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Quality of tuberculosis care and its association with patient adherence to treatment in eight Ethiopian districts

Mengiste M Mesfin,[1]* James N Newell,[1] John D Walley,[1] Amanuel Gessessew,[2] Tassew Tesfaye,[3] Frew Lemma[4] and Richard J Madeley[5]

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Background Little is known about the quality of tuberculosis (TB) service delivery in public health facilities in Ethiopia and its association with patients' non-adherence to TB treatment. This study assessed the organization, management and processes of TB care delivery, and their effects on patients' adherence to TB treatment.

Methods The quality of TB care was investigated in 44 public health facilities from three perspectives: structure, processes of TB care delivery and patient treatment outcome. Quality of care was determined by adherence to national TB guidelines. On-site observations of TB service delivery and interviews with health providers were conducted to evaluate structural factors. Patients ($n = 237$) in the health facilities were interviewed prospectively at completion of their treatment to determine the quality of tuberculosis care delivered. Three measures of treatment adherence [treatment interruption ($\geq$2 weeks), availability of unused TB drugs and treatment default] were quantified from a review of patient treatment registers and an audit of unused TB drugs at patients' homes. Effects were identified of poor quality structures and processes of service delivery on these three measures of adherence.

Results TB care providers were untrained in 18 (44%) of 44 facilities and daily outpatient TB care was not given in 13 of 44 (25%). Among the 237 patients, 43% interrupted treatment for $\geq$15 days and 30% had at least 1 day's dose of TB drugs unused. Patients tended to interrupt and default from treatment when their care provider had been inadequately supervised by district TB control experts and was incapable of dealing with patients' minor illnesses. Unavailability of daily TB care in health facilities was associated with missing daily doses.

Conclusion Better training of TB care providers and district supervisory support could be important interventions to improve the quality of care delivery and patient adherence to treatment.

Keywords Tuberculosis, quality of care, treatment adherence, tuberculosis programme, disease control, public sector

[1] Nuffield Centre for International Health and Development, Institute of Health Sciences, University of Leeds, Leeds, UK.
[2] Mekelle University Medical College, Mekelle, Ethiopia.
[3] Department for Diseases Prevention and Control of Tigray region, Mekelle, Ethiopia.
[4] South Bank University, London, UK.
[5] University of Nottingham Medical School, Division of Epidemiology and Public Health, School of Community Health Science, Nottingham, UK.
* Corresponding author. Nuffield Centre for International Health and Development, Leeds Institute of Health Sciences, University of Leeds, Charles Thackrah Building, 101 Clarendon Road Leeds, LS2 9JL, UK. Tel: +44 (0)113 3430833. Fax: +44 (0)113 246 0899. E-mail: M.melese@leeds.ac.uk

KEY MESSAGES

- To improve TB patient treatment outcomes in high HIV settings of sub-Saharan Africa, TB care delivery in health facilities needs to be accessible and effective in addressing patient needs.
- More emphasis should be given to the quality of training of health care providers and continued district TB control programme support (supervision, evaluation and monitoring of programme performance) to maintain the quality of patient care in public health facilities.

Introduction

In Ethiopia, the burden of tuberculosis (TB) remains high despite implementation since 1996 of the World Health Organization (WHO) recommended strategy known as 'DOTS', Directly Observed Treatment Short-course (Kochi 1997). The treatment success rate among smear-positive pulmonary TB (PTB+) patients is still below the international target and poor adherence to TB treatment is a major concern (WHO 2006). Several factors account for poor treatment adherence in Ethiopia and other African countries. Patient-related factors include age (Liefooghe *et al*. 1997; Shargie and Lindtjorn 2007), gender (Lienhardt *et al*. 1998; Comolet *et al*. 1999; Connolly *et al*. 2000), unemployment (Mishra *et al*. 2005), illiteracy (Chandrasekaran *et al*. 2007), low economic status (Comolet *et al*. 1999; Munro *et al*. 2007) and lack of awareness about TB and its treatment (Demissie and Kebede 1994; Tekle *et al*. 2002). Health service delivery and control programme factors include ineffective communication (Comolet *et al*. 1999; Mishra *et al*. 2006), poor supervision of health staff (Jin *et al*. 1993) and poorly accessible TB care (El-Sony *et al*. 2003).

Decentralization of TB care from tertiary to primary health care institutions has significantly improved TB treatment outcomes in Ethiopia and elsewhere (Edginton 1999; Dudley *et al*. 2003; Salaniponi *et al*. 2003). Further improving patients' access to TB care by using village volunteers has been shown to give as good outcomes as health institution-based TB care in many sub-Saharan countries (WHO 2003a). However, except in a few pilot studies (Edginton 1999; Kangangi *et al*. 2003), most countries of sub-Saharan Africa have failed to achieve the global target for treatment success rate, which is 85%, partly because of high mortality and treatment interruption from co-morbidity with human immunodeficiency virus (HIV) (Rubel and Garro 1992; Elliott *et al*. 1993; Richards *et al*. 1995; Harries *et al*. 1998).

The DOTS strategy also demands effective management of the TB control programme (Enarson *et al*. 2000), including continuous supplies, training and supervision of health providers (Jin *et al*. 1993), and programme monitoring and evaluation. Nevertheless, the relative importance of these managerial inputs on treatment outcome has never been properly investigated. Poor adherence to treatment arises from the interaction of multiple factors affecting the quality of TB care (Volmink *et al*. 2000), but there are very few studies that have looked beyond patient factors into the holistic organization and processes of TB service delivery. The objective of this study was to investigate aspects of the quality of TB care delivery in public health facilities and their association with patients' poor adherence to TB treatment.

Methods

Study setting

The study was conducted in the Tigray region of northern Ethiopia. The population of the region is estimated at 4.4 million, 86% of whom live in rural areas. The region has four administrative zones comprising 36 districts, each with an estimated population ranging from 70 000 to 90 000.

The TB control programme operates as an integral part of the public health system, with management structures at regional and district levels. A district health system typically comprises clinics, which are mainly staffed by primary health workers, one health centre and a district hospital. The district health office is responsible for the management of TB services in its catchment health facilities. The district TB control programme is run by a nurse (district TB coordinator) trained in TB management, with responsibility for training, supervision, monitoring and evaluation of TB care providers (TB focal persons) in his/her catchment health facilities (MOH 2002).

Patients have free access to diagnosis and treatment services in public health facilities. Patients with symptoms suggestive of TB must be referred from clinics to health centres and/or hospitals for diagnosis. Health centres can only diagnose smear-positive pulmonary TB by direct sputum-smear microscopy: suspects with a negative sputum-smear result and those with signs of extra-pulmonary tuberculosis (EPTB) disease must be diagnosed at district hospitals.

TB treatment comprises 2 months of daily treatment observed by a TB focal person, followed by 6 months of self-administered treatment with a fortnightly visit to a nearby public health facility (MOH 2002). New smear-positive pulmonary patients receive daily Streptomycin (S), Rifampicin (R), Isoniazid (H) and Pyrazinamide (Z) for the first 2 months, followed by 6 months of daily self-administered treatment with Ethambutol (E) and Isoniazid. Treatment for new smear-negative pulmonary tuberculosis (PTB-) and EPTB patients comprises RHZ for 2 months, followed by 6 months of EH. Patients must visit diagnostic centres (hospitals and health centres) for follow-up clinical assessment at the end of the 2nd, 5th and 7th months of treatment. The TB focal persons at clinics are expected to manage patients with minor adverse drug effects but refer those with serious medical illnesses to district hospitals or health centres. Patients who interrupt treatment for 14 days and more are traced by volunteer community health workers.

Both case detection and treatment completion rates among PTB+ patients remain below 35% and 75%, respectively (Health Bureau of Tigray 2005). High defaulter rates (range: 15 to 20%) and increasing trends of treatment failure (range: 0.1% to 2.5%) in PTB+ patients and of relapse rate (range: 0.9%

to 2%) among cases with all forms of TB are major concerns for TB control in Tigray (Health Bureau of Tigray 2004).

Study design and sampling

A cross-sectional assessment of health facilities, TB focal persons and respective patients was made in selected districts. Of the 36 districts which fully implemented the DOTS programme in all health facilities were selected from four zones (two districts from each zone). The study districts in each zone were selected randomly from those districts those that had fully integrated DOTS in all public health facilities. TB focal persons from each health facility (seven hospitals, nine health centres and 28 clinics) and all new patients ≥15 years of age who started treatment between July and December 2003 were prospectively interviewed at the completion of their TB treatment. Data collection was undertaken between April 2004 and January 2005.

Conceptual framework

Three aspects of the quality of TB care were evaluated (Donabedian 2003): structure and processes of TB service delivery and patient treatment outcomes. Structure includes the organizational and managerial factors at health facilities that define the availability, accessibility and convenience of TB care to patients (Campbell *et al*. 2000; Donabedian 2003). Process factors constitute ingredients of TB care delivered to patients by TB focal persons, while treatment outcomes are regarded as outcomes of structural and/or process factors. The structural aspects of the model were investigated taking into account the 'district health system' as a unit of operation for the DOTS strategy and the 'district health office' as the responsible authority for implementing the required managerial control activities in public health facilities (MOH 2002; WHO 2003b). The study assumed that the quality of patient care delivered by a TB focal person depends on the level of implementation of the WHO-recommended structural inputs by health facilities and the district TB control programme.

Study variables and data collection

The specific structural and process elements of TB care were identified from the NTCP guidelines (MOH 2002; WHO 2003b). Structural factors identified include the presence of a health worker trained in TB care, a separate TB treatment unit, the provision of daily outpatient TB care, fortnightly supervisory support, quarterly evaluation of TB services by a district TB control coordinator, uninterrupted supply of TB drugs and monitoring of patient treatment (Table 1). The quality of structural factors was evaluated by the extent to which these factors were implemented as per the recommended guidelines (MOH 2002; WHO 2003b) over the study period. Data on structural factors were collected from on-site observation of service delivery in health facilities and by interviews with TB focal persons. TB focal persons were interviewed, using a structured questionnaire, regarding their skills on patient care, and the number of supervisory and evaluation sessions conducted by the respective district TB control experts.

To assess the quality of the service delivery process, the essential elements of patient care were first defined from

Table 1 Study variables and data collection methods for assessing the quality of TB care in eight districts of Tigray region, northern Ethiopia

Factors evaluated[a]	Methods of data collection
A. Structural factors	On-site observation of practices in health facilities and interview with TB focal persons
• The presence of trained TB care provider	
• A separate TB unit in a health facility	
• Daily TB care in health facilities[b]	
• Monthly supervisory support to care providers by district TB control	
• A quarterly evaluation of the programme by district TB control	
• Standard diagnosis and treatment	
• Use of standard monitoring tools and regular supply of TB drugs	
B. Process factors	On-site observation of practices in health facilities and interview with TB focal persons
Ingredients of TB care that should be provided (TB focal person):	
• Patient counselling about TB and treatment, signs of side effects and actions to be taken	
• Two months of observation of treatment and fortnightly follow-up for 6 months	
• Management of minor illnesses arising during treatment[2]	
• The availability of daily TB care for patients who experience illness during treatment	
• Provision of daily TB services at referral centres	
Process quality measures from patients' perspective:	Interviews with patients at the completion of their treatment
• Level of awareness of TB and treatment	
• Level of knowledge of signs of side effects	
• Patients' level of awareness of actions to be taken when minor illnesses occur	
• Patients' access to support/consultations with their respective TB care provider when required	
• Problems encountered in getting care	
• Individualized TB care given the variations in demographic features of patients	
C. Treatment outcome indicators	Review of patient treatment registers in health facilities
• Treatment cure/completion rate	
• Defaulter rate	
• Treatment interruption days	Audit of TB drugs not taken at the end of treatment
• TB drugs not taken by patients at home	

[a]Quality criteria were drawn from the national TB control guidelines.

[b]This was not explicitly stated by the national TB control guidelines but agreed by a team of public health experts.

the NTLC guidelines (MOH 2002) and by a team of experts. These included proper patient counselling and education regarding TB and its treatment, effective management of illness arising during treatment, and the provision of daily TB care to patients, including referral. The quality of these ingredients of TB care delivered by TB focal persons was evaluated from the perspective of patients. House-to-house interviews were made by trained nurses using a pre-tested questionnaire translated into the local language (Tigregna) to collect information regarding patients' knowledge and experience about TB treatment.

Patients' treatment outcomes were assessed using recommended indicators (Enarson *et al*. 2000) and two unconventional measures of treatment adherence. Treatment outcome of PTB+ patients was determined by sputum microscopy, while clinical improvements were used to assess the outcomes of sputum smear-negative PTB and EPTB patients. Patients were classified as cured if they took treatment for 8 months and were confirmed to be sputum smear negative at the end of treatment or 1 month prior to the completion of treatment and on at least one previous occasion. Patients were classified as 'treatment completed' if they took treatment for 8 months but their smear results were not available on at least two occasions or they were PTB- or EPTB.

Patients who had been on treatment for at least 4 weeks but interrupted their treatment for 8 consecutive weeks or more were classified as defaulters. The default rate was used as one measure of interruption. However, many patients interrupt frequently but do not qualify as defaulters. Thus, the number of days' treatment the patient misses from the start to the completion of treatment was quantified as a second measure of poor treatment adherence. The total number of days of treatment interruption throughout the course of therapy was collected for each case.

Information on treatment interruptions and final treatment outcomes was collected from a review of patient treatment registers. An audit of TB drugs not taken by patients was made in order to evaluate their adherence to self-administered treatment during the continuation phase. Full daily doses of unused TB drugs found at home were counted to determine the number of daily doses missed by patients at the end of therapy. This measure of treatment adherence was useful particularly among PTB- and EPTB patients in whom treatment completion mainly depends on clinical evaluation; and among PTB+ cases in whom cure was not ascertained by sputum microscopy.

Data analysis

Data were entered and analysed using SPSS version 14 (SPSS, Inc., Chicago, USA). Data collected from patients were integrated into the data that were collected from their respective TB focal persons and health facilities. Descriptive and univariate analyses were employed to determine relative frequencies and strength of association of structure and process factors with poor treatment adherence. Crude odds ratios and 95% confidence intervals were calculated to measure the association between patients' demographic, structural and process factors and poor treatment adherence measures (i.e. interruption of treatment $\geq$14 days, $\geq$1 daily dose of unused TB drugs and treatment default). Multivariate logistic regression analysis was used to estimate adjusted odds ratios and 95% confidence intervals, using a backward model and an inclusion threshold of P value ≤ 0.2 with sequential dropping of the least significant variable until only those variables which were statistically significant ($P < 0.05$) remained. Verbal consent was obtained from each respondent. Ethical clearance was given by the regional Ethical Committee for Biomedical Research.

Results

Structural factors at health facilities

In all health centres, 5 out of 7 hospitals and 16 (57%) of the 28 clinics, TB care was run by trained TB focal persons (Table 2). Daily outpatient TB services were available in 31 (71%) of 44 health facilities, while in the remainder they were only available on specific days of the week. Patients were usually informed about TB and its treatment during the first day of treatment. None of the TB focal persons was trained on counselling techniques. In most health facilities, teaching materials were scarce and patients were taught in groups. Only 17 (39%) TB focal persons were able to manage adverse effects. The assessment showed only 8 (18%) of 44 TB focal persons were supervised on a monthly basis, while 10 (23%) of 44 were never supervised during the study period. Only 5 (11%) of 44 TB focal persons supervised received written feedback from their district TB coordinator. Twenty-five (57%) TB focal persons had never been involved in district TB programme evaluation in the preceding year. There was no interruption in supply of TB drugs and standard patient treatment registers were used by all health facilities.

Quality of TB care from the perspective of patients

The patient survey was used to study the quality of the structure and process of TB care delivery. Of the 237 patients, 40 PTB+, 103 PTB- and 94 EPTB were interviewed. Typically they were illiterate (61%), married (56%) and rural residents (56%). Forty-four per cent depended on farming for their livelihood and the median age of respondents was 34 years. The distribution of socio-demographic characteristics of patients was similar across the three subcategories of TB diagnosis.

Among the 237 patients, 151 (64%) had treatment follow-up from health centres and district hospitals and 36% were treated in clinics. Most patients (73%) had treatment follow-up from health assistants. Forty-seven (20%) of the 237 patients were supervised by health workers who did not have standard TB training. Most patients (225 of 237) had monthly treatment follow-up care from the same TB health workers. One hundred and eighty-one (76%) patients were allowed to visit their health care provider only during the usual monthly follow-up appointments. Patients had very limited general knowledge of TB and its treatment. Only 29 (12%) of the 237 patients mentioned bacteria as a cause of TB. Exposure to cold was mentioned by 92 (39%) respondents. Even though 186 (79%) stated that they could potentially transmit TB to others, only 39% knew the correct means of transmission. Over half knew neither the side effects nor the indications for stopping their

Table 2 The status of implementation of structural factors at health facilities ($n=44$) in Tigray region, northern Ethiopia

Structural factors	Hospitals $n=7$ (%)	Health centres $n=9$ (%)	Clinics $n=28$ (%)	Total $n=44$ (%)[a]
Health facilities with trained TB focal person	5 (71)	9 (100)	16 (57)	30 (68)
Health facilities delivering TB care on a daily basis	6 (86)	4 (44)	21 (75)	31 (71)
No. of health facilities with TB focal persons managing side effects	7 (100)	4 (44)	6 (21.5)	17 (39)
TB focal person teaching method:				
Patients taught in group	6 (86)	5 (56)	12 (43)	23 (52)
Person to person[b]	1 (14)	4 (44)	16 (57)	21 (48)
Monthly supervisory support given by district TB coordinators:				
0	1 (14)	0	4 (12)	5 (12)
1–2	2 (29)	4 (44)	13 (39)	19 (44)
3–4	2 (29)	2 (22)	6 (18)	10 (23)
5–6	2 (29)	3 (33)	5 (15)	10 (23)
Health institutions which received supervisory feedback in past 6 months	0	0	5 (18)	5 (11)
TB focal person participated in quarterly evaluation in past year:				
No evaluation	5 (71)	4 (44)	16 (57)	25 (57)
At least once	2 (29)	5 (56)	12 (43)	12 (43)

[a]Numbers in parenthesis are column percentages.
[b]Teaching method used during the first day of treatment.

medication. Of the 237 patients, 34% encountered problems during the continuation phase, and 30% were worried that someone might know about their illness.

Patient treatment outcome measures

From TB register data, of 246 eligible patients, 237 (98%) completed the intensive phase of treatment. Of these, 5% received the recommended 56 days of observed treatment while 93% were treated for more than 56 days (range 57–61 days). Only 37 (16%) of 237 did not miss any of their monthly appointments while the remaining missed at least one appointment (mean = 2.5, median = 2) during the continuation phase. Twenty-two per cent missed five or more monthly follow-up visits. Table 3 shows treatment interruption days, the number of daily doses of TB drugs unused and treatment default. Forty-three per cent of patients (102/237) had interrupted their treatment for 2 weeks or more (mean = 26 days, median = 9 days). Of patients who were discharged as cure or treatment completed, 71 (30%) of 237 missed at least one daily dose of TB drugs prescribed (mean = 5 daily doses). The overall treatment completion rate was 74%, while default and death rates were 22% and 3.8%, respectively.

Effects of structural and process factors on treatment adherence

Tables 4 and 5 show the distribution of treatment adherence indicators in relation to the structural and processes factors for TB care delivery. Table 6 shows crude and adjusted estimates of the association between structure and process factors and treatment interruption, poor adherence to self-administered treatment and default from treatment. Patients whose treatment supervisors were not properly trained and were incapable of managing illnesses arising during treatment were more likely to interrupt their treatment. This was significantly higher in patients whose follow-up treatment was from TB focal persons who had not been evaluated by the district TB coordinator during the study period. The likelihood of still having unused TB drugs was higher in patients whose follow-up treatment was at health centres and hospitals compared with those in clinics. It was also higher among those who had access to outpatient TB care only on limited days compared with those who had access on a daily basis. The rate of default was significantly higher in patients whose follow-up was from TB focal persons who were incapable of managing side effects; and among those whose treatment follow-up was from TB focal persons who had never been evaluated. Patients who believed 'vomiting' was a potential indication to stop TB medication were more likely to miss one or more daily doses of treatment.

Discussion

This study assessed the quality of TB care based on the national guidelines for TB care in public health care facilities. Structural factors relating to organization and management in health facilities were used to assess the extent to which TB care is accessible and convenient to patients. The key district TB control activities were evaluated for their systemic and direct effects on the quality of TB care. The study revealed that the required structural factors (presence of a health worker trained in TB care, a separate TB treatment unit, provision of daily outpatient TB care, fortnightly supervisory support, quarterly evaluation of TB services by a district TB control coordinator, uninterrupted supply of TB drugs and monitoring of patient treatment) have not been implemented optimally during the study period. The poor implementation of these structural factors affects the accessibility and effectiveness of TB care, and

Table 3 The status of TB treatment outcomes among patients ($n=237$) in Tigray region, northern Ethiopia

Adherence indicators	Total *n* (%)	New PTB+ $n=40$ (%)	New PTB− $n=94$ (%)	New EPTB $n=103$ (%)
Treatment interruption				
0 days	46 (19)	8 (20)	19 (18.4)	19 (20)
1–14 days	89 (38)	14 (35)	37 (36.9)	38 (40)
15–27 days	29 (12)	6 (15)	15 (14.6)	8 (9)
28–55 days	39 (17)	8 (20)	15 (14.6)	16 (17)
≥56 days	34 (14)	4 (10)	17 (16.5)	13 (14)
[mean, median days]	[26, 9]	[22, 7]	[30, 11]	[23, 7]
Daily doses missed				
0 daily doses	166 (70)	29 (72.5)	73 (72)	64 (68)
1–27 daily doses	63 (26.6)	10 (25)	26 (25)	27 (29)
28–56 daily doses	3 (1.3)	–	2 (1.9)	1 (1)
≥57 daily doses	5 (2.1)	1 (2.5)	2 (1.9)	2 (2)
[mean, median day]	[5, 0]	[4.5, 0]	[5, 0]	[5, 0]
Treatment outcome[a]	$n=246$	$n=42$	$n=105$	$n=99$
Cured	21 (8.5)	21 (50)	n.a.	n.a.
Completed	161 (65.4)	11 (26)	78 (74)	72 (73)
Defaulted	55 (22.4)	8 (19)	25 (24)	22 (22)
Died	9 (3.7)	2 (5)	2 (2)	5 (5)

[a]Treatment outcomes were calculated using all cohorts ($n=246$) including 9 patients who started treatment but died during the intensive phase.
n.a. = not applicable.

adherence to treatment. The study shows that the poor quality of TB service delivery and sub-optimal implementation of district control activities in public health facilities were key determinants of low adherence to treatment. The provision of TB care by poorly trained and inadequately supervised TB focal persons was related to high treatment interruption. Patients were more likely to miss their daily treatment when their follow-up was made in hospitals/health centres and they had limited access to daily TB care consultations. Patient default was also significantly higher when TB focal persons had poor capacity to treat minor illnesses and were rarely involved in programme evaluation.

The significance of treatment adherence measures

A 'defaulter' is a patient who completed at least the first 4 weeks of the intensive phase but then interrupted treatment for 8 consecutive weeks or more (MOH 2002; WHO 2003b). The default rate only measures continuous treatment interruption, and is sensitive only to major structural defects affecting the quality of TB care such as incompetence of health staff and poor programme monitoring. However, some patients (including some who resume treatment 'after default') interrupt their treatment intermittently. This 'intermittent interruption' is not considered in decisions pertaining to patient management even if it adds up to more than 8 weeks. In this study, poor capability of TB focal persons and lack of regular supervisory support and evaluation were significantly associated with high treatment interruption. This indicates that improved training and more regular supervisory support could improve TB focal persons' patient management skills to prevent interruptions that could potentially lead to relapse and resistant TB.

Another indicator used in this study was a measure of patients' non-adherence to self-administered treatment during the continuation phase. This cannot be determined by the existing health system or indirect methods (Palanduz *et al*. 2003). The high rate of non-adherence to self-administered treatment observed in this study risks continued transmission and drug resistance, particularly when frequent treatment interruption occurs. This study identified three PTB+ patients who interrupted their treatment for 4 to 8 weeks and missed 27 or more daily doses but were evaluated as treatment completed. Similarly, six PTB- patients who intermittently interrupted for 4 to 8 weeks and missed ≥28 daily doses were evaluated as treatment completed. Patients missing so many daily doses should be managed as defaulters, yet because they were not identified by the health system, they were not. These limitations in patient management might be contributing to the development of drug-resistant TB (Lambregts-van Weezenbeek and Veer 1995; Mitike *et al*. 1997; Behr *et al*. 1999).

Patients who believed 'vomiting' was an indication to stop medication were more likely to seek advice from TB focal persons when they had minor gastrointestinal disorders. Because of the inconvenience of accessing health facilities, however, patients could miss their daily treatment. The adherence of patients taking TB medication at home might be improved if they have easy access to medical advice when problems occur. Patients who failed to collect their TB drugs for more than 13 days were also found to be more likely to have missed their daily medication at home [OR 2.16; 95% CI (1.23, 3.81), $P=0.0007$]. The WHO guidelines and national programmes generally emphasize identifying continuous interruption (default). Programmes commonly do not give due emphasis to the identification and management of short term but multiple interruptions (MOH 2002). In this study, 22% of the total patients who interrupted treatment five or more times during the course of therapy were managed by extending the duration of treatment by the number of doses missed. The key problem is that the national guidelines are not explicit about the maximum number of interruptions and hence treatment extensions to allow. Determining the level of adherence to self-administered treatment is particularly important among PTB- and EPTB patients with recurrent multiple interruptions in whom treatment completion mainly depends on clinical evaluation, and among PTB+ cases in whom cure was not ascertained by sputum microscopy.

These findings suggest that patient treatment interruptions and non-adherence to self-administered treatment could be reduced by improving the quality of patient care in clinics and ensuring easy access to daily TB care at hospitals/health centres. Improving the capacity of clinic TB focal persons in

Table 4 Patients' adherence to TB treatment by quality of structural factors in their supervising health facilities in Tigray region, Ethiopia

Structural factors	Total	Treatment interruption		Daily doses missed		Treatment outcome	
		<14 days	≥14 days	0 days	≥1 days	Completed	Default
	$n=237$	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Patients treated:							
By trained TB care provider	190	102 (54)	88 (46)	130 (68)	60 (32)	142 (75)	48 (25)
By untrained TB care provider	47	33 (70)	14 (30)	36 (77)	11 (23)	37 (79)	10 (21)
Patients' TB care provider profession:							
Nurse	65	48 (74)	17 (26)	51 (78)	14 (22)	53 (82)	12 (18)
Health assistant	172	87 (51)	85 (49)	115 (67)	57 (33)	126 (73)	46 (27)
Type of health facility where patients treated:							
Clinic	86	54 (63)	32 (37)	68 (79)	18 (21)	70 (81)	16 (19)
Hospital or health centre	151	81 (54)	70 (46)	98 (65)	53 (35)	109 (72)	42 (28)
Patients who had access to consultations:							
On daily basis	56	34 (61)	22 (39)	48 (86)	8 (14)	48 (86)	8 (14)
On a fortnightly basis	181	101 (56)	80 (44)	118 (65)	63 (35)	131 (72)	50 (28)
Patients managed by TB care providers:							
Capable of managing side effects	166	88 (58)	78 (47)	109 (66)	57 (34)	123 (74)	43 (26)
Unable to treat side effects	71	47 (66)	24 (34)	57 (80)	14 (20)	56 (79)	15 (21)
Patients managed by TB care providers supervised by DTC[a] over the past 6 months:							
Inadequately (0–3 times)	114	65 (57)	49 (43)	77 (68)	37 (32)	81 (29)	33 (71)
Adequately (4–6 times)	123	70 (57)	53 (43)	89 (72)	34 (28)	98 (80)	25 (20)
Patients managed by TB care providers who:							
Had never been evaluated by DTC[a]	107	59 (55)	48 (45)	73 (68)	34 (20)	74 (69)	33 (31)
Were evaluated on a quarterly basis	130	76 (58)	54 (42)	93 (72)	37 (28)	105 (81)	25 (19)

[a]District tuberculosis control.

patient care through proper training and regular supervisory support by the district TB control programme can potentially reduce treatment interruptions arising from minor illnesses, and the costs to patients of referral.

Comparison with other studies

In common with other studies, age, sex, marital status and residence were not associated with defaulting, treatment interruption or non-adherence to self-administered treatment (Comolet *et al*. 1999). Patients who were aware of the cause of TB and those with knowledge of 'vomiting' as a sign of stopping medication were at increased risk of default and poor adherence to self-treatment, respectively. In this study, most patients believed TB was caused by exposure to a 'cold environment' and transmitted through physical contact including touching, sexual contact and sleeping together. Possibly patients may be more motivated to complete their treatment when they perceive a high risk of transmitting the disease to their families through these modalities. Similar observations have been reported from other African studies (Kaona *et al*. 2004).

In contrast to other Ethiopian studies (Demissie and Kebede 1994; Comolet *et al*. 1999), in this study default was not associated with low awareness of about the cause of TB. The knowledge of TB alone might not be enough to influence patients' decision to complete treatment. Studies elsewhere show that poor communication among patients and health providers can contribute to treatment non-adherence (Comolet *et al*. 1999; Liefooghe *et al*. 1999). This study did not assess the effectiveness of communication between TB focal persons and patients, and further studies on this issue are required.

Creating awareness can be paramount in high HIV-TB endemic countries like Ethiopia where stigma plays a role in early treatment and adherence to anti-TB chemotherapy. However, fear of revealing the disease to others was not shown to be significantly associated with the treatment adherence indicators. This may be due, at least in part, to the low awareness of TB and its means of transmission among patients and communities (Mengiste *et al*. 2005). Conceivably it could also be because of the Ethiopian perspective of the extended family that maintains support to patients.

Limitations of the study

A quarter of patients who needed to be treated for an extended duration (in order to compensate for treatment interruption days) were interviewed 2 months after the expected date of their treatment completion. It is possible that those interviewed late might have heard about the audit of TB drugs from others. Some TB drugs not taken by patients might not have been

Table 5 Comparison of measures of treatment adherence by quality of processes of TB care delivered to patients in Tigray region, Ethiopia

Process factors	Total	Treatment interruption		Daily doses missed		Treatment outcome	
	$n=237$	<14 days *n* (%)	≥14 days *n* (%)	0 dose *n* (%)	≥1 dose *n* (%)	Complete *n* (%)	Default *n* (%)
Patients' awareness about the cause of TB:							
Unaware of the cause of TB	208	122 (59)	86 (41)	146 (70)	62 (30)	164 (79)	44 (21)
Unaware of how TB is transmitted	145	88 (61)	57 (39)	105 (72)	40 (28)	111 (79)	34 (23)
Thought they could transmit the disease to others	51	28 (55)	23 (45)	40 (78)	11 (22)	39 (76)	12 (24)
Patients unaware of signs to stop medication:							
Severe skin itching	205	118 (58)	87 (42)	145 (71)	60 (29)	156 (76)	49 (24)
Change in eye colour	211	119 (56)	92 (44)	148 (70)	63 (30)	158 (75)	53 (25)
Impaired vision	209	119 (57)	90 (43)	147 (70)	62 (30)	158 (76)	51 (24)
Severe vomiting	218	124 (57)	94 (43)	157 (72)	61 (28)	165 (76)	53 (24)
Patients worried to reveal their disease	71	41 (58)	30 (42)	47 (66)	24 (34)	57 (80)	14 (20)
Patients who had problems getting TB care	81	41 (51)	40 (49)	63 (78)	18 (22)	58 (72)	23 (28)
Patient characteristics:							
Gender:							
Male	115	61 (53)	54 (47)	77 (67)	38 (33)	85 (74)	30 (26)
Female	122	74 (61)	48 (39)	89 (73)	33 (27)	94 (77)	28 (23)
Age:							
<35 years	107	57 (53)	50 (47)	78 (73)	29 (27)	86 (80)	21 (20)
≥35 years	130	78 (60)	52 (40)	88 (68)	42 (32)	93 (71)	37 (29)
Residence:							
Urban	104	61 (59)	43 (41)	68 (65)	36 (35)	76 (73)	28 (27)
Rural	133	74 (56)	59 (44)	98 (74)	35 (26)	103 (77)	30 (23)
Occupation:							
Farming	105	64 (61)	41 (39)	76 (72)	29 (28)	87 (83)	18 (17)
Other	132	71 (54)	61 (46)	90 (68)	42 (29)	92 (70)	40 (30)

identified during the study. Unused daily doses could also be underestimated as partially taken doses were not considered. The study was undertaken in eight districts selected from four zones of one regional state in the country, and may not be representative of the whole country.

Conclusions and policy recommendations

In Ethiopia many patients suffer from both TB and AIDS, and the occurrence of somatic and emotional stress is expected to be high. Unless TB focal persons have the necessary capability to deal with patient-specific problems, patients' trust of the effectiveness of TB treatment might be eroded. Thus, the TB control programme should be tailored based on the health care needs of patients. The institution of 'patient-centred care' in health facilities and effective management support of health care providers by district TB programmes are likely to improve patient adherence to TB treatment (Tuberculosis Coalition for Technical Assistance 2006). This should include daily access to TB care and effective management of side-effects and illnesses by a trained health worker. The quality of training of care providers at lower health facilities should be tailored to patients' care needs in a high HIV endemic setting and take into account the ongoing system of referral across health facilities in districts. The quality of patient care in health facilities should be monitored and strengthened on a continuous basis through optimal implementation of supervisory support and quarterly evaluations of TB focal persons by district TB control experts (MOH 2002; WHO 2003b).

The WHO and the NTLC (MOH 2002; WHO 2003b) guidelines do not define the management of patients who interrupt after 'return from default'. The same is true for PTB+ patients who interrupt after the 5th month of treatment but are not classified as 'defaulters' and in whom cure could not be ascertained by sputum microscopy. Treatment outcomes based on clinical evaluation could be unreliable in such cases since there is no way to ascertain whether patients were taking the prescribed TB drugs at home. In patients taking blister packed drugs it is relatively easy to monitor if pills have been taken at each clinic visit. A routine check of TB drugs not taken by a patient would guide actions regarding patient adherence. Routine consultation with patients regarding TB medication not taken at home during the continuation phase of treatment is required in order to provide the necessary care. We recommend that the national TB control programme guidelines should be explicit regarding patient management and number of short and multiple interruptions (<14 days) in conjunction

Table 6 Univariate and multivariate analysis of the association between structural and process factors and treatment interruption, missing daily doses of treatment and treatment default among TB patients ($n = 237$) in Tigray region, Ethiopia

Characteristics	Treatment interruption ≥14 days		Daily doses missed ≥1 day		Treatment default	
	Odds ratio (95% CI)[a]		Odds ratio (95% CI)		Odds ratio (95% CI)	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Structural factors						
TB follow-up by: untrained person	0.61 (0.2, 0.9)	R[b]	0.66 (0.3, 1.4)	R	0.81 (0.4, 1.7)	R
Type of health facility: hospital/health centre	1.45 (0.8, 2.5)	R	2.04 (1.1, 3.8)	3.16 (1.6, 6)	1.68 (0.9, 3.2)	R
Unavailability of TB care on a daily basis	1.21 (0.7, 2.3)	R	3.21 (1.4, 7.1)	4.2 (1.6, 10)	2.31 (1.2, 5.2)	R
Care by health workers unable to manage side effects	1.73 (1.0, 3.0)	2.50 (1.1, 5.5)	2.12 (1.1, 4.1)	R	1.31 (0.7, 2.5)	2.32 (1.1, 5.4)
Care by TB focal persons sub-optimally supervised by DTC[c] in the past 6 months	0.99 (0.6, 1.7)	2.41 (1.2, 5)	1.30 (0.7, 2.2)	R	1.89 (0.9, 3.9)	R
Care by TB focal persons never evaluated during the past year	1.15 (0.7, 2.0)	1.90 (3.3, 10)	1.21 (0.7, 2.0)	R	1.92 (1.1, 3.3)	3.01 (1.4, 5.0)
Process factors						
Gender: female	0.73 (0.4, 1.2)	R	0.75 (0.4, 1.3)	R	0.84 (0.5, 1.5)	R
Age: ≥35 year	0.76 (0.5, 1.3)	R	1.30 (0.7, 2.2)	R	1.62 (0.9, 3.0)	R
Residence: rural	1.13 (0.7, 1.9)	R	0.67 (0.4, 1.2)	R	0.79 (0.4, 1.4)	R
Occupation: farming	0.74 (0.4, 1.3)	R	0.80 (0.5, 1.4)	R	0.47 (0.3, 0.9)	R
Unaware of cause of TB	0.57 (0.3, 1.3)	R	0.94 (0.4, 2.0)	R	0.28 (0.1, 0.6)	0.32 (0.1, 0.8)
Unaware of means of TB transmission	0.67 (0.4, 1.1)	R	0.75 (0.4, 1.3)	R	0.86 (0.5, 1.6)	R
Did not know they could potentially transmit the disease	1.11 (0.6, 2.0)	R	0.57 (0.3, 1.2)	R	0.93 (0.5, 1.9)	R
Unaware of severe vomiting as a sign to stop medication	0.96 (0.4, 2.5)	R	2.90 (1.1, 3.3)	3.3 (1.3, 10)	1.12 (0.4, 1.3)	R
Encountered problems in getting TB treatment	1.47 (0.8, 2.5)	R	0.65 (0.3, 1.0)	R	1.37 (0.7, 2.5)	R
Patients worried to reveal their disease	0.95 (0.5, 1.7)	R	1.29 (0.7, 2.3)	R	0.68 (0.3, 1.3)	R

[a]95% confidence interval.
[b]Variables removed from the final model during stepwise multivariate analysis.
[c]District tuberculosis control.

with the methods currently used to assess end treatment outcomes of such patients.

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References

Behr MA, Warren SA, Salamon H *et al.* 1999. Transmission of Mycobacterium tuberculosis from patients smear-negative for acid-fast bacilli. *The Lancet* **352**: 444–49.

Campbell SM, Roland MO, Buetow SA. 2000. Defining quality of care. *Social Science and Medicine* **51**: 1611–25.

Chandrasekaran V, Balasubramanian R, Narayanan PR. 2007. Risk factors for non-adherence to directly observed treatment (DOT) in a rural tuberculosis unit, South India. *Indian Journal of Tuberculosis* **54**: 66–70.

Comolet TM, Rakotomalala R, Rajaonarioa H. 1999. Factors determining compliance with tuberculosis treatment in an urban environment, Tamatave, Madagascar. *International Journal of Tuberculosis and Lung Disease* **3**: 1049.

Connolly C, Davies GR, Wilkinson D. 2000. Who fails to complete tuberculosis treatment? Temporal trends and risk factors for treatment interruption in a community-based directly observed therapy programme in a rural district of South Africa. *International Journal of Tuberculosis and Lung Disease* **3**: 1081–7.

Demissie M, Kebede D. 1994. Defaulting from tuberculosis treatment at the Addis Ababa Tuberculosis centre and factors associated with it. *Ethiopian Medical Journal* **32**: 97–106.

Donabedian A. 2003. *An introduction to quality assurance in health care*. New York: Oxford University Press, Inc.

Dudley L, Azevedo V, Grant R *et al.* 2003. Evaluation of community contribution to tuberculosis control in Cape Town, South Africa. *International Journal of Tuberculosis and Lung Disease* **7**: S48–S55.

Edginton ME. 1999. Tuberculosis patient care decentralised to district clinics with community-based directly observed treatment in a rural district of South Africa. *International Journal of Tuberculosis and Lung Disease* **3**: 445–50.

El-Sony AI, Mustafa SA, Khamis AH *et al.* 2003. The effect of decentralization on tuberculosis services in three states of Sudan. *International Journal of Tuberculosis and Lung Disease* **7**: 445–50.

Elliott AM, Hayes RJ, Halwiindi B *et al.* 1993. The impact of HIV on infectiousness of pulmonary tuberculosis: a community study in Zambia. *AIDS* **7**: 981–7.

Enarson DA, Rieder HL, Arnadottir T, Trébucq A. 2000. *Management of tuberculosis: a guild for low income countries*. Paris: International Union Against Tuberculosis and Lung Disease.

Harries AD, Nyangulu DS, Kang'ombe C *et al.* 1998. Treatment outcome of an unselected cohort of tuberculosis patients in relation to human immunodeficiency virus serostatus in Zomba Hospital, Malawi. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **92**: 343–7.

Health Bureau of Tigray Region. 2004. *Annual report of tuberculosis and leprosy programme*. Mekelle: Health Bureau of Tigray Region of Ethiopia.

Health Bureau of Tigray Region. 2005. *Strategic Plan for health programmes*. Mekelle: Health Bureau of Tigray Region of Ethiopia.

Jin BW, Kim SC, Mori T, Shimao T. 1993. The impact of intensified supervisory activities on tuberculosis treatment. *Tubercle and Lung Disease* **74**: 267–72.

Kangangi JK, Kibuqa D, Muli J *et al.* 2003. Decentralisation of tuberculosis treatment from the main hospitals to the peripheral health units and in the community within Machakos district, Kenya. *International Journal of Tuberculosis and Lung Disease* **7**: S5–S13.

Kaona FA, Tuba M, Siziya S, Sikaona L. 2004. An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. *BMC Public Health* **4**: 68.

Kochi A. 1997. Tuberculosis control: is DOTS a breakthrough of the 1990s? *World Health Forum* **18**: 225–47.

Lambregts-van Weezenbeek CSB, Veen J. 1995. Control of drug-resistant tuberculosis. *Tubercle and Lung Disease* **76**: 455–59.

Liefooghe RG, Moran MB, Habib S, Muynck AO. 1997. Treatment adherence of tuberculosis patients in Bethania Hospital, Sialkot. *Journal of the College of Physicians and Surgeons – Pakistan* **7**: 140–44.

Liefooghe R, Suetens C, Meulemans H, Moran MB, De Muynck A. 1999. A randomised trial of the impact of counselling on treatment adherence of tuberculosis patients in Sialkot, Pakistan. *International Journal of Tuberculosis and Lung Disease* **3**: 1073–80.

Lienhardt C, Manneh K, Bouchier V *et al.* 1998. Factors determining the outcome of treatment of adult smear-positive tuberculosis cases in The Gambia. *International Journal of Tuberculosis and Lung Disease* **2**: 712–8.

Mesfin MM, Tesfay TW, Tareke IG, Mulugeta GWM, Madeley RJ. 2005. Community knowledge, attitudes and practices on pulmonary tuberculosis and their choice of treatment supervisor in Tigray, northern Ethiopia. *Ethiopian Journal of Health Development* **19**: 21–27.

Ministry of Health of Ethiopia. 2002. The manual of the National Tuberculosis and Leprosy Control Program. Addis Ababa: Ministry of Health of Ethiopia, Disease Prevention and Control Department.

Mishra P, Hansen EH, Sabroe S, Kafle KK. 2005. Socio-economic status and adherence to tuberculosis treatment: a case-control study in a district of Nepal. *International Journal of Tuberculosis and Lung Disease* **9**: 1134–9.

Mishra P, Hansen EH, Sabroe S, Kafle KK. 2006. Adherence is associated with the quality of professional-patient interaction in Directly Observed Treatment Short-course, DOTS. *Patient Education and Counseling* **63**: 29–37.

Mitike G, Kebede D, Yeneneh H. 1997. HIV infection and antituberculosis drug resistance among pulmonary tuberculosis patients in Harar Tuberculosis Centre, Ethiopia. *East African Medical Journal* **74**: 154–7.

Munro SA, Lewin SA, Smith HJ *et al.* 2007. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. *PLoS Medicine* **4**: 7, e238.

Palanduz A, Gultekin D, Erdem E, Kayaalp N. 2003. Low level of compliance with tuberculosis treatment in children: monitoring by urine tests. *Annals of Tropical Paediatrics: International Child Health* **23**: 47–50.

Richards SB, St Louis ME, Nieburg P *et al.* 1995. Impact of the HIV epidemic on trends in tuberculosis Abidjan, Côte d'Ivoire. *Tubercle and Lung Disease* **76**: 11–16.

Rubel AJ, Garro LC. 1992. Social and cultural factors in the successful control of tuberculosis. *Public Health Reports* **107**: 626–36.

Salaniponi FM, Gausi F, Mphasa N *et al.* 2003. Decentralisation of treatment for patients with tuberculosis in Malawi: moving from research to policy and practice. *International Journal of Tuberculosis and Lung Disease* **7**: S38–S47.

Shargie EB, Lindtjorn B. 2007. Determinants of treatment adherence among smear-positive pulmonary tuberculosis patients in southern Ethiopia. *PLoS Medicine* **4**: 2, e37.

Tekle B, Mariam DH, Ali A. 2002. Defaulting from DOTS and its determinants in three districts of Arsi Zone in Ethiopia. *International Journal of Tuberculosis and Lung Disease* **6**: 573–9.

Tuberculosis Coalition for Technical Assistance. 2006. *International standard for Tuberculosis Care (ISTC)*. The Hague: Tuberculosis Coalition for Technical Assistance.

Volmink J, Matchaba P, Garner P. 2000. Directly observed therapy and treatment adherence. *The Lancet* **355**: 1345–50.

WHO. 2003a. *Community contribution to TB care: Practise and policy*. Geneva: World Health Organization.

WHO. 2003b. *Treatment of tuberculosis: guideline for national programmes*. Geneva: World Health Organization.

WHO. 2006. *The Stop TB Strategy. Building on and enhancing DOTS to meet the TB related Millennium Development Goals*. Geneva: World Health Organization.