The Costs and Effects of the Practical Approach to Lung Health in South Africa

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ABSTRACT

The burden of respiratory diseases is large and, due to the HIV pandemic and increasing tobacco use, growing in many developing countries. In South Africa, responsibility for diagnosis, treatment and referral rests mainly upon primary care nurses who may have inadequate skills and training for the increasing clinical demand. Syndromic approaches have shown promise across other disease areas in similar settings, but have largely been implemented using offsite training courses of unknown effectiveness which have interrupted clinical services, limiting sustainability and coverage.

Based upon the World Health Organization's Practical Approach to Lung Health concept, PALSA (Practical Approach to Lung Health in South Africa) combined syndromic case management guidelines of priority adult respiratory diseases with educational outreach, a knowledge translation strategy known to change the practice of physicians towards evidence-based choices.

This thesis evaluates the effectiveness, cost and cost-effectiveness of the PALSA intervention on the processes and outcomes of respiratory care using a pragmatic cluster randomised controlled trial with prospective economic evaluation in 40 nurse-practitioner-staffed primary care clinics in the Free State province. Twenty clinics received the intervention in addition to usual support and training. Information about tests, treatment received, and costs, during and four months after PALSA outreach visits was obtained from 50 patients from each clinic.

Improvements in tuberculosis case detection (6.4% vs. 3.8%, OR 1.72, 95% confidence interval 1.04 to 2.85), inhaled corticosteroid use for obstructive lung disease (13.7% vs. 7.7%, OR 1.90, 95% confidence interval 1.14 to 3.18) and referral of severe cases (7.8% vs. 4.7%, OR 1.71, 95% confidence interval 0.95 to 3.09) suggested improved clinical processes. Increased costs associated with the intervention were largely

AUTHOR'S DECLARATION

The author contributed in obtaining funding for the study and played a leading role in its conduct. This included the development and piloting of the PALSA intervention, liaison and engagement with the Free State Department of Health, development of the questionnaire, co-ordinating translation (including leading translation of the EuroQol-5D into Sesotho), programming and testing the PDA version of the questionnaire, designing the fieldwork schedule, training and supervising fieldworkers, supervising data compilation and cleaning, compiling analysis plans, analysing data, and writing the papers, thesis and technical reports for funders. Merrick Zwarenstein conceived the idea to combine PAL with knowledge translation approaches to its implementation. Merrick Zwarenstein, Max Bachmann, Eric Bateman, Bosielo Majara, Carl Lombard, Gina Joubert, René English and Angeni Bheekie contributed to the study design and were co-applicants on the funding proposal. Dingie van Rensburg co-ordinated the fieldwork with assistance from Bosielo Majara, Marïette van Rensburg, Gloria Gogo and Neil Khoapa. Max Bachmann, Merrick Zwarenstein, Carl Lombard and Eric Bateman helped with statistical analysis and interpretation of data. Max Bachmann helped especially with the economic evaluation. Max Bachmann and Eric Bateman supervised the thesis.

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workshops during which the protocol and intervention were developed, with helpful inputs from Andy Oxman and Louis Niessen; Refiloe Matji for comments on the guideline and study protocol; Robert Scherpbier and Salah Eddine Ottmani from from the World Health Organization, who conceptualised PAL, the global model for a Practical Approach to Lung Health (PAL) from which PALSA drew its screening and syndromic approaches; Jennifer Jelsma for advice on the EuroQol translation; Claire Gudex for patient and meticulous review of the EuroQol translations at every stage; Miranda Mugford for advice on the economic evaluation; Edina Sinanovic for advice on unit costings; Gloria Rembe for assistance retrieving papers and costing information; Jani Brett Driskell and Linda Toews for assistance with retrieving papers; Tony Fairall for the final proofread; Nadine and Blaise Reynolds for providing me with a home away from home in Bloemfontein and finally my son, Thomas, for making me finish this. This thesis is dedicated to my husband, David.

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ABBREVIATIONS

AA	Automobile Association
AFB	Acid-fast bacilli
AIDS	Acquired Immunodeficiency Syndrome
ARI	Acute Respiratory Infection
ARV	Antiretroviral
CHAMP	CHestiness and Asthma in Mitchell's Plain
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CPIX	Consumer Price Index
CXR	Chest X-ray
DALY	Disability Adjusted Life Year
DARE	Database of Abstracts of Reviews of Effectiveness
DOTS	Directly Observed Therapy Short-course
EDL	Essential Drug List
EPOC	Effective Practice and Organisation of Care
EQ-5D	EuroQol-5D
FCTC	Framework Convention on Tobacco Control
FSDOH	Free State Department of Health
GCP	Good Clinical Practice
GDP	Gross Domestic Product
HAPI	Handheld Personal Interview (application)
HCP	Healthcare Provider
HIV	Human Immunodeficiency Virus
HRQoL	Health Related Quality of Life
ICC	Intracluster Correlation Coefficient
ICER	Incremental Cost-Effectiveness Ratio
ICU	Intensive Care Unit

1. INTRODUCTION

This study evaluates the South African adaptation of the World Health Organization's Practical Approach to Lung Health (PAL), specifically its impact on the effectiveness, cost and cost-effectiveness of respiratory care. PALSA, or the Practical Approach to Lung Health in South Africa, combined integrated case management symptom- and sign-based guidelines with knowledge translation approaches to their implementation. It targeted the primary care management of common respiratory conditions in adults and adolescents, including tuberculosis.

The requirement for such an intervention is clear if the burden that respiratory diseases impose on primary care services is considered. Section 1.1 describes the large and growing burden of respiratory diseases globally, in South Africa and the Free State. Section 1.2 describes the burden this imposes on primary care services. Section 1.3 briefly describes the organization of primary care services in South Africa and their dependence on primary care nurse practitioners who were the targets of the PALSA intervention.

This study contributes to two specific areas of evidence for primary care interventions. The first of these is for syndromic interventions, which use symptoms and signs to guide frontline health workers to provide the appropriate diagnosis and treatment using integrated case management guidelines. Examples that have been widely implemented throughout the developing world, including South Africa, are the syndromic management of Sexually Transmitted Infections and the Integrated Management of Childhood Illness. A general overview of these, and the PAL strategy, is provided in Section 1.4, and a more detailed appraisal of economic evaluations of these programmes in Section 1.5.

1.1 The burden of respiratory disease

The burden of respiratory disease is large and growing. The Global Burden of Disease Study estimated that in 1990, respiratory diseases, including lower respiratory tract infections, Chronic Obstructive Pulmonary Disease (COPD), tuberculosis and lung cancers, were among 4 of the top 10 causes of mortality worldwide and together accounted for 19% or 9.4 million deaths (Murray and Lopez 1997a). Lower respiratory tract infections are the leading cause of disability-adjusted life years (DALYs) worldwide, primarily affecting children of the developing world, and among adults, tuberculosis is the leading infectious cause of death and disability (Murray and Lopez 1997b). The burden of respiratory diseases is particularly severe in the low and middle-income countries of the developing world, where it is not limited to infectious causes. Chronic respiratory diseases are increasingly common and associated with increasing rates of tobacco use, low socio-economic status, frequent respiratory infections in childhood, previous tuberculosis, workplace pollution and exposure to indoor pollution from biomass fuels (Aït-Khaled et al. 2001). The spread of HIV/AIDS and the increasing consumption of tobacco will ensure that the burden imposed by respiratory diseases continues to grow well into the 21st century (Murray and Lopez 1997c).

1.1.1 Tuberculosis

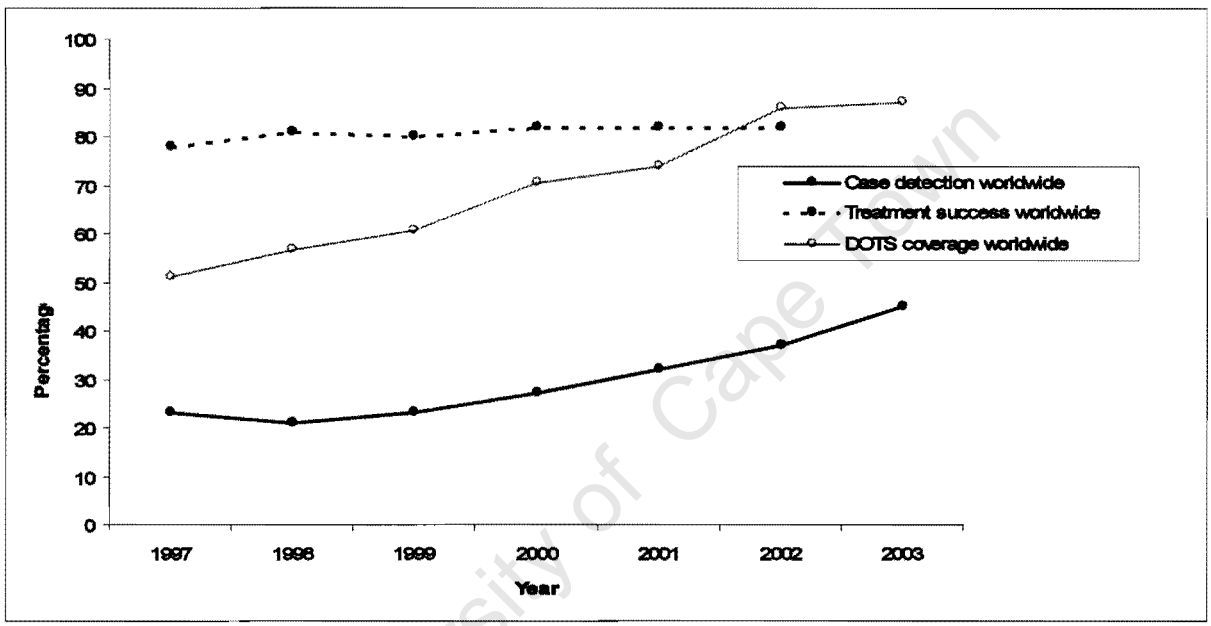
Annually tuberculosis (TB) is estimated to infect between 7 and 8 million people, and to kill between 2 and 3 million, 95% of whom live in the developing world (Raviglione 2003). Global efforts to control tuberculosis accelerated during the 1990s (Table 1.1), spurred on by a resurgence of tuberculosis among immigrants in the United States and Europe during the late 1980s (Reichman 1991; McKenna et al. 1995). In 1991 the World Health Assembly ratified global targets for TB control: to

Table 1.1 Milestones in global tuberculosis policy (1989 - 2002)

1989	Number of staff at the World Health Organization (WHO) assigned to tuberculosis numbers 2.
1991	World Health Assembly ratifies global targets for TB control: to successfully treat 85% of all smear positive cases, and detect 70% of all cases by 2000.
1993	World Bank endorses TB treatment as one of the most cost-effective health interventions. WHO declares TB a global emergency.
1994	WHO launches the Framework for Effective TB Control.
1995	The Framework is branded as DOTS (Directly Observed Treatment, Short Course) and aggressive marketing begins.
1997	WHO releases the first global monitoring report. South Africa adopts the DOTS strategy as its official national tuberculosis control policy.
1998	The Stop TB Partnership comprising >150 governments, non-governmental agencies and various institutions is established.
2000	The Amsterdam Declaration to Stop TB commits governments of high burden countries to achieving global TB targets by 2005. WHO launches the Global DOTS Expansion Plan. Millenium Development Goals include those targeting tuberculosis; by 2015 to: Reverse, or at least halt, the incidence of TB Halve the mortality due to TB compared with 1990 Halve the prevalence of TB compared with 1990
2001	The Global Drug Facility, which aims to provide free drugs to countries in need, is established.
2002	The Global Fund against Tuberculosis, AIDS and Malaria is created. The Strategic Framework to Decrease the Burden of TB/HIV is launched.

respectively (Raviglione 2003). Presently tuberculosis incidence is rising at 1.0% per year (WHO 2005a). Reductions in global prevalence and mortality would be greater, were it not for the unprecedented increase in tuberculosis in sub-Saharan Africa during the last decade.

Figure 1.1 DOTS coverage and progress towards global targets (from WHO 1998a, 1999, 2000a, 2001a, 2002a, 2003a, 2004a, 2005a)



1.1.1.2 The impact of HIV/AIDS on tuberculosis in sub-Saharan Africa

Key constraints to achieving the global tuberculosis targets and Millenium Development Goals include HIV/AIDS and the lack of skilled health workers (Dye et al. 2003). In sub-Saharan Africa the spread of HIV/AIDS has resulted in an unprecedented 300-400% increase in tuberculosis cases during the last decade (Raviglione et al. 1997), and co-infection rates in excess of 60% (Corbett et al. 2003). Mortality attributable to co-infection is high. Tuberculosis is the leading cause of death among HIV infected Africans (Grant et al. 1997, Rana et al. 2000, Ansari et al.

1.1.1.3 Tuberculosis control in South Africa

South Africa is currently in the grip of two historically unprecedented epidemics Not only is it home to the highest number of HIV infected people in the world (UNAIDS n.d.), but also to the 8th highest number of incident tuberculosis cases (WHO 2005a). Models predict that by the year 2010, 5.2 million South Africans will have lost their lives to HIV/AIDS (Dorrington et al. 2002), almost 20 times the number who died in the South East Asian tsunami of 2004 (Wall 2005). Many of these will die as a result of tuberculosis, and already tuberculosis and respiratory infections are the leading causes of death among young South African adults (Bradshaw et al. 2003).

The South African Department of Health adopted the DOTS strategy as its official national policy in 1997, and rapidly expanded the programme to cover 99.5% of the population. Notification rates have risen accordingly, but disproportionately to improvements in monitoring. Much of this coincides with increasing rates of HIV prevalence (Figure 1.2) (WHO 2004a; South African National Department of Health, 2005). HIV co-infection rates among tuberculosis cases are presently estimated at around 60% (WHO 2005a), and the proportion of tuberculosis cases directly attributable to HIV at one third (Churchyard and Corbett 2005).

patients to facilities and delayed diagnosis by health workers have been identified as priority challenges (Barr et al. 2005).

Table 1.3 Tuberculosis incidence, detection and outcomes for South Africa 1997 – 2003 (from WHO 1998a, 1999, 2000a, 2001a, 2002a, 2003a, 2004a, 2005a)

Indicator	1997	1998	1999	2000	2001	2002	2003
DOTS coverage	13	22	66	77	77	98	99.5
Global rank	8	8	9	9	7	9	8
Notification rate (all cases/ 100 000 pop)	271	326	323	344	334	481	505
Notification rate (ss+*/ 100 000 pop)	127	157	166	173	189	221	258
Incidence (all cases/ 100 000 pop/ year)	-	326	495	-	556	558	536
Detection of all cases (%)	80	90	90	74	68	94	94
DOTS case detection rate (new ss+, %)	6.2	22	68	91	95	106†	118†
TB cases aged 15-49yrs HIV positive (%)	45%	-	60	60	60	60	61
New cases multidrug resistant (%)	-	-	1.5	1.5	1.5	1.5	1.6
DOTS treatment success (new ss+, %)	69	74	60	66	65	68	-

* Smear positive pulmonary tuberculosis case defined as: at least two initial sputum smear examinations (direct smear microscopy) acid-fast bacilli (AFB) +; or one sputum examination AFB+ and radiographic abnormalities consistent with active pulmonary tuberculosis as determined by a clinician; or one sputum specimen AFB+ and culture positive for *M. tuberculosis* (WHO 2005).

† The case detection rate (reported cases/ estimated incidence) may exceed 100% because reported cases are derived from the prevalent pool in the community, and may arise from previous years.

Failure to improve treatment outcomes is also of concern. The percentage successfully treated remains well below target at around 65- 70%. Rising mortality associated with HIV infection is a contributing factor, and at 7% of those starting tuberculosis treatment, is considered an under-estimate of the real mortality associated with tuberculosis (WHO 2005a). Taken together, low rates of treatment success, high rates of treatment interruption and defaulting, and rising incidence, suggest that the country's largely nurse-driven tuberculosis service has been overwhelmed.

nurse co-ordinators, but this has been described as inadequate and rushed (Janse van Rensburg-Bonthuyzen 2005).

Drug supplies are generally secure, but clinics reported frequent difficulties in obtaining sputum jars. Among 9 nurse practitioners interviewed, knowledge of the National Tuberculosis Control Programme protocols was variable. Not all clinics possessed copies of the national treatment guidelines (Janse van Rensburg-Bonthuyzen 2005).

Tuberculosis treatment is provided in accordance with the DOTS strategy. Most patients attend the clinic daily for directly supervised treatment during the initial intensive phase, and twice weekly during the continuation phase. During this time, treatment is primarily supervised by lay health workers, known as DOTS supporters. These lay health workers deliver weekly supplies of medication to patients' homes, trace patients who interrupt treatment or do nor return to the clinic for sputum results, and are supervised by the clinic nurse practitioners. In the Free State DOTS supporters are required to register with a NGO recognised by the provincial health department, and in return received a monthly stipend of R500 for their services.

1.1.2 Acute respiratory infections

Acute respiratory infections (ARI) are one of the most common reasons for consulting primary care services worldwide. In a survey of respiratory care in 9 lower and middle-income countries during the late 1990s, ARI, predominantly upper tract infections, accounted for 80% of diagnoses among patients presenting with respiratory symptoms (WHO 2004b). Lower respiratory tract infections (LRTI) are an important cause of mortality worldwide (Murray and Lopez 1997a). Previously this was primarily among children under 5 years and the elderly, although recently they have been increasingly responsible for deaths among young adults co-infected

Tobacco was responsible for an estimated 3 million deaths worldwide in 1990, 4.9 million in 2000, and is projected to cause 8 million in 2020, making it what has been called the "most important determinant of human health trends" (Murray and Lopez 1997c). In the last 2 decades increases in smoking prevalence have been highest in countries of the developing world, and have followed aggressive marketing campaigns by the tobacco industry. Globally, the World Health Organization's Framework Convention on Tobacco Control (FCTC) aims to support national governments to develop and implement strategies to reduce smoking (WHO 2003b). The FCTC was adopted by the World Health Assembly in 2003.

1.1.3.1 Smoking prevalence and tobacco control in South Africa

In the Free State, smoking prevalence among men is slighter higher than the national average, and equal to the national average among women (Table 1.5; South African National Department of Health 1998a). The prevalence of self-reported emphysema was well below the national average for both men and women, although the prevalence of symptoms of chronic bronchitis and asthma were similar. Mining is a frequent occupation in the Free State, and a risk factor for both chronic respiratory disease and tuberculosis (Cowie and Mabena 1996; White and Ehrlich 1996; Cowie 1998; Steen et al. 1997; Churchyard et al. 2004; te WaterNaude et al. 2006).

sectors. This argument has been refuted by a local study of the economics of tobacco control, which concluded that income diverted from tobacco sales would generate more jobs than would be lost by the relatively labour un-intensive tobacco industry (Eberlee 2001).

These taxation and legislative measures appear to have impacted positively on smoking prevalence in the country (Table 1.6). Two surveys completed in 1995/6 estimated the national smoking prevalence to be 34% (Reddy et al. 1996, Reddy et al. 1998); later surveys completed in 1998 found that this had fallen to between 24 and 25% (South African National Department of Health 1998a; Meyer-Weitz et al. 2000). Most reassuring has been the decline in smoking among adolescents, presumably because this is the age group least likely to afford the increases in cigarette prices. The Global Youth Tobacco Survey completed two surveys of adolescent (ages 13-15 years) smoking patterns in 1999 and 2002, and found that the prevalence of current smokers has fallen from 23.0% to 18.5% and ever smokers from 46.7% to 37.6% (Medical Research Council 2003, Swart et al. 2004).

Table 1.6 Surveys of Smoking Prevalence in South Africa

Survey and Reference	Year	Participants	National smoking prevalence (%)
Reddy et al. 1996	1995	2238 adults ≥18 years from all 9 provinces	34.0
Reddy et al. 1998	1996	-	34.0
South African Demographic and Health Survey (South African National Department of Health 1998)	1998	13827 adults ≥15 years from 12 247 households in all 9 provinces	24.6
Meyer-Weitz et al. 2000	1998	-	25.0
Global Youth Tobacco Survey (Part 1) (Medical Research Council 2003)	1999	6045 learners 13–15 years from schools in all 9 provinces	23.0
Global Youth Tobacco Survey (Part 2) (Swart et al. 2004)	2002	8935 learners 13–15 years from 191 schools in all 9 provinces	18.5

1.2 The burden of respiratory disease in primary care

The increasing prevalence of respiratory diseases in developing countries is imposing a growing burden on primary care services. In the developed world, respiratory symptoms, primarily those associated with acute respiratory infections, have long been recognised as the most common reason for consulting primary care providers (Last 1963). In the late 1990s the World Health Organization attempted to quantify the burden in low and middle-income countries, and undertook surveys of patients 5 years or older attending 76 primary care facilities across 9 countries (WHO 2004b). They found a wide range in the prevalence of respiratory symptoms among primary care attendees from 8.5% in nurse-led facilities in Nepal to 33.7% in doctor provider facilities in Argentina. On the whole, it was estimated that respiratory symptoms accounted for one in five consultations. The distribution of respiratory diagnoses also varied significantly between the countries surveyed, but in general acute respiratory infections accounted for most visits, suspected tuberculosis for less than 10% of respiratory attendances and confirmed tuberculosis 1.4%. Variation was attributed to differences in risk factors (tobacco use, air pollution, HIV prevalence) between countries, but also to the lack of standardised diagnostic criteria for respiratory diseases.

In South Africa there are little data on the burden of respiratory conditions in primary care. Two surveys completed in private sector general practice in Cape Town during the 1960s and 1980s estimated the prevalence at around 25-35% of all primary care consultations (Silbert 1970; Bourne et al. 1991). A more recent survey, completed in a public sector primary care facility, estimated the prevalence at 28% of consultations (Fairall et al. 2001). Of these, acute respiratory infections accounted for 34% of consultations, obstructive lung disease for 55%, suspected tuberculosis for 12% and confirmed tuberculosis 3%. The prevalence of respiratory conditions, in

1.3 Organization of primary care services in South Africa

The South African health service is characterised by gross inequities in the financing and distribution of health services. The private healthcare sector services less than 20% of the country's population, but accounts for 60% of healthcare expenditure and employs most of the county's general practitioners, specialists, pharmacists and dentists (Blecher and Thomas 2004). Of the 8% of GDP spent on health, more than half is accounted for by medical schemes, and contributions towards the the medical schemes of civil servants represent a substantial government subsidy to the private sector. Prior to 1994, a disproportionate amount of public health expenditure was directed towards specialist-staffed urban hospitals, with the result that provinces with historically well-resourced urban centres, like Gauteng and the Western Cape, have a significantly higher number of health workers and better health infrastructure than poorer rural provinces. Since 1994 the ANC-led national government has sought to address these and other inequities by prioritising the expansion and development of primary care services, within a district-based management framework (McCoy and Engelbrecht 1999).

During the first decade of democracy 701 additional primary care clinics were built across the country, bringing the total number of primary care facilities close to 4500 (South African Government 2004). These facilities are for the most part, staffed by nurse practitioners with little or no support from doctors. Utilisation increased substantially following the announcement of free primary care services to pregnant women and children under 6 years in 1995, and to all citizens in 1996, but, at 2.3 visits per capita per year, remains well below the national target of between 3 and 3.5 visits per year as recommended by Lehmann and Sanders (2002).

primary care. Section 38A of the Nursing Act of 1978 makes provision for nurses to supply, administer and prescribe medications for "prescribed conditions" only if the services of a medical practitioner or pharmacist are not available, which is usual in primary care (Gray and Strasser 1999). However, it is not clear what is or isn't included in these "prescribed conditions", or what qualifications are required before a nurse can prescribe. In practice, clinical nurse practitioners have been granted Section 38A permits to prescribe medications specified for primary care use in the national Essential Drug List (EDL) (South African National Department of Health 2003a). Training prerequisites for clinical nurse practitioners are highly variable and poorly regulated, and range from part-time courses over the period of one year to three months or even 6 week short courses. More recently, the situation has become even more complex as Section 33 of the Act requires nurse prescribers to obtain permits to dispense, which has meant additional training from the Pharmacy Council.

The training demands on primary care nurses, who have been prepared for hospital-based practice, are therefore substantial, and require that nurses frequently leave their clinical posts to attend centralised short courses. This exacerbates already critical staff shortages and can also be disruptive to family life, as many nurses are women, and mothers of young children (Strachan 2000a). Removing nurses from clinical practice to attend courses has also limited the pace at which primary care nurses can be trained and supported, as nurses often miss out on training opportunities because there is no-one available to relieve them of their clinical responsibilities. It is therefore usual for only one nurse at a clinic to be selected for training in a particular course, the idea being that he/she will in turn train colleagues on returning to the clinic (the "cascade" model). Donahue (1998) emphasizes the requirement that effective trainers must possess both clinical competence and adult education skills, and that the assumption that those who are taught can teach others is the primary shortcoming of the cascade model.

poor compliance with EDL recommendations for prescribing and low levels of control of blood pressure and blood glucose.

In summary, training in the management of common primary care conditions can only be expected to lead to improvements in population health when adequate numbers of primary care nurses receive effective training. The demand for training is high, as nurses have been ill-equipped to practise as independent clinicians, and are facing increasing burdens of infectious and chronic diseases as the HIV epidemic unfolds. Decentralised, innovative and effective approaches to in-service training are required to skill nurses to provide a quality primary care service (Radebe 2000).

patients, who present with symptoms and signs, and not diagnoses. Syndromic approaches also make provision for treating more than one probable diagnosis at a time, an important attribute given the prevalence of multiple diagnoses in clinical medicine (WHO 2002b). Furthermore, they offer simplified and standardized protocols as the basis of training initiatives and clinical care.

This section provides a brief introduction to the four syndromic management programmes developed by the World Health Organization over the last 15 years, including the Practical Approach to Lung Health, on which PALSA is based. Although others exist, these four have by far dominated syndromic-approach-based training in developing countries.

1.4.1 Syndromic management of Sexually Transmitted Infections (STIs)

During the late 1980s and 1990s evidence emerged suggesting that sexually transmitted infections were an important co-factor in HIV transmission. Longitudinal studies showed increased risk of acquiring HIV infection if co-infected with other STIs (Stamm et al. 1988; Cameron et al. 1989; Plummer et al. 1991; Laga et al. 1993), and increased HIV shedding from the genital tracts of men and women with coexisting STIs which decreased when these were treated (Cohen et al. 1997; Ghys et al. 1997; Mostad et al. 1997).

These observations prompted debate as to the role of improved treatment of bacterial STIs in reducing HIV transmission (Cohen et al. 1997, Pepin et al. 1989). On the basis of this, and given the limited availability and high cost of diagnostic tests for STIs, the World Health Organisation began to promote syndromic management of STIs as a core component of national strategies to limit HIV transmission in the developing world, in particular sub-Saharan Africa where the epidemic was spreading rapidly (WHO 1991b). In the 1990s three large community trials in East Africa examined the

Table 1.7 Randomised trials of interventions based on the syndromic management of sexually transmitted infections

	Mwanza, Tanzania **Grosskurth et al. 1995**	**Rakai, Uganda** **Wawer et al. 1999**	**Masaka, Uganda** **Kamali et al. 2003**	**Lima, Peru** **Garcia et al. 1997**	**Hlabisa, South Africa** **Harrison et al. 2000**
Setting (period)	12 rural communities in Mwanza, Tanzania (1991-1994)	10 rural communities in Rakai, Uganda (1994-1998)	18 rural communities in Masaka, Uganda (1994-2000)	180 pharmacies in Lima, Peru	10 primary care clinics in Hlabisa, South Africa (1996-1997)
Intervention	Establishment of STI reference clinic/ laboratory Healthcare worker training (3 week course including 2 week's practical) Regular supply of drugs Supervisory visits 6 monthly health education visits to villages	Periodic mass directly – observed home-based STI treatment of adults with azithromycin, ciprofloxacin & metronidazole irrespective of symptoms (85% eligible and present). 2 rounds 10 months apart.	Healthcare worker training Regular supply of drugs Supervisory visits Community education: meetings, information leaflets, videos & drama groups	8 hour training course on STI management and prevention 1.5 hour on-site training session	Training and supervision of nurses in syndromic managment of STIs Provision of STI packs comprising drugs, condoms, contact cards, written health information
Study design	Community randomised controlled trial with closed cohort (n = 12, 12537 participants)	Community randomised controlled trial with open cohort (n = 10, 15127 participants)	Community randomised controlled trial with open cohort (n = 18, 20 000 participants)	Cluster randomised controlled trial (n = 180, 360 visits by simulated patients)	Cluster randomised controlled trial (n = 10, 100 visit by simulated patients)
Baseline STI prevalence	HIV: low (4%) and rising HSV2: <10% ulcers	HIV: 16% and stable HSV2: 43% of ulcers	HIV: 10% 7-10% with genital ulcer in preceeding year	Not reported	Not reported
Effect on HIV incidence	Significant 38% reduction in HIV incidence after 2 years	No reduction in HIV incidence after 2 rounds of treatment	No reduction in HIV incidence after 3 rounds of follow-up	Not measured	Not measured
Effect on prevalence of other STIs in general population	No significant effect	No significant effect	Significant decreases in gonorrohea and active syphilis cases	Not measured	Not measured
Quality of care	Not compared with control facilities. Compliance with protocols around 63% in intervention facilities.	Not applicable.	Not reported	No difference in diagnosis, referral, or appropriate treatment. Education and counselling more likely to be given in intervention pharmacies.	SSPs* significantly more likely to be given recommended drugs in intervention clinics No difference in provision of adequate counselling.

* Standardised simulated patients: fieldworkers trained to present to facilities complaining of symptoms from standardised scripts e.g. urethral discharge

intervention during the epidemic, and that syndromic management could lead to reduced HIV incidence in areas characterised by high risk sexual behaviour and high rates of co-factor STIs.

In spite of the controversies arising from these trials, most countries in sub-Saharan Africa, including South Africa, have included syndromic STI treatment programmes in their primary care packages. Even if these programmes have a limited effect on containing HIV transmission, implementation can be justified by the high burden of STIs among women of child-bearing age, second only to maternity related disorders (World Bank 1993).

Two studies have evaluated the impact of educational interventions on the quality of syndromic STI care provided in primary care facilities. The first of these completed in Lima, Peru, evaluated the impact of an 8 hour long off-site training course supplemented by a 1-1.5 hour on-site training session (Garcia et al. 1997). The second study completed in Hlabisa, South Africa, evaluated the impact of training for nurse practitioners combined with pre-packaged STI treatment packs comprising appropriate drugs, condoms, contact cards and written health information (Harrison et al. 2000). Both studies evaluated the impact of these interventions within cluster randomised controlled trials using standardised simulated patients to assess quality of care. Results from the Peru study were disappointing with no difference in appropriate diagnosis, treatment or referral. Furthermore, appropriate antibiotics were only prescribed in a low number of cases. By contrast, the Hlabisa study demonstrated improved prescription and treatment practices among simulated patients attending intervention clinics. No biological indicators were measured in either study.

The cost-effectiveness of syndromic treatment programmes for STIs has not been widely studied, and is restricted to a cost-effectiveness analysis alongside the

feasible, and consistent with national treatment guidelines and policies (WHO 2000b). Adaptation guides are available from the World Health Organization (2002b).

Health worker training usually lasts 11 days (a minimum of 80 hours is recommended), is centralised and combines modular lectures with a practical component (of at least 30%), including demonstration of clinical signs in patients, and supervised clinical examination (WHO 1998c).

Table 1.8 Components of the Integrated Management of Childhood Illness Strategy (adapted from WHO 1998c).

Facility-based IMCI (primary care):
Intensive short course training (11 days or 80 hours with a 30% practical component) of health workers in locally adapted integrated case management guidelines.
Health Systems components:
Improvements required for effective management of childhood illness (e.g. improving supplies of of essential drugs required to treat childhood illnesses, maintenance of immunisation cold chain)
Families and community components:
Improvement in 12 key family and community practices (including breastfeeding until 6 months of age, early care-seeking, compliance with treatments, interventions to improve family nutrition, use of insecticide-treated bed nets)

The Multi-Country Evaluation of IMCI Effectiveness, Cost and Impact (MCE) was launched in 1997 with the aim of evaluating the impact of IMCI on child health, and its cost-effectiveness (WHO 2002c). After worldwide review of 12 countries, 5 sites were selected for implementation studies. These include the United Republic of Tanzania, Bangladesh, Uganda, Peru and Brazil. Reasons for excluding countries

Schellenberg et al. 2004b). Improvements in observed quality of case management may not necessarily translate into population benefits if usual practice differs, and especially if health worker coverage remains limited, as in most countries where IMCI has been implemented (Nsungwa-Sabiiti et al. 2004; Huicho et al. 2005).

This notwithstanding, IMCI has been adopted by more than 100 developing countries, including South Africa (El Arifeen et al. 2004). In South Africa IMCI was first introduced in 1997 and training of health workers has followed the recommended intensive short course (11 day) model, with the result that coverage has been variable. About six years later, national IMCI training coverage, defined as the number of facilities with one or more nurses trained in IMCI, was estimated at 37%, but ranged from 12% in the Western Cape to 81% in Mpumalanga (Ramkissoon et al. 2004).

1.4.3 Practical Approach to Lung Health (PAL)

The Practical Approach to Lung Health, originally named Adult Lung Health Initiative, was a WHO strategy developed in the late 1990s as one of 5 components of the Global DOTS expansion plan designed to address slow progress towards the achievement of the global 85/70 tuberculosis target. Other components included accelerated DOTS coverage in areas where DOTS has not yet been implemented, public-private approaches to extend quality tuberculosis care to patients managed outside of national programmes, collaboration between tuberculosis and HIV programmes to address high tuberculosis incidence in areas with high HIV prevalence, and the involvement of communities in tuberculosis control activities in areas where access to health facilities is poor (WHO 2005b). PAL flowed out of experience with IMCI, and provided a useful starting point towards the development of an equivalent package for adults, now available as the Integrated Management of Adolescent and Adult Illness (WHO 2003c), because common respiratory conditions

reasonable evidence base for almost all interventions contained in the guideline but noted that few interventions were informed by studies completed in primary care settings in developing countries.

By 2006 PAL had been implemented in up to 14 countries (Eddine Ottmani – personal communication), although mainly on a limited scale as feasibility and effectiveness evaluations. Besides South Africa, evaluation activities are underway in Nepal, Morocco, Chile, Algeria, Tunisia and Kyrgyzstan. Initial results have yet to be widely disseminated and so opportunity for comparison with the findings of the South African evaluation is limited.

The impact of PAL on prescribing for respiratory diseases has been reported from Morocco, Kyrgyzstan, Tunisia and Nepal (WHO 2005b, Ottmani 2005, Shrestha et al. 2005). In all 4 countries the introduction of PAL was associated with significant reductions in the number of drugs per prescription (Table 1.9). Reduced prescription costs were also noted in Morocco, Kyrgyzstan and Tunisia, but not in Nepal. Antibiotic prescriptions were reduced in Morocco, Kyrgyzstan and Tunisia where baseline antibiotic prescription rates were high (71.7%, 57.5% and 71.5% respectively) and the guidelines used by doctors (except Nepal). However, the implementation of PAL in Nepal significantly increased generic prescribing and prescribing from the essential drugs list. Unfortunately the designs of the studies used to evaluate the impact of prescribing means that these results could well be confounded by other factors. The Morocco, Kyrgyzstan and Tunisian studies are before-after studies with no concurrent controls, and the Nepal study, while a cluster randomised controlled trial, was dependent on the correct diagnosis being recorded on carbon-copy prescription pads; this activity in itself is highly likely to be dependent on the intervention, resulting in non-comparability of interventions across different diagnostic categories.

1.4.4 Integrated Management of Adult and Adolescent Illness (IMAI)

The Practical Approach to Lung Health has since been incorporated into a new package for adolescents and adults called IMAI or Integrated Management of Adolescent and Adult Illness (WHO 2003c). Work on IMAI started in the late 1990s, and initial guideline drafts were reformulated as part of the World Health Organization's "3 by 5" campaign, with a strong focus on the clinical management of HIV, including the provision of antiretroviral (ARV) treatment.

Like IMCI and PAL, IMAI is syndromic and focuses on the clinical management of key symptoms. It attempts to balance management of acute illness with chronic disease management and prevention. Four modules are available (Table 1.10) for local country adaptation prior to implementation. At present implementation is underway in 6 African countries, including the Eastern Cape in South Africa (Ramzi Asfour – personal communication). Evaluations of its effectiveness are not yet underway.

Table 1.10 The four outpatient guideline modules of IMAI

- Acute Care
- General Principles of Good Chronic Care
- Chronic HIV Care with ARV Therapy
- Palliative Care

1.5.1 Description of studies reviewed

1.5.1.1 Cost-effectiveness of syndromic STI services in Mwanza, Tanzania

Gilson and co-workers (1997) completed this cost-effectiveness evaluation based on data from the Mwanza community randomised controlled trial which showed reduced HIV incidence following the introduction of syndromic STI services in 6 intervention communities (Grosskurth et al. 1995). Health service cost data were collected prospectively and combined with estimates of the prevalence of HIV in the community, average life expectancy values and Ugandan disability weights to estimate the cost per HIV infection averted, and per disability-adjusted life year (DALY) saved. These were estimated at 1993 US $217.62 and 1993 US $10.33 respectively. Sensitivity analysis carefully considered all sources of uncertainty arising from the study including the confidence limits for the effectiveness estimate (i.e. number of HIV infections averted), and found that the findings were most sensitive to the rate used to discount benefits, the estimated size of the catchment populations and uncertainty in the reduction of HIV incidence. At worst, the cost per DALY averted rose from 1993 US $10.33 to 1993 US $47.86. The study was the first to measure empirically the cost-effectiveness of syndromic STI management as a HIV control strategy, and concluded that it is highly cost-effective, with results applicable to many regions of the developing world.

1.5.1.2 Cost and consequence analysis of facility-based IMCI in Tanzania

The Multi-country Evaluation (MCE) of the costs and effects of IMCI team includes experienced health economists who devised standardised methods and data collection tools for estimating the cost, and cost-effectiveness, of the approach

investigators concluded that IMCI represents good value for money in the context of health sector reform, which in this instance had been facilitated by the TEHIP intervention.

1.5.1.3 Cost-effectiveness of the Practical Approach to Lung Health in Nepal

A prospective economic evaluation was undertaken alongside a 2002/2003 cluster randomised controlled trial of the PAL implementation in 40 health facilities in the Nawalparasi district of Nepal (Shrestha et al. 2005; Kumar 2006). Cost data and utility estimates obtained from the trial were combined with burden of disease parameters in a specially developed multi-disease (tuberculosis, pneumonia, COPD, asthma) multi-state (acute, chronic) projection model to estimate the cost per quality-adjusted life year (QALY) gained if PAL were implemented throughout Nepal (Kumar 2006). At 2003 US $111 per QALY gained, the investigators concluded that this represented a cost-effective implementation if compared with benchmarked standards of cost per DALY averted of per capita income. However, they noted that, because of uncertainty arising from data collected from the trial, the conclusion that PAL is cost-effective can only be made with a probability of 54%.

In a parallel analysis of prescription costs, Shrestha and co-workers (2005) found that PAL implementation resulted in a significant reduction in the number of items prescribed per visit, and significant increases in prescribing of generic drugs and from the essential drug list. These benefits, however, failed to translate into lower average prescription costs, and did not reduce wastage costs (defined as the difference between expected and actual costs per prescription).

IMCI and PAL-Nepal evaluations, but not specified in the STI study. Guideline development and implementation costs were treated as capital or start-up costs, and annualized over 10 years in both the IMCI and PAL-Nepal evaluations. This period was not justified in either evaluation, and seems optimistic given that Armstrong-Schellenberg (2004a) reported improvements in case management of children in health workers trained in IMCI up to 3 years previously, although durability beyond this has not been evaluated. Only the PAL-Nepal study made provision for refresher training after 5 years, but even this may be unrealistic. Furthermore Shekelle and co-workers (2001) evaluated the current validity of 17 quality guidelines and estimated that half the guidelines were outdated after 5.8 years. Reassuringly, the IMCI evaluation varied the period over which capital costs were annualized in a sensitivity analysis (5, 10 and 15 years) and found that this made little difference.

Changes in treatment costs were considered in all three evaluations. The cost of primary care staff time was not included in the STI analysis because STI care was considered to take up only 2% of staff time, although the impact of the intervention on this was not evaluated. The cost of hospital care was not considered in the STI or PAL-Nepal evaluations.

The alternatives being compared were clearly described in the STI and PAL-Nepal studies. It was more difficult to determine the comparison in the IMCI trial, where IMCI implementation occurred alongside other interventions including health sector reform initiatives (TEHIP), basket funding and social marketing of insecticide-treated bed nets. Careful reading of multiple sources was required to determine the alternatives being compared.

the clustered design of the trial. Adjustment for clustering was explicit in the PAL-Nepal prescription cost analysis. Also, the mortality benefit reported in the IMCI cost-consequence paper was of borderline significance, and its confidence interval included zero, corresponding to no effect, when adjustment for district-level clustering was made.

The PAL-Nepal model was based on differences in acute state utilities between the intervention and control groups, yet it was not clear whether this small difference was statistically significant (confidence limits not reported, adjustment for clustering not clear). The difference of 0.04 also falls short of what is considered the minimally important clinical difference (0.05) by the EuroQol group (Roset et al. 1999). Furthermore this model did not account for differences in the duration of disease states or incidence of acute exacerbations between groups, although both these are likely to change as a result of the intervention. The decision not to incorporate the differences in chronic state utilities observed in the trial was not justified.

The PAL-Nepal prescription cost analysis was likely confounded by assuming that the diagnosis made by the health worker and recorded alongside the prescription was correct, and not biased by the intervention, which it probably was. Also, the reason for applying different reference standards to intervention and control group prescriptions to determine prescription appropriateness, and therefore expected and wastage costs, was not justified.

Despite collection of economic data from patients and households, none of the economic evaluations reviewed used patient level data on costs and outcomes to quantify the uncertainty, or random error, of the cost-effectiveness analyses. Instead effectiveness estimates were combined with parameters estimated outside of the trials to determine cost per QALY gained (PAL-Nepal), or DALY averted (STI). This is discussed below.

investigation. Price years were reported in all three studies (STI: 1993; IMCI: 1999; PAL-Nepal: 2003) although methods for adjustment for inflation were only provided in the IMCI study. Currency conversions were clearly reported in all studies.

1.5.2.2.4 Details of models used

Both the STI and PAL-Nepal studies used mathematical models to extrapolate trial findings to population level. The STI model for estimating DALYs saved was relatively simple, combining trial costs and effectiveness estimates with local utility weights and average life expectancy values in five steps. All parameters included in the model were subjected to testing in the sensitivity analysis. The PAL-Nepal group developed a more complex multi-disease multi-state projection model to estimate the population benefits, measured in QALYs gained, should PAL be implemented at country level. In both cases, parameters for the models were well defined, and sources carefully documented and justified.

1.5.2.3 Criteria for evaluating methods of analysis

1.5.2.3.1 Discounting

Discounting was undertaken in all three studies, but to variable extents. The most comprehensive approach was in the STI evaluation, where a rate of 3% was justified, and used in the primary analysis to discount both costs and effects. Rates of 0% and 6% were explored in the sensitivity analysis. In the IMCI and PAL-Nepal studies, it was not clear whether discounting was applied equally across costs and benefits even though this was appropriate given that data collection spanned several years in both cases. The IMCI evaluation also did not specify whether costs other than capital

outcomes in cluster randomised trials are well developed (Donner and Klar 2000), but this is not true of economic evaluations conducted alongside cluster trials in which individuals' costs as well as outcomes are measured.

The PAL-Nepal cost effectiveness analysis used non-parametric bootstrapping to explore uncertainty related to cost and utility estimates derived from the trial. This is recognized as a gold standard for evaluating uncertainty related to patient-level economic data, which is typically skewed (Briggs 1999). It involves repeatedly sampling from costs and outcomes from the study sample, with replacement, assuming that distributions in the study sample are the same as the distributions in the population. With cluster randomised data, entire clusters rather than individuals should be sampled in keeping with the requirement that hierarchical data should only be bootstrap sampled at the highest level (e.g. clusters) to retain the data's hierarchical structure (Davison and Hinkley 1997). Most economic evaluations which have employed bootstrapping have used individual bootstrap sampling (Goodacre et al. 2004, Gilbert et al. 2004, Sullivan et al. 2005). So it is unlikely that cluster sampling was used in the PAL-Nepal evaluation. Analyses conducted for this thesis will show that intra- cluster correlation of costs and outcomes tends to reduce the estimated probability that an intervention is cost effective (Bachmann et al. 2005). This means that the estimated 54% probability that PAL-Nepal is cost-effective for a willingness to pay threshold of US $150 per QALY gained is likely to be an overestimate.

Recently, analysis of cost and outcomes by comparing net monetary benefits has been advocated for meta-analyses of multi-centered trial data, although it has yet to be used in cost-effectiveness analysis alongside cluster trials (Drummond et al. 2005).

1.6 The effectiveness of guideline dissemination and implementation strategies

In the 1980s and 1990s awareness concerning variations in health care, rising costs and failure to translate research findings into practice prompted increased interest in and production of clinical practice guidelines. Guidelines have been defined as "systematically developed statements to assist practitioners' and patients' decisions about appropriate health care" (Institute of Medicine 1992), and have been widely viewed as a means of updating busy health professionals of the latest research findings while promoting more appropriate and cost-effective care (Thorsen and Mäkelä 1999).

1.6.1 Trends in guideline development and implementation in developing and developed countries

Progress in guideline development has followed two distinct trends in the developed and developing worlds. In the developing world, guideline developers have focused largely on the production and implementation of symptom- and sign-based, or syndromic, guidelines focusing on the primary care management of common and important clinical conditions. These activities, chiefly co-ordinated by the World Health Organisation, have included initiatives such as the Syndromic Management of Sexually Transmitted Infections, the Integrated Management of Childhood Illness (IMCI), and more recently the Practical Approach to Lung Health (PAL) and Integrated Management of Adolescent and Adult Illness (IMAI), overviews of which were provided in Section 1.4. In terms of implementation strategy, decision-makers have relied largely on traditional didactic methods, usually in the form of intensive centralised short courses, often with a practical component, followed by limited

Models of change have been used to understand the behaviour of health professionals and to guide the development of interventions aimed at changing practice. These models include learning theory, social cognition models and models of organizational change (NHS Centre for Reviews and Dissemination 1999). Although the theoretical basis for changing the behaviour of health professionals is widely viewed as incomplete (Grimshaw et al. 2004), social marketing and the precede-proceed model have provided useful frameworks for informing the planning, design and implementation of various interventions, and in certain cases, have been shown to augment effectiveness (Thomson et al. 1999).

1.6.4 The evidence for dissemination and implementation strategies

Multiple reviews of the relative effectiveness of various implementation strategies have been completed during the past 15 years, in an attempt to guide policymakers as to how best to implement the growing number of clinical practice guidelines. Intervention strategies targeting health professionals have been described and categorised by the Cochrane Group on the Effective Practice and Organization of Healthcare (Bero et al. 2001), and include among others, the passive dissemination of educational materials, reminders, educational outreach visits, audit and feedback and the use of mass media (Table 1.11; Grimshaw et al. 2004).

Prior to 2004, systematic reviews of guideline implementation strategies drew similar conclusions (Oxman et al. 1995, Davis et al. 1995, Bero et al. 1998, NHS Centre for Reviews and Dissemination 1999, Grimshaw et al. 2001). Passive dissemination of guidelines was insufficient to change practice but may be useful for raising awareness. There was no single "magic bullet" for changing practice but active strategies including reminders and educational outreach appeared the most promising single interventions particularly when targeting prescribing behaviour (educational outreach) or ordering of investigations (reminders). Multifaceted interventions, which combine more than one type of intervention and address barriers to change, were likely to be the most effective. In all cases, reviewers acknowledged that the evidence base for changing professional practice was incomplete, and that the resource implications of competing strategies were rarely considered.

These reviews were limited in that they did not provide or compare the effect sizes due to various interventions, ignored unit of analysis errors, relied on the authors' descriptions of the intervention for classification thereby underestimating the number of multi-faceted interventions, and used vote-counting of statistically significant comparisons. In 2004 Grimshaw and co-workers published the most extensive and methodologically advanced review of interventions designed to change professional practice. They identified 235 studies reporting 309 comparisons from over 150 000 hits, extracted the main findings and estimated median effect sizes for main outcome measures, where possible adjusting for unit of analysis errors and interrupted time series designs (Grimshaw et al. 2004). Their findings challenged much of the conventionally held understanding of interventions to change professional practice.

Grimshaw and co-workers (2004) identified 18 studies involving the passive dissemination of educational materials. Most led to improvements in quality of care,

based care (Avorn and Soumerai 1983). Techniques of educational outreach are summarised in Table 1.12 (Fender et al. 1999).

Table 1.12 Techniques of educational outreach (from Fender et al. 1999)

- Investigating baseline knowledge and motivations for current practice.
- Defining clear educational and behavioural objectives.
- Establishing credibility through a respected organisational identity, referencing authoritative and unbiased sources of information, and presenting both sides of controversial issues.
- Simulating active participation in educational interactions.
- Using concise graphic educational materials that highlight and repeat essential messages.
- Providing positive reinforcement of improved practices at follow-up visits.

In the 1990s guideline implementation and dissemination reviews highlighted the potential of educational outreach to change professional practice, particularly its impact on prescribing behaviour (Thomson et al. 1999). However, Grimshaw and co-workers (2004) found it to be of only modest effectiveness with a median effect size of +6.01% (range -4.0 to +17.4) derived from 11 cluster randomised trials. Educational outreach was frequently included as a component of multi-faceted interventions, but subgroup exploratory analyses showed no advantage of combining it with dissemination of educational materials. The combination of educational outreach with educational materials *and* educational meetings proved most effective (median effect size from four cluster randomised trials +11.0%, range +8.4% to +16.4%). However, educational outreach was viewed as impractical by key informants in a survey of NHS decision-makers (Grimshaw et al. 2004). Concerns were also expressed about its resource implications, although these could not be adequately addressed given the low number of educational outreach studies (n=10) which have included some form of economic evaluation. Although published as recently as 2004, the review includes only studies published between 1966 and mid-1998. During a limited search, 40 studies of educational outreach interventions

The majority of studies (72.5%) originated from North America and Europe, although 8 studies were conducted in Australia. Three studies from the developing world were noted, all of them published in 2005. A randomised trial from Sudan evaluated the effectiveness of outreach in combination with audit and feedback on antibiotic prescribing in primary care practices, run by doctors and medical assistants, and found that it reduced the mean number of encounters during which antibiotics were prescribed (Awad et al. 2005; Eltayeb et al. 2005). Another randomised controlled trial from Thailand evaluated the impact of educational outreach combined with educational meetings on the quality of prescribing and general management of primary care delivered by nurses across a range of conditions (Pagaiya et al. 2005). This study noted mixed effects with improvements in some, but not all indicators of care. The final study from the developing world was from South Africa, where the effectiveness of educational outreach, in this instance combined with educational materials, on the provision of kangaroo mother care[c] was evaluated in 34 hospitals (Pattinson et al. 2005). This trial observed improvements in the provision of kangaroo care which exceeded those obtained with the distribution of educational materials alone. This brings the total number of studies evaluating the effectiveness of educational outreach in developing world settings to 6. Two studies excluded from the 2004 Grimshaw review both evaluated the impact of outreach on the management of diarrhoea in children in Indonesia, and noted mixed effects (Ross-Degnan et al. 1996, Santoso 1996). The CHAMP[d] study compared the impact of outreach to general practitioners in Cape Town with passive dissemination of guidelines on asthma control among children (Zwarenstein et al. 2005). It showed markedly improved asthma symptoms among children managed by intervention group practitioners.

[c] Kangaroo mother care is when infants are nursed skin-to-skin against the mother's chest.

[d] CHAMP stands for CHestiness and Asthma in Mitchell's Plain. Mitchell's Plain is a large socio-economically deprived suburb on the outskirts of Cape Town.

educational outreach visits (15/34 studies, 44%); in six studies two visits were conducted (6/34, 18%), and in 11 studies three or more visits were provided (11/34, 33%). This is despite recommendations that wherever possible, interventions be multi-event to maximise the effect on changing practice (Hulscher et al. 1999), and possibly reflects concerns that resource intensive interventions may be viewed as a barrier to scale-up (Grimshaw et al. 2004). The identity of the detailer may also be relevant in understanding the effectiveness of the various interventions. Pharmacists were most frequently used as detailers accounting for 12 of 29 studies in which the profession of the detailer was specified, presumably because of the focus on appropriate prescribing in the majority of studies. Specialist or local opinion leaders were used in nine studies (9/29, 31%) and peer doctor general practitioners in four studies (4/29, 41%). Denton and co-workers (2001) compared the effectiveness of a single educational outreach session provided by a specialist with one provided by a junior resident, and found the former to be more effective at changing prescribing for hypertension and cardiac failure.

Most (31/40, 78%) studies used cluster randomised controlled trials to evaluate the effectiveness of educational outreach. Seven studies (18%) used non-randomised controlled designs, and two used interrupted time series alongside routine implementation of the intervention. All studies reported the effect of the intervention on process outcomes, but only four studies reported the effect on health outcomes. Just over half of the studies (22/40, 55%) reported that the intervention was effective at changing process outcomes, 1/4 (10/40, 25%) that the effects were mixed, and only seven studies (7/40, 18%) reported no effect. No study reported that the intervention was associated with a deterioration in practice. A meta-analysis of observed effect sizes was beyond the scope of this review, but effect changes ranged from small (+5.2%, Freemantle et al. 2002) to substantial (+41%, Solomon et al. 2001).

Table 1.13a Characteristics of studies evaluating the effectiveness of educational outreach interventions 1998 – 2005 (n = 40)

Characteristic	n/N (%)	References
Year of publication		
1998 – 1999	4/40 (10%)	A7, A13, A16, A21
2000 – 2001	11/40 (28%)	A3, A5, A8, A10, A14, A17, A28, A31, A33, A34, A40
2002 – 2003	11/40 (28%)	A2, A9, A11, A18, A19, A25, A29, A30, A36, A37, A39
2004 – 2005	14/40 (35%)	A1, A4, A6, A12, A15, A20, A22, A23, A24, A26, A27, A32, A35, A38
Country		
United Kingdom / Europe	15/40 (38%)	A2, A4, A6, A7, A8, A9, A12, A13, A18, A22, A24, A29, A34, A36, A38
United States / Canada	14/40 (35%)	A3, A5, A10, A11, A16, A17, A19, A20, A25, A28, A31, A32, A33, A35
Australia	8/40 (20%)	A14, A15, A21, A23, A30, A37, A39, A40
Other	3/40 (8%)	A1 (Sudan), A26 (Thailand), A27 (South Africa)
Setting		
Primary care	35/40 (88%)	A1, A2, A3, A4, A6, A7, A8, A9, A10, A11, A12, A13, A14, A15, A16, A17, A18, A19, A20, A21, A23, A24, A25, A26, A28, A29, A31, A32, A34, A35, A36, A37, A38, A39, A40
Hospital-based care	5/40 (13%)	A5, A22, A27, A30, A33,
Study Design		
Randomised controlled trial	31/40 (78%)	A1, A2, A3, A4, A5, A6, A7, A8, A9, A10, A11, A12, A13, A14, A16, A17, A18, A19, A24, A25, A26, A27, A32, A33, A34, A35, A36, A37, A38, A39, A40
Controlled clinical trial	7/40 (18%)	A15, A20, A21, A23, A28, A30, A31,
Interrupted time series	2/40 (5%)	A22, A29
Targeted behaviour		
Prescribing	24/40 (60%)	A1, A2, A4, A5, A7, A8, A9, A14, A15, A17, A20, A21, A22, A23, A24, A25, A26, A30, A32, A33, A34, A36, A38, A40
General management	15/40 (38%)	A2, A3, A6, A10, A12, A13, A17, A18, A19, A24, A25, A26, A27, A28, A29
Test-ordering/ screening	10/40 (25%)	A2, A13, A16, A20, A25, A28, A29, A31, A35, A37
Counselling	2/40 (5%)	A11, A39

1.6.6 Implementation research in the developing world

There are few studies of the effectiveness of guideline dissemination and implementation strategies in developing countries. Only 2 studies from the developing world met the criteria for inclusion in the 2004 Grimshaw review. These included a cluster randomised trial of the effectiveness of reminder systems on urethral catherisation in Thai hospital wards (Danchaivijitr et al. 1992), and a multifaceted intervention to reduce antibiotic prescriptions among Mexican patients presenting to primary care facilities with the common cold (Perez-Cuevas et al. 1996). Both showed improvements in process outcomes following exposure to the interventions. It is encouraging to see that the limited search of educational outreach studies published after 1998 revealed three studies from the developing world, all published last year. These, including two studies excluded from the 2004 Grimshaw review and one unpublished study, were reviewed in section 1.6.5.

Noticing the dearth of studies of the relative effectiveness and efficiency of guideline implementation strategies in the developing world, European-based implementation researchers partnered with health systems researchers from Southern Africa in the late 1990s to promote the uptake of research findings in the region. AfroImplement was a European Union funded concerted action which aimed at developing rigorous implementation trials in Southern Africa (AfroImplement 1997). Over a period of six years, it nurtured collaborations between European and Southern African researchers during seven workshops, email discussions and exchange visits. Workshops involved interactive teaching sessions and opportunities to develop protocols for African implementation studies with input and support from expert implementation and health system researchers. The PALSA intervention and study protocol were both refined during several of these workshops.

1.6.7 Beyond changing professional practice – knowledge translation

More recently the concept of changing professional practice has broadened to acknowledge the range of stakeholders, including policymakers, clinicians, teams, managers, patients and populations required to act together to close the gap between evidence and practice. Knowledge translation can be defined as "the exchange, synthesis and ethically sound application of knowledge—within a complex system of interactions among researchers and users—to accelerate the capture of the benefits of research . . . through improved health, more effective services and products, and a strengthened health care system" (Canadian Institutes of Health Research 2005).

It is not limited to learning situations, but rather concerns the practice environment together with its social, organisational and policy dimensions. It targets all possible participants in the practice environment, and frequently includes patients and policymakers who are usually not addressed by professional interventions. As such, it permits greater emphasis on population health (screening, early diagnosis, preventive measures) and draws on a broader and interdisciplinary group of experts, including those from informatics, patient education, organisational learning and social marketing (Davis et al. 2003).

Table 1.15a Characteristics of educational outreach studies reporting resource use (1983 – 2005)

Characteristic	n/N (%)	References
Country		
United Kingdom / Europe	8/17 (47%)	B1, B2, B3, B4, B5, B10, B11, B16
United States / Canada	5/17 (29%)	B6,B9, B12, B14, B15
Australia	3/17 (18%)	B7, B8, B17
Other	1/17	B13 (Thailand)
Setting		
Primary care	13/17 (77%)	B1, B2, B3, B4, B5, B6, B7, B11, B12, B13, B14, B16, B17
Hospital-based care	4/17 (24%)	B8, B9, B10, B15
Study Design		
Randomised controlled trial	14/17 (82%)	B1, B2, B3, B4, B5, B7, B9, B11, B12, B13, B14, , B15, B16, B17
Controlled non-randomised trial	2/17 (12%)	B6, B8
Interrupted time series	1/17	B10,
Targeted behaviour		
Prescribing	12/17 (71%)	B1, B2, B3, B4, B7, B8, B9, B10, B12, B13, B14, B16
General management	3/17 (18%)	B3, B11, B13
Test-ordering/ screening	5/17 (29%)	B1, B4, B11, B12, B17
Counselling	2/17 (12%)	B3, B4
Intervention		
Educational outreach alone	1/17	B6
Educational outreach + educational materials	13/17 (77%)	B1, B2, B4, B5, B7, B8, B9, B10, B13, B14, B15, B16 , B17
Educational outreach + educational meetings	7/17 (41%)	B1, B8, B9, B11, B13, B15 , B17
Educational outreach + audit & feedback	3/17 (18%)	B3, B9, B13,

Almost all studies (71%) aimed to change prescribing practices; this is not unexpected since outreach had been earmarked as a promising tool for changing prescribing behaviour in the 1990s (Oxman et al. 1995, Thomson et al. 1999). Several studies also targeted test-ordering, general management and patient advice/education. Improved management and cost containment were the objectives of most of the studies, although one focused exclusively on cost containment (Hill et al. 2002).

1.7.2 Type of educational outreach evaluated

Most studies evaluated the effect of outreach in combination with educational materials. Other co-interventions included educational meetings and audit and feedback. The maximum number of interventions was six (Leviton et al. 1999). The majority of studies evaluated the effectiveness of a single educational outreach visit, and only four studies evaluated two or more visits (maximum four - Ofman et al. 2003). Around 40% were on a one-to-one basis and the rest were to groups of practitioners, or both. Pharmacists were the professionals most frequently employed as detailers, reflecting the emphasis on changing prescribing practices. In three studies specialist physicians provided the outreach training (Banait et al. 2003, Hill et al. 2002, Soumerai et al. 1983) and in two researchers did (Feder et al. 1995, Hansen et al. 1999).

1.7.3 Methodological quality of economic evaluations

Only two studies reported economic evaluations as separate publications (Mason et al. 2001, Stone et al. 2005). The primary focus of the remaining publications was mainly of the impact of educational outreach on the quality of care, with the result that reporting of economic data was very limited. For the purposes of this, and the 2004 Grimshaw review, the term "economic evaluation" was loosely

1.7.3.3 Estimates of costs

Methods for estimating and reporting of costs were poorly described in most studies, but this may reflect limited space in what are primarily publications describing effectiveness. Most studies restricted their cost analysis to an aspect of medical care, usually a limited number of drugs. Ofman's evaluation of a dyspepsia guideline intervention was a notable exception, and provided detailed, disaggregated information on health service expenditure with resource use reported separately (Ofman et al. 2003). The source of unit costs was stated in nine studies, and the price year in seven, although details of adjustment for inflation were never provided.

Eight studies reported intervention costs, usually restricted to the resource implications of implementing the outreach visits. Materials were variably included. Only Morrison and co-workers (1999) reported the cost of guideline development, despite several studies reporting extensive local tailoring and adaptation of guidelines specifically for the intervention. Mason and colleagues (2001) argued that guideline development costs could reasonably be excluded because guidelines for common primary care conditions are generated nationally, and readily available for implementation. They also argued that the opportunity cost of health worker time need not be considered, as health workers are expected to spend a portion of their time in continuing education activities. However, two studies noted that whether or not this opportunity cost of target practitioner time is considered, it is important in determining comparative cost effectiveness of competing intervention strategies (Watson et al. 2002, Simon et al. 2005). No study considered all costs relevant to guideline development, implementation and subsequent changes in treatment costs.

Morrison (1999) found increased primary care costs without improvement in outcomes for the investigation and management of infertility, and cautioned against the use of outreach for conditions that span the primary-secondary care interface. Feder (1995) and Simon (2005) provided no clear economic conclusion to their studies, although costs appeared similar between groups.

1.7.3.4 Summary

There are too few methodologically sound or sufficiently comprehensive studies of educational outreach interventions to draw any firm conclusions about its cost-effectiveness. Also, resource costs are likely to differ between different countries. Despite this, compared with alternative implementation approaches, educational outreach has been widely viewed as resource intensive, and many decision-makers have expressed resistance to its routine use in health services (Grimshaw et al. 2004). Gandjour (2005) makes an important distinction between the resources required to launch outreach initiatives and their cost-effectiveness. While resources required to launch outreach initiatives may appear substantial and serve as a disincentive to 3rd party payers who need to stay within a given budget, incremental cost-effectiveness may still be favourable, even if effect sizes for process outcomes are relatively small (Freemantle et al. 2002). Mason distinguishes between treatment cost-effectiveness, or the incremental costs and benefits of a treatment, and policy cost-effectiveness, which can be determined by combining treatment cost-effectiveness with the magnitude of change achieved by the implementation method. Many factors interact to influence policy cost-effectiveness. These "loading factors" include the treatment cost-effectiveness but also the prevalence of the target disease, duration of effect, effectiveness and cost of the implementation strategy.

So, while educational outreach might be perceived to be expensive, it may still be highly cost-effective if the prevalence of the disorder being targeted is high (like

1.8 Summary of literature review

This chapter has highlighted the large and growing burden of adult respiratory diseases in the developing world and in South Africa. Nurses in primary care facilities are facing increasing numbers of infectious diseases, many of which are manifestations of underlying HIV infection, superimposed on a moderate chronic respiratory disease burden. Traditional nurse training and short-course intensive workshops have failed to equip nurses adequately for independent clinical practice, although in reality many nurses assess and treat patients with no or extremely limited doctor support.

The response to suboptimal primary care has differed substantially in the developed and developing worlds. In the developing world, efforts have largely been channelled into the development of syndromic treatment guidelines although their implementation has been characterised by the use of traditional, largely didactic, and untested training methods. In the developed world, much has been done to develop, implement and evaluate the relative effectiveness of various implementation strategies which draw on theoretical frameworks for changing behaviour among adult professionals.

The PALSA project arose from the AfroImplement collaboration which sought to promote the uptake of evidence-based care in Southern Africa through rigorous implementation trials. It is unique in combining the syndromic approaches widely used in the developing world with evidence-based approaches to its implementation, in this case educational outreach visits, in a non-physician resource-limited setting like the Free State public health sector.

The pragmatic randomised controlled trial of its effectiveness, cost and cost-effectiveness undertaken in the Free State contributes to two areas of primary

1.9 The Practical Approach to Lung Health in South Africa (PALSA)

This thesis forms part of a larger collaborative project which developed, implemented and evaluated the PALSA intervention in the Free State. While a detailed explanation of intervention development is beyond the scope of this thesis, the events leading up to the trial will now be briefly described in order to provide background to the trial and economic evaluation.

1.9.1 Establishment of the research collaboration and engagement with the Department of Health

The South African adaptation of PAL, PALSA or Practical Approach to Lung Health in South Africa, arose out of a collaboration formed between health systems researchers, clinicians and Free State Department of Health managers in the late 1990s. A 1999 request from the Free State Department of Health to the Medical Research Council for assistance with research on priority setting and cost-effectiveness widened to a broader discussion of the need for health systems research in the province. At that time, Stop TB at the World Health Organisation had engaged the Medical Research Council as how to best adapt and implement the PAL guidelines in South Africa. Development of the PALSA intervention and study proposal was aided by AfroImplement workshops in late 1999 and 2001, and the Free State soon agreed to implement the package within a pragmatic randomised trial evaluation.

Contact with Stop TB at the World Health Organization led to important engagements with two further stakeholders. The first of these was with the head of the South African National Tuberculosis Control Programme, who supported the initiative and contributed technical expertise to the process of guideline

provided useful information on the distribution and prevalence of respiratory diseases in South African primary care settings (Fairall et al. 2001). The management of acute respiratory infections, tuberculosis and obstructive lung disease was emphasised and, due to high rates of HIV co-infection among patients with respiratory diseases, a section on HIV added. This guideline was adapted before antiretroviral treatment was made available through the South African public sector health service (South African National Department of Health 2003b), and so the HIV section instead emphasised the provision of cotrimoxazole prophylaxis to those with symptomatic HIV infection.

Several workshops were held with approximately 60 Free State clinicians, managers and nurses. A wide range of stakeholders, including the National Tuberculosis Control Programme Manager, Stop TB from WHO, and local respiratory and primary care physicians were consulted during the adaptation of the guideline. One key concern was to ensure consistency with national tuberculosis policies (South African National Department of Health 2000a) and the South African essential drugs list which regulates prescribing provisions for primary care nurse practitioners (South African National Department of Health 1998b).

Several deficiencies in the prescribing provisions relevant to the guideline were noted. Inhaled corticosteroid initiation was restricted to doctors in the Free State, and nurses were not permitted to prescribe short courses of oral corticosteroids for patients with acute exacerbations of obstructive lung disease, although they were allowed to provide intravenous corticosteroids prior to emergency referral. At a national level, the recently established Belgium government funded TB-HIV portfolio had successfully motivated for nurses to initiate cotrimoxazole prophylaxis in patients with symptomatic HIV infection, and the 2003 Primary Care Essential Drug List was revised to include Stages 3 and 4 HIV infection among the indications for primary prophylaxis (South African National Department of Health 2003a). Nurses in the Free State nonetheless reported feeling confused by conflicting recommendations as to when to start

1.9.3 Development of the PALSA training support materials and educational outreach intervention

Selection of the implementation strategy was informed by the AfroImplement collaboration (see section 1.6.6) which aimed to promote the development of rigorous implementation trials in Southern Africa. An earlier trial arising from the collaboration has investigated the impact of educational outreach to Cape Town general practitioners on the frequency and severity of asthma symptoms among children in their practices, and found marked improvements despite limited exposure to the intervention (Zwarenstein et al. 2006). We selected this model for implementation of PALSA in the Free State using nurse middle managers as outreach trainers, over offsite education because it was sustainable, drawing on and expanding the educational role of existing supervisory personnel, and because it minimised disruption in under-staffed front line facilities. Also, at the time systematic reviews of guideline implementation strategies identified educational outreach as a particularly promising strategy for changing provider behaviour, especially prescribing (Oxman et al. 1995, Thomson et al. 1999, Grimshaw et al. 2001). It was only later, with the publication of the state-of-the-art review by Grimshaw and colleagues in 2004, that it was considered not as effective as previously thought.

The selection of educational outreach as the primary implementation strategy was tested with nurses, nurse trainers and managers during further workshops in the Free State, where video-taped educational outreach sessions based on the childhood asthma intervention for general practitioners in Cape Town were presented. Nurses felt that the model was suitable, as a lack of onsite and clinical follow-up was perceived to be the main shortcoming of existing centralised training courses, where selected nurses were trained intensively but not re-evaluated or supervised once back at their clinic. The social marketing elements of outreach were recognised by nurses who emphasised that it was important to "sell" the package to nurse practitioners. Nurses provided many suggestions for

Table 1.16 PALSA Key Messages

Respiratory Syndrome	Key Message
Tuberculosis	Coughing ≥ 2 weeks → Send sputa for TB.
TB/HIV co-infection	Test for HIV because TB is common in HIV patients. Cotrimoxazole prophylaxis delays symptoms and prolongs healthy life in HIV patients.
Lower Respiratory Tract Infection (LRTI)	Diagnose LRTI in patients with cough plus difficult breathing and/or pain on coughing/breathing and/or fever. If severe refer; if new or purulent sputum prescribe amoxicillin for 7 days and follow-up in one week.
Upper Respiratory Tract Infection (URTI)	Diagnose URTI in patients with blocked or runny noses and/or sore throats and/or mild fever but *no* difficult breathing and *no* chest pain. Prescribe symptomatic treatments only.
Obstructive Lung Disease (Asthma and COPD – Chronic Obstructive Pulmonary Disease)	Diagnose asthma in patients with *recurrent* wheeze, difficult breathing and cough. Prescribe inhaled corticosteroids. Diagnose COPD in patients with *persistent* wheeze, difficult breathing and cough (and a history of smoking). Prescribe bronchodilators.
Smoking Cessation	People are more likely to stop smoking if advised to do so by a health professional....and smoking makes all lung conditions worse so tell your patients to quit today!

Eight nurse trainers, selected from among the district tuberculosis coordinators in the Free State, attended a 5 day workshop on techniques of interactive educational outreach and the clinical content of the guidelines, especially the key messages. The workshop was led by an experienced trainer, with specialist interests in facilitative training techniques, experiential learning and medical education. Content support was provided by two medical researchers, including the author and lead guideline developer. Free State nurse trainers were provided with the guideline and materials, and asked to model outreach sessions to their colleagues, and later in the week to groups of nurses in primary care clinics. These sessions were video-taped and reviewed, with feedback provided by content and process facilitators and colleagues. The training strategy for the trainers has been described in detail elsewhere (Bheekie et al. 2006).

considering whether or not to implement PALSA. Research questions for each dimension of the evaluation are provided in Table 1.17. They underpin a continuum of enquiry ranging from questions of effectiveness to those of efficiency, and together provide a comprehensive framework for understanding the impact of PALSA on health services.

- Health related quality of life
- Mortality
- Patient satisfaction
- Health care utilisation within and beyond the public sector
- Cost of respiratory care for the health service and for patients
- Patient productivity
- Cost per additional case of tuberculosis diagnosed, and per additional case appropriately treated

- To translate the EuroQol 5D generic health status questionnaire for use among Sesotho speakers, and to evaluate the construct validity of the translated version among primary care patients with cough and/or difficult breathing
- To estimate the incremental cost-effectiveness of PALSA in addition to usual training and support from the perspective of the health service and society.

2.2 Study Design

The study was a pragmatic cluster randomised trial with a prospective economic evaluation. The unit of randomisation was the clinic, and outcomes were assessed at the level of individual patients.

2.2.1 Reporting

Reporting is consistent with the CONSORT checklist for cluster randomised controlled trials, insofar as possible given the trial's pragmatic orientation (Campbell et al. 2004a). Similarly the economic evaluation conforms to guidelines for reporting economic evaluations (Drummond and Jefferson 1996).

tuberculosis protocol, received by fewer than 5% of staff each year, continued in both groups.

In the trial PALSA, in addition to usual training and support, was compared with usual practice. Ideally, PALSA should have been compared with, and not in addition to, usual training and support. However, this would have required that intervention clinic nurse practitioners be refused any usual training for the duration of the trial. This was considered unreasonable, especially given that such training generally applied to less than 5% of eligible nurse practitioners in any given year.

2.2.4 Economic Evaluation

2.2.4.1 Study question

Cost has been perceived as a barrier to implementation of similar interventions in other developing countries (Khan et al. 2000, Kolstad et al. 1998). The economic evaluation aimed to estimate the cost of PALSA and evaluate whether, in addition to usual training and support for respiratory diseases, it represented an effective and efficient use of scarce resources from the perspective of the health service and society.

2.2.4.2 Form of economic evaluation and hypotheses

Without a priori estimates of effectiveness, the economic evaluation set out to complete a cost consequence analysis, comparing the costs and effects of the PALSA intervention in addition to usual training and support. In the event that the trial showed a difference in outcomes (more or less effective) a cost-effectiveness analysis was planned; if no difference was observed a cost-minimisation analysis.

Table 2.1 Clinic Characteristics at baseline (beginning 2003)

Characteristic	PALSA Group	Control Group
Number of clinics	20	20
Total adult attendances (median per quarter during 2002)	12 749	12 935
Nurses per clinic (median)	9	8.5
TB Treatment Service available	19/20 (95%)	20/20 (100%)
24 Hour Emergency Service available	4/20 (20%)	2/20 (10%)
Distance from local referral hospital (median)	7km	5.5km

In general, these clinics service impoverished communities, predominantly in rural areas with high tuberculosis and HIV rates [tuberculosis notification rate (all cases) 494/100 000 in 2002 (South African National Department of Health 2003c), estimated HIV prevalence of 30.1% among antenatal attendees in 2003 (Makubalo et al. 2003)]. On a typical day around 200 patients attend one of these clinics; approximately 1/3 of these are children. A clinic is staffed by a median of nine nurses, some of whom see only pregnant women or children. Problem cases are referred to doctors who visit weekly.

2.2.5.2 Randomisation

Clinics were randomised to receive or not to receive PALSA in addition to usual training and support. Randomisation was completed in blocks of four and stratified by district (Figure 3.1). Randomisation was performed before outreach training commenced in clinics, by a statistician unfamiliar with the clinics or the intervention. After randomisation, but before educational outreach or data collection commenced, one clinic randomised to the control group closed down. Both staff and patients were moved to a nearby clinic. Given that the staff and patients to whom the intervention had been randomised had simply been

took two key factors into consideration: the number of patients in separate "fast track" queues for tuberculosis care, and the overall number of patients in the waiting room. These recruitment procedures were piloted before the trial, and guided the ratio which fieldworkers used to sample patients from the waiting room. Thus, if review of the daily headcounts suggested that total attendances numbered less than 70 patients, fieldworkers were asked to request *every* patient who reported cough and/or difficult breathing to meet with the team after consultation with the nurse. If the total attendances numbered between 71 and 140, *every second* patient was approached to meet them after the consultation, if total attendances numbered between 141 and 210, *every third* patient and if greater than 210, *every fourth* patient. This was necessary to ensure that patients with acute symptoms, who may present at any time, were not systematically excluded should sampling be completed early during the day.

The proportion of tuberculosis care visits for each clinic was also calculated before the trial, using 2002 statistics for each clinic collected routinely by the Free State Department of Health. This was used to guide recruitment from the general and tuberculosis queues. Thus, each clinic was set a "tuberculosis queue target", proportional to the burden of tuberculosis care visits in that particular clinic. For example in Pabollong clinic, where 24% of visits in 2002 were attributed to tuberculosis care, fieldworkers were instructed to recruit 38 (76%) patients from the general queue, and 12 patients (24%) from the tuberculosis queue. Inclusion and exclusion criteria were applied equally to patients recruited from either queue.

2.2.6.3 Patient interviews

Fieldworkers interviewed patients after their consultation, and three months later by appointment at the clinic (Figure 2.2). Those patients who did not return to the clinic for the follow-up interview were traced and interviewed at home or at their workplace. Interviews were conducted in one of five local languages, chosen by the patient. Questionnaire content, development and translation are

2.2.8 Outcomes

Multiple primary outcomes were pre-specified for the trial to accommodate the syndromic nature of the intervention whereby multiple conditions and behaviours were targeted. Outcomes are summarised in Table 2.2.

2.2.8.1 Effectiveness Outcomes

Primary outcomes included process indicators of quality care and were defined for four disease categories. For tuberculosis, the primary goal was to increase case detection, documented on the patient-held tuberculosis treatment card or as reported by the patient. Tuberculosis sputum testing, the South African standard for diagnosis (South African National Department of Health 2000a), was indicated by patient report. For obstructive lung disease, the primary goal was to improve therapy, indicated by inhaled corticosteroid prescription. For respiratory tract infections, the primary goal was to rationalise prescribing, indicated by antibiotic prescription. PALSA also aimed to improve HIV and AIDS care, indicated by cotrimoxazole prescription among tuberculosis patients. Outcomes were assessed one and four months after the intervention began and were deemed present if reported at either interview. This follow-up period is brief for an economic evaluation but was decided because of concerns about tracing patients in a difficult context characterised by urban migration of people in search of work, and the absence of infrastructure including road names in rural areas. We planned to extend follow-up if we received additional funding and wanted to interview participants on a third occasion, six to twelve months after the intervention started.

Secondary outcomes included counselling indicators (proportion receiving smoking cessation advice, readiness to quit, smoking cessation, motivation to undergo VCT), health related quality of life, frequency and severity of

2.2.9 Validation of the Sesotho Adaptation of the EuroQol-5D

The EuroQol was translated into Sesotho for use in the trial. A secondary objective was to assess the construct validity of the Sesotho translation for respiratory patients in an outpatient setting. The ability of the translated EuroQol to distinguish between sick and less sick patients, and diagnostic categories was examined using ordinal logistic regression. Results are reported in Chapter 6 Section 6.2.5.2.

2.2.10 Sample Size Calculations

Sample size calculations were based on the effectiveness outcomes given the lack of consensus on and methods for determining sample sizes for economic evaluations (Al et al. 1997). The minimally important health service improvement for tuberculosis case detection was specified by policymakers in advance of the trial to be 25%. Review of routine tuberculosis data showed that too few tuberculosis patients attend within a feasible study duration to detect this difference. A more common measure, sputum sampling for tuberculosis, was selected as a surrogate. It was estimated that 1000 patients per arm, in clusters of 50, provided 90% power (alpha = 0.05) to detect a 10% improvement in sputum screening for tuberculosis.

Further sample size calculations were based on preliminary survey work completed during piloting of the questionnaire. In total, 30 patients were interviewed. Of these, 70% reported receiving an antibiotic prescription, 17% an inhaled corticosteroid and half reported problems with their usual activities. From this it was estimated that 1000 patients per arm provided 90% power (alpha = 0.05) to detect a 10% improvement in inhaled corticosteroid prescriptions, a 10% reduction in antibiotic prescriptions, and a 10% reduction in the number reporting problems with usual activities. In all calculations, an intra-cluster correlation coefficient (ICC) of 0.02 was assumed, based on primary care studies elsewhere (Adams et al. 2004, Campbell et al. 2004b).

2.2.10 Ethical Issues

The study was approved by the Research Ethics Committee of the Faculty of Health Sciences, University of the Free State. In cluster randomised trials of guideline interventions, the risk to patient participants is low, given that the interventions do not target individual patients, and rarely introduce untested elements of care such as new drugs or investigations, but rather focus on the way in which proven interventions (like cotrimoxazole prohylaxis for HIV infection, or inhaled corticosteroids for asthma) are organised and delivered to patients attending health services.

Patients were required to be consented for their contribution to data collection, but not to the random allocation of the intervention. In this case data collection posed minimal risk to patients since it involved participation in two interviews and no invasive or additional monitoring. Access to routine clinical care was in no way disrupted, and fieldworkers were instructed to conduct exit interviews only once all care procedures had been completed. All patients were consented in their own language in accordance with South African Good Clinical Practice Guidelines (GCP), and gave written informed consent before participating. The English copy of the consent form is provided in the appendix.

2.3 Data Collection

Almost all data required for the analysis was obtained by patient report at exit and follow-up interviews. Record review was not used as a means of collecting data because clinical record-keeping is generally of poor quality. Furthermore, clinical records may have contributed potential bias as the intervention might have improved documentation of consultations by nurse practitioners.

Royal College of Physicians Asthma Control Measure contains 3 items covering night-time waking, day-time symptoms and interference with usual activity. Each item is answerable as a simple yes/no but can be supplemented with the Tayside grading system to improve responsiveness (Hoskins et al. 1998). The original instrument was intended for use among asthmatics but needed to be modified to accommodate all patients with respiratory symptoms in the trial. The word "asthma" was therefore substituted with generic terms including "chest symptoms" and "chest problem". The decision to use this instrument was later supported when the World Health Organization recommended its use in multi-country PAL evaluations at the first review meeting in Morocco in 2002 (WHO 2003d).

2.3.1.3 Generic health related quality of life (enrolment questionnaire, questions 61–72, follow-up questionnaire, questions 18–29)

The EuroQol-5D was chosen ahead of other measures because it is brief, has been widely tested across countries and conditions, had already been translated into several local languages and because it has a credible social preference weighting system capable of supporting cost-utility analysis (Brazier et al. 1999).

The EuroQol-5D comprises a descriptor section of five domains of health-related quality of life: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each domain in the descriptor section is divided into three levels indicating no problems (level 1), some problems (level 2) or extreme problems (level 3). The classification defines a total of 243 health states which can be combined with tariffs to yield a single index score with an upper limit of one, where one corresponds to perfect health, zero death, and scores less than zero to states considered worse than death.

Limited responsiveness to changes in clinical status among respiratory outpatient populations elsewhere (Harper et al. 1997) prompted correspondence

The questionnaire also made provision for collection of tuberculosis care details, if relevant. These included date of first dose of treatment, past tuberculosis history and frequency of clinic attendance to receive treatment. Date of first dose of treatment was validated by checking the patient-held tuberculosis treatment card.

2.3.1.5 Smoking cessation (enrolment questionnaire, questions 73- 91, follow-up questionnaire, questions 16 –168)

In addition to being asked whether they had been advised by the nurse practitioner to stop smoking, the stage of change (pre-contemplators, contemplators, preparation, action) was assessed among current smokers using questions developed by Prochaska and Climente (1986). These questions have been tested in other trials evaluating the effects of various interventions to increase smoking cessation (Riemsma et al. 2002). Patients were also asked whether they had actually quit smoking at the time of the follow-up interview.

2.3.1.6 Health care utilisation (enrolment questionnaire, questions 19 - 468, follow-up questionnaire, questions 30–98 and 280- 486)

Details on health care utilisation were collected for the economic evaluation. Patients were asked to provide details of care received at their index clinic and elsewhere for the preceding three months (three months before the enrolment interview, and the 3 months between interviews). Steps were taken to improve recall. In the Free State, most clinic records are patient-held, and interviewers were asked to refer to these to validate visit information. Patients were sensitised at the time of the first interview, and issued verbal and written reminders that information concerning health care utilisation would be required at the follow-up. For each clinic visit, interviewers were instructed to record the date, and reason for visit as reported by the patient. Provision was also made to capture a maximum of five visits to other health care providers; for these visits

2.3.1.10 Patient satisfaction (follow-up questionnaire, questions 527-547)

Patient satisfaction was assessed using a modified version of the Consultation Satisfaction Questionnaire, first developed for use in general practice in the United Kingdom (Baker 1990). It has since been used to assess satisfaction with nurse practitioner services (Shum et al. 2000) and demonstrates construct validity compared with other satisfaction indicators (Baker and Whitfield 1992, Poulton 1996). It comprises 18 statements graded using Likert scales. Formulae are available to convert responses to a score ranging from 0 to 100 for each of four domains: general satisfaction, professional care, depth of relationship and perceived time. Usual scores are in the range of 60 to 80.

2.3.2. Translation of the Questionnaire

The questionnaire was translated by researchers from the Centre for Health Systems Research and Development and Department of Community Health of the University of the Free State. Forward and back translations were completed in keeping with internationally accepted practices (Guillemin et al. 1993). The EuroQol was translated into Sesotho separately from the rest of the questionnaire in accordance with protocols from the EuroQol group (EuroQol Group 2003). The EuroQol translation is described in detail in Chapter 5.

2.3.3 Utilisation of handheld computer technology during fieldwork

An interview software application for handheld computers, developed by the Biomedical Informatics Research Division of the Medical Research Council, was used during the trial (Zwarenstein et al. 2006). This was the first time the application had been used to complete a large fieldwork exercise, and it has subsequently been used for several other large studies. Strengths and weaknesses of the application are discussed in Chapter 7 Section 7.2.

fieldworkers were shown how to operate them. Fieldworkers were also shown how to record a respiratory rate and how to mask this activity by simultaneously feeling the pulse to avoid prompting voluntary control of breathing by subjects. Fieldworkers were provided with an opportunity to test these skills on their colleagues, while researchers observed and gave feedback. Each team was provided with a video of a subject with respiratory distress using accessory muscles during breathing, so that they might recognise this when in the field. Should fieldworkers recognise a seriously ill patient they were advised to refer them back to the clinic nurse practitioner for management.

Three senior and experienced fieldwork supervisors were recruited, each to oversee between one and two teams. Supervisors visited teams once during each week of fieldwork at a clinic (enrolment and follow-up weeks). They assessed whether patient recruitment was being completed in accordance with the study protocol, were responsible for quality control procedures and helped solve any logistic difficulties (lack of transport etc.).

Researchers accompanied supervisors on field visits approximately once a month. During these visits they sat in on team meetings where feedback on quality control procedures was provided, witnessed interviews, provided feedback to interviewers and audited recruitment procedures. During later months of fieldwork, these visits provided important opportunities to resolve any queries arising from the reconciliation of enrolment and follow-up interviews for clinics where fieldwork had already been completed.

A second training workshop preceded the start of follow-up interviews. At this workshop, problems arising from past fieldwork were discussed, and the follow-up questionnaire was introduced and again worked through question by question. During follow-up fieldwork, team leaders were no longer required to recruit patients; instead they were asked to trace patients who did not arrive for follow-up interviews, and complete a time and motion work study of consultation duration (see section 2.3.7).

2.3.6 Cost identification, measurement and valuation

Patient-level costs were collected using a programme ingredients approach with resource quantities collected separately from unit costs (Drummond et al. 1989). Costs were considered from the perspective of the health system (health service costs and the cost of the PALSA intervention) and society (household and out-of-pocket health related expenditure). A template for measuring and valuing costs is provided in Table 2.3.

2.3.6.1 Intervention costs

The costs of developing the guideline and training intervention were determined after developing a diary template recording all related activity since the project's inception in 1999. Researchers were then interviewed to gauge their level of contribution, measured in time and valued using cost of employment. These costs were then inflated by 30% to reflect overhead costs borne by participating research institutions. The time of doctors and nurses who participated in workshops was valued using cost of employment obtained from the FSDOH Finance Division. Flight, accommodation, catering and graphic artist costs were obtained from project expenditure records. The opportunity cost of using university and health department venues for workshops and pilots was estimated using rates for a popular Bloemfontein conference centre.

Nurse trainers were required to complete attendance registers at all educational outreach visits. These forms also made provision for the collection of cost data directly related to visits (transport, refreshments etc.).

2.3.6.2 Treatment costs

Information on the quantities of health service and household resources used was collected during patient interviews. Unit costs were determined as follows:

- Clinic visits: 2003 equivalents for staff, management and administrative component costs were derived from a 1997/98 study of Cape Town primary care clinics (Daviaud 1999).
- Tuberculosis monitoring visits: Clinic visit unit costs were weighted using the findings of a tuberculosis treatment costing study (Sinanovic et al. 2001). Visits to monitor tuberculosis treatment were estimated to cost 52% that of a routine clinic visit.
- Inpatient days: An estimate generated during a study of inpatient care at a Cape Town district hospital was used (Haile 2000). The estimate was similar to the 2003 tariff for an inpatient day obtained from the FSDOH Finance Division.
- Outpatient visits: The inpatient day unit cost was weighted using the findings of a study completed at a Cape Town hospital (Cleary et al. 2004). Outpatient visits were estimated to cost 27% of an inpatient day.
- Ambulance trips: Public sector costs for emergency services were not available. Board of Healthcare Funder (2004) tariffs were used instead, and where applicable, adjustments made for trips in excess of 100km in keeping with the Board of Healthcare Funder fee structures.
- Medication: Acquisition costs were obtained from the Free State Pharmaceutical Services, and included a 8% handling fee. Patients were assumed to have received two packets of short course medications (e.g. antibiotics) if they reported receiving this medication at both interviews; one unit if reported at only one interview. Tuberculosis treatment and inhaled corticosteroids were assumed to have been taken for all three months between interviews. 15% of tuberculosis patients were assumed

elapsed time to be calculated. Stopwatches were not used in keeping with recommendations for completing such studies (International Labour Office 1969).

2.4 Analysis

2.4.1 Effectiveness

Effectiveness outcomes were analysed on an intention-to-treat basis. In the context of a cluster randomised controlled trial this means that clinics, and the patients recruited in these clinics, were analysed in the group to which they were randomised. Robust logistic regression models which accounted for the trial's design (cluster randomisation within district strata) were used to evaluate the effect of the intervention. Odds ratios are presented with 95% confidence intervals, corresponding p values and intra-cluster correlation co-efficients. Risk differences and numbers needed to treat (NNT) were estimated for effectiveness outcomes used in the economic evaluation.

2.4.2 Allocation of intervention costs

The cost of developing the guideline and training intervention, but not the cost of the training itself, was treated as a capital cost. This is because the guideline and training intervention represent an asset which will depreciate over time, owing to changes in medical knowledge and technology and in health services. Linear depreciation to zero over six years was assumed based on a study which evaluated the current validity of 17 quality guidelines and estimated that half the guidelines were outdated after 5.8 years (Shekelle et al. 2001). It follows that the cost of depreciation during the three months during which trial patients were followed-up was 3/72 times the total capital cost.

(Kind et al. 1998). During this survey over 3000 members of the United Kingdom general population were interviewed and asked to value EuroQol health states using time trade off and standard gamble exercises. This permitted the estimation of tariffs for all 243 states defined by the EuroQol classification (Dolan 1997). The York tariffs are the most widely used, and were combined with EuroQol-5D responses to calculate index scores for patients enrolled in the trial. A local set of EuroQol weights, derived from 2384 Zimbabweans using time trade off exercises, is available, and was applied in a secondary analysis (Jelsma et al. 2003). For analysis of the five level EuroQol scores, value decrements for levels 2 and 4 were set to the midpoint decrements for the three level version (Kind and Macran 2002). Patients were asked to reflect on their health status on the day of the interview, and separately during the course of the last month. Responses for the day of the interview were used in the primary analysis.

2.4.5 Valuation of Lost Productivity Time

This remains a controversial area of health economics especially when applied to populations with high rates of unemployment, where the friction period between replacing a person lost from the employed pool may be reduced compared with settings with lower rates of unemployment (Koopmanschap et al. 1995, Koopmanschap and Rutten 1996).

One common strategy is to value lost unemployed time at half the minimum wage. In some countries recommendations exist to ensure standard practice across evaluations (HM Treasury n.d.). This is not true for South Africa, although minimum wage categories have been determined (Basic Conditions of Employment Act 1997). In the trial employed days lost were valued at gross income, if provided, and full minimum wage if not. Unemployed days lost were valued at half minimum wage and school days lost were not assigned a monetary value.

Willingness to pay levels ranged from zero, in increments of 100 South African Rand (ZAR), up to ZAR2000.

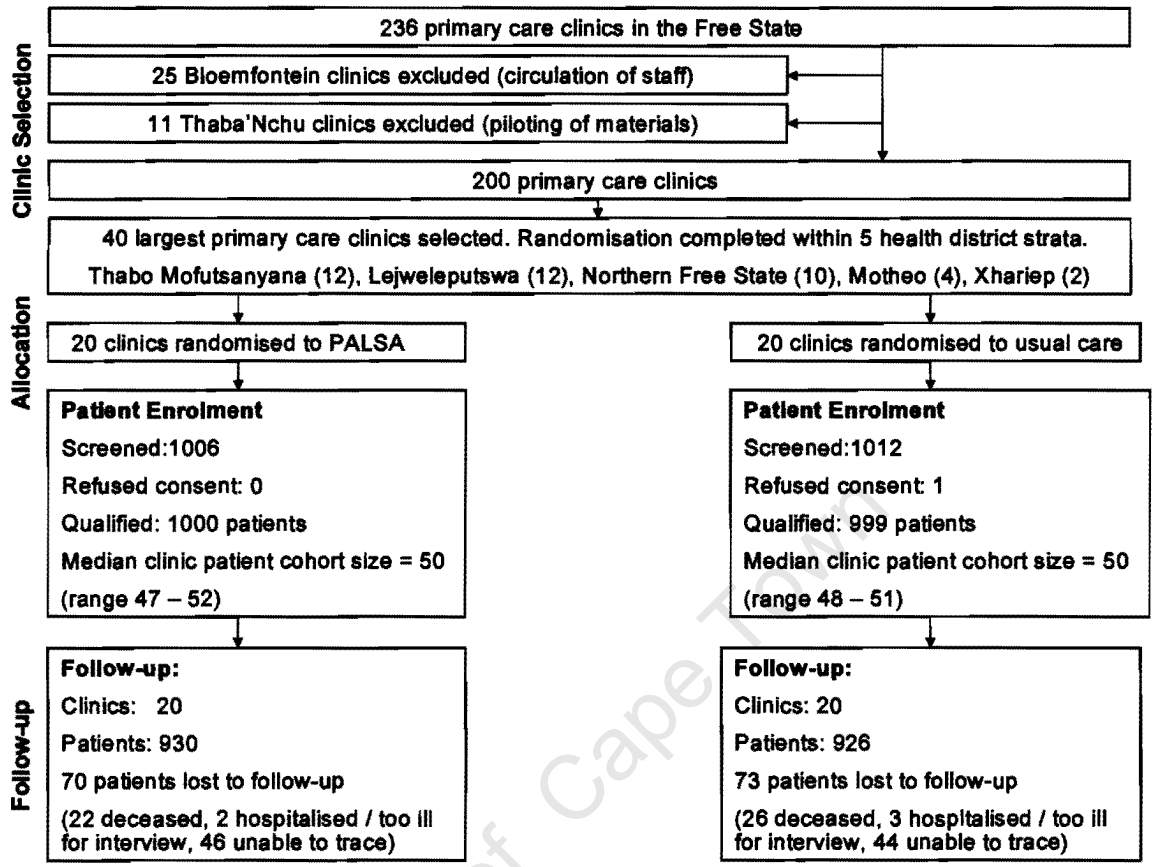
Non-parametric bootstrapping, with replacement, was conducted with Stata 9 software. Individual subjects' costs and outcomes were re-sampled 1000 times with Stata, with individual and then with cluster sampling. Differences in mean costs and mean effects for each individual bootstrap sample were plotted on a cost effectiveness planes. The cost difference, outcome difference, incremental cost effectiveness ratio, incremental net benefit and the probability that the intervention was cost effective was calculated at each willingness to pay level. Confidence intervals were estimated using the bias corrected accelerated percentile method (Carpenter and Bithell 2000).

Each individual's net benefits were individually bootstrapped with Stata. Also, entire clusters were sampled together and differences in mean net benefits were calculated for each bootstrap sample with Stata.

Linear regression analyses were conducted with Stata with robust adjustment for intra-cluster correlation of outcomes. Analyses were repeated without robust adjustment to provide the results that would be obtained if cluster randomisation was ignored.

For cost effectiveness acceptability curves, the probability that the intervention was cost effective at each level of willingness to pay was as follows. For 2D bootstrap, it was the proportion of samples for which the cost difference was less than the outcome difference multiplied by willingness to pay. For 1D bootstrap, it was the proportion of bootstrap samples for which the incremental net benefit was more than zero. For regression analyses the probability that the intervention was cost effective was one minus half the respective p value, if the mean incremental net benefit was greater than zero. If the mean incremental net benefit was less than one it was half the respective p value.

Figure 3.1 Trial Profile



Patient characteristics at enrolment are shown in Table 3.1. They did not differ between intervention and control arms. Around 2/3 of the patients were women, with a mean age in the forties (44.9 in the PALSA group and 44.2 in the controls). On the whole, patients were from very poor socioeconomic circumstances. 16% of patients had never attended school at all, and only 39% reported secondary school education while less than 10% completed school. Over half were unemployed, and 1/4 reported receiving welfare. Less than 20% indicated that they were employed.

and received a median of two educational outreach visits (range: 0 - 4, Table 3.2). In five clinics the median number of outreach visits received was less than two, and in one clinic where staff turnover during the study period was especially high (PAX clinic), zero. Sessions lasted on average 2 hours.

Table 3.2 Exposure to educational outreach visits at intervention clinics

District	Intervention Clinic	Location	Number of sessions delivered by outreach trainer	Number of eligible nurses	Median number of sessions per eligible nurse
Thabo Mofutsanyana	Riverside	QwaQwa	5	10	2.5
	Mpohadi	Bethlehem	3	6	3
	Bethlehem	Bethlehem	3	5	3
	Tseki	QwaQwa	2	7	2
	Tebang	QwaQwa	3	22	1
	Namahadi	QwaQwa	2	15	2
Lejweleputswa	Tshepong	Welkom	2	14	2
	K-Maile	Bothaville	3	7	2
	Albert Luthuli	Wesselsbron	3	6	3
	Phomolong	Henneman	2	5	2
	Welkom	Welkom	3	13	3
	Boithusong	Odendaalsrus	2	7	3
Northern Free State	Phahameng	Frankfort	5	5	3
	Thusanong	Kroonstad	6	9	4
	PAX	Viljoenskroon	3	15	0
	Seeisoville	Kroonstad	2	9	1
	Tumahole	Parys	3	8	2
Motheo	Botshabelo B	Botshabelo	3	18	1
	Botshabelo U & S	Botshabelo	3	11	1
Xhariep	Bophelong	Petrusburg	2	11	2

3.4 Effect on tuberculosis case detection and diagnostic processes

Sputum screening for tuberculosis (Table 3.4) was higher among intervention patients but not significantly so (OR 1.22, 95% CI 0.83 to 1.80). Despite this, 57 new cases of tuberculosis were diagnosed in intervention clinics during the study period compared with 34 new cases in controls (OR 1.72, 95% CI 1.04 to 2.85). The number of study patients diagnosed with tuberculosis before outreach commenced was ascertained by retrospective questioning and was similar in the two groups (108 in intervention and 109 in control clinics). Significantly higher rates of chest x-rays (Table 3.4) and within-clinic referrals to sessional doctors (see Section 3.7) suggest that the increased case detection may be attributed to increased compliance with the full range of diagnostic processes contained in the tuberculosis diagnostic algorithm.

Table 3.4 Effect of PALSA on TB case detection and diagnostic processes

Outcome	PALSA group		Control group		Odds ratio (OR)		p value	ICC*
	No.	%	No.	%	OR	95% CI		
Sputum screening for tuberculosis	226/ 1000	22.6%	193/ 999	19.3%	1.22	0.83 - 1.81	0.32	0.056
TB case detection among patients not known with tuberculosis at start of intervention period	57/ 892	6.4%	34/ 890	3.8%	1.72	1.04 - 2.85	0.04	0.007
Chest x-ray completed during study period	55/ 1000	5.5%	31/ 999	3.1%	1.83	1.13 - 2.96	0.01	0.015

*Intracluster correlation co-efficient

sample reported symptoms consistent with an URTI. All other patients reported more severe symptoms and, against the background of high tuberculosis and HIV prevalence, may have warranted antibiotic prescription. The effect of PALSA on antibiotic prescription for those with severe lower respiratory tract infections could not be examined as only 15 patients (<1%) met definition criteria (cough for less than two weeks with temperature ≥38°C).

Cotrimoxazole prophylaxis provision to tuberculosis patients, a group with a known high HIV co-infection rate (Corbett et al. 2003), was alarmingly low and similar in both groups (7.5% vs. 7.3%, OR 1.19, 95% CI 0.37 to 3.80). This is in part explained by the fact that only 16% of tuberculosis patients reported ever having undergone voluntary counselling and testing for HIV, all of them during the study period and significantly more of them from the intervention group (Table 3.7). In addition interruptions in cotrimoxazole drug supply during the study period were reported by nurse practitioners in two of the health districts included in the trial, affecting 24 clinics.

3.6 Effect of PALSA on counseling practices

Counseling practices highlighted in the PALSA intervention included advising smokers to quit and motivating patients, particularly tuberculosis patients, to undergo voluntary counseling and testing (VCT) for HIV infection (Table 1.16).

3.6.1 Smoking cessation counseling

112 smokers (68.3%) in the intervention group and 127 (65.8%) in the controls reported receiving advice to quit smoking from a nurse practitioner during the study period (OR 1.16, 95% CI 0.74 - 1.82; Table 3.5).

completed VCT was more than double that in the control group (21.1% vs. 10.1%, OR 2.49, 95% CI 1.27 - 4.89).

Table 3.6 Effect of PALSA on counselling to undergo VCT and VCT completion

Outcome	PALSA group		Control group		Odds ratio (OR)		p value	ICC*
	No.	%	No.	%	OR	95% CI		
Counselled to undergo VCT	249/ 1000	24.9%	237/ 999	23.7%	1.07	0.62 – 1.84	0.808	0.154
Tuberculosis patients counseled to undergo VCT	63/ 147	42.9%	45/ 138	32.6%	1.55	0.83 – 2.90	0.167	0.110
VCT completed	97/ 1000	9.7%	73/ 999	7.3%	1.37	0.85 – 2.20	0.202	0.032
VCT completed among tuberculosis patients	31/ 147	21.1%	14/ 138	10.1%	2.49	1.27 – 4.89	0.008	0.04

*Intracluster correlation co-efficient

3.7 Effect of PALSA on referrals

Referral to a doctor was more frequently reported by intervention group patients than by controls (7.8% vs. 4.7%, OR 1.71, 95% CI 0.95 to 3.09, Table 3.7). Within-clinic referral to a sessional doctor, and referral of patients with pre-defined markers of severe respiratory disease (see Chapter 2 Section 2.3.1.1) were both significantly higher among intervention group patients (Table 3.7).

intervention group patients reported more frequent symptoms than their control group counterparts. There was no difference in scores at follow-up even if unadjusted for scores at enrolment, or in the difference between scores at interviews.

Table 3.8 Effect of PALSA on respiratory symptoms (modified Royal College of Physicians Asthma Measure): index scores at enrolment and follow-up

Outcome	PALSA group	Control group	Odds ratio (OR)		p value	ICC*
			OR	95% CI		
At enrolment						
Mean	6.19	5.70	1.37	1.06	0.015	0.067
Median	7	6		–		
IQR	4, 9	4, 9		1.76		
At follow-up						
Mean	5.32	4.89	1.25	0.99	0.056	0.065
Median	6	6		–		
IQR	3, 9	2, 8		1.57		
Change						
Mean	-0.87	-0.80	0.98	0.76	0.866	0.033
Median	0	0		–		
IQR	-3, 1	-3, 1.5		1.26		
At follow-up adjusted for enrolment	-	-	1.17	0.93	0.184	-
Mean				–		
Median				1.47		
IQR						

*Intracluster correlation co-efficient

Examination of domain scores (Table 3.9) shows that the slightly higher index scores at enrolment among intervention group patients is explained by more patients reporting more frequent interference with their usual activities (OR 1.40, 95% CI 1.04 to 1.87).

usual activities (OR 1.39, 95% CI 1.06 to 1.81) although there was no difference in index scores, even when not adjusted for enrolment values (Table 3.9).

3.9 Effect of PALSA on health related quality of life

Health related quality of life was evaluated using the EuroQol 5D health status measure (Brooks 1996) which was translated into Sesotho for the purpose of the trial (see Chapter 6). The five level version (Kind and Macran 2002), where two additional categories are inserted between the three standard response categories (no problem, moderate problem, extreme problem), was used in the hope that this would improve responsiveness in a respiratory outpatient setting (see Chapter 2 Section 2.3.1.3). Differences in index scores, domain scores and visual analogue scale scores between groups were analysed and are presented in Tables 3.10 through 3.15. The primary analysis was restricted to participant's responses concerning their health status on the day of the interview, not in the preceding month.

Table 3.11 Effect of PALSA on health related quality of life (EuroQol): index scores at enrolment and follow-up (5 level EuroQol, York tariffs)

Outcome	PALSA group	Control group	Odds ratio (OR)		p value	ICC*
			OR	95% CI		
At enrolment						
Mean	0.40	0.44	0.86	0.65 – 1.15	0.318	0.093
Median	0.51	0.55				
Interquartile range	0.09, 0.70	0.16, 0.73				
At follow-up						
Mean	0.54	0.59	0.79	0.61 – 1.03	0.087	0.107
Median	0.69	0.73				
Interquartile range	0.19, 0.85	0.29, 0.86				
At follow-up adjusted for enrolment	-	-	0.81	0.63 – 1.03	0.089	-
Change						
Mean	0.14	0.15	0.94	0.76 – 1.17	0.601	0.036
Median	0.11	0.14				
Interquartile range	-0.10, 0.43	-0.08, 0.41				

*Intracluster correlation co-efficient

The analysis was repeated with Zimbabwean weights (Table 3.12), which are the only EuroQol weights to be valued and tested in sub-Saharan Africa (Jelsma et al. 2003). In general, index scores were higher than when the standard York tariffs were applied. This is because a different formula was fitted for the Zimbabwean weights. Nonetheless, no difference between groups was noted at enrolment or follow-up.

Table 3.13 Effect of PALSA on health related quality of life (5 level EuroQol): domain scores at enrolment

Domain	PALSA group		Control group		Odds ratio (OR)		p value	ICC*
	No.	%	No.	%	OR	95% CI		
Mobility								
No problem	440/996	44.2	496/997	49.8	1.29	0.90	0.163	0.115
Level 2	126/996	12.7	93/997	9.3		–		
Moderate problem	327/996	32.8	368/997	36.9		1.86		
Level 4	71/996	7.1	34/997	3.4				
Severe problem	32/996	3.2	6/997	0.6				
Self care								
No problem	785/996	78.8	811/997	81.3	1.21	0.77	0.414	0.098
Level 2	73/996	7.3	75/997	7.5		–		
Moderate problem	102/996	10.2	96/997	9.6		1.89		
Level 4	19/996	1.9	9/997	0.9				
Severe problem	17/996	1.7	6/997	0.6				
Usual activities								
No problem	272/996	27.3	329/997	33.0	1.47	1.15	0.002	0.048
Level 2	114/996	11.5	100/997	10.0		–		
Moderate problem	318/996	31.9	405/997	40.6		1.88		
Level 4	115/996	11.6	47/997	4.7				
Severe problem	177/996	17.8	116/997	11.6				
Pain/ discomfit								
No problem	142/996	14.3	185/997	18.7	1.25	0.95	0.116	0.078
Level 2	76/996	7.6	76/997	7.6		–		
Moderate problem	423/996	42.5	441/997	44.2		1.66		
Level 4	122/996	12.3	83/997	8.3				
Severe problem	233/996	23.4	212/997	21.3				
Anxiety/ depression								
No problem	182/996	18.3	190/997	19.1	0.88	0.68	0.370	0.069
Level 2	70/996	7.0	40/997	4.0		–		
Moderate problem	308/996	30.9	3101/997	31.1		1.16		
Level 4	119/996	12.0	98/997	9.8				
Severe problem	317/996	31.8	359/997	36.0				

*Intracluster correlation co-efficient

Table 3.15 Effect of PALSA on health related quality of life (EuroQol): visual analogue scores (VAS) at enrolment and follow-up (limited to patients with secondary school education)*

Outcome	PALSA group	Control group	Odds Ratio (OR)		p value	ICC†
			OR	95% CI		
At enrolment						
Mean	50.8	54.6	0.80	0.51	0.059	0.183
Median	50	50		–		
Interquartile range	40, 60	45, 60		1.01		
At follow-up						
Mean	59.8	61.3	0.79	0.62	0.053	0.116
Median	60	60		–		
Interquartile range	50, 70	50, 75		1.00		
At follow-up adjusted for enrolment	-	-	0.83	0.65	0.123	-
Mean				–		
Median				1.05		
Interquartile range						
Change						
Mean	8.8	7.1	1.02	0.77	0.885	0.075
Median	10	10		-		
Interquartile range	-5, 20	-5, 20		1.34		

* VAS scores were considered reliable in patients with more than 7 years' education (Gudex et al. 1996). The analysis was therefore limited to 363 intervention group patients (of whom 344 were re-interviewed at follow-up) and 409 control group patients (of whom 380 were re-interviewed at follow-up).

† Intracluster correlation co-efficient

3.10 Effect of PALSA on mortality

At follow-up 48 patients (2.4%) were reported by their families to have died since enrolment, 34 reportedly because of tuberculosis or other respiratory illnesses. Three month mortality was not different between the two groups (2.2% vs. 2.6%, OR 0.84, 95% CI 0.46 - 1.53).

Table 3.16 Effect of PALSA on patient satisfaction with clinic health services (modified Consultation Satisfaction Questionnaire)

Domain	PALSA group	Control group	Odds ratio		p value	ICC*
			OR	95% CI		
General satisfaction						
Mean	60.3	60.4	0.96	0.59	0.878	0.224
Median	58.3	58.3		–		
Interquartile range	50.0, 75.0	50.0, 75.0		1.57		
Professional care						
Mean	70.4	70.9	0.98	0.53	0.946	0.312
Median	75	75.0		–		
Interquartile range	60.7, 78.6	60.7, 82.1		1.81		
Depth of relationship						
Mean	50.6	51.7	0.92	0.57	0.720	0.358
Median	50.0	50.0		-		
Interquartile range	35.0, 65.0	40.0, 65.0		1.48		
Perceived time						
Mean	39.7	44.8	0.73	0.49	0.138	0.160
Median	33.3	41.7		–		
Interquartile range	25.0, 58.3	25.0, 75.0		1.10		

*Intracluster correlation co-efficient

3.12 Effectiveness outcomes used in the cost-effectiveness analysis

Two effectiveness outcomes were defined as the basis for the cost-effectiveness analysis. The first was tuberculosis case detection, because of its public health importance and as the driving force behind the rationale for PAL. The second was appropriate care which combined three process outcomes: case detection of tuberculosis, inhaled corticosteroid prescription for asthma and appropriate referral of patients with pre-defined markers of severe disease (see Chapter 2 Section 2.3.1.1). Such a composite indicator was necessary in evaluating a syndromic intervention like PALSA which targeted multiple diseases for improved management and outcome.

3.13 Summary

The randomized trial showed that, in spite of limited exposure to outreach training, PALSA markedly improved the quality of care across several priority respiratory illnesses.

Among patients with respiratory symptoms it increased case detection of tuberculosis (OR 1.72, 95% CI 1.04 – 2.85). It also increased VCT uptake among patients with tuberculosis (OR 2.49, 95% CI 1.27 – 4.89), although it failed to improve provision of cotrimoxazole prophylaxis to this subgroup (OR 1.19, 95% CI 0.37 – 3.80), presumably because, despite increased uptake of VCT in the intervention arm, overall HIV testing rates among those with tuberculosis remained low (16%).

Among patients with obstructive lung disease, it improved the provision of inhaled corticosteroids (OR 1.93, 95% CI 1.25 – 2.99) as well as other essential medicines, including beta-agonists and theophylline. There was no impact on the provision (OR 1.16, 95% CI 0.74 – 1.82) or uptake (OR 1.09, 95% CI 0.62 – 1.90) of smoking cessation advice. Nurse practitioners' inattention to smoking may be due to relatively low levels of smoking, both in terms of prevalence (16.5% in the PALSA group and 19.4% in the controls) and intensity (pack year history of 8.9 in the PALSA group and 8.3 in the controls), among the patients enrolled in the trial. Increases in the rate of within-clinic referral (OR 2.21, 95% CI 1.11 – 4.38) and referral of those with severe respiratory disease were also noted (OR 2.59, 95% CI 1.06 – 6.19).

Table 4.1 Cost of developing the PALSA guideline and training intervention

Year	Activity	Items and number included	Cost
2001	Guideline adaptation including workshop to review original WHO PAL guidelines and identify barriers to care	77 junior researcher days	87537
		9 senior researcher days	19162
		6 doctor and 6 nurse days	7602
		Venue and catering costs	1452
Subtotal in 2001 ZAR			*115 753*
2002	Guideline adaptation including two workshops to obtain end user input on drafts	110 junior researcher days	127540
		15 senior researcher days	33076
		3 doctor and 9 nurse days	7467
		7 local flights	19609
		Graphic layout	18488
		Venue and catering costs	2714
	Training development including two pilot sessions with nurses	75 junior researcher days	84317
		35 senior researcher days	42255
		8 nurse days	3021
		3 local flights	7297
		Illustrations & graphic layout	21407
		Venue and catering costs	925
	Liaison with World Health Organization	4 junior researcher days	4329
		3 senior researcher days	6547
		6 WHO consultant days	19092
		2 international and 3 local flights, 6 days' accommodation	39978
		Venue and catering costs	2473
Subtotal in 2002 ZAR			*442 946*
2003	Finalisation of guideline	4 junior researcher days	5028
		1 senior researcher day	2536
		Graphic layout	11264
	Finalisation of training and support materials	38 junior researcher days	48885
		8 senior researcher days	18880
		Graphic layout	4890
	Motivation for revised FSDOH nurse prescribing provisions	12 junior researcher days	15491
		1 senior researcher day	2536
		1 local flight and 2 days' accommodation	3057
Subtotal in 2003 ZAR			*112 570*
TOTAL (in 2003 ZAR) with 2001 and 2002 costs discounted at 3%* and adjusted for inflation using CPIX average†			**753 362**

* Russell et al. 1996

† Statistics South Africa

costs (25%). Local road travel costs were also quite high, as district trainers travelled from remote areas of the province to central airports.

Table 4.3 PALSA intervention costs: Training the Trainers workshop

Items and number included	Subtotal in 2003 ZAR	% total cost of training the trainers
10 junior researcher days	12740	8
10 senior researcher days	28881	18
55 nurse days	31650	20
11 local flights and 55 days' accommodation	39800	25
Road travel (4567 km)	10599	7
PALSA trainer material packs	14501	9
Venue and Catering	17935	11
Video hire	1700	1
Total in 2003 ZAR	**157805**	100

4.1.1.2 Educational Outreach Visits

Educational outreach took place between April and October 2003. The number of outreach sessions per clinic ranged between two and six. Relocation of nurses through night duty, leave and attendance at other offsite training courses meant that it was unusual for the same nurses to attend all sessions at a clinic (Mayers 2004). The median number of sessions received by an intervention clinic nurse practitioner was two, and in five intervention clinics it was one session or less.

Sessions ranged in length from 1 to 4.5 hours; on average a session lasted 2 hours. In total PALSA training occupied 893 health staff hours, including time spent travelling to clinics in remote areas. This is equivalent to the time required to train eight nurse practitioners in IMCI (assuming the standard 11 day offsite course and two trainers per course). By comparison 148 nurses were exposed to PALSA training during the study period.

Table 4.4 Cost of educational outreach visits to the 20 intervention clinics

Clinic	No. of staff trained*	No. of outreach sessions	Median no. of sessions per nurse	Km travelled†	Cost of FSDOH staff time† (2003 ZAR)	Cost of PALSA materials (2003 ZAR)	Cost of travel (2003 ZAR)	Cost of refreshments (2003 ZAR)	Total cost per clinic
Albert Luthuli	6	3	3	0	1190	907	0	141	2099
Bethlehem	5	3	3	601	2195	756	1034	360	3987
Boithusong (Odendaalsrus)	7	2	3	177	1191	1059	381	106	2632
Botshabelo B	13	3	1	89	3192	1966	117	95	5277
Botshabelo U&S	7	3	1	30	1881	1059	40	30	2981
K-Maile	5	3	2	317	1408	756	682	124	2848
Mpohadi	5	3	3	663	2790	756	1140	219	4688
Namahali	11	2	2	50	2103	1663	66	0	3834
PAX	7	3	0	322	1674	1059	692	0	3427
Bophelong (Petrusburg)	12	2	2	889	4788	1815	1911	0	8516
Phahameng	5	5	3	732	1715	756	1815	150	4289
Phomolong	4	2	2	240	1426	605	516	0	2548
Riverside	6	5	2.5	1117	2438	907	2770	150	6117
Seeisoville	6	2	1	19	1599	907	41	35	2549
Tebang	12	3	1	77	1926	1815	132	0	3875
Thusanong (Kroonstad)	9	6	4	114	3252	1361	245	54	4860
Tseki	4	2	2	20	955	605	26	0	1588
Tshepong	4	2	2	290	1190	605	624	0	2420
Tumahole	8	3	2	551	1933	1210	727	0	3872
Welkom	12	3	3	271	4357	1815	583	273	6757
Total cost of outreach visits in 2003 ZAR (% total)					(55%)	(28%)	(17%)	(2%)	**79165**

* In one clinic (Petrusburg), a doctor and 2 pharmacists also attended training sessions. The cost of their time has been included.

† FSDOH: Free State Department of Health. Several trainers conducted non-PALSA activities at the time of outreach training. In these cases travel costs, including time spent travelling and km travelled, have been weighted by the proportion of total time at the clinic spent delivering PALSA training.

4.1.1.3 Allocation of PALSA intervention costs

Intervention costs were allocated to patients' clinic visits as follows (Table 4.5). The cost of the guideline and training package, but not of the training itself, was treated as a capital cost, and linear depreciation to zero over six years was assumed. So the cost of depreciation over the three months during which trial patients were followed up was 3/72 times the total capital cost. Training the trainer and educational outreach visit costs were summed for all 20 intervention clinics. This was conservatively allocated (100% to the intervention clinics for the duration of the trial) on the assumption that the training would never be utilised outside of these 20 clinics, or beyond the time horizon of the trial. Total PALSA intervention costs allocated to the intervention clinics during the trial thus included 100% of training the trainer costs, 100% of educational outreach visit costs and 3/72 or 4.15% of guideline/intervention development costs.

The number of total attendances at the 20 intervention clinics during one quarter (corresponding to the three month period between interviews) was obtained from FSDOH data routinely reported by the chief nurse in each clinic and centrally collated. 30% of these patients were assumed to have cough and/or difficult breathing. This estimate was based on previous work completed in a Cape Town primary care clinic (Fairall et al. 2001). This is substantially lower than the 61% noted during the work study completed during the trial (Table 4.9). The higher estimate was explored in the sensitivity analysis and is reported in Section 4.4. The work study estimate was not used for the primary analysis because it was not based on a random sample of consultations, even though it was based on a random sample of clinics and days in intervention and control clinics. Also, as reported below, it found no significant difference in the duration of consultations between intervention and control clinics. Total PALSA costs for the trial were allocated

Patients attending intervention clinics reported more visits to clinics, mainly due to a near doubling of the number of tuberculosis monitoring visits in this group (Table 4.6). Control group patients reported more, and longer, hospital admissions, accounting for the difference in the number of inpatient days between groups. While these differences in tuberculosis monitoring visits and inpatient days are largely responsible for the difference in health service costs (Table 4.10), neither reached statistical significance, because of the low numbers of patients involved.

Table 4.6 Health service utilisation: visits and admissions

Item	No. in each group		IRR*	95% CI	p value
	PALSA	Control			
Clinic visits (excl. TB treatment monitoring)	1385	1284	1.08	0.89 – 1.31	0.466
TB treatment monitoring visits	2340	1215	1.91	0.91 – 4.03	0.088
Visits to non-trial primary care clinics	24	32	0.74	0.35 – 1.55	0.423
Outpatient visits	51	41	1.24	0.79 – 1.93	0.344
Hospital admissions	27	40	0.77	0.47 – 1.24	0.279
Inpatient days	119	193	0.61	0.36 – 1.06	0.078
Ambulance trips	37	44	0.80	0.55 – 1.15	0.240

* Incidence rate ratio from Poisson regression

Utilisation of respiratory drugs is reported in Table 4.7. It shows significant increases in the use of drugs for the treatment of obstructive lung disease (budesonide, inhaled salbutamol, fenoterol and theophylline). This is consistent with findings reported in Chapter 3. No difference in the use of antibiotics or symptomatic treatments was observed. Although the number of patients diagnosed with tuberculosis during the study period was higher in the intervention group, there was little difference in the use of tuberculosis medication, as the total number of patients who reported receiving tuberculosis treatment at follow-up (new and old cases) was similar between groups.

Table 4.8 Health service utilisation: number of investigations

Item	No. in each group		IRR*	95% CI	p value
	PALSA	Control			
Sputum tests for AFBs	676	506	1.34	0.91 – 1.98	0.143
Chest x-rays	84	51	1.67	1.08 – 2.57	0.020
HIV rapid test kits	92	72	1.28	0.82 – 1.99	0.275

* Incidence rate ratio from Poisson regression

Health service costs are summarised in Table 4.10. The work study (Table 4.9) timed 715 consultations in 19 trial clinics (10 intervention and 9 controls) and found no difference in the consultation duration for patients fulfilling trial eligibility criteria and those who didn't between groups (see Chapter 2 Section 2.2.6.1 for discussion of trial eligibility criteria). Consequently the same clinic visit unit cost was applied to both groups.

Table 4.10 Health service costs: mean per patient in 2003 ZAR for the 3 month period between enrolment and follow-up

Item	PALSA				Control			
	Mean	Median	IQR*	% Total†	Mean	Median	IQR*	% Total†
Visits, admissions								
Clinic visits	104.75	70.34	70.34 – 140.68	32.0	97.53	70.34	0 – 140.68	36.6
TB monitoring visits	92.04	0	0 – 0	28.1	48.00	0	0 – 0	18.0
Clinic visits (non-trial)	1.82	0	0 – 0	0.6	2.43	0	0 – 0	0.9
Outpatient visits	3.07	0	0 – 0	0.9	2.48	0	0 - 0	0.9
Inpatient days	27.04	0	0 – 0	8.2	44.04	0	0 - 0	16.5
Ambulance trips	19.69	0	0 – 0	6.0	25.86	0	0 - 0	9.7
Medication	39.61	7.04	0.62 – 54.70	12.1	29.35	5.86	0 – 24.30	11.0
Beta-agonists	7.63	0	0 – 0	(2.3)	4.82	0	0 - 0	(1.8)
Inhaled corticosteroids	5.12	0	0 – 0	(1.6)	2.60	0	0 - 0	(1.0)
Antibiotics (excluding TB drugs)	3.48	0	0 – 5.86	(1.1)	3.22	0	0 – 5.86	(1.2)
TB drugs	14.68	0	0 – 0	(4.5)	13.12	0	0 – 0	(4.9)
Other drugs	8.70	0.62	0 – 3.32	(4.0)	5.58	0.62	0 – 2.19	(2.9)
Investigations	22.77	0	0 – 24.93	7.0	16.70	0	0 - 0	6.3
Sputum tests for AFBs	18.12	0	0 – 0	(5.5)	13.62	0	0 - 0	(5.1)
Chest x-rays	3.25	0	0 – 0	(1.0)	1.98	0	0 - 0	(0.7)
HIV rapid test kits	1.39	0	0 – 0	(0.4)	1.10	0	0 - 0	(1.1)
PALSA	16.20	5.79	5.79 – 11.58	5.0	N/A	N/A	N/A	0
Total health service costs	326.98	160.74	78.27 – 282.07	99.9	266.39	144.02	70.34 – 241.18	100.00

* IQR: interquartile range

† % costs in parenthesis shown to demonstrate breakdown of drug and investigation costs. Total not equal to 100 because of rounding errors.

The mean cost of care for a patient attending a PALSA clinic was R60.59 more expensive than in the controls (R326.98 vs.R266.39). These costs reflect all health service costs, at primary, secondary and tertiary levels, for the three month period between interviews. Primary care clinic visits account for the bulk of the costs (60.7% in the PALSA group vs. 55.5% in the controls). Overall costs were consistently higher in the PALSA group, with the exception of costs of inpatient care and ambulance transport which were higher in controls. Differences in cost between groups tended to be small (<1%) except for the relatively large differences (5-10%) observed for tuberculosis monitoring visits, inpatient days and ambulance trips. Different unit costs for these items, and for clinic visits, were explored in the sensitivity analysis; results are reported in Section 4.4. The most important of these was the cost of tuberculosis treatment (tuberculosis monitoring visits + tuberculosis drugs) which accounted for 75% of the difference in health service costs between groups. In contrast with health care utilisation, PALSA intervention costs accounted for a relatively small proportion of total health service costs in the intervention group (5%).

4.2 Household costs

Household costs include out-of-pocket expenses associated with travel to the clinic and other health care providers, as well as any fees paid to these health care providers. In South Africa health care services have been provided free to pregnant women and children since 1994, and primary care service free to all citizens since 1996.

Most patients usually walk to the clinic; not surprising given that most South Africans live within a 5km radius of their local clinic (South African Human Rights Commission 2003). The next most popular form of transport is the minibus taxi, followed by private vehicles. Interestingly, no-one in the Free State

significantly more visits to private sector doctors reported among the PALSA group (OR 1.29, 95% CI 1.02 - 1.61), but use of other private providers was similar between groups.

Table 4.13 Visits to private health care providers

Item	No. in each group		IRR*	95% CI	p value
	PALSA	Control			
Private doctors	238	183	1.29	1.02 – 1.61	0.028
Pharmacy	49	56	0.87	0.48 – 1.55	0.632
Traditional healer	10	8	1.23	0.40 – 3.81	0.714
Work clinic	1	0	-	-	-

* Incidence rate ratio from Poisson regression

Table 4.14 Average fees (in 2003 ZAR) paid to private health care providers

Mode	Average fee (including medication)*	
	PALSA	Control
Private doctor	82.80	84.31
Pharmacy	30.67	29.06
Traditional healer / herbalist	102.00	65.29

* Average fee calculated only on respondents reporting a visit to a private health care provider.

Household costs are summarised in Table 4.15. All costs (taxi fare, private provider fees etc.) were derived directly from patient interviews, with the exception of the travel cost related to private vehicles. Door-to-door travel time was used to estimate distance travelled, and 2003 Automobile Association rates for a standard sedan vehicle were used to value these journeys (Automobile Association n.d.). Travel costs associated with clinic attendances were estimated by multiplying the cost of travel (taxi fare, car costs) by the number of attendances (including tuberculosis monitoring visits) during the period between interviews, assuming that the same mode of transport was used on each occasion. Travel costs associated with other health care providers include the cost of attending public (e.g. hospital) and private providers and were collected separately for each visit.

respiratory symptoms. In the case of employed patients, caregivers or companions, patients were asked to estimate the number of days of work lost as a result of illness or seeking care; in the case of scholars the numbers of days of school missed; and in the case of the unemployed, the number of days potentially spent looking for work that were lost. Numbers of productive days lost are summarised in Table 4.16.

Table 4.16 Changes in productivity among index patients, caregivers and companions

Item	No. in each group		IRR*	95% CI	p value
	PALSA	Control			
Index patients					
Employed days lost	442	372	1.19	0.58-2.4	0.631
Unemployed days lost	816	418	1.96	0.83-4.63	0.125
School days lost	26	77	0.34	0.12-0.97	0.043
Caregivers					
Employed days lost	124	85	1.47	0.79-2.76	0.225
Unemployed days lost	263	171	1.63	0.69-3.88	0.265
School days lost	68	175	0.39	0.19-1.26	0.114
Companion (trial clinics)					
Employed days lost	206	7	29.15	8.01-106.13	<0.001
Unemployed days lost	372	247	1.50	0.64-3.51	0.350
School days lost	25	10	2.46	0.83-7.28	0.105
Companion (other health care providers)					
Employed days lost	18	21	0.85	0.34-2.09	0.717
Unemployed days lost	18	5	3.61	0.53-24.2	0.186
School days lost	10	13	0.76	0.17-3.41	0.72

* Incidence rate ratio from Poisson regression

In total 3987 productive days were lost to illness during the three month period (1624 employed days, 1961 unemployed days and 404 school days). The distribution is highly skewed and 21 patients account for 19% of employed days lost (all in the PALSA group), 51% of unemployed days lost (31% in the PALSA group, and 20% in the controls) and 19% of school days lost (all in the control group). This explains why the median, 25th and 75th percentiles for all societal cost items equal zero (Table 4.17).

Table 4.17 Costs arising due to changes in productivity: mean* per patient in 2003 ZAR for 3 month period between enrolment and follow-up

Item	PALSA		Control	
	Mean	% Total	Mean	% Total
Among index patients	46.32	61.8	32.2	68.7
Among companions (trial clinics)	15.91	21.2	6.14	13.1
Among companions (other HCPs)	1.13	1.5	1.48	2.4
Among caregivers	11.71	15.6	7.02	15.0
Total	75.01	100	46.84	99.2

*Medians and interquartile ranges are not given, as all these values equal zero. That is, all costs were incurred by less than 25% of patients.

4.4 Sensitivity Analysis

One-way sensitivity analysis was used to explore assumptions concerning the allocation of intervention costs to trial patients, different unit costs for health service expenses (e.g. inpatient days) and the inclusion of tuberculosis treatment costs.

By far the most important factor affecting cost was the inclusion of tuberculosis treatment costs. Tuberculosis treatment costs were defined as the cost of tuberculosis medication and monitoring visits. In intervention clinics, not only were more cases of tuberculosis managed during the study period, but there was also increased compliance with five-times-a-week clinic-based directly observed treatment, resulting in a big difference in the number of monitoring visits (2340 visits among tuberculosis patients attending PALSA clinics vs. 1215 visits among tuberculosis patients attending controls, IRR 1.91, 95% CI 0.91 - 4.03, p = 0.088). This proved the most important driver of cost differences between arms, accounting for 75, 71 and 60% of the differences in health service, societal and societal - including lost productivity costs - respectively (Table 4.18).

Table 4.18 Summary of mean cost per patient in 2003 ZAR for 3 month period between enrolment and follow-up: disaggregated by perspective, and cost of tuberculosis treatment

Perspective	PALSA			Control			Difference		Intra-cluster correlation coefficient
	Mean	Median	Interquartile range	Mean	Median	Interquartile range	In means	95% CI*	
Health service (including TB treatment costs)	326.98	160.74	78.27 – 282.07	266.39	144.02	70.34 – 241.18	60.59	-7.67, 130.98	0.022
Health service (excluding TB treatment costs)	220.27	158.72	77.31 – 266.20	205.27	140.68	70.34 – 217.50	15.00	-20.90, 51.52	0.011
Societal (including TB treatment costs)	386.00	202.06	90.81 – 328.37	298.29	160.34	72.48 – 282.86	87.71	11.21, 168.60	0.018
Societal (excluding TB treatment costs)	261.27	190.04	88.89 – 312.50	235.52	152.68	72.14 – 253.42	25.75	-12.56, 65.06	0.009
Societal with lost productivity costs (including TB treatment costs)	460.76	228.92	114.27 – 392.66	345.13	190.00	76.82 – 326.34	115.63	40.01, 201.76	0.012
Societal with lost productivity costs (excluding TB treatment costs)	325.57	224.86	112.00 – 369.39	279.44	170.68	76.34 – 301.36	46.13	3.74, 95.00	0.009

* From cluster bootstrapping

Results for allocation of intervention costs to trial patients are presented in Table 4.19. In the base analysis the following applied (Table 4.5):

- Capital costs associated with the development of the guideline and training materials were discounted at 3% and linear depreciation to zero over six years was assumed.
- 100% of training costs were allocated to intervention clinics, assuming the training was never used outside of these clinics or beyond the time horizon of the trial.
- Intervention costs were equally allocated among intervention clinics and allocated to patient visits, on the assumption that 30% of adult attendances have respiratory symptoms, and stood to benefit from the intervention.

In general, sensitivity analysis revealed that the evaluation was robust to variations in these assumptions, presumably because intervention costs accounted for only 5% of health service costs for patients attending intervention clinics (Table 4.10). Changes in assumptions concerning the allocation of the cost of guideline and training material development (choice of discount rate, depreciation of asset over time) had almost no effect on costs, because these costs constituted a small fraction of the intervention cost per visit, in comparison to training costs.

Assumptions regarding allocation of these training costs were also explored. In the base analysis, 100% of these costs were allocated to trial patients assuming that this training did not benefit patients beyond the time horizon of the trial. In the sensitivity analysis depreciation of training over longer periods (up to 8 months) was explored. The proportion of patients with respiratory symptoms, to whom the cost of the intervention was allocated, was also varied, from 20% to 60%. Despite large effects on the cost of the intervention per visit (halved, and doubled) the effect on health service and societal costs was minimal, again reflecting the relatively low contribution of intervention costs to overall cost per patient.

unit cost is doubled. The results were also sensitive to the cost of inpatient days, clinic visits and ambulance trips, more so when tuberculosis treatment costs were excluded (Table 4.21). Modest changes were noted with differences in the cost of sputum tests, and small changes with asthma drugs (theophylline, budesonide, beta-agonists).

Table 4.20 Sensitivity Analysis: effect of unit costs on difference in health service costs when tuberculosis treatment costs are included

Item	% change in difference in health service costs between intervention and control						
Change in unit cost	***-0.5***	***-0.25***	***0.1***	***+0.1***	***+0.25***	***+0.5***	***+1.0***
TB monitoring visits	-38	-19	-8	+8	+19	+38	+75
Inpatient days	+14	+7	+3	-3	-7	-14	-22
Clinic visits	-6	-3	-1	1	3	6	12
Ambulance trips	-4	-2	-1	+1	+2	+4	+8
Sputum tests for AFBs	-4	-2	-1	+1	+2	+4	+8
Theophylline	-2	-1	0	0	+1	+2	+5
Budesonide	-1.8	-0.9	-0.4	+0.4	+0.9	+1.8	+3.5
Salbutamol	-1.6	-0.8	-0.3	+0.3	+0.8	+1.6	+3.2
TB drugs	-1	-1	0	0	+1	+1	+3
Chest x-rays	-1	-1	0	0	+1	+1	+2
Clinic visits (non-trial)	+1	0	0	0	0	-1	-1
Salmeterol	-1	0	0	0	0	+1	+1
Fenoterol	-0.2	-0.1	0	0	+0.1	+0.2	+0.3

than usual care; in large part it is due to the cost of tuberculosis treatment which accounts for 75, 71 and 60% of the differences in health service, societal and societal costs including lost productivity costs respectively. This does not necessary represent an unfavourable outcome as the costs associated with treating tuberculosis can be considered an appropriate and necessary use of resources.

- society (using health service and patient household costs) and
- society including lost productivity costs (using health service, patient household and lost productivity costs).

For patients with tuberculosis, a large proportion of their health service costs were due to treatment after diagnosis. As one of the primary outcomes was diagnosis of tuberculosis – which would have been before the costs were incurred – all analyses were repeated either including or excluding tuberculosis treatment costs.

Thus ICERS were estimated separately for each perspective with and without tuberculosis treatment costs yielding 12 scenarios (two outcomes, three perspectives each including/ excluding tuberculosis treatment costs). The two primary analyses of interest were those using health service costs (excluding tuberculosis treatment) and appropriate care or tuberculosis diagnosis as outcomes.

The cost-effectiveness analysis was undertaken using multiple methods as described in Chapter 2 Section 2.4.6. The appropriate methods of analysis for cluster randomised data are the cluster bootstrapping, and linear regression adjusted for stratification and clustering. The other analyses were conducted for methodological purposes, to assess the extent of cluster sampling design effects – that is, the potential bias that could result if the cluster randomised design were ignored.

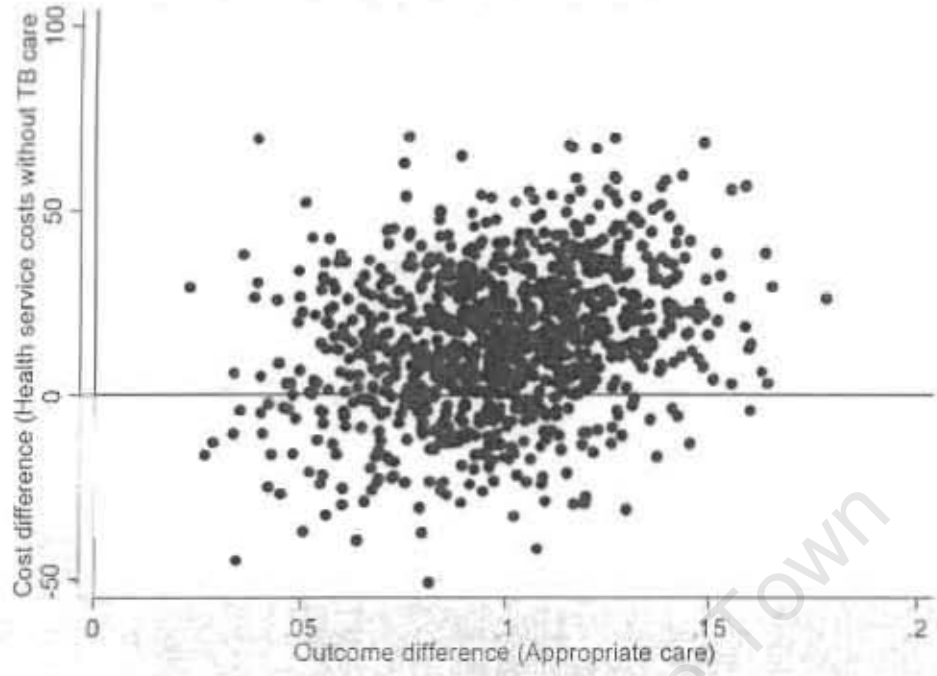
5.2 Cost-effectiveness planes

Cost-effectiveness planes were generated from 2D *cluster* bootstrap of differences in costs and effects using Stata (1000 resamples), and 2D *individual* bootstrap of differences in costs and effects using Excel (1000 and 10000 resamples). Planes for these methods, using 1000 resamples, are shown in Figures 5.1 through 5.12.

For appropriate care, the outcome difference was always greater than zero; the cost difference was also usually positive, but sometimes less than zero. Thus it appears

Figure 5.1 Cost-effectiveness planes: appropriate care (health service perspective excluding tuberculosis treatment costs)

From two dimensional cluster bootstrap of costs and effects (Stata)



From two dimensional individual bootstrap of costs and effects (Excel)

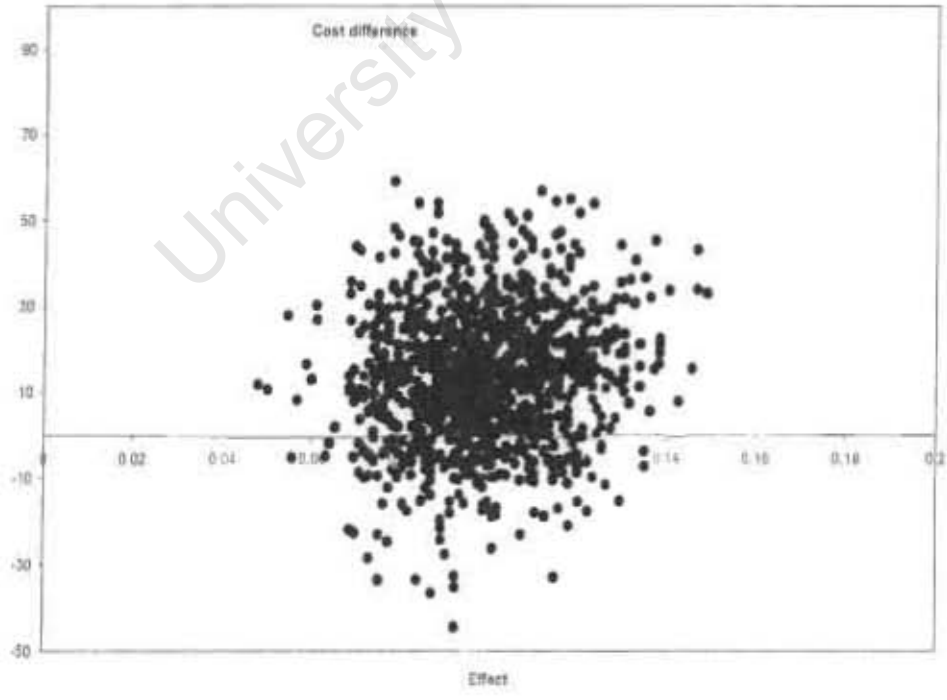
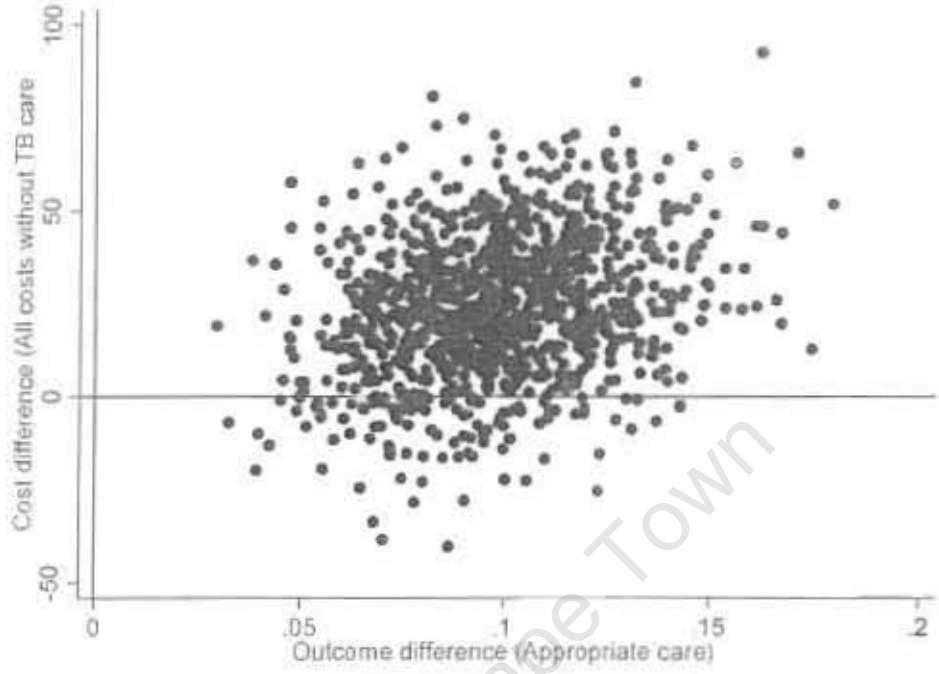


Figure 5.3 Cost-effectiveness planes: appropriate care (societal costs excluding tuberculosis treatment costs)

From two dimensional cluster bootstrap of costs and effects (Stata)



From two dimensional individual bootstrap of costs and effects (Excel)

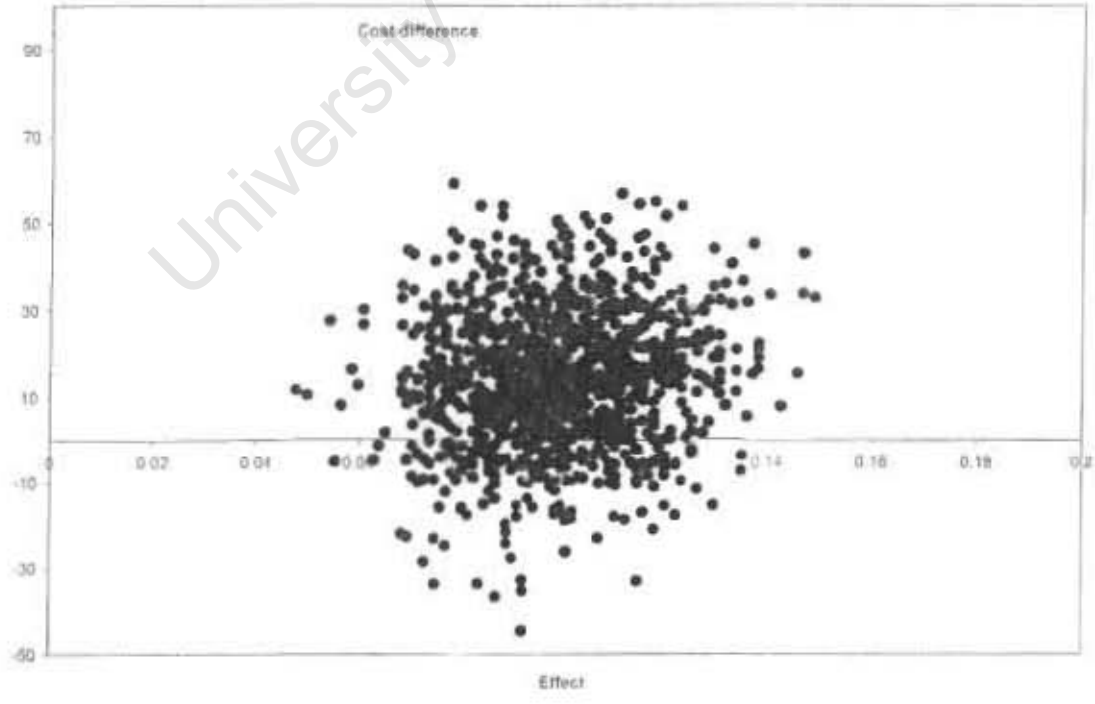
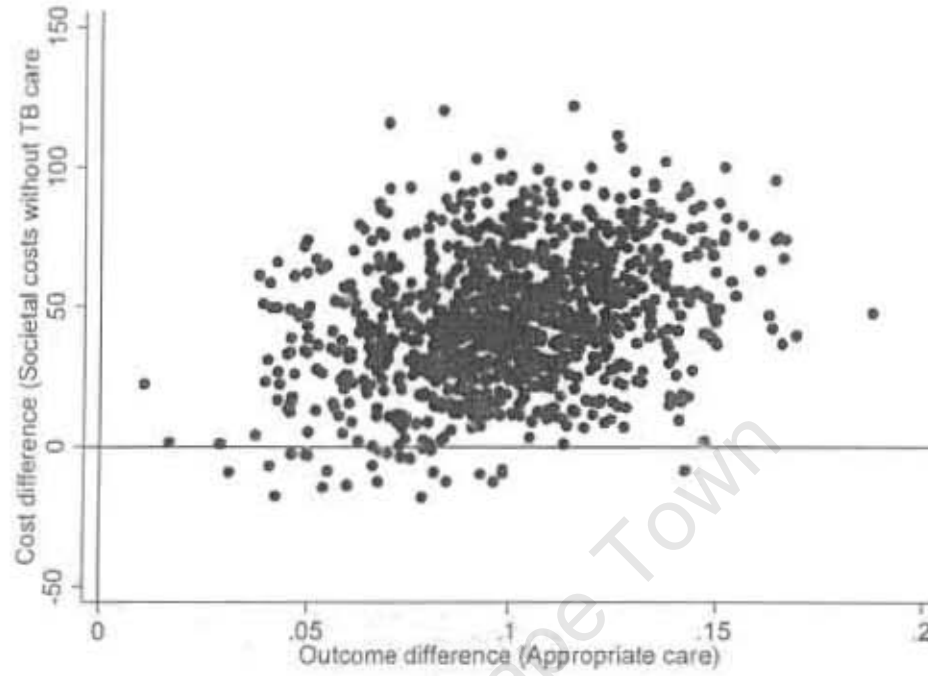


Figure 5.5 Cost-effectiveness planes: appropriate care (societal costs – including lost productivity costs - excluding tuberculosis treatment costs)

From two dimensional cluster bootstrap of costs and effects (Stata)



From two dimensional individual bootstrap of costs and effects (Excel)

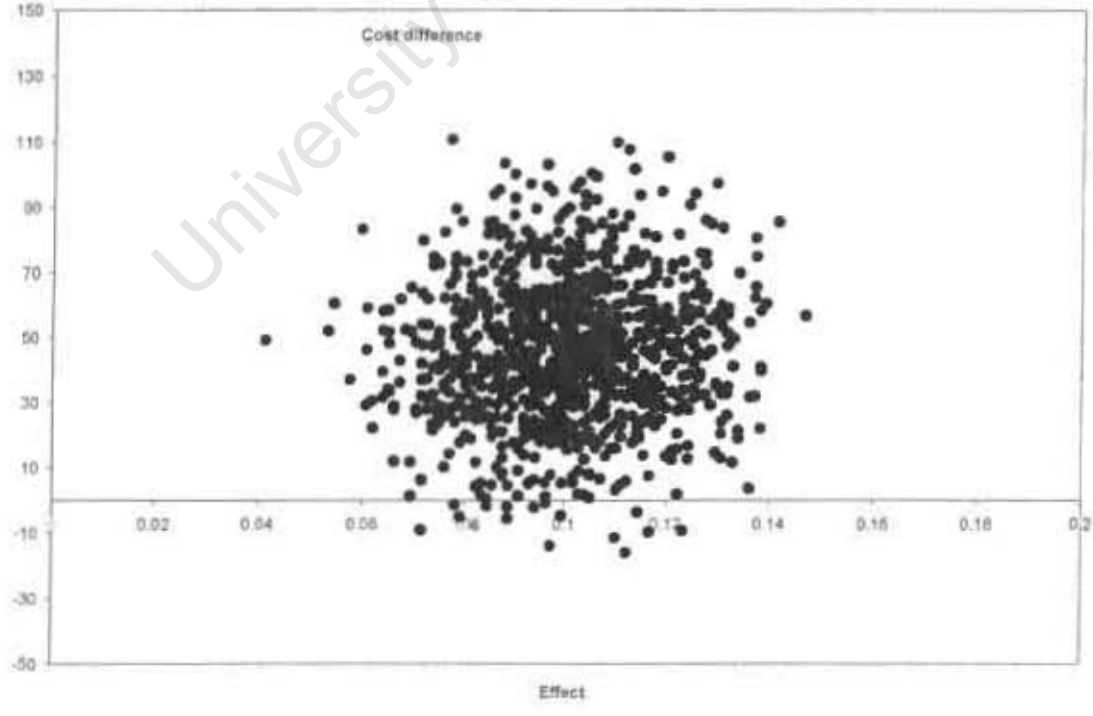
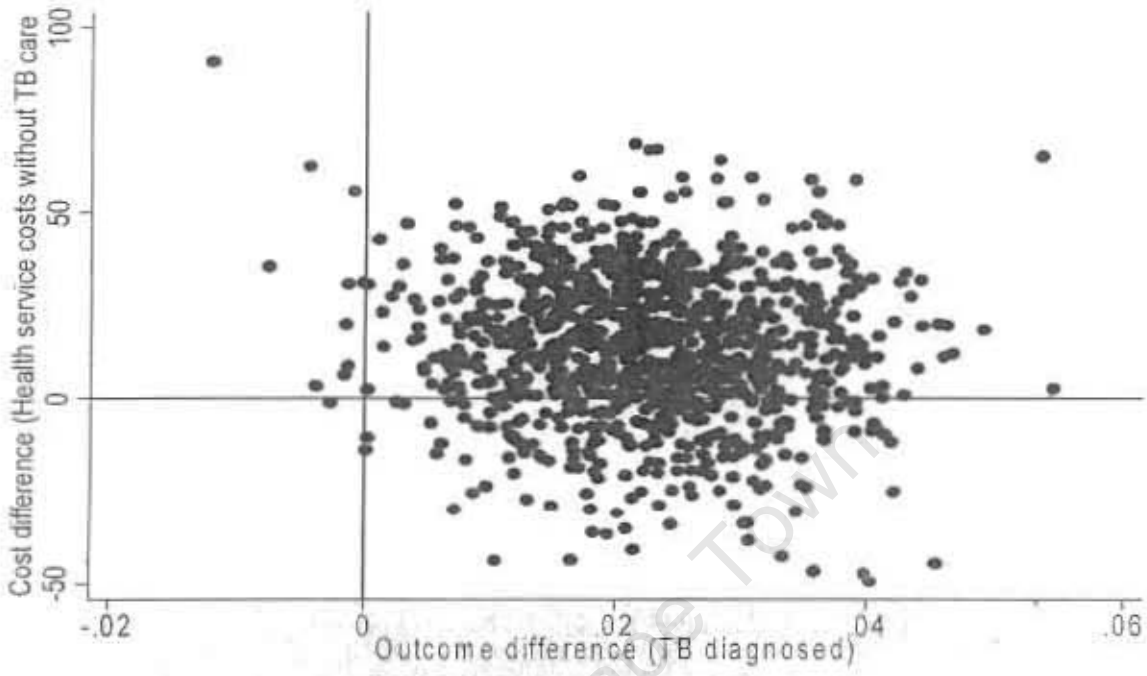


Figure 5.7 Cost-effectiveness planes: newly diagnosed TB (health service perspective excluding tuberculosis treatment costs)

From two dimensional cluster bootstrap of costs and effects (Stata)



From two dimensional individual bootstrap of costs and effects (Excel)

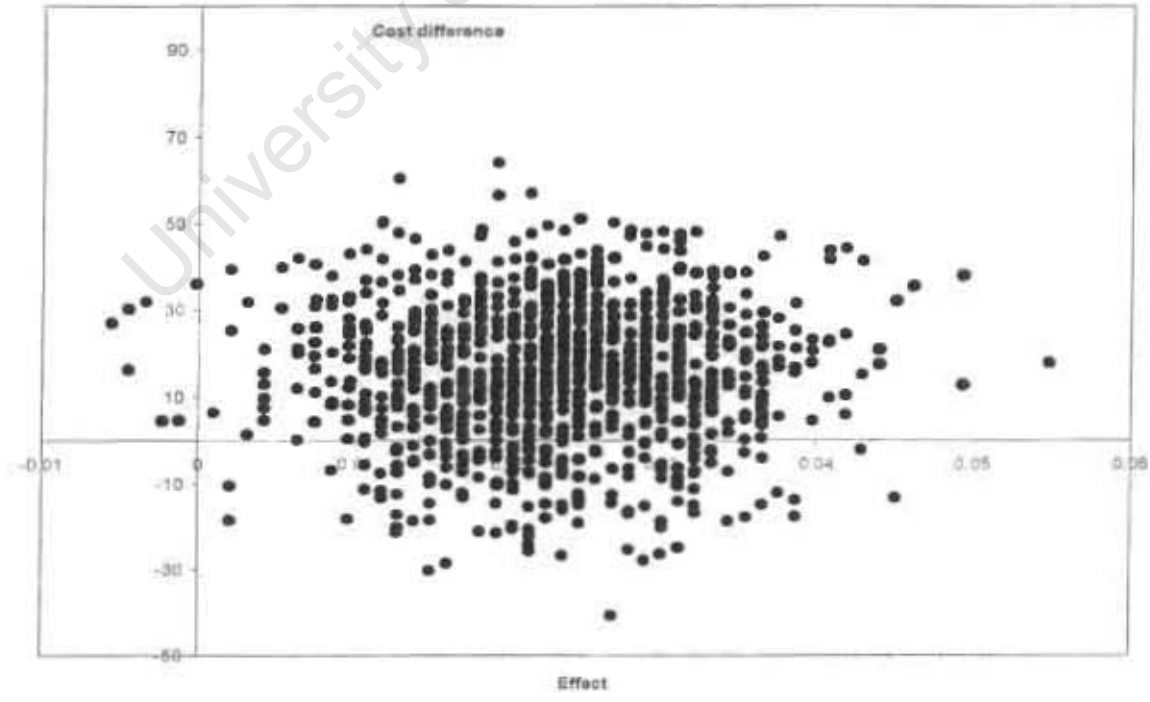
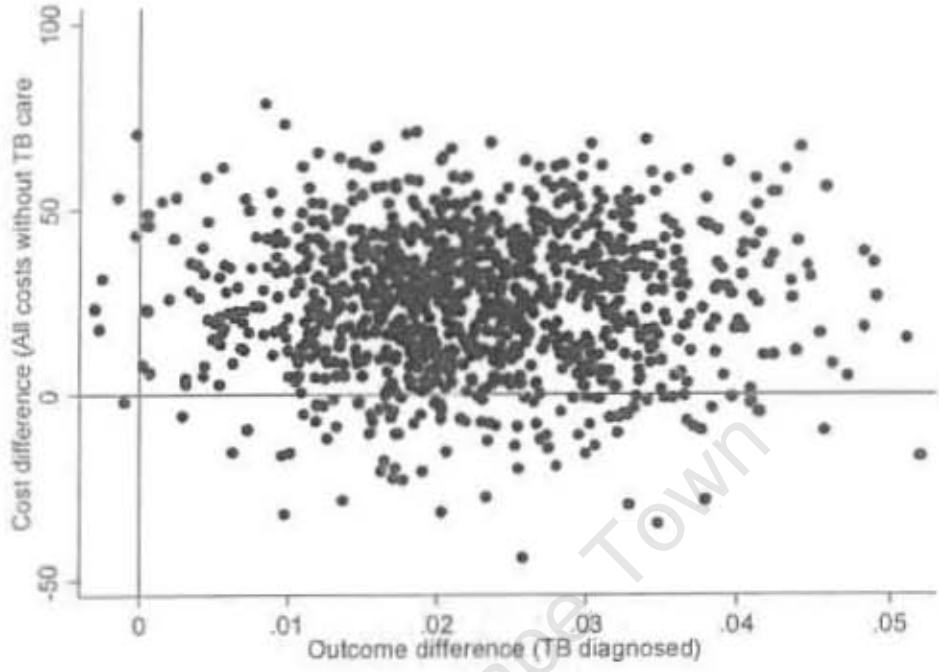


Figure 5.9 Cost-effectiveness planes: newly diagnosed TB (societal costs excluding tuberculosis treatment costs)

From two dimensional cluster bootstrap of costs and effects (Stata)



From two dimensional individual bootstrap of costs and effects (Excel)

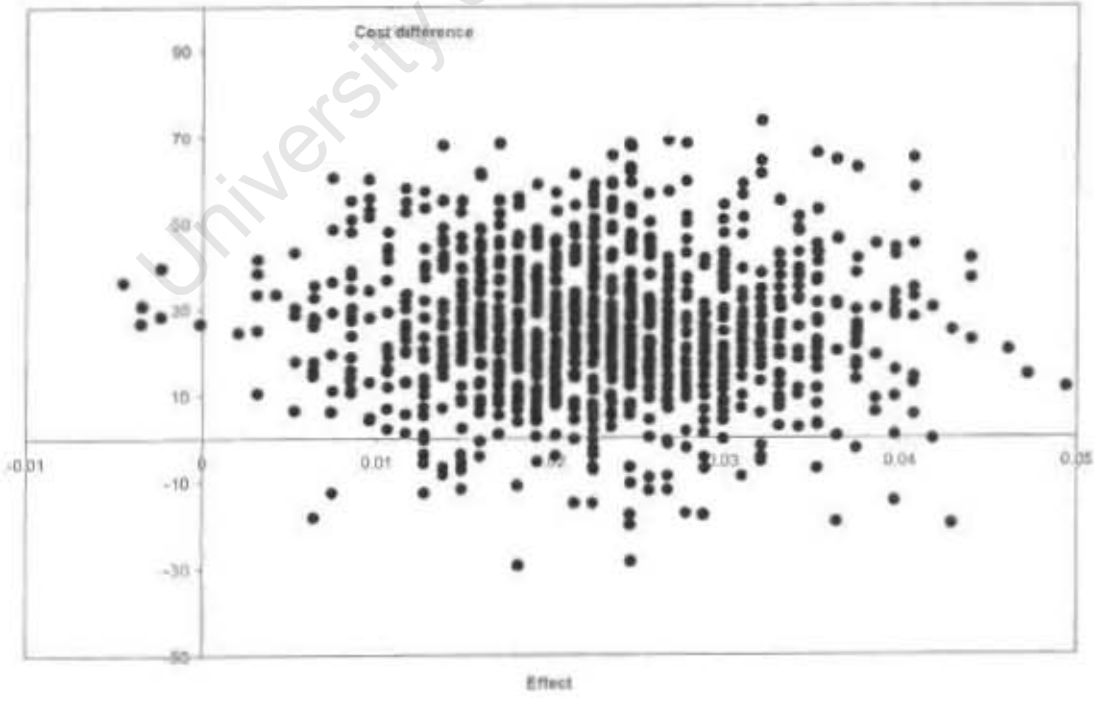
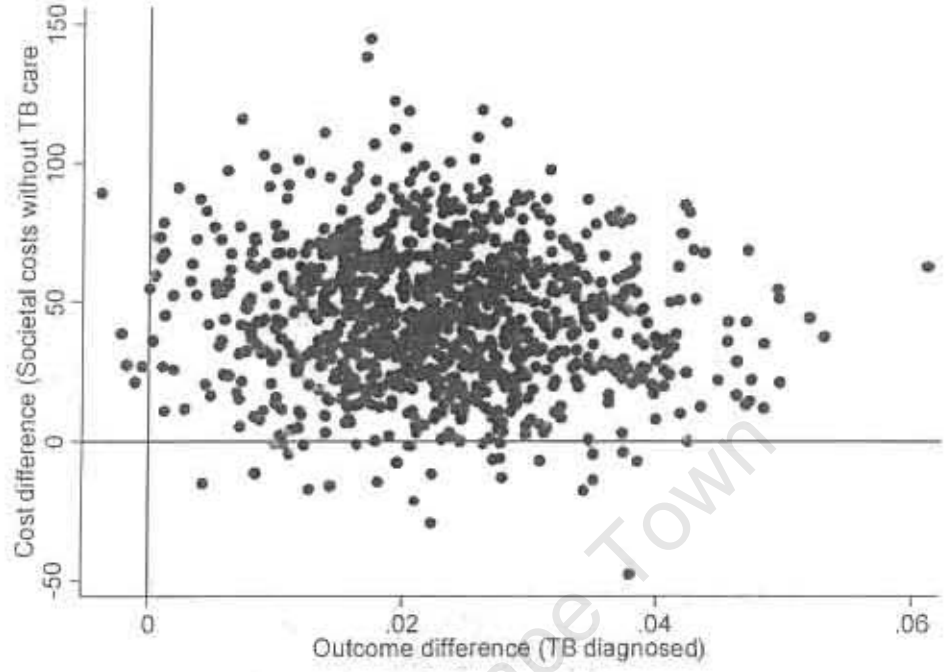
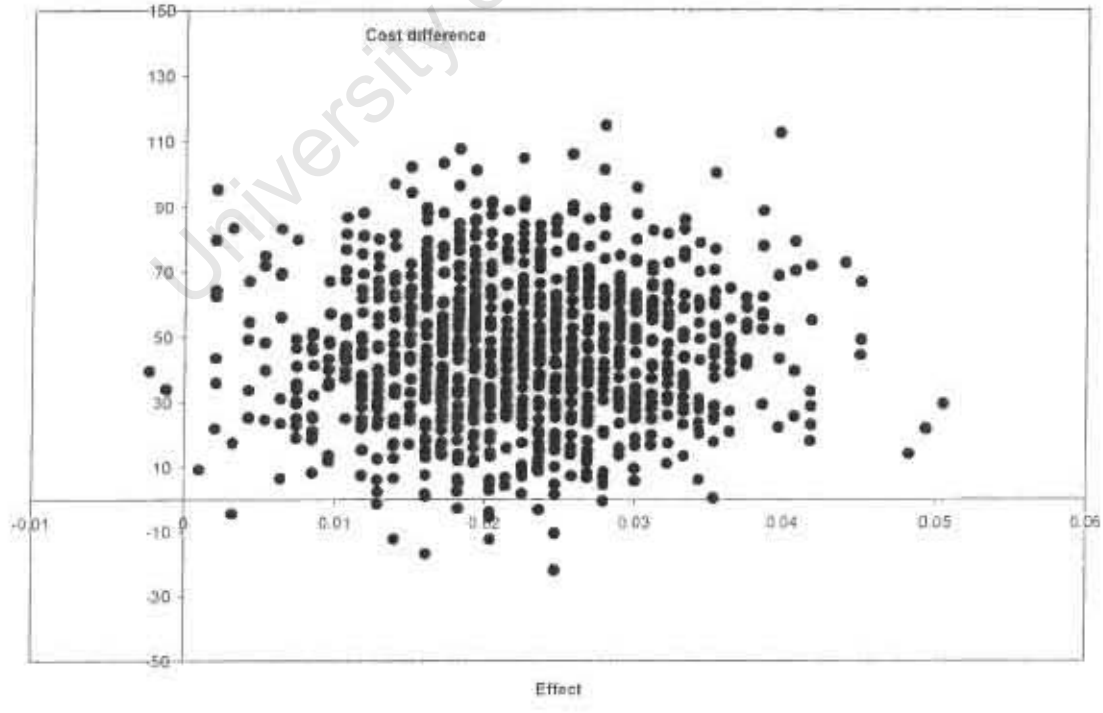


Figure 5.11 Cost-effectiveness planes: newly diagnosed TB (societal – including lost productivity costs - costs excluding tuberculosis treatment costs)

From two dimensional cluster bootstrap of costs and effects (Stata)



From two dimensional individual bootstrap of costs and effects (Excel)



5.3 Net Monetary Benefits

Differences in costs and effects were reduced to a single variable by calculating net monetary benefits for each subject, at willingness to pay levels from zero to R2000 in R100 increments, using the formula described in Chapter 2 Section 2.4.6.

5.3.1 Distribution of net monetary benefits

Figure 5.13 shows the distribution of net benefits at three willingness to pay levels (0, 1000, 2000) for appropriate care and newly diagnosed tuberculosis from a health services perspective (excluding tuberculosis treatment costs). The distribution of net benefits at most willingness to pay levels was roughly symmetrical for appropriate care, but less so for newly diagnosed tuberculosis because fewer patients experienced this outcome. Distribution also differed at different levels of willingness to pay. At willingness to pay of zero, the distributions were negatively skewed with net benefits equal to the negative of patient costs. At higher levels of willingness to pay, the distributions tended to be bimodal depending on whether or not patients had experienced the outcome. The net benefits are not Normally distributed, so it is possible that confidence intervals and P values from the following regression analyses that use these variables as outcomes may be invalid. However, the central limit theorem proves that, with large samples, they may indeed be valid (Altman 1999). Bootstrap methods do not assume Normal distributions of outcomes, so it is thus of methodological interest whether confidence intervals and probabilities from regression and bootstrap methods differ, as is shown towards the end of this chapter.

5.3.2 Incremental net benefits attributable to the intervention

Incremental net benefits attributable to the intervention were estimated in three different ways:

- Linear regression analysis of net benefits using Stata with the trial arm (intervention/ control) as the explanatory variable
- 2D individual bootstrapping using Excel (by calculating the means, and 2.5 and 97.5 percentiles of incremental net benefits for corresponding bootstrap replicates)
- 1D cluster bootstrapping of net monetary benefits using Stata

All analyses were conducted separately at each willingness to pay level. Incremental net benefits, with 95% confidence intervals, were plotted against willingness to pay levels (Figures 5.14 and Figures 5.15). Incremental net benefits predictably increased with increasing willingness to pay levels. They were higher for appropriate care than for newly diagnosed tuberculosis because more patients experienced this outcome. Confidence intervals were wider for those methods which adjusted for clustering (robust regression, cluster bootstrap) than for those which did not (regression without robust adjustment, individual bootstrap) (Figures 5.16 and 5.17).

Figure 5.16 Incremental net benefit at different levels of willingness to pay per unit of effect for appropriate care (health service costs without TB care): 95% confidence intervals estimated with different methods

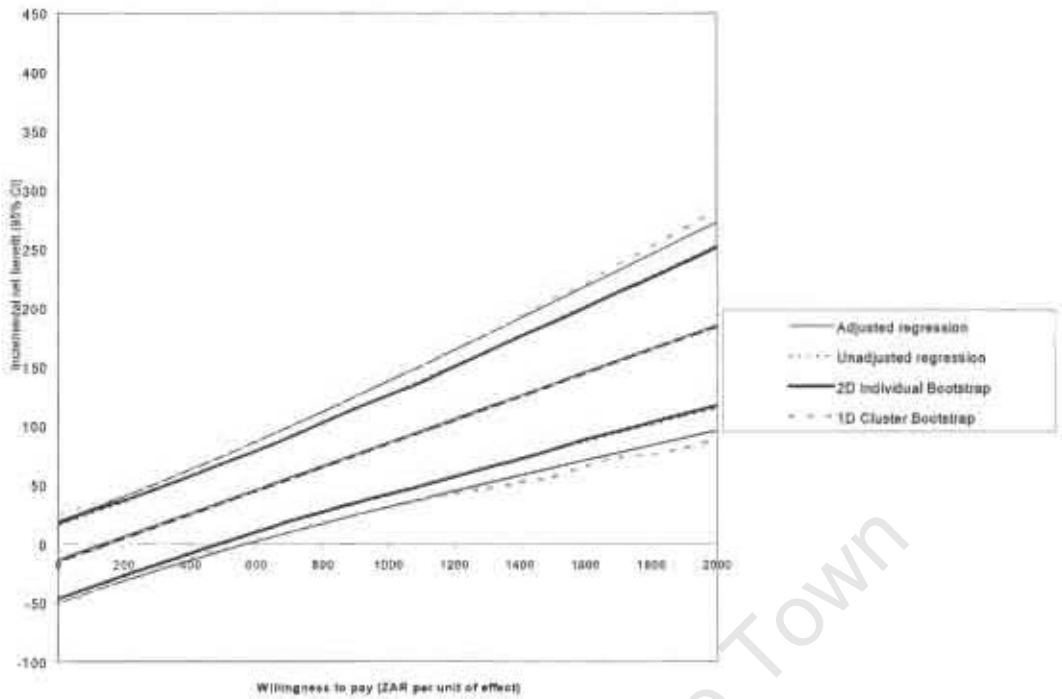
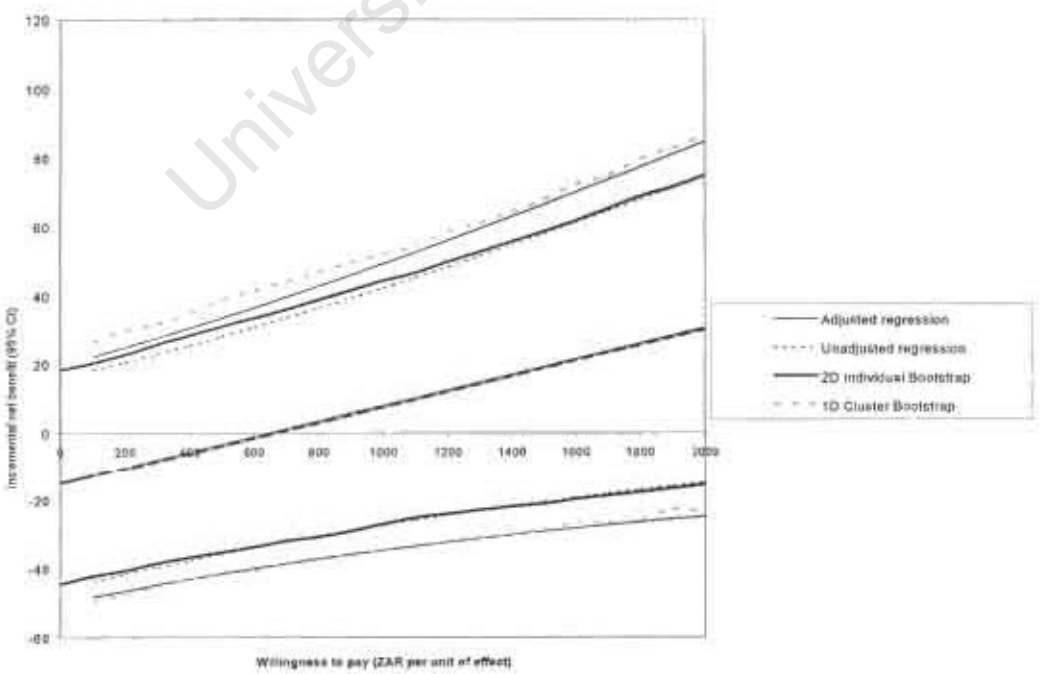


Figure 5.17 Incremental net benefit at different levels of willingness to pay per unit of effect for newly diagnosed tuberculosis (health service costs without TB care): 95% confidence intervals estimated with different methods



The cost-effectiveness plots obtained for these analyses show that the plots corresponding to negative confidence limits fell in the bottom right quadrant of the cost-effectiveness plane and that no plots fell in the top left quadrant. This suggests that the negative confidence limits reflect the possibility that the intervention is dominant (more effective and cost-saving) (Drummond et al. 2005). For newly diagnosed tuberculosis, analysis yielded negative confidence limit estimates for multiple scenarios. These could not be interpreted because the corresponding plots fell across all four quadrants of the cost-effectiveness plane (Figures 5.7 through 5.12).

Table 5.1 Incremental cost-effectiveness ratios per additional patient appropriately managed (means and 95% confidence intervals)

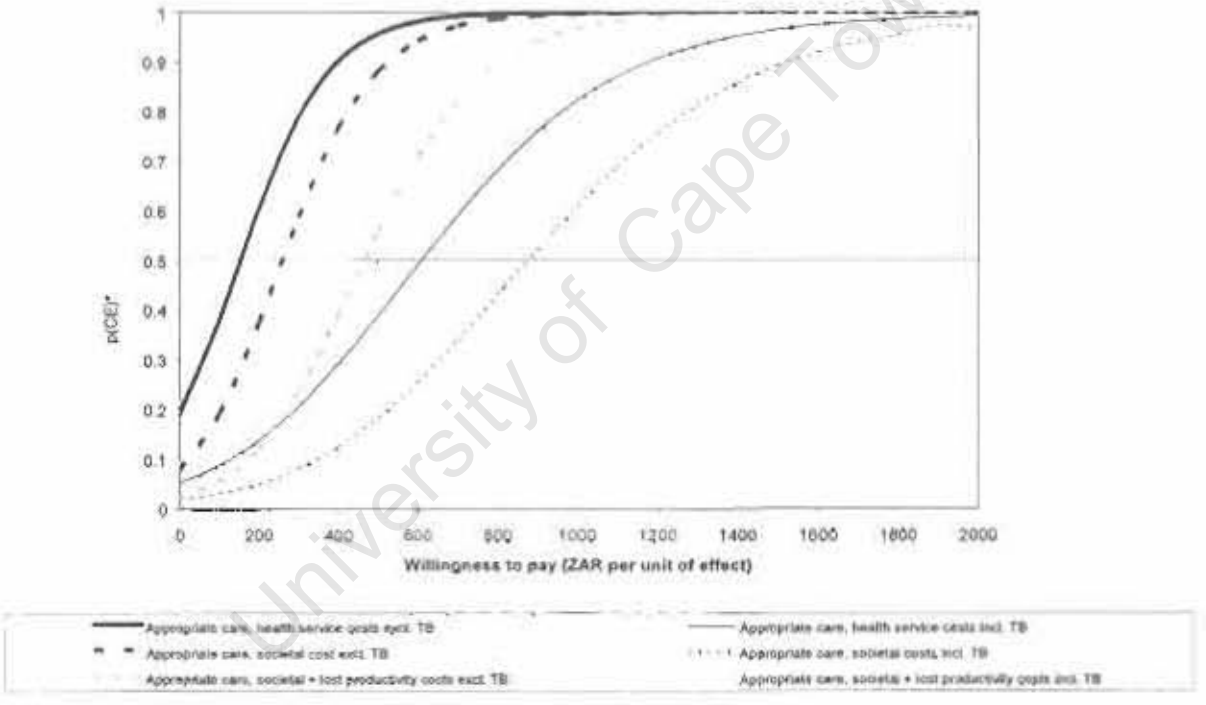
Perspective	Mean ICERS and 95% confidence intervals											
Statistical Method	Calculated	Regression		Bootstrap		Bootstrap		Regression		Bootstrap		Bootstrap	
Programme	-	Stata		Stata		Stata		Stata		Excel		Excel	
Adjustment for clustering	-	Yes		Yes		Yes		No		No		No	
One or two dimensional		One		One		Two		One		Two		Two	
No. of resamples	-	-		10000		1000		-		1000		10000	
Health Service (excl. TB treatment costs)	151	153	-155, 577	151	-198, 561	151	-305, 525	153	-137, 486	143	-178, 488	154	-159, 480
Health Service (incl. TB treatment costs)	609	609	-118, 1601	609	-59, 1681	609	-78, 1578	609	90, 1223	623	117, 1234	601	118, 1160
Societal Costs (excl. TB treatment costs)	259	259	-72, 723	259	-101, 3989	259	-218, 670	259	-50, 624	263	-60, 655	271	-92, 627
Societal Costs (incl. TB treatment costs)	882	877	64, 2008	881	122, 2191	881	143, 2124	881	261, 1659	899	283, 1620	913	270, 1681
Societal incl. lost productivity costs (excl. TB treatment costs)	464	465	27, 1062	464	14, 1066	464	-50, 1093	464	45, 975	469	29, 973	483	46, 975
Societal incl. lost productivity costs (incl. TB treatment costs)	1162	1158	323, 2403	1162	349, 2606	1162	261, 2303	1162	442, 2112	1176	505, 2061	1201	479, 2055

5.5 Cost effectiveness acceptability curves

Figures 5.18 and 5.19 show the probability that the intervention is cost-effective for different ceiling values of willingness to pay (from zero to 2000, in 2003 South African rands). Cost-effectiveness acceptability curves from robust regression are shown for all 12 scenarios. For appropriate care (Figure 5.18) the probability that the intervention was cost-effective exceeded 50% no matter what perspective was used, or whether the cost of tuberculosis care was considered. For the primary analysis (health service perspective excluding the cost of tuberculosis care) a 50% probability that the intervention corresponded to a willingness to pay value of R170 per additional case appropriately managed, and a 90% probability R400.

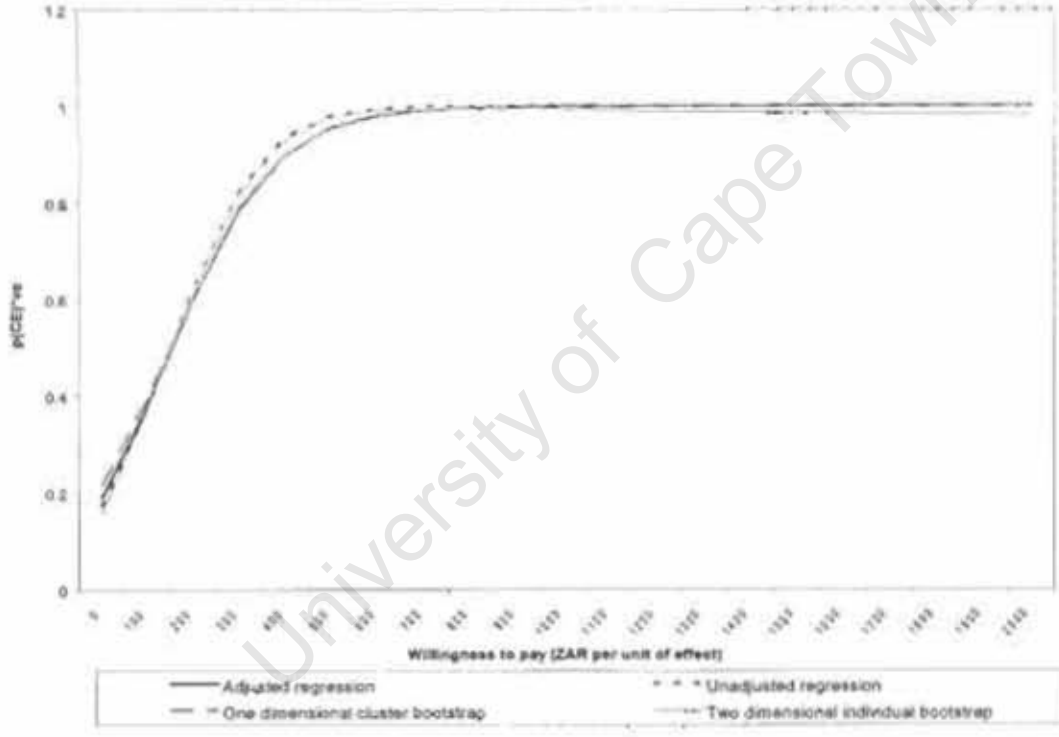
For newly diagnosed tuberculosis (Figure 5.19) the estimated probability that the intervention was cost-effective exceeded 50% for most scenarios except when tuberculosis treatment costs were included, and in the case of societal costs (including lost productivity costs), also when they were excluded. For the primary analysis (health service perspective excluding the cost of tuberculosis care) a 50% probability that the intervention corresponded to a willingness to pay value of R680 per additional case appropriately managed, and an 80% probability R2000 (90% probability would exceed R2000).

Figure 5. 18 Cost-effectiveness acceptability curves showing probability that the intervention is cost effective for willingness to pay ceiling values per additional patient appropriately managed (from robust regression)



* p(CE): Probability that the intervention is cost-effective

Figure 5.20 Cost-effectiveness acceptability curves showing probability that the intervention is cost effective for willingness to pay ceiling values per additional patient appropriately managed generated using multiple methods (health service perspective)



* p(CE): Probability that the intervention is cost-effective

Figure 5.20 shows cost-effectiveness acceptability curves for appropriate care from the health service perspective (excluding the cost of tuberculosis care) generated using multiple methods.

The probability that the intervention was cost-effective was lower for methods adjusting for clustering (robust regression and cluster bootstrap) than for those which didn't (individual bootstrap and unadjusted regression) at willingness to pay values above the incremental cost-effectiveness ratio. This suggests that methods which ignore the impact of clustering lead to excessive confidence that an intervention is cost-effective.

5.6 Summary

The cost effectiveness analysis shows that the intervention cost the health service about R150 extra for each extra patient appropriately managed, if tuberculosis treatment costs were not considered. But analyses of uncertainty showed that this ICER could be almost as high as R600 per patient, or even that the intervention could save almost R200 per patient appropriately managed. Similarly, the intervention was more likely than not to be cost effective if the health service was willing to pay more than about R150 per extra patient appropriately treated. This seems to be exceptionally good value for money. But when tuberculosis treatment, and societal costs were considered, ICERs were much higher.

If tuberculosis diagnosis was the only outcome of interest, the extra health service cost per extra patient diagnosed was over R600, and could be almost R5000 even if tuberculosis treatment costs were not considered. If all costs were considered the mean ICER for newly diagnosed tuberculosis cases was over R5000.

6.1.3 Translation Guidelines of the EuroQol Group

To date the EuroQol has been translated into 107 languages including many outside of Europe. Translation is guided by rigorous protocols (EuroQol 2003), and is co-ordinated by the EuroQol group based in Rotterdam. Groups wishing to undertake a translation are required to register with the EuroQol group, demonstrate that they have access to adequate resources and skills to perform the translation and sign an agreement. The EuroQol group then assigns a researcher experienced in translation and cross-cultural adaptation of health-related quality of life instruments to review reports of the translation process at every stage. The proposed Sesotho translation was registered with the Group in August 2002 and assigned a health economist as the EuroQol advisor.

The translation guidelines conform to internationally accepted protocols including forward and back-translation, comparison of back-translation with the source instrument, and review by a committee of translators and, finally, testing on a lay panel (Guillemin et al. 1993). In addition the EuroQol group requires that the forward and back translations each be carried out by two independent translators, that translators be qualified and/or experienced and that the forward translators be native speakers of the target language but fluent in English, and vice-versa for the back translators. An experienced EuroQol researcher who has undertaken the Shona and Xhosa translations advised that at least one of the back translators be a native Sesotho speaker (J Jelsma - personal communication). This was because she believed the cultural insights provided by a native speaker necessary to translate the instrument across widely diverse cultures. The EuroQol translation guidelines also specified the composition of the lay panel in that it must comprise at least 12 healthy speakers of the target language, and represent an even spread based on age, sex and educational characteristics.

6.1.4 A framework for understanding equivalence of HRQOL instruments across cultures

During the 1990s increased interest in patient-based outcomes (Fitzpatrick et al. 1998) alongside the proliferation of multi-national drug trials fuelled the translation and adaptation of HRQOL instruments across languages and cultures, rather than the development of new instruments in different cultures (Herdman et al. 1997). Much of this activity was limited to translation itself, and was accompanied by the publication of guidelines to standardise and improve the quality of translations (Gulleiman et al 1993). There was some debate as to what constituted equivalence, and whether rigorous translation processes alone were sufficient to guarantee this.

Herdman and colleagues (1998) reviewed equivalence constructs, their application in reporting of HRQOL translations and adaptations and proposed a model for assessing equivalence using a universalist approach adopted from cross-cultural psychology. This model requires that six types of equivalence be assessed during the process of cross-cultural adaptation and is summarised in Table 6.1. This model was used to appraise the cross-cultural adaptation of the EuroQol into Sesotho. The translation itself is summarised in Table 6.2. Further reporting of the cross-cultural adaptation process in this chapter is presented within the equivalence framework outlined by Herdman.

Table 6.2a The Sesotho EuroQol: results of the back and forward translations, and testing on the lay panel

Domain and Level	FORWARD TRANSLATION			BACK TRANSLATION			POST LAY PANEL	POST APPROVAL
	1st Translator	2nd Translator	Post consensus & feedback	1st Translator	2nd Translator	Post consensus & feedback		
MOBILITY								
Level 1	Ha ke na bothata ba ho tsamaya	Ha ke na le bothata ba ho tsamaya	Ha ke na bothata ba ho tsamaya	I do not have any problems with walking	I have no difficulty in walking	Ha ke na bothata ba ho tsamaya	Ha ke na bothata ba ho tsamaya	Unchanged
Level 2	Ha ke kgone ho tsamaya	Ke na le bothata bo itseng ba ho tsamaya	Ke na le bothata bo itseng ba ho tsamaya	I have some problems with walking	I have some difficulty in walking	Ke na le bothata bo itseng ba ho tsamaya	Ha ke na le bothata bo itseng ba ho tsamaya	Ke na le bothata bo itseng ba ho tsamaya
Level 3	Ke hlola ke robetse moalong (betheng)	Ha ke tsamaye ke dutse betheng.	Ke ba betheng ka taelo	I can stay in bed on command	I am confined to bed	Ke ba betheng ka taelo	Ke hlola betheng	Unchanged
SELF-CARE								
Level 1	Ha ke na bothata ka ho itlhokomela	Ha ke na bothata le ho itlhokomela	Ha ke na bothata le ho itlhokomela	I do not have problems with self-care	I have no difficulty in caring for myself	Ha ke na bothata ba ho itlhokomela	Ha ke na bothata ba ho itlhokomela	Unchanged
Level 2	Ke na le bothata ka ho itlhatswa kapa ho ikapesa	Ke na le bothata ba ho ithatswa le ho itentsha/ikapesa	Ke na le bothata bo itseng ka ho itlhatswa kapa ho itentsha/ikapesa	I have some/certain problems with washing or dressing myself	I have some difficulty in washing or dressing	Ke na le bothata bo itseng ka ho itlhatswa kapa ho itentsha/ikapesa	Ha ke na le bothata bo itseng ka ho itlhatswa kapa ho itentsha/ikapesa	Ke na le bothata bo itseng ka ho itlhatswa kapa ho itentsha/ikapesa
Level 3	Ha ke kgone ho hlapa kapa hona ho ikapesa	Ha ke kgone ho itlhatswa kapa ho itentsha	Ha ke kgone ho itlhatswa kapa ho itentsha/ikapesa	I am unable to wash or dress myself	I am unable to wash or dress myself	Ha ke kgone ho itlhatswa kapa ho itentsha/ikapesa	Ha ke kgone ho itlhatswa kapa ho itentsha/ikapesa	Unchanged

Table 6.2c The Sesotho EuroQol: results of the back and forward translations, and testing on the lay panel

Domain and Level	FORWARD TRANSLATION			BACK TRANSLATION			POST LAY PANEL	POST APPROVAL
	1st Translator	2nd Translator	Post consensus & feedback	1st Translator	2nd Translator	Post consensus & feedback		
PAIN/ DISCOMFORT								
Level 1	Ha ke opelwe kapa hona ho sulafallwa.	Ha ke opelwe kapa ho se ikutlwe monate.	Ha ke opelwe kapa ho se ikutlwe monate.	I have no pain or discomfit	I am not in pain nor feel unwell	Ha ke opelwe kapa ho se ikutlwe monate.	Ha ke opelwe kapa ho se ikutlwe monate.	Unchanged
Level 2	Ha ke opelwe hakaalo kapa ho sulafallwa hakaalo.	Ke opelwe hanyane kapa ho se ikutlwe monate.	Ha ke opelwe hakaalo kapa ho se ikutlwe monate hakaalo.	I do not have much pain or discomfit	I am not in great pain nor feel particularly unwell	Ha ke opelwe hakaalo kapa ho se ikutlwe monate.	Ha ke opelwe hakaalo kapa ho se ikutlwe monate.	Unchanged
Level 3	Ke opelwe haholo kapa ho sulafallwa haholo.	Ke opelwe haholo kapa ha ke e ikutlwe monate.	Ke opelwa hampe kapa ha ke ikutlwe monate ho hang.	I have severe pains and am very uncomfortable	I am in a lot of pain or I don't feel well at all	Ke opelwa hampe kapa ha ke ikutlwe monate ho hang.	Ha ke opelwe hampe kapa ha ke ikutlwe monate ho hang.	Ke opelwa hampe kapa ha ke ikutlwe monate ho hang.
ANXIETY/ DEPRESSION								
Level 1	Ha ke tshwenyeha kapa hona ho wa maikutlo.	Ha ke na kgatello ya maikutlo.	Ha ke a tshwenyeha kapa hona ho wa maikutlo kapa ha ke na kgatello maikutlo.	I am not worried or stressed	I am not worried or down or depressed	Ha ke a tshwenyeha kapa hona ho wa maikutlo.	Ha kea tshwenyeha kapa hona ho wa maikutlo.	Unchanged
Level 2	Ke tshwenyehile hanyenyane feela kapa ke wele maikutlo hanyenyane feela.	Ke na le kgatello ya maikutlo e tshesane.	Ke tshwenyehile hanyenyane kapa ho ba le kgatello ya maikutlo hakaalo.	I am a little worried or stressed	I am slightly worried or am particularly depressed	Ke tshwenyehile hakaalo kapa ke wele maikutlo.	Ha kea tshwenyeha hakaalo kapa ke wele maikutlo .	Unchanged.
Level 3	Ke tshwenyehile haholo kapa ke wele maikutlo hampe.	Ke opelwe haholo kapa ha ke maikutlo e mpe.	Ke tshwenyehile hampe kapa ke na le kgatello ya maikutlo e matla.	I am very worried and very stressed	I am very worried or severely distressed	Ke tshwenyehile hampe kapa ke wele maikutlo haholo.	Ha kea tshwenyeha hampe kapa ke wele maikutlo haholo.	Ke tshwenyehile hampe kapa ke wele maikutlo haholo.

6.2. 1 Conceptual equivalence

Both the forward and back-translators expressed concern that the constructs of anxiety and depression, as understood by Westerners, did not sit comfortably within the Sotho construction of HRQoL. The younger of the translators pointed out that while many younger generations of Sotho have adopted the Western terms in their everyday language, they often use them within an idiom which may sound confusing to a Westerner e.g. "I have an anxiety in my teeth". Although, unlike with the Shona and Xhosa translations (Jelsma et al. 2000, Mkoka et al. 2003), there was less concern that these constructs are not regarded as central to the Sotho construct of HRQoL because their origins are perceived to be spiritual or contextual, there was some discomfit at them being listed alongside the more physical and tangible manifestations of HRQoL. Depression and anxiety are understood within Sotho culture, but only in a normative sense relative to stressful life events like bereavement. Despite these reservations, the lay panel reported no difficulty in understanding the translation or the concept that was being conveyed.

The quantification of pain and discomfort also appeared to be foreign to the Sotho construct of HRQoL. In Sotho, one is either unwell or not, and the extent of the illness or pain is rarely described. This difficulty in quantification was also noted by the translators of the Shona version, but with regards to the mobility domain (Jelsma et al. 2000). Because the concept was not well understood, we encountered difficulty in selecting an appropriate word to convey "moderate". Two equivalents were considered including "hanyane", meaning "slight"or "a little", and "hakaalo"meaning "that much"or "to that extent". We eventually settled on "hakaalo"as colloquially it better conveyed the construct of "moderate" although it required we adjust the adverb for depression "tshwenyehile"to obtain grammatical agreement.

The minimum school leaving age ("Did your education continue after the minimum school leaving age?") posed difficulties in that many adults left school well before this age during the apartheid years, when compulsory education until the age of 16 was enforced only in "white" schools. Many still do, because of poor socio-economic circumstances. We therefore chose a more open-ended translation of this question, which allowed adults, whether they left school before, at or after the age of 16, to answer whether they had continued their education in any way.

6.2.3 Semantic equivalence

Several phrases required careful consideration before we were satisfied that semantic equivalence had been achieved. The first of these related to the translation of "walking about" (mobility domain, levels 1 and 2). When reviewing the back translations, we noted that the word "about" had been omitted. We decided against including it, as the Sotho equivalent implied idle purposeless walking, and not the spatial construct of the English original. Interestingly, a similar decision was taken by the group completing the Shona translation who noted that in a previous version, the Shona equivalent "kufamba-famba"literally meaning "to walk walk" had a connotation of hanging around street corners, which resulted in the questionnaire being viewed as relating to HIV/AIDS (Jelsma et al. 2000).

The phrase that proved most difficult to translate was "confined to bed" (mobility domain, level 3) for several reasons. Firstly, it proved difficult to provide an equivalent that was able to capture all forms of ill health which confine people to bed, whether they are severe but self-limiting illnesses like influenza or terminal illnesses like AIDS. Versions considered during the translation process were also not always free of causality (e.g. confined to bed literally because I cannot walk) or external factors (e.g. instructions for bed-rest from a health worker or family member). Ultimately two versions were put to the lay panel for consensus: "Ka ba

6.2.4 Operational equivalence

The EuroQol is intended for use as primarily a self-completed questionnaire although it is frequently administered by interviewers. We intended to use it as one component of a relatively lengthy questionnaire, and because of this, and the relatively low levels of literacy among our target users (patients attending predominantly rural primary care clinics), we chose to implement it using trained interviewers.

The lay panel testing provided an opportunity to implement the instrument using self-completed questionnaires. The mean time taken to complete the questionnaire during the lay panel was 17 minutes (range 11 - 19), slightly longer than the 10 - 15 minutes reported during the Shona lay panel (Jelsma and Chivaura 2000). Our single respondent with less than eight years of schooling reported difficulty understanding the instructions for completing the visual analogue scale. Her difficulties related to the formatting of the numbers on the scale (legend for values 10 through 90, are separated by the line of the scale itself, such that the "7" of "70" is positioned left of the scale, and the "0" of "70" to the right of it). Other participants reported that it felt odd to be instructed to draw a line from the box (labelled ""your own health state today") to the scale, and indicated that they felt it more intuitive to draw a line from the lower end of the scale to the point describing their health state. Given this feedback and the experience of others who have used the VAS among respondents with low literacy levels (Gudex et al. 1996), we restricted analysis of the visual analogue results to patients with more than primary education during the trial (Table 3.16).

During the trial, we also implemented the five level EuroQol in the hope that it would improve the instrument's responsiveness in a respiratory outpatient setting. This involves inserting two additional tick-boxes between levels 1 and 2, and 2 and 3

6.2.5.2 Construct validity of the Sesotho EuroQol among patients with respiratory illnesses

Construct validity was assessed using ordinal logistic regression of the collapsed three level Sesotho EuroQol scores with York tariffs applied. Analysis was restricted to the 1678 patients who completed Sesotho interviewer-administered questionnaires. Index scores were first compared with respiratory symptoms and signs, and diagnostic subgroups as defined in Table 6.3. Results are presented in Table 6.4.

Table 6.3 Description of diagnostic subgroups used in assessment of the Sesotho EuroQol's construct validity

Diagnostic subgroup*	Description
Upper respiratory tract infections	Cough for less than 2 weeks and no marker of severe illness (i.e. no difficult breathing, temperature ≥38°C, respiratory rate ≥30 breaths/min, use of accessory muscles or haemoptysis)
Lower respiratory tract infections	Cough and/or difficult breathing for less than 2 weeks and: temperature ≥38°C and/ or haemoptysis and/ or yellow/ green sputum
Suspected tuberculosis (definition 1)	Cough and/ or difficult breathing for 2 weeks or more and: temperature ≥38°C and/ or haemoptysis and/or self-reported weight loss and/ or night sweats
Suspected tuberculosis (definition 2)	Cough and/ or difficult breathing for 2 weeks or more and: temperature ≥38°C and/ or haemoptysis
Asthma	Cough and/ or difficult breathing of any duration and: responsive to beta-agonists and pack year history <10 years
COPD	Cough and/ or difficult breathing for 2 weeks or more and a pack year history ≥ 10 years or past tuberculosis

* Subgroups are not mutually exclusive and patients could fulfill criteria for more than one category.

also more likely to have lower index scores than those who didn't, with the exception of those with temperatures of 38°C or more, or respiratory rates of 30 or more, the latter applying only when the EuroQol was collapsed to three levels. Patients with symptoms and signs consistent with an upper respiratory tract infection (Table 6.3) were significantly more likely to have a higher index score than other trial patients with more severe disease, and those with suspected tuberculosis a lower index score. Interestingly, the EuroQol was unable to distinguish those with newly diagnosed, as opposed to suspected, tuberculosis. The Sesotho EuroQol was also unable to distinguish those with asthma, but those with COPD reported significantly lower index scores.

Convergent validity with the translated and modified Royal College of Physician's asthma control measure was also good, in that for every unit increase in the RCP score, the EuroQol index score decreased (Table 6.5, note that the two instruments are reversely scored). This is presumably in part because of shared domain constructs (usual activities).

Table 6.5 Association between deciles of the Sesotho EuroQol index score and modified Royal College of Physicians' (RCP) Asthma Measure

Comparison	Odds ratio (OR) of having a higher index score*		p value
	OR	95% CI	
Modified RCP Asthma Measure at enrolment	0.87	0.83 – 0.92	<0.001
Modified RCP Asthma Measure at follow-up	0.75	0.72 – 0.77	<0.001

* From ordinal logistic regression; per unit change in RCP score

Changes in Sesotho EuroQol index scores and the modified RCP score at follow-up were Normally distributed and so compared using linear regression (Table 6.6).

6.2.6 Functional Equivalence

In summary, the Sesotho EuroQol performed well across all five areas of equivalence. Many issues were identified and addressed during the rigorous translation process required by the EuroQol group. The most notable reservation concerned conceptual equivalence and whether the anxiety/ depression domain fitted within the Sotho understanding of HRQoL. This was raised by our team of academic translators but refuted by the lay respondents. The presentation of more than one alternative at each stage in the translation process helped identify issues requiring careful consideration and discussion. So it seems that the EuroQol requisite that two forward translators and two back translators undertake the task of translation is justified. The selection of a native English speaker as project manager (the candidate) resulted in an erroneous adjustment after testing on the lay panel. This could have been avoided if she had a working knowledge of Sesotho, and should be considered when undertaking additional translations. Nonetheless, once corrected, the translated version displayed good construct validity within the context of the trial and a respiratory outpatient setting, as well as convergent validity with a disease-specific measure for respiratory disease, the modified Royal College of Physician's asthma control measure.

of the intervention could be as high as R600 per patient appropriately managed, or even save R200 for every additional patient appropriately treated.

The results of this pragmatic trial are widely generalisable to other resource-limited settings where non-physicians provide primary care. It was delivered by existing staff, and was effective in spite of the low number of educational contacts. It suggests that equipping middle managers as outreach trainers is feasible within existing staff constraints and could improve quality of care, providing an alternative to traditional offsite centralised training courses.

This chapter provides an overview of results, considers the methodological strengths and weaknesses of the study, compares findings with those evaluating the effectiveness and efficiency of similar syndromic and educational outreach interventions, and discusses implications for policy and research methods.

patient-reported responsiveness to inhaled beta-agonists among inhaled corticosteroid recipients in the intervention group implies that the treated disease was indeed asthma. Taken together these observations suggest that the increased provision of inhaled corticosteroids in the intervention group was not solely due to expanded prescribing powers, but rather due to the appropriate detection and management of obstructive lung disease. Nonetheless, the effect of increasing prescribing provisions cannot be distinguished from the educational elements of the intervention. Expanded prescribing powers and access to a wider range of medications have typically been incorporated as elements of syndromic packages in South Africa (Harrison et al. 2000) and elsewhere (Grosskurth et al. 1995, WHO 1998c, Kamali et al. 2003).

Given the increase in appropriate inhaled corticosteroid prescription, it was disappointing that ***antibiotic prescription rates***, whether combined or for individual drugs, did not differ between arms (40.5% vs. 39.9%, OR 1.19, 95% CI 0.74 to 1.41). However, the antibiotic prescription rate was substantially lower than that noted during the data collection pilot or in comparable surveys (WHO 2004b). Additionally, it may well reflect appropriate use given the severe case mix observed among enrolled patients. Only 4.8% of the sample reported symptoms consistent with an uncomplicated upper respiratory infection, that is, cough for less than 2 weeks with no difficult breathing, haemoptysis, temperature or raised respiratory rate. All other patients reported symptoms consistent with more severe respiratory disease. High rates of past and/or current tuberculosis (23.6% in the PALSA group and 23.3% in the controls), current haemoptysis (12% in both PALSA and the control group), presence of any one of four pre-defined severity markers (25.7% in the PALSA group and 16.6% in the controls) and 3 month mortality (2.2% in the PALSA group and 2.6% in the controls) attest to this. This severe case mix may well have warranted antibiotics, and the intervention group nurse practitioners may have acted appropriately by not decreasing their use.

reported being current smokers (16.5% in the PALSA group and 19.4% in the controls), compared with 47% among the sample enrolled in the Cape Town primary care clinic used in the PALSA validation study (English et al. 2006). Smoking cessation may therefore have seemed less of a priority to Free State nurses facing high burdens of infectious diseases.

In summary improvements in quality of care suggest that the intervention was effective at changing the practice of target nurse practitioners. It was therefore disappointing that these improvements did not lead to improved ***health outcomes - respiratory symptoms, quality of life, patient satisfaction or mortality*** - during the study period. There are two plausible reasons for this: either there were no improvements in these health outcomes during the course of the trial, or improvements were not detected by the instruments used in the questionnaire. The follow-up period was short at only 3 months, and improvements in quality of life and respiratory symptoms may still not have manifested for patients only recently commenced on tuberculosis treatment or inhaled corticosteroids for their asthma. Inadequate instrument validity and/ or responsiveness may also explain the lack of effect on health outcomes; at the trial's outset no respiratory-specific or generic health status measure had been translated and tested in Sesotho. The modified Royal College of Physician's Asthma Control Measure and the EuroQol-5D were translated into Sesotho specifically for purpose of the trial. Care was taken with both translations, which included a minimum of a forward and back translation, and in the case of the EuroQol, a rigorous translation protocol was followed in accordance with the EuroQol group's translation requirements (EuroQol Group 2003). But neither translated version underwent testing before being used in the trial. The Sesotho EuroQol was evaluated after the trial and found to compare well with the original across 6 types of equivalence, including construct validity for patients with respiratory disease (see Chapter 6). This, however, does not necessarily mean that the instrument was responsive enough to the small, yet clinically meaningful, changes in quality of life one might expect among patients commenced on tuberculosis treated or inhaled corticosteroids. Limited responsiveness to changes in quality of life, as

priority health outcome, tuberculosis case detection, but also to consistent improvements in process outcomes across a range of indicators and conditions. It is true that absolute improvements were modest, but because target conditions were multiple and affect a high proportion of primary care attendees, these findings are of considerable public health interest. Table 3.17 shows that one PALSA trained nurse would need to treat only 11 respiratory patients for one person to benefit; this means that during the trial alone close on 3000[9] patients benefited from the intervention, assuming that around 30% of adults attended for respiratory symptoms. Should PALSA be scaled- up to cover all primary care facilities in the Free State, this figure could be as high as 46 000[10]. These are impressive gains given the limited exposure to the intervention.

7.1.2 Health care utilisation and costs

The cost analysis revealed substantial health service and household costs for patients attending both intervention and control clinics. PALSA was consistently more expensive than usual care, although much of this cost difference was due to treating tuberculosis in primary care.

The costing was based on an ingredients approach with resource use collected separately from unit costs (Drummond et al. 1989). Health care utilisation patterns were, in many instances, consistent with effectiveness outcomes. The single largest difference was in the number of ***tuberculosis treatment visits*** completed during the

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[9] Assumptions: 172 636 adult attendances per quarter in trial clinics, 30% of adult attendances have respiratory symptoms, 2003 PHC utilisation rate in the Free State of 2.2, NNT for appropriate care is 11.

[10] Assumptions: 3 700 000 adult attendances per year (B De Winnaar – personal communication), 30% of adult attendances have respiratory symptoms, 2003 PHC utilisation rate in the Free State of 2.2, NNT for appropriate care is 11.

complex because these reflect point in time estimates and are highly susceptible to changes in work load and staffing. For example, it appears that intervention clinics had sufficient capacity to increase the number of tuberculosis monitoring visits rapidly without employing additional staff. The impact of this on tuberculosis treatment outcomes is a priority for future research. On the one hand increased compliance with five-times-a-week clinic-based DOTS may be associated with improved outcomes. Alternatively, sudden steep rises in tuberculosis case detection may have overwhelmed treatment services undermining treatment outcomes. This concern was expressed by the National Tuberculosis Control Programme manager at the start of the trial. Furthermore, a previous randomised controlled trial found that, when compared with self-supervised treatment, clinic-based DOTS was not associated with better outcomes for new cases, and was actually associated with worse outcomes for retreatment cases (Zwarenstein et al. 1998).

One-way sensitivity analysis confirmed the sizable contribution of ***tuberculosis monitoring visit costs*** to the difference in health service costs between groups, and showed that results were sensitive to unit costs used for tuberculosis visits. Subsequent cost-effectiveness analyses were therefore conducted with and without tuberculosis treatment costs. Also, tuberculosis treatment costs constitute appropriate expenditure, given the public health implications of undiagnosed active tuberculosis and the proven high cost-effectiveness of short course tuberculosis treatment (World Bank 1993), and so the decision to exclude them from further analysis is justified. Health service costs were also sensitive, although less so, to the unit costs used for inpatient days and ambulance trips because of their high unit costs.

Compared with health service costs, ***household costs*** contributed relatively little to societal costs. Again, household costs were higher among patients attending intervention clinics mainly due to transport costs for a handful of tuberculosis patients attending the clinic frequently. After public sector primary care services,

treatment costs accounted for 75% and 71% of the difference in health service and societal costs respectively.

7.1.3 Cost-effectiveness

The primary ***incremental analysis of costs and effects (ICERs)*** showed that PALSA cost the health service an extra R150[11] for each additional patient appropriately treated, and around R650 for each additional patient diagnosed with tuberculosis ignoring all other outcomes. These calculations excluded the cost of treating tuberculosis. Cost-effectiveness was lower when the societal perspective was considered, particularly if lost productivity costs were included. Analyses of uncertainty showed that the intervention could cost as much as R600 for every patient appropriately treated, or even be dominant, saving up to R200 for every patient appropriately treated. Confidence intervals for tuberculosis diagnosis alone were particularly wide, but could not be interpreted as corresponding plots fell across all four quadrants of the cost-effectiveness plane. The cost-effectiveness acceptability curves for appropriate care showed that the estimated probability that the intervention was cost-effective exceeded 50% no matter what perspective was considered or whether or not tuberculosis treatment costs were included. A 50% probability that the intervention is cost-effective corresponded to a willingness to pay value of R170 and a 90% probability of R400 in the primary analysis.

The ***cost per quality adjusted life year gained*** could not be calculated because no difference in utilities was observed during the trial. An alternative would have been to extrapolate the effects of improved quality of care for tuberculosis and obstructive lung diseases beyond the time horizon of the trial. This was not pursued as it would have required a complex chronic multi-disease model, and some rather heroic

[11] All costs quoted in 2003 South African rands.

to include a further 40 facilities without incurring additional intervention costs (Gilson et al. 1997).

The syndromic nature of the intervention, and its effect on multiple target conditions, favourably influences the cost-effectiveness of the intervention. This is particularly true for respiratory diseases, because they affect a high proportion of patients attending health services. If implemented, large numbers of patients would stand to benefit from the intervention if one assumes that improvements in process outcomes will lead to improvements in health.

Sample sizes estimated from the pilot, were realised during the trial. All 40 clinics completed the trial. The recruitment target of 50 patients per clinic was met in all but four clinics which fell just short of it, and 92.8% of patients were re-interviewed after three months. This follow-up rate surpassed expectations as fieldworkers were, in some instances, working in particularly rural settings where respondents were unable to provide street addresses or were dependent on co-operative farmers for time off from work and transport to attend the follow-up interview. This follow-up rate can be attributed to two factors. Firstly, the fieldwork was overseen by the Centre for Health Services Research and Development who have extensive experience completing large fieldwork projects throughout South Africa, and in particular the Free State. Fieldworkers were recruited from a pool of experienced interviewers, and supervised closely throughout the trial. The decision to use five decentralised teams of local fieldworkers proved invaluable in contributing the local knowledge of community networks and systems required to track down patients who did not return for follow-up interviews. Fieldworkers also used their initiative to improve follow-up rates, in one instance eliciting the help of a local community radio station when patients were inadvertently given the incorrect date for their follow-up interviews. Secondly, respondents were provided with food parcels at follow-up interviews to thank them for their participation in the trial. The patients enrolled in the study were from very poor socioeconomic circumstances and over half were unemployed. The food parcel therefore represented a significant incentive to return for the follow-up interview and partly compensated them for their time. Almost no patients refused consent to participate in the study. This may in part be attributed to the offer of a food parcel within such a socioeconomically deprived context. Also, in South Africa patients attending primary care services are accustomed to spending the most part of the day at the facility, and so the burden of participating in an interview may have posed no additional inconvenience especially for the unemployed who were not rushing back to the workplace.

The intracluster correlation co-efficients (ICC) noted for the primary outcomes (Table 3.3) were substantially higher than what was adjusted for in the sample size calculations. This may have underestimated the study's power to detect differences

reported by patients attending clinics; consultations were not observed and all intervention group patients were included in the trial whether or not they had been exposed to a trained nurse practitioner, that is, we analysed by intention to treat. The improvements in quality of care are therefore likely to represent what would happen under usual circumstances, and not when a nurse practitioner is aware her or his performance is being evaluated. They also take into account variable exposure to the intervention, which was lower than expected, reportedly due to difficulties accommodating visits in clinic schedules and to absenteeism because of night shifts, usual and sick leave, and time off to attend offsite training courses (Mayers 2004).

The ***short duration of follow-up*** was by far the most serious limitation of the study. Typically trials of this nature follow-up participants for between six months and a year. In this case, six month follow-up interviews had to be curtailed owing to limited funding available for the fieldwork exercise. It is therefore difficult to be sure that improvements in quality of care led to improved health outcomes, although this seems plausible given the proven effectiveness of inhaled corticosteroids for asthma (Cates and FitzGerald 2001, Adams et al. 2001), and impact of diagnosing tuberculosis early. It also makes it difficult to comment on the durability of the training effect. Little is known about the durability of in-service training programmes. Evidence on the durability of active dissemination strategies is starting to emerge, and suggest that such interventions may well have lasting effects, with improvements in quality of care sustained, in some instances, even years later (Sanci et al. 2000; Morgenstern et al. 2003). The short duration of follow-up may have also biased cost estimates upwards especially for those patients diagnosed with tuberculosis and who required intensive monitoring during the initial stages of treatment. These short term expenses were included while health effects, which would plausibly have manifested several months later, were not captured.

It was unfortunate that ***tuberculosis case detection*** was demoted to a secondary outcome after initial sample size estimates, and replaced with sputum screening for

practice busy schedules and responsibility for up to 70 clinics at a time meant that monitoring and evaluation visits were infrequent and brief. The possibility that trainers would engage in educational outreach type activities during these visits was therefore limited, especially considering that they had each been assigned several other clinics to train, in addition to their usual activities. Support materials were distributed by the research team, and only exact numbers of materials were distributed to minimise the chance that excess copies would find their way into control clinics. Contamination may have also occurred if nurse practitioners transferred between clinics. Clinic managers were questioned about such transfers at the end of the trial, and reported none during the study period.

The failure to measure ***the effect of PALSA on tuberculosis treatment outcomes*** is another shortcoming of the study. Because of the duration of tuberculosis treatment, routinely collected outcomes are only finalised a year to 18 months later. This went beyond the funded timeline of the study, and so a decision was made not to include them in the primary analysis.

The ***economic evaluation*** represented a comprehensive attempt to estimate the costs, and cost-effectiveness of PALSA, in comparison with usual training and support for respiratory diseases. Wherever possible, it attempted to comply with internationally accepted guidelines for performing and reporting economic evaluations (Drummond and Jefferson 1996). A completed checklist of criteria from these guidelines can be found in the appendix.

The costing component of the evaluation was reasonably comprehensive, and included changes in treatment costs as well as all aspects of guideline development and implementation costs. The estimation and inclusion of guideline development costs sets it apart from most economic evaluations of guideline dissemination and implementation strategies. ***Intervention costs*** may therefore appear quite high when

estimate confidence intervals for incremental cost-effectiveness ratios (ICERs) and estimate probabilities that the intervention was cost-effective. To our knowledge, this was the first time regression of incremental net benefits was applied to data from a cluster randomised controlled trial. Comparison with standard methods showed that those methods which do not explicitly adjust for clustering yield confidence intervals that are misleadingly precise, and higher probabilities that the intervention is cost-effective.

Questionnaires to collect data on resource use and costs tend to be long, and must make provision for capturing relevant costs if respondents have made repeated use of health related services. Given that the distribution of health costs is typically right skewed, with few patients accounting for the majority of health service expenditure (Briggs and Gray, 1999), it can be inferred that, for most respondents, there will be large sections of the questionnaire that are not applicable. This imposes a burden on researchers and fieldworkers; bulky paper questionnaires are expensive to print, need to be transported to the field, are a disincentive to participation, and require that the fieldworker pay careful attention to instructions for skipping non-applicable questions. When skip instructions are not carefully followed, errors may arise and the rate of missing information increases. In practice, this requires careful editing of completed questionnaires, imposing yet further demands on fieldwork logistics.

The questionnaire compiled for the trial made provision for details of several visits to the trial clinic as well as other health care providers to be collected. Despite careful consideration of elements for inclusion, the final enrolment questionnaire numbered 36 pages and the follow-up questionnaire 34 pages. There were also multiple skip instructions to be followed by fieldworkers, presenting a substantial burden to both fieldworker and participant. At the time of going to the field, the Biomedical Informatics Research Division of the Medical Research Council had completed development of an interview software application for portable handheld computers or PDAs (personal digital assistants) (Zwarenstein et al. 2006). This ***Handheld Personal Interview application***, or HAPI, interfaced with available computerised

visual aid. Also, the application was dependent on a small amount of battery power. If the device battery was allowed to become completely exhausted, the application, together with any information stored on it, was lost. One such incident occurred during seven months of fieldwork. Six follow-up interviews were lost but fortunately the fieldworker was able to track down all patients and re-interview them the following day.

The PALSA intervention differs from the other syndromic interventions in that it did not depend on the usual intensive offsite short courses for implementation. IMCI training numbers 11 days, the PAL-Nepal training five days, and Syndromic STI Management in Mwanza three weeks. High levels of coverage were obtained within these research contexts, but this may not be the case when routinely implemented. Certainly in the case of IMCI many countries have struggled to achieve comparable levels of coverage with the result that the programme either petered out, was sub-optimally implemented or at such low coverage that it failed to net population level benefits (WHO 2002c, Nsungwa-Sabiiti et al. 2004; Huicho et al. 2005). PALSA equipped usual nurse middle managers as outreach trainers, making the intervention more likely to be sustainable and suitable for taking to a larger scale. The training of trainers, conducted by the research team and skilled contractors could now be conducted by the trainers who were trained for this province, with some initial assistance. Furthermore, PALSA prioritised the delivery of *some* training to *many* frontline health workers, instead of high-level training for a few. Improvements in quality of care were obtained despite a low number of educational contacts, and are therefore more likely to be reproduced when taken to scale.

The use of disparate methods for the economic evaluations of syndromic interventions makes it difficult to draw meaningful comparisons between studies. Like this study, the Mwanza cost-effectiveness analysis of the impact of syndromic STI care on HIV incidence, and the PAL-Nepal study are both based on cluster randomised controlled trials, whereas the IMCI economic evaluation is based on a non-randomised controlled study. Top-down costings were employed in the Mwanza and IMCI evaluations limiting the possibilities for a detailed assessment of the impact of uncertainty, like in the PALSA trial. Patient-level data were used in the PAL-Nepal cost-effectiveness analysis with individual bootstrapping of costs and effects to estimate the level of precision, ignoring the trial's cluster randomised design. The PALSA trial was methodologically more rigorous than the other evaluations in several respects. It considered both the health service and societal perspectives, as well as the impact of lost productivity costs; it undertook a detailed

guidelines (Awad et al. 2005, Santoso 1996). It should be noted that quality of care is generally very low in these health services, and *any* implementation strategy may be effective at improving practice in comparison to usual care.

recruiting extra nurses, although the impact on staff workload and morale should be considered. Decision-makers should also consider that widescale implementation would require managers to co-ordinate training of trainers, outreach training in clinics and distribution of guidelines and materials. This function was carried out by researchers during the trial, and was limited because of the relatively small number of clinics involved.

This study also provides evidence to support ***the role of integrated care programmes in improving quality of care and strengthening health services***. In sub-Saharan Africa the recent explosion in the tuberculosis epidemic has evoked responses which are vertical and selective. Examples include the WHO's declaration of tuberculosis as a global emergency (Raviglione 2003), and, in South Africa, the crisis status attributed to tuberculosis last year (2005) by the National Department of Health (Cullinan 2006). Amid these responses little attention is paid to horizontal programmes which favour medium to long-term service strengthening and sustainability (Victora et al. 2004b). Instead vertical programmes, frequently donor funded, which promise large and immediate gains are prioritised. Victora and colleagues (2004b) argue that multitrack approaches that address both short term gains, and longer term health system strengthening, are required, instead of forcing competition between approaches. Globally, PAL is slipping on the health care agenda, as tuberculosis and AIDS take centre stage amid initiatives such as the Global Fund for AIDS, Tuberculosis and Malaria, and the "3 by 5" campaign. Ironically, it is the skilling-up of frontline multipurpose health workers, as achieved through programmes like PALSA, that is required to ensure that Millennium Development Goals for priority diseases like tuberculosis and AIDS will be met (Task Force on Health Systems Research 2004).

This study is the first to demonstrate that an ***integrated approach to the case management of respiratory diseases*** can augment passive case detection of tuberculosis. This premise was central to PAL's inclusion as one of five components of the Global DOTS Expansion Plan in the late 1990s (Raviglione 2003). Until now,

public sector antiretroviral treatment programme (South African National Department of Health 2003b). The expanded package, which also included expanded support materials and outreach training, has since been tested in a second pragmatic randomised controlled trial, the results of which are expected before year end. Since upgrading PALSA to include HIV/AIDS, results of the trial have been disseminated to local decision-makers, both nationally and at provincial level, in the Free State, and in the Western Cape. This has led to several important developments. PALSA Plus is being implemented throughout approximately 300 clinics in the Western Cape, and a further 150 in the Free State. The Human Resources Directorate of the National Department of Health is supporting a bid for the programme to be adopted nationally as the official training strategy for the Comprehensive Care, Management and Treatment of HIV and AIDS Programme and PALSA Plus is being expanded yet again, this time to support fully nurse-initiated and nurse-monitored antiretroviral treatment. The initial invitation to expand the PALSA approach to include the management of HIV/AIDS occurred before the trial was completed, and followed positive feedback from managers and recipients of the educational outreach training. Decisions to adopt the programme widely in the Free State, the Western Cape and as national policy have followed dissemination of trial results over an extended period of time spent engaging local and national managers. Thus is appears that while high face validity is an important element in attracting initial attention from decision-makers, evidence *is* contributing substantively to decisions to take the programme to a larger scale.

This work has several ***implications for health services research methods***. The shortage of implementation research in middle and low income countries has been identified as one of the key constraints to equipping weak health systems towards realising the Millennium Development Goals (Task Force on Health Systems Research 2004; Sanders and Haines 2006). Evidence on the relative effectiveness and efficiency of delivery strategies in lower and middle-income countries is urgently needed to guide decision-makers to make the best use of scarce resources. This study

study used regression of incremental net benefits, adjusted for the trial's design, to estimate confidence intervals for ICERS, and compared it against a range of techniques including individual bootstrapping of costs and effects, cluster bootstrapping of incremental net benefits and unadjusted regression. Techniques that adjusted for clustering yielded wider confidence intervals, and lower probabilities that the intervention was cost-effective. Linear regression may be invalid if small samples are used, and results should be compared with those from cluster bootstrapping. This study is, to our knowledge, the first economic evaluation alongside a cluster randomised trial to explicitly account for cluster randomisation in reporting adjusted ICER confidence intervals and probabilities that the intervention is cost-effective. Comparison of techniques suggests that regression of incremental net benefits is valid and simple to perform. Furthermore, it permits adjustment for *all* aspects of trial design, including cluster randomisation and stratification, and if required, adjustment of outcomes for baseline characteristics. This represents an important methodological contribution to cost-effectiveness analysis based on patient-level data from cluster randomised trials.

In ***conclusion***, this pragmatic trial shows that combining syndromic integrated case management of adult respiratory diseases with educational outreach, delivered by nurse managers, provides a feasible, effective and efficient means of changing the practice of clinic nurse practitioners towards evidence-based choices. These findings are likely applicable to similar resource-limited settings characterised by high burdens of HIV and tuberculosis where non-physicians provide primary care. This model is being used to implement an expanded package, including guidelines on the management of HIV/AIDS and other sexually transmitted infections. The results of the trial suggest that such efforts should continue, and be accompanied by ongoing evaluation.

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9. APPENDICES

Title	**Cost-effectiveness of improved treatment services for STIs in Mwanza, Tanzania**
References	Grosskurth et al.1995 Gilson et al. 1997 Grosskurth et al. 2000
Description	Community randomised controlled trial (closed cohort followed-up for 2 years) with prospective economic evaluation and cost-effectiveness analysis reported
Country	Mwanza district in north-west Tanzania
Setting	12 rural communities matched into 6 pairs on basis of geographical location, type of community and rates of presentation with STIs
Period	1991 – 1994 Intervention implemented in intervention communities between 1991 and 1992, delivered to control communities starting in 1994. 2 community surveys of adults aged 15-54years living in the 12 communities completed 2 years apart. Cost data collected in December 1993 (reference year for cost analysis).
INTERVENTION	
Description	• Establishment of STI reference clinic and laboratory • Health care worker training in syndromic management (3 week course, including 1 week lectures and 2 week's practical) • Regular supply of drugs • Supervisory visits • 6 monthly health education visits to villages
EPOC classification	*Health care worker training:* Educational meetings and educational materials *Village health education:* Mass media
Level of training	Not stated.
Targeted behaviour	Diagnosis Prescribing Counselling (risk reduction)
STUDY DESIGN	
Design	Community randomised controlled trial
Unit of allocation	Communities
No. of allocation units in study	12
Group 1	5 component intervention as described above
Group 2	Usual STI services
Randomisation concealment	N/A.
Protection against contamination	Yes, communities well demarcated geographically and separated by large distances (>50km).
Blinded assessment:	Not clear.
Reliable outcomes	Yes. HIV incidence established from blood samples from survey participants according to clear protocols, including ELISA assay, confirmatory ELISAs and western blot tests.
Baseline measurement	Yes. First community survey preceded intervention.
Follow-up providers:	Coverage among health workers not reported at any time point.
Follow-up survey	71% of people included in original survey re-interviewed 2 years later; 83% if deaths and those who have moved away permanently

discussed	
Quantities of resources reported separately from their unit costs	Yes. Ingredients approach used to estimate costs.
Methods for estimation of quantities and unit costs described	Quantities: information obtained from 1993 survey of prescriptions in intervention and control communities, review of labour costs associated with training, supervision and administration and running of the reference clinic. Unit costs: Labour costs estimated using 1993 salaries, drug costs estimated using 1993 prices supplied from Essential Drugs List programme.
Details of currency, price adjustments for inflation, currency conversion given.	Yes. Costs converted from Tanzanian shillings to U$ dollars in December 1993 (U$1=479.87 Tanzanian shillings).
Details of any model used	Yes. Mathematical model to estimate cost per HIV infection averted, and per DALY saved.
Choice of model used and key parameters on which it is based justified	Yes.
Analysis	
Time horizon of costs and benefits stated	Yes.
Discount rate(s) stated	Yes – 3%.
Choice of rate(s) justified	Yes, in accordance with US Panel on Cost Effectiveness in Health and Medicine's recommendations.
Explanation given if costs and benefits are not discounted	Benefits discounted at same rates (0%, 3%, 6%).
Details of statistical tests and confidence interval given for stochastic data	Yes, for effectiveness estimates.
Approach to sensitivity analysis given	Yes – one-way and multivariate sensitivity analysis used.
Choice of variable for sensitivity analysis justified	Yes – discount rate used in costing and to estimate DALYs, proportion of prescribed drugs received, proportion of central support staff time allocated to the intervention, average catchment population, reduction in HIV incidence (CI limits from effectiveness study).
Ranges over which variables are varied stated	Yes.
Relevant alternatives	Yes. Communities with and without STI intervention.

Title:	**Effectiveness and cost of facility-based IMCI in Tanzania**
References	Adam et al. 2004a Adam et al. 2004b Adam et al. 2005 Armstrong Schellenberg et al. 2004a Armstrong Schellenberg et al. 2004b Gouws et al. 2004
Description	Controlled non-randomised trial with prospective economic evaluation (cost analysis and cost consequence reported, cost-effectiveness not yet reported)
Country	Tanzania
Setting	Public sector primary care facilities (health facilities and dispensaries)
Period	IMCI implementation commenced in intervention districts in 1997; 80% coverage of healthcare workers achieved by mid 2000. Implementation commenced in control districts in 2002. Effectiveness data collected in 2000 (quality of care), and 2000–2002 (mortality from demographic surveillance systems). Cost data collected in 1999 (household and hospital costs), and 2000 (national, district and primary care facility costs). Cost data includes start-up costs incurred since 1997. Reference year for cost data is 1999.
INTERVENTION	
Description	*Facility based IMCI:* 11 day centralized training workshops based on locally adapted integrated case management guidelines, with 30% of time allocated to practical case management. Minimum of one follow-up visit in health facility within one month of training. *Health system IMCI:* Basic drugs need for IMCI case management not included in national essential drugs list available for purchase in special kits from medical stores. Integrated supervision cascade (component of TEHIP): health centres charged with supervision of dispensaries in local catchment areas, and provided with solar operated radios and motorcycles to facilitate this. *Community-based IMCI:* Not implemented but strategies consistent with the approach (e.g. social marketing of insecticide-treated bed nets) present in all 4 districts.
EPOC classification	*Facility based IMCI:* Educational meetings (workshops, traineeships) and educational materials.
Level of training	High; within 3 years of implementation 80% of health workers were trained.
Targeted behaviour	General management Diagnosis Prescribing Referral
STUDY DESIGN	
Design	Non-randomised controlled clinical trial ("plausibility"study)
Unit of allocation	District
No. of allocation units in study	4

effectiveness study	
Methods of synthesis of estimates of health given	N/A, because CEA for pre-defined indicators (years life saved, child appropriately treated) not reported.
Primary outcome measure clearly stated	Yes - Total cost of start up and implementation of IMCI in a district. Incremental cost of introducing and running IMCI in a district.
Methods to value health states and other benefits stated	N/A because health states not included.
Details of subjects from whom valuations were obtained given	N/A (see above).
Productivity changes (if included) reported separately	Collected, but not reported. Not valued monetarily and included in estimate of total cost.
Relevance of productivity changes to study question discussed	No. Unclear why productivity changes were not reported. May be planned for future publications.
Quantities of resources reported separately from their unit costs	Collected separate from unit costs; not always reported separately. Hospital costs reported separately, but not drug costs.
Methods for estimation of quantities and unit costs described	Quantities: information obtained from 1999 household survey and 2000 health facility survey Unit costs: From various sources including national department (salaries), and previous studies (cost per hospital day).
Details of currency, price adjustments for inflation, currency conversion given.	Limited to methods for adjustment – costs incurred pre-1999 were inflated to 1999 using gross domestic product deflators. 1999 costs in Tanzanian shillings were converted to U$ using official exchange rates but exact rate not specified.
Details of any model used	Ordinal least squares regression model used to explore whether the facility cost of caring for under 5s was correlated with IMCI after controlling for other factors influencing cost (facility clustering, type of facility, annual number of U5 attendances, capital availability). Proxys for complexity of services offered (presence of dental chairs and microscopes) exclude due to multicollinearity. Note that district was not included in the model as a dummy variable.
Choice of model used and key parameters on which it is based justified	Yes – key parameters described above.
Analysis	
Time horizon of	Yes, but not clear whether adjustments were made when relating costs (referenced to 1999) to quality of care indicators (measured in

	been suitably detailed, including a time and motion study to estimate the effect of IMCI on consultation time. • Methodology of economic evaluation appears reasonable with adequate attention to detail regarding cot measurement and valuation, inclusion of a regression model to explore factors impacting on facility-based costs, and a sensitivity analysis.
Weaknesses	• Non-randomised design with high level of commitment to IMCI in intervention districts, and rapid achievement of 80% coverage compared with other countries, consistent with bias. • Small number of allocation units. • Co-intervention effect of strengthened district management (TEHIP) may explain reductions in mortality. • Training interventions in comparison district not well described; unclear whether similar interventions occurred in intervention districts. • Claim that the 4 study districts are typical of others in rural Tanzania not well substantiated, as have introduced demographic surveillance systems not implemented elsewhere. • Unit of error analysis errors probable in cost analysis and quality of care indicators (inconsistent adjustment for clustering by health facility, and stratification by district). • Mortality reduction non-significant when results adjusted for clustering, and may be explained by interventions other than IMCI (e.g. social marketing of treated bed nets given that malaria leading cause of death in this region). • Start up costs, including training of health workers, annualised over 10 years without justification for choosing such a prolonged period. Reassuring that varying this period between 5 and 15 years did not impact on results, but 5 years may have been too long. Difficult to assess this without further information on coverage after mid 2000. • National level costs associated with TEHIP not included in costing. • Reference year for cost is 1999, yet effects to which they relate were collected in 2000 (health facilities) and 2000 – 2002 (mortality). Effects have not been discounted, or costs inflated to represent the year in which the effects occurred.

ECONOMIC EVALUATION	
Design of economic evaluation	
Research question	What is the cost-effectiveness of PAL?
Importance of research question	Concern whether it merits the best use of scarce health resources in Nepal.
Viewpoint	Societal (health service and households). Productivity costs data collected from patients, but subsequently excluded because of 'measurement problems'.
Alternative clearly defined	Yes, but not described in any detail. Usual care, implementation of STS (standard treatment schedule) guidelines assumed.
Form of economic evaluation stated	Cost analysis (prescription costs). Cost-effectiveness (cost-utility) analysis.
Choice of form of economic evaluation justified	Cost analysis justified because of concerns around increasing prescribing costs. Cost-effectiveness analysis based on projection model justified using recommended WHO methodology for modeling the cost-effectiveness of health interventions.
Data collection	
Source of effectiveness estimate stated	Yes – from cluster randomized trial. Difference in acute state utilities used in model, but not clear whether the difference in acute state utilities between intervention and control groups is a) statistically significant (only difference in mean and SD reported, no CIs) or b) clinically significant (not compared with clinically significant improvement in HRQoL).
Details, design and results of effectiveness study	Yes – see above.
Methods of synthesis of estimates of health given	Yes. Methods for estimating acute state utilities clearly described.
Primary outcome measure clearly stated	Prescription cost analysis: Average cost per prescription Wastage cost per prescription (Actual cost per prescription less expected cost per prescription) Cost-effectiveness analysis: Incremental cost of introducing and running IMCI in Nepal per QALY gained by the Nepal population.
Methods to value health states and other benefits stated	Choice of tariffs for converting EQ5D responses to index scores not specified. Sources for selection of model parameters based on burden of disease estimated for Nepal, and literature (number and duration of exacerbations).
Details of subjects from whom valuations were obtained given	N/A (see above).
Productivity changes (if included) reported separately	Collected, but not reported because of 'measurement problems'.
Relevance of productivity changes to study question discussed	No.

Ranges over which variables are varied stated	Yes – see above.
Relevant alternatives compared	Yes.
Incremental analysis reported	Yes.
Major outcomes presented in aggregated as well as disaggregated form	Yes.
Answer to study question given	Cost analysis: Yes. Significant reduction in number of items prescribed per visit, and significantly increased prescribing of generics and from the essential drug list did not reduce average prescription or wastage costs. Cost-effectiveness analysis: Country wide implementation of PAL, considered cost-effective compared with DALY/ GDP benchmarks.
Conclusions follow from data reported	Cost analysis: Yes. Cost-effectiveness analysis: Yes.
Conclusions accompanied by appropriate caveats	Cost analysis: Further cost-effectiveness analysis recommended. Cost-effectiveness analysi: Yes. Substantial uncertainty limits probability that intervention is cost-effective.
Strengths	• Draws on effectiveness estimates from well-designed and implemented cluster randomized trial. • Costing appears to have considered almost all relevant costs at multiple levels (national and district, patient including facility and out-of-pocket costs). • Unique multi-disease model developed to extrapolate trial findings to country-wide implementation. • Uncertainty of cost-effectiveness estimates considered using bootstrapping.
Weaknesses	• Analysis of prescription costs may have been confounded by diagnosis recorded by health workers in intervention and control facilities. • Different criteria applied to prescription details in intervention and control groups to assess appropriateness. • Prescription cost outliers were excluded from the analysis without justification. • Logistic regression of transformed cost data was used to determine difference between groups, but bootstrapping may have been more appropriate. • Not clear whether the difference in utilities between groups is statistically or clinically significant, yet this forms the basis of the comparison in the model. • Not clear why the model is based only on the acute state utilities, and not the chronic state ones, given the dominance of chronic conditions in the model. • The model does not account for differences in the duration of disease states between groups, or the incidence of acute exacerbations for chronic conditions, which could be expected to change as a result of the intervention. • Many effects (mortality, admissions) were not considered. • Depreciation of training effects was not considered, and adaptation costs were written off over a prolonged period (10 years) without justification. • Cost analysis, but not the cost-effectiveness analysis, explicating adjusted for clustering.

Bibliographic details of reviewed papers

Syndromic STI management in Mwanza, Tanzania

Grosskurth H, Mosha F, Todd J, et al. 1995. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet*. **346**: 530–36.

Grosskurth H, Gray R, Hayes R et al. 2000. Control of sexually transmitted diseases for HIV-1 prevention: understanding the implications of the Mwanza and Rakai trials. *Lancet*. **355**: 1981-87.

Gilson L, Mkanje R, Grosskurth H et al. 1997. Cost-effectiveness of improved treatment services for sexually transmitted infections in preventing HIV-1 infection in Mwanza region, Tanzania. *Lancet*. **350**:1805-09.

Facility-based IMCI in Tanzania

Adam T, Manzi F, Kakundwa C, Schellenberg J, Mgalula L. de Savigny D, Mbuya C, Wilczynska K and the MCE team in Tanzania. 2004a. Analysis report on the costs of IMCI in Tanzania. Available from: http://www.who.int/imci-mce/Publications/Tanzania_CostsR.pdf [cited 15 April 2006].

Adam T, Bishai D, Khan M, Evans D. 2004b. Methods for the Costing Component of the Multi-Country Evaluation of IMCI. World Health Organization: Department of Child and Adolescent Health. Available from: http://www.who.int/imci-mce/Publications/Costing_Methodology.pdf [cited 15 April 2006].

Shresta N, Samir KC, Baltussen R, Kafle KK, Bishai D, Niessen L. Practical approach to lung health in Nepal: better prescribing and reduction of cost. *Trop Med Int Health.* **11**(5):765-72.

No.	Reference/ country/ setting/ study design	Area of interest/ targeted behaviour	Intervention groups	Main findings
A1	Awad et al. 2005 Eltayeb et al. 2005 Sudan, doctor and medical assistant primary care cRCT (n=20)	Prescribing (antibiotics)	Grp 1: Audit & feedback Grp 2: Audit & feedback, educational meetings Grp 3: Audit & Feedback, educational outreach (individual, single visit, detailer = clinical pharmacologist) Grp 4: Usual care/ no intervention	Effective (Grps 2 and 3) Reduced mean no. of encounters where antibiotics prescribed Educational outreach more effective than adding meetings to audit and feedback
A2	Banait et al. 2003 United Kingdom, doctor-led primary care cRCT (n=114)	General management, prescribing, test-ordering (acid-related disorders)	Grp 1: Educational outreach (group, 2 visits, detailer = hospital specialist), educational materials Grp 2: Educational materials	Effective Increases in H. Pylori testing and appropriate referrals in Grp 1
A3	Brown et al. 2000 US, doctor-led primary care cRCT	General management (depression)	Grp 1: Educational outreach Grp 2: Usual care/ no intervention	Mixed effects Increase in treatment rates but no improvement in symptoms or functional status
A4	Coenen et al. 2004 Belgium, doctor-led primary care	Prescribing (antibiotics for cough lasting < 30 days in adults)	Grp 1: Educational outreach (individual, single visit, detailer = pharmacist), educational materials Grp 2: Usual care/ no intervention	Effective Reduction in no. of patients receiving an antibiotic prescription

No.	Reference/ country/ setting/ study design	Area of interest/ targeted behaviour	Intervention groups	Main findings
A6	Dey et al. 2004 United Kingdom, doctor-led primary care cRCT (n=24)	General management (acute lower back pain)	Grp 1: Educational outreach, educational materials Grp 2: Usual care/ no intervention	Mixed effects No effect on referral for Xray, issuing of sick certificates, prescribing of opiods or muscle relaxants Increased referral to a physio, and educational programme
A7	Fender et al. 1999 United Kingdom, doctor-led primary care cRCT (n=100)	Prescribing and referrals (menorrhagia)	Grp 1: Educational outreach (group, 2 visits 6 months apart, detailer = researcher) Grp 2: Usual care/ no intervention	Effective Lower no. of referrals and more use of tranexamic acid among intervention practices
A8	Figueiras et al. 2001 Spain, doctor-led primary care cRCT (n=595)	Prescribing (non-steroidal anti-inflammatory drugs [NSAID] in primary care)	Grp 1: Educational outreach (individual, single visit, detailer = pharmacist) Grp 2: Educational outreach (group, single visit, detailer = pharmacist) Grp 3: Usual care/ no intervention	Effective Improved NSAID prescribing sustained after 9 months' follow-up (individual > group educational outreach)
A9	Freemantle et al. 2002 United Kingdom, doctor-led primary care cRCT (n=60)	General management, prescribing across 4 disease areas (aspirin as antiplatelet therapy, ACE inhibitors in cardiac failure, NSAIDS for pain due to osteoarthritis, antidepressants), EBOR (Evidence-based outreach) trial	Grp 1: Educational outreach (group, 4 visits, detailer = community pharmacist) in 2/4 guideline topics, educational materials Grp 2: Educational outreach (group, 4 visits, detailer = community pharmacist) in 2/4 guideline topics, educational materials	Effective Improvement in prescribing practices and compliance with guidelines (smaller practices > larger practices)

No.	Reference/ country/ setting/ study design	Area of interest/ targeted behaviour	Intervention groups	Main findings
A15	Jackson et al. 2004 Australia, doctor-led primary care CCT (n=2)	Prescribing (antithrombotics for stroke prevention in patients with atrial fibrillation)	Grp 1: Educational outreach (individual, multiple visits, detailer = not specified), educational materials Grp 2: Usual care/ no intervention	Effective Increase in warfarin prescriptions among patients attending intervention group GPs
A16	Kim et al. 1999 US, doctor-led primary care cRCT (n=41)	General management of preventive medicine (immunisation, cancer screening, smoking cessation counselling)	Grp 1: Educational outreach (individual/ group, 2 visits, detailer = pharmacist), educational materials, educational meetings Grp 2: Educational materials, educational meetings	No effect
A17	Lin et al. 2001 US, doctor-led primary care cRCT (n=109)	General management, prescribing (depression)	Grp 1: Educational outreach (individual, single visit, detailer = psychiatrist), educational meetings, audit and feedback Grp 2: Usual care/ no intervention	No effect On diagnosis or prescribing
A18	Lobo et al. 2002 The Netherlands, doctor-led primary care cRCT	General management (cardiovascular preventive care)	Grp 1: Educational outreach (group, 15 visits over 21 months, detailers = nurses) Grp 2: Usual care/ no intervention	Effective Improved provision of cardiovascular preventive care
A19	Majumdar et al. 2003 Canada (rural), doctor-led primary care cRCT (n=2)	General management (type 2 diabetes)	Grp 1: Educational outreach (group, 2-6 visits, detailer = specialist physician), educational outreach (individual, 6 visits, detailer = pharmacist), educational meetings Grp 2: Educational meetings	Mixed effect Significant improvement in BP control, non-significant improvement in HbA1C and cholesterol Improved patient satisfaction
A20	Majumdar et al. 2005 US, doctor-led primary care CCT (n=14)	Test-ordering, prescribing (acid-related disorders)	Grp 1: Educational outreach (group, no. of visits not specified, detailer = gastroenterologist [initial] and pharmacist [follow-up]), educational materials Grp 2: Educational materials Grp 3: Usual care/ no intervention	Educational outreach effective – increased test-ordering for H. Pylori and reduced PPI prescriptions

No.	Reference/ country/ setting/ study design	Area of interest/ targeted behaviour	Intervention groups	Main findings
A26	Pagaiya et al. 2005 Thailand nurse-led primary care cRCT (n=18)	Prescribing (antibiotics for childhood ARI & diarrhoea, diazepam for adults), general management (diabetes in adults)	Grp 1: Educational outreach (group, single visit, detailer not specified), educational meetings (3 day workshop) Grp 2: Usual care/ no intervention	Mixed effects Improved management of ARI, provision of rehydration solution for diarrhoea, no improvement in antibiotic prescribing for diarrhoea, diazepam prescribing
A27	Pattinson et al. 2005 South Africa, hospital-based practice cRCT (n=34)	General management (provision of kangeroo mother care)	Grp 1: Educational outreach (group, 3 visits, detailer = not specified), educational materials Grp 2: Educational materials	Effective Increase in provision of kangeroo care in educational outreach hospitals after 8 months
A28	Preston et al. 2000 US, doctor-led primary care CCT (n=not specified clearly)	Screening (mammography among women aged 65-74 years)	Grp 1: Educational outreach, audit & feedback, local opinion leaders, reminders, educational materials Grp 2: Usual care/ no intervention	Effective Increase in mammography rates among women attending intervention practices
A29	Ricordeau et al. 2003 France, doctor-led primary care ITS	General management, test-ordering (diabetes)	Intervention: Educational outreach (individual/ group, single visit, detailer = not specified, telephone calls)	Effective Increase in number of HbA1C and urine microalbuminuria tests ordered
A30	Shaw et al. 2003 Australia, hospital-based practice CCT (n=2)	Prescribing (errors in prescriptions for drugs of addiction)	Grp 1: Educational outreach (individual, single visit, detailer = not specified), educational materials Grp 2: Usual care/ no intervention	Effective Reduced error rates in prescriptions
A31	Sheinfeld Gorin et al. 2000 US, doctor-led primary care Non-randomised CBA (n=122)	Cancer screening (cervical, breast, lung, colorectal, prostate)	Grp 1: Educational outreach (individual, 2.65 visits on average, detailer = research staff), educational materials Grp 2: Usual care/ no intervention	No effect No change in screening rates among patients

No.	Reference/ country/ setting/ study design	Area of interest/ targeted behaviour	Intervention groups	Main findings
A36	Watson et al. 2002 United Kingdom, community-based pharmacies cRCT (n=60)	Prescribing (over-the-counter antifungals for vulvovaginal candidiasis)	Grp 1: Educational outreach (group, single visit, detailer = pharmacist), educational meeting Grp 2: Educational outreach(group, single visit, detailer = pharmacist) Grp 3: Educational meeting Grp 4: Usual care/ no intervention	No effect
A37	Weller et al. 2003 Australia doctor-led primary care cRCT (n=40)	Screening (PSA for prostate cancer)	Grp 1: Educational outreach (two visits, detailer = trained pharmacist), educational materials Grp 2: Educational materials Grp 3: Usual care/ no intervention	Mixed effects Significantly lower PSA testing rates among 70-79 year old men (only age grp with effect) in outreach group, but not sustained at 12 months
A38	Witt et al. 2004 Denmark doctor-led primary care cRCT (n=100)	Prescribing (asthma medication among children)	Grp 1: Educational outreach (individual, single visit, detailer = peer doctor), educational materials Grp 2: Educational materials	No effect No change in prescribing in the short or long (1 year follow-up) term
A39	Young et al. 2002 Australia, doctor-led primary care cRCT (n=39), balanced incomplete block design	Counselling (smoking cessation)	Grp 1: Educational outreach (group, 3 sessions, detailer = peer doctor) for smoking cessation Grp 2: Educational outreach (group, 3 sessions, detailer = peer doctor) for cervical screening	Mixed effects Increased use of nicotine replacement but nothing else (advice etc.)
A40	Zwar et al. 2000 Australia, doctor-led primary care RCT (n=157)	Prescribing (benzodiazepines)	Grp 1: Educational outreach (individual, single visit, detailer = not specified) Grp 2: Usual care/ no intervention	No effect

Bibliographic details of included papers

A1 Awad (2005), Eltayeb (2005)

Awad AI, Elyayeb IB, Baraka OZ. 2005. Changing antibiotic prescribing practices in health centres of Khartoum State, Sudan. *Eur J Clin Pharmacol*. **62**(2): 135-42.

Eltayeb IB, Awad AI, Mohamed-Salih MS, Daffa-Alla MA, Ahmed MB, Ogail MA, Matowe L. 2005. Changing the prescribing patterns of sexually transmitted infections in the White Nile Region of Sudan. *Sex Transm Inf*. **81**:426-427.

A2 Banait (2003)

Banait G, Sibbald B, Thompson D, Summerton C, Hann M, Talbot S; Salford and Trafford Ulcer Research Network. 2003. Modifying dyspepsia management in primary care: a cluster randomised controlled trial of educational outreach compared with passive guideline dissemination. *Br J Gen Pract*. **53**(487):94-100.

A3 Brown (2000)

Brown JB, Shye D, McFarland BH, Nichols GA, Mullooly JP, Johnson RE. 2000. Controlled trials of CQI and academic detailing to implement a clinical practice guideline for depression. *Jt Comm J Qual Improv*. **26**(1):39-54.

A4 Coenen (2004)

Coenen S, Van Royen P, Michiels B, Denekens J. 2004. Optimising antibiotic prescribing for acute cough in general practice: a cluster randomised controlled trial. *J Antimicrob Chemother*. **54**:661-672.

A10 Goldberg (2001)

Goldberg HI, Deyo RA, Taylor VM, Cheadle AD, Conrad DA, Loeser JD, Heagerty PJ, Diehr P. 2001. Can evidence change the rate of back surgery? A randomized trial of community-based education. *Eff Clin Pract.* **4**(3):95-104.

A11 Goldstein (2003)

Goldstein MG, Niaura R, Willey C, Kazura A, Rakowski W, DePue J, Park E. 2003. An academic detailing intervention to disseminate physician-delivered smoking cessation counseling: smoking cessation outcomes of the Physicians Counseling Smokers Project. *Prev Med.* **36**(2):185-96.

A12 Griffiths (2004)

Griffiths C, Foster G, Barnes N, Eldridge S, Tate H, Begum S, Wiggins M, Dawson C, Livingstone AE, Chambers M, Coats T, Harris R, Feder GS. 2004. Specialist nurse intervention to reduce unscheduled asthma care in a deprived multiethnic area: the east London randomised controlled trial for high risk asthma (ELECTRA). *BMJ.* **328**:144-149.

A13 Hansen (1999)

Hansen LJ, Olivarius N, Beich A, Barfod S. 1999. Encouraging GPs to undertake screening and a brief intervention in order to reduce problem drinking: a randomized controlled trial. *Fam Pract.* **16**(6):551-7.

A14 Ilett (2000)

Ilett KF, Johnson S, Greenhill G, Mullen L, Brockis J, Golledge CL, Reid DB. 2000. Modification of general practitioner prescribing of antibiotics by use of a therapeutics adviser (academic detailer). *Br J Clin Pharmacol.* **49**(2):168-73.

A20 Majumdar (2005)

Majumdar SR, Ross-Degnan D, Farraye FA, Lee M, Kemp JA, Lecates RF, Henning JM, Tunis SR, Schrammel P, Soumerai SB. 2005. Controlled trial of interventions to increase testing and treatment for Helicobacter pylori and reduce medication use in patients with chronic acid-related symptoms. *Aliment Pharmacol Ther.* **21**(8): 1029-39.

A21 May (1999)

May FW, Rowett DS, Gilbert AL, McNeece JI, Hurley E. 1999. Outcomes of an educational-outreach service for community medical practitioners: non-steroidal anti-inflammatory drugs. *Med J Aust.* **170**(10):471-4.

A22 Mol (2005)

Mol PG, Wieringa JE, NannanPanday PV, Gans ROB, Degener JE, Laseur M, Haaijer-Ruskamp FM. 2005. Improving compliance with hospital antibiotic guidelines: a time-series intervention analysis. *J Antimicrob Chemother.* **55**:550-7.

A23 Naunton (2004)

Naunton M, Peterson GM, Jones G, Griffin GM, Bleasel MD. 2004. Multifaceted educational program increases prescribing of preventive medication for corticosteroid induced osteoporosis. *J Rheumatol.* **31**(3):550-6.

A24 New (2004)

New JP, Mason JM, Freemantle N, Teasdale S, Wong L, Bruce NJ, Burns JA, Gibson JM. 2004. Educational outreach in diabetes to encourage practice nurses to use primary care hypertension and hyperlipidaemia guidelines (EDEN): a randomised controlled trial. *Diabetes Medicine.* **21**: 599-603.

A30 Shaw (2003)

Shaw J, Harris P, Keogh G, Graudins L, Perks E, Thomas PS. 2003. Error reduction: academic detailing as a method to reduce incorrect prescriptions. *Eur J Clin Pharmacol.* **59**(8-9):697-9.

A31 Sheinfeld Gorin (2000)

Sheinfeld Gorin S, Gemson D, Ashford A, Bloch S, Lantigua R, Ahsan H, Neugut A. 2000. Cancer education among primary care physicians in an underserved community. *Am J Prev Med.* **19**(1):53-8.

A32 Simon (2005)

Simon SR, Majumdar SR, Prosser LA, Salem-Schatz S, Warner C, Kleinman K, Miroshnik I, Soumerai SB. 2005. Group versus individual academic detailing to improve the use of antihypertensive medications in primary care: a cluster randomised controlled trial. *Am J Med.* **118**:521-8.

A33 Solomon (2001)

Solomon DH, Van Houten L, Glynn RJ, Baden L, Curtis K, Schrager H, Avorn J. 2001. Academic detailing to improve use of broad-spectrum antibiotics at an academic medical center. *Arch Intern Med.* **161**(15):1897-902.

A34 van Eijk (2001)

van Eijk ME, Avorn J, Porsius AJ, de Boer A. 2001. Reducing prescribing of highly anticholinergic antidepressants for elderly people: randomised trial of group versus individual academic detailing. *BMJ.* **322**(7287):654-7.

A40 Zwar (2000)

Zwar NA, Wolk J, Gordon JJ, Sanson-Fisher RW. 2000. Benzodiazepine prescribing by GP registrars. A trial of educational outreach. *Aust Fam Physician.* **29**(11):1104-7.

Bibliographic details of excluded papers

Papers excluded on the basis of study design

Albert D, Ahluwalia KP, Ward A, Sadowsky D. 2004. The use of 'academic detailing' to promote tobacco-use cessation counselling in dental offices. *JADA.* **135**:1700-06.

Blackstien-Hirsch P, Anderson G, Cicutto L, McIvor A, Norton P. 2000. Implementing continuing education strategies for family physicians to enhance asthma patients' quality of life. *J Asthma.* **37**(3):247-57.

Grupper A, Grupper A, Rudin D, Drenger B, Varon D, Gilon D, Gielchinsky Y, Menashe M, Mintz Y, Rivkind A, Brezis M. 2005. Prevention of perioperative venous thromboembolism and coronary events: differential responsiveness to an intervention program to improve guidelines adherence. *Int J Qual Health Care.* **18**(2):123-126.

Scott IA, Denaro CP, Bennett CJ, Hickey AC, Mudge AM, Flores JL, Sanders DCJ, Thiele JM, Wenck B, Bennett JW, Jones MA. 2004. Achieving better in-hospital and after-hospital care of patients with acute cardiac disease. *Med J Aust.* **180**:S83-S88.

Valk GF, Renders CM, Kriegsman DMW, Newton KM, Twisk JWR, van Eijk JTM, van der Wal G, Wagner EH. 2004. Quality of care for patients with type 2 diabetes

Gonzales R, Steiner JF, Lum A, Barrett PH Jr. 1999. Decreasing antibiotic use in ambulatory practice: impact of a multidimensional intervention on the treatment of uncomplicated acute bronchitis in adults. *JAMA*. **281**(16):1512-9.

Martin CM, Doig DS, Heyland DK, Morrison T, Sibbald WJ. 2004. Multicentre, cluster-randomised clinical trial of algorithms for critical-care enteral and parenteral therapy (ACCEPT). *CMAJ*. **170**(2):197-204.

Richards D, Toop L, Graham P. 2003. Do clinical practice education groups result in sustained change in GP prescribing? *Fam Pract*. **20**(2):199-206.

Schlienger RG, Luscher TF, Schoenenberger RA, Haefeli WE. 1999. Academic detailing improves identification and reporting of adverse drug events. *Pharm World Sci*. **21**(3):110-5.

No.	Reference(s) / Country / Setting Area of interest / Targeted behaviour	Intervention Study design and main effectiveness findings	Type of economic evaluation Main findings Comment on quality of evaluation
B1	**Ref:** Banait et al. 2003 **Country:** England (North West) **Setting:** Primary care (doctor-led) **Area of interest:** Dyspepsia in adults **Targeted behaviour:** Prescribing (acid-suppressing drugs) Test ordering (Helicobater Pylori)	**Intervention:** Educational outreach (single visit, group, hospital specialist detailer) Educational meeting Educational materials **Study design and main effectiveness findings:** From cRCT (n=113) Mixed effects: increase in appropriate referrals and H. pylori testing in intervention group; no increase in proportion of major findings at endoscopy and increase in prescribing costs of acid-suppressing drugs	**Type of economic evaluation:** Cost analysis limited to drug (H2 receptor antagonists, proton pump inhibitors) costs (reported in methods, results and discussion) **Main findings:** Significant, and unexpected, increase in cost of acid suppressing drugs in intervention group. **Comment on quality:** Not all methods for costing (price year, inflation adjustment) given. Source of unit costs and no. of units given.
B2	**Ref:** Coenen et al. 2004 **Country:** Belgium **Setting:** Primary care (doctor-led) **Area of Interest:** Acute cough in adults (<30 days) **Targeted behaviour:** Prescribing of antibiotics	**Intervention:** Educational outreach (single visit, individual, pharmacist detailer) Educational materials (key messages) **Study design and main effectiveness findings:** From cRCT (n=85) Effective: reduction in number of adults with acute cough prescribed antibiotics with no difference in time to symptom resolution, re-consultation or hospitalisation rates.	**Type of economic evaluation:** Cost analysis limited to drug (reimbursed antibiotics only) costs (reported in methods, results and discussion) and cost of intervention (implementation only, €236 per visit [2000, 2001]). **Main findings:** Significantly reduced antibiotic costs per patient in intervention group without compromising patient outcomes. **Comment on quality:** Not all methods for costing (price year, inflation adjustment) given. Source of unit costs given. Discounting appropriate (>1 year) but not clear if done. Guideline development costs not reported yet process extensive.

No.	Reference(s) / Country / Setting Area of interest / Targeted behaviour	Intervention Study design and main effectiveness findings	Type of economic evaluation Main findings Comment on quality of evaluation
B5	**Ref:** Hansen et al. 1999 **Country:** Denmark **Setting:** Primary care (doctor-led) **Area of interest:** Problem drinking in adults **Targeted behaviour:** Screening Patient education/ advice	**Intervention:** Educational outreach (single visit, individual, GP researcher detailer) Educational materials (key messages on advice, questionnaire to screen for problem drinkers) **Study design and main effectiveness findings:** Direct mailing vs. telephone vs. educational outreach using educational material From cRCT (n=143) Effective: Telephone and educational outreach increased requests for package. Utilisation of package with outreach similar with mailing, but lower for telephone.	**Type of economic evaluation:** Cost analysis limited to comparison of intervention costs for different dissemination strategies. Cost implications reported in results and discussion. **Main findings:** Costs of educational outreach 16 times, and cost of telephone 10 times, higher than direct mailing. Costs reported in Danish kroner (year?). **Comment on quality:** Very limited costing (methods not given), based exclusively of cost of time related to implementation. Costs not considered: treatment costs, material development.
B6	**Ref:** Hill et al. 2002 **Country:** United States **Setting:** Primary care (doctor-led HMO) **Area of interest/ Targeted behaviour:** Prescribing	**Intervention:** Educational outreach (single visit, individual, physician peer detailer) **Study design and main effectiveness findings:** CCT (n=>600) Main outcome is change in drug costs per physician.	**Type of economic evaluation:** Cost analysis limited to drug costs (reported in results). **Main findings:** Drug expenditure among intervention group physicians increased by 0.9% compared with 2.9% in the control group (estimated cost saving: US$ 232 219 [2000]). **Comment on quality:** Significance of difference in groups not reported, and not adjusted for case-mix differences. Price year and source of unit costs given. Discounting appropriate (>1 year) but not clear if done. Intervention costs not considered.

No.	Reference / Country / Setting Area of interest / Targeted behaviour	Intervention Study design and main effectiveness findings	Type of economic evaluation Main findings Comment on quality of evaluation
B9	**Ref:** Leviton et al. 1999 **Country:** United States **Setting:** Inpatient **Area of interest Targeted behaviour:** Corticosteroids for preterm labour/ rupture of membranes	**Intervention:** Educational outreach (single visit, individual, pharmacist detailer) Multiple others: Educational materials, educational meetings, reminders, audit and feedback, local opinion leaders, local consensus process **Study design and main effectiveness findings:** cRCT (n=27) Effective: significant increase in prescription of corticosteroids.	**Type of economic evaluation:** Comment on cost implications in discussion only. **Main findings:** Favourable policy cost-effectiveness ($77 to $1231 per neonate) given high treatment cost effectiveness ($3000 saved per neonate treated). **Comment on quality:** Insufficient detail provided to comment.
B10	**Ref:** Mol et al. 2005 **Country:** The Netherlands **Setting:** Hospital care (internal medicine) **Area of interest/ targeted behaviour:** Antimicrobial prescribing among inpatients.	**Intervention:** Educational materials (tailored guideline) introduced first Educational outreach (group and individual) with audit/feedback component followed. **Study design and main effectiveness findings:** From ITS No additional effect of educational outreach: guideline led to increased compliance (up to 86%) with antimicrobial prescribing. No additional improvement noted following outreach (limited by ceiling effect?).	**Type of economic evaluation:** Cost analysis limited to drug (antimicrobials only) costs (reported in methods, results and discussion). **Main findings:** No significant change in drug costs following introduction of guideline or outreach. Increased compliance with guidelines not associated with cost savings. **Comment on quality:** Price year and source of unit costs given. Discounting appropriate (>1 year) but not clear if done. Guideline development costs not reported yet process 'intensive'.

No.	Reference / Country / Setting Area of interest / Targeted behaviour	Intervention Study design and main effectiveness findings	Type of economic evaluation Main findings Comment on quality of evaluation
B13	**Ref:** Pagaiya et al. 2005 **Country:** Thailand **Setting:** Primary care (nurse-led) **Area of interest:** Chidren: ARTI, diarrhoea Adults: diabetes, anxiety **Targeted behaviour:** Prescribing: antibiotics for childhood illness, diazepam for adults General management: diabetes	**Intervention:** Educational meetings (3 day workshop) Educational materials (guidelines) Educational outreach (single visit, group) Audit and feedback (at outreach) **Study design and main effectiveness findings:** From cRCT (n=18) Mixed effects: improved antibiotic prescribing for ARTI, ORS for diarrhoea, diazepam for anxiety. No change in diabetes management or antibiotics for diarrhoea.	**Type of economic evaluation:** Cost analysis limited to drug costs (reported in methods, results and discussion). **Main findings:** Significantly reduced drug costs per patient in intervention group (because less antibiotics and diazepam prescribed). **Comment on quality:** Methods for costing (price year, inflation adjustment, source of unit costs) not given.
B14	**Ref:** Simon et al. 2005 **Country:** United States **Setting:** Primary care (doctor-led) **Area of interest** Hypertension **Targeted behaviour:** Prescribing (diuretics and beta-blockers)	**Intervention:** Educational outreach (single, group vs. individual, 'physican educator' detailer) Educational materials Compared passive dissemination vs. group vs. individual outreach **Study design and main effectiveness findings:** cRCT (n=9) Mixed effects: increased prescription of diuretics and beta-blockers with outreach (group and individual); no improvement in BP control.	**Type of economic evaluation:** Cost analysis limited to anti-hypertensive costs (reported in methods, results and discussion). **Main findings:** Reduction of drug costs in passive dissemination group and individual outreach groups, no change in group outreach group. Not clear whether differences significant. Individual outreach costs more than group outreach. **Comment on quality:** Price year and source of unit costs given. Discounting appropriate (>1 year) but not clear if done. Not clear what is included in intervention costs.

No.	Reference / Country / Setting Area of Interest / Targeted behaviour	Intervention Study design and main effectiveness findings	Type of economic evaluation Main findings Comment on quality of evaluation
B17	**Ref:** Weller et al. 2003; Stone et al., 2005 **Country:** Australia **Setting:** Primary care (doctor-led) **Area of Interest** PSA screening for prostate cancer **Targeted behaviour:** Screening/ test-ordering	**Intervention:** Educational outreach (2 visits, individual, trained pharmacist detailer) Educational meetings (single group seminar) Educational materials **Study design and main effectiveness findings:** From cRCT (n=40) Mixed effects: reduction (19.1%) in PSA testing, but only in >70 year age group, and not sustained at 12 months.	**Type of economic evaluation:** Cost-effectiveness analysis reported separately. Model used developed for cancer programmes. **Main findings:** Cost-effectiveness comparable with that estimated for colorectal cancer screening programmes. **Comment on quality:** Model of CEA and details provided. Excluded cost of guideline development; not clear what was included in cost of educational outreach visit. Methodologically advanced with discounting of costs and benefits, sensitivity analysis, reporting of 95% confidence intervals.

Bibliographic details of included papers

B1 Banait (2003)

Banait G, Sibbald B, Thompson D, Summerton C, Hann M, Talbot S; Salford and Trafford Ulcer Research Network. 2003. Modifying dyspepsia management in primary care: a cluster randomised controlled trial of educational outreach compared with passive guideline dissemination. *Br J Gen Pract.* **53**(487):94-100.

B2 Coenen (2004)

Coenen S, Van Royen P, Michiels B, Denekens J. 2004. Optimising antibiotic prescribing for acute cough in general practice: a cluster randomised controlled trial. *J Antimicrob Chemother.* **54**:661-672.

B3 Feder (1995)

Feder G, Griffiths C, Highton C, Eldridge S, Spence M, Southgate L. 1995. Do clinical guidelines introduced with practice based education improve care of asthmatic and diabetic patients? A randomised controlled trial in general practices in east London. *BMJ.* **311**:1473-78.

B4 Freemantle (2002), Mason (2001)

Freemantle N, Nazareth I, Eccles M, Wood J, Haines A. 2002. A randomised controlled trial of the effect of educational outreach by community pharmacists on prescribing in UK general practice. *Br J Gen Pract.* **52**(477): 290-295.

B9 Leviton (1999)

Leviton LC, Goldenberg RL, Baker CS, Schwartz RM, Freda MC, Fish LJ, Cliver SP, Rouse DJ, Chazotte C, Merkatz IR, Raczynski JM. 1999. Methods to encourage the use of antenatal corticosteroid therapy for fetal maturation: a randomised controlled trial. *JAMA*. **281**(1):46-52.

B10 Mol (2005)

Mol PG, Wieringa JE, NannanPanday PV, Gans ROB, Degener JE, Laseur M, Haaijer-Ruskamp FM. 2005. Improving compliance with hospital antibiotic guidelines: a time-series intervention analysis. *J Antimicrob Chemother*. **55**:550-7.

B11 Morrison (1999)

Morrison J. 1999. *Improving quality of referral: a cost-effectiveness evaluation of clinical guidelines for infertility management across the interface. Final report. Project No. 2-09*. Glasgow: Department of General Practice, University of Glasgow.

B12 Ofman (2003)

Ofman JJ, Segal R, Russell WL, Cook DJ, Sandhu M, Maue SK, Lowenstein EH, Pourfarzib R, Blanchette E, Ellrodt G, Weingarten SR. 2003. A randomized trial of an acid-peptic disease management program in a managed care environment. *Am J Manag Care*. **9**(6):425-33.

B13 Pagaiya (2005)

Pagaiya N, Garner P. 2005. Primary care nurses using guidelines in Thailand: a randomised controlled trial. *Trop Med Int Health*. **10**(5):471-77.

9.4 Consent form

I,.....
(Name of Patient in block letters)

have read and understood all the information given to me about my participation in this study and I have been given the opportunity to discuss it and ask questions. I voluntarily agree to take part in this study and understand that I will receive a copy of this consent form.

....
Signature of Patient Date

.....
Printed name of Patient

I have explained the nature and purpose of the study to the Patient named above.

....
Signature of Principal Investigator or delegate **Date**

.....
Printed name of Principal Investigator or delegate

Patient Initials:		Date:		Clinic:		Interviewer code:	

FREE STATE LUNG HEALTH SURVEY
SCREENING QUESTIONNAIRE

PATIENT DETAILS							
3	Enter first name:				4	Enter surname:	
5	Gender: (Mark with an X)	Male		Female			
6	Enter folder no:				7	Re-enter folder no:	

DOES THE PATIENT QUALIFY FOR THE FULL INTERVIEW?							
8	What is your date of birth? If you don't know your date of birth, enter age at last birthday.						
	9	Date:		Month		Year	→ 1987 of after? → do not continue
	11	Age at last birthday:					→ 14 years or younger? → do not continue

12	Have you participated in this study before (full questionnaire ± 1 hour)?		
	YES		→ do not continue
	NO		→ go to the next question

13	Were you seen ONLY by a doctor today?		
	YES		→ do not continue
	NO		→ go to the next question

14	Were you seen by a nurse/nursing sister today?		
	YES		→ go to the next question
	NO		→ do not continue

15	Do you have difficult breathing (tight chest, shortness of breath, wheeze) today?		
	YES		→ CONSENT → skip to question 17
	NO		→ go to the next question

16	Have you had difficult breathing (tight chest, shortness of breath, wheeze) in the last 6 months?		
	YES		→ CONSENT → go to the next question
	NO		→ go to the next question

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

MORE QUESTIONS ON DIFFICULT BREATHING (tight chest, shortness of breath, wheeze)

	Do you have difficult breathing (tight chest, shortness of breath, wheeze) today?		
28	YES		→ skip to question 30
	NO		→ go to the next question

	Have you had difficult breathing (tight chest, shortness of breath, wheeze) in the last 6 months?		
29	YES		→ go to the next question
	NO		→ Skip to Question 36 (top of page 4)

	For how long have you had or did you have difficult breathing (tight chest, shortness of breath, wheeze? Choose *one* option and enter number.		
30	Days		→ 31. Enter number:
	Weeks		→ 31. Enter number:
	Months		→ 31. Enter number:
	Years		→ 31. Enter number:

32	Does this difficult breathing trouble you continuously, so that your breathing is never quite right, or does it trouble you repeatedly but always gets completely better?	
	Continuously	
	Repeatedly	

33	Does this difficulty breathing trouble you only when walking fast on the flat or uphill or also when resting?	
	Only when walking fast / uphill	
	When resting (sitting etc.)	

34	Do you experience sharp chest pain on breathing in deeply with this current illness?	
	YES	
	NO	

35	Does your chest wheeze (make a whistling sound) when you breathe with your current illness?	
	YES	
	NO	

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

OTHER SYMPTOMS OF THIS CURRENT ILLNESS

44	With this current illness, do you sweat a lot at night so that your pajamas or bed clothes are wet?		
	YES		
	NO		

45	Do you have a runny or blocked nose with this current illness?		
	YES		
	NO		

46	Do you have a sore throat with this current illness?		
	YES		
	NO		

47	Is your ear leaking pus with your current illness?		
	YES		
	NO		

48	Are you losing weight these days?		
	YES		
	NO		

49	Has a nurse or doctor told you that you might have TB recently?		
	YES		
	NO		

50	Before this illness now, have you ever had TB before?		
	YES		
	NO		

51	Have you ever worked underground in a mine?			
	YES		→ 52: For how many years?	
	NO			

53	Interviewer: Is the patient breathless now during the interview (e.g. breathless while seated, breathless while talking, unable to speak in full sentences without stopping to breathe)?	
	YES	
	NO	

54	Interviewer: Is the patient straining his/her neck muscles in order to breathe?	
	YES	
	NO	

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed	Fieldworker tick if completed	Please correct/complete the following question (s)	Fieldworker tick if completed	Fieldworker tick if completed	Capturer tick if completed

Patient Initials:		Date:		Clinic:		Interviewer code:	

HEALTH-RELATED QUALITY OF LIFE TODAY

Read to patient (and complete with the help of the visual aid)
By placing a tick in one box in each group below, please indicate which of the following statements best describe your own state of health TODAY.

MOBILITY

61

☐	☐	☐	☐	☐
I have no problems in walking about		I have some problems in walking about		I am confined to bed

SELF-CARE

62

☐	☐	☐	☐	☐
I have no problems with self-care		I have some problems washing or dressing myself		I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

63

☐	☐	☐	☐	☐
I have no problems with performing usual activities		I have some problems with performing usual activities		I am unable to perform usual activities

PAIN / DISCOMFORT

64

☐	☐	☐	☐	☐
I have no pain or discomfort		I have moderate pain or discomfort		I have severe pain or discomfort

ANXIETY / DEPRESSION

65

☐	☐	☐	☐	☐
I am not anxious or depressed		I am moderately anxious or depressed		I am extremely anxious or depressed

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed	Fieldworker tick if completed	Please correct/complete the following question (s)	Fieldworker tick if completed	Fieldworker tick if completed	Capturer tick if completed

Patient Initials:		Date:		Clinic:		Interviewer code:	

HEALTH-RELATED QUALITY OF LIFE IN THE LAST MONTH

Read to patient (and complete with the help of the visual aid)
By placing a tick in one box in each group below, please indicate which of the following statements best describe your own state of health IN THE LAST MONTH.

MOBILITY

67

☐	☐	☐	☐	☐
I have no problems in walking about		I have some problems in walking about		I am confined to bed

SELF-CARE

68

☐	☐	☐	☐	☐
I have no problems with self-care		I have some problems washing or dressing myself		I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

69

☐	☐	☐	☐	☐
I have no problems with performing usual activities		I have some problems with performing usual activities		I am unable to perform usual activities

PAIN / DISCOMFORT

70

☐	☐	☐	☐	☐
I have no pain or discomfort		I have moderate pain or discomfort		I am have severe pain or discomfort

ANXIETY / DEPRESSION

71

☐	☐	☐	☐	☐
I am not anxious or depressed		I am moderately anxious or depressed		I am extremely anxious or depressed

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed	Fieldworker tick if completed	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

SMOKING

73	**Have you ever smoked?**		
	YES		→ go to the next question
	NO		→ skip to question 91 (top of page 12)

74	**Do you smoke currently?**		
	YES		→ go to the next question
	NO		→ skip to question 83 (this page)

75 to 77	**On average how many of the following items do you smoke per day?** Mark appropriate boxes and enter average number smoked per day. Check all that apply.		
	Shop-bought cigarettes		→ 75. Enter no. smoked per day:
	Hand-rolled cigarettes		→ 76. Enter no. smoked per day:
	Pipefuls of tobacco		→ 77. Enter no. smoked per day:

78	**When did you start smoking regularly (at least one cigarette / pipe per day)?** Interviewer: You may enter the age OR the year:		
	AGE		→ 79. Enter age:
	YEAR		→ 80. Enter year:

81	**Did the nurse who saw you today advise you to reduce or quit smoking?**		
	YES		
	NO		

82	**Which of the following best describes your thoughts about stopping smoking now?** Interviewer: Read all 3 statements to patient and ask them to choose one.		
	I will stop smoking		→ skip to question 92 (top of page 12)
	I plan to stop smoking but not now		→ skip to question 92 (top of page 12)
	I do not plan to stop smoking soon		→ skip to question 92 (top of page 12)

83	**When did you stop smoking?** Interviewer: You may enter age OR year:		
	AGE		→ 84. Enter age:
	YEAR		→ 85. Enter year:

86	**When did you start smoking regularly (at least one cigarette / pipe per day)?** Interviewer: You may enter the age OR the year:		
	AGE		→ 87. Enter age:
	YEAR		→ 88. Enter year:

89 to 91	**On average how many of the following items did you smoke per day?** Mark appropriate boxes and enter average number smoked per day. Check all that apply.		
	Shop-bought cigarettes		→ 89. Enter no. smoked per day:
	Hand-rolled cigarettes		→ 90. Enter no. smoked per day:
	Pipefuls of tobacco		→ 91. Enter no. smoked per day:

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed	Capturer tick if completed

Patient Initials:		Date:		Clinic:		Interviewer code:	

PRESCRIPTION DETAILS – Inhalers (Visual Aid pages 28 – 29)

Interviewer: Show patient photo's of inhalers in visual aid (pages 28 and 29).
First ask patient to identify inhalers *they received to take home today*. Complete the tables below.
Then ask them to identify the inhalers *they usually use at home*. Complete the second set of tables below.

101	**Did you receive an inhaler to take home today?**		
	YES		→ complete the following 2 tables (Reliever & Preventer inhalers)
	NO		→ skip to question 117 (this page)

RELIEVER INHALERS RECEIVED TODAY (Interviewer: Check all that apply)				YES	NO
102	Fenoterol (Berotec)		→ 103. Does this inhaler improve your difficult breathing minutes after using it?		
104	Fenoterol/Ipratropium (Duovent)		→ 105. Does this inhaler improve your difficult breathing minutes after using it?		
106	Ipratropium (Atrovent)		→ 107. Does this inhaler improve your difficult breathing minutes after using it?		
108	Salbutamol (Asthavent)		→ 109. Does this inhaler improve your difficult breathing minutes after using it?		
110	Salbutamol/Ipratropium (Combivent)		→ 111. Does this inhaler improve your difficult breathing minutes after using it?		
112	Salmeterol (Serevent)		→ 113. Does this inhaler improve your difficult breathing minutes after using it?		

PREVENTER INHALERS RECEIVED TODAY (Interviewer: Choose one)			No. of times to be taken each day		No. of puffs to be taken each time	
114	Budesonide 100		115		116	
114	Budesonide 200		115		116	
114	Budesonide (don't know the dose)		115		116	

117	**If you didn't receive an inhaler today, do you usually use an inhaler?**		
	YES		→ complete the following 2 tables (Reliever & Preventer inhalers)
	NO		→ skip to question 133 (top of page 14)

RELIEVER INHALERS USUALLY USED AT HOME (Interviewer: Check all that apply)				YES	NO
118	Fenoterol (Berotec)		→ 119. Does this inhaler improve your difficult breathing minutes after using it?		
120	Fenoterol/Ipratropium (Duovent)		→ 121. Does this inhaler improve your difficult breathing minutes after using it?		
122	Ipratropium (Atrovent)		→ 123. Does this inhaler improve your difficult breathing minutes after using it?		
124	Salbutamol (Asthavent)		→ 125. Does this inhaler improve your difficult breathing minutes after using it?		
126	Salbutamol/Ipratropium (Combivent)		→ 127. Does this inhaler improve your difficult breathing minutes after using it?		
128	Salmeterol (Serevent)		→ 129. Does this inhaler improve your difficult breathing minutes after using it?		

PREVENTER INHALERS USUALLY USED AT HOME (Interviewer: Choose one)			No. of times to be taken each day		No. of puffs to be taken each time	
130	Budesonide 100		131		132	
130	Budesonide 200		131		132	
130	Budesonide (don't know the dose)		131		132	

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s):	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s):	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

PRESCRIPTION DETAILS – Antibiotics (Visual Aid pages 30 – 31)

Interviewer: Show patient photo's of antibiotics in visual aid (pages 30 and 31).
First ask patient to identify the antibiotics *they received to take home today*. Complete the tables below.
Then ask them to identify the antibiotics *they usually use at home*. Complete the second set of tables below..

140	**Did you receive an antibiotic to take home today?**		
	YES		→ complete the following table (Antibiotics received today)
	NO		→ skip to question 177 (this page)

ANTIBIOTICS RECEIVED TODAY (Interviewer: Check all that apply)

			No. of times to be taken each day		No of tablets/capsules to be taken each time		No. of days to be taken for (duration of course)	
141	Amoxicillin 250mg capsules (Betamox 250)		142		143		144	
145	Amoxicillin 500mg capsules (Betamox 500)		146		147		148	
149	Amoxicillin/calvulanic acid tablets (Bio-Amoksiklav)		150		151		152	
153	Cotrimoxazole tablets (Cozole / Bactrim)		154		155		156	
157	Doxycycline capsules (Doxyclin)		158		159		160	
161	Erythromycin tablets (Rubimycin)		162		163		164	
165	Flucloxacillin capsules (Floxapen)		166		167		168	
169	Fluconazole tablets (Diflucan)		170		171		172	
173	Penicillin VK tablets / Pen VK tablets (Betapen)		174		175		176	

177	**If you didn't receive an antibiotic today, do you usually use an antibiotic at home on a regular basis?**		
	YES		→ complete the following table (Antibiotics usually used)
	NO		→ skip to question 187 (top of page 16)

ANTBIOTICS USUALLY USED AT HOME (Interviewer: Check all that apply)

			No. of times taken each day		No of tablets/capsules taken each time	
178	Cotrimoxazole tablets (Cozole / Bactrim)		179		180	
181	Doxycycline capsules (Doxycyclin)		182		183	
184	Fluconazole tablets (Diflucan)		185		186	

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

DETAILS OF CONSULTATION cont'd

FOLLOW-UP APPOINTMENT

191 **Did the nurse ask you to return for a follow-up appointment?**
Interviewer: Check all that apply. Mark boxes with an **X**.

On a specific date	
If you feel worse	
If you don't get better	
When you run out of medication	
Before you run out of medication	
No instructions	

REFERRALS

192 **Did the nurse who saw you today refer you to a doctor?**

YES		→ go to the next question
NO		→ skip to question 194 (top of page 18)

193 **Did the nurse refer you to a doctor...**
Interviewer: Choose *one*. Mark appropriate box with an **X**.

in a hospital casualty or ward	
at this clinic to be seen today	
at this clinic for another day	
in a hospital outpatient department	

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

VISITS TO THIS CLINIC IN THE LAST 3 MONTHS cont'd

200 201	Date of Visit 1 to this clinic in last 3 months			
	Date:		Month:	

202	What was the reason for attendance for clinic visit 1? Interviewer: Check all that a; ; ly.	
	Check-up for high blood pressure	
	Check-up for diabetes ("sugar")	
	Check-up for a respiratory problem	
	Check-up for other problem	
	First visit for a respiratory problem	
	First visit for other problem	
	Other (please specify): 203	

204	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 205 (next block)
	NO	→ skip to question 232 (top of page 21)

205	Date of Visit 2 to this clinic in last 3 months			
	Date:		Month:	

206	What was the reason for attendance for clinic visit 2? Interviewer: Check all that a; ; ly.	
	Check-up for high blood pressure	
	Check-up for diabetes ("sugar")	
	Check-up for a respiratory problem	
	Check-up for other problem	
	First visit for a respiratory problem	
	First visit for other problem	
	Other (please specify): 207	

208	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 209 (next block)
	NO	→ skip to question 232 (top of page 21)

209	Date of Visit 3 to this clinic in last 3 months			
	Date:		Month:	

210	What was the reason for attendance for clinic visit 3? Interviewer: Check all that apply.	
	Check-u; for hi ;h blood ; ressure	
	Check-u; for diabetes ("su ;ar")	
	Check-up for a respiratory ; roblem	
	Check-u; for other ; roblem	
	First visit for a res; iratory problem	
	First visit for other ; roblem	
	Other (; lease s; ecify): 211	

212	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 213 (next block)
	NO	→ skip to question 232 (top of page 21)

213	Date of Visit 4 to this clinic in last 3 months			
	Date:		Month:	

214	What was the reason for attendance for clinic visit 4? Interviewer: Check all that apply.	
	Check-u; for hi ;h blood ; ressure	
	Check-u; for diabetes ("su ;ar")	
	Check-u; for a respiratory problem	
	Check-u; for other ; roblem	
	First visit for a res; iratory ; roblem	
	First visit for other ; roblem	
	Other (; lease s; ecify): 215	

216	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 217 (next block)
	NO	→ skip to question 232 (top of page 21)

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s):	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s):	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

VISITS TO THIS CLINIC IN THE LAST 3 MONTHS cont'd

Interviewer: Show patient transport photo's in visual aid (page 34).

232 How do you usually travel to this clinic?
Use visual aid to select a mode of transport. Choose *one* (Mark box with an **X**)

Walk				
Bicycle				
Animal (e.g. donkey)				
Taxi	233		→234. Enter amount paid for return fare to clinic by taxi:	R:
Bus	235		→236. Enter amount paid for return fare to clinic by bus:	R:
Train	237		→238. Enter amount paid for return fare to clinic by train:	R:
Private motor vehicle				
Ambulance	239		→241. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
Other				

242 How long does it usually take you to travel to the clinic and back home again (travel time + time spent at clinic)?
Choose *one* (Mark box with an X)

Overnight		→244. Enter rands spent on accommodation	R:
		→246. Enter rands spent on food and drink	R:
Between 2 and 12 hrs			
Less than 2 hours			

247 Does someone usually accompany/escort you to the clinic?

YES		→ go to the next question
NO		→ skip to question 263 (top of page 22)

248 What is the employment status of your usual companion/escort?
Choose *one* (Mark box with an X)

Employed	249		→ go to question 250 (next block)	
Self-employed	249		→ go to question 250 (next block)	
Unemployed			→ skip to question 263 (top of page 22)	
Student/Scholar	259		→260. Days unable to attend school/ college because of accompanying you to the clinic: (then go to question 263)	
Looking for work	261		→262. Days unable to look for work because of accompanying you to the clinic: (then go to question 263)	
Receiving Grant/Pension			→ skip to question 263 (top of page 22)	
Other			→ skip to question 263 (top of page 22)	

250 On what basis is your companion/escort employed?
Choose one (Mark box with an **X**)

Casual	251		→252. Enter average no. of days worked per week	
			→253. Enter average amount brought home per day (after deductions e.g. tax)	
			→258. Enter no. of days unable to work to accompany you to the clinic	
Weekly	254		→255. Enter average amount brought home per week (after deductions e.g. tax)	
			→258. Enter no. of days unable to work to accompany you to the clinic	
Monthly	256		→257. Enter average amount brought home per month (after deductions e.g. tax)	
			→258. Enter no. of days unable to work to accompany you to the clinic	

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

273 **How did you travel to this health care provider for that visit / admission?**
Use visual aid to select a mode of transport. Choose *one* (Mark box with an **X**)

Walk				
Bicycle				
Animal (e.g. donkey)				
Taxi	274		→275. Enter amount paid for return fare to HCP by taxi:	R:
Bus	276		→277. Enter amount paid for return fare to HCP by bus:	R:
Train	278		→279. Enter amount paid for return fare to HCP train:	R:
Private motor vehicle				
Ambulance	280		→282. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
Other				

283 **How long did it take you to visit the HCP from the time you left home until the time you got back home again (travel time + time spent at HCP)?**
Choose *one* (Mark box with an X)

Overnight		→285. Enter rands spent on accommodation	R:
		→287. Enter rands spent on food and drink	R:
Between 2 and 12 hrs			
Less than 2 hours			

288 **Did someone accompany you to the health care provider?**

YES		→ go to the next question
NO		→ skip to question 304 (at bottom of page)

289 **What is the employment status of your companion?**
Choose *one* (Mark box with an X)

Employed	290		→ go to question 291 (next block)	
Self-employed	290		→ go to question 291 (next block)	
Unemployed			→ skip to question 304 (bottom of page)	
Student/Learner	300		→301. Days unable to attend school/ college because of accompanying you to HCP: (then go to question 304)	
Looking for work	302		→303. Days unable to look for work because of accompanying you to HCP: (then go to question 304)	
Receiving Grant/Pension			→ skip to question 304 (bottom of page)	
Other			→ skip to question 304 (bottom of page)	

291 **On what basis is your companion/escort employed?**
Choose one (Mark box with an **X**)

Casual	291		→293. Enter average no. of days worked per week	
			→294. Enter average amount brought home per day (after deductions e.g. tax)	
			→299. Enter no. of days unable to work to accompany you to the HCP	
Weekly	295		→296. Enter average amount brought home per week (after deductions e.g. tax)	
			→299. Enter no. of days unable to work to accompany you to the HCP	
Monthly	297		→298. Enter average amount brought home per month (after deductions e.g. tax)	
			→299. Enter no. of days unable to work to accompany you to the HCP	

304 **Is there another visit in the last 3 months to a health care provider other than this clinic which we have not discussed?**

YES		→go to the next question (top of page 23)
NO		→ skip to question 469 (top of page 32)

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

314	How did you travel to this health care provider for that visit / admission? Use visual aid to select a mode of transport. Choose *one* (Mark box with an **X**)				
	Walk				
	Bicycle				
	Animal (e.g. donkey)				
	Taxi	315		→318. Enter amount paid for return fare to HCP by taxi:	R:
	Bus	317		→318. Enter amount paid for return fare to HCP by bus:	R:
	Train	319		→320. Enter amount paid for return fare to HCP train:	R:
	Private motor vehicle				
	Ambulance	321		→323. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
	Other				

324	How long did it take you to visit the HCP from the time you left home until the time you got back home again (travel time + time spent at HCP)? Choose *one* (Mark box with an X)			
	Overnight		→326. Enter rands spent on accommodation	R:
			→328. Enter rands spent on food and drink	R:
	Between 2 and 12 hrs			
	Less than 2 hours			

329	Did someone accompany you to the health care provider?		
	YES		→ go to the next question
	NO		→ skip to question 345 (at bottom of page)

330	What is the employment status of your companion/escort? Choose *one* (Mark box with an X)				
	Employed	331		→ go to question 332 (next block)	
	Self-employed	331		→ go to question 332 (next block)	
	Unemployed			→ skip to question 345 (bottom of page)	
	Student/Learner	340		→342. Days unable to attend school/ college because of accompanying you to HCP: (then go to question 345)	
	Looking for work	343		→344. Days unable to look for work because of accompanying you to HCP: (then go to question 345)	
	Receiving Grant/Pension			→ skip to question 345 (bottom of page)	
	Other			→ skip to question 345 (bottom of page)	

332	On what basis is your companion/escort employed? Choose one (Mark box with an **X**)				
	Casual	333		→334. Enter average no. of days worked per week	
				→335. Enter average amount brought home per day (after deductions e.g. tax)	
				→340. Enter no. of days unable to work to accompany you to the HCP	
	Weekly	336		→337. Enter average amount brought home per week (after deductions e.g. tax)	
				→340. Enter no. of days unable to work to accompany you to the HCP	
	Monthly	338		→339. Enter average amount brought home per month (after deductions e.g. tax)	
				→340. Enter no. of days unable to work to accompany you to the HCP	

345	Is there another visit in the last 3 months to a health care provider other than this clinic which we have not discussed?		
	YES		→go to the next question (top of page 26)
	NO		→ skip to question 469 (top of page 32)

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s):	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s):	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

355 **How did you travel to this health care provider for that visit / admission?**
Use visual aid to select a mode of transport. Choose *one* (Mark box with an **X**)

Walk				
Bicycle				
Animal (e.g. donkey)				
Taxi	356		→357. Enter amount paid for return fare to HCP by taxi:	R:
Bus	358		→359. Enter amount paid for return fare to HCP by bus:	R:
Train	360		→361. Enter amount paid for return fare to HCP train:	R:
Private motor vehicle				
Ambulance	362		→364. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
Other				

365 **How long did it take you to visit the HCP from the time you left home until the time you got back home again (travel time + time spent at HCP)?**
Choose *one* (Mark box with an X)

Overnight		→367. Enter rands spent on accommodation	R:
		→369. Enter rands spent on food and drink	R:
Between 2 and 12 hrs			
Less than 2 hours			

370 **Did someone accompany you to the health care provider?**

YES		→ go to the next question
NO		→ skip to question 386 (at bottom of page)

371 **What is the employment status of your companion/escort?**
Choose *one* (Mark box with an X)

Employed	372		→ go to question 373 (next block)	
Self-employed	372		→ go to question 373 (next block)	
Unemployed			→ skip to question 386 (bottom of page)	
Student/Learner	382		→383. Days unable to attend school/ college because of accompanying you to HCP: (then go to question 386)	
Looking for work	384		→385. Days unable to look for work because of accompanying you to HCP: (then go to question 386)	
Receiving Grant/Pension			→ skip to question 386 (bottom of page)	
Other			→ skip to question 386 (bottom of page)	

373 **On what basis is your companion/escort employed?**
Choose one (Mark box with an **X**)

Casual	374		→375. Enter average no. of days worked per week	
			→376. Enter average amount brought home per day (after deductions e.g. tax)	
			→381. Enter no. of days unable to work to accompany you to the HCP	
Weekly	377		→378. Enter average amount brought home per week (after deductions e.g. tax)	
			→381. Enter no. of days unable to work to accompany you to the HCP	
Monthly	379		→380. Enter average amount brought home per month (after deductions e.g. tax)	
			→381. Enter no. of days unable to work to accompany you to the HCP	

386 **Is there another visit in the last 3 months to a health care provider other than this clinic which we have not discussed?**

YES		→go to the next question (top page 28)
NO		→ skip to question 469 (top of page 32)

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

396	How did you travel to this health care provider for that visit / admission? Use visual aid to select a mode of transport. Choose *one* (Mark box with an **X**)				
	Walk				
	Bicycle				
	Animal (e.g. donkey)				
	Taxi	397		→398. Enter amount paid for return fare to HCP by taxi:	R:
	Bus	399		→400. Enter amount paid for return fare to HCP by bus:	R:
	Train	401		→402. Enter amount paid for return fare to HCP train:	R:
	Private motor vehicle				
	Ambulance	403		→405. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
	Other				

406	How long did it take you to visit the HCP from the time you left home until the time you got back home again (travel time + time spent at HCP)? Choose *one* (Mark box with an X)			
	Overnight		→408. Enter rands spent on accommodation	R:
			→410. Enter rands spent on food and drink	R:
	Between 2 and 12 hrs			
	Less than 2 hours			

411	Did someone accompany you to the health care provider?		
	YES		→ go to the next question
	NO		→ skip to question 427 (at bottom of page)

412	What is the employment status of your companion/escort? Choose *one* (Mark box with an X)				
	Employed	413		→ go to question 414 (next block)	
	Self-employed	413		→ go to question 414 (next block)	
	Unemployed			→ skip to question 427 (bottom of page)	
	Student/Learner	423		→424. Days unable to attend school/ college because of accompanying you to HCP: (then go to question 427)	
	Looking for work	425		→426. Days unable to look for work because of accompanying you to HCP: (then go to question 427)	
	Receiving Grant/Pension			→ skip to question 427 (bottom of page)	
	Other			→ skip to question 427 (bottom of page)	

414	On what basis is your companion/escort employed? Choose one (Mark box with an **X**)				
	Casual	415		→416. Enter average no. of days worked per week	
				→417. Enter average amount brought home per day (after deductions e.g. tax)	
				→422. Enter no. of days unable to work to accompany you to the HCP	
	Weekly	418		→419. Enter average amount brought home per week (after deductions e.g. tax)	
				→422. Enter no. of days unable to work to accompany you to the HCP	
	Monthly	420		→421. Enter average amount brought home per month (after deductions e.g. tax)	
				→422. Enter no. of days unable to work to accompany you to the HCP	

427	Is there another visit in the last 3 months to a health care provider other than this clinic which we have not discussed?		
	YES		→go to the next question (top of page 30)
	NO		→ skip to question 469 (top of page 32)

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

437	How did you travel to this health care provider for that visit / admission? Use visual aid to select a mode of transport. Choose *one* (Mark box with an **X**)				
	Walk				
	Bicycle				
	Animal (e.g. donkey)				
	Taxi	438		→439. Enter amount paid for return fare to HCP by taxi:	R:
	Bus	440		→441. Enter amount paid for return fare to HCP by bus:	R:
	Train	442		→443. Enter amount paid for return fare to HCP train:	R:
	Private motor vehicle				
	Ambulance	444		→446. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
	Other				

447	How long did it take you to visit the HCP from the time you left home until the time you got back home again (travel time + time spent at HCP)? Choose *one* (Mark box with an X)			
	Overnight		→449. Enter rands spent on accommodation	R:
			→451. Enter rands spent on food and drink	R:
	Between 2 and 12 hrs			
	Less than 2 hours			

452	Did someone accompany you to the health care provider?		
	YES		→ go to the next question
	NO		→ skip to question 469 (top of next page)

453	What is the employment status of your companion/escort? Choose *one* (Mark box with an X)				
	Employed	454		→ go to question 455 (next block)	
	Self-employed	454		→ go to question 455 (next block)	
	Unemployed			→ skip to question 468 (bottom of page)	
	Student/Learner	464		→465. Days unable to attend school/ college because of accompanying you to HCP: (then go to question 468)	
	Looking for work	466		→467. Days unable to look for work because of accompanying you to HCP: (then go to question 468)	
	Receiving Grant/Pension			→ skip to question 468 (bottom of page)	
	Other			→ skip to question 468 (bottom of page)	

455	On what basis is your companion/escort employed? Choose one (Mark box with an **X**)				
	Casual	456		→457. Enter average no. of days worked per week	
				→458. Enter average amount brought home per day (after deductions e.g. tax)	
				→463. Enter no. of days unable to work to accompany you to the HCP	
	Weekly	459		→460. Enter average amount brought home per week (after deductions e.g. tax)	
				→463. Enter no. of days unable to work to accompany you to the HCP	
	Monthly	461		→462. Enter average amount brought home per month (after deductions e.g. tax)	
				→463. Enter no. of days unable to work to accompany you to the HCP	

468	Is there another visit in the last 3 months to a health care provider other than this clinic which we have not discussed?		
	YES		→ maximum number of visits entered, go to question 469 (top of page 32)
	NO		→ go to question 469 (top of page 32)

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Please correct/complete the following question (s)	Fieldworker tick if completed:	Fieldworker tick if completed:	Capturer tick if completed:

Patient Initials:		Date:		Clinic:		Interviewer code:	

ECONOMIC IMPACT OF ILLNESS

Read: We would like to understand what the economic impact of your illness has been on you and your household. In order to do this we need to know some background about your education, employment status, history and household income. We would like to remind you that all the information you give us is confidential.

485 **What was the highest standard/grade you passed at school?**
Choose *one* (Mark box with an ***X***)

Did not attend school	
Sub A or Grade 1	
Sub B or Grade 2	
Standard 1 or Grade 3	
Standard 2 or Grade 4	
Standard 3 or Grade 5	
Standard 4 or Grade 6	
Standard 5 or Grade 7	
Standard 6 or Grade 8	
Standard 7 or Grade 9	
Standard 8 or Grade 10	
Standard 9 or Grade 11	
Standard 10 or Grade 12	

486 **Which of the following best describes your employment status?**
Choose *one* (Mark box with an X)

Employed	487		→ go to question 488 (next block)
Self-employed	487		→ go to question 488 (next block)
Unemployed			→ skip to question 499 (top of page 34)
Student/Learner	500		→501. Days unable to attend school/ college because of *any* illness in the last 3 months (then go to question 499 – top of page 33)
Looking for work	502		→503. Days unable to look for work because of *any* illness in the last 3 months: (then go to question 499 – top of page 33)
Receiving Grant/Pension			→ skip to question 499 (top of page 34)
Other			→ skip to question 499 (top of page 34)

488 **On what basis are you employed?**
Choose one (Mark box with an ***X***)

Casual	489		→490. Enter average no. of days worked per week
			→491. Enter average amount brought home per day (after deductions e.g. tax)
			→498. Enter no. of days unable to work because of *any* illness in the last 3 months
Weekly	492		→493. Enter average number of weeks worked per month
			→494. Enter average amount brought home per week (after deductions e.g. tax)
			→498. Enter no. of days unable to work because of *any* illness in the last 3 months
Monthly	495		→496. Enter average number of months worked per year
			→497. Enter average amount brought home per month (after deductions e.g. tax)
			→498. Enter no. of days unable to work because of any illness in the last 3 months

COMMENTS FROM EDITOR			COMMENTS FROM DATA CAPTURER			
Please correct/complete the following question (s)	Fieldworker tick if corrected	Fieldworker tick if corrected	Please correct/complete the following question (s)	Fieldworker tick if corrected	Fieldworker tick if corrected	Capturer tick if corrected

Patient Initials:		Date:		Clinic:		Interviewer code:	

PATIENT CONTACT DETAILS

511	**What is your home address?**		

512	**Do you have a telephone at home?**		
	YES		→ 513. Enter number:
	NO		

514	**Do you have a cellphone?**		
	YES		→ 515. Enter number:
	NO		

516	**Do you have a work address?** Enter below:		

518	**Do you have a work telephone number?**		
	YES		→ 519. Enter number:
	NO		

520	**Do you have an alternative telephone number (friend, relative, neighbour)?**		
	YES		→ 521. Enter number:
			→ 522. Enter name of contact:
			→ 523. Enter how you are related to this contact (son, friend, neighbour):
	NO		

525	**SCHEDULE PATIENT FOR FOLLOW-UP INTERVIEW AFTER 3 MONTHS** Enter date below:					
	DATE:		MONTH:		YEAR:	

END OF BASELINE INTERVIEW

LUNG HEALTH SURVEY FOLLOW-UP QUESTIONNAIRE *(English version)*

University of Cape Town Lung Institute
Centre for Health Services Research and Development, University of the Free State
Department of Community Health, University of the Free State
Medical Research Council

Patient initials:		Date:		Clinic:		Interviewer code:	

PATIENT DETAILS

3	Enter first name:				4	Enter last name:	
5	Gender: (Mark with an X)	Male		Female			
6	Enter folder no:				7	Re-enter folder no:	

8	**Do you know the year of your birth?**			
	YES		9	→ Enter year of birth & go to question 11:
	NO		10	→ Enter age at last birthday & go to question 11:

11	**Remember when we last spoke to you here at the clinic 3 months ago. Think carefully back to that day. Compared with your state of health on the day of the first interview, do you think your state of health today is...** Interviewer: Choose ONE. Mark box with an X.		
	Better		
	The same		
	Worse		

SYMPTOM SEVERITY IN THE LAST MONTH

I am now going to ask you some questions about how your chest has been in the last month. You will recognize the questions from the first interview. Please think carefully about your symptoms IN THE LAST MONTH before answering each question.

12	**Have you had difficulty sleeping because of difficulty in breathing and/or cough in the last month?**		
	YES		→ go to the next question
	NO		→ skip to question 14

13	**Select a category:** (Interviewer: Choose ONE. Mark box with an X)		
	1 – 2 times per month		
	1 – 2 times per week		
	Most nights		

14	**Have you has your usual chest symptoms during the day (cough, wheeze, breathlessness) in the last month?**		
	YES		→ go to the next question
	NO		→ skip to question 16

15	**Select a category:** (Interviewer: Choose ONE. Mark box with an X)		
	1 – 2 times per month		
	1 – 2 times per week		
	Most days		

16	**Has your chest problem interfered with your usual activities (e.g. work, study, housework, family or leisure activities) in the last month?**		
	YES		→ go to the next question
	NO		→ skip to question 18 (top of page 2)

17	**Select a category:** (Interviewer: Choose ONE. Mark box with an X)		
	1 – 2 times per month		
	1 – 2 times per week		
	Most days		

Patient Initials: | Date: | Clinic: | Interviewer code:

HEALTH-RELATED QUALITY OF LIFE TODAY cont'd

23. Read:

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale, in your opinion, how good or bad your own health is TODAY. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.

Your own state of health today

Patient initials: | Date: | Clinic: | Interviewer code:

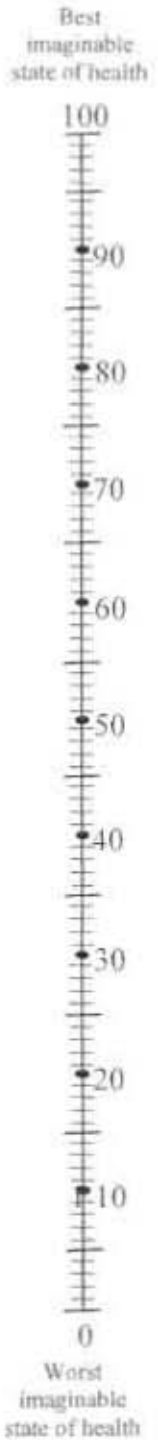
HEALTH-RELATED QUALITY OF LIFE IN THE LAST MONTH cont'd

29. Read:

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale, in your opinion, how good or bad your own health has been IN THE LAST MONTH. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health has been IN THE LAST MONTH.

Your own state of health in the last month



Patient Initials: Date: Clinic: Interviewer code:

VISITS TO *THIS* CLINIC IN THE LAST 3 MONTHS cont'd

35	VISIT 1 BACK TO *THIS* CLINIC IN THE LAST 3 MONTHS		43	VISIT 2 BACK TO *THIS* CLINIC IN THE LAST 3 MONTHS	
	Month of visit:			Month of Visit:	
36	What was the reason for attendance for clinic visit 1? Interviewer: Check ALL that apply.		44	What was the reason for attendance for clinic visit 2? Interviewer: Check all that apply.	
	Check-up for high blood pressure			Check-up for high blood pressure	
	Check-up for diabetes ("sugar")			Check-up for diabetes ("sugar")	
	Check-up for a respiratory problem			Check-up for a respiratory problem	
	Check-up for other problem			Check-up for other problem	
	First visit for a respiratory problem			First visit for a respiratory problem	
	First visit for other problem			First visit for other problem	
	Other (please specify):	37		Other (please specify):	45
38	**On that occasion, who did you see at the clinic?** Choose ONE. Mark box with an *X*.		46	**On that occasion, who did you see at the clinic?** Choose ONE. Mark box with an *X*	
	A clinic nurse			A clinic nurse	
	A doctor			A doctor	
	A clinic nurse AND a doctor			A clinic nurse AND a doctor	
	None of these			None of these	
39	Interviewer: Did the patient indicate that he/she had seen a nurse on this occasion whether or not he/she also saw a doctor?		47	Interviewer: Did the patient indicate that he/she had seen a nurse on this occasion whether or not he/she also saw a doctor?	
	YES	→ go to the next question		YES	→ go to the next question
	NO	→ skip to question 42		NO	→ skip to question 50
40	**Did the nurse tell you what was wrong with you on that occasion?**		48	**Did the nurse tell you what was wrong with you on that occasion?**	
	YES	→ go to the next question		YES	→ go to the next question
	NO	→ skip to question 42		NO	→ skip to question 50
41	**What did he/she tell you?** Interviewer: Enter response below.		49	**What did he/she tell you?** Interviewer: Enter response below.	
42	Interviewer: Enter data for another clinic visit?		50	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 43 (next block)		YES	→ go to question 51 (next page)
	NO	→ skip to question 99 (top of page 11))		NO	→ skip to question 99 (top of page 11)

Patient Initials: | Date: | Clinic: | Interviewer code:

VISITS TO *THIS* CLINIC IN THE LAST 3 MONTHS cont'd

67	VISIT 5 BACK TO *THIS* CLINIC IN THE LAST 3 MONTHS	
	Month of visit:	

68	What was the reason for attendance for clinic visit 5? Interviewer: Check ALL that apply.	
	Check-up for high blood pressure	
	Check-up for diabetes ("sugar")	
	Check-up for a respiratory problem	
	Check-up for other problem	
	First visit for a respiratory problem	
	First visit for other problem	
	Other (please specify):	69

70	On that occasion, who did you see at the clinic? Choose ONE. Mark box with an X.	
	A clinic nurse	
	A doctor	
	A clinic nurse AND a doctor	
	None of these	

71	Interviewer: Did the patient indicate that he/she had seen a nurse on this occasion whether or not he/she also saw a doctor?		
	YES		→ go to the next question
	NO		→ skip to question 74

72	Did the nurse tell you what was wrong with you on that occasion?		
	YES		→ go to the next question
	NO		→ skip to question 74

73	What did he/she tell you? Interviewer: Enter response below.

74	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 75 (next block)
	NO	→ skip to question 99 (top of page 11))

75	VISIT 6 BACK TO *THIS* CLINIC IN THE LAST 3 MONTHS	
	Month of Visit:	

76	What was the reason for attendance for clinic visit 6? Interviewer: Check all that apply.	
	Check-up for high blood pressure	
	Check-up for diabetes ("sugar")	
	Check-up for a respiratory problem	
	Check-up for other problem	
	First visit for a respiratory problem	
	First visit for other problem	
	Other (please specify)	77

78	On that occasion, who did you see at the clinic? Choose ONE. Mark box with an X.	
	A clinic nurse	
	A doctor	
	A clinic nurse AND a doctor	
	None of these	

79	Interviewer: Did the patient indicate that he/she had seen a nurse on this occasion whether or not he/she also saw a doctor?		
	YES		→ go to the next question
	NO		→ skip to question 82

80	Did the nurse tell you what was wrong with you on that occasion?		
	YES		→ go to the next question
	NO		→ skip to question 82

81	What did he/she tell you? Interviewer: Enter response below.

82	Interviewer: Enter data for another clinic visit?	
	YES	→ go to question 83 (next page)
	NO	→ skip to question 99 (top of page 11)

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

CARE RECEIVED AT *THIS* CLINIC IN THE LAST 3 MONTHS

99	**Has a nurse at this clinic collected any phlegm/sputum samples for testing in the last 3 months after our first interview?** Interviewer: Show patient pictures of sputum jars in the visual aid (pages 26 - 27).		
	YES		→ 100. How many did she collect?
	NO		

101	**Has a nurse at this clinic *asked you* to collect any phlegm/sputum samples at home in the last 3 months after our first interview?** Interviewer: Show patient pictures of sputum jars in the visual aid (pages 26 -27).		
	YES		→ 102. How many did she ask you to collect?
	NO		

103	**Have you been diagnosed with TB in the last 3 months after our first interview?**		
	YES		→ go to the next question
	NO		→ skip to question 108 (this page)

104	**Where were you diagnosed with TB?** Interviewer: Choose ONE. Mark box with an *X*.		
	In a hospital		
	At this clinic		
	At another clinic		

105	**Where are you receiving your TB treatment?** Interviewer: Choose ONE. Mark box with an *X*.		
	This clinic		
	Another clinic		

106	**When did you start your TB treatment at this clinic?** Interviewer: Ask patient to show you their TB treatment card if available					
	Date:		Month		Year	

107	**How often do or did you attend the clinic for TB treatment?** Interviewer: Choose ONE. Mark box with an *X*.		
	Once		Once every 2 weeks
	Twice		Once every 3 weeks
	Three times		Once a month
	Four times		
	Five times (Every day)		

108	**Have you had any blood tests in the last 3 months after our first interview?**		
	YES		
	NO		

109	**Have you had a chest X-ray in the last 3 months after our first interview?**		
	YES		→ 110. How many Chest X-Rays have you had?
	NO		

Patient Initials: | Date: | Clinic: | Interviewer code:

TRAVEL TO THIS CLINIC IN THE LAST 3 MONTHS

125 **Thinking back, in the last 3 months how have you usually travelled to the clinic?**
Use visual aid to select a mode of transport. Choose *ONE*. Mark box with an *X*.

Walk				
Bicycle				
Animal (e.g. donkey)				
Taxi	126		→127. Enter amount paid for return fare to the clinic by taxi:	R:
Bus	128		→129. Enter amount paid for return fare to the clinic by bus:	R:
Train	130		→131. Enter amount paid for return fare to the clinic train:	R:
Private motor vehicle				
Ambulance	132		→133. Tariff paid? Enter amount : (enter 0 if no tariff paid)	R:
Other				

135 **How long did it usually take you to visit the clinic and back home again (travel time + time spent at the clinic)?**
Choose *ONE*. Mark box with an *X*.

Overnight		→137. Enter rands spent on accommodation	R:
		→139. Enter rands spent on food and drink	R:
Between 2 and 12 hrs			
Less than 2 hours			

140 **Thinking back in the last 3 months, has someone usually accompanied you to the clinic?**

YES		→ go to the next question
NO		→ skip to question 169 (top of page 15)

141 **What is the employment status of your usual companion/escort?**
Choose *one* (Mark box with an X)

Employed	142		→ go to question 143 (next block)	
Self-employed	142		→ go to question 143 (next block)	
Unemployed			→ skip to question 169 (top of page 15)	
Student/Learner	152		→153. Days unable to attend school/ college because of accompanying you to HCP: (then skip to question 169, top of page 15)	
Looking for work	154		→155. Days unable to look for work because of accompanying you to HCP: (then skip to question 169, top of page 15)	
Receiving Grant/Pension			→ skip to question 169 (top of page 15)	
Other			→ skip to question 169 (top of page 15)	

143 **On what basis is your companion/escort employed?**
Choose one (Mark box with an *X*)

Casual	144		→145. Enter average no. of days worked per week	
			→146. Enter average amount brought home per day (after deductions e.g. tax)	
			→151. Enter no. of days unable to work to accompany you to the HCP: (then skip to question 169, top of page 15)	
Weekly	147		→148. Enter average amount brought home per week (after deductions e.g. tax)	
			→151. Enter no. of days unable to work to accompany you to the HCP: (then skip to question 169, top of page 15)	
Monthly	149		→150. Enter average amount brought home per month (after deductions e.g. tax)	
			→151. Enter no. of days unable to work to accompany you to the HCP: (then skip to question 169, top of page 15)	

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

MEDICATION

169	Interviewer: Are you conducting this interview at the patient's home or at the clinic?		
	At the patient's home		→ skip to question 230 (top of page 17)
	At the clinic		→ go to the next question

170	**Have you come to the clinic today just for the purpose of this interview or also to see a nurse/doctor?**		
	Just for the purpose of the interview		→ skip to question 230 (top of page 17)
	Also to see a nurse/doctor		→ go to the next question

MEDICATION RECEIVED TODAY

INHALERS RECEIVED TODAY

Interviewer: Show patient photo's of inhalers in visual aid (pages 28 and 29).

171	**Did you receive an inhaler to take home today?**		
	YES		→ complete the following 2 tables (Reliever & Preventer inhalers)
	NO		→ skip to question 187 (this page)

RELIEVER INHALERS RECEIVED TODAY (Interviewer: Check ALL that apply)				YES	NO
172	Fenoterol (Berotec)		→ 173. Does this inhaler improve your difficult breathing minutes after using it?		
174	Fenoterol/Ipratropium (Duovent)		→ 175. Does this inhaler improve your difficult breathing minutes after using it?		
176	Ipratropium (Atrovent)		→ 177. Does this inhaler improve your difficult breathing minutes after using it?		
178	Salbutamol (Asthavent)		→ 179. Does this inhaler improve your difficult breathing minutes after using it?		
180	Salbutamol/Ipratropium (Combivent)		→ 181. Does this inhaler improve your difficult breathing minutes after using it?		
182	Salmeterol (Serevent)		→ 183. Does this inhaler improve your difficult breathing minutes after using it?		

PREVENTER INHALERS RECEIVED TODAY (Interviewer: Choose ONE).

			No. of times taken each day		No. of puffs taken each time	
184	Budesonide 100		185		186	
184	Budesonide 200		185		186	
184	Budesonide (don't know the dose)		185		186	

PREDNISONE RECEIVED TODAY

Interviewer: Show patient photo's of prednisone tablets in visual aid (page 29).

			No. of times to be taken each day		No. of tablets to be taken each time		No. of days to be taken for	
187	Interviewer: Did the patient receive any Prednisone tablets to take home today?							
	YES		188		189		190	

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

MEDICATION THAT YOU ARE USING NOW

INHALERS THAT YOU ARE USING NOW

Interviewer: Show patient photo's of inhalers in visual aid (pages 28 and 29).

230	**Are you currently using an inhaler(s) at home?**		
	YES		→ complete the following 2 tables (Reliever & Preventer inhalers)
	NO		→ skip to question 247 (this page)

RELIEVER INHALERS THAT YOU ARE USING NOW (Interviewer: Check ALL that apply)				YES	NO
231	Fenoterol (Berotec)		→ 232. Does this inhaler improve your difficult breathing minutes after using it?		
233	Fenoterol/Ipratropium (Duovent)		→ 234. Does this inhaler improve your difficult breathing minutes after using it?		
235	Ipratropium (Atrovent)		→ 236. Does this inhaler improve your difficult breathing minutes after using it?		
237	Salbutamol (Asthavent)		→ 238. Does this inhaler improve your difficult breathing minutes after using it?		
239	Salbutamol/Ipratropium (Combivent)		→ 240. Does this inhaler improve your difficult breathing minutes after using it?		
241	Salmeterol (Serevent)		→ 242. Does this inhaler improve your difficult breathing minutes after using it?		

243	Interviewer: Is the patient using a preventer inhaler at home?		
	YES		→ complete the following table (Preventer inhalers)
	NO		→ skip to question 247 (this page)

PREVENTER INHALERS THAT YOU ARE USING NOW (Interviewer: Choose ONE)					
			No. of times taken each day		No. of puffs taken each time
244	Budesonide 100		245		246	
244	Budesonide 200		245		246	
244	Budesonide (don't know the dose)		245		246	

PREDNISONE THAT YOU ARE USING NOW

Interviewer: Show patient photo's of prednisone tablets in visual aid (page 29).

247	Interviewer: Is the patient using Prednisone tablets at home on a regular basis (this means daily or almost every day)?				
			No. of times taken each day		No. of tablets taken each time
	YES		248		249	
	NO	→ go to the next question (top of page 18)			

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

VISITS TO OTHER HEALTH CARE PROVIDERS IN THE LAST 3 MONTHS

Show patient: Pictures of other health care providers on visual aid
Read: As in the first interview, we wish to know whether you have been to any other health care provider *besides this clinic* in the last 3 months after the last interview. Other health care providers include hospitals (public, private, mine), other primary care clinics besides this one, private doctors, traditional healers etc. We would like to know about *all* visits to other health care providers, whether you attended as an outpatient or were admitted.

280	**Have you been to another health care provider besides this clinic in the last 3 months after our first interview?**		
	YES		→ go to the next question
	NO		→ skip to question 487 (top of page 29)

281	**How many times have you been to another health care provider besides this clinic in the last 3 months after our first interview?** Interviewer: Enter number below. Then enter details for the visits.

VISIT 1 to other health care provider in the last 3 months: questions 282 - 322

282 **When was your first visit to another health care provider other than this clinic in the last 3 months after our first interview?**
Choose *ONE* (Mark with an **X**)

Jan		Feb		March		April		May		June	
July		August		Sept		Oct		Nov		Dec	

283 **On this occasion, which of the following health care providers did you visit?**
Use visual aid (page 35) to select a health care provider. Choose *one* (Mark box with an **X**)

Hospital (Public or Private or Mine)		→284. Enter name of hospital:
Other PHC Clinic		
Mobile Clinic		
Workplace / Mine Clinic		
Private Doctor		
Traditional Healer		
Pharmacy / Chemist		
Other		

285 **What was the reason for this visit?**
Check all that apply. Mark boxes with **X**.

Check-up for high blood pressure		
Check-up for diabetes ('sugar")		
Check-up for a respiratory problem		
Check-up for other problem		
First visit for a respiratory problem		
First visit for other problem		
Other		→286. Specify:

287	**Did you stay overnight at this health care provider?**		
	YES		→288. Enter number of nights:
	NO		

289	**Did the health care provider charge you for that visit/ admission (consultation fee + medication)?**		
	YES		→290. How much? (consultation fee + medication): R
	NO		

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

VISITS TO OTHER HEALTH CARE PROVIDERS IN THE LAST 3 MONTHS cont'd

VISIT 2 to other health care provider in the last 3 months: questions 323 - 363

323 **When was your second visit to another health care provider other than this clinic in the last 3 months?**
Choose *ONE*. Mark with an **X**.

Jan		Feb		March		April		May		June	
July		August		Sept		Oct		Nov		Dec	

324 **On this occasion, which of the following health care providers did you visit?**
Use visual aid (page 35) to select a health care provider. Choose *ONE*. Mark box with an **X**.

Hospital (Public or Private or Mine)		→325. Enter name of hospital:
Other PHC Clinic		
Mobile Clinic		
Workplace / Mine Clinic		
Private Doctor		
Traditional Healer		
Pharmacy / Chemist		
Other		

326 **What was the reason for this visit?**
Check all that apply. Mark boxes with **X**.

Check-up for high blood pressure		
Check-up for diabetes ('sugar")		
Check-up for a respiratory problem		
Check-up for other problem		
First visit for a respiratory problem		
First visit for other problem		
Other		→327. Specify:

328 **Did you stay overnight at this health care provider?**

YES		→329. Enter number of nights:
NO		

330 **Did the health care provider charge you for that visit/ admission (consultation fee + medication)?**

YES		→331. How much? (consultation fee + medication): R
NO		

Patient Initials: | Date: | Clinic: | Interviewer code:

VISITS TO OTHER HEALTH CARE PROVIDERS IN THE LAST 3 MONTHS cont'd

VISIT 3 to other health care provider in the last 3 months: questions 364 - 404

364 When was your third visit to another health care provider other than this clinic in the last 3 months?
Choose *ONE*. Mark with an **X**.

Jan		Feb		March		April		May		June	
July		August		Sept		Oct		Nov		Dec	

365 On this occasion, which of the following health care providers did you visit?
Use visual aid (page 35) to select a health care provider. Choose *ONE*. Mark box with an **X**.

Hospital (Public or Private or Mine)		→366. Enter name of hospital:
Other PHC Clinic		
Mobile Clinic		
Workplace / Mine Clinic		
Private Doctor		
Traditional Healer		
Pharmacy / Chemist		
Other		

367 What was the reason for this visit?
Check all that apply. Mark boxes with **X**.

Check-up for high blood pressure		
Check-up for diabetes ("sugar")		
Check-up for a respiratory problem		
Check-up for other problem		
First visit for a respiratory problem		
First visit for other problem		
Other		→368. Specify:

369 Did you stay overnight at this health care provider?

YES		→370. Enter number of nights:
NO		

371 Did the health care provider charge you for that visit/ admission (consultation fee + medication)?

YES		→372. How much? (consultation fee + medication): R
NO		

Patient Initials: | Date: | Clinic: | Interviewer code:

VISITS TO OTHER HEALTH CARE PROVIDERS IN THE LAST 3 MONTHS cont'd

VISIT 4 to other health care provider in the last 3 months: questions 405 - 445

405 **When was your fourth visit to another health care provider other than this clinic in the last 3 months?**
Choose *ONE*. Mark with an **X**.

Jan		Feb		March		April		May		June	
July		August		Sept		Oct		Nov		Dec	

406 **On this occasion, which of the following health care providers did you visit?**
Use visual aid (page 35) to select a health care provider. Choose *ONE*. Mark box with an **X**.

Hospital (Public or Private or Mine)		→407. Enter name of hospital:
Other PHC Clinic		
Mobile Clinic		
Workplace / Mine Clinic		
Private Doctor		
Traditional Healer		
Pharmacy / Chemist		
Other		

408 **What was the reason for this visit?**
Check all that apply. Mark boxes with **X**

Check-up for high blood pressure		
Check-up for diabetes ('sugar')		
Check-up for a respiratory problem		
Check-up for other problem		
First visit for a respiratory problem		
First visit for other problem		
Other		→409. Specify:

410 **Did you stay overnight at this health care provider?**

YES		→411. Enter number of nights
NO		

412 **Did the health care provider charge you for that visit/ admission (consultation fee + medication)?**

YES		→413. How much? (consultation fee + medication): R
NO		

Patient Initials: | Date: | Clinic: | Interviewer code:

VISITS TO OTHER HEALTH CARE PROVIDERS IN THE LAST 3 MONTHS cont'd

VISIT 5 to other health care provider in the last 3 months: questions 446 - 486

446 **When was your fifth visit to another health care provider other than this clinic in the last 3 months?**
Choose *ONE*. Mark with an X.

Jan		Feb		March		April		May		June	
July		August		Sept		Oct		Nov		Dec	

447 **On this occasion, which of the following health care providers did you visit?**
Use visual aid (page 35) to select a health care provider. Choose *ONE*. Mark box with an *X*.

Hospital (Public or Private or Mine)		→448. Enter name of hospital:
Other PHC Clinic		
Mobile Clinic		
Workplace / Mine Clinic		
Private Doctor		
Traditional Healer		
Pharmacy / Chemist		
Other		

449 **What was the reason for this visit?**
Check all that apply. Mark boxes with *X*.

Check-up for high blood pressure		
Check-up for diabetes ('sugar')		
Check-up for a respiratory problem		
Check-up for other problem		
First visit for a respiratory problem		
First visit for other problem		
Other		→450. Specify:

451 **Did you stay overnight at this health care provider?**

YES		→452. Enter number of nights:
NO		

453 **Did the health care provider charge you for that visit/ admission (consultation fee + medication)?**

YES		→454. How much? (consultation fee + medication): R
NO		

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

CAREGIVER COSTS IN THE LAST 3 MONTHS

Read: For those of you who have been ill in the last 3 months, we wish to understand what the illness has cost your family and friends in terms of time caring for you at home. We would like you to tell us about the person who has cared for you IN THE LAST 3 MONTHS after our first interview. We only want to know about people who have looked after you because of poor health, not because of any other reasons. If more than one person has cared for you, please tell us about the person who looked after you the most.

487	**Has anyone (including family or friends) looked after you at home because of any illness in the last 3 months?**		
	YES		→ go to the next question
	NO		→ skip to question 442 (top of page 28)

488	**What is the employment status of your caregiver?** Choose one (Mark box with an X)				
	Employed	489		→ go to question 490 (next block)	
	Self-employed	489		→ go to question 490 (next block)	
	Unemployed			→ skip to question 503 (top of page 30)	
	Student/Learner	499		→500. Days unable to attend school/ college because of looking after you at home in the last 3 months (then go to question 503 – top of page 30)	
	Looking for work	501		→502. Days unable to look for work because of looking after you in the last 3 months (then go to question 503 – top of page 30)	
	Receiving Grant/Pension			→ skip to question 503 (top of page 30)	
	Other			→ skip to question 503 (top of page 30)	

490	**On what basis is your caregiver employed?** Choose one (Mark box with an X)				
	Casual	491		→492. Enter average no. of days worked per week	
				→493. Enter average amount brought home per day (after deductions e.g. tax)	
				→498. Enter no. of days unable to work because of looking after you at home in the last 3 months	
	Weekly	494		→495. Enter average amount brought home per week (after deductions e.g. tax)	
				→498. Enter no. of days unable to work because of looking after you at home in the last 3 months	
	Monthly	496		→497. Enter average amount brought home per month (after deductions e.g. tax)	
				→498. Enter no. of days unable to work because of looking after you in the last 3 months	

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

ECONOMIC IMPACT OF ILLNESS cont'd

523	**In the last year what did the household do to cope with your medical costs?** Interviewer: Choose *all* that apply. (Mark boxes with X)	
	Used own income	
	Used savings	
	Sold assets e.g animals, appliances, clothes	
	Medical Aid	
	Help from relatives	
	Help from friends	
	Borrowed money	
	Other	
	Not applicable	

524	**Has a nurse at this clinic spoken to you about HIV in the last 3 months after the first interview?**	
	YES	
	NO	

525	**Has a nurse at this clinic referred you for HIV counselling and/or testing in the last 3 months after the first interview?**	
	YES	
	NO	

526	**Have you had an HIV test (rapid test/ fingerprick method or drawing of blood from your arm) in the last 3 months after the first interview?**	
	YES	
	NO	

Patient Initials: | **Date:** | **Clinic:** | **Interviewer code:**

PATIENT SATISFACTION WITH SERVICES PROVIDED AT THE CLINIC cont'd

536	**I thought the nurse took notice of me as a person.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
537	**The time I was allowed to spend with the nurse was not long enough to deal with everything I wanted.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
538	**I understand my illness much better after seeing the nurse.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
539	**The nurse was interested in me as a person, not just my illness.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
540	**The nurse knows all about me.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
541	**I felt the nurse really knew what I was thinking.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
542	**I wish it had been possible to spend a little longer with the nurse.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
543	**I was not completely satisfied with my visit to the nurse.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
544	**I found it difficult to tell the nurse about some private things.** Interviewer: Choose *ONE*. Mark the box with an *X*.				
	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree

545	**Compared with the care provided by the nurses at the clinic 3 months ago, do you think the care provided by the nurses now is...** Interviewer: Choose ONE. Mark box with an *X*.	
	Better	
	The same	
	Worse	

	Finally, do you have any other comments or thoughts on the care you receive at this clinic? Remember this information will not be shown to any clinic staff members and will be kept entirely confidential so feel free to say what you wish.	
546	Number of positive points raised	
547	Number of negative points raised	

Thank you very much for participating in our study and returning to the clinic today for the follow-up interview. The results of the study will be used to improve primary care services for patients with respiratory illnesses. Please accept this food parcel as a sign of our appreciation for your participation.

Effect of educational outreach to nurses on tuberculosis case detection and primary care of respiratory illness: pragmatic cluster randomised controlled trial

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logistic constraints of typical, real world situations.[13 14] The unit of randomisation was the clinic, although we collected outcome data from individual patients.

Intervention

Educational outreach (non-commercial, short, face to face, in-service interactive education by a trusted outsider) is an effective strategy for promoting evidence based choices among physicians (median improvement 6%, range −4% to 17%).[15] We selected this model (box) over off-site education because it was sustainable, drawing on and expanding the educational role of existing supervisory staff, and because it minimised disruption in understaffed front line facilities.

We developed an algorithmic guideline using symptoms and simple signs for the diagnosis and management of respiratory diseases in adults, including tuberculosis, asthma and chronic obstructive pulmonary disease, acute upper and lower respiratory tract infections, and opportunistic infections in patients with HIV. We collaborated with front line clinicians and managers to ensure local applicability and consistency with national tuberculosis policies[16] and essential drugs lists.[17] We incorporated key messages from the guideline (fig 1 and see bmj.com) into a colourful, illustrated flip chart for use by the nurse trainers during educational outreach visits, and into a desk blotter (see bmj.com) for the nurse practitioners whom they trained. These were tested in pilot sites and adapted before implementation.

Eight senior nurses running the tuberculosis programme attended a five day workshop on the techniques of interactive educational outreach and the clinical content of the guidelines, especially the key messages. They were to deliver three or four educational outreach sessions, each lasting one to three hours to all clinical staff, in groups, in each of their intervention clinics over a three month period.

The Free State department of health permitted nurse practitioners in intervention clinics to newly prescribe inhaled corticosteroids for asthma (with review by a physician within one month), short course oral corticosteroids for exacerbations of obstructive lung disease, and cotrimoxazole prophylaxis for symptomatic HIV infection. The nurses had long been permitted to renew physician initiated prescriptions.

Components of the practical approach to lung health in South Africa (PALSA) intervention

- A median of two educational outreach sessions to groups of primary care nurse practitioners delivered by trained nurse supervisors
- Expanded prescribing provisions for nurse practitioners to include inhaled corticosteroids for asthma, short course oral corticosteroids for exacerbations of obstructive lung disease, and cotrimoxazole prophylaxis for symptomatic HIV infection
- Illustrated support materials for outreach sessions: flip chart for nurse trainers and desk blotters (incorporating key messages) for the nurse practitioners they trained
- Locally tailored, evidence based, brief (22 pages), symptom and sign based guideline on common respiratory conditions in adults (tuberculosis, TB/HIV coinfection, respiratory tract infections, and obstructive lung disease)

Respiratory Syndrome	Key Message
Tuberculosis	Coughing ≥ 2 weeks ⟶ Send sputa for TB.
TB/HIV co-infection	Test for HIV because TB is common in HIV patients. Cotrimoxazole prophylaxis delays symptoms and prolongs healthy life in HIV patients.
Lower Respiratory Tract Infection (LRTI)	Diagnose LRTI in patients with cough plus difficult breathing and/or pain on coughing/breathing and/or fever. If severe refer, if new or purulent sputum prescribe amoxicillin for 7 days and follow-up in one week.
Upper Respiratory Tract Infection (URTI)	Diagnose URTI in patients with blocked or runny noses and/or sore throats and/or mild fever but *no* difficult breathing and *no* chest pain. Prescribe symptomatic treatments only.
Obstructive Lung Disease (Asthma and COPD – Chronic Obstructive Pulmonary Disease)	Diagnose asthma in patients with *recurrent* wheeze, difficult breathing and cough. Prescribe inhaled corticosteroids. Diagnose COPD in patients with *persistent* wheeze, difficult breathing and cough (and a history of smoking). Prescribe bronchodilators.
Smoking Cessation	People are more likely to stop smoking if advised to do so by a health professional, and smoking makes all lung conditions worse so tell your patients to quit today!

Fig 1 Key messages as presented to front line nurses

Control clinics received no new training. Usual off-site training, received by fewer than 5% of staff each year, continued in both groups.

Participants and randomisation

The estimated prevalence of HIV among people attending antenatal clinics in impoverished communities of the Free State, predominantly in rural areas with high rates of tuberculosis and HIV (tuberculosis notification rate (all cases) 494/100 000 in 2002),[18] was 30.1% in 2003.[16] On a typical day around 200 people attend one of these clinics; about one third of these are children. A clinic is staffed by a median of nine nurses, some of whom see only children or pregnant women. Problem cases are referred to doctors who visit weekly.

On the basis of total annual attendances, we included in our study the 40 largest eligible primary care clinics. Randomisation was stratified by district. Clinics were ranked by size and allocated to intervention or control arms using a random number table in blocks of four. Allocation was carried out by a trial statistician before intervention or patient recruitment.

Patient recruitment

In each clinic waiting room a trained fieldworker screened all adult patients, independent of the nurse practitioners, for cough or difficult breathing on presentation or within the past six months. Patients aged 15 years or over who answered yes to either query and who were willing to take part in the study, were invited to meet the research team after their consultation with the nurse. Fieldworkers then obtained written consent and interviewed patients with any one of the following: difficult breathing on the day of interview or during the past six months; current cough for seven days or more; recurrent cough in the past six months; and current cough with a temperature above 38°C or a respiratory rate of 30 breaths per minute or more. We excluded patients who had been urgently referred elsewhere by

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Of the 2000 patients enrolled, 1999 completed the initial interview and one refused consent; 1856 (92.8%) were re-interviewed at four months. Forty eight patients (2.4%) were reported by their families to have died. The groups had similar mortality (intervention, 22/1000; control, 26/999; odds ratio 0.84, 95% confidence interval 0.46 to 1.53).

Training intensity fell short of the targets. Nurses in intervention clinics received a median of two educational outreach visits (range 0-4 visits).

Outcome measures

Tuberculosis

Sputum screening for tuberculosis was higher among patients in the intervention arm but not significantly so (odds ratio 1.22, 0.83 to 1.80; table 2). During the three months of the study period 57 new cases of tuberculosis were diagnosed in intervention clinics compared with 34 in control clinics (odds ratio 1.72, 1.04 to 2.85). The groups had similar numbers of patients diagnosed as having tuberculosis before outreach started (intervention clinics, 108; control clinics, 109).

Obstructive lung disease

Almost twice as many prescriptions were filled out for inhaled corticosteroids in the intervention group than in the control group (13.7%, 137/1000 *v* 7.7%, 77/999; odds ratio 1.90, 1.14 to 3.18; table 2).

At enrolment 164 patients in the intervention group and 193 patients in the control group reported that they were current smokers. The groups had similar rates for counselling on smoking cessation (68.3%, 112/164 *v* 65.8%, 127/193 in controls) and smoking cessation for the period between interviews (12.2%, 20/164 *v* 10.4%, 20/193).

Antibiotic prescriptions

The prescription rates of antibiotics commonly used for respiratory indications did not differ between the groups (odds ratio 1.01, 0.74 to 1.38; table 2).

HIV/AIDS

The groups were similar for voluntary counselling and testing (9.7%, 97/1000 *v* 7.3%, 73/999 in controls) and for prescriptions for co-trimoxazole among patients with a diagnosis of tuberculosis during the study (7.8%, 13/167 *v* 7.5%, 11/147 in controls).

Referral

A higher proportion of severely ill patients in the intervention group were referred to a doctor than in the control group (10.5%, 27/257 *v* 4.8%, 8/166; odds ratio 2.59, 1.06 to 6.19).

Discussion

An educational outreach intervention on syndromic management of respiratory diseases in adults improved the case detection of tuberculosis and the treatment of asthma by nurse practitioners working in typical South African primary care clinics. In this pragmatic trial, the intervention was a "black box" and the relative contributions of the various elements of this multifaceted intervention cannot be distinguished. Although trainers reported using almost all of their visit time for education, they were also middle managers and may, in passing, have provided some managerial support.

Clinic and patient follow-up were exceptionally high, enhancing the internal validity of our trial. The cluster randomised design was accounted for in the analysis. Follow-up was short (only four months); longer term effects could be diluted by the turnover of staff and could decline with time. Emerging studies, however, suggest that evidence based education strategies may trigger long term change in practice.[24 25]

Appropriateness of care improved across several of the most important conditions: the effect of the intervention on tuberculosis case detection was higher than expected. By contrast, the effect on sputum collection was small. This suggests that the intervention improved clinical selection of cases for sputum sampling.

Inhaled corticosteroid prescribing for asthma also increased, which may be appropriate given that these drugs are known to be underprescribed in South Africa.[3] A post hoc analysis also suggested that these prescriptions were clinically appropriate, in that response to β agonists was more often reported by patients who were prescribed inhaled corticosteroids in the intervention group than in their equivalent controls (85%, 117/137 *v* 73%, 56/77), suggesting that the treated disease was asthma.

The lack of change in antibiotic prescribing may well be appropriate for this severe case mix; only 4.8% of the sample reported symptoms consistent with uncomplicated upper respiratory tract infection, lower than in comparable surveys. In patients with predefined markers of severe disease, referral to physicians was higher in the intervention group.

The number of patients receiving voluntary counselling and testing remained unchanged. Nurses may have seen little point in this practice at a time before antiretroviral treatment was made available in South Africa.[26] Repeated central drug shortages prevented the intervention from achieving increases in prescribing of co-trimoxazole prophylaxis. The failure to increase advice on smoking cessation may reflect light smoking at low prevalence (table 1) and thus the low salience of this issue for nurse practitioners dealing with patients with acute severe infectious disease.

Table 2 Trial outcomes

Outcome	No (%) in outreach group	No (%) in control group	Odds ratio (95% CI)	P value	Intracluster correlation coefficient
Sputum screening for tuberculosis	226/1000 (22.6)	193/999 (19.3)	1.22 (0.83 to 1.80)	0.33	0.049
Tuberculosis case detection	57/892* (6.4)	34/890* (3.8)	1.72 (1.04 to 2.85)	0.04	0.007
Prescriptions for inhaled corticosteroids	137/1000 (13.7)	77/999 (7.7)	1.90 (1.14 to 3.18)	0.006	0.019
Prescriptions for antibiotics	397/1000 (39.7)	394/999 (39.4)	1.01 (0.74 to 1.38)	0.95	0.042

*Denominator limited to all patients who had not been diagnosed as having tuberculosis before educational outreach started.

What is already known on this topic

Secondhand smoke has adverse effects on health, including respiratory health

Smoke-free policies are associated with decreased exposure in the hospitality sector and possibly a rapid improvement in respiratory health in bar workers, though the size of these effects relative to underlying trends is unknown

What this study adds

After the introduction of comprehensive smoke-free workplace legislation in the Republic of Ireland, exposure to secondhand smoke and respiratory symptoms declined in non-smoking bar staff

The reductions were significantly higher than the unanticipated reductions observed in the control region

The small number not followed up differed from the overall group but because of the paired design, this does not compromise study validity. Although the numbers enrolled from Northern Ireland were small, they were sufficient to detect significant changes.

Implications of findings

The smoke-free workplace law in the Republic of Ireland seems to have provided protection for one of the most heavily exposed occupational groups. The increase in support for the law in the Republic since its introduction, even among smokers, underpins its effectiveness.[11] These findings have implications for legislators in other countries currently considering smoke-free workplace legislation.

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Competing interests: SA is a member of the Board of the Irish Office of Tobacco Control (unpaid position). IJP is chairman of the Irish Research Institute for a Tobacco Free Society.

Ethical approval: Research ethics committee of the Faculty of Public Health Medicine, Royal College of Physicians of Ireland; the St James's Hospital and Federated Dublin Voluntary Hospitals joint research ethics committee; the clinical research ethics committee of the Cork Teaching Hospitals; and the healthcare committee and senior management team of the Western Health and Social Services Board and the Western Investing for Health Partnership.

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Corrections and clarifications

Effect of educational outreach to nurses on tuberculosis case detection and primary care of respiratory illness: pragmatic cluster randomised controlled trial

In this Primary Care paper by Lara R Fairall and colleagues (*BMJ* 2005;331:750-4, 1 Oct) we inadvertently misspelt the name of one of the authors, Pat Mayers (not Myers). This has now been corrected online. A process error in the editorial office led to the figure seriously overstating the number of patients lost to follow-up in the intervention group: 70 (not 7000) patients were lost. Additionally, the authors have sent us a fuller acknowledgment for two of the contributors, Robert Scherpbier and Salah-Eddine Ottmani (http://bmj.bmjjournals.com/cgi/content/full/331/7519/750/DC2).

Cervical cancer, human papillomavirus, and vaccination

We wrongly made a last minute change to the title of the box in this editorial by Catherine M Lowndes and O Noel Gill (*BMJ* 2005;331:915-6, 22 Oct). The title should have remained as agreed with the authors, as "Some important questions for a programme for HPV vaccination" (not "Questions before starting an HPV vaccination programme"—as many of the questions listed would be impossible to answer before the vaccine is introduced). For more discussion on this, see rapid responses accompanying the editorial (http://bmj.bmjjournals.com/cgi/content/full/331/7522/915).

9.8.1 CONSORT checklist for reporting of cluster randomised trials (Campbell et al. 2004a)

Section and topic	Item	Description	Reported
TITLE & ABSTRACT	1	How participants were allocated to interventions specifying that allocation was based on clusters. (e.g., "random allocation", "randomized", or "randomly assigned").	Abstract Allocation: randomised
INTRODUCTION Background	2	Scientific background and explanation of rationale including the rationale for using a cluster design.	Chapter 1
METHODS Participants	3	Eligibility criteria for participants and clusters and the settings and locations where the data were collected	Clinics: 2.2.5.1 Patients: 2.2.6.1
Interventions	4	Precise details of the interventions intended for each group, whether they pertain to the individual level, the cluster level or both, and how and when they were actually administered.	Intervention components: 2.2.2 Intervention delivery: 3.2
Objectives	5	Specific objectives and hypotheses and whether they pertain to the individual level, the cluster level, or both.	2.1
Outcomes	6	Clearly defined primary and secondary outcome measures, whether they pertain to the individual level, the cluster level, or both, and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	Outcomes: 2.2.8 and Table 2.4 Training of fieldworkers: 2.3.4 Quality control procedures: 2.3.5
Sample size	7	How sample size was determined (including method of calculation,number of clusters, cluster size, a coefficient of intracluster correlation (ICCor k), and an indication of its	2.2.10

		together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	2.2.6 Recruitment: May to September 2003 Follow-up 12 weeks after recruitment (Figure 2.2)
Baseline data	15	Baseline demographic and clinical characteristics for the individual and cluster levels as applicable.	Clinics: Table 2.1 (baseline characteristics) Patients: Table 3.1 (enrolment characteristics)
Numbers analyzed	16	Number of clusters and participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	Numbers reported for all analyses Analysis by intention-to-treat: 2.4.1
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group for the individual or cluster level as applicable and the estimated effect size and its precision (e.g., 95% confidence interval) and a coefficient of intracluster correlation (ICC or k) for each primary outcome.	Primary outcomes: Table 3.3 Secondary outcomes: Tables 3.4 through 3.17
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	Exploratory analysis for inhaled corticosteroids: 3.5.1
Adverse events	19	All important adverse events or side effects in each intervention group.	Mortality: 3.10
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Interpretation of results: Effectiveness: 7.1.1

9.8.2 Checklist of criteria for the completion and reporting of economic evaluations of healthcare interventions (Drummond and Jefferson 1996)

Section and topic	Reported
DESIGN OF ECONOMIC EVALUATION	
Research question stated	Tabe 1.17 2.2.4.1
Importance of question stated	Assess efficiency and describe resource implications 2.1 Cost may be viewed as a disincentive to implementation: 2.2.4.1
Viewpoint of analysis stated and defined	2.2.4.2 Health service and societal
Rationale for choosing alternative programmes or interventions compared stated	2.2.3
Alternatives being compared clearly defined	2.2.2 Intervention 2.2.3 Comparator
Form of economic evaluation used stated	2.2.4.2 Planned: cost analysis, cost-effectiveness (including cost-utility) if intervention more or less effective than usual care, cost-minimisation if equivalent to usual care Completed: cost analysis, cost-effectiveness analysis as PALSA more effective thar usual care, cost-utility analysis not completed because no difference in utilities observed during the trial

Choice of model used and key parameters on which it is based justified	N/A
ANALYSIS	
Time horizon of costs and benefits stated	2.4.3
Discount rate(s) stated	2.4.3 Base analysis: 3%
Choice of rate(s) justified	2.4.3 Russell et al. 1996
Explanation given if costs and benefits are not discounted	2.4.3 Benefits and costs incurred in 2003 not discounted
Details of statistical tests and confidence intervals given for stochastic data	Table 4.18 Means cost per patients for 3 month period between interviews Table 5.1 Cost per additional case appropriately managed Table 5.2 Cost per additional tuberculosis case detected
Approach to sensitivity analysis given	2.4.7
Choice of variables for sensitivity analysis justified	2.4.7
Range over which variables are varied stated	2.4.7, 4.4
Relevant alternatives compared	Yes. PALSA + usual training and support for respiratory diseases vs. usual training and support for respiratory diseases
Incremental analysis reported	Chapters 4 and 5
Major outcomes presented in an aggregated as well as a disaggregated form	Chapters 4 and 5
Answer to study question given	7.1.2 and 7.1.3
Conclusions follow from data reported	7.1.2 and 7.1.3
Conclusions accompanied by appropriate caveats	7.1.2, 7.1.3, 7.2