labelling them as "the poorest of the poor" as was the case for some recipients of conditional cash transfers in Turkey (Adato *et al* 2011) but rather because they felt that all patients needed them, to a greater or lesser degree. Interestingly, patients who felt that they did not need the voucher at a particular point in time would not take it, feeling that others who needed it more could benefit from it. The same feeling is echoed in a qualitative study amongst recipients of the Child Support Grant in KwaZulu-Natal; caregivers would not apply for the grant if they had other regular sources of material support (Hunter and Adato 2007). For communities with high levels of poverty, these feelings are extraordinarily altruistic.

Logistical problems also impacted on the fidelity to the intervention. In some clinics, it was administratively easier for nurses to give out all the vouchers at month end, but this required patients to come back to the clinic at this time to receive them. Because the study team was small, there were also logistical difficulties with delivering vouchers to all clinics on time. Voucher books were personally delivered to all clinics and collected from all shops by the principal investigator and one assistant, with staff at clinics and shops required to sign proof of delivery or collection. This meant that vouchers were sometimes not available for patients on

their appointment dates, which necessitated another visit to the clinic to collect them. Although the frequency of these occurrences were not quantified, they were raised by some interviewees in this process evaluation.

These issues of logistics are important considerations for the replication of this intervention in other settings. The co-ordination of delivery of vouchers to clinics and collection of vouchers from shops requires considerable organization and a dedicated staff complement. Setting up the infrastructure to manage the voucher system may be difficult where health systems are weak and resources very limited.

Like patients in Mexico's conditional cash transfer programme (Adato *et al* 2011), we found that many patients shared their voucher purchases with their families, and that this was consistent with their social values. Although this may have diluted the effect of the vouchers for the index patients, for many it was inconceivable that they should keep the voucher to themselves. Like other social grants in South Africa, the material benefits of the grant are generally distributed throughout the household, so that the household is the unit that benefits, rather than the individual recipient (Case and Menendez 2011). For this voucher therefore, as for other social grants, it is important to note that the impact of policies targeted at individuals will be mediated by household dynamics (Rosenzweig 1986). If the value of the voucher had been larger, the dispersion of this benefit may have improved the nutritional status of other household members and so reduced their risk of contracting or developing TB (Cegielski *et al* 2012, Tverdal 1986, Edwards *et al* 1971). However, because it was relatively small, these sharing practices may have meant that neither the index patient nor their households could

benefit maximally from the vouchers. Given that the impact of the voucher on overall household expenditure was small (reported in Chapter 5), it is likely that this is the case.

Leakage or misuse of the voucher

There were very few cases of "leakage" of the vouchers to those who for whom they were not intended. In only one case was the theft of a voucher reported and even in this case, the theft was reported before the voucher could be redeemed. More common was the fear that lay DOT supporters, who might collect vouchers on behalf of patients who were too ill to collect them themselves, would either not give the vouchers to the patients or would buy food for themselves. Even this, however, was expressed by only a few participants. The level of leakage of vouchers in this study is thus very small, compared to the levels experienced at provincial and national level with other social grants. For example, in the Eastern Cape alone, 3000 cases of social grant fraud were recently handed over to the Special Investigating Unit for prosecution (Plaatjie 2012). Although it is possible that cases of leakage would increase if vouchers were delivered on a larger scale, the system used in this study is promising in terms of minimising that potential.

Relationship between the voucher and adherence to treatment

Nurses were of the view that patients who received the voucher came back to the clinics to collect their tablets regularly, and that even known defaulters returned to the clinic to resume treatment. One of the reasons for the perceived improvement in adherence is that most patients interviewed valued the food purchases that they could make with their vouchers, and that this food helped to avoid having to take tablets on an empty stomach. This is consistent with the model for the mechanism of action that we proposed for the voucher (and is

illustrated in Chapter 1), that is, that it would enable adherence by minimising some of the barriers to adherence imposed by poverty.

Another reason for possible improved adherence may have been the improved nurse-patient relationships cited by many nurses in this study (although these were not cited by patients). Poor relationships with nurses undermine treatment adherence (Munro *et al* 2007a; Noyes and Popay 2007) because patients simply do not want to attend health care facilities. Even where conditional cash transfers are offered, patients who feel badly treated by staff prefer not to attend, even if this means losing their grant (Adato *et al* 2011). Although an improved nurse-patient relationship was not an aim of this trial, it may have been an unintended consequence that had an impact, albeit unquantified, on patient adherence to treatment. On the other hand, the strain that the voucher placed on nurses' relationships with patients not eligible to receive the voucher may have undermined the health related behaviour of those patients. Although this was not specifically investigated in this trial, it may be an important potential consequence of economic support targeted at patients with specific illnesses and should be considered in further research in this field.

The value of the voucher relative to the aims of the trial

This trial essentially asks two questions about the monetary value of the voucher. In this chapter and in the report of the main trial (Chapter 3), it asks if the value of the voucher was sufficient to change adherence behaviour and so change patients' outcomes on TB treatment. In Chapter 5 (which reports on the effect of the voucher on household expenditure), it asks if the value of the voucher was sufficient to significantly increase patients' household expenditures.

This qualitative analysis showed that patients generally felt that the value of the voucher (R120.00) was small, and indeed, compared to the Child Support Grant (valued at R250.00 per month at the time of the trial), the Old Age Pension and the Disability Grant (both valued at R1080.00 per month at the time of the trial), it was. However, it was about a fifth of the value of the median per capita income in KwaZulu-Natal around the time of the trial (Hall *et al* 2010), and most participants said it was helpful, particularly in enabling them to buy the food to take their tablets with. This was a powerful theme in the patients' interviews, with most saying that it was impossible to take tablets on an empty stomach. In this sense, the voucher enabled patients to take tablets where this may have been difficult without it.

Continuing the voucher scheme: addressing poverty or creating dependency?

Acknowledging the link between poverty and TB, the TB managers and nurses interviewed in this study agreed in theory with the principle of social assistance for people who are poor and ill. However, managers raised concerns about the impact of a financial transfer to patients with TB, based on the development of dependency on the grant which is a widespread concern in the country (Humanitarian News and Analysis 2007). However, this fear was not realized in our study, which suggested that the more often patients received vouchers, the more likely they were to be cured or to complete their treatment (dose-response analysis reported in Chapter 3). Similarly, an analysis of the trends in teenage pregnancy rates in South Africa has shown that these are not linked to access to the Child Support Grant (Makiwane *et al* 2006). Firstly, increasing trends of teenage pregnancy pre-date the introduction of the Child Support Grant in 1998 and secondly, only a minority of pregnant teenagers are eligible to receive the grant (ibid).

It is interesting to note however that concerns around dependency on grants and their perverse incentive effects go back a long way in South Africa's history, and were important debates held at the time of the Lund Commission in 1995 (Lund 2008: 116) and the Carnegie Commission in 1932 (Seekings 2006). These concerns persist today and relate largely to the concept of the "deserving poor" which were first articulated in the Poor Laws of Elizabethan England and remain areas of debate for welfare states today (Bowlby 2010). In essence, the poor who deserve assistance from the state are felt to be those who are unable to work, such as the very young, the elderly and the disabled. However, in South Africa today, the opportunities for formal employment are diminishing and those which are available are increasingly for people with a completed secondary or tertiary education (Leibbrandt *et al* 2012). Social grants are an important, perhaps even a crucial, means of survival for the poor in this country (Coetzee 2011) and further research is needed to explore whether these perverse effects are indeed found in practice, in order to inform ongoing debates.

Limitations of this sub-study

Firstly, the use of research assistants for much of the data collection in this sub-study may have introduced some information bias. Although the research assistants were perhaps less intimidating to participants than the principal investigator, they may have been less familiar with the core questions being addressed in this sub-study and therefore been less adept at probing. This may have resulted in loss of information depth from the interviews.

Secondly, in an effort to ensure continuation of the voucher scheme, patients and, to a lesser extent, nurses, may have overstated their perception of the benefits of the vouchers.

Thirdly, most clinics and patients included in the trial and in this sub-study were situated in urban areas, because relatively few rural clinics met the criteria for inclusion in the trial. The under-representation of rural participants in this sub-study may limit its generalizability to rural settings.

Conclusions

This qualitative analysis provides evidence of the importance of contextual factors in influencing the implementation and thus the effectiveness of economic support to patients with TB in South Africa.

The delivery of a voucher to enable better adherence to TB treatment was well received by patients, health workers and shop personnel in this trial. Patients and nurses felt that it improved adherence, and nurses felt that it improved the relationship between patients and nurses. Patients particularly felt that the voucher enabled them to buy food with which to take their tablets, thereby making treatment taking easier.

However, a number of factors limited the reach of the voucher to all eligible patients. Some of these factors were a consequence of the beliefs and values of the nurses who distributed them, and others were logistical. Nurses felt strongly that vouchers should be given out on the basis of need, rather than on trial eligibility, and this is likely to have reduced the extent to which the intervention was delivered as intended. Administrative difficulties that may have impacted on fidelity included the inability on the part of investigators to ensure that all clinics had an uninterrupted supply of vouchers, and a preference in some clinics for giving out vouchers in batches at month end, instead of at the time of the patients' appointments. These factors

explain some of the reasons for the non-significant results of this trial, and must be addressed in further research around such interventions.

Finally, managers of the TB Control Programme raised concerns about the development of dependence on the vouchers, and a perverse incentive effect. Although neither of these fears were realised in our trial, and are not supported by data from other studies, they are deeply felt by many in South African society, and have been prevalent in the country since early in the development of its social welfare system. More research on existing social grants, as well as further trials on new types of grants, are important to ascertain how best to deliver social assistance to those who need it most.

Chapter 5

Process evaluation (part two): A cross-sectional study of poverty, and the impact of the voucher, among patients participating in the trial

Introduction

This chapter constitutes the second part of the process evaluation of this trial, following on from the qualitative analysis discussed in Chapter 4. It focuses specifically on the patients participating in the trial, investigating their levels of poverty, the extent to which the voucher assisted them financially, and the goods on which they spent their vouchers.

This analysis is an important component of the thesis as a whole because it investigates the mechanism of action of the voucher. In designing this trial, it was postulated that, if the voucher did assist patients in adhering to their TB treatment, it would be through its poverty alleviating effects – it would increase the food available to the patient, and free up cash that would have been spent on food for other necessities such as transport to the clinic. As depicted in the model shown in Chapter 1, we envisaged that the voucher would work in a similar way to conditional cash transfers, and enable adherence by lowering some of the barriers imposed by poverty. This chapter thus explores how the voucher might have affected the link between poverty and adherence to TB treatment.

The chapter also investigates an important concern raised by several stakeholders in the preparatory phases of this trial, and in the context of social grants in South Africa generally; that is, how the vouchers would be spent by patients. A number of people in management, clinical and political positions expressed concerns during discussions that patients would spend their vouchers on damaging items such as cigarettes or alcohol. Indeed, these concerns have been raised throughout the history of social grants in South Africa (Lund 2008: 116; Seekings 2006) and remain prevalent today. Thus the second aim of this chapter is to present evidence around patients' use of the voucher.

Background

Poverty is a complex phenomenon, and an extensive body of literature exists on the many ways in which poverty can be defined. At the most basic level, poverty is defined using measures of income or expenditure, with "the poor" being defined relative to a level that is considered adequate (a poverty line or threshold). This level can be absolute, in that it is the minimum of material goods that are necessary to sustain life (Alcock 2006: 64), or it can be relative to the context in which poverty is being measured; relative poverty can thus be defined as "the inability to participate in the ordinary life of that society owing to a lack of resources" (Expert Group on Poverty Statistics 2006). More complex perspectives on poverty include Sen's capabilities approach (Sen 1999), which maintains that that the freedoms that are precious to individuals and societies require certain material and non-material inputs in order to be actualised. Although these more complex approaches are important in that they acknowledge

the multi-dimensional nature of poverty, they make the measurement of poverty both more subjective and more difficult, and were not used in this thesis.

In this study, poverty lines were used as yardsticks against which patient expenditure was measured, and as a threshold below which people were described as poor. Poverty lines are essentially arbitrary measurements because they are subjective. For example, the poverty lines of wealthier countries are usually set higher than those of poor countries (World Bank 2005). Several poverty lines have been used in South Africa. These include the $1 and $2 a day lines which are measures of absolute poverty, or the 40% or 50% of median national income lines which are measures of relative poverty (Leibbrandt *et al* 2010: 17). Although poverty lines have been used in South Africa since the Second World War (Wilson and Ramphele 1989: 16), at the time of the study the country did not have an official poverty line (Bhorat and van der Westhuizen 2010). The line chosen for analysis in this study was the food poverty line, because this most clearly defines people's access to adequate nutrition, which is an important factor influencing both the risk of developing TB and patients' outcomes on TB treatment (Hargreaves *et al* 2011).

South Africa is classified as a middle income country, but high levels of inequality mean that poverty remains extensive (Armstrong *et al* 2008). South Africa's consumption Gini co-efficient in 2009 was 0.63, making it one of the most unequal countries in the world (World Bank 2012). Using a poverty line of R515 per capita income per month,[10] the poverty headcount ratio in the country at the time of the study was 0.54 (Leibbrandt *et al* 2010: 36). This was highest in

[10] This was the "lower bound" poverty line for South Africa and indicates extreme absolute poverty. The "upper bound" poverty line for the same year was R949 per capita per month (Leibbrandt *et al* 2010: 65).

households headed by African females (0.68) and African males (0.60). The poverty rate in KwaZulu-Natal is the second highest in the country, at 58.5%, and just over a quarter (25.5%) of all poor individuals in the country live in this province (Armstrong *et al* 2008).

Social grants have, to a certain extent, lessened the depth of poverty in the country in the past decade (Armstrong *et al* 2008), and are the main source of income for 47.7% and 51.0% of households in the poorest two quintiles in the country, respectively (ibid). Social grants have been shown to improve household food security in South Africa (Case and Menendez 2007), and may thus reduce under-nutrition, which is an important risk factor for the development of TB disease (Cegielski and McMurray 2004) and may predispose to more severe disease (Van Lettow *et al* 2004).

For reasons of equity and stigma, social protection programmes are much more commonly directed at poor people in general, rather than poor people who are ill (Hargreaves *et al* 2011). However, there is a need to protect the latter group from the costs of illness which may be catastrophic for the household (Russell 2004), and also to support them through an illness so that they may become economically active again at the end of treatment. As Hargreaves *et al* (2011) state, “it may be possible (and necessary) to address selected factors in the daily living conditions of TB patients and their communities that might influence TB epidemiology”.

Indeed, as has been discussed earlier in this thesis, social support is provided to patients with TB in South Africa, in the form of a disability grant and food parcels from public sector clinics. However, neither the disability grant nor the food parcels are tied to any conditions such as adherence on the part of TB patients, and neither has been evaluated for its effect on poverty,

food security, or disease outcomes. Because of the high burden of TB and poor outcomes on treatment in South Africa, and because poverty in the country remains extensive, it is important to investigate whether economic support targeted at patients with TB improves outcomes on treatment (and this is discussed in Chapter 3), and if so, whether this improvement is related to the alleviation of poverty among patients and their households.

Aims:

To investigate indicators of poverty among TB patients participating in this trial, and the effect of the voucher on these; and to analyse the expenditure of the vouchers by recipients.

Objectives:

For all patients participating in this sub-study:

- To describe patients' main sources of income, in terms of their employment status, receipt of social grants and any other important sources of income
- To determine the main source of income of patients' households, in terms of the employment status of other household members, the receipt of social grants by others in the household, and any other important sources of income in the household
- To determine patients' levels of education
- To determine patients' average household expenditure on food, household goods, health care and transport
- To determine levels of food security in patients' households.

For patients attending intervention clinics:

- To investigate whether patients perceived the voucher as assisting in their adherence to treatment and if so, how
- To investigate whether patients perceived the voucher to be helpful financially
- To determine in which area of household expenditure the voucher had been most helpful, if at all
- To investigate on which goods the vouchers were spent.

Methods

The aims and objectives of this part of the process evaluation were met by using two separate methodologies, described in sections A and B below. The assessment of levels of poverty among patients, and the impact of the voucher on patient household expenditure were achieved through conducting a survey of a sample of patients included in the trial. The assessment of the goods that patients bought with their vouchers was achieved through an analysis of a sample of till slips (receipts) that participating shops retained for each voucher that was spent.

A. Survey of indicators of patient poverty and the effect of the voucher on these

Study design

This was a quantitative cross-sectional study nested in the trial. The focus of the poverty assessment in this study was patient household expenditure, since this is more likely to be

reported accurately by participants than income (Oosthuizen 2008) and because it varies less over time and is therefore more likely to give an accurate picture of chronic poverty, than is income (Chaudhuri & Ravallion 1994). A food poverty line was used in this analysis for three main reasons: firstly, because food is one of the most basic requirements of life; secondly, because nutrition affects outcomes on TB treatment (Hargreaves *et al* 2011); and, thirdly, because food consumption is more stable over time than either income or general expenditure (Chaudhuri and Ravallion 1994). The food poverty line is a measure of absolute poverty and is calculated according to how much an "average" individual should spend on food in order to meet his/her daily calorie requirements. For the poverty line used in this study, these requirements were set at 2 230 kilocalories per day (Oosthuizen 2008) and the cost of purchasing these calories (the food poverty line) was calculated to be R326 per month (adjusted to 2009 prices) (personal communication: Morne Oosthuizen, Development Policy Research Unit, University of Cape Town, 2012).

Participants

All patients who were in their fourth to sixth month of treatment for pulmonary TB in intervention and control clinics at the time of the trial were eligible for inclusion in this study. We chose participants who were approaching the end of their treatment period to ensure that they had had sufficient experience of the voucher to enable them to report on it, and to allow the voucher sufficient time to have had an impact on their expenditures.

Sampling

The calculation of this sample size was pragmatic in that it was based on the number of fieldworkers and amount of time available for this sub-study. Patients were recruited by two fieldworkers who moved between intervention and control clinics every week day for a four month period, and included in the survey every eligible patient at the clinic on that day.

Three hundred and seventeen trial participants (7.8% of the total) participated in this sub-study. Two hundred and sixteen were from intervention clinics (who had received the voucher) and 101 were from control clinics.[11] Six patients refused to participate. This sample size enabled the detection of R170.00 difference in total monthly household expenditure between patients who received the voucher and those who did not, with a power of 80% and a confidence interval of 95% (SPSS, two sample T-test power analysis). A difference in expenditure higher than the amount of the voucher was chosen in order to take into account the purchase of "productive inputs" such as chickens or goats that might further have further enabled increased expenditure (Creti 2010), and of improved household well being that might have facilitated job-seeking and employment by household members (Case and Menendez 2007).

Data collection

All data collection took place at intervention and control clinics, either in a quiet room within the clinic or in the clinic grounds, to ensure privacy. Using technology called Mobile

[11] Patients from intervention clinics were relatively over-sampled in order to estimate more precisely the effects of the voucher on expenditure.

Researcher,[12] the questionnaire was loaded onto mobile phones and read out by trained fieldworkers, who entered the patients' responses electronically into the phone. Once the questionnaire was completed, the fieldworkers submitted it to a central database by sending it in a similar way to a mobile text message. Data uploaded to this database was password protected and available to the principal investigator only, via a web-based interface. The complete Excel database was downloaded at the end of data collection, and analysis performed.

Information on the following variables was collected from survey participants:

- Age, gender, area of residence and educational status
- Type of residence
- Ownership of assets
- Employment status of index patient and household members (formal/informal/part time/full time/self-employed)
- Receipt of grants by index patient and household members
- Average monthly household expenditure
- Average monthly expenditure on food
- History of TB for the index patient
- Receipt of voucher
- Effect of voucher on household expenditure and adherence to treatment.

[12] Mobile Researcher is a technology that enables survey questionnaires to be loaded onto cell phones, the questionnaires to be completed on the cell phones and the completed forms to be sent to a central web-based database. More information on the technology is available from http://www.mobenzi.com/researcher/Features/Mobile-Application

The full questionnaire for the survey is presented in Appendix 5A.

Fieldworkers were trained by a member of the Mobile Researcher team, who assisted the principal investigator in their supervision. Fieldworkers were visited at clinics on a weekly basis, and were also in contact with the principal investigator by phone whenever the need arose. Checks on the data as these were entered were built into the Mobile Researcher programme. For example, answers outside a certain range were not permitted for questions where these limitations were appropriate (such as age). Most questions on the survey had a limited number of legitimate answers; keys pressed on the mobile phones that did not correspond to these answers were not permitted. For some questions, only one response was permitted, whilst for others, multiple responses could be entered. Omission of important questions by fieldworkers was prevented by making such questions mandatory; it was impossible to move on to the next question in the survey if a mandatory question had not been answered. Entered data was checked manually for extreme values and duplicated data.

The Mobile Researcher programme also allowed remote supervision of fieldworkers, by showing the time taken for each interview (interviews that were conducted too quickly implied rushed work or fabrication of data) and the time at which each interview was done (interviews conducted outside working hours could imply fabrication of data). These facilities complemented the on-site supervision of fieldworkers.

Data analysis

Uni-, bi- and multivariate analyses were performed. The main focus of the analysis was the total expenditure and food expenditure of the patients' households, and the impact of the voucher on these.

Statistical methods

SPSS version 15.0 was used to analyse the data. A p value of less than 0.05 was used to indicate statistical significance. Frequency tables were used to describe categorical data whereas summary statistics such as mean and standard deviation were used to summarise numerical variables with a normal distribution, and non-parametric measures such as median and inter-quartile range were used in the case of skewed numerical data.

Total monthly household expenditure was calculated by summing up reported monthly expenditure on various commodities, including food and meat. ANOVA tests were used to analyse variables with more than 2 levels and t-tests were used when the variables were binary. Pearson's and Spearman's correlation co-efficients were used to assess strength of relationships between quantitative variables. Because information on household size was only given by 129 participants, individual expenditure on food and meat was calculated by dividing household expenditure on food and meat by the national average household size (Statistics South Africa and National Treasury 2007).

Multivariate analysis

Stata version 12 was used for the Generalized Linear Modelling and the analysis was performed at the household level. The log transformed total monthly household expenditure was the dependent variable, and a normal distribution and identity link were specified. We aimed in this analysis to determine which variable(s) were most important in affecting household expenditure when confounding factors were taken into account; specifically, we aimed to determine whether the voucher was one of these factors. It was a principled analysis, in that variables that had been identified in the literature as affecting expenditure, or were in practice known to affect expenditure, were included. Robust clustered standard errors were used with the clustering variable being the clinic.

B. Investigation of expenditure of vouchers

The till slips, which listed each patient's purchases and the prices of these, were retained by all participating shops and fixed to a copy of the patient's voucher. These till slips and the vouchers were collected by the investigators and a 15% sample of all till slips (1182 of 8022) was randomly selected. The sample size was again pragmatic, and influenced by the number of data capturers available to work on this sub-study. The information from these till slips was entered onto an Excel database and a descriptive analysis of patient expenditure was performed in SPSS (version 15.0).

Results

Three hundred and seventeen patients were interviewed, 216 from intervention clinics (who had received the voucher) and 101 from control clinics.

Patient demographics

One hundred and eighty two (57.4%) of all participants were women, and the mean age of all participants was 31.9 years. The mean household size of participants was 4 adults (standard deviation 2.5) and 2 children (standard deviation 1.9).

Although 161 participants (50.8%) had had some secondary (high) school education, only 67 (21%) had completed secondary school; 85 (26.8%) had never attended secondary school and 24 (7.6%) had never attended school at all.

Consistent with the urban location of most (16) of the 20 participating clinics, 197 (62.1%) of patients lived in a township, 43 (13.6%) in an informal settlement, whilst 58 (18.3%) lived in a rural area.

Household economic status

Employment and income among trial participants enrolled in the survey

One hundred and twenty six participants (39.7%) said that they earned money in some way (including formal and informal, part-time employment and odd jobs). Those who did not earn any money at all gave reasons as listed in Table 1 below.

Table 1: Patients' explanations of why they were not able to earn any money

Reason	**Number (%)**
Too sick to work	93 (48.7)
Unable to find job	54 (28.3)
Studying	23 (12.0)
Retired	2 (1.0)
Pregnant or caring for a child	3 (1.6)
Household duties	1 (0.5)
Other*	15 (7.8)
Total	191 (100)

*"Other" reasons for patients not working were most commonly age (too young or too old) (n=5), or receipt of a disability grant (n=3).

Only 9 patients (2.8%) received the disability grant for TB or HIV. These patients were all adults between the ages of 18 and 50 years,and most (6) were women. Importantly, six of these patients came from a single clinic, which suggests that nurse-related factors (such as their knowledge of how to access the disability grant) are important in the equity of the distribution of the grant. Seventeen patients (5.4%) received the child support grant and only one patient (0.3%) received the old age pension. One hundred and twenty patients (37.9%) were supported financially by others in their household.

Employment and income among household members of trial participants

One hundred and seventy six participants (55.5%) said at least one person in their households (other than themselves) earned an income.

Two hundred and thirty three participants (73.5%) said that at least one person in their households (other than themselves) received a grant from the state. Of these, the child support grant (160 households) was the most common, followed by the old age pension (79 households). The foster care grant (7 households) and unemployment insurance (one household) were rarely received.

Household expenditure

Participants estimated their monthly household expenditure for a variety of items, listed in Table 2 below.

Table 2: Monthly household expenditure for various items (in South African Rand)

	Food (excluding meat)	**Meat**	**Clothes and shoes**	**School fees**	**Cell phone and airtime**	**Cigarettes or tobacco**	**Alcohol**	**Transport**	**Health care**
Mean	584.77	273.02	345.00	253.88	78.40	105.42	313.64	252.03	142.27
Standard deviation	305.51	183.19	410.20	277.71	100.01	69.09	238.84	201.04	105.02
Minimum	50	20	50	0	5	20	50	10	30
Maximum	2000	1200	3000	2000	700	300	700	1200	1000

Because the consumption of cigarettes and alcohol is important for public health, this expenditure was analysed further. The median expenditure on cigarettes or tobacco was R100 per month, and on alcohol it was R200 per month. The majority (79%) of patients who spent money on tobacco products were adult men between the ages of 18 and 56, and none had achieved higher than a grade 5 education. The majority (64%) of patients who spent money on alcohol were adult men between the ages of 23 and 56, and in this group again, the highest level of education achieved was grade 5.

Household deprivation, including food security

Participants were asked to recall how often in the three months prior to the interview they had been unable to meet their usual expenditure commitments on important items. Their responses are listed in Table 3 below.

Table 3: Frequency with which households went without specific items, in the three months prior to the interview

	Food (%)	**Clothing and shoes (%)**	**School fees (%)**	**Fuel for cooking and heating (%)**	**Basic household items e.g. for cleaning/cooking (%)**	**Health care (%)**
Never	204 (65.60%)	198 (67.12%)	239 (80.74%)	175 (56.82%)	104 (40.15%)	250 (79.37%)
Once	16 (5.14%)	7 (2.37%)	14 (4.73%)	30 (9.74%)	17 (6.56%)	14 (4.44%)
A few times	83 (26.69%)	78 (24.44%)	40 (13.51%)	94 (30.52%)	125 (48.26%)	44 (13.97%)
Often	8 (2.57%)	12 (4.07%)	3 (1.01%)	9 (2.92%)	13 (5.02%)	7 (2.22%)
Total number of patients who responded to question	311 (100%)	295 (100%)	296 (100%)	308 (100%)	259 (100%)	315 (100%)

One hundred and sixty nine (53.3%) of participants said that in the three months prior to the interview, they had had to borrow money or food in order to survive.

Individual expenditure on food

Mean individual monthly expenditure on food (including meat) was R142.85, and median expenditure was R133.33. One hundred and seventy one patients (54%) reported expenditure on food (including meat) less than the food poverty line of R326 per month (adjusted to 2009 prices) (personal communication: Morne Oosthuizen, Development Policy Research Unit, University of Cape Town, 2012).

Receipt of vouchers from intervention clinics

Two hundred and sixteen participants received the voucher from their clinics. All 216 patients said the voucher had helped them in taking their TB treatment, in the ways listed in Table 4 below.

Table 4: How the voucher helped participants in taking their TB treatment

Reason*	**Number**
I've been able to eat enough to take my tablets comfortably	198
I've been able to save use the money saved on foodstuffs for transport to the clinic	13
I've been able to help my family financially so they are more supportive of me	36
I eat more and feel better able to come to the clinic	94

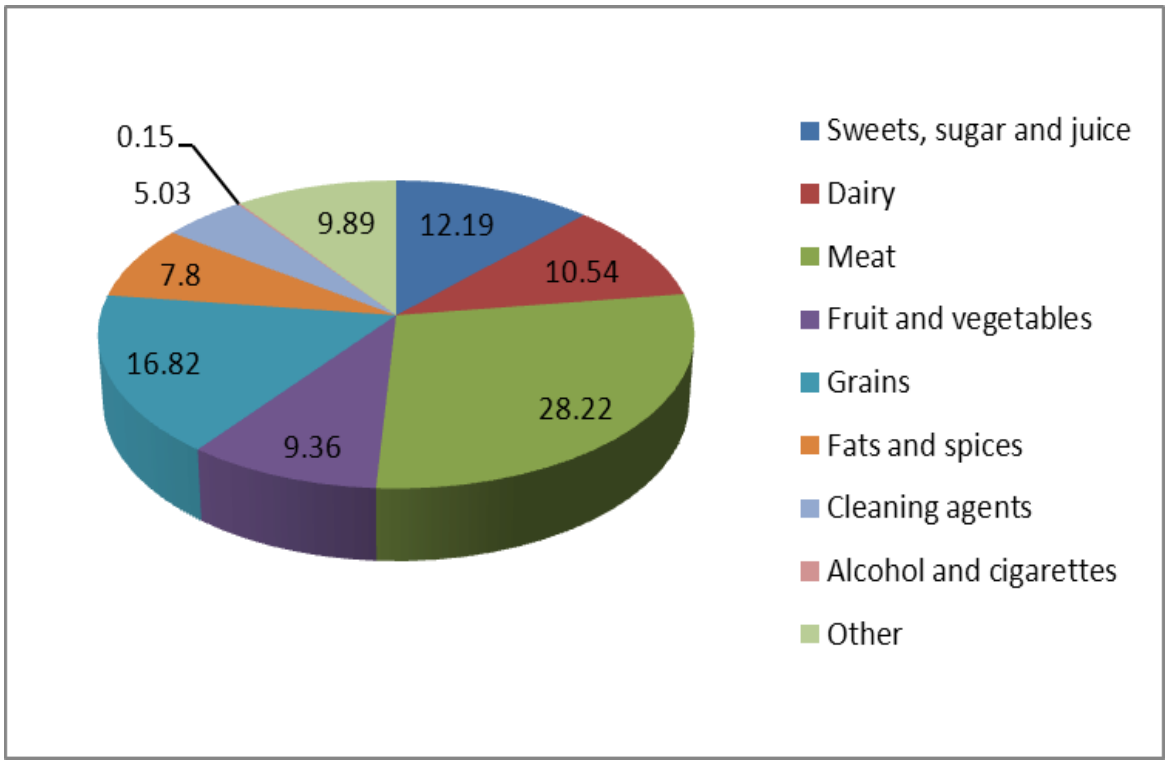
*Note: Patients were allowed to choose more than one option for this question.

Most participants (97.70%) felt the voucher had helped considerably in meeting household expenditure on food, whilst some (22.7%) said it had helped considerably in buying fuel for cooking and heating. The voucher was not found to be helpful in meeting other expenses such as those for other consumables, or for health care. A fifth (20.4%) of patients said the voucher had helped considerably to reduce the need to borrow food or money.

Expenditure of the vouchers

Vouchers were spent primarily on foodstuffs. Figure 1 below shows that 85% of the value of all vouchers analysed was spent on food. Importantly, 28.22% was spent on buying meat, 16.82% on grains, 10.54% on dairy products and 9.36% on fruit and vegetables.

Figure 1: Expenditure of vouchers (%)



Note that "other" expenditure included paraffin for heating and cooking, candles for lighting, airtime for mobile phones and toys.

Although there were some differences in expenditure between urban and rural areas and between the genders, most of these were not statistically significant. In urban areas, 0.15% of voucher expenditure was on alcohol and cigarettes, whilst in rural areas it was 0.17%. (chi^2=0.00, p=0.95). Rural patients tended to spend a higher proportion of their vouchers on meat (39.22% versus. 26.37% in urban areas) (chi^2=11.87, p<0.01). On the other hand, patients in urban areas spent more (11.02%) on dairy products compared to their counterparts in rural areas who only spent 7.67% (chi^2=2.10, p=0.15). Men also spent more on meat than women did

(31.18% versus 25.8% respectively) (chi^2=2.25, p=0.13) whereas women spent more on grains (17.69% versus 15.77%) (chi^2=0.42, p=0.12).

Bivariate analysis

Effect of employment and income on household expenditure

Those participants who had some form of earnings reported significantly higher monthly household expenditure than those who did not (p <0.01), but there was no association between the receipt of state grants or any other financial assistance with monthly household expenditure on bivariate analysis.

There was a significant association between mean total monthly expenditure and both the need to borrow food or money because of shortages (p<0.01) and food security. Participants who were least food secure had the least total expenditure of the group (p<0.01). Both these associations are expected and confirm the internal validity of this survey.

Other factors affecting expenditure

There was no association between the geographic areas in which participants lived, and their total monthly expenditures (p = 0.97), or their monthly expenditures on food (p = 0.46). However, the total monthly expenditure of men was significantly higher than that of women (p = 0.02), although food expenditure was not different between the genders (p = 0.35).

Both total monthly expenditure and monthly food expenditure were higher in those who had completed more than a primary school education, compared to those with a primary school education or no schooling (p = 0.07 and p = 0.05 respectively).

Effect of voucher on household expenditure

As shown in Table 5, there was no difference between the total monthly household expenditure of participants who received the voucher and those who did not (p=0.77). The monthly expenditure on food and meat was higher in the households of participants who received the voucher, although these did not reach statistical significance (p=0.21 and p=0.08 respectively).

Table 5: Effect of voucher on monthly household expenditure

	Mean total monthly expenditure (standard deviation)	**Mean monthly expenditure on food (standard deviation)**	**Mean monthly expenditure on meat (standard deviation)**
Received voucher	1225.42 (856.16)	834.21 (461.39)	292.21 (169.74)
Did not receive voucher	1257.54 (875.69)	757.62 (408.45)	245.94 (198.54)

Differential effect of voucher on expenditure in population sub-groups

Overall, there were no differences in the effect of the voucher on total and monthly food expenditure between men and women, or between patients of different educational or employment status or between participants living in different areas. The effect of the voucher on total monthly expenditure and monthly food expenditure was similar across all areas in which participants lived.

Multivariate analysis

Two hundred and sixty three patients were included in this analysis (168 who received the voucher and 95 who did not). Those who were excluded from this analysis were those for whom information on total monthly household expenditure was not available.

Receipt of a voucher did not influence total monthly household expenditure, even after controlling for confounders ($p=0.557$). Factors which did affect total expenditure significantly were whether the respondent was earning money ($p<0.001$), whether the respondent was receiving a disability grant ($p=0.017$) and whether there were any household members receiving social grants ($p=0.025$). All of these factors increased the mean total expenditure, as might be anticipated. In addition, participants who lived in a city spent more than those who lived in a township ($p<0.01$).

Table 6: Results of multi-variate analysis†

Parameter	Significance
Gender: male	.244
Age	.452
Education level: primary school and below (versus secondary and tertiary education)	.969
Household location: informal settlement (versus township)	.657
Household location: city (versus township)	<0.001
Household location: rural area (versus township)	.582
Respondent earns money (versus respondent does not earn money)	<0.001
Respondent does not receive a disability grant (versus respondent does receive disability grant)	.017
Respondent does not receive child support grant (versus respondent does receive child support grant)	.338
Members of household do earn money (versus members of household do not earn money)	.067
Members of household receive social grants (versus members of household do not receive grants)	.025
Respondent does receive voucher[#] (versus respondent does not receive voucher)	.557

† This is an abridged table. The full table for the results of the multivariate analysis is available in Appendix 5B.

[#]Note that these were respondents who received at least one voucher during the trial.

Discussion

Levels of poverty among participants

There is little doubt that the participants in this study needed economic support. Consistent with the observation that TB is a "barometer of poverty" in South Africa (Andersson 1990), the participants in this survey came from poor households. Less than 40% of participants said that they earned an income in any way, and, as other research has found, the households of patients who did not earn money spent less than those of patients who did (Goudge *et al* 2009, Armstrong *et al* 2008). This is an important point for discussion in this thesis, given the arguments against the provision of social grants (and this voucher), in favour of people finding paid work (reported in Chapter 4). It is important to note that it is difficult for people who are less well educated to find employment in South Africa (Leibbrandt *et al* 2012), and that besides social grants, the poor have few alternatives for survival. Unemployment has risen in the country in the last decade, and the demand for labour in South Africa is increasingly for those who have, at a minimum, completed their secondary schooling (ibid). In our study, only the minority of patients had completed secondary education and, as expected from national findings (Armstrong *et al* 2008), those with lower levels of education reported lower monthly household expenditure. Although the average length of schooling in the country has increased since 1994, the number of scholars who complete their secondary education or who go on to tertiary education have not (Leibbrandt *et al* 2012). Thus formal employment has been increasingly difficult to reach for many South Africans. The rate of unemployment in the country remains high, with an official unemployment rate of 25% and a rate of unemployment

among young people of 51% (Kane-Berman and Cronje 2010). In KwaZulu-Natal, the official unemployment rate at the time of the study was 20.9% (Department of Labour 2011). In spite of this, the current social security system in South Africa seems to rest on the premise that income from employment is readily available to all those who are willing and able to work, and that only when an individual is disabled or too ill to work, should the state intervene with economic support (Hardy and Richter 2008). It can be argued that this is not an appropriate approach for South Africa (ibid).

For patients with TB, for whom employment may be even more difficult because of illness (Munro *et al* 2007a), social protection from the state may be the only means of household survival. Indeed, 27.8% of patients in this survey said that they were too sick to work. Even assuming that paid work was available for these patients if they were well enough, such patients should have been eligible for and received disability grants to cushion their households against the economic shock of loss of employment during their episode of TB. However, only 2.8% of patients in this study received the disability grant for HIV or TB. In spite of the fact that the total number of disability grants issued by the state has increased in the recent past (Hardy and Richter 2008), these do not seem to be reaching households disabled by illness, either in this study, or in others conducted in South Africa (Daftary and Padayatchi 2012, Booysen 2004, Steinberg *et al* 2002).

Recognising the importance of other social grants in alleviating extreme poverty in the country (Armstrong *et al* 2008), and as other research has shown (Case and Menendez 2007), the receipt of state grants was an important source of income for households with almost three

quarters of all patients saying that at least one person in their household received a state grant (most commonly the child support grant). Indeed, the receipt of a disability grant by the index patient or any social grant by a household member was significantly associated with increased household expenditure on multivariate analysis. It is interesting to note that the receipt of a child support grant by the index patient was not associated with higher household expenditure; this is likely to be because the value of the child support grant is much smaller than of the value of the disability grant (R250 versus R1080.00 per month at the time of the trial). Therefore, like the voucher, the child support grant is likely to be too small to have significantly influenced household expenditure in this survey.

Consistent with the experience of poor populations in general, food security among patients in this study was low. Over half (54%) of all patients surveyed reported individual expenditure on food (including meat) which was lower than the food poverty line for 2009 and almost a third (29%) reported that their households had gone without food often or a few times in the three months preceding the interview. Food insecurity has been found to be an important social determinant of TB (Hargreaves *et al* 2011, Murray *et al* 2011), and these findings show the high levels of food insecurity in the households of people with TB in KwaZulu-Natal. Such food insecurity has important implications for the risk of developing TB (including among others in the index patient's household) and for poorer outcomes on treatment (Villamore *et al* 2008, Range *et al* 2006, Karyadi *et al* 2002).

Impact of the voucher on household expenditure

In contrast to other research, which shows that conditional cash transfers increase the consumption of households (Rawlings and Rubio 2005), our analysis of patient expenditure showed that the voucher did not increase the total expenditure of patients' households. It did increase slightly the household expenditure on food and meat, but these increases were not statistically significant. In addition, receipt of the voucher did not differentially improve expenditure in specific vulnerable groups, such as among women or those with lower levels of education.

Subjectively however, almost all patients felt that the voucher had helped considerably in meeting household expenditure on food, whilst a fifth felt it had helped considerably to reduce the need to borrow food or money. These results reflect those of the qualitative analysis reported in Chapter 4, where patients said that the main value of the voucher had been in increasing the amount of food available with which to take their tablets. Assessment of the nutritional status of patients was beyond the scope of this study. However, given that the voucher did not significantly improve expenditure on food, it is unlikely that it impacted very directly on the nutritional status of patients. Indeed, although cash transfers have been shown to have beneficial effects on the nutritional and health status of children (Lagarde *et al* 2009), a recent review found that they have had limited or no impact on levels of adult malnutrition (Boccia *et al* 2011).

It is perhaps because the value of our voucher was small in relation to the food poverty line, that it had no significant impact on overall household expenditure or food expenditure. It is

likely that cash transfers will have the most impact if they are large in comparison to household expenditure, and shift expenditure up to or over a specific poverty line. However, the value of cash transfers varies across countries (Lagarde *et al* 2009) and it is difficult to relate the amount transferred to the level of poverty in individual households, since this data is not available for most cash transfer programmes (ibid). In our study, the value of the voucher (R120) was less than half the value of the food poverty line (R326 at the time of the trial). The value of the voucher was limited by stakeholders' fear that too large a voucher would act as a disincentive to work, or as a perverse incentive to remain ill.

In South Africa, social grants from the state, especially the old persons' grant (old age pension) have been shown to improve household food security (Case and Menendez 2007). In households where there is a chronic illness, social grants may help households to meet the direct and indirect costs of illness, and protect against further impoverishment (Goudge *et al* 2009). Indeed, the social grants received by households in this study were found to significantly improve household expenditure on multivariate analysis, supporting national findings that these grants have reduced the depth and extent of poverty in the country (Armstrong *et al* 2008). (The lack of a statistically significant association between social grants and total household expenditure on bivariate analysis was probably due to confounding factors which were controlled for in the multivariate analysis). However, the value of our voucher (R120 per month) was small in comparison to the social grants offered by the state. The Child Support Grant was valued at R250 per month at the time of the study, whilst the old persons grant and disability grant for TB or HIV were valued at R1080.00 per month (South African Social Security Agency 2011). The perception of patients that the voucher did help "considerably" with food

purchases may be explained by the fact that the voucher enabled the purchase of a reasonable basket of food, as illustrated in Table 1 of Chapter 1.

The direct and indirect costs of an illness are more burdensome for poorer than for wealthier households (McIntyre *et al* 2006). For poorer households, even relatively minor costs like travel to a clinic may necessitate reducing expenditure elsewhere (Goudge *et al* 2009). The vouchers helped to reduce the need to borrow food and money in some of the households included in this study. Since the creation of debt as a result of illness is a common cause of further household impoverishment (McIntyre *et al* 2006), the voucher may have mitigated somewhat against this. In addition, it may have made recipients more "creditworthy" in the eyes of their communities, thus strengthening social networks for borrowing and lending in the future (Goudge *et al* 2009). Similarly, one of the reasons patients gave for finding the voucher helpful was that it enabled them to give financial assistance to their families, who were in turn more supportive of them. This is consistent with theories relating to the allocation of resources in households, where household members who bring in financial income may be valued more highly than those who do not (Rosenzweig 1986).

Expenditure of the vouchers

Patients in this study were advised by clinic nurses to spend their vouchers on healthy foodstuffs, but at the shops where vouchers were redeemed no restrictions were placed on patient expenditure. However, analysis of their expenditure shows that most patients did spend their vouchers on food. Although concerns have been raised in South Africa that social grants are spent on unhealthy or even damaging items (Coetzee 2011), and although this was a

concern raised often by stakeholders in the preparatory phases of this study, analysis of the expenditure of this voucher shows that less than 1% of expenditure was on alcohol or cigarettes and that the greatest expenditure by far was on healthy foodstuffs. This reflects the findings of other studies in the country (Patel *et al* 2012: 20; Coetzee 2011), and contradicts the findings of studies internationally (Oxman *et al* 2009). Although the expenditure of such transfers may be contextual, the results of this study seem to suggest that in South Africa, recipients of grants tend to spend them on what is best and most needed for households. Whilst in this study, patients were restricted to spending the voucher on consumables, unrestricted cash grants are generally spent on foodstuffs, school fees and school uniforms, medicines and health care, and transport (Patel *et al* 2012).

Limitations of this sub-study

This survey was based on relatively small sample sizes and therefore its generalizability may be limited. In addition, the survey focused on expenditure rather than income as the former is considered to be more accurately reported by patients (Oosthuizen 2008). However, expenditure is also subject to recall bias especially if the detail required is great (Bhorat and van der Westhuizen 2010). The information requested for the purposes of this study was not detailed in comparison to that required for income and expenditure surveys, and so the risk of recall bias may have been lower. However, this lower level of detail may have resulted in the omission of important information that might have enabled greater precision in the analysis of patient expenditure.

Patients appear to have under-estimated their total household expenditure, which is small relative to the expenditure reported for individual consumables. This suggests that patients' estimates of expenditure were imprecise and this must be borne in mind in the interpretation of the findings.

Patients in intervention clinics were not asked to differentiate their expenditure with and without the voucher, and some may thus have reported their usual expenditure, as opposed to their expenditure with the voucher. This may have reduced the ability of the analysis to detect an effect of the voucher on expenditure.

Analysis of individual expenditure may not have been an accurate reflection of reality, because information on the composition of households was only available for 129 participants. The use of the national average household composition to calculate individual expenditure from household expenditure may have led to inaccuracies in figures for individual expenditure.

A limitation of the trial generally, as well as of this sub-study, is that most clinics and patients in the trial were situated in urban areas because most rural clinics did not meet the trial's inclusion criteria. This under-representation of rural participants and clinics mean that the findings of the trial and of this sub-study should be generalized to rural areas with caution.

The multivariate analysis was confined to those patients for whom information on total monthly household expenditure was available (263 participants). Although it is possible that those who did not report their expenditure were a random sample of the total, it is more likely that they did not report because they were unwilling to disclose this information. This suggests

that their expenditure might be significantly different from that of the sample who did report on it and, if so, this may have introduced some bias into the findings.

Conclusions

The voucher did not impact significantly on the poverty levels of patients in this study. Its value of R120 (approximately US$15) was considerably lower than that of most other social grants at the time of the study, and it did not significantly increase patients' total monthly expenditure or monthly expenditure on food. However, it was perceived by patients to be helpful in improving the amounts of food available to the household and in reducing the need to borrow food or money. There was no differential effect of the voucher on the expenditure of vulnerable groups. Although patients were not restricted in their purchases at shops, vouchers were spent primarily on food stuffs, with less than 1% of expenditure being on alcohol or cigarettes.

Because of its relatively small value, the impact of the voucher on the role of poverty in undermining the outcomes of patients on TB treatment is likely to have been small. Further research should investigate the effects of higher levels of economic support for their impact on household and patient poverty, and TB outcomes. Future research should also investigate whether economic support directed at patients with active TB should be shared with household members or used exclusively by the index patient. These and other research questions arising from this trial and its sub-studies are discussed further in Chapter 6.

Chapter 6

The evidence that informed this trial, and the contribution of the trial to current evidence

Introduction

This chapter aims to summarise the evidence generated by this trial and its process evaluation, and to demonstrate how it extends the evidence already available in the field of economic support for the improvement of TB outcomes. By critically examining the strengths and limitations of the trial, I lay the foundations for the final chapter, which focuses on the research that is still needed in this field.

What evidence informed this trial?

The conduct of this trial was motivated by the fact that, in the face of strong evidence that links TB to poverty (Cegielski *et al* 2012; Ploubidis *et al* 2012; Baker *et al* 2008; ASSAF 2007; Van Lettow *et al* 2004, Tverdal 1986; Edwards *et al* 1971) and substantial interest in the field of the socio-economic determinants of health, including of TB (Hargreaves *et al* 2011; Lonnroth *et al* 2010; WHO 2008), data on the efficacy or effectiveness of socio-economic interventions to improve TB control is very thin. This may be because, as was discussed in Chapter 1, studies that intervene in the linkages between poverty and disease are complex and difficult to conduct. It may be also, as discussed in Chapter 4, because some stakeholders feel that social

welfare for the poor, including for the poor who are ill, may lead to dependence and act as a perverse incentive. Finally, it may be because the concept of using economic interventions to improve health outcomes is still a new one, which exists on the periphery of the public health imagination. The perception of economic interventions as tools which should be tested and rigorously evaluated, like new treatment or prevention modalities, is still not widely entrenched.

The Cochrane systematic review reported in Chapter 2 showed that 10 of the 11 included studies that investigated the use of economic incentives or enablers for patients with TB were conducted in the United States, among marginalized groups such as injection drug users or homeless adults (Lutge *et al* 2012). Thus the findings of these studies must be generalized with caution. In addition, most studies included in this review focused on adherence to TB preventive therapy or on return to clinics for the receipt of the results of diagnostic tests. Only one included study investigated patients on treatment for active TB (Martins *et al* 2009). The review concluded that economic incentives or enablers showed promise as short term interventions; cash incentives might improve rates of return for the collection of TB diagnostic tests (although the quality of the evidence was low), and would probably improve rates of return to the health services for initiation of TB treatment (here the quality of the evidence was moderate). For long term TB prophylaxis, the review concluded that economic incentives or enablers might improve patients' outcomes in some settings, but the quality of the evidence was low. However, it was unable to draw conclusions about the effect of economic support on

completion of treatment for active TB because only one included study had addressed this issue and the quality of evidence in this study was very low (Martins *et al* 2009).

Previous reviews documented a similar lack of evidence for the use of economic support to improve TB outcomes. In a review investigating the use of conditional cash transfers and microfinance for the improvement of TB control (Boccia *et al* 2011), which focused on the household level and included non-randomised study designs, it was found that no conditional cash transfer programmes focused on TB per se, and only one microfinance programme did so (Thim *et al* 2004). In this study, participation in a microfinance programme showed a beneficial effect on TB cure rates (ibid). An earlier review of large scale conditional cash transfer programmes for the improvement of access to health care and various indicators of health, focused only on direct monetary transfers and included non-randomised study designs (Lagarde *et al* 2009). This review also found that no conditional cash transfer programmes had focused on TB outcomes. Finally, in a review of reviews of results-based financing which included both conditional cash transfers and economic incentives targeted at "patients, providers, organizations, or governments", Oxman and Fretheim (2009) discussed one review of financial incentives which had included studies on tuberculosis (Giuffrida and Torgerson 1997). Both of the studies on TB in the review by Giuffrida and Torgerson (Pilote *et al* 1996 and Morisky *et al* 1990) were considered in the Cochrane review reported in Chapter 2 (Lutge *et al* 2012).

Trial setting

Our pragmatic, cluster randomized controlled trial to test the feasibility and effectiveness of economic support for patients on TB treatment was conducted in South Africa, "where the health crisis intersects most forcefully with issues of social justice and human rights" (London 2008). Although in many regions of the world the incidence of TB has fallen, and outcomes on TB treatment have improved (WHO 2011), rates of death and default from treatment remain high in Africa (Lonnroth *et al* 2010). In South Africa, incidence rates continue to rise (WHO 2011) and TB remains the most important cause of death in the country (Statistics South Africa 2011). Although HIV has played an important role in the increasing incidence of TB in South Africa (Day *et al* 2012: 89-90), conditions of poverty have also remained central to the continuing significance of the epidemic (Abdool Karrim *et al* 2009). KwaZulu-Natal, where this trial was set, is one of the poorest provinces in the country (Armstrong *et al* 2008), and is the epicenter of both the TB and the HIV epidemics (Day *et al* 2012: 89 and 203).

Working in public health in South Africa, it is difficult not to note, and try to address, the important links between poverty and TB. Some of South Africa's most eminent academics have commented on the profound importance of addressing poverty in order to improve TB control, and the urgency of their call has not decreased over time. In 1986, Professor Solly Benatar of the University of Cape Town wrote "Without doubt the most important factor in the control of TB is improvement in living standards. Unless there is improvement in nutritional status, reduction in overcrowding, and improvement in the overall level of education, no TB programme can hope to be more than marginally effective" (Benatar 1986). In 2005, Professor

Dingie van Rensburg of the University of the Free State wrote, “We have to recognize that TB is a socio-economic disease par excellence, and that the neglect of socio-economic factors was and still is the reason why TB control has constantly failed” (van Rensburg *et al* 2005). In South Africa, it is very difficult to ignore the association between poverty and TB, and the investigation of the use of economic interventions to improve TB indicators can be seen as a public health imperative.

Thus the trial that is the core of this thesis was undertaken to investigate whether It was feasible to implement economic support to patients with pulmonary TB as part of the routine TB control programme in public sector clinics in South Africa and whether this support would be effective in improving patients’ outcomes on TB treatment.

What were the main findings of the trial and what are the implications of these?

The trial was conducted over a period of 14 months, from 01/07/2009 to 30/09/2010. Twenty clinics and a total of 4091 patients were included. There was no loss of clinics in this trial and minimal loss of patients to follow up (Lutge *et al* 2013, reported in Chapter 3). The main findings of the trial and its process evaluations are as follows:

- A monthly voucher given to patients with active pulmonary TB in public sector clinics in South Africa resulted in a small and nonsignificantimprovement in their treatment success rates

- Fidelity to the trial protocol was low, which may have contributed to this inconclusive result
- Nurses' preference for giving vouchers to patients who were relatively more deprived probably had an important impact on this fidelity
- Both nurses and patients perceived the vouchers as helpful in improving adherence to treatment
- The voucher did not significantly increase the household expenditure of recipients
- Managers of the TB Control Programme were concerned about the perverse incentive effects of the vouchers (although there was no evidence of such effects in the data from this trial).

As in all epidemiological studies, there are a number of possible explanations for the very modest effect found in the intention to treat analysis. The first is that this was due to chance; however, given the power of this study (90%), this is unlikely. The second, that it was due to confounding, is also unlikely because of the randomized nature of the trial. The third, that is was due to bias, is possible. The clinics selected for inclusion in this trial may, due to the selection criteria used, have been different in their management and administration from other clinics. Indeed, it was important that clinics which may have been very poorly administered be excluded from the trial, so that poor administration did not affect the delivery of the voucher (Lutge *et al* 2013, reported in Chapter 3). However, because included clinics were geographically scattered throughout the two districts, it is unlikely that the patients themselves were different in selected clinics compared to clinics which were not selected. Within the trial,

we know that selection bias (in terms of which patients were given the voucher) did occur and this is extensively reported on in Chapters 3 and 4 and in this chapter. Nurses in intervention clinics preferentially allocated vouchers to patients whom they perceived to be more needy. Since patients who are more deprived are likely to find it more difficult to adhere to treatment (Munro *et al* 2007a), it is possible that this may have weakened the effect of the voucher if the voucher was unable to overcome the barriers that they experience. In addition, many other eligible patients who may have responded to the voucher did not receive it, and this may also have diluted the effect of the voucher in the intention to treat analysis.

The fourth explanation for the intention to treat finding of our trial is that the intervention itself (the economic support in the form of a voucher) was not efficacious. This is entirely plausible; the voucher may simply not have been the most appropriate intervention to address the factors undermining patients' outcomes on TB treatment, or its Rand value may have been too low to have had a more substantial effect (this was commented on by several participants and is reported in Chapter 4). Finally, the context in which this pragmatic trial took place may have affected its conduct and results. Some important programme- and people-related factors that impacted on the delivery of our voucher, and which may have impacted on the findings of the effectiveness of the voucher, were elicited in the process evaluation of this trial; these are discussed further below. A summary of factors internal and external to the trial that may have affected its findings, is presented in Table 1.

Table 1: Factors affecting the conduct and findings of the trial

	Factor	**Explanation**
Internal to trial	Chance	Unlikely to have affected findings because of high statistical power of trial (90%)
	Confounding	The use of randomization in the trial reduces the likelihood that the findings are due to confounding
	Bias	Intention to treat findings may have been affected by selection bias of clinics into trial (only clinics meeting inclusion criteria were selected for randomization) Intention to treat findings may have been diluted by selection bias of patients for the receipt of the voucher (nurses gave vouchers to patients who they perceived to be more deprived)
External to trial (contextual)	Communities' perceptions of social justice	Nurses' re-interpretation of trial eligibility criteria (giving voucher to more deprived patients) may have diluted intention to treat findings of trial (see point above).
	Stakeholders' concern around perverse incentive effect of voucher	Low value of voucher (prompted by stakeholders' concern that patients might try to remain ill in order to continue receiving the voucher) may have lowered its benefit for patients in terms of how much food could be bought with the voucher, and how long this food could last in a household in which it was shared.
	Stakeholders' concern around the creation of dependence on voucher	Low value of voucher (also prompted by stakeholders' concern that patients would become dependent on voucher and no longer seek work) may also have lowered its benefit for patients in terms of how much food could be bought with the voucher, and how long this food could last in a household in which it was shared.

The pragmatic nature of the trial generated valuable lessons regarding the implementation of economic interventions for health at scale, and reaffirmed the dictum that "science is social" (that is, that scientific research is not only motivated by social values but that its results are affected by the social context in which it takes place) (Venkatapuram and Marmot 2009). Although the participants in this trial, including the nurses and shop personnel who were responsible for issuing and redeeming the voucher, said that it was easy to administer, the voucher was not administered as intended in the protocol. Experience from this trial suggests that the system of voucher administration tested in this trial was technically feasible in the setting of public sector clinics in KwaZulu-Natal. However, two factors prevented the full operationalisation of the voucher system, and I now discuss these in more detail. The first, and probably the most important, was the fact that nurses delivering the voucher reinterpreted the eligibility criteria for the trial, based on their own perceptions of patients' need.

As discussed earlier, there is widespread and deep poverty within KwaZulu-Natal, and the patients who present with TB to public sector clinics are almost universally poor in terms of their levels of employment, their monthly incomes and their living conditions (survey of household expenditure, reported in Chapter 5). However, even within this general poverty there is a range of deprivation which, at its worst extreme, is almost untenable. Thus it seemed unfair to participating nurses to give the vouchers to eligible patients who seemed relatively less deprived; nurses felt that vouchers should be "rationed" so that the most needy patients received them. This is an understandable compassionate response. It is not uncommon for the

implementers of policies to adjust or modify the implementation of a policy because it seems to them to be unjust or otherwise inappropriate (Walker and Gilson 2004, Lipsky 1980). This makes the implementation of policies more complex, and may fundamentally alter the intended effects thereof. The role of the implementor in re-interpreting a policy through its implementation should therefore not be under-estimated.

A second group of factors that may have impacted on the fidelity to the implementation of our voucher system was logistical issues experienced by both nurses and investigators (reported in Chapter 4). Although the effect of these issues was not quantified, they may also have lowered the fidelity to our intervention, and so may have diminished the effectiveness findings of the intention to treat analysis. They are also important to consider for the replication of this trial in other settings. Indeed, they point to the conclusion that this system of voucher delivery may in fact not be feasible for settings where staffing levels are low. Although the voucher system used for the trial protected to a large extent against misuse of the vouchers, such as theft, fraud and "leakage" to patients not eligible to receive them, it was resource intensive in that vouchers were delivered to clinics and collected from shops in person and upon the signatures of investigators, nurses and shop personnel. Where gains may have been made in reducing corruption around the vouchers, these gains may have been lost because some eligible patients did not receive the vouchers when, and as often as, they should have. The issue of ensuring that all those who are eligible receive social assistance is also problematic on a national scale. In South Africa, not all of those who are eligible for social grants actually receive them. This is because they either do not know they are eligible, do not know how to access the grants, or are

unable to access them consistently over time (Richter 2006). Developing a system for the delivery of economic support to poor patients, including for those who are ill, that is best suited to local contexts, remains a subject for further research.

In addition to its modest effect on treatment success rates, our voucher did not significantly increase the expenditure of patients' households. This most likely was because, as discussed in Chapter 5, the amount at which the voucher was valued was small. It was less than half the value of the food poverty line at the time of the trial (personal communication: Morne Oosthuizen, Development Policy Research Unit, University of Cape Town, 2012) and about a quarter of the value of the national median per capita monthly income (Hall 2010). This value was set however because TB managers who were involved in the planning phase of the trial were concerned that a higher amount might act as a perverse incentive for patients to remain ill so that they could continue receiving the voucher. This fear does not seem to have been realized in this trial. Although reverse causality may have contributed to these results, the dose-response analysis suggested that the more often patients received the voucher, the higher the treatment success rates. This finding tends to support that of the exploratory analysis, and also argues against a perverse incentive effect; it is expected that if patients had tried to remain ill in order to continue receiving a voucher, treatment success rates would have fallen with increasing duration of receipt. In addition, although the low value of the voucher may have limited its effectiveness, it is possible that a voucher with a higher value might have had a perverse incentive effect. It is also not clear how affordable a larger financial transfer may be

for South Africa, and it is therefore a recommendation of this thesis that more research be conducted into the optimal value of economic support for TB patients in various local contexts.

Although the voucher did not have a significant effect on patients' household expenditures, it was perceived to be very helpful by patients, both in the quantitative survey reported in Chapter 5 and in the in-depth interviews reported on in Chapter 4. Patients in this trial were predominantly (over 60%) unemployed, and a large proportion (over 50%) were not able to meet their household needs with their regular incomes. As directed by the nurses who distributed the vouchers, patients by and large used their vouchers for the purchase of food (reported in Chapter 5), which was useful because it helped them to avoid taking their tablets on an empty stomach (reported in Chapters 4 and 5). This confirms the findings of other studies (Patel *et al* 2012: 20; Richter 2006) that patients who receive financial assistance from the State generally spend it on worthwhile items. However, because the value of the voucher was low and because most patients shared their purchases with their households, the benefit of the voucher to the individual patient was probably limited. This finding raises important questions for further research on poverty and TB. For example, is it sufficient for TB control to limit economic support to individuals on treatment (Hargreaves *et al* 2011)? Given the effect of poverty and specifically, poor nutrition, on the incidence of the disease (Cegielski *et al* 2012, Edwards *et al* 1971, Tverdal 1986), should economic support not be directed at the household so that two goals can be achieved simultaneously: the outcome of the index patient on TB treatment can improve, and new cases of TB arising from the same household can be prevented? Perhaps even more effective for TB control would be to direct economic support to

all people below a certain poverty threshold? However, given that such support already exists in South Africa in the form of social grants, and that despite this the incidence of TB continues to rise and outcomes on TB treatment remain poor, it seems that questions around the best way to impact on TB epidemiology remain.

What does the trial add to the current evidence?

This trial adds to the current evidence on the use of economic support to improve the outcomes of patients on TB treatment, both in terms of the trial findings themselves and in terms of the process evaluation.

The effect of economic support on TB treatment outcomes

To examine the global evidence for the effects of economic support in patients on treatment for active pulmonary tuberculosis, we combined the findings of our trial with that of the only other randomized controlled trial we know of that examines this question (Martins *et al* 2009). The trials are compared in Table 2 and the results of this meta-analysis are presented in Figure 1 and discussed further below.

Table 2: Comparison of trials investigating the use of economic support to improve the outcomes of patients on treatment for active pulmonary TB

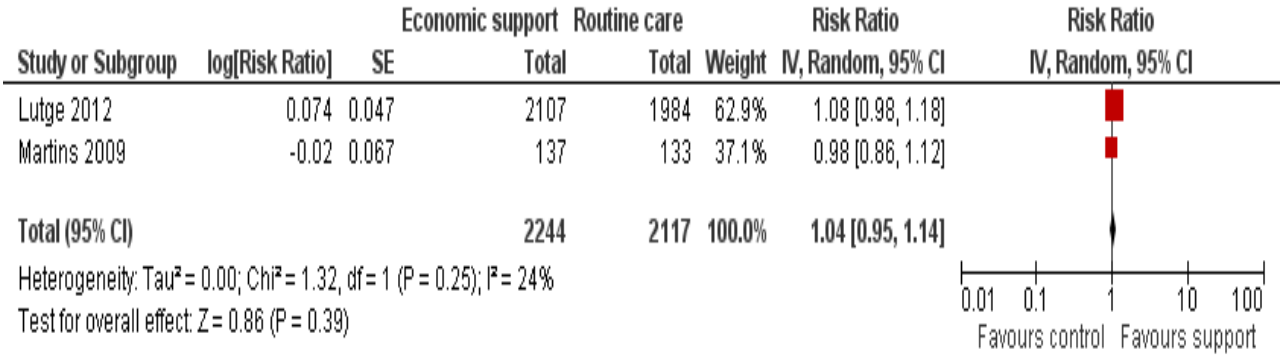
	Lutge *et al*	**Martins *et al***
Primary outcome measure	Treatment success (treatment completion + cure)	Treatment completion[13]
Participants	Patients with pulmonary tuberculosis (both smear positive and smear negative) (n = 4091)	Patients with pulmonary tuberculosis (both smear positive and smear negative) (n = 270).
Intervention	Monthly voucher, redeemable at local stores. Patients were encouraged to buy food with their vouchers.	Culturally appropriate daily meal for the intestive phase of treatment, followed by a food parcel containing sufficient food for a meal for one person, for the continuation phase.
Control group	Routine care	Routine care + nutritional advice
Methodology	Cluster randomized	Individually randomised

Because one of the trials in this meta-analysis was cluster randomized, the generic inverse variance method was used to perform the meta-analysis (Higgins and Green 2011). The natural

[13] Martins (2009) defined treatment completion as "clearance of acid fast bacilli from the sputum after treatment or the completion of eight months of treatment, or both". Thus the primary outcome of both trials is the same, although the terminology used is different.

logs of the risk ratios and their standard errors were calculated and entered into RevMan; the forest plot showing the results of this analysis is below.

Figure 1: Pooled results from two trials of the effect of economic support on the outcomes of patients on treatment for active pulmonary TB



As shown in figure 1 above, the degree of variation between the trial results due to true heterogeneity rather than chance alone was relatively small (24%). The meta-analysis suggests that the effect of economic support for patients on treatment for active TB is still very undertain, although the confidence intervals include a potentially important benefit. Given the evidence that suggests that poverty undermines the outcomes of patients on TB treatment (Hargreaves *et al* 2011, Zachariah 2002), the finding of this meta-analysis is surprising. However, the quality of the evidence must be taken into account. Since my own assessment of the quality of this evidence may be biased, an independent assessment of the evidence was undertaken by an editor of the Cochrane Infectious Diseases Group based at the Liverpool School of Tropical Medicine.

Folllowing an assessment of the risk of bias in our trial (Lutge *et al* 2013), the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system was used to assess the quality of the evidence of this meta-analysis. This system is one of the most objective and transparent ways of categorizing the quality of evidence (Guyatt *et al* 2008) and is used by the Cochrane Collaboration. The GRADE approach considers several aspects of a body of evidence in order to classify its quality; these include the study design (randomized controlled trials are considered high quality evidence), the risk of bias in the studies, and the precision, consistency and directness of study results (Balshem *et al* 2011). In the GRADE assessment of this meta-analysis, the starting point was to identify the evidence as high quality because both included studies were randomised controlled trials. The application of the remaining criteria are presented in the Summary of Findings Table and the GRADE assessment of the meta-analysis below.

Figure 2: Summary of findings table and GRADE assessment of meta-analysis

<table>
<tr><td colspan="6">Material incentives/enablers compared to routine care for improving patient adherence to treatment for active TB</td></tr>
<tr><td colspan="6">Patient or population: People engaged in tuberculosis programmes
Settings: Middle- and low-income settings
Intervention: Material incentives/enablers (vouchers or food)
Comparison: Routine care</td></tr>
<tr><td rowspan="3">Outcomes</td><td colspan="2">Illustrative comparative risks* (95% CI)</td><td rowspan="3">Relative effect (95% CI)</td><td rowspan="3">No of participants (studies)</td><td rowspan="3">Quality of the evidence (GRADE)</td></tr>
<tr><td>Assumed risk</td><td>Corresponding risk</td></tr>
<tr><td>Routine care</td><td>Material incentives/enablers</td></tr>
<tr><td>Treatment sucess (Completion or cure)</td><td>750 per 1000</td><td>780 per 1000 (728 to 848)</td><td>RR 1.04 (0.97 to 1.13)</td><td>4356 (2 studies)</td><td>⨁⊖⊖⊖ very low[1,2,3,4]</td></tr>
<tr><td colspan="6">The assumed risk is taken from the control groups in the trials. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
CI: Confidence interval; RR: Risk ratio;</td></tr>
<tr><td colspan="6">GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.</td></tr>
</table>

Footnotes

[1] No serious risk of bias: Both studies adequately concealed allocation to be at low risk of selection bias. Neither study was blinded.
[2] Downgraded by 1 for serious inconsistency: Although neither study showed a statistically significant difference, the study from Timor Leste showed a trend towards harm with the intervention while the study from South Africa showed a trend towards benefit.
[3] Downgraded by 1 for serious indirectness: The study from Timor Leste was conducted among malnourished men and provided an incentive as a daily hot meal. The study from South Africa provided all TB patients with a monthly voucher worth $15 when medication was collected. Qualitative research around these studies suggest that the daily hot meal was not well liked by patients as it interfered with daily life, whereas the voucher was well received. It is difficult to generalize these interventions to other settings.
[4] Downgraded by 1 for imprecision: Neither study showed a statistically signficiant benefit. However the study from South Africa where the intervention was well recieved has a confidence interval which includes a 15% increase in treatment success, which may be deemed worthwhile.

Thus the GRADE assessment describes the quality of the evidence provided in this meta-analysis as being of very low quality. The official definition of this assessment is "We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect" (Balshem *et al* 2011). In terms of this meta-analysis then, it is likely that the finding that "economic support for patients on treatment for active TB probably has little or no effect on TB treatment outcomes" will be refuted by future research. The importance of conducting this research, and some suggestions as to important foci for this research, are discussed later in this chapter.

The consideration of these two trials together also emphasizes the importance of the context in which the research took place. Although Martins *et al* (2009) do not present a separate process evaluation for their trial, they do report that civil conflict in the country during the conduct of their trial "dramatically increased" the default rate of participating patients, and "led to a significant decrease in treatment completion (168/199 (84%) before conflict v 35/66 (53%)) after conflict" (Martins *et al* 2009). In our trial, poor fidelity to the trial protocol may have contributed to our failure to detect a significant effect. Both trials highlight the difficulties of implementing economic interventions in real world settings, and emphasize the imperative to take context into account in studies that investigate the effect of economic support on TB outcomes.

Factors that influenced the conduct of our trial and its findings

The process evaluation of our trial provided valuable information on how the context in which an economic intervention is delivered may have a profound effect on its administration, and its reach. It supports other studies that show that different settings influence the response of recipients and administrators to economic transfers; for example, whereas in one context very poor people may not wish to receive economic interventions for fear of being stigmatized as "the poorest of the poor" (Adato *et al* 2011), in the context of this trial, that was the very reason why nurses and patients felt that people should receive it. However, where poverty is extensive, our trial also shows that targeting such interventions to specific groups may be problematic for both administrators and recipients.

The issue of targeting social assistance at poor patients who are ill in South Africa has been extensively discussed by Richter (2006), in relation to patients with HIV/AIDS. Richter argues that social support for patients who have HIV/AIDS in South Africa is crucial because most patients are poor and food insecure. By improving patients' access to food, and providing funds for transport to the clinic, the disability grant received by patients with HIV/AIDS improves patients' prognosis; in addition, it acts as a "de facto poverty alleviation grant" (Taylor Report 2002) because it is shared with the patient's family. Richter notes that there are probably grounds within the South African Constitution (Act 108 of 1996) for compelling the government to provide longer term support for patients living with HIV/AIDS than the current disability grant allows. However, although such support is crucial for the well-being of these patients who are mostly living in poverty, this targeting of individuals with HIV/AIDS may have an important

perverse incentive effect (Nattrass 2006) and may also be considered unjust by those who are living in similar conditions of poverty but who have other chronic diseases such as diabetes and hypertension (Richter 2006). Both of these issues were raised in our trial. Although our vouchers did not seem to have a perverse incentive effect, several concerns around this were raised by policy makers and managers in the planning phase of the trial and by managers in the in-depth interviews conducted as part of the process evaluation (reported in Chapter 4). Issues around targeting were also found by our trial to be problematic for both nurses and patients, and fundamentally altered the delivery of our vouchers.

In light of the findings of this trial and the views of Richter (2006) and Nattrass (2006), significant concerns around the targeting of economic support to patients with a specific disease, including those with TB, remain. Recognizing these concerns, and the fact that the results of this trial were inconclusive, the question remains: given that TB is strongly associated with poverty, how best should economic interventions be delivered in order to improve TB outcomes in South Africa?

Both Richter (2006) and Nattrass (2006) feel that universal social protection in the form of a basic income grant (BIG)[14] to all South Africans would circumvent the problems of perverse incentives and social division associated with more targeted economic support. It would also be easier to administer than the current system of social grants in the country because means

[14] The Basic Income Grant would be a universal cash transfer, given to every single South African, but recovered from the financially better off by a progressive tax. At the height of debates around its implementation, the amount postulated for the grant was R100 per month (Catholic Bishops Conference 2003).

testing or other forms of assessment would no longer be required. The social security system of the democratic government has not been as efficient as hoped, and it has been reported that it has incurred annual losses of up to R1. 5 billion due to massive problems of maladministration and corruption (Reddy and Sokomani 2008). From the perspective of TB control, universal social protection has much more potential to reduce the incidence of the disease (by improving household nutrition and living standards) than does a grant that is targeted to patients who are already ill. It would even be superior to the current system of social grants in the country in this respect, because there are millions of poor households in South Africa that slip through the social protection safety net because they do not qualify for any of the grants available (Richter 2006).

However, as evidenced by some of the findings of this trial, it is questionable whether the proposed Basic Income Grant of only R100 per month (adjusted to R162.37 in 2013 prices) would be effective in improving household economies to the extent that nutritional status and living standards could be improved. It was seen in this trial that the amount of R120 per month provided by the voucher was perceived by patients as being very little, and it did not significantly impact on patients' household expenditures. Increasing the value of a universal Basic Income Grant may be more effective but may also be unaffordable for the country; providing a larger amount that is targeted at the poorest and most deprived groups may be difficult to administer and open to corruption; providing a larger amount targeted to patients with a specific disease such as TB may generate resentment in patients who are not the subjects of such targets, create perverse incentives to contract or prolong TB infection, and be

similarly difficult to administer according to the policy. Finding the ideal way to provide economic support in order to improve TB outcomes requires a great deal more effort, and given the burdens of both poverty and TB in South Africa, should be the subject of much research and debate in this country in the years to come.

Strengths and limitations of this study

In this section, I consider the most important strengths and limitations of the trial and its process evaluation, and discuss how its limitations impacted on the results and interpretation of this study as a whole.

Strengths

This trial was the first to investigate the use of economic support to improve the outcomes of patients on TB treatment in Africa, and is particularly relevant for this continent because of its high burden of TB and extensive levels of poverty. It was an important trial for South Africa, where studies testing the use of economic interventions to improve health outcomes are rarely conducted and where concerns around the provision of social welfare remain prevalent.

The pragmatic nature of the trial enabled an assessment of how the real world conditions of a relatively poorly resourced TB programme would impact on the delivery of the intervention, and highlighted many factors that are important for both policy and future research in this field. This trial was much larger than the only other trial known to have investigated economic support for the improvement of TB outcomes in a low or middle income country, and

demonstrates that it is possible to implement economic interventions for the improvement of health outcomes on a fairly large scale in this setting.

The trial was based on a strong foundation of prior research; the Cochrane systematic review reported on in Chapter 2 summarised the evidence around the use of economic incentives and enablers for patients with TB, and identified an important gap in the use of such interventions for patients with active TB in low and middle income countries. An earlier study investigating the levels of poverty among patients with TB in KwaZulu-Natal, and the material support available to these patients, laid the groundwork for this trial and supported the rationale for its conduct (Lutge *et al* 2009). Extensive consulation with a wide range of stakeholders before the trial not only enabled the trial to run smoothly, but also raised some of the issues that were investigated further in the qualitative component of the process evaluation (reported in Chapter 4).

Limitations

Poor fidelity to the intervention was probably the most important limitation of this trial. It makes the inconclusive results of the trial more difficult to interpret as these results may be due to poor implementation of the voucher, or limited efficacy of the voucher, or both. However, the reasons for the poor fidelity as elicited in the process evaluation do provide important information for the conduct of future trials and for the development of policy in this field.

The eligibility criteria for the inclusion of clinics in this trial may have resulted in selection bias, and may limit the generalizability of the findings of this trial. Conducting this trial in all public sector clinics providing TB care in KwaZulu-Natal may have resulted in different findings. Specifically, including clinics with poorer TB outcomes, which may have weaker administration, may have reduced even further the modest effect found in the intention to treat analysis of this trial.

Patients were not asked about whether or how they felt that their adherence behavior was "rewarded" by the voucher; the focus of the investigation was on the enabling effect of the voucher with the result that its incentivizing effect was neglected. Thus only a partial picture of the effects of the voucher was painted.

Because of extensive missing data on HIV status, we were unable to include HIV in the ancillary analysis of the trial. It may be that the voucher has a different effect, or an effect of a different magnitude, in HIV positive as opposed to HIV negative patients. Given the high prevalence of HIV in South Africa, and the high rates of co-infection with HIV and TB, the possible modifying effect of HIV on responses to economic support may have important policy implications.

The small sample size of the household expenditure survey (reported in Chapter 5), and the imprecision of reports of household expenditure, mean that the results of this survey and the implications of these for the effect of the voucher on household expenditure, should be treated with caution. Because of this, and because the incentivizing effect of the voucher was not

adequately investigated, it was not possible for this study to confirm the mechanism of action of the voucher proposed in the model presented in Chapter 1. However, the qualitative data presented in Chapter 4 support the enabling effect of the voucher on which this model is based.

Conclusions

This trial and its process evaluations have contributed important evidence for the design and implementation of economic interventions to support poor patients on TB treatment. However, the field is complex, not least because the implementation of such interventions is heavily dependent on the context in which they are delivered, and the attitides and perceptions of those who implement and receive them. It is clear that this trial has raised several more questions on how best to provide economic support to poor patients, so as to improve their outcomes on TB treatment. These question are discussed further in Chapter 7.

Chapter 7

Conclusions: taking forward our understanding of economic support for people with TB

Introduction

This chapter aims to identify the most important questions raised by this thesis, and to outline a way forward in terms of the research that needs to take place in order to better inform public health policy on the use of economic interventions to improve the outcomes of patients on TB treatment. Finally, it describes the ethical principles that underpin my view that future research on the use of economic support to improve the outcomes of patients with TB, is fundamentally important.

What further research is needed to better inform public health policy?

This trial has raised many fundamental questions about the use of economic support for the improvement of outcomes of patients on TB treatment and for the improvement of TB control in general. What seems unequivocal, since it is based on decades of research and centuries of observation, is that tuberculosis is powerfully related to poverty and is the "consequence of gross defects in social organization" (Dubos and Dubos: xxxviii). What is not clear, however, is what to do about it. Possible research questions are outlined and discussed further below.

These research questions address key issues raised in this trial and in other related studies regarding the use of economic support to improve TB control.

At what level/s should economic interventions for TB control be aimed? Is the improvement of outcomes of patients on TB treatment a worthwhile goal or should such interventions also aim to reduce the incidence of TB in patients' households and in poor communities in general?

Possible levels for intervening in the pathway between poverty and TB are at:

- The *individual patient level*, for the improvement of patient outcomes on treatment, as demonstrated in this study
- The patient's *household level*, to improve the economic well being and nutrional status of both the patient (to improve outcomes on treatment) and household members (to reduce their risk of developing TB disease)
- The *community level*, to improve the nutritional status and living standards of whole communities and thereby reduce their risks of developing TB disease and improve their outcomes on treatment.

It can be argued that the ideal economic intervention for TB control is one that is broad-based and reaches all those whom poverty makes vulnerable to infection with and development of TB. Such interventions may be more cost-effective than those which target patients who already have TB, by reducing the numbers of patients who need to be treated for the disease.

Indeed, the Commission on the Social Determinants of Health seems to favour this broad approach; two out of its three main recommendations are to "improve daily living conditions" and to "tackle the inequitable distribution of power, money and resources" that may foster the development of disease (WHO 2008: 2). However, both of these are much easier said than done, and rely on the political philosophy of governments in power. Acknowledging that these aims will not be achieved simply or in the short term, it is important to develop and test interventions that will contribute to their achievement, both because the alleviation of poverty is a moral imperative in its own right, and because the sum of the public's health will be increased by reducing the impact of poverty on it.

What interventions are the most feasible and effective, for the different levels?

It is likely that interventions will need to be crafted differently, to best suit the level at which they are targeted. Whilst it might be feasible to issue vouchers to individual patients on a small (clinic) scale, it might be logistically easier to deposit cash into peoples' bank accounts on a large (community) scale. Similarly, as has been shown in a study from the United States (Malotte 1999), it may be that cash is more effective than vouchers for some or all levels of targeting. The feasibility and effectiveness of implementing different interventions may be highly dependent on context, and so research should take place in a number of different settings to best inform the public health policy of individual countries or regions.

What interventions are the most feasible for low and middle income countries?

As noted in Chapter 4, the logistics of delivering and collecting vouchers from clinics and shops in this trial were resource-intensive. Low income countries may find this system of delivering economic support unfeasible in their settings. Furthermore, whilst it might be financially feasible for middle income countries like South Africa to target economic interventions broadly, at large sectors of society such as those falling below a specific income threshold, this may be unaffordable for low income countries. Poorer countries might have to aim their interventions at smaller, more clearly defined groups.

In addition, more complex studies have shown that multiple simultaneous interventions can positively impact on a number of TB indicators (Rocha *et al* 2011). However, the specific effect of economic support may be difficult to disentangle from other interventions given simultaneously (Oxman and Fretheim 2009) and implementing all these interventions may be unaffordable for some countries.

What interventions and levels of targeting are most acceptable to the communities who receive economic support and the health workers or other staff who implement this? Are there any additional unintended consequences of such targeting?

The perceptions of those who implement and receive economic support are crucial to the administration and effectiveness of this support, as this trial has shown. Depending on the context in which such support is given, the more defined the target group for receipt of such support, the less acceptable the programme of support might be. Clearly defined targeting may

also increase the stigma associated with the disease and further alienate recipients from their communities.

If targeted at patients with a specific disease, such as TB, important research questions around economic support include the following:

- What are the perceptions of patients with other health problems, who are not targeted to receive economic support?
- How do these perceptions affect the relationship of such patients with health care providers, and their own health related behavior?
- How do these perceptions affect the recipients of this support and their positions in their communities?

If economic support is targeted at poorer patients, regardless of their illness status, the following questions should be considered:

- Would it be feasible to deliver these vouchers (or a similar form of economic support) to poorer patients only?
- How feasible would the means testing inherent in such delivery be?
- Would such means testing be susceptible to manipulation and corruption?
- Would the effect demonstrated in this pragmatic trial be replicated or increased if this voucher were only given to more deprived patients?
- What would the reaction of other patients be, to the targeting of poorer patients for the receipt of a voucher?

What is the potential for misuse of economic support in various contexts? How realistic are the perspectives of stakeholders around this potential for misuse? If misuse is likely to be important, how can it be minimized by the design and administration of the economic support so that its administration remains feasible in various settings?

Economic support can be misused by those who are eligible for it (in terms of what it is used for), by those who are not eligible for it (in terms of theft and fraud to obtain the support) and by those who administer it (in terms of theft and fraud to obtain the support for themselves, or in terms of poor administration). All of these factors need to be considered for different types of economic support in various settings. In addition the following are crucial considerations for future research: the perceptions of stakeholders (such as managers, policy makers and health workers) around such misuse, the relationship of these perceptions to evidence regarding the use and misuse of economic support, and the effect of these perceptions on the development and implementation of programmes of economic support for TB control.

What value should an economic intervention have, to maximize its benefit on TB outcomes but minimize its potential to cause dependence and/or a perverse incentive effect?

It is likely that larger values of economic support will have a greater impact on individual and household nutritional status and well-being, but it is also possible that, if the support is tied to a particular illness, larger values may cause recipients to try to remain ill in order to continue receiving such support. If the value of the support approaches or exceeds the value of the minimum wage in any setting, it may also dis-incentivise work and create dependence on the support. The thresholds at which these effects occur, if at all, may depend on the levels of

poverty in communities to whom the support is given. Research into the optimal value of economic interventions should therefore be conducted in several different contexts to best inform practice across a range of settings.

Is the use of economic support to improve TB treatment outcomes, or reduce the incidence of TB, worth pursuing?

It is clear that several crucial questions around the use of economic support to improve TB control in general, and the outcomes of patients on TB treatment in particular, remain. A further fundamental question which may be asked is this: is it worthwhile to continue to conduct research that aims to answer these questions? It is the strong view of this researcher that studies that investigate and attempt to intervene in the relationship between poverty and ill health should be high on the public health research agenda. This is in spite of the difficulties inherent in such research – the complexity of the relationship between poverty and ill health, the mistrust of several stakeholders of economic interventions to improve health and the difficulty in elucidating the mechanisms of action of economic interventions to improve health. This view is based not only on the principle that the alleviation of poverty is in itself a moral imperative but also, on the public health principle that the determinants of disease should be addressed just as much as disease itself.

Two fundamental ethical principles inform this stance, and these principles also underpin efforts to address the social determinants of health in general. The first, which is commonly felt to be the most important ethical principle in public health, is that of beneficence (the obligation to bring about "a certain kind of human good, the good of health") (Powers and Jaden 2008: 9).

Diminishing the number of cases of TB that arise through poverty, and improving the outcomes of patients on TB treatment through the amelioration of conditions of poverty, increase the sum of the public's health. The second ethical principle is social justice. Social justice is less often considered in health research but is fundamental in research on the social determinants of health (Venkatapuram and Marmot 2009) and is increasingly recognized as an important principle underlying public health (Powers and Jaden 2008: 10). Indeed, intervening in the cases of tuberculosis that arise through poverty can be seen as marrying both of these ethical obligations, and it has been argued that it is "an appropriate, if not obligatory, function of public health to reduce poverty…. – if for no other reason than to reduce the incidence of disease" (Kass 2001).

Concluding remarks

This thesis centres around the use of economic support to improve the outcomes of patients on TB treatment. The background to the work includes a systematic review of material incentives and enablers in the management of TB, whilst the main body of the thesis is a report of a pragmatic cluster randomized controlled trial, and its process evaluation, that tested the use of a voucher in patients on treatment for active TB in South Africa. The rationale for the trial was that, although convincing evidence exists for a strong association between poverty and TB, and although there is substantial interest in the socio-economic factors that might affect TB epidemiology, there is very little evidence available that can inform the use of socio-economic

interventions to improve TB control, specifically to improve the outcomes of patients on TB treatment.

This was the first trial conducted in Africa to investigate the use of economic support to improve patients' outcomes on TB treatment. Because the context in which our trial was to be conducted was one of general poverty, we postulated that the economic support we provided (a voucher for a general store) would have its effect through enabling patients to overcome the barriers poverty posed to adherence to treatment (depicted in the model presented in Chapter 1). Although the findings of the trial based on an intention to treat analysis were not significant, the exploratory and dose-response analyses suggest that economic support to patients with active TB in a middle income setting has the potential to improve their outcomes on treatment. However, the context in which such support is delivered is an important consideration; attitudes of staff and patients towards the economic support may affect its delivery, which may in turn impact on its effectiveness. In addition, the logistics of the delivery of such support may be burdensome, particularly in resource-poor settings and when complex administrative procedures are put in place to prevent "leakage" of the economic support.

Although this trial and its process evaluation add to the available evidence on the use of economic support to improve patients' outcomes on TB treatment, the evidence is probably not yet convincing enough to change public health policy. Many research questions remain, which are outlined in this thesis. Because research in the field of the socio-eonomic determinants of health is complex and difficult to do, it may be asked whether the effort of

undertaking such research is worth it. I argue that it is, for a few important reasons: firstly, because it is a fundamental philosophy of public health to consider not only disease but also the determinants thereof; secondly, because addressing poverty as a determinant of disease will increase the sum of the public's health; and thirdly, because it is socially just to ensure that the burdens of any disease are not disproportionately borne by any sector of society.

Thus, although research that intervenes in the relationship between poverty and TB is still rarely conducted, I suggest that it moves to a more central place in the public health research agenda. This will expand the armamentarium of current interventions to improve TB control and result in a more just world, where some of the remediable determinants of TB are addressed and the burden of TB disease and death are not disproportionately borne by the poor.

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Appendix 2A: Detailed search strategies

Search set	CIDG SR^	CENTRAL	MEDLINE^^	EMBASE^^	LILACS^^	SCI-EXPANDED and SSC
1	tuberculosis	tuberculosis	tuberculosis	tuberculosis	tuberculosis	tuberculosis
2	adherence	PATIENT COMPLIANCE	PATIENT COMPLIANCE	PATIENT-COMPLIANCE	adherence	adherence
3	compliance	PATIENT DROPOUTS	PATIENT DROPOUTS	TREATMENT-REFUSAL	compliance	compliance
4	Monitor*	MOTIVATION	MOTIVATION	MOTIVATION	Monitor$	Monitor*
5	Incentive*	SOCIAL SUPPORT	SOCIAL SUPPORT	SOCIAL SUPPORT	Incentive$	Incentive*
6	Reward*	CONTRACTS	CONTRACTS	COMPENSATION	Reward$	Reward*
7	Voucher*	Adherence	Adherence	Adherence	Voucher$	Voucher*
8	Payment*	Incentive*	Incentive*	Incentive$	Payment$	Payment*
9	Reimbursement*	Reward*	Reward*	Reward$	Reimbursement$	Reimbursement*
10	Concordance	Voucher*	Voucher*	Voucher$	Concordance	Concordance
11	Cash transfer*	Payment*	Payment*	Payment$	Cash transfer$	Cash transfer*
12	2-11/OR	Reimbursement*	Reimbursement*	Reimbursement$	2-11/OR	2-11/OR
13	1 AND 12	Concordance	Concordance	Concordance	1 AND 12	1 AND 12
14		Cash transfer*	Cash transfer*	Cash transfer$		
15		2-14/OR	2-14/OR	2-14/OR		
16		1 AND 15	1 AND 15	1 AND 15		
17			Limit 16 to Human	Limit 16 to Humans		
18						
19	^ Cochrane Infectious Diseases Group Specialized Register		^^Search terms used in combination with the search strategy for retrieving trials			

			developed by The Cochrane Collaboration (Higgins 2006); Upper case: MeSH or EMTREE heading; Lower case: free text term			
20						

Appendix 2B: Characteristics of included studies

Chaisson 2001

Methods	Individually randomized controlled trial, factorial design Duration of enrolment: June 1995 - August 1997
Participants	Number enrolled: 300 Inclusion criteria: Injection drug users over 18 years old, with tuberculin skin test reading of more than 5 mm induration if HIV positive or 10 mm if HIV negative, on preventive treatment for TB. Exclusion criteria: evidence of active TB, history of serious adverse reaction to INH (isoniazid) treatment, previous INH treatment for 6 months or longer, serum ALT elevated more than 5 times normal levels, or HIV disease with CD4 count of less than 200/mm3. (Isoniazid is a standard TB medication used for both prophylaxis and treatment of active TB).
Interventions	All participants were randomly assigned to receive either: 1. An immediate stipend of $10 per month (for each monthly appointment kept), or 2. A deferred amount, equal to $10 for each monthly appointment kept. The immediate payment was given at the end of each month when the patient had completed a routine assessment for adherence and drug toxicity. The deferred payment was credited each month a patient in this group completed assessment for adherence and toxicity, but payment was made when treatment was completed or when the patient withdrew from the study. Each arm was on prophylaxis for TB.
Outcomes	Completion of 6 months of INH preventive treatment (reporting for each of 6 monthly visits and taking at least 80% of medication).
Notes	Independent of the material incentive, all patients were randomly assigned to directly observed preventive therapy (i.e. outreach meeting with a nurse twice a week; peer support counselling (i.e. monthly support group meetings); or routine care (i.e. monthly clinic visits). Trial location: Baltimore, United States Setting: Community based tuberculosis clinic Source of funding: National Institute on Drug Abuse (DA 08992) and the National Institute of Allergy and Infectious Diseases (AI 01637).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence generation performed by computer algorithm.
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment was given.
Blinding (performance bias and detection bias)	Unclear risk	Not known if outcome assessors were blind
Incomplete outcome data (attrition bias)	Low risk	Numbers presented for whole group and each arm, intention to treat analysis. Withdrawals included "failure to return (37 patients), voluntary withdrawal (4)...and other reasons (13)". These do not seem to be related to the material incentives
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Malotte 1998

Methods	Individually randomized controlled trial Duration: April 1994 to August 1995.
Participants	Number enrolled: 1004 Inclusion criteria: Injection drug and crack cocaine users, who had had tuberculin skin tests and were required to return for the reading. Exclusion criteria: None stated
Interventions	Participants were divided into 6 arms, which received the following interventions: 1. 5-10 minute session of motivational education 2. 5-10 minute session of motivational education plus $10 on return for tuberculin skin test reading 3. 5-10 minute session of motivational education plus $5 on return for tuberculin skin test reading 4. $10 on return for tuberculin skin test reading 5. $5 on return for tuberculin skin test reading 6. Routine care.
Outcomes	Return for tuberculin skin test reading within 96 hours.
Notes	Trial location: Long beach, California, United States Setting: Urban research clinic Source of funding: National Institute on Drug Abuse (grant RO1-DA08799)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomization not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	Low risk	No omissions from final analysis. 1004 enrolled, intention to treat analysis.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Malotte 1999

Methods	Individually randomized controlled trial Duration: September 1995 to September 1997
Participants	Number enrolled: 1078 Inclusion criteria: Injection drug and crack cocaine users who had tuberculin skin tests and were required to return for the reading (age restrictions not specifically stated but all participants were over age of 18 years). Exclusion criteria: Participation in group's previous studies.
Interventions	1. $10 on return for tuberculosis skin test reading. 2. Grocery store coupons worth $10 on return for tuberculosis skin test reading. 3. Patient's choice of bus passes or coupons for fast food restaurant worth $10 on return for tuberculosis skin test reading. 4. Motivational education session of 5 - 10 minutes. 5. Routine care.
Outcomes	Return for tuberculosis skin test reading within 96 hours.
Notes	Study was a follow up to Malotte 1998 - authors wanted to test effectiveness of non-cash incentives, as they felt health departments might object to giving cash out to patients as this was considered controversial. Trial location: Long beach, California, United States Setting: Urban research clinic Source of funding: National Institute on Drug Abuse (grant RO1-DA08799)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of randomization.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	Low risk	No omissions from final analysis. 1078 randomized, intention to treat analysis.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Malotte 2001

Methods	Individually randomized controlled trial Duration: April 1994 to September 1997 (recruitment period).
Participants	Number enrolled: 169 Inclusion criteria: Injection drug or crack cocaine users, needing INH treatment for TB prophylaxis. Exclusion criteria: Active TB or medical contraindications to the use of isoniazid.
Interventions	1. Twice weekly directly observed therapy (DOT) by study outreach worker at location chosen by patient, plus $5 per visit. 2. Twice weekly DOT by study outreach worker at location chosen by patient. 3. Twice weekly DOT at study site plus $5 per visit. Participants in both arms received INH prophylaxis.
Outcomes	Completion of course of INH (6 months if patient HIV negative, 12 months if patient HIV positive). Also percentage of medications taken on time (all doses in all arms were directly observed).
Notes	Trial location: Long beach, California, United States Setting: Urban research clinic Source of funding: National Institute on Drug Abuse (grant RO1-DA08799)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization in blocks of 18, assumed to have been done by computer.
Allocation concealment (selection bias)	Low risk	Allocation was kept in "numbered, opaque, sealed envelopes" and "staff ... were unaware of block size".
Blinding (performance bias and detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	Low risk	169 patients randomized. Six excluded from analysis for medical reasons which were unlikely to have been related to the study outcome. Intention to treat analysis.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Martins 2009

Methods	Individually randomized controlled trial conducted at three sites in Dili, Timor Leste. Duration: Enrollment 16 March - 9 November 2005; Follow up continued until July 2006.
Participants	Patients with newly diagnosed pulmonary tuberculosis, both positive and negative results on sputum tests. Eligible: 833 (563 excluded) Randomized: 270 (133 control, 137 intervention group). Most participants were poor, malnourished men living close to the clinics.
Interventions	1. Nutritious, culturally appropriate daily meal (weeks 1-8) and food packages (weeks 9-32). 2. Control group given nutritional advice. Both groups received standard TB treatment.
Outcomes	Primary outcomes: Completion of treatment, including cure Secondary outcomes: Adherence to treatment, weight gain, and clearance of sputum smears.
Notes	Outbreak of civil conflict in the country three months before completion of study disrupted service delivery and access of patients to health care (70% of the population were displaced). However, it is likely that this affected intervention and control groups similarly. Most participants were poor and malnourished men who lived close to the clinics and this may limit the external generalisability of the study. Substantial missing data for intermediate outcomes implies that participants did not attend clinics regularly. Also, intervention was not well received by many participants as it was inconvenient to attend the clinics at midday for the meal (this was also the reason for a high number of patients' refusal to participate in the trial). 70% of participants had negative smear results, which means that cure could not be objectively verified. Adherence was not objectively assessed. Adverse events: None necessitated stopping treatment. Itch with or without rash was more than twice as likely to occur in the intervention group (RR 2.27; 95% CI 1.20-4.26).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated random allocation sequence with randomly varying block sizes (done by independent statistician using STATA). Allocation was stratified by community health clinic and by diagnosis of TB (positive or negative smear).
Allocation concealment (selection bias)	Low risk	Concealed from all investigators with sequentially numbered opaque sealed envelopes prepared distant from study site.
Blinding (performance bias and detection bias)	Unclear risk	Blinding of participants and treatment providers not done, but independent observer who determined the primary outcome was blinded.
Incomplete outcome data (attrition bias)	Low risk	All participants received allocated intervention and loss to follow up (transfer to another clinic during treatment) was very small (1% in intervention group and 4% in control group). Intention to treat analysis.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Morisky 2001

Methods	Individually randomized controlled trial. Duration: Not stated
Participants	Number enrolled: 794. Inclusion criteria: Adolescents aged 11 - 19 years who needed treatment for latent TB infection. Exclusion criteria: Not stated
Interventions	1. Peer counselling (at least once every two weeks) 2. Incentive (participant-parent contingency contract, where parent and patient negotiated a reward for adherence to treatment. This was provided by the parent and given at a frequency negotiated by the parent and participant). Examples of incentives included a special meal at home, going out to eat, clothing, going to movies or renting a video, or anything agreeable to both parent and adolescent. 3. Combined peer counselling and incentive (participant-parent contingency contract). 4. Usual care. Participants in intervention and control arms received INH prophylaxis.
Outcomes	Completion of 6 months of INH prophylaxis; measured using the discharge summary recorded in the patient's medical chart.
Notes	Trial location: Los Angeles County, United States Setting: Urban community based clinics Source of funding: National Heart, Lung and Blood Institute (ROI-55770).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	Low risk	Authors state that intention to treat model was used (page 570). 794 adolescents enrolled and analysed. No omissions from final analysis.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	Over and above the interventions described above, patients were interviewed three times during the study and at each interview received $15. The additional interest in the participants, plus the cash which may have acted as a further incentive to adhere, may be regarded as interventions in themselves. However, this applied to all participants and would not have introduced bias.

Pilote 1996

Methods	Individually randomized controlled trial. Duration: June 1992 to April 1994.
Participants	Number enrolled: 244 Inclusion criteria: Homeless "men and women", age not specified (but all over 18 years as listed in Results section), who had a tuberculin skin test and were required to attend a clinic to initiate treatment for latent or active TB. Exclusion criteria: Recent investigation for TB.
Interventions	1. Peer health advisers plus usual care (advisers accompanied patients to clinics and assisted with filling out forms etc.) 2. Incentive of $5 cash if participant came to clinic within 3 weeks of randomisation plus usual care 3. Usual care (appointment at TB clinic plus a bus token for transport to clinic).
Outcomes	Attendance at clinic appointment within three weeks of positive reading of tuberculin skin test.
Notes	Second phase of this study reported in Tulsky *et al* 2000. Trial location: San Fransisco, California, United States Setting: Urban community based TB clinic (attached to San Fransisco General Hospital) Source of funding: Kaiser Family Foundation, AcqUired Immunodeficiency Syndrome Clinical Research Center, San Francisco, Calif; Universitywide Acquired Immunodeficiency Syndrome Research Program, University of California; and by grant R01-DA04363-07 from the National Institute on Drug Abuse, Bethesda, MD.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"treatment group was assigned by sampling without replacement from blocks of nine". Assumed to be done by computer.
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	Low risk	244 patients randomized, 244 analysed.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Tulsky 2000

Methods	Individually randomized controlled trial Duration: June 1992 to May 1995 (recruitment period June 1992 to December 1994, plus 6 months of patient follow up time).
Participants	Number enrolled: 118 Inclusion criteria: Homeless adults, with positive tuberculin skin test or credible history of prior positive tuberculin skin test but no follow up for this in the 6 months prior to the study. Exclusion criteria: Receiving treatment or prophylaxis for TB at the time of the study, or HIV positive.
Interventions	1. Usual care (self-supervised daily dosing with INH and monthly clinic visits for assessment and refill of tablets) 2. Taking of 900 mg INH directly observed at each of two weekly visits to study site; plus an incentive of $5 cash. 3. Peer health advisor (who directly supervised taking of treatment twice weekly, accompanied patient to clinic and looked for the patient if lost to follow up). Participants in intervention and control arms received INH prophylaxis.
Outcomes	Completion of 6 months of INH preventive treatment as documented in patients' clinic charts; number of months of INH dispensed.
Notes	Trial location: San Francisco, California, United States Setting: Community-based TB clinic Source of funding: Not stated

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomization used, therefore allocation sequence assumed to have been generated by computer.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	Low risk	Of 330 patients randomized, 195 found to require further evaluation and 37 needed further diagnostic tests (sputum cultures and liver function tests). Of 121 who were prescribed INH, 118 were analysed - 3 were excluded from study because of "toxic effects of INH". These reasons unlikely to be related to final outcome.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

Tulsky 2004

Methods	Individually randomized controlled trial. Duration: May 1996 to May 1998 (based on recruitment period of May 1996 to December 1997, plus 6 months for patient follow up).
Participants	Number enrolled: 119 (85% male; median age 41 years [range 21-79]). Inclusion criteria: Homeless adults who were eligible for preventive TB treatment. Adults who were "truly homeless" (living in street and shelter dwellings) and those who were "marginally housed" (living in residential hotels) were recruited into the study. Exclusion criteria: active TB or HIV positive.
Interventions	1. $5 cash incentive for each twice weekly appointment kept. 2. Non-cash incentive with face value of $5 for each twice weekly appointment kept (patients could choose between fast food or grocery store coupons, phone cards or bus tokens). Participants in intervention and control arms received INH prophylaxis.
Outcomes	1. Completion of preventive treatment (assessed by reviewing TB clinic records) 2. Length of time needed to look for participants who had missed scheduled appointments and didn't respond to letters or phone calls. (A tracking form including names and mailing addresses of family, friends, and case workers was completed for each participant. After the first missed appointment, staff made phone calls and sent reminder letters. If the participant did not attend the next scheduled visit, outreach efforts were initiated and were guided by the information on the tracking form.)
Notes	Because the cash incentive arm did so much better than the non-incentive arm in the study performed by this group previously (Tulsky 2000), the authors felt it would be unethical to continue to randomize one group to no incentive. Trial location: San Francisco, California, United States Setting: Urban, community-based TB clinic Source of funding: National Heart, Lung, and Blood Institute (grant HL55729) and the National Institute of Mental Health (grant MH54907).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence was generated "...from a list of randomly generated numbers"
Allocation concealment (selection bias)	Unclear risk	"...numbers previously sealed into individual envelopes and selected in consecutive order". Not clear if these envelopes were opaque.
Blinding (performance bias and detection bias)	Low risk	"TB clinic physicians were blinded with respect to the results of the randomisation"
Incomplete outcome data (attrition bias)	Low risk	141 patients randomized but 16 not prescribed INH (4 in cash incentive arm, 12 in non-cash incentive arm). Reasons for exclusion were clinical and unlikely to be related to allocation. 6 patients censored (5 for clinical reasons, 1 because died in hotel fire). Again, reasons for exclusion unlikely to be related to allocation or outcome. 119 patients analysed.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	High risk	The study groups were not the same with respect to their primary housing in the year prior to the study. In the cash incentive arm, 23% had lived in a shelter or on the street, whilst 41% of the non-cash incentive arm had done so.

White 1998

Methods	Individually randomized controlled trial Duration: One year (1996)
Participants	Number enrolled: 79 (98% male, mean age 32.0 years) Inclusion criteria: Jail inmates eligible for INH prophylaxis for latent TB infection. Exclusion criteria: Unable to speak English or Spanish, or sequestration from jail population due to violence or mental illness.
Interventions	1. Promise of $5 cash incentive (to be provided) on making first visit to community TB clinic to continue INH prophylaxis after release from jail plus standardised TB education. 2. Standardised TB education (about TB and the importance of taking INH prophylaxis). Participants in intervention and control arms received INH prophylaxis.
Outcomes	Attendance at first visit to community TB clinic to continue INH prophylaxis after release from jail.
Notes	Trial location: San Francisco, California, United States Setting: Prison Source of funding: Academic Senate of the University of California, San Francisco.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization done using table of random numbers.
Allocation concealment (selection bias)	Low risk	Previously sealed, ordered, opaque envelopes used.
Blinding (performance bias and detection bias)	Low risk	Research assistants collecting clinic data (as to whether participant attended first appointment or not) were blinded as to participants' assignments.
Incomplete outcome data (attrition bias)	Low risk	Of the 79 inmates enrolled in the study, 18 remained in prison for the full duration of their INH treatment (and so were never required to present at a community TB clinic). 61 were analysable, and there were no differences between treatment allocations in this group. "Data were rechecked for internal validity and there were no differences by study group in any of the variables collected for this analytic sample of 61 persons" (page 508).
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes.
Other bias	Low risk	The study appears to be free of other bias.

White 2002

Methods	Individually randomized controlled trial Duration of enrolment: 1 March 1998 to 31 May 1999.
Participants	Number enrolled: 558 (82% male; median age 28.5 years in incentive arm, 29.7 years in routine care arm, and 29.5 years in education arm) Inclusion criteria: Jail inmates with latent TB infection, eligible for and agreeable to INH prophylaxis. Exclusion criteria: HIV positive, not able to speak English or Spanish, assessed by Sherriff's personnel to be violent, or by mental health staff to have a serious psychiatric illness.
Interventions	1. Promise of incentive ($25 equivalent in food or transportation vouchers), provided at the first visit to the community TB clinic after release from jail 2. Education, provided every two weeks whilst in jail 3. Usual care (neither intervention).
Outcomes	1. Attendance at first visit to community TB clinic to continue INH prophylaxis within one month after release from jail; 2. Completion of full course of INH treatment.
Notes	HIV positive patients on INH prophylaxis receive very different programme of treatment, including incentives. Trial location: San Francisco, California, United States Setting: Prison Source of funding: National Institute of Nursing Research, National Institutes of Health, Bethesda, Md. (grant R01 NR04456).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization done using table of random numbers.
Allocation concealment (selection bias)	Low risk	Ordered, opaque, sealed envelopes used.
Blinding (performance bias and detection bias)	Low risk	Research assistants collecting clinic data (as to whether participant attended first appointment or not) were blinded as to participants' assignments.
Incomplete outcome data (attrition bias)	Low risk	Of 558 inmates enrolled, 48 discontinued INH treatment whilst in jail, and 185 completed INH treatment whilst in jail. Thus 325 were eligible for analysis. There were no differences between study group in either the 325 analysable patients or 558 initially enrolled patients. Reasons for exclusion from analysis not likely to be related to final outcome. Intention to treat analysis for those released while taking INH.
Selective reporting (reporting bias)	Unclear risk	Study protocol not available and there is no earlier methods paper listing the pre-specified outcomes
Other bias	Low risk	The study appears to be free of other bias.

Appendix 2C: Characteristics of excluded studies

Cheng 1997

Reason for exclusion	Not a randomized controlled trial, as allocation to treatment interventions was done by day of the week.

Filho 2009

Reason for exclusion	Not a randomized controlled trial; essentially two cross-sectional studies where first group was not given incentive and second group was.

FitzGerald 1999

Reason for exclusion	Not a randomized controlled trial; essentially two cross-sectional studies where first group was not given incentive and second group was.

Jahnavi 2010

Reason for exclusion	A trial of community health worker delivered tuberculosis treatment combined with food supplements; and not a trial of food incentives per se.

Morisky 1990

Reason for exclusion	Not a randomized controlled trial, as allocation to treatment interventions was done by the last digits of the participants' clinic numbers.

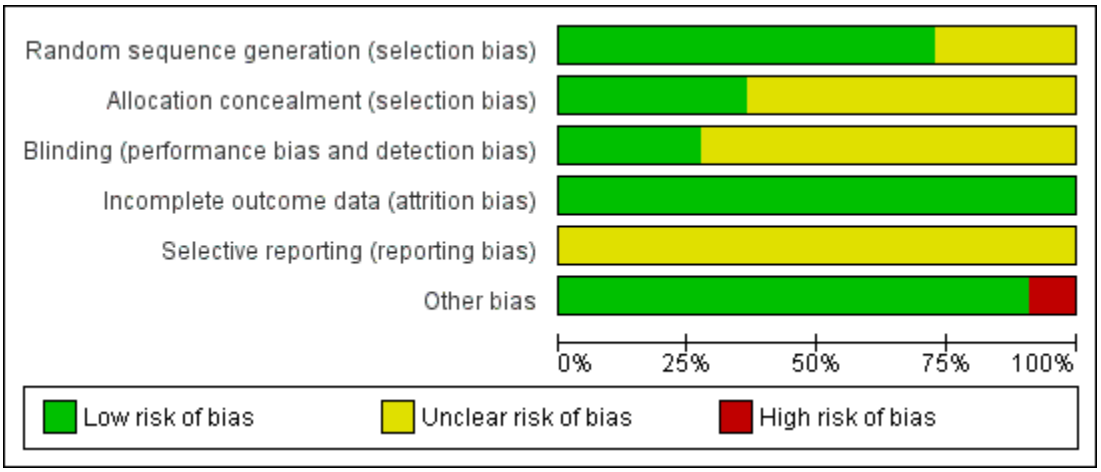
Nyamathi 2006

Reason for exclusion	Both the intervention and control arms received a $5 cash incentive for each dose of INH prophylaxis taken. It was therefore not possible to assess the effect of the incentive in this study. The main intervention was a nurse case management programme.

Yao 2008

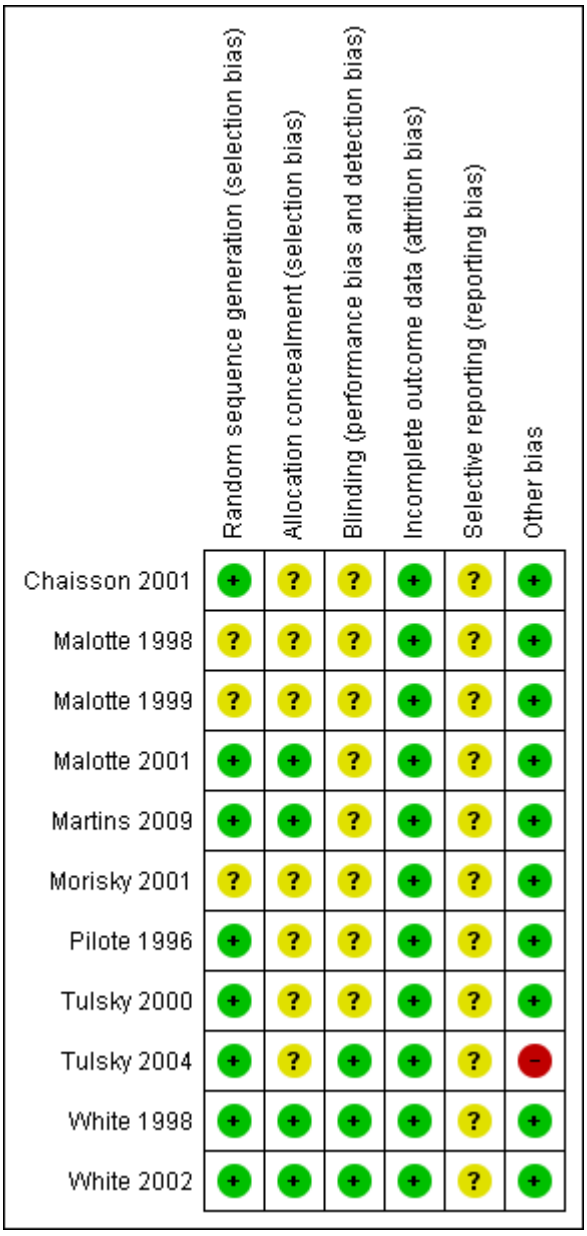
Reason for exclusion	Quasi-experimental study (controlled before-after study), with no evidence of randomisation to control or intervention groups. Incentives were provided to health care workers as well as patients, and the effect of patients' incentives only is not disaggregated.

Appendix 2D: Risk of bias graph



Risk of bias graph: reviews authors' judgments about each risk of bias item presented as percentages across all included studies.

Appendix 2E: Risk of bias summary



Risk of bias summary: reviews authors' judgments about each risk of bias item for each included study.

Appendix 2F: Data and analyses

1 Incentive versus routine care

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Return for tuberculin skin test results	2	1371	Risk Ratio (M-H, Random, 95% CI)	2.16 [1.41, 3.29]
1.2 Clinic visit to start or continue TB prophylaxis	3	595	Risk Ratio (M-H, Fixed, 95% CI)	1.58 [1.27, 1.96]
1.3 Completion of TB prophylaxis	3	869	Risk Ratio (M-H, Random, 95% CI)	1.79 [0.70, 4.58]
1.4 Completion of treatment for active TB	1	265	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.86, 1.12]

2 Immediate versus deferred incentive

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Completion of TB prophylaxis	1	300	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.98, 1.24]

3 Cash incentive versus non-cash incentive

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 Return for tuberculin skin test reading	1	652	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [1.07, 1.19]
3.2 Completion of TB prophylaxis	1	141	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [1.02, 1.56]

4 Different values of cash incentive

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 Return for tuberculin skin test reading	1	404	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [1.01, 1.16]

5 Incentives versus any other intervention

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 Return for tuberculin skin testing	2	1366	Risk Ratio (M-H, Random, 95% CI)	2.16 [1.56, 3.00]
5.2 Clinic visit to start or continue TB prophylaxis	2	535	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.92, 1.31]
5.3 Completion of TB prophylaxis	3	837	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.59, 1.83]

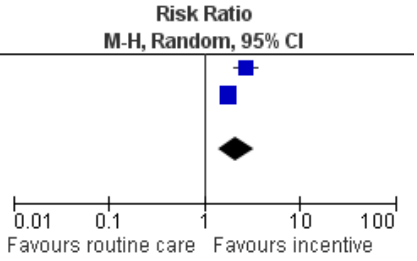
Appendix 2G: Forest plots

Comparison one: Any incentive versus routine care

Outcome: Return for tuberculin skin test results

Study or Subgroup	Any incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Malotte 1998	361	404	33	100	45.8%	2.71 [2.04, 3.59]
Malotte 1999	572	652	106	215	54.2%	1.78 [1.55, 2.04]
Total (95% CI)		**1056**		**315**	**100.0%**	**2.16 [1.41, 3.29]**
Total events	933		139			

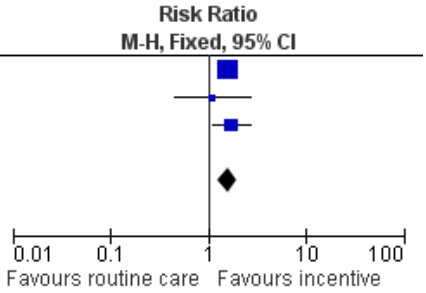
Heterogeneity: Tau² = 0.08; Chi² = 7.29, df = 1 (P = 0.007); I² = 86%
Test for overall effect: Z = 3.57 (P = 0.0004)



Outcome: Clinic visit to start or continue TB prophylaxis

Study or Subgroup	Any incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pilote 1996	69	82	42	79	57.3%	1.58 [1.26, 1.99]
White 1998	8	31	7	30	9.5%	1.11 [0.46, 2.67]
White 2002	42	185	25	188	33.2%	1.71 [1.09, 2.68]
Total (95% CI)		**298**		**297**	**100.0%**	**1.58 [1.27, 1.96]**
Total events	119		74			

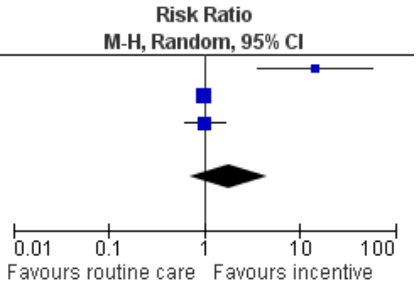
Heterogeneity: Chi² = 0.74, df = 2 (P = 0.69); I² = 0%
Test for overall effect: Z = 4.16 (P < 0.0001)



Outcome: Completion of TB prophylaxis

Study or Subgroup	Any incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Malotte 2001	28	53	2	55	21.8%	14.53 [3.64, 57.98]
Morisky 2001	152	199	147	189	41.2%	0.98 [0.88, 1.09]
White 2002	26	185	26	188	37.0%	1.02 [0.61, 1.68]
Total (95% CI)		**437**		**432**	**100.0%**	**1.79 [0.70, 4.58]**
Total events	206		175			

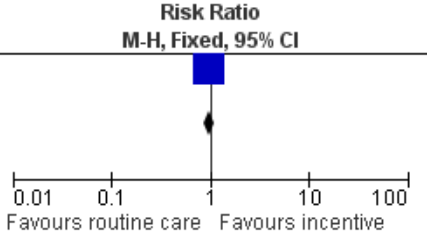
Heterogeneity: Tau² = 0.55; Chi² = 20.12, df = 2 (P < 0.0001); I² = 90%
Test for overall effect: Z = 1.21 (P = 0.22)



Outcome: Completion of treatment for active TB

Study or Subgroup	Incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Martins 2009	103	136	100	129	100.0%	0.98 [0.86, 1.12]
Total (95% CI)		**136**		**129**	**100.0%**	**0.98 [0.86, 1.12]**
Total events	103		100			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)

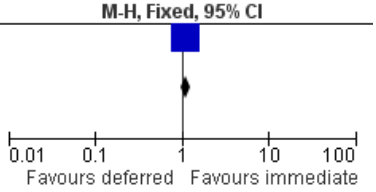


Comparison 2: Immediate versus deferred incentive

Outcome: Completion of TB prophylaxis

Study or Subgroup	Immediate incentive Events	Total	Deferred incentive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chaisson 2001	126	152	111	148	100.0%	1.11 [0.98, 1.24]
Total (95% CI)		**152**		**148**	**100.0%**	**1.11 [0.98, 1.24]**
Total events	126		111			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.67 (P = 0.10)

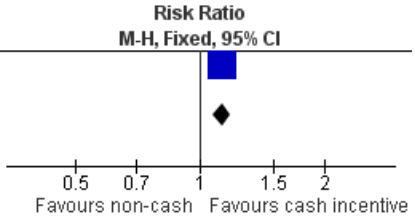


Comparison 3: Cash incentive versus non-cash incentive

Outcome: Return for tuberculin skin test reading

Study or Subgroup	Cash incentive Events	Total	Non-cash incentive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Malotte 1999	206	217	366	435	100.0%	1.13 [1.07, 1.19]
Total (95% CI)		**217**		**435**	**100.0%**	**1.13 [1.07, 1.19]**
Total events	206		366			

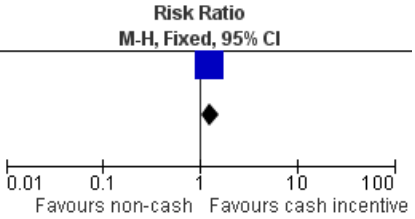
Heterogeneity: Not applicable
Test for overall effect: Z = 4.63 (P < 0.00001)



Outcome: Completion of TB prophylaxis

Study or Subgroup	Cash incentive Events	Total	Non-cash incentive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tulsky 2004	58	72	44	69	100.0%	1.26 [1.02, 1.56]
Total (95% CI)		**72**		**69**	**100.0%**	**1.26 [1.02, 1.56]**
Total events	58		44			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.17 (P = 0.03)

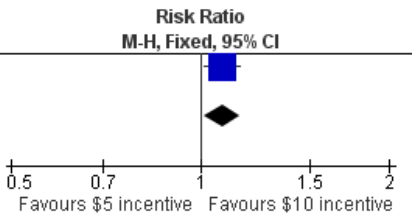


Comparison 4: Different values of cash incentive

Outcome: Return for tuberculin skin test reading

Study or Subgroup	$10 cash incentive Events	Total	$5 cash incentive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Malotte 1998	186	200	175	204	100.0%	1.08 [1.01, 1.16]
Total (95% CI)		**200**		**204**	**100.0%**	**1.08 [1.01, 1.16]**
Total events	186		175			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.34 (P = 0.02)

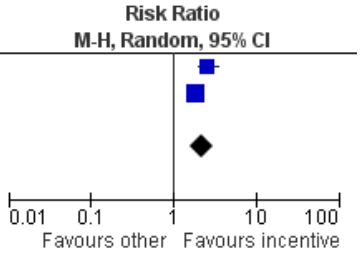


Comparison 5: Incentives versus any other intervention

Outcome: Return for tuberculin skin testing

Study or Subgroup	Incentive Events	Incentive Total	Any other intervention Events	Any other intervention Total	Weight	Risk Ratio M-H, Random, 95% CI
Malotte 1998	361	404	34	99	43.8%	2.60 [1.98, 3.42]
Malotte 1999	572	652	99	211	56.2%	1.87 [1.62, 2.16]
Total (95% CI)		**1056**		**310**	**100.0%**	**2.16 [1.56, 3.00]**
Total events	933		133			

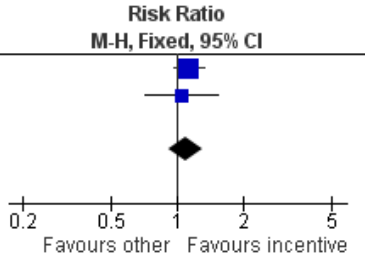
Heterogeneity: Tau² = 0.04; Chi² = 4.50, df = 1 (P = 0.03); I² = 78%
Test for overall effect: Z = 4.62 (P < 0.00001)



Outcome: Clinic visit to start or continue TB prophylaxis

Study or Subgroup	Incentive Events	Incentive Total	Any other intervention Events	Any other intervention Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pilote 1996	69	82	62	83	60.6%	1.13 [0.96, 1.32]
White 2002	42	185	40	185	39.4%	1.05 [0.72, 1.54]
Total (95% CI)		**267**		**268**	**100.0%**	**1.10 [0.92, 1.31]**
Total events	111		102			

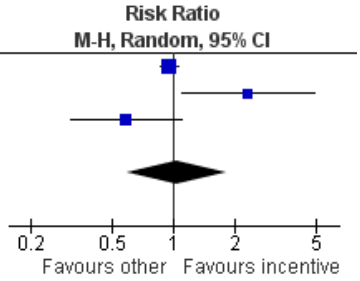
Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 1.03 (P = 0.31)



Outcome: Completion of TB prophylaxis

Study or Subgroup	Incentive Events	Incentive Total	Any other intervention Events	Any other intervention Total	Weight	Risk Ratio M-H, Random, 95% CI
Morisky 2001	152	199	151	188	45.1%	0.95 [0.86, 1.06]
Tulsky 2000	19	43	7	37	25.5%	2.34 [1.11, 4.93]
White 2002	14	185	24	185	29.4%	0.58 [0.31, 1.09]
Total (95% CI)		**427**		**410**	**100.0%**	**1.04 [0.59, 1.83]**
Total events	185		182			

Heterogeneity: Tau² = 0.18; Chi² = 7.90, df = 2 (P = 0.02); I² = 75%
Test for overall effect: Z = 0.12 (P = 0.90)

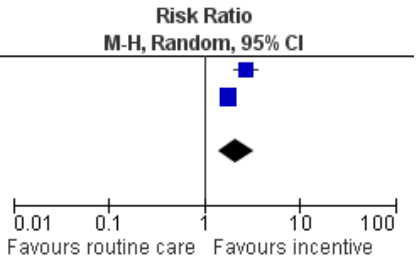


Comparison 6: Incentive versus routine care

Outcome: Return for tuberculin skin test results

Study or Subgroup	Any incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Malotte 1998	361	404	33	100	45.8%	2.71 [2.04, 3.59]
Malotte 1999	572	652	106	215	54.2%	1.78 [1.55, 2.04]
Total (95% CI)		**1056**		**315**	**100.0%**	**2.16 [1.41, 3.29]**
Total events	933		139			

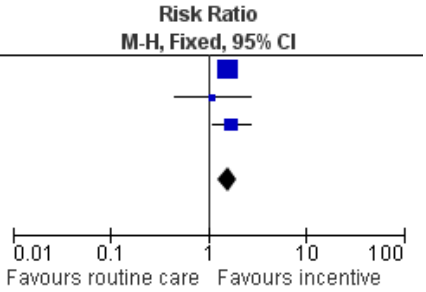
Heterogeneity: Tau² = 0.08; Chi² = 7.29, df = 1 (P = 0.007); I² = 86%
Test for overall effect: Z = 3.57 (P = 0.0004)



Outcome: Clinic visit to start or continue TB prophylaxis

Study or Subgroup	Any incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pilote 1996	69	82	42	79	57.3%	1.58 [1.26, 1.99]
White 1998	8	31	7	30	9.5%	1.11 [0.46, 2.67]
White 2002	42	185	25	188	33.2%	1.71 [1.09, 2.68]
Total (95% CI)		**298**		**297**	**100.0%**	**1.58 [1.27, 1.96]**
Total events	119		74			

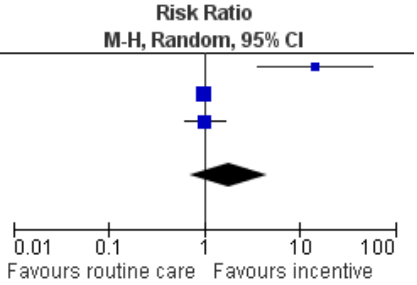
Heterogeneity: Chi² = 0.74, df = 2 (P = 0.69); I² = 0%
Test for overall effect: Z = 4.16 (P < 0.0001)



Outcome: Completion of TB prophylaxis

Study or Subgroup	Any incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Malotte 2001	28	53	2	55	21.8%	14.53 [3.64, 57.98]
Morisky 2001	152	199	147	189	41.2%	0.98 [0.88, 1.09]
White 2002	26	185	26	188	37.0%	1.02 [0.61, 1.68]
Total (95% CI)		**437**		**432**	**100.0%**	**1.79 [0.70, 4.58]**
Total events	206		175			

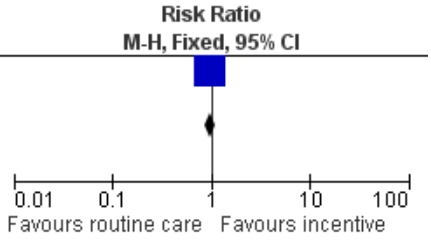
Heterogeneity: Tau² = 0.55; Chi² = 20.12, df = 2 (P < 0.0001); I² = 90%
Test for overall effect: Z = 1.21 (P = 0.22)



Outcome: Completion of treatment for active TB

Study or Subgroup	Incentive Events	Total	Routine care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Martins 2009	103	136	100	129	100.0%	0.98 [0.86, 1.12]
Total (95% CI)		**136**		**129**	**100.0%**	**0.98 [0.86, 1.12]**
Total events	103		100			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)



Appendix 2H: Summary of findings tables

1 Material incentives/enablers compared to routine care for improving patient adherence to TB management

Material incentives compared to routine care for improving patient adherence to TB management					
Patient or population: People engaged in tuberculosis programmes **Settings:** High- and low-income settings **Intervention:** Material incentives (such as cash, grocery vouchers or food) **Comparison:** Routine care					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	Routine care	**Material incentives**			
Return for tuberculin skin test reading	**441 per 1000**	**953 per 1000** (622 to 1000)	**RR 2.16** (1.41 to 3.29)	1371 (2 studies)	⨁⨁⊖⊖ **low**[1,2]
Return to clinic to start or continue treatment	**249 per 1000**	**393 per 1000** (316 to 488)	**RR 1.58** (1.27 to 1.96)	595 (3 studies)	⨁⨁⨁⊖ **moderate**[2]
Completion of TB prophylaxis	**405 per 1000**	**725 per 1000** (283 to 1000)	**RR 1.79** (0.70 to 4.58)	869 (3 studies)	⨁⨁⊖⊖ **low**[2,3]
Completion of treatment for active TB	**775 per 1000**	**760 per 1000** (669 to 868)	**RR 0.98** (0.86 to 1.12)	265 (1 study)	⨁⊖⊖⊖ **very low**[4,5]
The **assumed risk** is taken from the control groups in the trials. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.					

Footnotes (pto)

Footnotes

[1] Downgraded by 1 for risk of bias: Neither study adequately described the method of randomization.

[2] Downgraded by 1 for indirectness: These trials were conducted in specific subpopulations from the USA and the result may not be applicable in other settings.

[3] Downgraded by 1 for inconsistency: Two studies found no suggestion of a benefit with the incentive, and just one study found a clinically and statistically significant benefit in drug users.

[4] Downgraded by 2 for indirectness: Qualitative research around this trial suggests that the form of the incentive was not appropriate as patients did not like having to attend the clinic at midday for a meal.

[5] Downgraded by 1 for imprecision: The 95% CI includes what may be clinically important benefits and no effect.

2 Summary of findings table: Immediate versus deferred incentive

Immediate compared to deferred incentive for improving patient adherence to TB management					
Patient or population: People at high risk of developing TB **Settings:** High- and low-income settings **Intervention:** Immediate incentive (received on a regular basis during treatment) **Comparison:** Deferred incentive (received only at end of treatment).					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	deferred incentive	**immediate**			
Completion of TB prophylaxis	**750 per 1000**	**832 per 1000** (735 to 930)	**RR 1.11** (0.98 to 1.24)	300 (1 study)	⨁⨁⊖⊖ **low**[1,2]
The **assumed risk** is taken from the control group in the trial. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.					

[1] Downgraded by one for indirectness: This trial was conducted in specific subpopulations from the USA and the result may not be applicable in other settings.

[2] Downgraded by one for imprecision: The 95% CI of the estimate of effect includes both clinically important benefit and no effect.

3 Summary of findings table: Cash versus non-cash incentive

Cash compared to non-cash incentive for improving patient adherence to TB management					
Patient or population: People at high risk of developing TB **Settings:** High- and low-income settings **Intervention:** Cash incentive **Comparison:** Non-cash incentive					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	non-cash incentive	**cash**			
Return for tuberculin skin test reading	**841 per 1000**	**950 per 1000** (900 to 992)	**RR 1.13** (1.07 to 1.18)	652 (1 study)	⨁⨁⊖⊖ **low**[1]
Completion of TB prophylaxis	**638 per 1000**	**804 per 1000** (651 to 995)	**RR 1.26** (1.02 to 1.56)	141 (1 study)	⨁⨁⊖⊖ **low**[1]
The **assumed risk** is taken from the control group in the trial. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.					

[1] Downgraded by two for indirectness: These trials were conducted in specific subpopulations from the USA and the results may not be applicable in other settings.

4 Summary of findings table: Comparison of different values of cash incentives

Comparison of different values of cash incentives for improving patient adherence to TB management					
Patient or population: People at high risk of developing TB **Settings:** High- and low-income settings **Intervention:** Higher cash value ($10) **Comparison:** Lower cash value ($5)					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	lower cash value	**higher cash value**			
Return for tuberculin skin test reading	**858 per 1000**	**927 per 1000** (867 to 995)	**RR 1.08** (1.01 to 1.16)	404 (1 study)	⨁⨁⊖⊖ **low**[1]
The **assumed risk** is taken from the control group in the trial. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.					

[1] Downgraded by two for indirectness: This trial was conducted in a specific subpopulation from the USA and the result may not be applicable in other settings.

5 Summary of findings table: Material incentives versus educational or motivational interventions

Incentives compared to educational or motivational interventions for improving patient adherence to anti-TB treatment					
Patient or population: Patients at high risk of developing TB **Settings:** High- and low-income settings **Intervention:** an incentive **Comparison:** any educational or motivational intervention					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	any other intervention	**material incentives**			
Return for tuberculin skin test reading	**429 per 1000**	**927 per 1000** (669 to 1000)	**RR 2.16** (1.56 to 3.00)	1366 (2 studies)	⨁⨁⊖⊖ **low**[1,2]
Return to clinic to start or continue treatment	**381 per 1000**	**419 per 1000** (351 to 499)	**RR 1.10** (0.92 to 1.31)	535 (2 studies)	⨁⨁⊖⊖ **low**[2,3]
Completion of prophylaxis for latent TB	**444 per 1000**	**462 per 1000** (262 to 813)	**RR 1.04** (0.59 to 1.83)	837 (3 studies)	⨁⨁⊖⊖ **low**[2,4]
The **assumed risk** is taken from the control group in the trial. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.					

[1] Downgraded by 1 for risk of bias: Neither study adequately described the method of randomisation.

[2] Downgraded by 1 for indirectness: These trials were conducted in specific subpopulations from the USA and the result may not be applicable in other settings.

[3] Downgraded by 1 for imprecision: The 95% CI includes what may be clinically important benefits and no effect.

[4] Downgraded by 1 for inconsistency: Two studies found no suggestion of a benefit with the incentive, and just one study found a clinically and statistically significant benefit in drug users.

Appendix 3A: Description of pragmatic/explanatory approach to the trial

Domain	Predominant approach	Description
Participant eligibility criteria	Pragmatic	All patients with drug sensitive pulmonary TB enrolled; no additional exclusion criteria were applied
Experimental intervention — flexibility	Pragmatic-explanatory	Instructions were given for each element of voucher delivery, but practitioners were not rigorously monitored in this.
Experimental intervention — practitioner expertise	Pragmatic	The voucher was delivered by the same Department of Health nurses who would have cared for patients and administered TB treatment had there not been a trial, and this included nurses at all levels of experience and seniority
Comparison intervention — flexibility	Pragmatic	Patients in control clinics received routine TB care
Comparison intervention — practitioner expertise	Pragmatic	TB care in control clinics was delivered by the same Department of Health nurses who would have cared for patients and administered TB treatment had there not been a trial, and this included nurses at all levels of experience and seniority
Follow-up intensity	Pragmatic	There was no additional follow

		up of trial participants beyond what was usually performed by the Department of Health. Data for all trial participants were obtained from clinic registers and patients' files.
Primary trial outcome	Pragmatic	The primary outcomes of the trial were the same as those used by the Department of Health, and no additional measurements were used.
Participant compliance with "prescribed" intervention	Explanatory	Patient adherence was measured as routinely done by Department of Health nurses (i.e. by checking the patients' clinic cards and by doing pill counts). Patients who were adherent to treatment were given vouchers.
Practitioner adherence to study protocol	Pragmatic explanatory	Nurses were encouraged to adhere to study protocol but meetings only took place every 4 to 6 weeks and there was no censure for failing to adhere.
Analysis of primary outcome	Explanatory	Intention-to-treat analysis was supplemented by an exploratory analysis (based on a per-protocol analysis) and a dose-response analysis in order to estimate "maximum achievable treatment effect".

Source: Thorpe KE, Zwarenstein M, Oxman AD, Treweek S, Furburg CD, Altman DG et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. Journal of Clinical Epidemiology 62 (2009) 464-475.

Appendix 3B: Voucher

HEALTH SYSTEMS TRUST

MRC

Voucher for patients on TB treatment
I-voucher yeziguli ezidla amaphilisi esifo sofuba i-TB

This voucher is redeemable for goods to the value of R120.00 only.
Le-Voucher ingathenga izimpahla zenani elingu R120.00 kuphela.

UNIVERSITEIT STELLENBOSCH UNIVERSITY

Patient name
Igama lesiguli .....

Gender
Ubulili .....

Patient ID or Birth date (yy/mm/dd)
Noma usuku lokuzalwa .....

Patient clinic number
Inombolo yasemtholampilo yesiguli .....

.....
Signature of nurse/sister and date
Isignesha yomhlengikazi, nosuku

Serial number of voucher:
Inombolo ye-voucher:
007901

Clinic Stamp / Isitembu Somtholampilo

The Health Systems Trust/Medical Research Council undertake to pay the dealer R120.00 for each voucher presented to the shop.

This voucher is valid for thirty (30) days from the date above.
Le-voucher ingasetshenziswa uma zingakapheli izinsuku ezingamashumi amathathu (30) kusukela osukwini olubhalwe ngenhla.

The dealer should supply any goods to the patient to the value of R120.00. No amounts may be carried over. No cash change should be given.
Umthengisi kumele anike isiguli noma iluphi uhlobo lwezimpahla zenani elingu R120.00. Kumele isetshenziswe yonke le-voucher zingakapheli izinsuku ezibekiwe ngenhla. Ngeke ukwazi ukusebenzisa ingxenye ye-voucher uma sekudlule izinsuku ezibekiwe ngenhla. Awutholakali ushintshi oyimali kule-voucher.

SHOP FOR REDEMPTION OF VOUCHER:

The goods purchased should be indicated on the list below.
Izimpahla ezithengiwe kumele zikhonjiswe ohlwini olungenzansi.

	Quantity/Ubuningi	Price/inani
Mealie meal/imphupu		
Whole maize/izinkobe		
Bread/isinkwa		
Flour/ufawa		
Potatoes/amazambane		
Beans/ubhontshisi		
Lentils/udali		
Nuts/amakinati		
Cooking oil/ukalakateni		
Margarine/ibhotela		
Peanut butter/ibhotela lamantongomane		
Baked beans/ubontshisi osethinini		
Vegetables/imfino		
Eggs/amaqanda		
Milk/maas/ubisi/umasi		
Meat/fish/inyama/inhlanzi		
Other, please specify/okunye, sicela uchaze:		

Dealer's stamp/igama lesitolo

Date/usuku .....

PLACE STICKER HERE

Sticker must be in place in order for the voucher to be valid.

TBCTA The Tuberculosis Coalition for Technical Assistance

USAID FROM THE AMERICAN PEOPLE

wellcome trust

Appendix 3C: Information for clinics

Vouchers for patients with TB

Study conducted in eThekwini and Uthungulu Districts, 2009

Thank you for participating in this study! Here follow some guidelines for the distribution of vouchers to patients. If you require further information, or in case of problems, please contact Dr Elizabeth Lutge on 083 4192787.

1. Every patient receiving TB treatment from the clinic will receive the voucher for the duration of their treatment, or a maximum of 8 months (for re-treatment patients)
2. The patient should take the voucher from the clinic to the allocated shop, and present it to the shopkeeper with his/her green clinic card.
3. The patient will be able to take goods to the value of R120.00 from the shop
4. The patient may take any goods he or she wishes, but should be encouraged to take healthy foods that will support his/her recovery
5. The patient must spend as much of the voucher as possible. No change will be given by the shop.
6. The patient will not be able to keep credit at the shop. Each voucher must be spent on one day
7. The voucher may not be exchanged for cash at the shop
8. The shopkeeper will be reimbursed for all vouchers redeemed at his/her shop.
9. Copies of distributed vouchers will be collected from the clinics and the shops every month by the Health Systems Trust.

How to answer questions from the patient

Here follow some examples of questions the patients might ask, and ideas on how you could answer them. We hope this is helpful. However, if you need support or further information, please don't hesitate to contact Elizabeth Lutge at the Health Systems Trust (work phone 033 – 3473967, email Elizabeth@hst.org.za, cell phone 0834192787).

1. Can someone take the voucher to the store for me?

Only if you are too ill to take the voucher yourself. If you can't go to the shop yourself, we will indicate on the voucher that someone else is taking it for you. The clinic sister will judge if you are really too ill to take the voucher to the shop, and will indicate this on the voucher.

2. Do I have to spend it all at once?

Yes. The shop will not keep credit for you. Whatever you don't spend when you first take the voucher to the shop will be lost.

3. Will I get change?

No, the shops will not give you change for the money you haven't spent. So it's best that you spend as much of the R120.00 as you can, all at once.

4. I don't have my ID book – can I still participate in the study?

Yes. The clinic sister will record your date of birth and your gender on the voucher and this will be acceptable to the shops.

5. What can I buy from the shop?

You can buy anything you like, but it's best to buy nutritious foodstuffs that will help you recover from your TB.

6. I can't go to the shop today – when do I need to spend the voucher by?

You need to spend the voucher within one month of receiving it. The shops will not accept the voucher if more than one month has gone by after you received it.

7. How long can I get the voucher for?

You will receive the voucher every month until you have completed 6 months of TB treatment (or 8 months if you are a re-treatment case). You will not receive the voucher beyond this period, even if your treatment is continued.

8. If I get TB again, will I get the voucher?

No. These vouchers are part of a study. Once the study is over, the vouchers will not be issued unless the results of the study show that they are beneficial, and unless the Department of Health feels they will be worthwhile.

9. Why aren't patients at other clinics getting the voucher?

Because this study is comparing TB cure rates at clinics where patients do receive the voucher, with cure rates where patients don't receive the voucher. This is how we will know if the voucher is effective in improving cure rates or not.

10. Can I tell my friends with TB to come to this clinic so that they can get the voucher?

No. It's important that patients with TB stay at the clinics where they are registered. If patients cross to this clinic, it will change the cure rates at other clinics and we will not be

able to see if the vouchers have improved cure rates at this clinic or not. Also, it will result in a much greater workload for the nurses at this clinic. It is best for people to receive treatment from the clinic that is closest to them.

11. Can I tell my friends and family to come to this clinic to test for TB, so that they can get the voucher?

It is important that anyone who suspects they might have TB, tests at a clinic. Patients can come to this or any other clinic to test for TB.

12. Why am I not eligible for the study (for patients starting TB treatment after the trial has ended)?

The study that was looking at whether vouchers helped patients take their TB treatment has ended. Patients were only bought into the study for a few months, although the study will last until they have finished their treatment. At the end of the study, the results will be given to the Department of Health. If the results show that vouchers did improve cure rates for TB patients, and the Department feels that it is worthwhile, the Department of Health may implement the voucher system in clinics.

Appendix 3D: Letter of ethics approval for trial

7 February 2008

Dr EE Lütge
Health Systems Trust
PO Box 808
DURBAN
4000

Dear Dr Lütge

RESEARCH PROJECT: "ECONOMIC INCENTIVES FOR IMPROVING CLINICAL OUTCOMES IN PATIENTS WITH TB IN SOUTH AFRICA: A STUDY OF FEASIBILITY AND EFFECTIVENESS"

PROJECT NUMBER : N07/10/245

At a meeting of the Committee for Human Research that was held on 12 November 2007 the above project was approved on condition that further information that was required, be submitted.

This information was supplied and the project was finally approved on 6 February 2008 **for a period of one year from this date**. This project is therefore now registered and you can proceed with the work. Please quote the above-mentioned project number in all further correspondence.

Please note that a progress report (obtainable on the website of our Division) should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly and subjected to an external audit.

Patients participating in a research project in Tygerberg Hospital will not be treated free of charge as the Provincial Government of the Western Cape does not support research financially.

Due to heavy workload the nursing corps of the Tygerberg Hospital cannot offer comprehensive nursing care in research projects. It may therefore be expected of a research worker to arrange for private nursing care.

Yours faithfully

FRANKLIN WEBER
RESEARCH DEVELOPMENT AND SUPPORT (TYGERBERG)
Tel: +27 21 938 9657 / E-mail: fweb@sun.ac.za

Appendix 3E: Patient consent form for in-depth interview

(similar form used for all participants).

We would like to talk to you about your experience with the voucher you have received over the past few months. Your input is very important to help assess whether the voucher has helped patients to take their TB treatment, as well as how the delivery of the voucher has been, and what changes could be made to improve this.

We will be asking you several questions which we would like you to answer openly and honestly. Everything you say will be treated confidentially. Your name will not be noted anywhere in our data or our reports, and everything that we write will be safely stored in a locked drawer in the office of the Health Systems Trust. After two years, all these papers will be destroyed.

We would like to tape-record this interview, as well as record it by taking notes. If you would prefer that we do not tape record, then we will respect your wishes.

We have received ethical approval for this study (including these interviews) from the University of Stellenbosch, and permission to conduct the study from the KwaZulu-Natal Department of Health. If you have any queries regarding this study, you can contact:

Dr Elizabeth Lutge

The Health Systems Trust

Phone: 031 - 3072954 / 083 4192787

Fax: 031 – 3040775.

If you consent to participate in this interview, we will sign the consent form below. If not, we will close this interview now. Please note that if there are any questions that you do not want to answer, you are free to refuse to do so. Also, you may withdraw from this interview at any time.

Patient consent given: Yes No

Signed (interviewee)…….

Signed (interviewer)…….

Date: ……

Thank you!

Appendix 3F: Patient consent form for household economic survey

Patient survey: experience of TB and its financial effect on household

We would like to talk to you about your experience of TB, and how having TB has affected your work and your income. If you have received a voucher, we will be asking you about that too. We will use the answers you give to inform the Department of Health about how TB affects people financially.

We will be entering your answers to our questions on a cell phone. Once the interview is completed, we send the interview via sms to a central computer at the Health Systems Trust, where it will be analysed. The interview is deleted from this phone as soon as it is sent. Your name will not be used at any time during this study, and you will not be able to be identified from this interview.

We have received ethical approval for this study (including these interviews) from the University of Stellenbosch, and permission to conduct the study from the KwaZulu-Natal Department of Health. If you have any queries regarding this study, you can contact:

Dr Elizabeth Lutge
The Health Systems Trust
Phone: 031 - 2669090 / 083 4192787.

We hope that you will consent to this interview, which will take about 40 minutes.
If you do consent to participate in this interview, we will sign the consent form below. If not, we will close this interview now. Please note that if there are any questions that you do not want to answer, you are free to refuse to do so.

Patient consent given: Yes No

Signed (patient)…….
Date: ……
Signed (interviewer)…….
Date: ……
Place: …….

Thank you!

Appendix 3G: Protocol for trial and its process evaluation

Economic incentives for improving clinical outcomes in patients with TB in South Africa: a study of feasibility and effectiveness.

Principal investigator: Dr EE Lutge (Health Systems Trust)

In collaboration with Professor JA Volmink (University of Stellenbosch) and Dr SA Lewin (Medical Research Council South Africa)

Additional technical assistance for protocol development and data analysis provided by KNCV Tuberculosis Foundation.

Funded by the National Department of Health (South Africa), the Tuberculosis Control Assistance Program (TB CAP), (the Netherlands, through the National TB Directorate) and the Wellcome Trust (United Kingdom).

Background:

Tuberculosis (TB) is widely acknowledged as a disease of poverty (Lancet 2005) and much work internationally has gone into establishing the vulnerability of poor people to TB (StopTB Partnership 2002b).

In Piot's model of the different aspects of a TB programme, a patient needs an awareness of possible TB infection and a motivation to seek treatment, in order to access it (Piot 1967). However, even when these are present, studies have shown that poverty is a barrier to seeking treatment, for TB (Sanou *et al* 2004, Xu *et al* 2004) and other illnesses (Taffa & Chepngeno 2005, Goldman *et al* 2002). Many more primarily qualitative studies show that after diagnosis of TB and initiation of treatment, poverty fundamentally undermines adherence by rendering the patient unable to cope with the direct and indirect costs of treatment (Munro *et al* 2007, Greene 2004, Needham *et al* 2004, Watkins & Plant 2004, Khan *et al* 2000, Johansson *et al* 1999, Johansson *et al* 1996). The conclusion from these studies (that poor patients are more likely than wealthier to default from treatment) has been reinforced by a recent survey in Brazil, where the defaulter rate amongst the poorest 20% of patients was ten times higher than among the wealthiest 20% (Belo *et al* 2006).

The inability to cope with the costs of treatment is especially true in low and middle income countries (McIntyre *et al* 2006), where the burden of TB is also highest (StopTB Partnership 2002b). However, in poor countries little work has been done on interventions that may lessen the impact of the economic shock of TB on household economies, or the potential for these interventions to improve TB outcomes such as adherence and cure.

In the literature on adherence in South Africa, few studies have investigated the role of patient economic factors. Those that have been done to date have concluded that financial constraints are major obstacles to the completion of TB treatment (Loveday *et al* 2006, Lutge *et al* 2005, Yach 1988) and TB preventive therapy (Rowe *et al* 2005). In Rowe's qualitative study, financial limitations were universally reported by patients as general barriers to adherence, and cited again as preventing access to the clinic because of the expense of transport. Two of the other studies (Loveday *et al* 2006, Lutge *et al* 2005) both concluded that financial constraints were important factors in a patient's failure to complete TB

treatment, in populations where knowledge of TB was generally good (Lutge *et al* 2005), and trust in the public health system was fairly high (Loveday *et al* 2006). In this latter study, the cost of reaching the clinic (between R3 and R80, depending on the distance from the patients' homes) was said to be a major constraint to their access to treatment by 40% of patients. Most (84%) of the patients interviewed in the study were unemployed.

To date in South Africa, support to TB patients has been provided in the form of free treatment at government hospitals and clinics (Department of Health 2001), nutritional supplementation[15] and social grants (Department of Social Development 2006). Nutritional supplementation is meant to be given in the form of powdered food supplements or food parcels to patients at primary care clinics, and is complemented by involving patients in gardening projects. However, problems in delivering this supplementation has resulted in patchy and suboptimal implementation, and to date this programme has not been formally evaluated. The social (disability) grant is given, in conjunction with the Department of Social Development, to patients who are certified by a doctor to be incapacitated by TB. This criterion makes most TB patients, who are not incapacitated by the disease, ineligible for the grant. In addition, this criterion has led to significant corruption in some areas, with certain private general practitioners becoming known as "disability doctors" as they will provide certification for grants whether this is warranted or not. This intervention has also not been formally evaluated. A further failing of the nutritional and social grant support is that neither has been linked to TB outcomes, such as adherence to or completion of treatment.

Economic incentives to patients with TB may diminish the multi-faceted impact of poverty on TB control, both by preventing the deepening of household poverty when affected by TB, and by limiting the extent to which poverty undermines treatment outcomes. Indeed, poor TB patients in Brazil ranked financial incentives highest in a range of interventions which included improved health services support and better administrative organization, such as being able to schedule appointments (Belo *et al* 2006).

A variety of incentives (such as cash, vouchers for shops, telephone cards or bus tokens) have been tested and evaluated for their effects on patient adherence to tuberculosis management (either treatment or preventive therapy) (Tulsky et al 2004). In particular, cash incentives have been found in a systematic review to be effective (Volmink & Garner 2000) and in studies subsequent to this review, were found to significantly improve rates of completion of TB preventive therapy (Malotte *et al* 2001, Tulsky *et al* 2000), and to reduce the amount of follow up necessary to assist patients to complete TB preventive therapy (Tulsky *et al* 2004).

To date no rigorous intervention studies of incentives for tuberculosis control have been conducted in high burden developing countries. This was noted in Volmink and Garner's review (2000) which concluded that "Future studies in low income countries are a priority and should measure adherence and clinical outcomes." In South Africa, tuberculosis ranks as the third most common cause of death among adults (Bradshaw *et al* 2003), adherence rates are low (only 50% of patients in the country are cured, with a further 13% completing treatment) (Grimwood *et al* 2006), 57% of people live below the poverty income line[16] and

[15] Personal communication, Mr Simiso Masondo, TB Control Programme of the KZN Provincial Department of Health, July 2006.

[16] The poverty income line varies according to household size. For a household of 4, the poverty income is R1290.00 per month (Human Sciences Research Council 2004).

the poverty gap[17] is increasing (Human Sciences Research Council 2004). South Africa is therefore an ideal setting in which to investigate the effect of economic incentives on TB outcomes.

Aim:

To test the feasibility and effectiveness of economic incentives in patients with TB in South Africa.

Objectives:

1. To evaluate the effectiveness of an economic incentive in improving clinical outcomes in patients with TB
2. To assess the responses and attitudes of health care managers, workers and patients towards the incentive
3. To investigate the technical, administrative and financial feasibility of delivering the incentive
4. To assess the impact of the incentive on patients' household economies

Definition of terms:

Incentive: Any form of inducement to adhere to or complete treatment, such as cash, vouchers for groceries, transport etc. and other forms of rewards. As preferred by the National TB Director, vouchers for local shops will be used for this study (personal communication, Dr Lindiwe Mvusi, April 2008). Vouchers are preferred to cash because they avoid connotations of being another social grant, which is controversial in South Africa. At the same time they give the patient a relatively high degree of choice as to what the voucher can be spent on, as compared to food parcels which have been used in the past in KwaZulu-Natal.

Methods:

This study will use both quantitative and qualitative methods. The basic design will be a cluster randomised trial (quantitative) within which qualitative studies will be nested. The methods will be described and discussed under the objectives to which they apply.

Objective 1: To evaluate the effectiveness of the incentive

Design

This will be a pragmatic, un-blinded two-arm cluster randomized trial with before and after data on TB outcomes. Clinics will be randomly allocated to intervention (voucher) and control (no voucher) groups, with each clinic and the patients attending it acting as a cluster. A cluster design was chosen because providing incentives to selected individuals within one clinic in a poor population could result in high levels of dissatisfaction in those patients not receiving these incentives. Also it is logistically easier to implement the intervention across a

[17] The poverty gap measures the required annual income transfer to all poor households to bring them out of poverty (Human Sciences Research Council 2004).

whole facility than by individual patient as health providers can use the same procedure for each person.

All TB patients within the intervention clinics will receive the incentive, but the focus for analysis will be on smear positive patients who present at the clinic for the first time during the study (see "study population" below).

Patients in the control and intervention clinics will receive TB care as routinely provided by the health service.

Follow up and outcomes

Patients will be followed up for the duration of their TB treatment, which is usually 6 months.

The effectiveness of the intervention will be assessed by comparing intervention and control sites for the following outcomes:

1. Primary outcomes: Cure and treatment completion
2. Secondary outcomes: Default and failure rates.

The World Health Organisation definitions of these outcomes will be used (WHO 2004).

These data will be obtained from each clinic, where it is routinely collected for submission to the National TB Register.

Intervention

Monthly vouchers of R120.00 will be given to patients, redeemable at shops in close proximity to the clinics. The amount was informed by arguments proposing a universal system of social protection in South Africa, and has been adjusted for inflation since these debates took place. Proponents of the Basic Income Grant suggested that a monthly amount of US$20 would more than double the average consumption of the poorest 20% of the population. The amount suggested for this study is greater than the $5 per visit that achieved a significant effect in an American study with a similar aim (Malotte *et al* 2001).

Shops in close proximity to the clinic will be chosen as outlets where patients can redeem their vouchers. Shops will be chosen in consultation with nursing staff at the intervention clinics, to ensure that they are easily accessible for patients but also are among the least expensive in the area. Patients will receive the voucher from the clinic, containing the patient's name and their clinic number, as well as the signature of the nurse in charge of TB services, and the clinic stamp and date stamp. The clinic will keep a copy of each voucher for the records of the study. On discussion with the participating shops, patients will be allowed to spend their vouchers over the following month, and will not be required to spend it all at once. However, credit will not be maintained beyond any one month, and cash change will not be given to patients who do not spend the entire amount within that period. Shops will record on each voucher, what goods were bought and at what price.

Study period

Patient recruitment will take place over a period of 3 months. Patients will be followed up for the following six months (for new patients) and eight months (for retreatment patients), resulting in a total study duration of 11 months. All patients on TB treatment during the recruitment period will receive the voucher, for the remainder of the duration of their treatment. However, the focus for analysis will be on the new smear positive patients starting their treatment during this time.

Study sites

This study will be conducted in KwaZulu-Natal, one of South Africa's poorest and most populous provinces (Barron et al 2007). One urban district (eThekwini, also known as the city of Durban) and one rural district (Uthungulu) have been selected for the study. In terms of cure rates, eThekwini ranks 47th (with a cure rate of 41%) and Uthungulu 45th (with a cure rate of 42%) out of 53 districts in the country (Barron et al 2007).

eThekwini, the second most densely populated district in the country (ibid) is one of four districts in the country identified for special intervention in the Department of Health's National TB Crisis Management Plan (Department of Health 2006). The city has the best socio-economic profile in KwaZulu-Natal, with good infrastructure (just over 96% of residents have access to piped water. However, many of its health outcomes remain poor, and its TB cure rate, and perinatal mortality rate are among the worst in South Africa (Barron et al 2007). Uthungulu is a poorer district than eThekwini, with over half of its residents living on less than R800.00 per month (ibid). Infrastructure has improved recently, with 73.4% of its households having access to piped water, as has the TB cure rate (from 18% in 2004) but there is still much room for improvement.

Study population

Clinics:
Clinics with cure rates of between 40% and 70% for the previous year will be eligible for inclusion in the study. The upper limit is set because a demonstration of a clinically meaningful effect in clinics with cure rates higher than 70% would not be possible with this sample size. The lower limit is set to exclude clinics where poor service provision may contribute to poor cure rates. Also, because the average cure rate in South Africa is 57% (Barron *et al* 2005) included clinics will be more representative of the country as a whole. Cure rates for the country range from 31.4% in Nkangala (Mpumalanga province) to 83.6% in Overberg in the Western Cape province. Seventy five percent of districts achieved cure rates of above 50% (ibid). Finally, only clinics with 20 or more new smear positive patients per quarter will be included, to ensure that smaller clinics do not bias the results.

Patients:

Although all TB patients will receive the incentive, the new smear positive adult TB patients (that is, those who are newly diagnosed during the study period) will be the focus of the analysis. Children below the age of 18 years will be analysed both within the main cohort and as a sub-group analysis. The proportion of new smear positive TB patients varies between clinics, but in most clinics, these patients constitute the majority of TB cases (in Uthungulu

district, there were 1400 new TB patients and only 324 re-treatment patients in 2007[18]) . Retreatment patients will be analysed separately. This is at the explicit request of the Uthungulu District, where these patients are perceived as problematic (personal communication, Jacqueline Ngozo, HAST co-ordinator, Area 3, KwaZulu-Natal. September 2008).

Only patients who join the study in the initial three month recruitment period will receive the incentive. This is at the explicit request of the eThekwini Municipality, who want to limit where possible the cross over of patients from control to intervention clinics.

All TB patients, regardless of their HIV status and treatment for HIV, will be included in the study. .

Patients with MDR- or XDR-TB will be excluded from the analysis because of the very poor outcomes associated with these strains. However, they will receive the vouchers for a maximum of 8 months of the study, as will retreatment cases.

Study sample

There are a total of 144 clinics in eThekwini[19], and 68 provincial clinics in Uthungulu, providing TB care. From all these clinics in the districts, a list of those meeting the cure rate and new smear positive patient inclusion criteria will be constituted. A random sample of 20 clinics will be selected from this sub-population - 16 in eThekwini, and 4 clinics in Uthungulu. Half of the selected clinics in each district will be randomly allocated to the intervention group and half to the control group. All eligible patients within intervention clinics will be recruited for the study.

Power calculations are based on an intracluster correlation co-efficient of 0.031 (within the range commonly encountered in health outcomes from primary care clinics).[20] Comparing cure rates between two arms using a two sided test with 5% significance level, this study will be powered (90%) to detect a 15% difference between the intervention and control arms. Although the effect size is large, it is anticipated that a large effect size will be necessary to justify the roll out of this intervention on a large scale.

Analysis

Analysis will be by intention to treat at the clinic as well as at the patient level. The baseline characteristics of the two groups will be compared, although no significant differences are expected because of randomisation.

Because the study outcomes are binary (cured or not cured etc.) a generalised linear mixed model (GLMM) will be used to evaluate the intervention effect with clinics used as a random effect. This method will take into account the cluster randomised design and the number of clinics planned for this study will be appropriate for use of this method.

[18] Uthungulu TB data 2007.
[19] Approximately 40% of clinics in eThekwini are run by the Local Government (eThekwini Municipality) and 60% by the KwaZulu-Natal Provincial Department of Health.
[20] Personal communication: Dr Carl Lombard, Biostatistician, Medical Research Council (South Africa). May 2007.

Sub-group analyses based on gender, age, HIV status, anti-retroviral treatment, and socio-economic indicators are planned.

Objective 2: To assess the responses and attitudes of health care managers, workers, shopkeepers and patients towards the incentives

Design

This objective will be addressed through a qualitative study, nested within the intervention study above. Semi-structured qualitative interviews will be used to gather data. A sample of approximately 35 patients from intervention clinics in eThekwini and 15 patients from Uthungulu will be interviewed at the clinic at month 3 of treatment and again on exit (month 6), focusing on their experience of TB and TB treatment, and their perceptions of the health system and the incentive (please see Patient Interview Guide attached). Data collection will continue until saturation is reached. Patients will be requested to give investigators their cell phone numbers or other contact details, which will be used to contact them for the second interview.

Patients will be selected purposively to include men and women of different age groups, socio-economic status and places of residence, to ensure that a range of experiences are investigated. As far as possible, patients will be selected from the TB register, independently by the study staff. Although nurses will not select patients, their advice will be sought in identifying patients who have struggled to complete treatment, patients from different residential areas, patients who have received TB treatment previously etc. Where consent is given, these interviews will be recorded on audiotape and later transcribed. If consent for the recording is not given, interviews will be transcribed at the time.

HIV tests will not be performed as part of the study, but patients will be asked to disclose their status. If not known, they will be encouraged to test using the clinics' voluntary counselling and testing programme. Since HIV has a profound effect on TB cure rates, as well as on a household's economy, this will be an important variable to include in analysis. However, patients will be assured that all information they disclose, including their HIV status, will be treated with confidentiality and that all data will be anonymised.

A sample of twenty four nurses involved in providing direct TB care to patients in intervention clinics will be asked to participate in semi-structured interviews in months 6 and 9 of the study period. Inter alia, their attitudes to TB patients, perceptions about adherence and efforts to encourage this, and their attitudes towards the incentive will be investigated (please see Health Worker In-depth Interviews, attached).

The shop owners or managers of all eight shops participating in this study will be interviewed to ascertain their views on the administration of this voucher, and the impact that the voucher had on their businesses, both financial and administrative. (Interview Guide and consent form attached).

All interviews will be recorded on audiotape and subsequently transcribed.

For qualitative interview data, thematic analysis will be undertaken to identify issues seen as important by respondents. At this stage, it is anticipated that this analysis will be manual, but after viewing the data, a software programme may be used for analysis.

Objective 3: To investigate the technical, administrative and financial feasibility of delivering an economic incentive to patients with TB

Together with a health economist, the cost of delivering the intervention will be calculated for the intervention clinics, and used as a basis for modelling these costs for the province, and the country as a whole. The cost per additional patient cured will be calculated. This data will be presented to TB managers at district, provincial and national levels to discuss the financial feasibility of providing the incentive on a large scale.

The additional technical and administrative burdens imposed by the incentive programme will be documented throughout the study. The process for delivering the vouchers to patients, confirming their adherence to treatment and authorising payment of the incentive every month will be developed and streamlined over the course of the study. Unanticipated issues will be addressed and additional new systems supporting the delivery of the intervention will be developed during the study. Specifically, the feasibility of making the incentive conditional on demonstration of adherence will be investigated. Because this will require input from directly observed treatment (DOT) supporters, whether these are community or clinic based, the study will answer the question of whether it will be simpler to make the incentive unconditional.

Twelve managers at clinic, district, provincial and national TB programme levels will also be interviewed to explore the administrative and technical feasibility of the intervention (please see Manager In-depth Interviews, attached). Only those managers who are directly involved with the intervention clinics, or under whose line management these clinics fall, will be interviewed. Provincial and national managers involved with the management of service provision for TB will be interviewed. The effectiveness data, costs, and patient, provider and manager responses will form the basis of assessments regarding the feasibility of the intervention.

Objective 4: To assess the impact of the incentive on patients' household economies

Design

This will be a quantitative cross-sectional study nested in the intervention study, involving a 40% sample of patients attending both intervention and control clinics (approximately 400 patients in total). This will enable the detection of differences of 30% between the groups, with a power of 80% and a confidence interval of 95%.

Patients will be approached to complete a questionnaire (please see Impact of incentive on household economy: questionnaire, attached) in month 6 of treatment. Using this structured questionnaire, data on household income and consumption will be collected, as well as, amongst others, direct and indirect expenditure due to TB and coping mechanisms of households to offset expenditure (Sauerborn *et al* 1996). In intervention clinics, data on the incentive will also be collected. This will include what goods/services the incentive is spent on, and the extent to which the incentive has protected the household from further poverty.

Fieldworkers will enter all information onto cell phones at the time of the administration of the questionnaire (no paper will be used for this section of data collection). This method of data collection has been used successfully by the Health Systems Trust in other studies. However, funds have been set aside for paper-based collection of data if required.

Data analysis

Uni-, bi- and multivariate analyses will be performed. Associations between patient, household and facility variables and treatment outcomes will be explored.

Ethical considerations

This study has been approved by the Committee for Human Research at the University of Stellenbosch (South Africa) (see approval letter attached), and is supported by the Director of TB services at the National Department of Health (Dr Lindi Mvusi).

Permission to conduct the study has been obtained from the Health and Safety Sub-Committee of elected City Counsellors and the Research Committee of the eThekwini Municipality, the Durban District Office, the Uthungulu District Management Team and the KwaZulu-Natal Provincial Research Committee.

Consent for this study will be sought at a clinic level, and individual patient consent will be requested from those patients who are interviewed. The nature of the study, and the reasons why it is being conducted, will be explained to all patient participants in an indigenous language of their choice. This will be done verbally and in writing. Patients will be assured that non-participation will not compromise their treatment. Written informed consent will be obtained from all participants (nurses, managers and patients) who are interviewed for the purposes of this study (consent forms attached in appendices). However, written consent will not be sought from patients receiving the vouchers. Individual patient consent will be implied if patients take and use the vouchers. We feel that the waiver of individual consent can be justified because patients will be receiving their routine TB treatment, and the voucher is only intended to increase adherence to this. Therefore patients will be exposed to no or very little additional risk. Also, the intervention is applied at the organizational level, and nothing further will be required from the majority of patients (written informed consent will be asked from patients who are interviewed, as above). Waiving individual patient consent will make the distribution of vouchers logistically easier at intervention clinics.

Fieldworkers will be trained to treat all information given by patients, especially HIV status, in the strictest confidence. All data will be confidential. Data will be safely stored in a locked drawer at the Health Systems Trust offices in Durban, and only accessible to the investigators.

No clinical interventions will be performed as part of this study, and participants will not be subjected to risks beyond those of other patients receiving treatment for TB.

Because this study has relevance for social and financial policy, as well as for health, a wide range of stakeholders will be informed of the results. Results will be reported to the eThekwini Municipality, the KwaZulu-Natal Provincial Department of Health, the TB and Research Directorates in the National Department of Health, the National Department of

Social Development and the National Treasury. Workshops for the discussion of results and their implications for policy will be arranged with these stakeholders.

Results will also be published in international peer reviewed journals, so that the international community can engage with the issues raised.

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Appendix 4A: Interview guide for patients

Demographic information:

Age

Gender

Number of years of education

Type of residence (shack, or formal residence)

Employment (unemployed, self employed, piece work, employed full time)

Month and year when diagnosed with TB

Any breaks in treatment in current episodes of TB (if so, record duration)

Previous episodes of TB – date (year) and whether or not treatment was completed.

In-depth questions:

1. What makes it difficult for you to take your TB treatment?
2. What makes it easier?
3. Does lack of money affect your ability to take your TB treatment? Prompt: money for transport to the clinic, for food with which to take tablets, unwillingness to leave work to go to clinic etc.
4. In addition to these problems, does having TB have an effect on your finances or those of your household at all?
5. Some people are HIV positive – do you think this impacts on their experience of TB, or their ability to take TB treatment? In what way?
6. Do you think that this voucher has made it easier for you to take your treatment? Please explain. (Prompt: Please discuss how the money is used generally - include “luxuries” such

as airtime, cigarettes etc. Is it used only for the index patient or also for other household members? Etc).

7. Please tell me about your experience of receiving the voucher. Did everything run smoothly? Were there any problems you experienced? Please explain.
8. Did anyone else know that you were receiving this voucher? How did they react when they heard?
9. Do you think this voucher is worthwhile? Why/why not?
10. Would you advise that it be given to all patients receiving TB treatment? Why/why not?
11. What else could be done to make it easier for you to take your TB treatment?
12. Do you have any other comments on your experience of receiving treatment at this clinic? (Prompting: satisfaction with the staff; opening hours of the clinic; availability of treatment etc.)

Appendix 4B: Interview guide for nurses

You have been administering this voucher to patients for a few months now. We'd like to learn about your experiences with it, what you think of it, and how it can be improved.

1. How have you found the administration of this voucher?
    a. Prompt: What things have been difficult? Please give concrete examples.
    b. Was there anything that made things run more smoothly? What has been easy?
    c. Is it getting easier or more difficult over time? Why is this so?

2. How have patients reacted to the voucher?
    a. Prompt: Have patients receiving the voucher responded differently to treatment compared to when there was no voucher?
    b. Do you think it has attracted more patients to the clinic?
    c. Do you think it has improved patients' adherence?
    d. What have patients said to you about the new voucher?
    e. Has it had negative effects on the patients?
    f. Has it improved the relationship between patients and the health services, or made it worse?
3. Did you give the voucher to every patient with PTB, or only certain patients? If only certain patients, how did you choose who received it?
4. How did you check that the patient had taken all his tablets? Did you check the green card? Are there any other ways in which you can check adherence?
    a. If a patient had missed some doses, did you say s/he couldn't get the voucher? What happened if a patient missed an appointment or missed some time of treatment? Did you still give the voucher for the time missed? Did you give the voucher when the patient returned as usual?

5. Compared with other interventions to improve adherence, such as DOTS support, how do you feel about this voucher? Prompt: effectiveness in improving adherence, ease of administration, reaction of patients etc.
6. Are there any TB patients in your clinic receiving the disability grant for TB or HIV? Does this help them to take their treatment and to complete their treatment? Please explain.
7. What support did you receive in administering this voucher? Did your management provide support? Did you get support from the study team?
8. What do you think about the voucher? Do you think it is a worthwhile intervention? Why/why not?
9. How could it be improved?
10. What further support would help in administering the voucher?
11. Do you think it should be expanded to include all clinics treating patients with TB? Why/why not?
12. What other interventions might be useful in improving the adherence of patients to TB treatment in your clinic?
13. Do you think it is right to pay the patient to behave in a healthy way?

Additional questions asked in follow up interviews:

1. Besides the vouchers do you give any other kind of support to patients at the clinic like food parcels, disability grant for TB, disability grant for HIV?
2. Do you give these to everyone with TB? If not, how do you decide who should get them? Do you decide who should get the voucher in the same way?

3. How do you make sure that the patients who are getting the vouchers are actually taking their treatment?
4. Do you have DOT supporters at this clinic? How many? Do the patients come here for their DOT support or do the DOT supporters go to the patient's house?
5. Did anyone ask you to give them the voucher after they had stopped the treatment, like when they had finished their six months?
6. Some people say that the voucher must not be given out because patients will try to stay sick so that they can get the voucher for longer. Do you think that is a problem?
7. If the department had decided to give the voucher out now to all the clinics, do you think there should give it to everyone with TB or just the ones who are really needy, who are poor and those who don't have a job?

Appendix 4C: Interview guide for managers in TB Control Programme

1. Have you been directly involved in the administration of this voucher?
2. If so, how have you found the administration of this voucher? Prompt: What things have been difficult? Was there anything that made things run more smoothly? What has been easy? Is it getting easier or more difficult over time? Why is this so?
3. If not, what have you heard from your staff about the administration of this voucher? Prompt: What things have been difficult? Was there anything that made things run more smoothly? What has been easy? Is it getting easier or more difficult over time? Why is this so?
4. What are your impressions of this voucher? What do you feel is good about it and what is not good? Please elaborate.
5. What in your opinion are the most important challenges in delivering this voucher? Please explain.
6. How could these challenges be overcome?
7. From your perspective, how do you think the administration of this voucher could be improved? Please give concrete examples.
8. Do you think the costs of offering and administering the voucher are worth the benefits? Please elaborate. How could these costs be reduced, if at all?
9. How do you feel about social assistance for patients who are ill? Like the disability grant for TB and HIV or food parcels. Do you think it helps to promote adherence?
10. What do you think of the most important challenges in delivering a kind of social support for patients with TB?
11. What would you say about role of poverty in developing TB disease?

12. Do you think that research into social interventions for medical problems like TB is important?
13. Do you think the voucher is a worthwhile intervention? Please explain why/why not.
14. Do you think this voucher should be offered at all clinics to all patients with TB across the country? Please explain why/why not.

Appendix 4D: Interview guide for shop personnel

1. How have you found the administration of this voucher? Prompt: What things have been difficult? Please give concrete examples. Was there anything that made things run more smoothly? What has been easy? Is it getting easier or more difficult over time? Why is this so?
2. How have you found the payments for the voucher from HST? Have you been paid on time, and the full amount? Have you experienced any other problems with payment?
3. Can you suggest ways in which these could be improved?
4. Do you feel you have been visited often enough and supported adequately by HST staff? If not, how could this support to you be improved?
5. Have you incurred any additional costs as a result of the voucher? If so, have these been substantial or minor? What sort of costs are they?
6. How has the voucher impacted on your staff at the tills? Have they found it easy or difficult to administer? Has their experience of the voucher changed over time (e.g. got easier as they became more used to doing it?)
7. Have you had any specific problems with the patients? For example:
    a. Have most patients come themselves to redeem the voucher or have they sent friends or relatives to redeem it? If the latter, have you allowed the friends/relatives to redeem the voucher?
    b. Have patients always bought their green clinic cards with them when redeeming the vouchers?
    c. Have most patients bought their ID books with them to redeem the vouchers? Did you always ask for ID books? (note: this was not a requirement for redeeming the voucher as many patients do not have IDs)
    d. Do patients ask for change? If so, what do you do?

e. How do you ensure that the patients spend as much of the voucher as possible, to avoid having money left over?

f. Have you ever intervened in patients' purchases? i.e. have you ever asked them to return goods that they have chosen in favour of something else? For example, if patients were buying alcohol or cigarettes or some other unhealthy item, have you asked them to exchange it? Have you asked them to buy cheaper items instead of the more expensive ones they have chosen? Etc.

8. Have you found that the volume of people coming through your shop has increased dramatically since you joined this voucher scheme?
9. What proportion of your monthly turnover does the voucher represent? If you would prefer not to answer this question, could you just tell us if it is a large, medium or small proportion?
10. How would you do this study differently, knowing what you know as a result of having participated?
11. Would you be interested in continuing to participate in such a voucher programme if it was rolled out on a national basis?
12. If yes, why and how would you suggest the running of the programme could be improved? If no, why not?

Appendix 5A: Questionnaire for household economic survey

Impact of Incentive on Household Economy

Last Modified by: Clyral Support **on** 30 Jun 2010 09:29:34 **Revision number:** 1006 **Field Count:** 149

Section 1. Introduction

1.1 Introductory Prompt

We would like to talk to you about your experience with TB, and how your household finances have been affected by this. Your input is very important in helping to develop ways of supporting patients who have TB, so that they are better able to take their treatment.

1.2 Intro 2

We will be asking you several questions which we would like you to answer openly and honestly. Everything you say will be treated confidentially. Your name will not be noted anywhere in our data or our reports.

1.3 Intro 3

This interview should take about 45 minutes. We have received ethical approval for this study from the University of Stellenbosch, and permission to conduct the study from the KwaZulu-Natal Department of Health.

1.4 Intro 4

If you have any queries regarding this study, you can contact: Dr Elizabeth Lutge, The Health Systems Trust, Phone: 031 - 260 9090/ 083 419 2787.

1.5 Consent

Do you consent to participate in this interview? Please note that if there are any questions that you do not want to answer, you are free to refuse to do so. Also, you may withdraw from this interview at any time.

Expects a single option response (**required**)

- e Yes [1]
- e No [2]

Branches

If response **Equals 'No [2]'** then skip to ***End of Interview (12.1)***

Section 2. Demographic Information

2.1 Gender

Is the participant male or female?

Expects a single option response (**required**)

- Male [1]
- Female [2]

2.2 Age

How old are you?

Expects a numeric response (**required**)

2.3 Clinic location

Please select the clinic at which this interview is being conducted.

Expects a single option response (**required**)

- Mlazi N [1]
- Mlazi L [2]
- Mbumbulu [3]
- Folweni [4]
- Goodwins [5]
- Amathikwe [6]
- Khandisa [7]
- Dondotha [8]
- Msunduzi [9]
- Kwandengezi [10]
- Mpumalanga [11]
- Fredville [12]
- Mpola [13]
- Danganya [14]
- Sivananda [15]
- Osizweni [16]
- Ntuzuma [17]
- Mlazi G [18]
- Ntambanana [19]
- Ndlangubo [20]

Section 3. Education

3.1 Highest Level of Education

What is the highest level of education you have completed?

Expects a single option response (**required**)

- Never went to school [1]
- Did some primary school but did not complete it [2]
- Completed primary school (grade 7/ standard 5) [3]
- Did some high school but did not complete it [4]
- Completed high school (grade 12) [5]
- Attended technical/ vocational college after school [6]
- Attended university after school [7]
- Don't know [8]
- Refused to respond [99]

3.2 Read

Can you read in at least one language?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

3.3 Write

Can you write in at least one language?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Section 4. Household Information

4.1 Household Location

Where do you live?

Expects a single option response (**required**)

- ė Township [1]
- ė Informal settlement [2]
- ė City [3]
- ė Suburb [4]
- ė Rural area [5]
- ė Other [6]
- ė Refused to respond [99]

Prerequisites
Skip when ***Household Location (4.1)*** Not Equal 'Other [6]'

4.2 Household Location_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

4.3 Land for Produce

Does your household have land on which it grows its own produce?

Expects a single option response (**required**)

- ė Yes [1]
- ė No [2]
- ė Refused to respond [99]

4.4 Money for Renovation

Please estimate the amount of money that has been spent in renovating or improving this household during the last year (give amount in rands).

Expects a numeric response (**required**)

Section 5. Assets

5.1 Assets

Do you, or anyone living in your household, own any of the following?

Expects multiple selected options (**required**)

- ë Any land [1]
- ë Cars or motorcycles [2]
- ë Televisions [3]
- ë Hi-Fis [4]
- ë Fridges [5]
- ë Bicycles [6]
- ë Cell phones [7]
- ë Don't own any of these items [8]
- ë Refused to respond [99]

5.2 Assets Animals

Do you, or anyone else living in your household, own any of the following animals?

Expects multiple selected options (**required**)

- ë Cows [1]
- ë Goats [2]
- ë Chickens [3]
- ë Don't own any of these animals [4]
- ë Refused to respond [99]

Branches

If response **Includes 'Refused to respond [99]'** then skip to ***First TB Episode (6.1)***

If response **Includes 'Don't own any of these animals [4]'** then skip to ***First TB Episode (6.1)***

Prerequisites
Skip when ***Assets Animals (5.2)*** **Excludes 'Cows [1]'**

5.3 Number of Cows

How many cows do you or anyone else living in your household own?

Expects a numeric response (**required**)

Prerequisites
Skip when ***Assets Animals (5.2)*** **Excludes 'Goats [2]'**

5.4 Number of Goats

How many goats do you or anyone else living in your household own?

Expects a numeric response (**required**)

Prerequisites
Skip when ***Assets Animals (5.2)*** **Excludes 'Chickens [3]'**

5.5 Number of Chickens

How many chickens do you or anyone else living in your household own?

Expects a numeric response (**required**)

Section 6. TB Illness

6.1 First TB Episode

Is this your first episode of TB?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Branches

If response Equals 'Yes [1]' then skip to *Number of Months Current Treatment (6.6)*

If response Equals 'Refused to respond [99]' then skip to *Number of Months Current Treatment (6.6)*

6.2 Number of TB Episodes

How many episodes of TB have you had in your life?

Expects a numeric response (**required**)

6.3 Last TB Episode

When was your last episode of TB (please capture the year only)?

Expects a numeric response (**required**)

Constraints

Response must be ***Less Than or Equal '2010'***

6.4 Complete Treatment

Did you complete treatment for that previous episode?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Prerequisites

Skip when *Complete Treatment (6.4)* Equals 'Yes [1]'

6.5 Number of Months on Treatment

How many months of treatment did you complete?

Expects a numeric response (**required**)

6.6 Number of Months Current Treatment

How many months of treatment have you taken in this current episode of TB?

Expects a numeric response (**required**)

6.7 Stopped Current Treatment

Have you stopped taking treatment for any period during this episode of TB?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Branches

If response Equals 'No [2]' then skip to *Finish Current TB Treatment (6.11)*

If response Equals 'Refused to respond [99]' then skip to *Finish Current TB Treatment (6.11)*

6.8 Stopped Current Treatment Why

Why did you stop?

Expects multiple selected options (**required**)

- I felt better [1]
- It was too expensive to get to the clinic to collect tablets [2]
- I felt too sick to get to the clinic to collect tablets [3]
- I had no transport to get to the clinic to collect tablets [4]
- I was too busy to get to the clinic to collect tablets [5]
- Other [6]
- Don't know [7]
- Refused to respond [99]

Prerequisites

Skip when *Stopped Current Treatment Why (6.8)* Excludes 'Other [6]'

6.9 Stopped Current Treatment Why_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

6.10 Time Stopped Taking Current Treatment

How long did you stop taking your tablets for?

Expects a single option response (**required**)

- Less than two weeks [1]
- Two weeks to one month [2]
- One to two months [3]
- More than two months [4]
- Refused to respond [99]

6.11 Finish Current TB Treatment

Do you think you will be able to finish your TB treatment?

Expects a single option response (**required**)

- Yes, definitely [1]
- Yes, maybe [2]
- No [3]
- Don't know [4]
- Refused to respond [99]

Section 7. Employment

7.1 Earn Money

I want to ask you a bit about your household finances now, and how your TB has affected your financial situation. Do you do anything to earn money? This includes having a job, doing domestic work, selling things, making things to sell, casual jobs, odd jobs, working in your family's business, having your own business, or anything else you do to earn money.

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]
- Refused to respond [99]

Branches

If response **Equals 'Yes [1]'** then skip to ***TB Affected Work Ability (7.5)***

7.2 Not Earning Money Reason

Why don't you earn any money?

Expects a single option response (**required**)

- Too sick to work [1]
- Unable to find job [2]
- Important things to do at home [3]
- Studying [4]
- Retired (on pension) [5]
- Pregnant/caring for child [6]
- Caring for adult (e.g. someone who's sick) [7]
- Housework [8]
- Other [9]
- Don't know [10]
- Refused to respond [99]

Prerequisites

Skip when ***Not Earning Money Reason (7.2)*** **Not Equal 'Important things to do at home [3]'**

7.3 Important things to do at home_specify

Please specify what important things you have to do at home (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

Prerequisites

Skip when ***Not Earning Money Reason (7.2)*** **Not Equal 'Other [9]'**

7.4 Not Earning Money Reason_specify

Please specify other reasons you're not earning any money (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

7.5 TB Affected Work Ability

Has TB affected your ability to work?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Branches

If response **Not Equal 'Yes [1]'** then skip to ***TB Affected Work Ability Money (7.9)***

7.6 TB Affected Work Ability Reason

In what way has TB affected your ability to work ?

Expects a single option response (**required**)

- I am too sick to work now [1]
- I was asked to leave work because I was sick [2]
- I couldn't look for work because I was sick [3]
- No one would employ me because I was sick [4]
- I had to miss days of work because I was sick [5]
- Other [6]
- Refused to respond [99]

Prerequisites
Skip when *TB Affected Work Ability Reason (7.6)* Not Equal 'I had to miss days of work because I was sick [5]'

7.7 TB Affected Work Ability Days

How many days of work did you miss in the past 6 months, because you were sick with TB?

Expects a numeric response (**required**)

Prerequisites
Skip when *TB Affected Work Ability Reason (7.6)* Not Equal 'Other [6]'

7.8 TB Affected Work Ability Reason_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

Prerequisites
Skip when *TB Affected Work Ability (7.5)* Equals 'Yes [1]'

7.9 TB Affected Work Ability Money

What do you do to earn money?

Expects a single option response (**required**)

- Work for one employer [1]
- Work for more than one employer [2]
- Work for yourself [3]
- Work for another household member [4]
- Do odd jobs/piece jobs [5]
- Other [6]
- Don't know [7]
- Refused to respond [99]

Prerequisites
Skip when *TB Affected Work Ability Money (7.9)* Not Equal 'Other [6]'

7.10 TB Affected Work Ability Money_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

7.11 Assistance from Others

Do you receive any assistance in terms of money or goods from others?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Branches

If response **Not Equal 'Yes [1]'** then skip to ***Household Members Earn Money (7.14)***

Prerequisites
Skip when ***Assistance from Others (7.11)*** **Not Equal 'Yes [1]'**

7.12 Assistance Type

What type of assistance do you receive from others?

Expects multiple selected options (**required**)

- Supported by others in household [1]
- Supported by persons not in the household [2]
- Supported by charity or church [3]
- Unemployment Insurance Fund (UIF) [4]
- State old age pension [5]
- Private pension [6]
- Child support grant [7]
- Foster care grant [8]
- Care dependency grant/single care grant [9]
- Disability grant [10]
- Other grant or transfer [11]
- Other [12]
- Don't know [13]
- Refused to respond [14]

Prerequisites
Skip when ***Assistance Type (7.12)*** **Excludes 'Other [12]'**
Skip when ***Assistance from Others (7.11)*** **Not Equal 'Yes [1]'**

7.13 Assistance Type_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

7.14 Household Members Earn Money

Does anyone else in your household do anything to earn money? This includes having a job, doing domestic work, selling things, making things to sell, casual jobs, odd jobs, working in your family's business, having your own business, or anything else they do to earn money.

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]
- Refused to respond [99]

Branches

If response **Not Equal 'Yes [1]'** then skip to ***Household Members Recieve Grants (7.16)***

7.15 Household Members Regular Paid Work

How many people in your household have regular paid work?

Expects a numeric response (**required**)

7.16 Household Members Recieve Grants

Does anyone else in your household receive a grant?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Prerequisites
Skip when ***Household Members Recieve Grants (7.16)*** Not Equal 'Yes [1]'

7.17 Grant Received Type

Which types of grants do the household members receive?

Expects multiple selected options (**required**)

- Old age pension [1]
- Child support grant [2]
- Foster care grant [3]
- Care dependency grant/single care grant [4]
- UIF [5]
- Private maintenance e.g. from father of children [6]
- Other [7]
- Don't know [8]
- Refused to respond [99]

Prerequisites
Skip when ***Grant Received Type (7.17)*** Excludes 'Other [7]'

7.18 Grant Received Type_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

Section 8. Household Expenditure

8.1 Expenditure Prompt

I would like to ask you about household expenditure. I will read you a list of items. Please tell me how much the household spends on each of these in a normal month.

8.2 Expenditure Food

In your household, is there monthly expenditure on food other than meat?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Food (8.2)* Not Equal 'There is expenditure and I know how much [Y]'

8.3 Expenditure Food Yes

How much does the household spend on food other than meat in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.4 Expenditure Meat

What is your normal monthly household expenditure on meat?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Meat (8.4)* Not Equal 'There is expenditure and I know how much [Y]'

8.5 Expenditure Meat Yes

How much does the household spend on meat in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.6 Expenditure Clothing and Shoes

Is there monthly household expenditure on clothing and shoes?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Clothing and Shoes (8.6)* Not Equal 'There is expenditure and I know how much [Y]'

8.7 Expenditure Clothing and Shoes Yes

How much does the household spend on clothing and shoes in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.8 Expenditure School Uniforms

Is there monthly household expenditure on school uniforms?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure School Uniforms (8.8)* Not Equal 'There is expenditure and I know how much [Y]'

8.9 Expenditure School Uniforms Yes

How much does the household spend on school uniforms in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.10 Expenditure School Fees

Is there monthly household expenditure on school fees?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure School Fees (8.10)* Not Equal 'There is expenditure and I know how much [Y]'

8.11 Expenditure School Fees Yes

How much does the household spend on school fees in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.12 Expenditure Cell phone/Airtime

Is there monthly household expenditure on cell phones/ airtime?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Cell phone/ Airtime (8.12)* Not Equal 'There is expenditure and I know how much [Y]'

8.13 Expenditure Cell phone/Airtime Yes

How much does the household spend on cell phones/ airtime in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.14 Expenditure Cigarettes/Tobacco

Is there monthly household expenditure on cigarettes/ tobacco?

Expects a single option response (**required**)

- None [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Cigarettes/ Tobacco (8.14)* Not Equal 'There is expenditure and I know how much [Y]'

8.15 Expenditure Cigarettes/Tobacco Yes

How much does the household spend on cigarettes/ tobacco in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.16 Expenditure Beer/Wine/Spirits

Is there monthly household expenditure on beer/ wine/ spirits?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Beer/ Wine/ Spirits (8.16)* Not Equal 'There is expenditure and I know how much [Y]'

8.17 Expenditure Beer/Wine/Spirits Yes

How much does the household spend on beer/ wine/ spirits in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.18 Expenditure Transport

Is there monthly household expenditure on transport?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Transport (8.18)* Not Equal 'There is expenditure and I know how much [Y]'

8.19 Expenditure Transport Yes

How much does the household spend on transport in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.20 Expenditure Health Care

Is there monthly household expenditure on health care (doctor visits, medicine, medical aid)?

Expects a single option response (**required**)

- There is no expenditure [0]
- I don't know if there is any expenditure [DKN]
- There is expenditure but I don't know how much [RRR]
- There is expenditure and I know how much [Y]
- Refused to respond [99]

Prerequisites
Skip when *Expenditure Health Care (8.20)* Not Equal 'There is expenditure and I know how much [Y]'

8.21 Expenditure Health Care Yes

How much does the household spend on health care (doctor visits, medicine, medical aid) in a normal month (amount in rands)?

Expects a decimal response (**required**)

8.22 Household Financial Situation

How would you classify the financial situation of your household these days?

Expects a single option response (**required**)

- Comfortable [1]
- Poor [2]
- Extremely poor [3]
- Don't know [4]
- Refused to respond [99]

8.23 Effect of TB on Financial Situation

What effect has your TB had on the household finances?

Expects a single option response (**required**)

- None - we have enough money anyway [1]
- A small effect - we are not as well off now as we were before I contracted TB [2]
- A big effect - we have lost money because of my illness [3]
- A very big effect - it has dramatically reduced the money available to us [4]
- Refused to respond [99]

8.24 Food availability

Now I would like to talk about food availability over the last 7 days. In the past one week, has it happened that because of insufficient food you experienced the following during at least one or more days:

8.25 Food availability - none

You had a day without eating anything all day?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]

8.26 Food availability - reduced

You reduced the size and/or number of meals eaten?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]

8.27 Food availability - cheaper food

You changed the family diet to cheaper or less-preferred foods?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]

8.28 Shortage Prompt

In the last 3 months, did you or your children ever go without any of the following things you really needed because of a shortage of resources (money)?

8.29 Shortage: Food

In the last 3 months, have you or your children ever gone without any food?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: Food (8.29)* Equals 'Don't know [5]'
Skip when *Shortage: Food (8.29)* Equals 'Refused to respond [99]'

8.30 Shortage Food_clarify

Please clarify:

Expects a single line text response (**required**)

8.31 Shortage: Clothing and Shoes

In the last 3 months, have you or your children ever gone without any clothing and shoes?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: Clothing and Shoes (8.31)* Equals 'Don't know [5]'
Skip when *Shortage: Clothing and Shoes (8.31)* Equals 'Refused to respond [99]'

8.32 Shortage Clothing/Shoes_clarify

Please clarify:

Expects a single line text response (**required**)

8.33 Shortage: School uniforms

In the last 3 months, have you or your children ever gone without any school uniforms?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: School uniforms (8.33)* Equals 'Don't know [5]'
Skip when *Shortage: School uniforms (8.33)* Equals 'Refused to respond [99]'

8.34 Shortage School Uniforms_clarify

Please clarify:

Expects a single line text response (**required**)

8.35 Shortage: School fees

In the last 3 months, have you or your children ever gone without school fees?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: School fees (8.35)* Equals 'Don't know [5]'
Skip when *Shortage: School fees (8.35)* Equals 'Refused to respond [99]'

8.36 Shortage School Fees_clarify

Please clarify:

Expects a single line text response (**required**)

8.37 Shortage: Fuel

In the last 3 months, have you or your children ever gone without any fuel (for cooking/heating)?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: Fuel (8.37)* Equals 'Don't know [5]'
Skip when *Shortage: Fuel (8.37)* Equals 'Refused to respond [99]'

8.38 Shortage Fuel_clarify

Please clarify:

Expects a single line text response (**required**)

8.39 Shortage: Basic household items

In the last 3 months, have you or your children ever gone without any basic household items (for cleaning, cooking, sleeping)?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: Basic household items (8.39)* Equals 'Don't know [5]'
Skip when *Shortage: Basic household items (8.39)* Equals 'Refused to respond [99]'

8.40 Shortage Basic Household Items_clarify

Please clarify:

Expects a single line text response (**required**)

8.41 Shortage: Health care

In the last 3 months, have you or your children ever gone without any health care (paying for services or the transport to get to a clinic or hospital)?

Expects a single option response (**required**)

- Never [1]
- Once only [2]
- A few times [3]
- Often [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Shortage: Health care (8.41)* Equals 'Don't know [5]'
Skip when *Shortage: Health care (8.41)* Equals 'Refused to respond [99]'

8.42 Shortage Health Care_clarify

Please clarify:

Expects a single line text response (**required**)

8.43 Ask for Food or Money?

In the last 3 months, has anyone in your household had to go to another house to ask for food or money because of a shortage?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Section 9. Care for current episode of TB

9.1 Transport Type

What means of transportation do you use? Select all that apply for one round trip.

Expects multiple selected options (**required**)

- ë Bus [1]
- ë Train [2]
- ë Taxi [3]
- ë Own car [4]
- ë Get a lift in someone else's car [5]
- ë Walk [6]
- ë Other [7]
- ë Don't know [8]
- ë Refused to respond [99]

Prerequisites
Skip when *Transport Type (9.1)* Excludes 'Other [7]'

9.2 Transport Type_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

9.3 Travel Costs to Clinic

Approximately how much money does it cost you to get to the clinic (amount in rands)?

Expects a numeric response (**required**)

9.4 Travel Cost Expensive

Is this expensive for you?

Expects a single option response (**required**)

- ë Yes, very [1]
- ë Yes, quite expensive [2]
- ë No, not expensive [3]
- ë Refused to respond [99]

9.5 Hours queued

How many hours do you spend queuing for you TB treatment per month?

Expects a numeric response (**required**)

9.6 Difficult to get to Clinic

Is it difficult for you to get to the clinic to keep your TB appointments?

Expects a single option response (**required**)

- Always [1]
- Often [2]
- Sometimes [3]
- Never [4]
- Refused to respond [99]

Branches

If response **Equals 'Never [4]'** then skip to ***Other Money Spent (9.10)***

If response **Equals 'Refused to respond [99]'** then skip to ***Other Money Spent (9.10)***

9.7 Difficult to get to Clinic Reason

What makes it difficult to get to the clinic to keep your TB appointments? Select all that apply.

Expects multiple selected options (**required**)

- Lack of money [1]
- Lack of transport [2]
- Responsibilities at home [3]
- Feel too sick to travel [4]
- Don't want people to know I have TB [5]
- Other [6]
- Don't know [7]
- Refused to respond [99]

Prerequisites
Skip when ***Difficult to get to Clinic Reason (9.7)*** **Excludes 'Other [6]'**

9.8 Difficult to get to Clinic Reason_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

Prerequisites
Skip when ***Difficult to get to Clinic Reason (9.7)*** **Includes 'Don't know [7]'**
Skip when ***Difficult to get to Clinic Reason (9.7)*** **Includes 'Refused to respond [99]'**

9.9 Most Important Factor

Please select the most important reason that makes it difficult to get to the clinic to keep your TB appointments.

Expects a single option response (**required**)

- Lack of money [1]
- Lack of transport [2]
- Responsibilities at home [3]
- Feel too sick to travel [4]
- Don't want people to know I have TB [5]
- Your other option [6]
- Refused to respond [99]

9.10 Other Money Spent

What else do you need to spend money on because of your TB?

Expects multiple selected options (**required**)

- ë Other medicines, like cough mixtures [1]
- ë Consulting other health care workers, e.g. private doctors, traditional healers [2]
- ë Special foods/more food [3]
- ë Payment for others to do chores in household while you are too sick to do them [4]
- ë Payment for someone to take care of others in household while you are sick [5]
- ë Payment for someone to take care of you while you are sick [6]
- ë Other payments [7]
- ë Refused to respond [99]

Branches

If response **Includes 'Refused to respond [99]'** then skip to ***Other Payments Amount (9.21)***

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Other medicines, like cough mixtures [1]'**

9.11 Other Medicines

What amount do you spend on other medicines for treatment of TB symptoms each month?

Expects a decimal response (**required**)

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Other medicines, like cough mixtures [1]'**

9.12 Expensive: Other Medicines

Is this expensive for you?

Expects a single option response (**required**)

- ë Yes, very expensive [1]
- ë Yes, quite expensive [2]
- ë No, not expensive [3]
- ë Refused to respond [99]

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Consulting other health care workers, e.g. private doctors, traditional healers [2]'**

9.13 Consulting Fees

What amount do you spend on consulting other health care workers for treatment of TB symptoms, e.g. private doctors, traditional healers, each month?

Expects a decimal response (**required**)

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Consulting other health care workers, e.g. private doctors, traditional healers [2]'**

9.14 Expensive: Consulting fees

Is this expensive for you?

Expects a single option response (**required**)

- ë Yes, very expensive [1]
- ë Yes, quite expensive [2]
- ë No, not expensive [3]
- ë Refused to respond [99]

9.10 Other Money Spent

What else do you need to spend money on because of your TB?

Expects multiple selected options (**required**)

- ë Other medicines, like cough mixtures [1]
- ë Consulting other health care workers, e.g. private doctors, traditional healers [2]
- ë Special foods/more food [3]
- ë Payment for others to do chores in household while you are too sick to do them [4]
- ë Payment for someone to take care of others in household while you are sick [5]
- ë Payment for someone to take care of you while you are sick [6]
- ë Other payments [7]
- ë Refused to respond [99]

Branches

If response **Includes 'Refused to respond [99]'** then skip to ***Other Payments Amount (9.21)***

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Other medicines, like cough mixtures [1]'**

9.11 Other Medicines

What amount do you spend on other medicines for treatment of TB symptoms each month?

Expects a decimal response (**required**)

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Other medicines, like cough mixtures [1]'**

9.12 Expensive: Other Medicines

Is this expensive for you?

Expects a single option response (**required**)

- ë Yes, very expensive [1]
- ë Yes, quite expensive [2]
- ë No, not expensive [3]
- ë Refused to respond [99]

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Consulting other health care workers, e.g. private doctors, traditional healers [2]'**

9.13 Consulting Fees

What amount do you spend on consulting other health care workers for treatment of TB symptoms, e.g. private doctors, traditional healers, each month?

Expects a decimal response (**required**)

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Consulting other health care workers, e.g. private doctors, traditional healers [2]'**

9.14 Expensive: Consulting fees

Is this expensive for you?

Expects a single option response (**required**)

- ë Yes, very expensive [1]
- ë Yes, quite expensive [2]
- ë No, not expensive [3]
- ë Refused to respond [99]

Prerequisites
Skip when *Other Money Spent (9.10)* Excludes 'Payment for others to do chores in household while you are too sick to do them [4]'

9.15 Payment Household Chores

What amount do you spend on payments for others to do chores in the household while you are too sick to do them each month?

Expects a decimal response (**required**)

Prerequisites
Skip when *Other Money Spent (9.10)* Excludes 'Payment for others to do chores in household while you are too sick to do them [4]'

9.16 Expensive: Payment Household Chores

Is this expensive for you?

Expects a single option response (**required**)

- Yes, very expensive [1]
- Yes, quite expensive [2]
- No, not expensive [3]
- Refused to respond [99]

Prerequisites
Skip when *Other Money Spent (9.10)* Excludes 'Payment for someone to take care of others in household while you are sick [5]'

9.17 Payment Sick Care

What amount do you spend on payments for someone to take care of others in the household while you are sick each month?

Expects a decimal response (**required**)

Prerequisites
Skip when *Other Money Spent (9.10)* Excludes 'Payment for someone to take care of others in household while you are sick [5]'

9.18 Expensive: Payment Sick Care

Is this expensive for you?

Expects a single option response (**required**)

- Yes, very expensive [1]
- Yes, quite expensive [2]
- No, not expensive [3]
- Refused to respond [99]

Prerequisites
Skip when *Other Money Spent (9.10)* Excludes 'Payment for someone to take care of you while you are sick [6]'

9.19 Payment Sick Care You

What amount do you spend on payments for someone to take care of you while you are sick each month?

Expects a decimal response (**required**)

Prerequisites
Skip when *Other Money Spent (9.10)* Excludes 'Payment for someone to take care of you while you are sick [6]'

9.20 Expensive: Payment Sick Care You

Is this expensive for you?

Expects a single option response (**required**)

- Yes, very expensive [1]
- Yes, quite expensive [2]
- No, not expensive [3]
- Refused to respond [99]

Prerequisites
Skip when ***Other Money Spent (9.10)*** **Excludes 'Other payments [7]'**

9.21 Other Payments Amount

How many other payments do you have each month?

Expects a numeric response (**required**)

Repeat this section for value of *Other Payments Amount (9.21)*

Section 10. Other Payments

10.1 Other Payments Type

What type of payment is payment #REPEAT IDX:

Expects a single line text response (**required**)

10.2 Other Payments Amount Spent

How much do you spend on ***Other Payments Type (10.1)*** each month (amount in rands)?

Expects a numeric response (**required**)

10.3 Expensive: Other Payments

Is paying for ***Other Payments Type (10.1)*** expensive for you?

Expects a single option response (**required**)

- Yes, very expensive [1]
- Yes, quite expensive [2]
- No, not expensive [3]
- Refused to respond [99]

Section 11. Receipt of Voucher

11.1 Material Support

What form of material support do you receive from the clinic? Select all that apply.

Expects multiple selected options (**required**)

- Food parcels [1]
- Vegetables from the clinic garden [2]
- Disability grant for TB or HIV [3]
- Other [4]
- Don't know [5]
- Refused to respond [99]

Prerequisites
Skip when *Material Support (11.1)* Excludes 'Other [4]'

11.2 Material Support_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

11.3 R120 Voucher

Have you received the R120 voucher since starting TB treatment this last episode?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Refused to respond [99]

Branches
If response Equals 'No [2]' then skip to *Most Helpful Support (11.30)*

11.4 R120 Voucher Every Month

Have you received it every month?

Expects a single option response (**required**)

- Yes, every month [1]
- Most months [2]
- Some months [3]
- Refused to respond [99]

11.5 Voucher Helped TB Treatment

Has the voucher helped you to take your TB treatment in any way?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]
- Refused to respond [99]

Branches
If response Not Equal 'Yes [1]' then skip to *R120 Voucher Helped (11.8)*

11.6 Voucher Helped TB Treatment How

In what way has the voucher helped you with regards to taking your TB treatment?

Expects multiple selected options (**required**)

- I have been able to eat enough to take my tablets comfortably [1]
- I have been able to use the money I saved on foodstuffs for transport to the clinic [2]
- I have been able to help my family with money/commodities and so they are more supportive of me [3]
- I eat more and so feel better, so am better able to come to the clinic [4]
- Other [5]
- Refused to respond [99]

Prerequisites
Skip when *Voucher Helped TB Treatment How (11.6)* Excludes 'Other [5]'

11.7 How Voucher Helped TB Treatment_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

11.8 R120 Voucher Helped

Has it helped you financially?

Expects a single option response (**required**)

- Yes very much - we need it to survive [1]
- Yes, quite a lot - it would be difficult to do without it [2]
- Yes - it enables us to buy things we would otherwise do without [3]
- Not really - it doesn't really make a difference as we have enough money already [4]
- Refused to respond [99]

11.9 Voucher Helped: Food

Has the voucher helped in meeting your expenditure on food?

Expects a single option response (**required**)

- Yes, it has helped a lot [1]
- Yes, it has helped a little [2]
- No, it hasn't helped at all [3]
- Refused to respond [99]

11.10 Voucher Helped: Clothing and Shoes

Has the voucher helped in meeting your expenditure on clothing and Shoes?

Expects a single option response (**required**)

- Yes, it has helped a lot [1]
- Yes, it has helped a little [2]
- No, it hasn't helped at all [3]
- Refused to respond [99]

11.11 Voucher Helped: School Uniforms

Has the voucher helped in meeting your expenditure on school uniforms?

Expects a single option response (**required**)

- Yes, it has helped a lot [1]
- Yes, it has helped a little [2]
- No, it hasn't helped at all [3]
- Refused to respond [99]

Prerequisites
Skip when *Money Spent on Who (11.17)* Not Equal 'Other [4]'

11.18 Money Spent on Who_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

11.19 Problems Getting Voucher

Have you had any problems in getting this voucher at the clinic?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Don't know [3]
- Refused to respond [99]

Branches

If response Not Equal 'Yes [1]' then skip to *Voucher Used to get to Shops (11.22)*

11.20 Problems Getting Voucher Reason

Why have you had a problem getting a voucher?

Expects a single option response (**required**)

- Other patients were angry with me because they did not get the voucher [1]
- There were no vouchers at the clinic when I came to get my TB treatment [2]
- Other [3]
- Refused to respond [99]

Prerequisites
Skip when *Problems Getting Voucher Reason (11.20)* Not Equal 'Other [3]'

11.21 Problems Getting Voucher Reason_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

11.22 Voucher Used to get to Shops

Did you find it easy to get to a shop to use the voucher?

Expects a single option response (**required**)

- Yes, very easy [1]
- No, there were some difficulties [2]
- No, it was very difficult [3]
- Refused to respond [99]

Branches

If response Equals 'Yes, very easy [1]' then skip to *Voucher Used at Shops (11.26)*

11.23 Voucher Used to get to Shops Difficult

If you found it difficult, please explain what made it difficult.

Expects multiple selected options (**required**)

- The shop was far away from the clinic and my home [1]
- It was expensive to get to the shop [2]
- I didn't know where the shop was [3]
- The shop is not in a safe area [4]
- I had no one to help me to get to the shop [5]
- Other [6]
- Refused to respond [99]

Prerequisites
Skip when *Voucher Used to get to Shops Difficult (11.23)* Excludes 'Other [6]'

11.24 Voucher Used to get to Shops Difficult_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

11.25 Voucher - getting to the shop

How much money did you spend (in rands) on getting to the shop to redeem the voucher every month?

Expects a numeric response (**required**)

11.26 Voucher Used at Shops

Did you find it easy to use the voucher at the supermarket/shop?

Expects a single option response (**required**)

- Yes, very easy [1]
- No, there were some difficulties [2]
- No, it was very difficult [3]
- Refused to respond [99]

Branches
If response **Equals 'Yes, very easy [1]'** then skip to *Voucher Helpful (11.29)*

11.27 Voucher Used at Shops Difficult

Why did you find it difficult to use the voucher at the supermarket/ shop?

Expects multiple selected options (**required**)

- The shopkeepers made it difficult for me [1]
- The shopkeepers wouldn't let me buy the goods that I wanted [2]
- I tried to save up the vouchers and spend more than one at once, but was not allowed to [3]
- I asked a friend/relative to buy the goods for me, but they were not allowed to [4]
- I lost the voucher and could not get it replaced [5]
- I didn't want to show anyone the voucher as I don't want people to know I have TB [6]
- Other [7]
- Refused to respond [99]

Prerequisites
Skip when *Voucher Used at Shops Difficult (11.27)* Excludes 'Other [7]'

11.28 Voucher Used at Shops Difficult_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

11.29 Voucher Helpful

Do you feel that this voucher is helpful to patients with TB?

Expects a single option response (**required**)

- Yes, very helpful [1]
- Yes, quite helpful [2]
- No, not helpful [3]
- Refused to respond [99]

11.30 Most Helpful Support

What support would be most helpful to you in completing your TB treatment?

Expects multiple selected options (**required**)

- Food parcels [1]
- Financial assistance - cash [2]
- Financial assistance - vouchers for shops [3]
- Being able to make appointments at the clinic instead of waiting in a queue [4]
- More time with the nurses to talk about TB [5]
- Transport to take you from your house to the clinic [6]
- Being able to take all your tablets home with you instead of fetching them regularly from the clinic [7]
- Other [8]
- Don't know [9]
- Refused to respond [99]

Prerequisites
Skip when *Most Helpful Support (11.30)* Excludes 'Other [8]'

11.31 Most Helpful Support_specify

Please specify (capture 99 if respondent refuses to specify):

Expects a single line text response (**required**)

Section 12. End

12.1 End of Interview

Thank you, we have completed the interview now. Thank you for taking the time to talk to us.

12.2 Complete

Fieldworker: Please press BACK to review/ make changes to the responses or press NEXT to complete the survey.

Appendix 5B: Full table showing multivariate analysis

Parameter	Coefficient	Robust standard error	z	P value	95% confidence interval: lower limit	95% confidence interval: upper limit
Gender: male	-.0656871	.0563807	-1.17	0.244	-.1761913	.0448172
Age	.0020533	.0027329	0.75	0.452	-.0033031	.0074097
Education level: primary school and below (versus secondary and tertiary education)	.0014061	.0362644	0.04	0.969	-.0696708	.072483
Household location: informal settlement (versus township)	.03689	.0829803	0.44	0.657	-.1257484	.1995284
Household location:	.8096406	.1262826	6.41	0.000	.5621312	1.05715

city (versus township) (city spent more than township)						
Household location: rural area (versus township)	.0629823	.1142968	0.55	0.582	-.1610354	.2869999
Respondent earns money (versus respondent does not earn money) (those who earned money spent more)	-.1668177	.0411727	-4.05	0.000	-.2475146	-.0861208
Respondent does not receive disability grant (versus respondent does receive disability grant)	.0962788	.0403915	2.38	0.017	.017113	.1754447

(those who received grant spent more)						
Respondent does not receive child support grant (versus respondent does receive child support grant)	-.1106019	.1155463	-0.96	0.338	-.3370685	.1158648
Members of household do earn money (versus members of household do not earn money)	-.0870196	.0474675	-1.83	0.067	-.1800542	.006015
Members of household receive social grants (versus members of household do not receive grants) (those who received grants spent more)	-.1284743	.0571574	-2.25	0.025	-.2405008	-.0164479
Respondent does receive voucher[#] (versus respondent does not receive	.042015	.0715954	0.59	0.557	-.0983095	.1823394

voucher)						

#Note that these were respondents who received at least one voucher during the trial.