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Factors Contributing to Delay in Seeking Treatment among Pulmonary Tuberculosis Patients in Suneka Sub-County, Kenya

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Abstract

Tuberculosis is a major global public health problem and a leading cause of morbidity and mortality in Kenya. TB control has remained a major challenge for the TB control programme especially in this HIV/AIDS era and the emergence of multi-drug resistant TB (MDR-TB). Early identification of cases and commencement of effective chemotherapy is an effective method to control the spread of TB. Reliance on passive case finding means that patients play a key role in reducing delay to diagnosis and treatment. Patient delay (duration from onset of symptoms to first contact with a health care provider at a public health facility) is a major challenge to TB control and is dependent on several factors. The purpose of this study was to determine the duration from onset of symptoms to seeking appropriate TB treatment among pulmonary TB (PTB) patients and investigate the factors associated with patient delay in Suneka sub-County, Kisii County, Kenya. A cross-sectional survey, using a semi-structured questionnaire, was carried out at five public health facilities in the sub-County. Data entry, management and analysis were done using SPSS Version 15. The mean patient delay and associations between length of patient delay and the various independent variables was determined. Multiple logistic regression was performed to determine the factors independently associated with patient delay. The mean patient delay was 54 days and 65.4% of the study subjects had delayed for more than 30 days. Delay in seeking appropriate TB treatment among PTB patients in Suneka sub-County was associated with poor perception of services in public health facilities (OR=4.91; CI=1.6-15.3; P=0.0061), visiting a private clinic (OR=4.24; CI=1.5-11.6; P=0.0052) and stigma (OR=2.46; CI=1.9-12.2; P=0.0178). Most PTB patients in Suneka sub-County delay in presenting at public health facilities after the onset of major TB symptoms and the main factors responsible for this delay include having a poor perception of the quality of services offered in public health facilities, prior attendance at a private clinic and stigma associated with the disease. Delay was not found to be associated with the patient socio-demographic characteristics, knowledge of TB, distance or transport cost to the nearest public health facility. Since TB services are integrated in the general health care system, the findings highlight the need by the Ministry of Health (MOH) to improve service delivery at public health facilities and thereby encourage patients to seek early diagnosis and treatment of communicable diseases or reduce patient delays. Educational campaigns should go beyond providing general information about TB to emphasize embracing a positive attitude of transmission reduction through early treatment.

Keywords: Delay; Treatment; Pulmonary tuberculosis; Patients

Background Information

Tuberculosis is an infectious bacterial disease caused by Mycobacterium tuberculosis which commonly affects the lungs but can affect other parts of the body [1]. The disease which is a major global public health problem was declared a global emergency by the World Health Organization (WHO) in 1993. In Africa, the WHO Regional Committee for Africa also declared the disease an emergency [2].

The risk of infection is high from a person who is not on treatment especially if the contact occurs in poorly light and poorly ventilated environments [3]. In most cases, the body is able to contain the infection thus majority of individuals do not develop TB disease [4]. However, in the old and very young children (especially those under one year), the poorly nourished and individuals with poor immune defenses (such as persons infected with HIV), the risk of developing TB disease following an infection is high [3].

Kenya is one of the highest TB burdened countries in the world. The burden is increasing as a result of poverty, population growth and HIV/AIDS [5]. The number of TB cases related in the country increased tenfold from 11,625 in 1990 to 116,723 in 2008 [3]. The incidence of all forms of TB in Kenya (353 new cases per 100, 000 populations per year) is higher compared to that of Tanzania (297 new cases per 100, 000 populations per year) and Uganda (330 new cases per 100,000 populations per year) [1].

Although the Ministry of Health and Public Health and Sanitation [3] have made tremendous progress in the fight against TB, scanty information on the extent and factors influencing patient delay in rural areas like Suneka sub-County pose a challenge to TB control efforts.

Statement of the problem

TB is a major global public health problem and a leading cause of morbidity and mortality in Kenya. Control of the disease in this HIV era has been made difficult by the emergence of MDR-TB [5] case finding, initiation of effective chemotherapy are cornerstones in TB control. However, where TB case finding is largely passive as is the case in Kenya, the patient plays an important role in reducing delay to diagnosis. Delay in seeking appropriate TB treatment is a challenge in TB control [3].

The MOH estimates that about 50% of TB cases in Kenya remain undiagnosed in the population [3]. These cases contribute to increase in transmission, mortality and morbidity and the effects are severe in TB patients co-infected with HIV. The burden of undiagnosed TB may be attributable to patients' late presentation [6,7]. In spite of its importance in case finding, quantitative information on the extent and factors influencing patient delay in seeking appropriate TB treatment particularly in the high HIV prevalence area of Suneka sub-County is lacking.

It`s against this background that the researcher was prompted to investigate the predictors of patient delay in PTB control in Suneka sub-County.

Purpose of the study

The purpose of this study was to determine the duration from onset of symptoms to seeking appropriate TB treatment among pulmonary TB (PTB) patients and factors associated with patient delay in the high HIV prevalence area of Suneka sub-County.

Objectives of the study

General objective: To determine the factors influencing patient delay in seeking appropriate TB treatment in Suneka sub-County.

Specific objectives: To find out the socio-demographic characteristics influencing patient delay in seeking appropriate PTB treatment in Suneka sub-County.

To determine the prevalence of patients delay in seeking appropriate TB treatment in Suneka sub-County.

To determine the duration from onset of major symptoms to the time of seeking appropriate TB treatment among PTB patients in Suneka sub-County.

Research questions

What are the socio-demographic characteristics influencing patient delay in seeking appropriate PTB treatment in Suneka sub-County?

What is the prevalence of patients' delay in seeking appropriate TB treatment among PTB patients in Suneka sub-County?

What is the duration from onset of major symptoms to the time of seeking appropriate TB treatment in PTB patients in Suneka sub-County?

Significance of the study

A good understanding of the predictors of patient delay is important in TB control. Information from this study may be useful to the Ministry of Health (MOH) in developing interventions aimed at improving early identification of pulmonary TB cases so as to initiate effective chemotherapy and minimize the potential of disease transmission in the population. When PTB cases are identified early and effective treatment is started, the burden of morbidity is greatly lessened in the patient.

Justification

Early diagnosis and treatment of Tuberculosis is crucial for reduction of infection rate and improving outcome of the treatment. Despite efforts made through media to sensitize community of the warning symptoms of TB, still there is a significant delay in health care seeking among TB patients.

Limitations of the study

Respondents who might treat the researcher with suspicion and withhold some information which may hamper the outcome of the research.

Scarcity of finances to cover the entire population of PTB patients.

Assumptions of the study

The questionnaires were answered properly, accurately and without major personal bias.

The sample selected was a true representation of the population of the people involved in influencing delay in seeking treatment among pulmonary tuberculosis patients in Suneka sub-County.

Conceptual framework

The duration from onset of TB symptoms to initiation of effective TB chemotherapy is generally referred to as total delay. This delay is divided into two:

Delay due to patient related factors (patient delay).

Delay due to health system related factors (health systems delay). Health system delay comprises of diagnostic and treatment delay.

TB patients may delay in seeking appropriate TB treatment promptly due to factors related to access to health care services such as socio, economic and demographic factors, stigma and perceptions of disease and health care services (Figure 1).

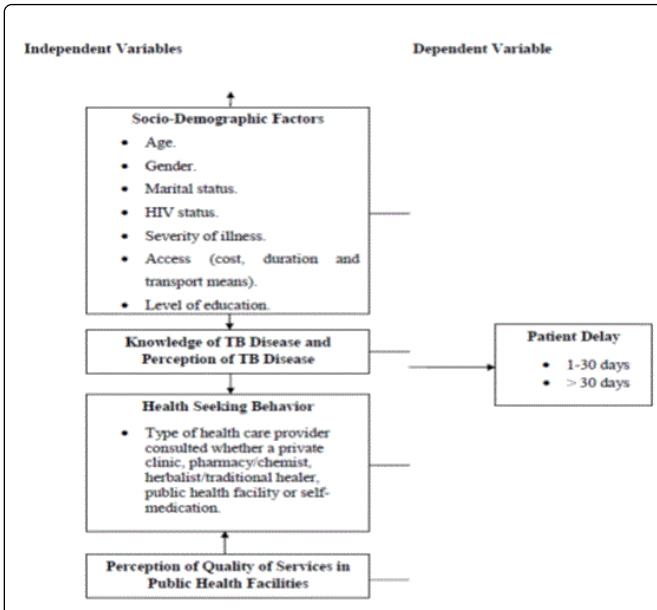

Figure 1: Independent variable and dependent variables.

Methodology

Introduction

This chapter seeks to describe the research area, research design, target population, the sample size, and the sampling method, and data collection, procedure for data collection, ethical issues and communication of results.

Study area

The research was carried out in Suneka Sub-County. The area is located along the Kisii-Migori route. Majority of the population are poor and depend on rain fed subsistence agriculture.

The area experiences adequate rainfall in 2 seasons March and August. The soil is mainly loam which is conducive for growth of maize, tea, cassava and coffee at large scale as major economic activity hence most people practice farming though the pieces of land are not large enough for huge productions. About 50% of the population is economically stable. Sources of income are small scale farming, small scale business, casual labour etc. The region's staple food is ugali from maize served with locally available vegetables, milk, meat and eggs.

Topography of the area is flat with low ridges, valleys and rivers. This favours easy communication due to well-constructed tarmacked roads. However, other roads are untarmacked hindering transport and communication especially during rainy season. Modes of transport include; public vehicles, motor bikes and rarely bicycles.

Study design

A cross sectional survey was conducted in which questionnaires were administered to PTB patients seeking treatment from Iyabe District Hospital, Itiero, Riana, Riotanchi and Itibo Health Centres. This design has various advantages such as the ease of assessing the study participants and at relatively low cost. It is disadvantaged as in the inability to establish causal relationship to enable the capture of adequate responses.

Target population

The study targeted PTB patients aged 15 years and above in high HIV prevalence rural areas in Suneka Sub-County.

Study population

The study population consisted of newly diagnosed PTB patients and PTB patients in the intensive phase of TB treatment aged 15 years and above who sought treatment from the five public health facilities in Suneka sub-County during the eight week period of survey.

Inclusion and exclusion criteria

Inclusion criteria: Patients with proven TB. PTB patients aged 15 years and above. Residents in the study area.

Exclusion criteria: **Patients aged below 15 years**

PTB patients who had been on TB treatment for a period of over two months. Patients who do not reside in the study area.

Sampling procedure

Purposive sampling technique was used to identify the public/government health facilities in Suneka sub-County namely Iyabe District Hospital, Itiero, Riana, Riotanchi and Itibo Health Centres. These were selected as study sites because they reported high TB caseloads in 2012 and also because all except Iyabe had sputum microscopic equipment. Purposively identifying these facilities made it possible to capture newly diagnosed PTB patients thus minimizing recall bias. The inclusion of Iyabe level Four Hospital served to ensure that the sample was more representative since the hospital serves patients from the entire Suneka region. The patient sample in each health facility was a convenience sample.

Sample size determination

The sample size was determined using the formula by Fisher's et al. for determining the sample size when the population is less than 10,000. The confidence interval was set at 95% with 5% margin of error.

$$nf = \frac{n}{(1+n)/n}$$

Where;

nf=Desired sample size (when the target population is less than 10, 000).

n=Desired sample size (when the target population is more than 10, 000).

N=Estimate population of PTB patients in the intensive phase of TB treatment aged 15 years and above in Suneka Sub-County. In the last quarter of 2015, N was 128 PTB patients.

$$n = \frac{Z^2 pq}{d^2}$$

Z=The standard normal deviate at the required confidence level (1.96) which corresponds to 95% confidence interval.

p=Proportion in the target population estimated to have the characteristics being measured (proportion of TB patients who delay for more than one month is assumed to be 50%).

q=1-p

d=Level of statistical significance set (0.05)

$$n = \frac{(1.96)^2 \times (0.5) \times (0.5)}{(0.05)^2}$$

$$= \frac{0.9604}{0.0025}$$

=384 patients

Therefore;

$$nf = \frac{384}{1 + 384/128} = 128$$

However at the data collection stage, the researcher administered questionnaires to 133 PTB patients.

Methods of data collection

The researcher visited each health facility at least three times during the 8 week study period. Each visit was planned to coincide with a clinic day (usually a week day) when all the newly diagnosed patients and those in the intensive phase of treatment went for review and to collect drugs for the following week. The questionnaire was administered in a private room after the patients had been seen by the clinician. It took ten to twenty minutes to administer the questionnaire to each respondent after informed consent was sought. A closed-ended questionnaire was used and the sort of questions asked include; socio-demographic information, first symptoms and health seeking behaviors, knowledge and perception of TB disease.

Data was analyzed using SPSS version 16. Descriptive statistics performed include determining the means, median, Standard Deviation (SD) and range.

Validity

The validity of the questionnaire was based on expert opinion and a field test. The supervisors examined the questionnaire and the appropriate changes they recommended on; content, construct, criterion and face validity were made in consideration to the field test results.

Reliability

A pilot test was carried out involving at least 20 respondents not included in the actual sample to obtain data that was analyzed by SPSS to determine the reliability coefficient.

Pilot study

The questionnaire was translated into Kiswahili and Gusii and transcribed to check accuracy then pre-tested on 20 PTB patients in two other health facilities namely; Gakero and Motonto in Suneka sub-County. The questionnaire was administered in English, Kiswahili or Gusii depending on the patient's preference. Ambiguities in translations were clarified and appropriate modifications done on affected items.

Ethical and logistical considerations

Permission to carry out the study was sought from the Board of Post Graduate studies of JOOUST and the University of Eastern Africa Baraton Ethical Review committee, and also from KisiiTeaching and Referral Hospital, further clearance was sought from Suneka sub-County Public Health Officer. Informed consent from the respondents was sought by informing them the objectives of the study and completing the consent form. The respondents were assured of confidentiality with all the information that they provided in the questionnaire.

Results

Socio-demographic characteristics of the study subjects

One hundred and thirty three (133) study participants were interviewed in five public health facilities in Suneka Sub-County representing 104% of the targeted sample size. The proportion of study subjects interviewed in each health facility is shown in Figure 2.

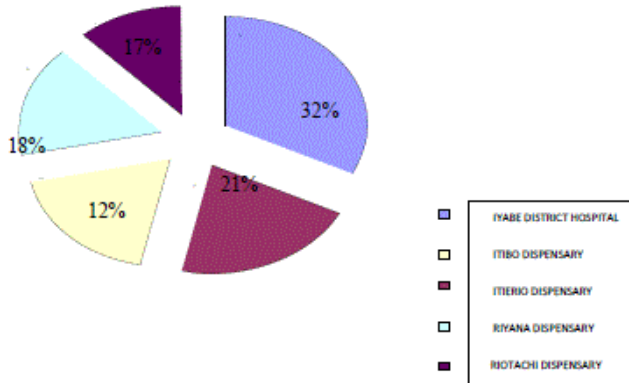

Figure 2: Proportion of study subjects interviewed in the five public health facilities (n=133).

The sample consisted of approximately 53% males and 47% females (Table 1). The mean and median age was 35 and 33 years respectively. Fifty two (39%) of the study subjects were aged between 25-34 years (Figure 3).

Variable	Frequency	Percentage (%)
Gender		
Male	70	52.6
Female	63	47.4
Level of Education		
None	10	7.5
Primary	73	534.9
Secondary	41	30.8
College graduate	9	6.8
Marital Status		
Single	42	31.6
Married	77	57.9
Widow/widower	14	10.5
HIV Status		
Positive	60	45.1
Negative	55	41.4
Do not know	18	13.5
Severity of Illness		
Not hampered	22	16.5
Moderate	61	45.9
Severe	50	37.6

Table 1: Socio-demographic characteristics of study subjects (n=133).

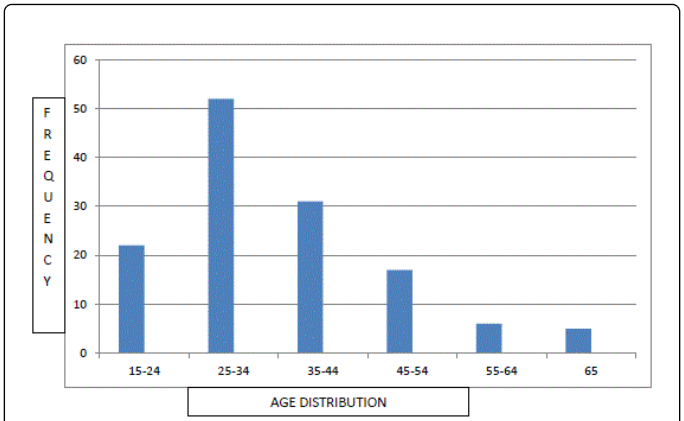

Figure 3: Age distribution of study subjects (n=133).

Seventy seven (57.9%) were married and 60 (45.1%) of the patients were HIV positive. Eighty three (62.4%) of the study subjects had either primary education or had no formal education. Sixty one (45.9%) could only perform light chores in their homes (were moderately ill) by the time of seeking TB treatment from a government/public health facility while 50 (37.6%) were severely ill (house bound or bed ridden) and 22 (16.5%) were not hampered by the TB (could still do a full day's work) by the time of first visit to a public health facility.

Fifty seven (42.1%) of the patients took 2-3 hours to reach the nearest public health facility and 33 (24.8%) took over 4 hours. Seventy seven (57.9%) spent more than Kenya Shillings (Ksh) 100 (US$1.3) as transport to and from the public health facility. Matatus (public transport vehicles) were the most frequently used means of transport used by 68 (51.1%), followed by Boda Boda (bicycle taxi) which were used by 40 (30.1%) of the patients (Table 2).

Patient delay

The mean patient delay was 54.1 days (SD=14; median=53.5) and a range of 7-120 days. Eighty seven (65.4%) of the PTB patients had delayed for more than 30 days before seeking treatment from a government/public health facility.

Variable	Number	Percentage (%)
Duration		
0-1 hrs	43	33.1
2-3 hrs	57	42.1
Over 4 hrs	33	24.8
Means of transport		
Walk	25	18.8
Boda Boda	40	30.1
Matatu	68	51.1
Cost of transport		
Less than Ksh 100	56	42.1
Ksh 101 and above	77	57.9

Table 2: Distribution of study subjects by duration, cost and means of transport used to access a Government/public health facility (n=133).

Patient delay and socio-demographic factors

Age and gender: The mean age of males was 40 years (SD=13; median=39) and that of females was 29 years (SD=7; median=28). Forty nine (67.1%) of the males compared to 38 (63.3%) of the females had delayed for more than 30 days (Table 3).

Males had a mean patient delay of 51.2 days (SD=9; median= 51), while females had a mean patient delay of 57.6 days (SD=11.6; median 56).

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (> 30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Age					
15-44	34 (32.4)	71 (67.7)	105	0.70 (0.3-1.6)	0.5422
45-65+	12 (42.9)	16 (57.1)	28	2.2 (0.2-20.3)	0.4268
Gender					
Male	24 (32.9)	49 (67.1)	73	0.65 (0.4-2.6)	0.5321
Female	22 (36.7)	38 (63.3)	60	0.78 (0.5-3.8)	0.6426

Table 3: Proportion of PTB patients with longer delay according to age and gender (n=133).

No significant association was established between age and longer patient delay {delay of more than 30 days}, (p=0.4268). Similarly the role of gender in patient delay was not significant (p=0.5321) (Table 3).

Marital status

The number of widows/widowers who had a longer delay was smaller 7 (50%), than that of single 29 (69.0%) and married 51 (63.6%) patients. About four (57.0%) of the widows/widowers were HIV positive. The role of marital status in patient delay was not found to be significant by this study {(p=0.1015) (Table 4).

HIV Status

Forty one (68.3%) of the HIV positive PTB patients reported longer delays compared to 34 (61.8%) of the HIV negative and 12 (66.7%) of the patients who did not know their status (Table 4). The role of HIV status in patient delay was not statistically significant (p=0.0950).

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (> 30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Marital status					
Single	13 (31.0)	29 (69.0)	42	0.85 (0.4-1.9)	0.8309
Married	26 (33.8)	51 (62.6)	77	0.80 (0.4-1.7)	0.7028
Widow/widower	7 (50.0)	7 (50.0)	14	3.25 (0.7-15.0)	0.1015
HIV status					
Positive	19 (31.7)	41 (67.1)	60	2.03 (1.0-4.3)	0.0982
Negative	21 (38.7)	34 (61.8)	55	0.55 (0.3-1.2)	0.16
Do not know	22 (36.7)	12 (66.7)	18	0.73 (0.3-2.1)	0.7579

Table 4: Proportion of PTB patients with longer delay according to marital and HIV status (n=133).

Level of education

Sixty percent (60.0%) of those with no formal education had a longer delay compared to 57.5% of those who had primary level of education, 61.0% of those with secondary level of education and 55.6% of the college graduates (Figure 4). The level of education was however not found to be significantly associated with longer patient delay (p=0.5332).

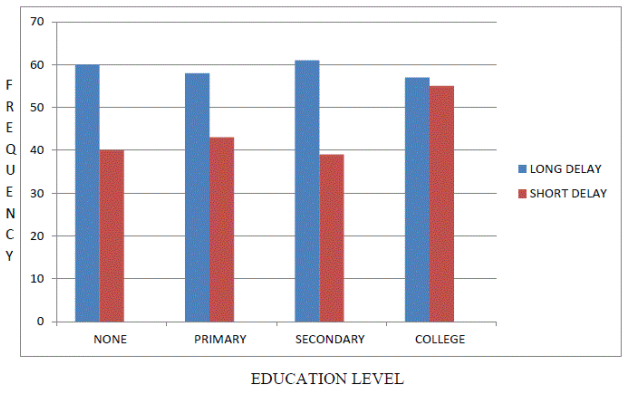

Figure 4: Patients with long and short delay according to education level (n=133).

Severity of illness

Forty five (90.0%) of the severely ill patients reported a longer delay compared to 8 (33.3%) of the patients who were not hampered and 33 (55.9%) of those who were moderately ill (Figure 5).

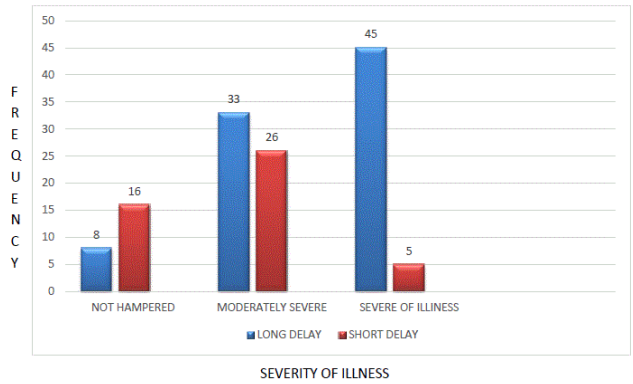

Figure 5: Patients with long and short delay according to severity of illness (n=133).

A significant association was established between longer patient delay and the severity of illness at the time of first visit to public health facility in the univariate analysis (p=0.00001). This association did not remain significant in the Multiple Logistic Regression Analysis.

Duration to the health facility, cost and means of transport

The PTB patients who took more than 2 hours to get to a public health facility tended to delay longer. Thirty five (61.4%) of those who lived 2-3 hours away and 29 (87.9%) of the patients who took over 4 hours reported delay of more than 30 days (Table 5).

Fifteen (60.0%) of the PTB patients who had to walk to the public health facility, 26 (65.0%) of those patients who used a Boda Boda and 46 (67.6%) of those who used a Matatu reported longer delay (Table 5).

The proportion of patients with longer delay among those who spent less than Ksh100 (<US$1.3) and those who spent more than Ksh 100 (>US$ 1.3) was over 60.0%. Forty six (67.6%) of patients who used Matatus to access the health facility reported longer delay. Using a Matatu to access the health facility was significantly associated with having to commute a distance of over 4 hours (OR=2.37; CI: 0.95-5.25; p=0.0132) and spending over Ksh 100 (>US$1.3) on transport costs (OR=20.75; CI: 7.69-56.0; p=0.00001). In the univariate analysis, the means of transport used to get to the health facility (p=0.1445) and the amount of money spent on transport (p=0.0580) were not significantly associated with longer delay (Table 5).

However the association between longer patient delay and having to commute for over 4 hours to the health facility found to be significant in the univariate analysis (p=0.0003) (Table 5), did not remain so in the Multiple Logistic Regression Analysis.

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (> 30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Duration					
0-1 hrs	20 (46.5)	23 (53.5)	43	0.44 (0.2-0.9)	0.0553
2-3 hrs	22 (38.6)	35 (61.4)	57	0.61 (0.3-1.3)	0.02574
Over 4 hrs	4 (12.1)	29 (87.9)	33	11.5 (2.6-50.0)	0.0003
Means of transport					
Walk	10 (40.0)	15 (60.0)	25	0.64 (0.3-1.6)	0.4775
Boda Boda	14 (35.0)	26 (65.0)	40	0.67 (0.3-1.5)	0.424
Matatu	22 (32.4)	46 (67.6)	68	1.86 (0.9-3.9)	0.1444
Cost of transport					
<Ksh 100	21 (37.5)	35 (62.5)	56	0.44 (0.2-1.0)	0.058
>Ksh 101	25 (32.5)	52 (67.5)	77	0.57 (1.0-2.9)	0.1679

Table 5: Proportion of PTB patients with longer delay according to duration to the health facility, cost and means of transport (n=133).

Patient delay and the choice of first health care provider

Sixty (45.1%) of the patients sought treatment from a private clinic first, 42 (31.6%) sought treatment from chemists/pharmacy, 16 (12.0%) went to a public hospital first, 12 (9.0%) went to a public health centre or dispensary, and 3 (2.3%) consulted an herbalist/traditional healer (Figure 6).

Forty nine (81.7%) of the patients who visited a private clinic, 27 (64.3%) of those who visited chemist/pharmacy and 2 (66.7%) of those who visited an herbalist reported longer delay (Table 6). A significant association was found between the choice of first health care provider and longer delay. Seeking treatment from a private clinic first was significantly associated with longer patient delay in the univariate analysis (p=0.00001) whereas visiting a health centre/dispensary (OR=5.85; CI: 1.47-23.4; p=0.0090) or a government hospital (OR=9.88; CI: 2.61-37.3; p=0.0003) first were significantly associated with lesser patient delay (Table 6).

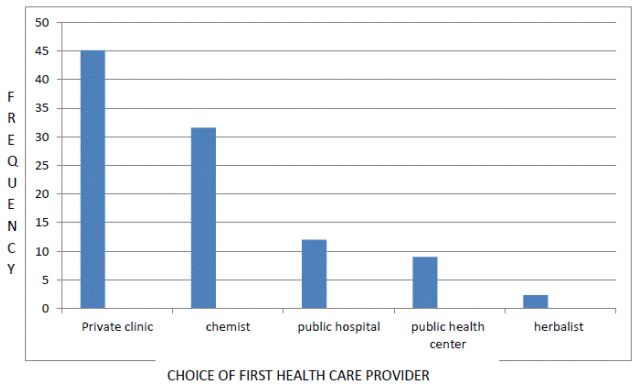

Figure 6: Patient delay and the choice of first health care provider.

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (>30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Health provider					
Chemist /pharmacy	15 (35.7)	27 (64.3)	42	0.99 (0.5-2.2)	0.8509
Health center/ dispensary					
Government hospital	9 (75.75.0)	3 (25.0)	12	0.17 (0.04-0.7)	0.009
Private clinic					
Herbalist	10 (62.5)	6 (37.5)	16	0.10 (0.03-0-4)	0.0003
	11 (18.3)	49 (81.7)	60	5.31 (2.3-12.0)	0.0001
	1 (33.3)	2 (66.7)	3	-	0.4217

Table 6: Proportion of PTB patients with longer delay according to the choice of first health care provider.

Patients were more likely to visit a private clinic if they had to commute for 2 or more hours to get to the nearest public health facility (OR=11.5; CI: 2.6-50.9; p=0.0003).

Patient delay and knowledge and perception of TB disease

Fifty five (41.4%) of the patients had an average score on TB knowledge, 42 (31.6%) had a good knowledge score and 36 (27.0%) had a poor knowledge score (Figure 7). Eighty one (60.9%) knew that there is a relationship between TB and HIV. Fifty two (39.1%) believed that TB is a very serious disease, 60 (45.1%) believed that it is serious, 10 (7.5%) said TB was slightly serious and 11 (8.3%) believed that TB disease was not serious (Table 7).

Most (94.0%) of the 133 patients reported that TB can be transmitted from person to person and 96.2% said that TB was curable.

There was no significant difference between the proportion of patients who delayed longer among those with poor TB knowledge score (69.4%) and those with an average TB knowledge score (67.3%) (Table 7). The contribution of this factor to patient delay was not statistically significant in this study (OR=0.39; CI: 0.2-0.8; p=0.0264). Similarly the proportion of PTB patients who delayed longer among those who perceived TB to be a "very serious disease" (63.5%) and those who perceived the disease as "not serious" (63.6%) was not significant. The perceived seriousness of TB disease was not found to have significant influence on patient delay in this study (p=0.5005).

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (>30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Knowledge of TB					
Poor	11 (30.6)	25 (69.4)	36	1.86 (0.6-4.6)	0.2509
Average	18 (34.5)	37 (67.3)	55	1.51 (0.7-3.2)	0.3734
Good	17 (40.5)	25 (59.5)	42	0.39 (0.2-0-8)	0.0264
Perception of TB					
Very serious	16 (30.8)	36 (69.2)	52	1.44 (07-3.1)	0.4472
Serious	21 (35.0)	39 (65.0)	60	0.61 (0.3-1.3)	0.2681
Slightly serious	5 (50.0)	5 (50.0)	10	1.08 (0.1-12.2)	0.721
Not serious	4 (36.4)	7 (63.6)	11	1.23 (0.4-4.3)	0.5005

Table 7: Proportion of PTB patients with longer delay according to level of TB knowledge and perception of TB disease (n=133).

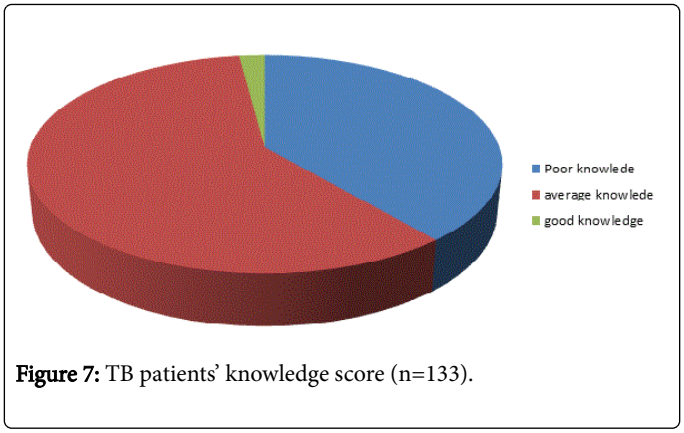

Figure 7: TB patients' knowledge score (n=133).

Fifty seven (42.9%) of the patients reported low stigma, 56 (42.1%) reported average stigma and 20 (15.0%) reported high stigma. The proportion of patients with longer delay was large among PTB patients who reported "average stigma" (78.6%) and "high" stigma (80.0%) and both levels of stigma were associated with delay in the univariate analysis (Table 8).

Patient delay and perception of the quality of health services

Fifty two (39.1%) patients had a poor perception of the quality of services offered in public health facilities, 44 (33.1%) perceived services as average and 37 (27.8%) perceived the services as being of good quality. Although 94.7% of the sample size felt that staff in public health facilities were qualified to diagnose and treat TB, 68% felt that the waiting time was long, 72% felt that the staff did not enquire about the patients" progress and 82% felt that the staff did not give patients time to ask questions where they needed clarification. Shortage of drugs was also reported by 53% of the patients.

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (>30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Stigma					
Low	30 (52.6)	27 (47.4)	57	0.30 (0.1-0.6)	0.0028
Average	12 (21.4)	44 (78.6)	56	1.54 (1.2-4.6)	0.0076
High	4 (25.5)	16 (80.0)	20	6.10 (0.6-15.1)	0.0004

Table 8: Proportion of PTB patients with longer delay according to stigma (n=133).

Most 46 (88.5%) of the patients who had a poor perception of the quality of health services in public health facilities reported a longer delay compared to 18 (48.8%) of those who had a good perception (Table 9).

Indeed a significant association was found between poor perception of the quality of services and longer delay in both univariate (p=0.0005), (Table 9) and Multiple Logistic Regression Analysis (p=0.0061) while good perception was associated with lesser patient delay (OR=2.86; CI: 1.3-6.4; p=0.01784).

Variable	Lesser delay (≤ 30 days) n (%)	Longer delay (>30 days) n (%)	Total	OR {Long delay 95%CI}	p-value
Total interviews	46 (34.6)	87 (65.4)	133	-	-
Perception of services					
Poor					
Average	6 (11.5)	46 (88.5)	52	6.99 (2.7-18.3)	0.00005
Good	21 (47.7)	23 (52.3)	44	0.47 (0.2-1.0)	0.07717
	19 (51.4)	18 (48.6)	37	0.35 (0.2-0.8)	0.01784

Table 9: Proportion of PTB patients with longer delay according to perception of the quality of services in government/public health facilities (n=133 Conclusion).

Multiple logistic regression analysis

The factors found to be significantly associated with longer patient delay in the univariate analysis were; having visited a private clinic (p=0.0001), poor perception of the quality of services in public health facilities (p=0.00005), being severely ill at the time of first visit to a public health facility (p=0.00001) and having to commute for over 4 hours to get to a public health facility (p=0.0003) and experiencing Average "(p=0.0076)" and High "(p=0.0004)" levels of stigma.

The results of Logistic Regression Analysis showed that poor perception of the quality of services in public health facilities (p=0.0061), visiting a private clinics (p=0.0052) and experiencing "High" (p=0.0178) stigma remained independent predictors of longer patient delay (delay of more than 30 days) (Table 10).

The mean patient delay among PTB patients in Suneka sub-County is long and majority of the PTB patients had delayed for more than 30 days before seeking treatment from a public health facility. The factors associated with patient delay were found to be related to perception of

quality of health care in public health facilities, prior attendance at private clinics and stigma. This study also established that good knowledge of TB and perception of TB as a serious disease did not translate to early care seeking.

Risk factor	Odds ratio (95% CI)	P-value
Duration of 4 hrs	2.126 (0.364-12.438)	0.4026
Severely ill	3.006 (0.805-11.673)	0.1016
Visiting private clinic	4.238 (1.539-11.673)	0.0052
Poor perception of quality of services	4.918 (1.576-15.348)	0.0061
Stigma		
Average	0.786 (0.894-2.316)	0.6082
High	2.456 (1.919-12.24)	0.0178

Table 10: Predictors of longer patient delay (n=133).

Discussion

The study sample consisted of more males than females. Similar trends have been established in other related studies [8-10]. This may imply gender bias in passive case finding [11-13] or that more men than women are indeed affected by TB in Suneka sub-County The Ministry of Health reported that men are 1.4 times more likely to have TB than women.

Tuberculosis affects the economically productive age of 15-45 years and the most affected age group is 25-35 years [14]. In this study 78.9% of the PTB patients were aged 15-44 years and those aged 25-35 years constituted 39.1% of the sample size. Twenty eight (54%) of patients in this age group were HIV positive, the highest among the all age groups. This finding is in line with the NLTP 2007 report that the same age group had the highest sero-prevalence [15].

Mean patient delay and proportion of ptb patients with longer delay

Patient delay was long (mean=54.1 days; median=53.5 days) and majority (65.4%) of the patients presented at a public health facility more than 30 days after the onset of the symptoms. Demissie et al. [8] and Cambanis et al. [9] reported similar proportions of 58.4% and 65.0% respectively in Ethiopia. The mean patient delay for this study was however found to be shorter compared to 78.2 days and 272 days in Ethiopia [8,9] respectively, 89.6 days in Ghana [16] and 161.7 days in Tanzania [17].

This may be a reflection of improved awareness of health problems and better access to health care in the study population.

Age, gender and marital status

The mean patient delay was slightly shorter for males (51 days) than for females (54 days) although a larger proportion of the males delayed longer than the females. The slight difference may be because the women may have had to depend on their husbands or other family members to raise money for transport. Women are also the primary care givers in homes and lack of time may be a contributor to the slightly longer delay. Long patient delays have been reported in women by Needham et al. [11].

Although the role of gender, age and marital status in longer patient delay was not statistically significant, this study revealed that male PTB patients were older (mean age=40) than female patients (mean age=29), a finding similar to that of a study in Uganda [10]. This may be attributed to the high HIV prevalence in TB patients. Females infected with HIV tend to be younger than the males because of early sexual debut in girls. Rampant poverty makes young girls in Suneka Sub-County tend to have male sexual partners who are older and have a source of income. Some of these males may already have been exposed to HIV/AIDS.

HIV status

Eighty four (63.2%) of the patients of the patients knew that there is an association between TB and HIV. A study in Thailand [18] found patient delays to be shorter in HIV positive PTB patients because these suffered more symptoms.

This study did not find the role of HIV status significant in patient delay. However slightly more of the HIV positive PTB patients delayed longer than the HIV negative patients. There is a possibility that HIV positive PTB patients may have been aware of their HIV status and this may have made them loose hope of recovery hence hesitating to seek treatment. The observed difference, albeit small, may be also due depletion of financial resources in the course of seeking treatment for their HIV.

Level of education

Educated people may have a better awareness of health problems such as TB and therefore seek treatment promptly. But studies in Zambia [19], Uganda [10] and Nigeria [20] found no association between education level and patient delay. In this study, PTB patients with low levels of education (lack formal education or have primary level of education) tended to have longer patient delay. However no association was established between the level of education and longer patient delay.

Severity of illness

Majority (90.0%) of the patients who were severely ill at the time of first visit to a public health facility had delayed for more than 30 days. This may be because the patients had to be carried to the health facility which is expensive but it could also be that those who delay longer develop more severe symptoms [21]. This study did not find the association between the severity of illness and longer patient delay significant; a finding similar to that of a study in Uganda [10].

The significant association observed between haemoptysis and longer patient delay may be because the patients may not perceive the prolonged cough as serious unless it is accompanied by other severe symptoms like coughing blood.

Duration, cost and means of transport

The duration, cost and means of transport used to get to the public health facility was used to get an indication of how accessible these facilities were. Although most (66.9%) of the PTB patients of the patients had to commute for 2 or more hours to the nearest public health facility and 57.9% spent over Ksh 100 (US$1.3) in transport, this

study did not find the role of these factors in longer patient delay statistically significant. Some studies carried out in urban Ethiopia [8] and Zambia [19] reported a significant association between duration taken to reach the centre and longer patient delay. It must be noted that this study was done in a rural setting and therefore the study population may have been significantly different from those in Addis Ababa and Lusaka.

Choice of health care provider

The increasing population poses the challenge of providing quality health care services in Kenya. Private clinics and chemists/pharmacies have mushroomed to take advantage of the increasing health care needs. This study found that private clinics were most frequently visited first, followed by the chemists/pharmacies. Kiwuwa et al. [10] also reported that PTB patients sought treatment from private clinics and pharmacies/drug stores more commonly than from government health units. Most of these are however run by personnel who do not have formal training in the medical field particularly TB and lung diseases which makes diagnosis and management of TB inadequate [19]. A recent study in Oman [22] established that private practioners had significantly lower TB knowledge scores and TB suspicion compared to public practioners. The significant association between visiting a private clinic and longer delay observed in this study may therefore be due to the repeated administration of doses of non-specific antibiotics when the patients returned due to failure of symptoms to disappear.

Repeated visits to the private clinics also depletes the patients limited financial resources needed for the TB diagnostic process and this may cause delay [16,23,24]. Significant associations were also established between being severely ill and visiting a private clinic (OR=2.84; CI: 1.3–6.0; p=0.0087) and also having to commute for two and more hours and visiting a private clinic (OR=2.50; CI: 1.1–5.8; p=0.02163).

Visiting private clinics by patients who had to commute for two and more hours to get to the nearest health facility may be an indicator of constrained access to appropriate TB treatment in this group. Several other studies found significant association between visiting a private clinic and prolonged patient delay [11,16,19,20,25].

This study also established that of all the PTB patients who sought treatment from the private clinics, only 8.3% reported having been influenced to seek the appropriate TB treatment by the personnel at the private clinic. This finding concurs with findings by Tesena et al. [26] who found progression towards specialized TB services to be poor among patients who sought treatment from a private clinic. This may be because health personnel"s knowledge on TB symptoms is inadequate hence low suspicion index or that the private clinics may be more interested in profit making and thus try to "hold" the patients as long as possible.

Knowledge and perception of TB disease

Knowledge is an important component of self-care and many studies and literature advocate increasing awareness of TB as a means to shorten patient delay [5,10,27-29].

Majority of the patients in this study had average knowledge of TB and the number of patients with good knowledge of TB increased with the increasing levels of education. Most (85.7%) of the patients in this study said that TB was a "very serious" or "serious" disease while the minority (13.0%) did not think that TB was serious.

Almost all the patients believed that TB is curable a probable indication that campaigns by NLTP emphasizing the curability of TB in print and electronic media are changing the past perception that the disease is incurable [30].

This study did not find the perceived seriousness of TB to have a role in patient delay. This may mean that there may be other factors like health, economic and social impacts of TB disease [31] which influence decisions to seek effective treatment.

In this study, having a good score in TB knowledge and perceiving TB as a serious disease did no translate to early seeking of care. Experience in HIV/AIDS control programs has shown that knowledge of HIV/AIDS and of risks does not translate to appropriate behavioral change. This finding may have the implication that strategies aimed at controlling TB through improving awareness on TB symptoms and mode of transmission of the disease may not be successful unless emphasis is made on developing positive attitudes towards prevention and early treatment [32]. Like similar studies by Odusanya et al. [20], Godfrey-Faussett et al. [12] the role of TB knowledge and the perceived seriousness of TB disease in patient delay could not established in this study.

Stigma

The stigma attached to TB due its close association with HIV [33] or the perceived incurability and contagiousness of the disease have been linked to patient delay [30,34].

Studies [35-38] have recommended the importance of information on stigma to help understand how it influences health-seeking behavior. In this study most of the patients who reported experiencing "average" and "high" stigma sought treatment at a public health facility 30 days after the onset of symptoms. This study established a significant association between longer delay and stigma. Stigma attached to TB in many cultures may make people want to conceal their illness thus increasing the risk of transmission and also delaying health-seeking [31]. Studies in different socio-cultural contexts [28,30,39] have shown evidence that stigmatization of TB results in delayed health care seeking and in Kenya. Liefooghe et al. [30] and the Ministry of Public Health and Sanitation reported stigma as a challenge in TB control [3]. However a study in Zambia [11] did not find stigmatizing attitudes to be associated with patient delay.

Perception of quality of services

The study found that a large proportion (88.5%) of patients who had a poor perception of the quality of services delayed longer. The study also established that poor perception of the quality of services in public health facilities to be associated with longer patient delay, a finding similar to that by Godfrey-Fausett et al. [19] in a study on patient delay in Zambia, and Jaramillo [34] in a Colombian study.

Although poor perception of health services has been found to be a risk factor for long delay among TB patients by studies outside Africa [34,40-60], the role of this factor in patient delay has been given little attention in Africa [19]. And this is in spite of the challenges faced by many public health care systems in the continent like drug shortages and inadequate health care personnel. Since TB services are integrated in the general health care system in Kenya, the findings of this study

underscore the need to improve the quality of public health care services as a means to promote early care seeking [61-79].

Conclusions and Recommendations

Implications of findings

Promoting early care seeking through increasing awareness of TB in the population is still an effective way to ensure that TB cases are identified early and treated using effective chemotherapy. But such efforts are unlikely to be successful if the public have a poor perception of the quality of services in the public health facilities which almost exclusively offer TB diagnostic and treatment (DOTs) recommended by WHO in Suneka Sub-County. The role of private clinics in health care provision in Suneka Sub-County can no longer be overlooked. These are widely accepted and frequently used health care providers even though many are run by personnel without any formal training in management of TB. Stigma attached to TB is a constraint to seeking effective treatment early.

Conclusion

The mean patient delay among PTB patients in Suneka Sub-County is long and majority of the PTB patients had delayed for more than 30 days before seeking treatment from a public health facility. The factors associated with patient delay were found to be related to perception of quality of health care in public health facilities, prior attendance at private clinics and stigma. This study also established that good knowledge of TB and perception of TB as a serious disease did not translate to early care seeking.

Recommendations

The particular aspects of health care services in public health facilities that most patients reported being most dissatisfied with were: the long waiting time, lack of encouragement and support in the course of recovery and failure of staff to give patients time to ask questions where they needed clarification and drug shortages. There is need for the Ministry of Medical Services to ensure that public health facilities have adequate staff and essential drugs. Addressing these issues vigorously can contribute towards changing the poor perception and promoting early care seeking. Communication skills training for health care workers in public health facilities can help change how the staff relate to patients hence improve the poor perception.

PTB patients frequently visited private clinics when they developed initial TB symptoms. Very few if any private clinics in Suneka Sub-County have the equipment for TB diagnosis or offer the TB DOTS, independently or in collaboration with the MoPH and S. Visiting a private clinic first was significantly associated with longer delay in this study. This finding highlights the need to integrate the private clinics in rural areas into the National TB control programme. Personnel running private clinics need to be trained on signs and symptoms (to enhance their suspicion index), diagnosis and management of TB. Private clinics can also be allowed access to sputum microscopy and culture services in addition to availing TB drugs to them. A referral system can be developed to ensure rapid referral of patients from private clinics for more specialized services at the public hospitals.

Since strict adherence to the guidelines on TB diagnosis and treatment is critical in prevention of MDR-TB, the MoPH/S can consider strengthening the ability of DLTLD to supervise, monitor and evaluate activities in private clinics in order to promote adherence to set standards. Active case finding with the help of community workers can also be explored as an option to improve early case detection.

Educational programmes aimed at reducing stigma need to be conducted.

Since good knowledge of TB and perception of TB as a serious disease did not translate to seeking effective treatment early, health awareness campaigns should go beyond providing general information about TB to emphasize embracing a positive attitude to prevention of transmission through early treatment.

Further research

Financial constrains limited this study to public health facilities in Suneka Sub-County. Similar studies can be done to determine the extent and contribution of various health care providers to patient delays at a national level. Delays to diagnosis and commencement of effective chemotherapy attributable to the health system factors can also be investigated.

References

1. WHO (2013) Research for universal health coverage: World health report, World Health Organization.
2. WHO (2005) WHO Declares Tuberculosis an Emergency in Africa. Genava. World Health Organization.
3. MOPH & S (2013) Division of Leprosy Tuberculosis and Lung Disease: Annual Report 2013. Ministry of Public Health and Sanitation, Nairobi, Kenya.
4. WHO (2013) Treatment of Tuberculosis: Guidelines for National programs. Geneva, World Health Organization.
5. MOH (2013) What health care workers need to know about implementing TB/HIV collaborative activities. Ministry of Health, Nairobi, Kenya.
6. Pronyk RM, Makhubele MB, Hargreaves JR, Tollman SM, Hausler HP (2001) Assessing health seeking behaviour among tuberculosis patients in rural South Africa. Int J Tuberc Lung Dis 5: 619-627.
7. Yimer S, Bjune G, Alene G (2005) Diagnostic and treatment delay among pulmonary tuberculosis patients in Ethiopia: a cross sectional study. BMC Infect Dis 5: 112.
8. Demissie M, Lindtjorn B, Berhane Y (2002) Patient and health service delay in the diagnosis of pulmonary tuberculosis in Ethiopia. BMC Public Health 2: 23.
9. Cambanis A, Yassin MA, Ramsay A, Bertel Squire S, Arbide I, et al. (2005) Rural poverty and delayed presentation to tuberculosis services in Ethiopia. Trop Med Int Health 10: 330-335.
10. Kiwuwa MS, Charles K, Harriet MK (2005) Patient and health service delay in pulmonary tuberculosis patients attending a referral hospital: a cross-sectional study. BMC Public Health 5: 122.
11. Needham DM, Foster SD, Tomlinson G, Godfrey-Faussett P (2011) Socio economic gender and health service factors affecting diagnostic delay for tuberculosis patients in Zambia. Tropical Medicine and International Health 6: 256-259.
12. Kasse Y, Jasseh M, Corrah T, Donkor SA, Antonnio M, et al. (2006) Health seeking behaviour, health system experience and tuberculosis case finding in Gambians with cough. BMC Public Health 6: 143.
13. Cassel A, Heine E, Le Clerq S (2012) Tuberculosis case finding in Eastern Nepal. Tuberc 63: 173-185.
14. NLTP (2015) Annual Report. Ministry of Health, Nairobi, Kenya.
15. NLTP (2013) Guidelines. Ministry of Health, Nairobi, Kenya.
16. Lawn SD, Afful B, Acheampong JW (1998) Pulmonary tuberculosis: diagnostic delay in Ghanaian adults. Int J Tuberc Lung Dis 2: 635-640.

17. Wandwalo ER, Mørkve O (2000) Delay in tuberculosis case-finding and treatment in Mwanza, Tanzania. Int J Tuberc Lung Dis 4: 133-138.
18. Ngamvithayapong J, Yanai H, Winkvist A, Diwan V (2001) Health seeking behaviour and diagnosis for pulmonary tuberculosis in an HIV-epidemic mountainous area of Thailand. Int J Tuberc Lung Dis 5: 1013-1020.
19. Godfrey-Faussett P, Kaunda H, Kamanga J, van Beers S, van Cleeff M, et al. (2002) Why do patients with a cough delay seeking care at Lusaka urban health centres? A health systems research approach. Int J Tuberc Lung Dis 6: 796-805.
20. Odusanya OO, Babafemi JO (2004) Patterns of delays amongst pulmonary tuberculosis patients in Lagos, Nigeria. BMC Public Health 4: 18.
21. Madebo T, Lindtjorn B (2013) Delay in treatment of pulmonary tuberculosis; an analysis of symptom duration among Ethiopia patients. Med Gen Med 18: E6.
22. Al-Maniri AA, Al-Rawas OA, Al-Ajmi F, De Costa A, Eriksson B, et al. (2008) Tuberculosis suspicion and knowledge among private and public general practitioners: Questionnaire Based Study in Oman. BMC Public Health 8: 177.
23. Lienhardt C, Rowley J, Manneh K, Lahai G, Needham D, et al. (2001) Factors affecting time delay to treatment in a tuberculosis control programme in a sub-Saharan African country: the experience of The Gambia. Int J Tuberc Lung Dis 5: 233-239.
24. Gibson N, Boillot F, Jalloh H (1998) The cost of tuberculosis to patients in Sierra Leone's war zone. Int J Tuberc Lung Dis 2: 726-731.
25. Rojpibulstit M, Kanjanakiritamrong J, Chongsuvivatwong V (2006) Patient and health system delays in the diagnosis of tuberculosis in Southern Thailand after health care reform. Int J Tuberc Lung Dis 10: 422-428.
26. Tesena N, Chiun N, Supannawong P, Buphratrakul K (2011) Delay in case finding in 6th zonal tuberculosis centre. Thai J Tuberc Chest Dis 12: 187-194.
27. Lewis KE, Stephens C, Shahidi MM, Packe G (2003) Delay in starting treatment for tuberculosis in east London. Commun Dis Public Health 6: 133-138.
28. Steen TW, Mazonde GN (1999) Ngaka ya setswana, ngaka ya sekgoa or both. Health seeking behaviour in Batswana with pulmonary tuberculosis. Soc Sci Med 48: 163-172.
29. Rajeswari R, Chandrasekaran V, Suhadev M, Sivasubramaniam S, Sudha G, et al. (2002) Factors associated with patient and health system delays in the diagnosis of tuberculosis in South India. Int J Tuberc Lung Dis 6: 789-795.
30. Liefooghe R, Michiels N, Habib S, Moran MB, De Muynck A (1995) Perception and social consequences of tuberculosis: a focus group study of tuberculosis patients in Sialkot, Pakistan. Soc Sci Med 41: 1685-1692.
31. Karki DK (2014) Delay in tuberculosis treatment in Kathmandu valley, Nepal. Department of Community Medicine, Mahaajgunj Institute of Medicine. Tribhuvan University Kathmandu.
32. dos Santos MA, Albuquerque MF, Ximenes RA, Lucena-Silva NL, Braga C, et al. (2005) Risk factors for treatment delay in pulmonary tuberculosis in Recife, Brazil. BMC Public Health 5: 25.
33. Ngamvithayapong J, Winkvist A, Diwan V (2000) High AIDS awareness may cause tuberculosis patient delay: results from an HIV epidemic area, Thailand. AIDS 14: 1413-1419.
34. Jaramillo E (1998) Pulmonary tuberculosis and health-seeking behaviour: how to get a delayed diagnosis in Cali, Colombia. Trop Med Int Health 3: 138-144.
35. Long NH, Johansson E, Diwan VK, Winkvist A (2001) Fear and social isolation as consequences of tuberculosis in VietNam: a gender analysis. Health Policy 58: 69-81.
36. Borges S, Silva J, Teixeira P (2014) The role of lactobacilli and probiotics in maintaining vaginal health. Arch Gynecol Obstet 289: 479-489.
37. Johansson E, Long NH, Diwan VK, Winkvist A (2000) Gender and tuberculosis control: perspectives on health seeking behaviour among men and women in Vietnam. Health Policy 52: 33-51.
38. Lönnroth K, Tran TU, Thuong LM, Quy HT, Diwan V (2001) Can I afford free treatment: Perceived consequences of health care provider choices among people with tuberculosis in Ho Chi Minh City, Vietnam. Soc Sci Med 52: 935-948.
39. Long NH, Johansson E, Lönnroth K, Eriksson B, Winkvist A, et al. (1999) Longer delays in tuberculosis diagnosis among women in Vietnam. Int J Tuberc Lung Dis 3: 388-393.
40. Asch S, Leake B, Anderson R, Gelberg L (1998) Why do symptomatic patients delay obtaining care for tuberculosis. Am J Respir Crit Care Med 157: 1244-1248.
41. Auer C, Sarol J Jr, Tanner M, Weiss M (2000) Health seeking and perceived causes of tuberculosis among patients in Manila, Philippines. Trop Med Int Health 5: 648-656.
42. WHO conference (2015) Montego Bay, Jamaica.
43. Hoa NP, Thorson AE, Long NH, Diwan VK (2003) Knowledge of tuberculosis and associated health-seeking behaviour among rural Vietnamese adults with a cough for at least three weeks. Scand J Public Health Suppl 62: 59-65.
44. Hooi LN (1994) Case-finding for pulmonary tuberculosis in Penang. Med J Malaysia 49: 223-230.
45. Tipping G, Segall M (2015) Health care seeking in developing countries. An annotated bibliography and literature review. Development Bibliography number 12, Brighton, UK: Institute of Development Studies, University of Sussex.
46. WHO (2015) Fact sheets on tuberculosis, Geneva, World Health Organization.
47. WHO (2012) Diagnostic and treatment delay in tuberculosis. Geneva. World Health Organization.
48. WHO (2015) Global Tuberculosis control: Surveillance, Planning, Financing: WHO Report.
49. WHO (2011) WHO/AFRO Tuberculosis Surveillance Report, Geneva. World Health Organization
50. Delley M, Bruttin A, Richard M, Affolter M, Rezzonico E, et al. (2015) In vitro activity of commercial probiotic Lactobacillus strains against uropathogenic Escherichia coli. FEMS Microbiol Lett 362: fnv096.
51. Ulett GC, Totsika M, Schaale K, Carey AJ, Sweet MJ, et al. (2013) Uropathogenic Escherichia coli virulence and innate immune responses during urinary tract infection. Curr Opin Microbiol 16: 100-107.
52. Nielubowicz GR, Mobley HL (2010) Host-pathogen interactions in urinary tract infection. Nat Rev Urol 7: 430-441.
53. Carey AJ, Sullivan MJ, Duell BL, Crossman DK, Chattopadhyay D, et al. (2016) Uropathogenic Escherichia coli Engages CD14-Dependent Signaling to Enable Bladder-Macrophage-Dependent Control of Acute Urinary Tract Infection. J Infect Dis 213: 659-668.
54. Jepson R, Craig J, Williams G (2013) Cranberry products and prevention of urinary tract infections. JAMA 310: 1395-1396.
55. Blango MG, Mulvey MA (2010) Persistence of uropathogenic Escherichia coli in the face of multiple antibiotics. Antimicrob Agents Chemother 54: 1855-1863.
56. Tsai CC, Huang LF, Lin CC, Tsen HY (2004) Antagonistic activity against Helicobacter pylori infection in vitro by a strain of Enterococcus faecium TM39. Int J Food Microbiol 96: 1-12.
57. Tsai CC, Hsih HY, Chiu HH, Lai YY, Liu JH, et al. (2005) Antagonistic activity against Salmonella infection in vitro and in vivo for two Lactobacillus strains from swine and poultry. Int J Food Microbiol 102: 185-194.
58. Tsai CC, Lin PP, Hsieh YM (2008) Three Lactobacillus strains from healthy infant stool inhibit enterotoxigenic Escherichia coli grown in vitro. Anaerobe 14: 61-67.
59. Barrons R, Tassone D (2008) Use of Lactobacillus probiotics for bacterial genitourinary infections in women: a review. Clin Ther 30: 453-468.

60. Reid G (2008) Probiotic Lactobacilli for urogenital health in women. J Clin Gastroenterol 42 Suppl 3 Pt 2: S234-236.
61. MacPhee RA, Hummelen R, Bisanz JE, Miller WL, Reid G (2010) Probiotic strategies for the treatment and prevention of bacterial vaginosis. Expert Opin Pharmacother 11: 2985-2995.
62. Atassi F, Servin AL (2010) Individual and co-operative roles of lactic acid and hydrogen peroxide in the killing activity of enteric strain Lactobacillus johnsonii NCC933 and vaginal strain Lactobacillus gasseri KS120.1 against enteric, uropathogenic and vaginosis-associated pathogens. FEMS Microbiol Lett 304: 29-38.
63. Juárez Tomás MS, Saralegui Duhart CI, De Gregorio PR, Vera Pingitore E, Nader-Macías ME (2011) Urogenital pathogen inhibition and compatibility between vaginal Lactobacillus strains to be considered as probiotic candidates. Eur J Obstet Gynecol Reprod Biol 159: 399-406.
64. Rammelsberg M, Radler F (1990) Antibacterial polypeptides of Lactobacillus species. J Appl Bacteriol 69: 177-184.
65. Gilliland SE, Walker DK (1990) Factors to consider when selecting a culture of Lactobacillus acidophilus as a dietary adjunct to produce a hypocholesterolemic effect in humans. J Dairy Sci 73: 905-911.
66. Gopal PK, Prasad J, Smart J, Gill HS (2001) In vitro adherence properties of Lactobacillus rhamnosus DR20 and Bifidobacterium lactis DR10 strains and their antagonistic activity against an enterotoxigenic Escherichia coli. Int J Food Microbiol 67: 207-216.
67. Chapman CM, Gibson GR, Todd S, Rowland I (2013) Comparative in vitro inhibition of urinary tract pathogens by single- and multi-strain probiotics. Eur J Nutr 52: 1669-1677.
68. Karlsson M, Jass J (2012) Lactobacilli differently regulate expression and secretion of CXCL8 in urothelial cells. Benef Microbes 3: 195-203.
69. Asahara T, Nomoto K, Watanuki M, Yokokura T (2001) Antimicrobial activity of intraurethrally administered probiotic Lactobacillus casei in a murine model of Escherichia coli urinary tract infection. Antimicrob Agents Chemother 45: 1751-1760.
70. Kruse R, Demirel I, Säve S, Persson K (2014) IL-8 and global gene expression analysis define a key role of ATP in renal epithelial cell responses induced by uropathogenic bacteria. Purinergic Signal 10: 499-508.
71. Chan FK, Moriwaki K, De Rosa MJ (2013) Detection of necrosis by release of lactate dehydrogenase activity. Methods Mol Biol 979: 65-70.
72. Totsika M, Kostakioti M, Hannan TJ, Upton M, Beatson SA, et al. (2013) A FimH inhibitor prevents acute bladder infection and treats chronic cystitis caused by multidrug-resistant uropathogenic Escherichia coli ST131. J Infect Dis 208: 921-928.
73. Forde BM, Ben Zakour NL, Stanton-Cook M, Phan MD, Totsika M, et al. (2014) The complete genome sequence of Escherichia coli EC958: a high quality reference sequence for the globally disseminated multidrug resistant E. coli O25b:H4-ST131 clone. PLoS One 9: e104400.
74. Mathoera RB, Kok DJ, Verduin CM, Nijman RJ (2002) Pathological and therapeutic significance of cellular invasion by Proteus mirabilis in an enterocystoplasty infection stone model. Infect Immun 70: 7022-7032.
75. Reid G, Bruce AW (2006) Probiotics to prevent urinary tract infections: the rationale and evidence. World J Urol 24: 28-32.
76. Falagas ME, Betsi GI, Tokas T, Athanasiou S (2006) Probiotics for prevention of recurrent urinary tract infections in women: a review of the evidence from microbiological and clinical studies. Drugs 66: 1253-1261.
77. Zhou X, Bent SJ, Schneider MG, Davis CC, Islam MR, et al. (2004) Characterization of vaginal microbial communities in adult healthy women using cultivation-independent methods. Microbiology 150: 2565-2573.
78. de Arellano AR, Sánchez M, Vera R, Jara S, González M, et al. (2012) Effect of orally-administered Lactobacillus plantarum LPLM-O1 strain in an immunosuppressed mouse model of urinary tract infection. Benef Microbes 3: 51-59.
79. Pascual L, Ruiz F, Giordano W, Barberis IL (2010) Vaginal colonization and activity of the probiotic bacterium Lactobacillus fermentum L23 in a murine model of vaginal tract infection. J Med Microbiol 59: 360-364.