Improving Tuberculosis Control in Ethiopia: *performance of TB control programme, community DOTS and its cost-effectiveness*

Daniel Gemechu Datiko

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Improving Tuberculosis Control in Ethiopia:

performance of tuberculosis control programme, community DOTS and its cost-effectiveness

By

Daniel Gemechu Datiko

Centre for International Health,

University of Bergen , Norway

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to my late mother Mrs. Mulunesh Wata

&

Sr. Liv Ekeland

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Original papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

PAPER I. Yassin MA, Datiko DG, Shargie EB (2006) Ten-year experiences of the tuberculosis control programme in the southern region of Ethiopia. Int J Tuberc Lung Dis 10: 1166-1171.

PAPER II. Datiko DG, Yassin MA, Chekol LT, Kabeto LE, Lindtjorn B: The rate of TB-HIV co-infection depends on the prevalence of HIV infection in a community. *BMC Public Health* 2008, 8:266.

PAPER III. Datiko DG, Lindtjørn B (2009) Health Extension Workers Improve Tuberculosis Case Detection and Treatment Success in Southern Ethiopia: A Community Randomized Trial. PLoS ONE 4(5): e5443. doi:10.1371/journal.pone.0005443

PAPER IV. Datiko DG, Lindtjørn B (2010) Cost and Cost-Effectiveness of Treating Smear-Positive Tuberculosis by Health Extension Workers in Ethiopia: An Ancillary Cost-Effectiveness Analysis of Community Randomized Trial. PLoS ONE 5(2): e9158. doi:10.1371/journal.pone.0009158

PAPER V. Datiko DG, Lindtjorn B: Tuberculosis recurrence in smear-positive patients cured under DOTS in southern Ethiopia: retrospective cohort study. *BMC Public Health* 2009, 9:266.

PAPER VI. Datiko DG, Lindtjørn B (2009) Mortality in successfully treated tuberculosis patients in southern Ethiopia: retrospective follow-up study. Int J Tuberc Lung Dis 14 (7): 866-871

List of abbreviations

AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
ANC	Ante Natal Clinic
BCG	Bacille Calmette-Guérin
CDR	Case Detection Rate
CNR	Case Notification rate
CHRL	Centre for Health Research and Laboratory
CDOT	Community DOT
CHWs	Community Health Workers
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment Short course
EPTB	Extra Pulmonary Tuberculosis
GHWs	General Health Workers
HEP	Health Extension Program
HEWs	Health Extension Workers
HFDOT	Health facility DOT
HIV	Human Immunodeficiency Virus
LTBI	Latent Tuberculosis Infection
MDR TB	Multidrug Resistant Tuberculosis
MTB	Mycobacterium Tuberculosis
NTLCP	National Tuberculosis and Leprosy Control Programme
PTB	Pulmonary Tuberculosis
PYO	Person-Years of Observation

SNNPRS	Southern Nations, Nationalities and Peoples' Regional State
SMR	Standard Mortality Ratio
TSR	Treatment Success Rate
TB	Tuberculosis
WHO	World Health Organization

Summary

World Health Organization (WHO) recommends directly observed treatment short course (DOTS) strategy to control tuberculosis (TB). It aims to detect 70% of new smear-positive cases and cure 85% of them. Implementing the DOTS strategy has improved the case detection rate (CDR) and treatment success rate (TSR) in many settings.

We reviewed the performance of TB control programme of the southern Ethiopia. Low CDR mainly because of inability to access the health service was the limit. We also explored alternatives that could improve access to the health service, its cost-effectiveness; estimated the recurrence rate and mortality in successfully treated TB patients under DOTS strategy and the rate of human immunodeficiency virus (HIV) infection in TB patients.

In ten years, TB control programme of southern Ethiopia has improved the case detection (from 22% to 45%) and treatment success (from 53% to 85%). However, the target of CDR seemed unachievable. Some of the reasons were low health service coverage, shortage of general health workers (GHWs), HIV epidemic and poor socioeconomic conditions. Ethiopia launched community-based programme that deployed huge number of health extension workers (HEWs) to the community. Nevertheless, the possible contribution of HEWs in TB control programme of Ethiopia has not been explored.

We, therefore, employed community-based approach to identify alternatives that improve the performance of TB control programme. The HEWs were involved in sputum collection and providing directly observed treatment (DOT). This improved the CDR,

more significantly for women. This could be mainly because of the community-based sputum collection that had increased access to the diagnostic service. Moreover, community-based treatment improved the TSR of smear-positive patients (90%) compared with to health facility-based DOT (83%). This could be due to the improved access to the service that was created through the provision of DOT in the community where TB patients live, with in reachable distance.

The decision to employ effective interventions by policy-and decision-makers depends on the available resources and existing supporting evidences. This is more important in resource-constrained settings with high disease burden. We, therefore, estimated the cost and cost-effectiveness of involving HEWs in providing DOT. In our study, treating smear-positive cases in the community reduced the total, patient and caregiver costs by 62.6%, 63.9% and 88.2%, respectively.

We also estimated the recurrence rate and mortality in TB patients cured under DOTS strategy and the rate of HIV infection in TB patients and the community. The rate of recurrence in smear-positive TB patients cured under DOTS strategy was 1 per 100 PYO (0.01 per annum). The rate of TB-HIV co-infection varied with the prevalence of HIV in the community. We found mortality rate of 2.5% per annum in successfully treated TB patients. The mortality was associated with sex, age and occupation.

We have shown that the performance of TB control programme could be improved by involving HEWs in TB control programme as we found improved the CDR and TSR. Community-based DOT is economically attractive option to the patient, the household and the health service. We recommend planned scaling up and implementation of community-based TB care in Ethiopia to improve the performance of National TB Leprosy Control Programme (NTLCP). Currently the Federal Ministry of Health of Ethiopia has accepted and endorsed the implementation of community-based TB care by involving HEWs. National guideline for implementing community-based TB care is being developed to apply it at larger-scale in Ethiopia.

1.0. Introduction

1.1. Tuberculosis epidemiology

1.1.1 Cause, transmission and risk factors

Tuberculosis (TB) is a chronic infectious disease mainly caused by *mycobacterium tuberculosis* (MTB). The main source of infection is untreated smear-positive pulmonary tuberculosis (PTB) patient discharging the bacilli. It mainly spreads by airborne route when the infectious patient expels droplets containing the bacilli. It is also transmitted by consumption of raw milk containing *Mycobacterium bovis* [1-3].

The risk of infection depends on the susceptibility of the host, the extent of the exposure and the degree of infectiousness of the index case [3-5]. Once an individual inhales the infectious aerosols, the bacilli lodge into the alveoli where it multiply and form a primary lesion [6]. Under normal condition, in most of the cases, the immune system either clears the bacilli or arrests the growth of the bacilli within the primary lesion in which case the host is said to harbor latent TB infection (LTBI). However, in 5 - 10% of the cases, the bacilli overwhelm the immune system resulting in a primary TB within a few months to years. In the rest, post-primary TB occurs when reinfection occurs or the LTBI is reactivated. The lifetime risk of developing active TB is 5 - 10 %. It could be higher because of the underlying conditions (like human immunodeficiency virus (HIV) infection, diabetes and other medical conditions that suppress immunity) and poor socioeconomic status [3, 7].

Although TB affects many parts of the body, it mainly affects the lung. Its clinical presentation, therefore, depends on the site of infection, the organ affected and its severity. Patients with PTB present with pulmonary symptoms (like productive cough, haemoptysis, chest pain and shortness of breath), constitutional symptoms (like fever, poor appetite, weight loss, night sweats and anorexia) and other symptoms depending on the site of the infection [8-11]. Understanding of the symptoms is important to inform the community about the symptoms to seek medical advice and to inform health workers in order to increase the index of suspicion to easily pick suspects and detect tuberculosis cases presenting to health institutions.

Early detection of the cases and prompt treatment are crucial for TB control. TB diagnosis mainly depends on the clinical presentation of the disease and identification of the offending bacilli. Many TB diagnostic tests are available although no single diagnostic test for TB exists that can be performed rapidly, simply, inexpensively, and accurately as a stand-alone-test. Thus, the diagnosis of active TB is a clinical exercise; and sputum microscopy remains the mainstay of diagnosis because of its availability, operational feasibility and ability to identify the highly infectious forms of TB, the smear-positive PTB cases [12-14].

The significance of TB diagnosis is high if and only if it is complemented by prompt treatment. If not treated in the earliest five years, 50% of PTB cases die, 25% self cure and 25% remain sick and infectious. Untreated smear-positive PTB patient can infect 10 - 15 people per year on average [15]. Thus, treatment of TB is not only a matter of treating the individual patient, but also is an important public health intervention. Treatment is the centerpiece of TB control and can reduce the risk of infection if implemented with adequate coverage and acceptable quality [16, 17]. So far, DOTS remains a cost-effective intervention to control TB [7, 18, 19].

1.1.2. Morbidity and mortality

TB has been a scourge of humanity throughout recorded history. Even today after the availability of effective drugs for more than half a century, it is a major cause of morbidity and mortality worldwide. One-third of world's population is estimated to be infected with MTB [6, 20]. There were about 9.27 million new TB cases (including 4.1 million new smear-positive cases) and 1.3 million deaths from TB in 2008. There were about 11.1 million prevalent TB cases and half million multidrug resistant (MDR) TB cases (resistance at least to isoniazid and Rifampcin) in the world. 95 % of TB cases and 98% of TB deaths occurred in developing countries [21, 22]. TB also is a leading infectious cause of death among women in the reproductive age group and affects the productive segment of a population[23]. TB is the sixth cause of mortality (2.5%) next to HIV infection and accounts for 26% of preventable deaths in the world [21, 24-26].

1.1.3. Risk factors of acquiring tuberculosis

Age

The risk of acquiring TB infection increases with age from infancy to early adult life, probably, because of increasing number and frequency of contacts [27]. TB is mainly a disease of adults in the age group of 15 - 49 years. In a population where the transmission has been stable or increasing, the incidence rate is higher in children mostly because of recent infection or reinfection. As transmission falls, the case load shifts to older adults mainly because of reactivation of LTBI at later ages [14].

Gender

Reports show that men account for high proportion of notified TB cases than women [28, 29]. This was explained by sex (biological determinant - progression from TB infection to disease is likely to be faster for women compared with men in their reproductive years) and gender (socio-cultural determinants influencing access to TB care leading to differential access to health care (like economic problem, inability to make decisions, poor health seeking behaviour and stigma) that compromise the women's ability to utilize the available health service [11, 30-36]. In addition, higher risk of HIV infection among women makes them susceptible to develop active TB. TB is the leading infectious cause of death in young women in developing countries [35, 37, 38]. This could be worse in settings with health services insensitive to gender-specific needs [39]. Studies that consider the interplay of biological, socio-cultural and health system determinants of sex and gender-based differences are needed to understand how and why women are affected.

Residence

More TB patients were reported from urban than rural areas because of overcrowding, poverty and HIV infection [40]. In contrast, the presumed lower risk of TB infection in rural settings could be misleading and should be cautiously taken in high burden countries. In the rural settings, access to the health service is limited; health seeking behaviour is poor and the living condition favour disease transmission. As a result, understanding the burden of TB in rural areas will have a wider implication for TB control in such settings [41, 42].

Socio-economic conditions

TB has been associated with factors linked to socioeconomic deprivation: poverty, overcrowding and malnutrition. The magnitude of TB is high among the poor, displaced, homeless, drug addicts, elderly, malnourished and women [14]. The association between TB and poverty was shown by the decline in TB burden with the improved living condition in developed countries prior to the introduction of treatment. Improved living condition was also found to reduce the risk of infection from 4 - 6 % per annum. In contrast, the resurgence of TB in developing countries as the living condition worsens shows its association with poor living conditions. TB was also found to disproportionately affect the poor [43-45]. Therefore, free diagnosis and treatment was offered to TB patients (mainly to smear-positive PTB cases) to reduce the economic burden for seeking diagnosis and treatment and treat the highly infectious cases [46]. However, limited access to the service because of the poor socioeconomic condition of the patients and their households has reduced the utilization of the available service [42, 46-51]. Thus, interventions that improve access to health service need serious consideration.

1.2. Tuberculosis and HIV co-infection

A complex interaction exists between TB and HIV infection. HIV increases the risk of infection, as it reactivates LTBI and increases the progression to active disease. TB-HIV co-infection has fatal consequences as TB becomes the leading cause of death in HIV infected individuals and patients with acquired immunodeficiency syndrome (AIDS). HIV lowers the host's immune response to MTB. The lifetime risk of developing active TB in HIV infected individuals is 10% per year compared with lifetime risk of 5 - 10% in individuals without HIV. As a result, the TB case notification rate (CNR) has increased four to six fold in sub-Saharan Africa [52-54].

HIV affected the performance of TB control programmes by increasing the number of TB cases and by compromising the treatment outcomes. It created a huge challenge to the already overstretched and under staffed health system in high burden countries. It reduced the proportion of smear-positive cases; and increased the rate of treatment failure, defaulter and death, which in turn compromised the progress towards achieving the targets recommended for TB control under DOTS strategy.

Globally 1.37 million TB cases (14.8% of 9.27 million cases) were co-infected with HIV. 70% of TB-HIV co-infections occurred in countries with high burden of TB. Moreover, half million deaths occurred in HIV infected people due to TB which accounted for a quarter of deaths among HIV positive people [21, 55-58]. There is an epidemiological and clinical association between the two diseases. Therefore, TB-HIV collaboration is an appropriate intervention to improve TB case finding in HIV infected individuals and reduce the risk of HIV infection in TB patients [6, 59-62].

1.3. Global tuberculosis control

History of TB control started from attempts of treating unidentified cause to treating cases infected with the bacilli, from no remedy to effective treatment, from compulsory isolation to chemical isolation (treating infectious cases with anti-TB drugs), and from vertical to integrated approach where the service delivery was progressively decentralized to peripheral health institutions in the communities [63, 64].

Robert Koch's identification of the bacilli and the proposal to isolate patients was followed by compulsory isolation of the patients as the main principle of TB control. This included social support and contact examination in TB clinics (that were accessible and open at convenient time for the patients) [65, 66].

After the introduction of effective treatment, TB control was organized as a vertical programme staffed with health workers particularly assigned to run the programme. This reduced the annual risk of infection by 5 -13% in developed countries due to the available resources and improved general living conditions [67]. However, similar results were not achieved in developing countries due to the associated high cost [68]. Hence, TB control was integrated into general health service to ensure effective and efficient use of resources [69, 70]. However, lack of technical efficiency by the GHWs, neglect of TB control activities, health sector reform (that resulted in collapse of TB structure because of hasty implementation or lack of appropriate attention to TB control) and resurgence of TB due to HIV epidemic weakened the TB control efforts [71, 72]. This was also complicated by socioeconomic deterioration: increased poverty, malnutrition and overcrowding.

The affordability of rifampicin, poor treatment adherence and high TB burden paved way to the introduction of DOTS strategy [73, 74]. The components of the strategy are government commitment to ensure lasting and comprehensive TB control, case detection by sputum smear microscopy among self-reporting symptomatic patients, standardized short course chemotherapy using six to eight months treatment regimens, regular and uninterrupted supply of anti-TB drugs and standardized recording and reporting system [64, 75].

DOTS strategy aims to detect 70% of new smear-positive cases and to cure 85% of them. Epidemiological modelling suggested that achieving these targets will reduce TB incidence, prevalence of smear-positive cases and the number of infected contacts [14, 76]. Decentralization of DOTS to peripheral health facilities has increased the number of TB cases that were detected and treated [77] even in settings with high HIV infection and MDR TB [18, 78]. However, its effectiveness was limited in settings with low health service coverage.

To improve TB control efforts, the Stop TB partnership further envisioned eliminating TB as a public health problem (one smear-positive case per 10^6 population) and, ultimately, to achieve a world free of TB. The partnership promotes TB control as an element for health-system development, a basic human right, and an integral part of poverty alleviation strategies [6, 60-62]. Stop TB partnership, therefore, advocates comprehensive TB control approach that includes providing high quality DOTS expansion and enhancement, addressing TB-HIV, MDR TB and address the needs of the poor and vulnerable people (women, children, prisoners, migrants and ethnic minorities), strengthening the health system, engaging all care providers, empowering TB patients and the community with partnership, and enabling and promoting research to alleviate human suffering [79].

1.4. The health system of Ethiopia

1.4.1. General background of Ethiopia

Ethiopia is a located in East Africa. It covers an estimated area of 1.1 million km^2. The Government of Ethiopia has nine ethnic-based administrative regions, which are referred to as Regional States and two Federal City Administrations. There are 611districts and 15000 kebeles (lowest administrative unit with an average population of 5000 people) [80]. Ethiopia has a population of about 76 million people, of which 85% lives in rural areas. It has huge topographic variations ranging from the lowest 116 meters below sea level to 4, 620 meters above sea level. Most of the population lives in highland areas on subsistence farming.

1.4.2. Health service in Ethiopia

General health service

The National health policy of Ethiopia emphasizes the development and provision of equitable and acceptable health service to the people. Under this provision, the Government of Ethiopia follows a four-tier health service with a major emphasis on community-based health services. Primary health care unit (a health centre and five satellite health posts) is the lowest unit in the health system (Figure 1). Health centres provide curative and preventive health service while health posts mainly focus on disease prevention and health promotion activities and selective curative services in the community.

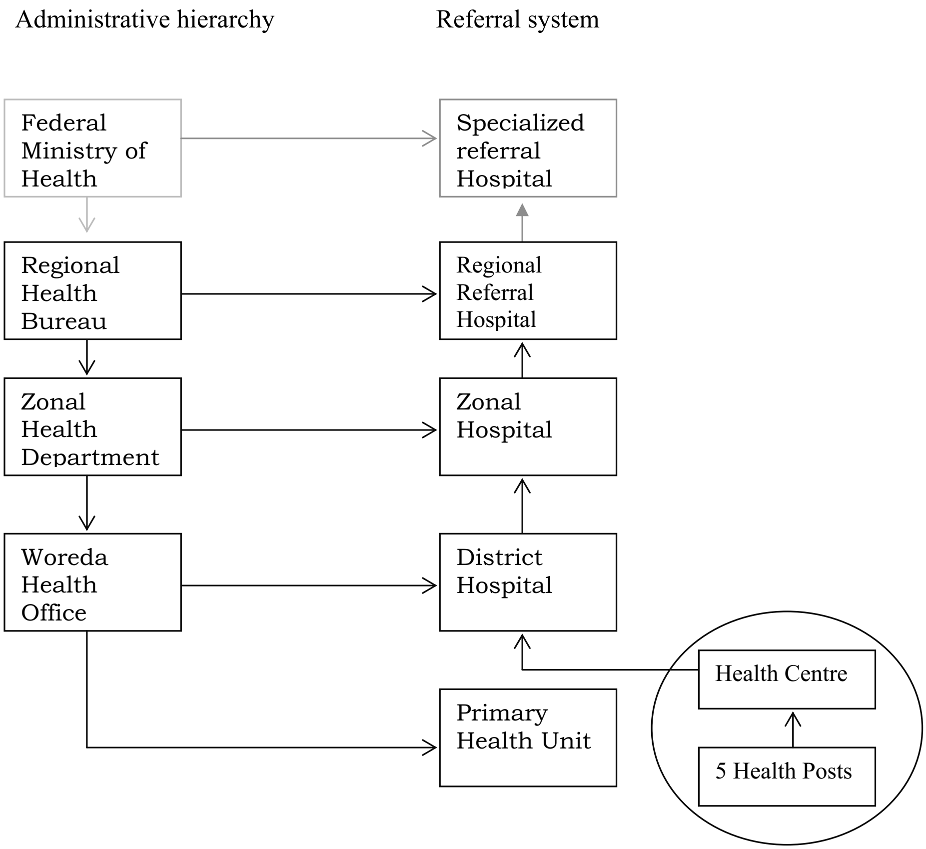
Community-based initiative: Health Extension Programme

In year 2004, the Government of Ethiopia launched a community-based initiative under health extension programme (HEP) with an emphasis to establish reflective and responsive health delivery system to the people living in rural areas. This was accompanied by accelerated health post construction in each kebele. HEP programme focuses on promoting health and providing preventive and selected curative services to ensure equitable access to the community under three major categories: disease prevention and control, family health service, hygiene and environmental sanitation, and health education and communication as a cross cutting issue [81, 82].

The local health authorities in consultation with kebele leaders select two women from each kebele, who have completed 10th grade. The women receive one-year training before they are placed as HEWs in their respective kebeles. TB control is included in the training of HEWs as one of the components under Disease Prevention and Control. HEWs are responsible to provide health education, identify and refer TB suspects, trace defaulters and ensure treatment adherence.

Assigned to health post, HEWs spend about three-fourth of their time on outreach activities in the communities, the kebele in particular. Each HEW is responsible for 500 - 1000 households in each kebele. They receive salary from the government and are accountable to health centre and the kebele administration [83, 84]. However, their contribution to TB control has not been evaluated. The health system, administrative hierarchy and referral system is shown in figure 1.

Figure 1 - The health system of Ethiopia



1.4.3. Tuberculosis control in Ethiopia

TB is among the leading causes of morbidity and mortality in Ethiopia [80]. The NTLCP was started in 1992. Ethiopia adopted the WHO recommended DOTS strategy in 1995. Since then TB control efforts have been decentralized to public health facilities (hospitals, health centres and health stations) where GHWs are responsible for the diagnosis and treatment of TB. [80, 83, 85].

Ethiopia has one of the highest TB burden in the world. The annual incidence and prevalence of all forms of TB was 378 and 579 per 10^5 populations, respectively [21]. DOTS is implemented in public health facilities in hospitals and health centres [80]. The CNR for all forms TB was 155 per 10^5 populations. The incidence of smear-positive cases was 163 cases 10^5 populations. The CNR and CDR of new smear-positive cases was 46 per 10^5 populations and 28 %, respectively. The TSR, the proportion of patients who were cured and completed treatment, was 84 % [21].

1.4.4. Tuberculosis control in the southern Ethiopia

Southern Nations, Nationalities and People's Regional State (SNNPRS) is one of the Federal States of Ethiopia. It has a population of about 15 million. Ninety-three per cent of its population lives in the rural areas. The health service coverage and user rate is about 73.5 % and 32 %, respectively [80].

The SNNPRS Health Bureau started DOTS in three zones and four health facilities as a vertical program in 1995. Later, the programme was integrated into the general health service, and decentralized to zones, districts and health facilities (hospitals, health centres and health stations). Over ten years, implementation the DOTS strategy tripled TB case notification (45 to 143 per 10^5 population), doubled the case detection rate (22 to 45%), increased the treatment success rate (from 53 to 85%), reduced the defaulter rate (from 26 to 6%) and treatment failure rate (from 7 to 1%) [86].

TB remains the leading cause of morbidity and mortality in southern Ethiopia. It was 4th cause of total admission, 5th cause of female admission and 5th cause of admission in children less than five year. It was the 3rd cause of inpatient deaths, 2nd cause of deaths in women and 6th cause of death in children less than five years [80].

1.5. Rationale for the present study

Over the last two decades, the load of TB has increased in sub-Saharan Africa mainly because of HIV infection. This has compromised the already overstretched health services due to the associated morbidity. The implication is more in settings with low health service coverage and shortage of health workers [6, 62].

DOTS strategy advocates passive case finding and provision of DOT under the direct observation of GHWs or treatment supervisors. Passive case finding mainly serves those who have better socioeconomic status (better knowledge and health seeking behaviour) and geographic access to health facilities. This affects the poor and patients living in rural and remote areas leading to delay in presentation and disease transmission [42, 44]. Moreover, seeking diagnosis and treatment in health facilities is costly and difficult for TB patients and their families [47, 87-89]. In TB patients who have accessed the service, adherence and completion of treatment remains a challenge to successful completion of treatment.

Therefore, alternative approaches that improve access to diagnosis and treatment are needed [90-95].

Ethiopia has one of the highest TB burden in the globe. TB is among the leading causes of morbidity and mortality. Over the last two decades implementing DOTS strategy has increased the number of TB patients diagnosed and treated. However, the CDR for smear-positive patients remained far below the target despite increasing number of health workers and health facilities providing DOT. This was mainly because of the limited access to the health service. However, decentralization and performance of DOTS strategy in the era of HIV epidemic has not been documented in Ethiopia.

In 2004, the government of Ethiopia introduced a community-based initiative under HEP to provide health service in each kebele by a new cadre of health workers. However, the role of HEWs in TB control has not been explored. Therefore, we aimed to measure the performance DOTS, identify the role of HEWs in improving the performance of the TB control programme and its cost-effectiveness to implement in resource-constrained Ethiopia.

2.0. Study aims

2.1. Aim

The aim of this research was to improve the performance of TB Control in Ethiopia

2.2. Objectives

1. To find out ten-year performance of TB control programme in southern Ethiopia
2. To estimate the rate of HIV infection in TB patients and its association with the prevalence of HIV in the community
3. To find out if involving HEWs in TB control improves the CDR and TSR of smear-positive patients
4. To compare the cost and cost-effectiveness of treating smear-positive patients by HEWs in the community compared to treatment by GHWs in health facilities
5. To determine the recurrence rate in smear-positive patients cured under DOTS
6. To determine mortality in TB patients after successful treatment under DOTS

3.0. Methods

3.1. Study area and population

3.1.1. Study area

Ethiopia is the third largest and populous country in Africa (Figure 2). It covers an area of 1.1 million km^2 and has a population of 76 million people. 85% of the population lives in rural areas. It has nine regional states and two city administration. It is undergoing enhanced health facility construction and training of health workers to improve the delivery of health service to the community.

Ethiopia is a poor country with one of the worst health indicators in the world [96]. Communicable diseases and nutritional deficiencies are the main causes of morbidity and mortality. However, the country is making remarkable changes by expanding health service delivery and extending affordable primary health care to the community [80, 97].

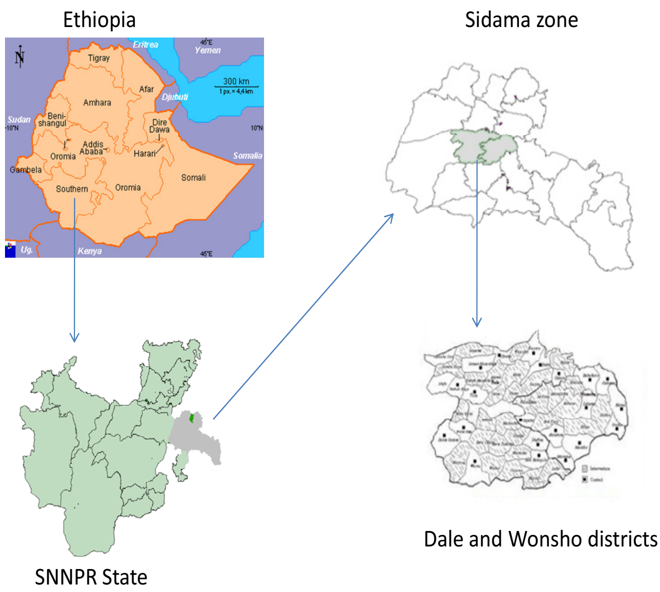
Table 1 selected demographic and health indicators for Ethiopia

Indicators	**Rates**	
	2008	**2009**
Life expectancy at birth [98]	56	55.4
Incidence of TB all forms per 10^5	379	378
Incidence of smear-positive TB per 10^5	168	163
Prevalence of TB per 10^5	643	579
Case detection rate of new smear-positive cases	27%	28%
DOTS treatment success rate per 10^5	84%	-
TB mortality per 10^5	84	92
Adult HIV prevalence (urban/rural) [99]	3.0(9.5/1.6)	2.9(9.4/1.5)
TB HIV co-infection (new TB cases)	6.3%	19%
MDR TB new(retreatment)	1.6% (12%)	-

SNNPRS is the third largest and populous region in Ethiopia. It is located in the south-west part of the country. It shares international borders with Sudan and Kenya. It covers 118, 000 square km (10% of national area). It has a population of about 15 million (20% of the national population). It has 13 zones, one city administration and eight special districts. 93% of the population lives in rural areas. The health service coverage and user rate was 73.5 % and 32%, respectively. TB treatment is provided in all hospitals and health centres (DOTS coverage was 100% in hospitals and health centres). However, only 16% (354/2230) of health facilities provide treatment to TB patients inclusive of health posts. Nevertheless, DOT has not been implemented in health posts and HEWs do not provide DOT to TB patients.

Sidama zone is located in SNNPRS. It has 19 districts and two towns. It has about 3.2 million people in an area of 6,981 square km. It is one of the most densely populated zones of the region with a population density of 463 people per square km. Fifty-five per cent of the population lives at a two-hour walking distance from the health facilities. Dale and Wonsho are rural districts in Sidama zone located about 50 kms from Hawassa, the SNNPRS capital. There are 51 kebeles in the two districts.

Figure 2 - Map of the study area



3.1.2. Study population

The SNNPRS Health Bureau started implementing DOTS strategy in 1995. TB control programme was decentralized to hospitals, health centres and health stations. TB case finding and treatment outcome reports were complied on quarterly basis. TB patients reported from 1995 - 2004 were enrolled to measure the performance of TB control programme of southern Ethiopia (Paper I).

In 2005, after implementation of DOTS strategy for ten years, the prevalence of HIV and its association with the rate of TB-HIV co-infection was estimated by enrolling pregnant women and TB patients in the southern Ethiopia. This was performed as part of regular HIV surveillance conducted by the SNNPRS Health Bureau. Paper II was based on the data obtained from TB patients and pregnant women attending health facilities for antenatal care (ANC) for the first time during the study period.

In 2006, TB patients who were successfully treated (declared cured or treatment completed) under DOTS strategy in two rural districts of Sidama zone (Dale and Wonsho) were retrospectively followed to the first cohort that received DOT (Paper V & VI).

Smear-positive patients from intervention and control kebeles were enrolled in a community randomized trial conducted in the two rural districts of Sidama zone. TB patients identified from intervention and control kebeles received DOT. These patients were followed until they completed treatment for TB (Paper III). Prospectively cost data was collected for these patients, caregivers and health workers to find out the cost and cost-effectiveness of providing DOT by HEWs (Paper IV). Smear-negative and EPTB cases were excluded from the study. However, they received the treatment available in intervention or control kebeles (see additional results - 5, table - 3).

3.2. Study design

The main study design was community randomized trail (Paper III). In this study, 51 kebeles from two rural districts were randomly allocated to intervention and control groups. Kebele was the unit of randomization. We used table of random numbers for allocation. TB patients diagnosed from the intervention kebeles were started on DOT under the direct observation of HEWs while patients from the control kebeles received health facility-based DOT under the direct observation of GHWs. Cost data was prospectively collected for these patients along the main study to estimate the cost and cost-effectiveness of providing DOT under the two treatment options (Paper IV).

In Paper II, TB patients and pregnant women were enrolled in a cross-sectional study to find out the rate of TB-HIV co-infection and the prevalence of HIV in southern Ethiopia. TB patients and pregnant women presenting to the health facilities were consecutively enrolled after obtaining informed consent. HIV testing was done (from the remaining serum after routine blood test for pregnant women and from sample collected for surveillance of HIV in TB patients) at the Centre for Health Research Laboratory (CHRL) at SNNPRS Health Bureau.

Paper I reports a cross-sectional study conducted to assess the ten-year performance of the TB control programme based on the reports compiled at the SNNPRS Health Bureau. We also conducted a retrospective cohort study to find out the recurrence and mortality rate in

TB patients after successfully receiving treatment under DOTS strategy. TB patients who were declared treatment completed or cured were traced to their home (Paper V & VI).

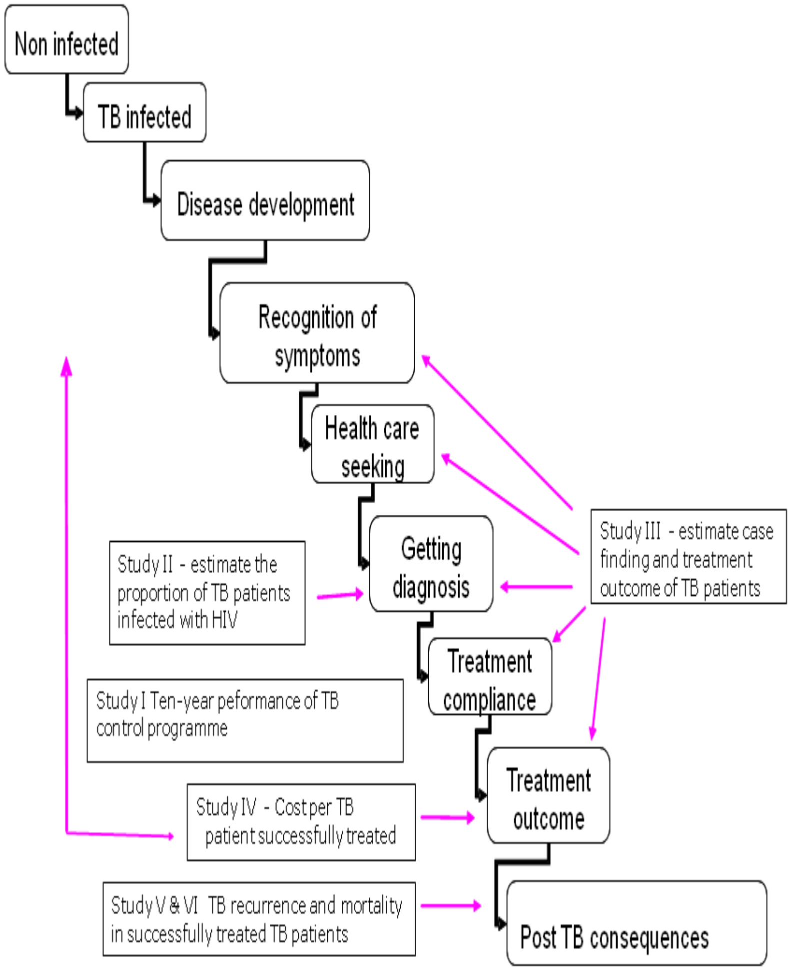
Table - 2 Summary of the studies conducted: the design, population and the study period

Paper	Titles	Study design	Study population	Study period
I.	Ten-year experiences of TB control in southern Ethiopia	Cross sectional	136 572 TB patients	1995 - 2004
II.	The rate of TB HIV co-infection	Cross sectional	1308 TB patients 4199 Pregnant women	2005 - 2006
III.	HEWs improved the case detection and treatment	Community randomized trial	318 TB patients	2006 - 2008
IV.	Cost-effectiveness of TB treatment	Community randomized trial	229 TB patients, 30 HEWs, 10 GHWs	2006 - 2008
V.	TB recurrence in smear-positive patients	Retrospective cohort study	368 TB patients	1998 - 2006
VI.	Mortality in successfully treated TB patients	Retrospective cohort study	725 TB patients	1998 - 2006

To achieve the targets of DOTS strategy, understanding the transmission of the disease, the progress from infection to disease and effective control measures that early identify the cases, cure the disease and maintain disease free survival of the cases and the community is important. Therefore, increasing the awareness of the community in prevention of the transmission, recognizing the symptoms and seeking diagnosis should be complemented by the ability of health workers to identify the cases, provide prompt treatment and encourage the patients to adhere to the treatment. Studies and intervention that address these issues will be of great significance to TB control.

The aim of our study as described earlier was to improve the performance of TB control in Ethiopia. We tried to address the challenges of TB control in southern Ethiopia in relation to the patient, community and health system. To put our study in context we have depicted how our studies fitted into the public health model of TB control adopted from simulation model of case-finding and treatment in tuberculosis control programme [100, 101]. We focused on improving symptom recognition, health seeking, diagnosis, treatment compliance, its cost-effectiveness and post-treatment consequences as shown below (Figure 3).

Figure 3 - The schematic presentation of the studies in the public health model of TB control



3.3. Data collection and management

3.3.1. Data collection tools and methods

NTLCP uses standard recording and reporting formats to monitor TB control efforts. Case finding and treatment outcome data were complied and reported on quarterly basis from lower to higher administrative levels (from District Health Offices → Zonal Health departments → Regional Health Bureaus → Federal Ministry of Health) and copies of the reports were kept at all levels for official documentation (Figure - 1). Ten-year TB programme review (Paper I) was based on the copies of reports remaining at SNNPRS Health Bureau.

In Paper II, TB patients and pregnant women were enrolled from health facilities to find out the rate of HIV infection. Trained laboratory technicians and GHWs collected the data using a pretested questionnaire prepared for HIV surveillance among pregnant women and TB patients.

In paper III, smear-positive patients from intervention and control kebeles were registered in the health facilities and were treated under the two treatment options: under the direct observation of GHWs or HEWs. During supervision, district TB experts transcribed the list of patients from unit TB registers in the health facilities to district TB registers. They also cross-checked the sputum results of smear-positive cases in the TB unit register against the smear results recorded in the laboratory register. TB case finding and treatment outcome data were quarterly reported from district TB register using standard reporting formats.

In Paper IV, smear-positive patients from intervention and control kebeles were prospectively enrolled and cost data was obtained using a structured questionnaire. Trained GHWs and HEWs interviewed the patients and caregivers about the travel time, transport cost and costs related to visit to health facilities or health posts for treatment. Similarly, the cost data for HEWs and GHWs was collected by trained data collectors from the two districts. The salary of established positions, budget expenditures, medical equipments, vehicles and buildings were obtained from health facilities, district health and finance offices. Joint costs were shared based on the proportion of time used for TB control. Capital items were annualized using 30 years for buildings, 10 years for equipments and 5 years for motorbikes as an expected useful life. The base year for valuing cost was 2007, and the applicable exchange rate was 8.6 Ethiopian birr for 1 USD.

In Paper V & VI, TB patients who were treated since the start of DOTS in the study area were retrospectively followed in the two districts. The lists of TB patients who were declared treatment completed or cured were obtained from unit TB registers in the health facilities and district TB registers. HEWs collected the data about the current status of the patients if they were alive or dead. This was done by taking registered history of TB patients from unit registers for prior successful treatment in health facilities and recent history of TB was obtained by making house-to-house visits. The data about recurrence or rediagnosis of TB after successful treatment was confirmed by cross-checking with the list of TB patients on unit or district TB registers.

3.3.2. Study management

The study team consists of HEWs, GHWs, district HEP experts and TB programme experts at Districts, Zone and Region including the principal investigator and the supervisor.

The HEWs were responsible for case finding and provision of DOT in an intervention kebeles. They also conducted house-to-house visit to collect data about post-treatment follow-up of TB patients and cost data for patients receiving treatment in their kebeles.

The GHWs were responsible for supervising the TB control activities conducted by HEWs, registration of TB patients in the unit TB register, provision of drugs and supplies to the health post and providing DOT for patients receiving treatment in health centres.

The district HEP experts were responsible for coordinating the activities of HEWs in TB control; and District TB programme experts were responsible for providing drugs and supplies, coordinating the activities, ensuring the completeness and consistency of the recording and reporting in the health facilities and report the quarterly performance of district TB control programmes. TB and Leprosy Control Programme experts from zone and region also conducted supportive supervision to the districts, health facilities and kebeles.

The principal investigator was responsible for organizing and supervising the overall conduct of the studies and reports the activities to the supervisor who also facilitated the administrative and technical issues to accomplish the work and conducted the field visits.

3.3.3. Data safety and quality assurance

Effective delivery of an intervention requires both that the providers adhere to the intervention procedure and that the participants cooperate appropriately [102]. To ensure this, HEWs, GHWs and TB programme experts were trained about community-based TB care and its implementation. The trainees received copies of training documents and field guides prepared in Amharic (official language of Ethiopia) to use it as a reference. This was accompanied by supportive supervision: GHWs supervised HEWs, reviewed the conduct of case finding and treatment, and checked the completeness and accuracy of the cost and post-treatment follow-up data. They also crosschecked patient data by making home visits and interviewed the patients in their kebeles.

District TB programme experts conducted supportive supervision to health facilities and kebeles. The district programme experts checked the completeness and accuracy of the data, the recording and reporting of patients, the patient follow-up and the availability of resources. The experts also cross-checked the data from unit TB register with the laboratory register in the same health facility, the data from health facilities against the data from the kebeles and the patients. They also collected slides from diagnostic units for blind rechecking as part of external quality assurance and it was done at CHRL as per the recommendation of the NTLCP. The district health office reviewed the community-based TB care and other health activities on quarterly basis. Regular supervision was also conducted by the investigator and TB programme experts from the SNNPRS Health Bureau. The six months performance of the community-based TB care was conducted in Yirgalem.

Definition of terms

TB Diagnosis, classification, case definitions and treatment outcomes were dealt with in individual papers. Some important terms are defined below.

Failure: refers to a patient who remains or becomes smear positive at 5th month or later.

Cured: refers to smear-positive patient who is smear-negative at the last month of treatment and at least on the previous occasion (at 2nd or 5th month).

Treatment completed refers to a smear-positive patient who completed full course of treatment but does not have smear result at 7th month of treatment or does not fulfil the criteria to be classified as failure; or smear-negative and EPTB patients who completed the full course of treatment.

Case detection rate: is the number of smear-positive patients detected of the estimated new smear-positive patients expressed in percentage.

Treatment success rate: is the number of TB patients cured or treatment completed of the total TB cases reported expressed as percentage

Relapse*:* refers to rediagnosis of smear-positive TB in patients after successful treatment.

Recurrence: refers to rediagnosis of TB in patients who were declared cured or treatment completed in the past with or without smear positive result. It also included relapse cases.

3.4. Study outcome measures

The main study outcomes were CDR, TSR, proportion of HIV infected, mortality, recurrence of TB and cost per patient successfully treated.

TB patients were classified into smear-positive, smear-negative and EPTB cases based on the smear result and the site involved. The treatment outcomes were cured, treatment completed, default, failure, transfer out and died (appendix I & II). In Paper I, CDR and TSR were used to measure the performance of TB control programme as recommended by WHO [77].

In Paper V & VI, recurrence and mortality were used to measure the post-treatment condition of the TB patients. In Paper II, HIV test results were done using ELISA test. A societal perspective of cost estimation was used to find out the average cost per patient successfully treated (Paper IV).

3.5. Sample size and statistical analysis

For the community randomized trial, we used the CDR of 41% (an average of previous three years from 2003 - 2005 for the study area) [additional results -1, table - 1]. We estimated the number of clusters needed on the basis that community-based case finding to increase the CDR by 30% using power of 80%, 95% confidence interval and accounting for 30% loss to follow-up. Based on the principle of allocating unequal clusters, 21 kebeles were assigned to control while 30 were allocated to intervention groups. TB patients who received treatment in the study area were included in the cost-effectiveness study (Paper III & IV). As indicated in the individual papers, we enrolled and analyzed the available data as a whole and the number of patients evaluated was large enough for multiple comparisons (Paper I, II, V & VI).

Microsoft Excel and SPSS for Windows 14 were used for data entry and analyses. Independent t-test and one way analysis of variance were used to compare the mean CDR and TSR for cluster level values and to determine the intraclass correlation coefficient

(Paper III), respectively. Average cost of treating smear-positive patients was divided by the number of patients treated successfully. One way sensitivity analysis was done to determine the cost-effectiveness of the intervention (Paper IV)

Logistic regression analysis was used to estimate the effect of predictor variables on the rate of HIV infection among TB patients and pregnant women. Linear regression analysis was used to estimate the amount of variation explained by predictor variables (Paper II).

Kaplan-Meier and Cox Regression method were used to evaluate event free (death or recurrence) survival and the relative effects of selected variables, respectively. Log rank test and hazard ratios were used for statistical significance. We calculated SMR using indirect standardization method (Paper V).

3.6. Ethical considerations

The Ethical Review Committee of the SNNPRS Health Bureau approved the studies. In consultation with the NTLCP, discussion was held with TB programme experts at zone, districts and health facilities about community-based TB care. Subsequently similar discussion was held with kebele leaders and we obtained community consent. Enrolment of the study participants was done after obtaining informed consent from individual study participants. The participants were also informed about the right to withdraw from the study without compromising their future care. PTB suspects that were smear-negative for acid fast bacilli were given free antibiotic treatment as part of diagnostic work up recommended by the NTLCP. In Paper II, study participants who wanted to know their

HIV status were advised to visit the voluntary counselling and testing unit in the same health facility or in the nearby.

4.0. Synopsis of the Papers

4.1. Paper I: Ten-year Experiences of Tuberculosis Control Programme in Southern Region of Ethiopia

Implementation of the DOTS strategy started in 1995. It was decentralized to zones, districts and health facilities. Monitoring and evaluation is one of the components of the DOTS strategy to understand its performance. We aimed to find out the effectiveness decentralization on TB case finding and treatment outcome in southern Ethiopia.

The result of the study was based on the official reports of TB control programme over ten years. The diagnosis and treatment, case notification and treatment outcome reports were based on the recommendations of NTLCP.

In 2004, 94% of the health facilities (hospitals, health centers and health stations) implemented the DOTS strategy. 136 572 cases were registered in ten years; of these, 47% were smear-positive, 25% were smear-negative and 28% had EPTB. The smear-positive case notification rate increased from 45 to 143 per 10^5 population. Similarly, the CDR increased from 22% to 45%, and the TSR from 53% to 85%. The defaulter rate decreased from 26% to 6%.

Decentralization of DOTS strategy improved the case detection and treatment success of TB patients. TB control programme achieved 85% treatment success; however, with the current low CDR (45%), the 70% WHO target seems unachievable in the absence of alternative case-finding mechanisms.

4.2. Paper II: The rate TB-HIV Co-infection Depends on the Prevalence of HIV Infection in a Community

Limited knowledge about the rate of HIV infection in TB patients and the general population compromises the planning, resource allocation and prevention and control activities. We aimed to determine the rate of HIV infection in TB patients and its correlation with the rate HIV infection in pregnant women attending ANC.

TB patients and pregnant women attending health facilities were enrolled in 2004 - 2005. TB diagnosis, treatment and HIV testing were done as per the National guideline. Logistic regression and linear regression analysis were used to determine the risk factors and the correlation between HIV infection in TB patients and pregnant women, respectively.

Of the 1308 TB patients enrolled, 226 (18%, 95%CI: 15.8 - 20.0) were HIV positive. The rate of HIV infection was higher in TB patients from urban (25%) than rural areas (16%) [AOR = 1.78, 95%CI: 1.27- 2.48]. Of the 4199 pregnant women, 155 (3.8%, 95%CI: 3.2 - 4.4) were HIV positive. The rate of HIV infection was higher in pregnant women from urban (7.5%) than rural areas (2.5%) [OR = 3.19, 95% CI: 2.31- 4.41]. In the study participants attending the same health facilities, the rate of HIV infection in pregnant women correlated with the rate of HIV infection in TB patients (R^2 = 0.732).

The rate of HIV infection in TB patients and pregnant women was higher in urban areas. The rate of HIV infection in TB patients was associated with the prevalence of HIV infection in pregnant women attending ANC.

4.3. Paper III: Health Extension Workers Improve Tuberculosis Case Detection and Treatment Success in Southern Ethiopia: A Community-Randomized Trial

Early case finding and prompt treatment of smear-positive cases is at the centre of DOTS strategy. Unfortunately, the CDRs remain low in many countries. We aimed to find out if involving HEWs in TB control improves smear-positive CDR and TSR in Southern Ethiopia.

Community randomized trial was conducted in 51 kebeles in two rural districts of southern Ethiopia. HEWs from the intervention kebeles were trained on how to identify suspects, collect sputum specimen and provide DOT.

230 smear-positive patients were identified from the intervention and 88 smear-positive patients from control kebeles. The mean CDR was higher in the intervention than in the control kebeles (122·2% v*s.* 69·4%, p < 0·001). More females were identified in the intervention kebeles (149·0% *vs.* 91·6%, p < 0·001). The mean TSR was higher in the intervention than control kebeles (89·3% *vs.* 83·1%, p = 0·012) and for females (89·8% *vs.* 81·3%, p = 0·05).

Involving HEWs in sputum collection and treatment improved smear-positive CDR and TSR possibly because of an improved access to the service that reduced socioeconomic burden on TB patients. This could be applied in settings with low health service coverage and shortage of health workers.

4.4. Paper IV: Cost and Cost-effectiveness of Treating Tuberculosis by HEWs in Ethiopia: An ancillary Cost-effectiveness Analysis of a Community Randomized Trial

Increasing number of TB cases due to HIV infection and worsening socioeconomic conditions have affected the already overstretched health system. Therefore, alternative strategies that increase the effectiveness of identifying and treating TB patients at lower cost are required. We present the cost and cost effectiveness of involving HEWs in TB treatment.

Comparison of two treatment options, DOT by HEWs and GHWs was done along a community randomized trial. Costs were analyzed from societal perspective in 2007 in US $ using standard methods. Cost-effectiveness was calculated as the cost per smear-positive patient successfully treated.

The total cost per successfully treated smear-positive patient was higher in health facilities ($161.9) compared to the treatment in the community ($60.7). Community DOT (CDOT) reduced the total, patient and caregiver cost by 62.6%, 63.9% and 88.2%, respectively. The cost of involving HEWs ($8.8) was 14.3% of total cost per patient for CDOT.

Involving HEWs in TB treatment is a cost-effective treatment option to health service, patients and caregivers. There is an economic and public health reason to involve HEWs in TB treatment in Ethiopia. However, due attention should be paid to ensuring initial start up investment to implement CDOT, resources, training and regular supervision.

4.5. Paper V: Tuberculosis Recurrence in Smear-positive Patients Cured Under DOTS in Southern Ethiopia: Retrospective Cohort Study

Decentralization of DOTS has increased the number of cured smear-positive patients after completing treatment. However, the rate of recurrence has increased mainly due to HIV infection. Thus, recurrence rate could be taken as an important measure of long-term success of TB treatment. We aimed to find out the rate of recurrence in smear-positive patients cured under DOTS strategy in southern Ethiopia.

We retrospectively enrolled smear-positive patients who were reported cured from 1998 to 2006. Recurrence of smear-positive TB was used as an outcome measure. Person-years of observation (PYO) were calculated per 100 PYO from the date of cure to date of interview or date of recurrence as registered in unit TB registers. Kaplan-Meier and Cox-regression methods were used to determine the survival and the hazard ratio (HR).

368 cured smear-positive patients cured under DOTS were followed for 1463 person-years. Of these 15 smear-positive patients had recurrence. The rate of recurrence was 1 per 100 PYO (0.01 per annum). Recurrence was not associated with age, sex, occupation, marital status and level of education.

High recurrence occurred among smear-positive patients cured under DOTS strategy. Further studies are required to identify factors contributing to high recurrence rates to improve disease free survival of TB patients after treatment.

4.5. Paper VI: Mortality in Successfully Treated Tuberculosis Patients in Southern Ethiopia: Retrospective Follow-up Study

Tuberculosis control programme aims at identifying the highly infectious TB cases and successfully treat them. However, there is no routine monitoring of TB patients after treatment completion.We aimed to measure excess mortality in successfully treated TB patients.

We retrospectively enrolled TB patients who were treated and reported cured or treatment completed from 1998 to 2006. Mortality was used as an outcome measure. Person-years of observation (PYO) were calculated per 100 PYO from the date of completing treatment to date of interview if the patient was alive or to date of death. Kaplan-Meier and Cox-regression methods were used to determine the survival and the hazard ratio (HR). Indirect method of standardization was used to calculate the standard mortality ratio (SMR).

725 TB patients were followed for 2602 person-years. 91.1% (659 of 723 patients) were alive while 8.9% (64 of 723 patients) had died. The mortality was 2.5% per annum. Sex, age and occupation were associated with high mortality. More deaths occurred in non-farmers (SMR=9.95, 95%CI: 7.17 - 12.73).

The morality was high in TB patients compared with the general population. More deaths occurred in non-farmers, men and elderly. Further studies are required to identify the causes of death in these patients.

Additional results

To enrich the understanding of the context and the significance of the studies, some important data that were not part of the individual studies were added here. These are the baseline data, the duration of presentation for seeking diagnosis in the community, cases identified, cost of seeking diagnosis in public health facilities and treatment outcome of smear-negative and EPTB cases.

1. Baseline data: smear-positive case detection and treatment success rates

Table 1. CDR and TSR of smear-positive cases in the study area, 2003 - 2005

Kebeles	Case detection rate				Treatment success rate			
	2003	2004	2005	Average	2003	2004	2005	Average
Control kebeles	35%	53%	40%	43%	86%	91%	82%	86%
Intervention kebeles	23%	50%	42%	38%	80%	87%	84%	84%
Total	28%	51%	41%	40%	82%	88%	84%	85%

* 3 years average TSR for smear-negative and EPTB cases was 77% and 79%, respectively.

2. Duration of cough on presentation: in the intervention kebeles, of the total 723 PTB suspects who produced sputum for examination, more females (65%) were enrolled than males (35%). Most of the suspects (75%) visited health post within 2 - 4 weeks of the onset of cough. The duration of cough was in the range of two weeks to six months in the first month of the intervention. It decreased as the sputum collection continued from the first month to the last month of the intervention.

3. smear-positive cases identified: case notification rates of smear-positive cases

Table 2. Smear-positive case notification rates in the study area, 2006 - 2007

Variable	Intervention	Control	Mean difference (95%CI)	P - value
CNR per 10^5	124	69	55.2 (8.4 - 102.1)	0.022
Men	115	79	35.8 (-11.9 - 83.5)	0.138
Women	134	65	68.5 (7 - 130)	0.030
By season				
Spring	96	73	23.8 (- 48.2 - 95.8)	0.510
Winter	121	40	80.9 (33.8 - 127.9)	0.001
Autumn	79	55	23.8 (-27.1 - 74.7)	0.352
Summer	107	48	59.3 (-1.5 -120.2)	0.056

4. The cost of seeking diagnosis in control kebeles: household cost of seeking TB diagnosis in public health facilities for smear-positive patients from control kebeles accounts for the loss of about 10 working days or US$ 12.9 [10% of the GDP in 2007($130)], at its least estimate. This did not include the waiting time in the health facilities (at outpatient department, laboratory, x-ray unit and TB room).

5. Treatment outcome smear-negative and EPTB cases: Of 265 smear-negative and EPTB cases, 171 cases were from the intervention while 94 cases were from control kebeles. Of these, 75% (128/171) from intervention and 42% (39/94) from control kebeles were treated successfully. The TSR was higher in the intervention than control kebeles for smear-negative cases (p-value = 0.01). However, the TSR for EPTB cases was higher in the control than intervention kebeles (p-value = 0.004). This was due to six deaths in EPTB cases of which four deaths occurred after admission to hospital.

Table 3. Treatment outcome of smear-negative and EPTB cases in the study area, 2006 - 2008

TB	Groups	Number of cases			TSR*			ICC**
		Male	Female	Total	Female	Male	Total	
PTB -	Control	21	53	74	53%	62%	58%	
	Intervention	54	50	104	89%	82%	87%	0.0000714
EPTB	Control	13	7	20	86%	92%	90%	
	Intervention	40	27	67	74%	63%	70%	0.0000797

* TSR - treatment success rate **ICC - intraclass correlation coefficient

NB: the TSR was adjusted for clustering under the two treatment options.

6. Baseline comparison of TB cases enrolled for post-treatment follow-up

Table 4. Comparison of TB cases enrolled and lost to follow-up in the study area, 1998 - 2006

Variables	*TB patients followed-up n (%)*	*TB cases lost to follow-up n (%)*	X^2	*p-value*
Age (mean/SD†)	26.9(13.9)	26.6(10.5)	0.2*	0.84
sex			0.07	0.79
Male	379(52%)	37(53.6%)		
Female	350(48%)	32(46.4%)		
TB classification			4.9	0.85
PPOS	429(59.2%)	32(46.4%)		
PNEG	165(22.8%)	23(33.3%)		
EPTB	131(18.0%)	14(20.3%)		
TB category			0.28	0.59
New	718(99.2%)	68(98.6%)		
Others ‡	6(0.8%)	1(1.4%)		
Treatment outcome			4.88	0.03‡‡
Cured	403(55.9%)	29(42.0%)		
Treatment completed	318(44.1%)	40(58.0%)		

* df = 92.3 mean difference = 0.28, † SD = standard deviation, ‡others = relapse and transfer-in

‡‡ More cases were lost to follow-up among treatment completed (missed sputum examination at 7th month)

5.0. Discussion

5.1. Discussion of the methods

5.1.1. Study design

The main study design was community-randomized trial in which intact social units or group of individuals are assigned to intervention or control groups. This study design is applied when individual allocation is not possible or desirable. It is a preferred design when an intervention involves groups is applied at the level of health organizational units or geographic area, is unethical to administer it to individuals, cheaper and convenient to administer and when reduction of contamination is required [103-106]. This design may be more important in developing countries, particularly in rural areas where the sense of community is strong, and community consent and cooperation are essential [107]. We conducted our study in two rural districts (Dale and Wonsho) at programme (health organizational unit) level using health workers in the districts (Paper III).

Cluster randomization trials lack the independence of observations and violate the main assumption of statistics. This influences the design and analysis; the standard approaches to sample size estimation and analysis no longer apply. Moreover, during recruitment, clusters may withdraw (in our case HEWs in a cluster may not recruit participants) which may lead to empty clusters. However, the shortcomings may be overcome by randomized allocation, increasing number of clusters (small sized clusters are more efficient), follow-up during the intervention and adjusting for clustering during analysis. Randomization ensures similar distribution of known or unknown sources of bias except for a chance or a real effect of an intervention [104, 108-110].

In Paper III, we completely randomized the clusters using table of random numbers, adjusted for clustering and used intention-to-treat analysis that is a pragmatic approach. We did not have cluster level withdrawal but had three empty clusters one from intervention and two from control groups which reflects what happens in practice under programme conditions. However, this is less likely to affect the results of our study due to fact that we added thirty percent of calculated clusters as a contingency to compensate for loss to follow-up. The conduct of the study requires two level ethical consideration due to participant involvement at individual and cluster level [107]. We obtained informed consent at the two levels, from the community leaders and the patients.

Cohort studies can be thought as natural experiments in which outcomes are measured in realistic setting [111]. Cohort studies follow two or more groups from exposure to outcome. It can be done ahead in time from present (prospective), in the opposite direction (retrospective), or in both directions. Retrospective cohort studies require good records of past exposure for a group of people who can be traced to find out their current status [112]. In Paper V & VI, TB patients who were successfully treated under DOTS strategy were retrospectively followed-up. The list of patients was obtained from unit TB registers in health facilities and this was crosschecked with the list of patients in the district TB register and the quarterly reports. Then the patients were traced to their place of residence.

Cohort studies are useful to find out incidence and natural history of a disease. They allow estimation of incidence rates, relative risks and other outcome measures using survival methods. It also reduces the risk of survivor’s bias in conditions that are rapidly fatal [43, 112, 113]. The design is appropriate for studying rare exposures and helps to measure multiple outcomes that might follow an exposure. Selection bias and loss to follow-up can be a problem. In Paper V & VI, patients were followed to the place of their residence by house-to-house visit and the degree of loss to follow-up was minimal (less than seven percent). Cohort studies by nature are time consuming and expensive. However, the benefit: cost ratio of efficient cohort study is high and retrospective cohort studies generally reduce cost [43, 112]. In Paper V & VI, we believe that the cost of conducting the studies was low for we involved HEWs, used unit TB registers at health facilities and employed standard population for comparison of mortality.

Cross-sectional study defines the scope of a problem (descriptive), identifies possible casual risk factors (analytic) and captures its prevalence. It is useful to generate hypothesis, to examine unchanging exposures (sex, blood group) that occurred many years back. However, cross-sectional studies have in built 'chicken or egg' dilemma and selection bias [114]. We enrolled all TB patients and pregnant women available during the study period. Therefore, selection bias is less likely to affect the results.

5.1.2. Validity of the studies

The results of any research are only as good as the data upon which they are based. However, data may be affected by the study participants, instruments used, people's memories and biological variation. As a result, no epidemiological study will ever be perfect except to minimize errors as far as possible, and then assess the practical effects of any unavoidable error [115]. The validity of epidemiological study, therefore, depends on the study design, the study conduct and data analysis [112]. In relation to the population to which the conclusion is drawn, the term validity refers to two population groups, the study population (internal validity) and general population (external validity).

Internal validity

Internal validity refers to the accuracy of measuring what the study is designed to measure in the study participants or refers to the extent to which the results of the study reflect the true situation in the study sample. It is natural to take delight in interesting findings. However, the findings of a study could be explained by other facts than the study itself. It could be due to chance, bias and confounding that should be ruled out through closer evaluation of the study design, the selection of the study participants and the data analysis. The possible alternative explanations for study results are briefly discussed below.

Chance (random sampling error)

It refers to random error or the probability that variability in sampling explains the observed result. The role of chance is measured by conducting the test of statistical significance or by estimating the confidence interval. It could be reduced by taking adequate sample size [115, 116]. In Paper I, II, V & VI, we consecutively enrolled TB cases diagnosed in public health facilities employing adequate sample size.

Properly conducted intervention studies reduce the probability of chance. It is assumed that randomization could take care of the chance occurrences of outcomes under study [102, 104]. In Paper III & IV, due to the random allocation of adequate number of clusters it is less likely that the results were affected by chance.

Selection bias (systematic sampling error)

This is a systematic distortion that results from procedures used to select subjects and from factors that influence study participation. This occurs when study participants are selected inappropriately, using different criteria, or upon prior knowledge about their exposure or outcome. Selection bias could also arise due to self-selection of volunteers, ascertainment of exposure or outcome on basis of prior knowledge, one-sided low response rate or loss to follow-up and enrolling healthy workers. It should be considered and reduced in the design and conduct of a study by using a clearly defined eligibility criteria [112, 115, 117].

In Paper I, TB patients reported over ten years were included in the study. It is possible that poor outcomes might not be reported. However, the treatment outcome data was crosschecked against the previously reported case finding which was used to calculate the treatment outcomes. In addition, only about 4% of all TB cases were not evaluated for which incomplete recording could be one of the reasons [118]; in one of the zones in the region, as high 17.5% of TB cases were not evaluated and treatment was not registered for them[119]. TB patients were prospectively (Paper III & IV) and retrospectively (Paper V & VI) followed to their place of residence. In Paper V & VI, the list of patients was obtained from the TB unit registers available in the health facilities where the patients received treatment; in this case the registration was less likely to be affected by the outcomes of the cases. In Paper II, we consecutively enrolled all TB patients and pregnant women available during the study period. Therefore, it is less likely that the results are affected by selection bias. However, ecological fallacy could be a problem for we used aggregate data of few study sites to estimate the correlation (Paper II).

In intervention studies, participants lost to follow-up and protocol deviation can occur at the level of the cluster (cluster withdrawal or lost to follow-up or inactive cluster) or the individual (participant withdrawal or lost to follow-up, or transfer from one cluster to another). However, this could be improved by regular follow-up and by intention-to-treat analysis [110]. In Paper III and IV, there was no cluster level withdrawal and individual level loss to follow was minimal to affect the comparability of the groups. Moreover, analysis using cluster as unit of analysis and cluster level values maintains comparability of the groups.

In Paper V, we found that no baseline difference between the cases enrolled in the study compared to those who were lost to follow-up and moved to other places except in the difference in treatment outcome (additional results - 6, table - 4). However, there was no difference in mortality and recurrence among those who were reported cured or treatment completed (Paper V & VI).

Information (measurement) bias

It is a systematic error that results from systematic differences in the way exposure or outcome data are obtained. This can be reduced by using eligibility criteria, defined exposure or outcome, objective and structured questionnaire and maintain blinding of the participants to exposure or outcome. In addition, implementation of standardized training using written protocol, administering the data collection under uniform conditions, conducting regular supervision and quality check could reduce information bias [117].

In our studies, standard case and treatment outcome definitions, laboratory examination method, registers and reporting formats were used. GHWs and laboratory technicians were trained. CHRL prepared reagents for sputum examination and distributed to the districts. Slides were collected for quality control to assure the quality of the tests as per the recommendation of NTLCP (CHRL reported 98% concordance with the slides from the peripheral laboratory in the study area). In addition, TB control programme experts and the investigator supervised the health facilities to follow the conduct of the studies. The data about rediagnosis was confirmed by cross-checking the report against unit TB registers in health facilities (Paper V). The diagnosis of smear-negative and EPTB had a component of subjective decision by the clinicians. However, the use of uniform training materials and case definitions based on the NTLCP guideline and working under similar setting (GHWs and the health facilities providing diagnostic service) could reduce the effect of subjective decision.

In the cost-effectiveness study (Paper IV), we included smear-positive cases diagnosed during the study period. The travel time and related costs were cross-checked against the travel distance and existing market price by the HEWs and GHWs who know the estimates of travel time and related costs. The fact that we did not give incentives or refund the expenses makes the estimate reasonable for the travelled distance and related expenses. Thus, we believe that the measurements were less prone to bias to significantly affect the study results.

Confounding

It refers to a mixing of effects that can occur when the results of a study are confused by effect of a third factor that is associated with both the exposure and the outcome but not an intermediate between them. Confounding occurs when a confounding variable is distributed unevenly across study groups and can lead to either overestimation or underestimation of the effect size, completely hide and in extreme cases reverse the direction. This is a major problem in observational studies and in some non-randomized trials if they are small. In such cases, increasing the size of the study does not make any difference to the size of confounding. However, it can be reduced at design stage by randomization, matching and restriction; and at stage of analysis by stratification and multivariable modelling [112, 115, 117, 120, 121].

In our studies, randomization (Paper III & IV), multiple logistic regression (Paper II) and Cox proportional hazard regression (Paper V & VI) were done to control for confounders. Randomization deals not only with confounders that are known and can be measured but also with other unrecognizable or unmmeasurable confounders in the study group that makes the results less likely to be affected by confounding except for the play of chance. In addition, in the analysis, we stratified the data by age, sex, residence, TB classification and category (Paper II) and by sex, level of education, marital status, occupation and TB classification (Paper V) to control for confounders in the analysis. However, in Paper II, using aggregate data made it difficult to control for confounding factors. Generally, if confounding is not evaluated, invalid and potentially dangerous results could be extrapolated to the study and general population [121] while controlling for cofounding ensures the internal validity of the study, a prerequisite for external validity.

External validity (Generalizability)

It refers to the applicability of the results to the people outside the study population. The applicability of the study results outside the study setting depends on the feasibility of conducting it under routine care and its acceptability [122]. In addition, using broader eligibility criteria increases the applicability of the findings to a wider population [123].

The results of Paper III could be applied in settings with low health service coverage (low DOTS coverage and limited number of TB laboratories), where HEWs have the first contact with the people to provide health education, and collect and transport sputum specimens and provide DOT. It is considered that, this makes the service patient-centred and improve the case finding and treatment adherence [124]. The study area is a densely populated agrarian community, typical of the rural population on the Ethiopian highlands. It could also be applied in areas with a shortage of health workers, especially laboratory technicians, with or without adequate health service coverage.

In the studies, we used the existing health service (health centres and health posts) and health workers (GHWs and HEWs) within the policy provision of community-based initiative. The study employed the routine TB care and decentralized service to the community without requiring the patients to make extra visits for the purpose of the study. This reduced the distance travelled by the patients and caregivers, travel time and related expenses. This might have increased the time for productivity by caregivers and possibly by the patients.

We believe that it was acceptable by the community as the patients received treatment under direct observation of HEWs (a member of their kebele) at health post in the kebele (the closest health facility to their living place) and possibly culturally acceptable as the patients did not travel out of their kebeles and were treated by HEWs who understand the culture and speak their language. Moreover, the improved TSR for smear-negative and EPTB add to the applicability of the intervention to all forms of TB (additional results - 5, table - 3). However, TB patients should be carefully evaluated for their general condition at diagnosis and during follow-up. Generally the implementation of our intervention in different kebeles with different TB incidence, prevalence and varying performance of TB control programme makes it more applicable.

The intervention required initial investment to start community-based TB care. But, compared to the benefits of improving case finding, reducing disease transmission and improving the treatment outcome; and cost implication to the patients, households and the health service, the researchers strongly believe that it is valid to apply to broader population. The results of the study could be applied in settings with limited health service coverage and shortage of health workers including laboratory technicians, which exists in many developing countries. The implementation should be done step-by-step to learn from the experience and improve its performance by dealing with emerging challenges.

5.2. Discussion of main findings

Decentralization of TB control programme to peripheral health facilities increased access to the service and increased the number of cases identified and treated. In our study area, involving HEWs in TB control improved the case detection and treatment success rates. It was also economically attractive for the patients, the household and the health service. This is one of the ways to overcome the challenges of the TB control programme in settings with low health service coverage and shortage of health workers in the face of HIV epidemic.

5.2.1. The role of general health workers in health facility DOT

The introduction of DOTS strategy, in response to the increasing global burden of TB, is an important landmark in the history TB control. DOTS strategy aims to detect 70% of incident smear-positive cases and cure 85% of them through early case finding and providing prompt treatment.

The implementation of DOTS strategy was started in hospitals followed by decentralization to peripheral health facilities and later involved all care providers and the community. Decentralized implementation of the DOTS strategy has successfully improved the TSR of smear-positive cases. However, its effectiveness in CDR was limited mainly due to low health service coverage, shortage of health workers, HIV epidemic, MDR TB and inadequate involvement of the available care providers [19, 124-127]. In Paper I, decentralization of DOTS to peripheral health facilities increased the TSR from 53% to 85%. However, its effectiveness in improving the CDR was limited; it increased from 22% to 45%, far below the target to effectively reduce the incidence of smear-positive cases [14]. Similarly low CDR was reported in a study conducted in rural districts of southern Ethiopia. However, the possible explanations given were treatment of adequate number of TB cases by the decentralized implementation of DOTS that reduced the incidence and prevalence of TB or low disease burden in the study area [119]. However, our findings suggested that backlog of cases were not adequately reached by the DOTS strategy to reduce the incidence and prevalence of TB due to the prevailing low health service coverage and its utilization.

Moreover, TB diagnosis and treatment was limited to health centres and hospitals. In such cases, TB suspects and patients travel long distance; have out of pocket expense and loss of productivity to seek diagnosis and treatment. This could be improved by creating awareness about TB in the community. However, this can also have impact on case finding if optimally functioning diagnostic and treatment facilities are available within the reach of the community. It is therefore required of TB control programme to identify alternatives that reduce the cost of the health service and the community to access the service. The contributions of the community health workers specifically HEWs in our settings are discussed below.

5.2.2. Community involvement in TB control

Community participation and contribution to health system was recognized as an essential element of public health interventions and primary health care [128]. After long silence, the following reasons called for renewed interest to look for cost-effective alternatives to deliver diagnostic and treatment services to TB patients. Decentralization of TB services did not increase the access to the services as expected mainly because of inadequate health service coverage, insufficient decentralization of both diagnostic and treatment services and shortage of health workers and resources. This was worsened by the increased burden of TB that overstretched the existing health services in many countries [69, 129].

In Ethiopia the main challenge for NTLCP continues to be low CDR. Attempts to increase CDR through deploying HEWs and training GHWs to identify and refer suspects has not yet demonstrated an increase in CDR. This suggests the existence of problems in the health system that needs alternative approaches to improve the programme performance [130].

Community-based case finding

TB diagnosis depends on examination of patients that visit health facilities. However, the awareness about TB, socioeconomic status, culture, access to the health service, the quality of the service and the interplay among these factors affect the health seeking behaviour of the community. Cognizant of the interplay between these factors, TB diagnosis was primarily considered to be the role of GHWs. However, evidences show geographic expansion DOTS strategy to have less effect on improving case finding [125]. Similarly, in our setting (Paper I), DOTS expansion (treatment and diagnostic units) improved the TSR while the CDR remained far below the target.

To improve the CDR in our setting, the role of community in TB case finding that involves activities such as raising awareness of TB, advocacy for adequate resources and proper care, identification and referral of TB suspects and supporting patients during treatment was revisited [14]. In Paper III, we involved HEWs in identifying PTB suspects, sputum collection and transportation to diagnostic units and administration of DOT. This has successfully increased the CDR in the intervention group (122%) compared to the control group (69%). The main reasons were increased access to diagnostic facilities that was created (by sputum collection in the kebeles and its transportation to diagnostic units by HEWs). The intervention improved geographic and economic access to the rural community. In addition, more women suspects were examined (additional results - 2) and more smear-positive cases were detected among them. This could be one of the explanations why less women TB cases are reported in DOTS strategy. We believe that our intervention addressed socio-cultural and economic factors that affected the heath seeking behaviour of women. In addition, for every smear-positive case detected in health facilities existed two undetected smear-positive cases in the community. Though, attractive the case fining is the adherence of the patients to treatment and the cost effectiveness of involving HEWs in TB control should be clearly outlined.

Community-based DOT

DOT is only one range of measures aimed at promoting treatment adherence. Thus, the fight against TB, a scourge to humanity, requires a concerted effort of the health system, care providers and the community. This presupposes a patient-centred service that is easily accessible, convenient and acceptable without compromising the treatment success. To this end a range of community members, TB patients, families, community leaders and CHWs were involved in providing DOT. Community DOT was found to be as effective as the health facility based DOT [126, 131-133]. The study (Paper III) has shown community DOT - treatment by HEWs to be more effective than the health facility DOT in our setting. The TSR was 89% in the community and 83% under health facility DOT. In addition, the rate of defaulter, failure and transfer out was low in the community-based approach. This could be mainly due to the improved geographic and socioeconomic access created by providing DOT in the community.

Cognizant of the argument that treatment success should be improved prior to increasing the case detection, except for improving the TSR the effectiveness of CHWs in improving the CDR was limited [133, 134]. This could be due to the fact that the role of CHWs was limited to improving treatment adherence and providing health education. Is this a failure of DOTS strategy? [127] In our study, we have explored option of involving HEWs in sputum collection and improved the CDR. However, the cost-effectiveness of involving HEWs in sputum collection required further study.

Cost-effectiveness of community DOT

Health interventions of public health importance should be cost-effective. This is of most use in situations where a decision maker, operating with a given budget, is considering a limited range of choices within a given field.

Studies show that involving CHWs in providing DOT is a cost-effective alternative for economic reasons for the patients, household and health service. Compared to health facility DOT, community DOT is effective without compromising the TSR [135-138]. But, its cost-effectiveness varied with the type and the role of the CHWs involved in community-based approaches, the health service coverage and other related factors [139-144]. In Paper IV, the cost per successfully treated smear-positive patient in the intervention area ($61) was lower compared to health facility DOT ($162). It reduced the cost per successfully treated smear-positive case by 63%. For the same amount of cost of treating a patient in health facilities more than two patients could be treated in their communities. This was due to the decentralization of the service and reduced the travelled distance and time and associated costs for seeking treatment.

In addition, the high cost incurred for seeking diagnosis in public health facilities ($13, about 10% of GDP loss or loss of 10 working days) could also be one of the reasons for low CDR at its least estimate excluding the cost related to visits made to other health facilities and traditional healers (additional results 4). Other studies reported that the cost of seeking diagnosis to be prohibitively high for the patients and their household [47-51]. In this study, stronger belief is held that community-based sputum collection has reduced the cost of seeking diagnosis in public health facilities due to the reduced travel distance, time and related costs.

As cost-effective as it may be, implementation of community DOT at larger scale was limited due to high turnover and/or exhaustion of the CHWs, additional cost incurred to run community-based programme and lack of sustainability [124, 133]. Hence, community-based efforts to control TB should be patient centred, sustainable and integrated into the general health service in such a way that it complements the existing health service delivery.

In Paper III & IV, involving HEWs improved the CDR and TSR and was cost-effective compared to the health facility DOT. The health workers involved in our study operated under the provision of the health policy of the country, employed and received salary and supervised by public health professional in health centre. In addition, two HEWs were assigned in each kebele and training schools deploy new graduates to address the attrition [145]. This ensures the sustainability of involving HEWs in TB control in Ethiopia.

5.2.3. Long term efficacy of DOT

Effective disease control strategy should be efficient in identifying the cases early, providing prompt treatment and ensuring long term disease free survival of the patients. Therefore, understanding the long term efficacy of the DOTS strategy in reducing the rate of recurrence (either due to relapse or reinfection) [146-150], mortality, development of MDR TB and its effectiveness in the face of HIV epidemic and socioeconomic deprivation is crucially important [151-156].

In Paper V & VI, we found high recurrence rate and mortality among successfully treated TB patients. The plausible explanations were HIV infection, MDR TB and possibly continued transmission due to high backlog of untreated cases in the community. In Paper II, the prevalence of HIV infection in the community was 3.8% and the rate of TB-HIV co-infection was 17.5%. This is high enough to affect the survival of TB patients after successful treatment.

Moreover, we reported excess mortality (Paper VI) in TB patients after successful treatment. The mortality was higher in non-farmers (SMR=9.95, 95%CI: 7.17 - 12.73). This could also be explained by HIV infection and to some extent by prevalence of MDR TB. Thus, TB control programmes should strengthen patient follow-up, provide HIV counselling and testing for TB patients during follow-up period and after successful treatment. This requires decentralized implementation of provider initiated HIV counselling and testing for TB patients that is performing in limited health institutions. Less than five percent of TB patients were tested for HIV during the study period which has now increased by three fold [21]. Further study is needed to estimate the prevalence of MDR TB and causes of death in successfully treated TB patients.

Strategies that enhance TB-HIV collaboration activities are needed in such settings. All TB patients should be encouraged to be tested for HIV and enrolled for antiretroviral treatment and management of other opportunistic infections. HIV negative TB cases should also be advised to reduce their risk and be encouraged to live HIV free life. The health facilities should organize their facilities in such a way that it encourages simple patient flow and convenience.

In addition, the role of the community and HEWs in prevention and control of the two diseases should be clearly outlined and implemented. This should be accompanied by decentralization and scaling up of DOTS strategy and provision of antiretroviral treatment. This will increase the number of patients accessing and receiving the service to benefit from the available treatment that will contribute to the long term efficacy of DOTS strategy.

We demonstrated the significance of community-based intervention in TB control within the existing health system in Ethiopia. The recommendations of our study were taken up by the Federal Ministry of Health of Ethiopia. The SNNPRS Health Bureau required larger scale implementation of the community-based TB care to provide evidence-based decision making for policy change to make sure that the benefits of the study were shared by TB patients, the community and TB control programme of the country.

We therefore recommend further larger scale intervention to strengthen the health system and improve the performance of the NTLCP of Ethiopia through community-based approaches based on evidences from the field. In such cases, health system strengthening should also be part of the intervention where the GHWs and HEWs will receive adequate training and necessary resources made available. The service should then be progressively scaled up and based on the lessons learned should be used to improve the model of the implementation. This should also be accompanied by monitoring and evaluation of the impact and quality of the community-based approach to improve the role of HEWs and the community in TB control.

The NTLCP has recognized the role of HEWs in TB control and decided to start case finding and treatment by HEWs. The WHO in collaboration with the NTLCP has started a pilot project of implementing community-based case finding through referral of suspects and decentralization of treatment to health posts under the direct observation of HEWs in four big regions of the country. Currently the Federal Ministry of Health of Ethiopia has accepted the implementation of community-based TB care by employing HEWS in referring suspects and encouraging adherence to treatment. National guideline for implementing community-based TB care was developed to start implementing the service at larger-scale.

6.0. Conclusions and recommendations

6.1. Conclusions

1. Decentralization of DOTS strategy to peripheral health facilities improved the CDR and TSR under the observation of GHWs
2. The rate of TB-HIV co-infection is high and is associated with the prevalence of HIV infection in the community
3. Beyond achieving the treatment success rate of 85%, the recurrence and mortality rate was high in successfully treated TB patients. Therefore, identifying the causes of recurrence and death is important to ensure disease free survival of TB patients.
4. Involving HEWs in community-based case finding and treatment of smear-positive TB cases improved the CDR and TSR. More women smear-positive cases were identified and treated in the community-based approach.
5. Involving HEWs in TB treatment is cost-effective and increased the number of treated TB cases for the same amount of cost under health facility DOT. This is economically attractive option for the patients, households and the health service.

6.2. Recommendations

6.2.1. Clinical practice

1. GHWs should be trained about identifying TB cases that require closer follow-up in health centres and hospital before referring them for treatment in the community under HEWs and vice versa.
2. HEWs should be trained about identifying seriously ill TB patients and patients with side effects that need referral and follow-up in health centres and hospitals.

3. GHWs and HEWs should inform TB patients to be tested for HIV during treatment and even after completing treatment to benefit from the available care.
4. TB patients should be advised to seek medical care if they develop symptoms of TB after completing treatment.

6.2.2. Public health implications

1. Decentralization and implementation of DOTS strategy should be accompanied by regular monitoring and evaluation of its performance.
2. Routine TB data reported from districts to higher levels should be analysed and utilized locally to improve the performance of TB control programme in the districts.
3. Regular surveillance of HIV prevalence, TB-HIV co-infection and MDR TB should be incorporated into TB and HIV Prevention and Control Programmes
4. Early identification and prompt treatment of smear-positive TB cases should be emphasized to reduce the risk of transmission in the community
5. Supportive supervision should be strengthened to improve the performance of community-based interventions as part of strengthening the delivery of health service to the community. It should be clearly outlined and practiced at all levels.

6.2.3. Future research

1. Conduct a community-based smear-positive prevalence survey to estimate the burden and the impact of the interventions on the incidence and prevalence of smear-positive TB

2. Determine the causes of recurrence in smear-positive cases after successful treatment under DOTS
3. Estimate the cost-effectiveness of community-based sputum collection in improving case finding of smear-positive cases.
4. Determine the causes of death among successfully treated TB patients to better estimate mortality related to TB
5. Evaluate the significance of community-based case finding and treatment at larger scale as an integral part of strengthening the health system of the country.

6.2.4. Policy

1. The role of HEWs in TB case finding and treatment should be clearly stated and its implementation should be supported by measurable indicators to increase the contribution of the HEP in the efforts to prevent and control TB in Ethiopia
2. In collaboration with the HEP, the NTLCP should incorporate the role of HEWs in TB control. This should be supported by including it in the NTLCP guideline and implementation documents specifically prepared for HEWs.
3. Community-based DOT is cost-effective intervention in an effort to reduce the diseases burden and save lives, worth adopting in resource constrained settings
4. Community-based DOT is cost-effective intervention. However, it is not without cost. Therefore, initial investments related to involving HEWs in TB control should be clearly identified and planned before embarking on scaling it up

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Annexes

I. CASE FINDING FORMAT

TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME ETHIOPIA

Quarterly report on tuberculosis case-finding

Level of report (tick on the appropriate box): **Region** ☐ **Zone** ☐ **Woreda** ☐

Quarter during which patients were registered: **Quarter** ☐ **Year (EC)** ☐

Region: ______ Zone: ______ Woreda: ______

Name of Co-ordinator: ______ Date: ______ Signature: ______

ALL CASES REGISTERED DURING THE QUARTER:

Pulmonary tuberculosis											Extra-pulmonary TB		Totals		
Smear positive									Smear negative						
New cases			Relapses		Failures		Defaulters						All male	All female	Grand total
M	F	Total	M	F	M	F	M	F	M	F	M	F			

SMEAR POSITIVE NEW CASES BY AGE AND SEX:

0 - 14		15 - 24		25 - 34		35 - 44		45 - 54		55 - 64		65+		All male	All female	Total
M	F	M	F	M	F	M	F	M	F	M	F	M	F			

NUMBERS OF NEW SMEAR POSITIVE CASES PUT ON SCC OR LCC:

SCC	
LCC	

NUMBERS OF NEW SMEAR NEGATIVE AND EPTB CASES PUT ON SCC OR LCC

SCC	
LCC	

SMEAR CONVERSION AT 2 MONTHS OF NEW SMEAR-POSITIVE CASES PUT ON SCC **DURING THE PREVIOUS QUARTER**

New cases	2 month smear result		
	pos	neg	not done

II. TREATMENT OUTCOME FORMAT

TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME ETHIOPIA

Quarterly report on the results of treatment of all TB patients registered 13 - 15 months earlier

Patients registered during quarter: Year (EC):

Region: Zone: Woreda: Date:

Name of Co-ordinator: Function Signature: Date received by TLCT:

	PTB SMEAR POS	PTB SMEAR NEG	EPTB
Total number of new patients registered during the quarter being reported:			
Total number of cases registered for re-treatment during the reported quarter:			

Regimen		Number registered	Cured	Treatment completed	Died	Failure	Defaulted	Transferred out	Total number evaluated*
New cases PTB-POS.	SCC								
	LCC								
New cases PTB-NEG.	SCC								
	LCC								
New cases EPTB	SCC								
	LCC								
Re-treatment									

* if number evaluated is less than no.registered, comment COMMENTS:

III. UNLINKED ANONYMOUS SEROSURVEY IN TB PATIENTS

Study site ______________

Date ___________

Patient code no _______________

Age __________

Sex __________

Address   Urban ___________ Rural _______________

Diseases category   a) New   b) Relapse   c) treatment after default

Disease classification   a) PTB+ve   b) PTB -ve   c) EPTB

Name of responsible health worker ________________ Signature ____________

Note: From ANC surveillance format we included study site, date, client code, age, sex and address as variables for paper II.

IV. CHECKLIST OF SYMPTOMS IN TB SUSPECTS IN THE COMMUNITY

Questionnaire no.________ Name of interviewer __________ Date___________________

1. Socio-demographic variables

1.1 Name of suspect ____________________ 1.2. Age________1.3. Sex _____________

1.4. Cluster __________ Kebele _________Residence urban _____ rural ______________

1.5. Marital status Single___________ Married__________ Divorced________________

Widowed________ other (specify) ____________________________

1.6. Educational status No schooling ____ Grade ____ other (specify) ______________

1.7. Occupation of suspect Farmer ____ student ____ merchant ____________ ______

House wife ________government employee____________ _______

daily labourer__________ others (specify) _____________________

2. Tuberculosis symptoms and history

2.1. Did you experience cough for two or more weeks? Yes __________ No ________

If yes, for how many weeks _________

2.2. Is the cough productive of sputum? Yes __________ No ________

If yes, does it contain blood? Yes __________ No ________

2.3. Did you have fever and night sweats? Yes __________ No ________

If yes, for how many weeks _________

2.4. Did you have loss of appetite? Yes __________ No ________

If yes, for how many weeks _________

2.5. Did you loss weight? Yes __________ No ________

2.6. Did you have chest pain? Yes __________ No ________

If yes, for how many weeks _________

2.7. Did you have shortness of breath? Yes _________ No ________

If yes, for how many weeks _________

2.8. Did you have history of tuberculosis treatment? Yes __________ No ________

2.9. Did you have closer contact with known TB patient? Yes __________ No ________

V. LABORATORY REGISTER

LABORATORY REGISTER FOR AFB

Month(s): ____________ **Year:** ___________

Patient number	Health Unit	Date	Lab. Serial number	Name and address of patient	Age	Sex	Name and address of contact person	New patient	Follow-up	Woreda TB/Lep number	Results			Sign	Remarks
											1	2	3		

VI. UNIT TB REGISTER - INTENSIVE PHASE TREATMENT

Unit TB Number	Name (in full) and address of patient	Sex M/F	Name and address of contact person	Smear result	Category N.R.F.D.T.O	Intensive phase			Intensive phase treatment monitoring chart																													
Woreda TB No.		Age		Lab. no.	P/Pos, P/Neg or EP	Drug	Dose		Days:																													
				Weight				Mth	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30

VII. UNIT TB REGISTER - CONTINUATION PHASE TREATMENT

Sputum results, lab.name, serial nr.& wt			Continuation phase		Continuation phase treatment monitoring chart 4 - weekly attendance: Month:													Date treatment stopped (enter date in appropriate column):						Remarks
2nd month	5th month	7th/11th month	Drug	Dose	Ham	Neh	Pag	Mes	Tik	Hid	Tah	Tir	Yek	Meg	Mia	Gin	Sen	Cured	Treatment completed	Died	Failure	Default	Transfer out: name of unit	

VIII. COST OF TB TREATMENT - INTENSIVE PHASE

Cost items for intensive phase treatment for TB patients											
Questionnaire number			Name of interviewer								
Background											
1. Name of TB case											
2. Age											
3. Sex											
4. Kebele											
5. Religion											
6. Marital status											
7. Educational status											
8. Occupation											
Cost of TB case											
	date	means of transport	travel time in minutes	travel cost	type of meal	cost	type of drinks	cost	accommodation (if stayed overnight)		
Visit to GHWs or HEWs									place	amount paid	reason

Cost of companion											
Visit to GHWs or HEWs	date	means of transportation	travel time in minutes	travel cost	type of meal	Cost	type of drinks	Cost	accomodation (if stayed overnight)		
									place	amount paid	reason

IX. COST OF TB TREATMENT - CONTINUATION PHASE

Cost items for continuation phase treatment for TB patients											
Questionnaire number			Name of interviewer								
Background											
1. Name of TB case											
2. Age											
3. Sex											
4. Kebele											
5. Religion											
6. Marital status											
7. Educational status											
8. Occupation											
Cost of TB case											
	date	means of transport	travel time in minutes	travel cost	type of meal	cost	type of drinks	cost	accommodation (if stayed overnight)		
Visit to GHWs or HEWs									place	amount paid	reason

Cost of companion											
Visit to GHWs or HEWs											
	date	means of transportation	travel time in minutes	travel cost	type of meal	Cost	type of drinks	Cost	accomodation (if stayed overnight)		
									place	amount paid	reason

Note: Use extra sheet for more than one care takers

X. COMMUNITY-BASED POST-TREATMENT FOLLOW-UP FORMAT

Questionnaire no.________ Name of interviewer ______________________

Date______/_______/________

Socio-demographic variables during past treatment

1. Name of TB patient___________________ 2. Sex ___________

3. Age at first diagnosis ___________ 4. Kebele ______________

5. Health facility _______________________ 6. TB unit register number ___________

7. TB classification PTB +ve __________ PTB -ve _________ EPTB ________

8. Treatment category New ____ Relapse _____ Failure ____ Defaulter ____ others ___

9. TB treatment regimen ____

10. Date treatment started _____/_________/________

11. Treatment outcome Cured __________ Treatment completed __________

12. date treatment completed _____/_________/________

Current sociodemographic character after completing treatment for TB

1. Current condition Alive ______ Dead ______ Date of death _____/______/______

2. Marital status Single___ Married___ Divorced___ Widowed____ other___________

3. Educational status No schooling ____ Grade ____ other _____________________

4. Occupation of suspect Farmer ____ student ___ merchant ___others ____________

History related to tuberculosis after first treatment for TB

1. History of diagnosis for TB Yes ____ No ____ 2. Health facility _________

2. TB classification PTB +ve __________ PTB -ve _________ EPTB ________

3. TB category New ____ Relapse _____ Failure ____ Defaulter ____ others ________

4. Date treatment started ____/___/____ 5. Date treatment completed ____/___/_____

6. Treatment outcome Cured ___Completed ___ Died ___ Failure __ Default __ TO ___

7. History of cough Yes____ duration in months _______

Note: 1. Collect sputum specimen for patients with productive cough of two weeks or more

2. Advise and refer patients who have other medical conditions