Local problems, local solutions: improving tuberculosis control at the district level in Malawi

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Objective To examine the causes of a low cure rate at the district level of a tuberculosis (TB) control programme and to formulate, implement, and evaluate an intervention to improve the situation.
Methods The study setting was Mzuzu (population 60 000), where the annual smear-positive pulmonary TB incidence was 160 per 100 000 and the human immunodeficiency virus (HIV) seroprevalence was 67% among TB patients. There is one TB treatment unit, but several other organizations are involved with TB control. An examination of case-holding activities was carried out, potential areas for improvement were identified, and interventions performed.
Findings In 1990–91, the cure rate was 24% among smear-positive cases (29% among survivors to end of treatment). Problems identified included a fragmented TB control programme; inadequate training and supervision; suboptimal recording of patients' addresses; and nonadherence to national TB control programme protocols. These problems were addressed, and in 1992–93 the cure rate rose to 68% (relative risk (RR) = 2.85 (95% confidence interval (CI) = 1.63, 4.96)) and to 92% among survivors to the end of treatment (RR = 3.12 (95% CI = 1.84, 5.29)). High cure rates are therefore achievable despite high HIV prevalence.
Conclusions Simple, inexpensive, local programmatic interventions can dramatically improve TB case holding. This study demonstrates the need for evaluation, training, and supervision at all levels of the programme.

Keywords: tuberculosis, multidrug-resistant, drug therapy; antitubercular agents, administration and dosage; AIDS-related opportunistic infections; acquired immunodeficiency syndrome; community health services; community health aides, education; treatment outcome; Malawi.

Mots clés: tuberculose pharmacorésistante, chimiothérapie; antituberculeux, administration et posologie; infections opportunistes liées au SIDA; SIDA; service de santé publique; auxiliaire de santé publique, enseignement; évaluation des résultats de traitement; Malawi.

Palabras clave: tuberculosis resistente a multidrogas**,** quimioterapia; agentes antituberculosos, administración y dosificación; infecciones oportunistas relacionadas con SIDA; síndrome de inmunodeficiencia adquirida; servicios de salud comunitaria; auxiliares de salud comunitaria, educación; resultado del tratamiento; Malawi.

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Introduction

Much has been written about the WHO strategy of directly observed therapy, short-course (DOTS), which has been promoted in the control of tuberculosis (TB) (*1*). Indeed, great strides have been made recently in introducing the strategy worldwide (*2*). However, by the end of 1998, 68% of the world's population remained uncovered by this strategy for TB control (*2*). Doubts have been expressed whether DOTS alone is the answer in TB control, and a more holistic approach has been advocated (*3*). A recent South African randomized controlled trial (*4*) showed no significant increase in cure rates among patients receiving directly observed therapy (DOT). The findings of the last-mentioned study are controversial, and concerns about the validity of the findings have been outlined elsewhere (*5*–*7*). Controversy notwithstanding, it is worthwhile examining the elements of successful district TB control programmes in developing countries where DOT is not in place.

The hypothesis tested was that if well implemented, the DOTS strategy could achieve high cure rates at the district level, even in the presence of a high prevalence of seropositivity for human immunodeficiency virus (HIV). The objective of the present study was thus to examine the reasons for the low cure rate in a peripheral district of a TB control programme in a resource-poor, high-prevalence country in sub-Saharan Africa. The problems that were identified by cohort analysis of sputum smear-positive pulmonary TB patients are presented, the local solutions that were

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put into place outlined, and their effects demonstrated. It is argued that the method is applicable to other settings where resources are scarce, but where goodwill among those working in TB control at the district level is abundant.

Study setting

Malawi

Malawi is a small, landlocked country in Central Africa with a population of about 10 million. It is also one of the poorest countries in the world, with a gross domestic product (GDP) of less than US$ 200 per capita. The country has been hard hit by the dual epidemics of HIV and TB. Over 30% of antenatal women in urban areas are HIV-positive (*8*). Since 1985, Malawi has operated an International Union against Tuberculosis and Lung Diseases (IUATLD) model TB control programme. Nevertheless, smear-positive pulmonary TB notification rates doubled between 1985 and 1993 (*9*). Most of this increased caseload was probably due to the rapid spread of the HIV epidemic in the corresponding period, as has been documented elsewhere in sub-Saharan Africa (*10, 11*).

The Malawi national tuberculosis control programme

The Malawi national tuberculosis control programme (NTP) has a similar administrative structure to other government departments and is supported by IUATLD and foreign donors. The government of Malawi is politically committed to the programme and provides an annual budgetary allocation of funds to the Ministry of Health (MOH). The central TB unit coordinates the programme at a national level, and three regional TB officers have key roles in evaluating the programme. District TB officers are responsible for registration and case holding as well as coordination with other programmes, especially primary health care. Nongovernmental organization (NGO) hospitals and health centres contribute significantly to health care in Malawi, operating outside the formal government structure to deliver 35% of all health care services. Some NGO hospitals participate as treatment centres within the NTP, follow NTP guidelines for diagnosis and treatment of TB patients, and fulfil their recording and reporting requirements.

Mzuzu

Mzuzu is the administrative centre of the northern region of Malawi, has a population of 60 000, and is located 360 km north of the nearest tertiary referral hospital in the capital, Lilongwe. The smear-positive TB incidence is 160/100 000, and HIV seroprevalence amongst TB patients is 67% (*12*).

TB control in Mzuzu

TB treatment and control activities in Mzuzu and the surrounding area follow the Malawi NTP guidelines. In 1991, several agencies were involved in TB control activities in Mzuzu. The TB treatment unit was based at an NGO hospital. Public health officers based at the Mzuzu Health Department had responsibility for the follow-up of patients who defaulted from treatment. Both organizations reported to a district TB officer situated at the MOH hospital 100 km away, but they were never directly supervised. An MOH health centre offered continuation phase treatment and reported to a different district TB officer. There were no formal or informal links between these organizations, except at the regional level.

In 1991, there was a general lack of interest in TB control among clinicians and administrators at the hospital. A medical officer diagnosed and prescribed therapy for TB patients. Most other aspects of the TB service at the hospital were run by a hospital employee with no formal post-primary school education. He was responsible for enrolling and registering patients and for administering drugs to them. He was also responsible for follow-up of patients in continuation phase treatment. However, due to his other duties, he was rarely able to leave the hospital premises. He had no formal training in TB control. This lack of training, combined with a lack of personal experience in defaulter tracing, resulted in his entering inaccurate addresses into the TB register and made follow-up of defaulters almost impossible. Supervision and evaluation by the regional TB officer was intermittent and did not investigate the reasons underlying the poor performance of the TB control programme in Mzuzu. Training in TB control excluded nongovernment staff.

Methods

Two periods were used for comparison: before (1 April 1990–30 September 1991) and after (1 November 1991–31 May 1993) an intervention aimed at increasing cure rates. A before/after study design was employed to compare the results of cohort analysis in 1990–91 versus 1992–93. During the study period, all patients presenting with cough were investigated for TB (*13*). All previously untreated sputum smear-positive pulmonary TB patients diagnosed at St John's Hospital, Mzuzu, were included. Sputa were examined using the Ziehl–Neelsen technique to detect alcohol-acid fast bacilli (AAFB) (*14*). The slides were examined on site within 3 days of collection by one of four trained and experienced laboratory technicians. Quality control was provided by the Malawi NTP. Patients were treated according to the Malawi NTP guidelines, with a 2-month intensive phase in hospital of directly observed daily streptomycin, rifampicin, isoniazid, and pyrazinamide. This was followed by a 6-month continuation phase of daily thioacetazone and isoniazid. Ethambutol replaced thioacetazone in the case of toxic reactions. During the continuation phase of therapy, a 1-month supply of oral TB medication was supplied

according to the treatment protocol of the Malawi NTP. Monthly attendance for review and resupply of medication was taken to be proof of compliance with treatment (*15, 16*). All drugs were obtained from reputable international suppliers and given in recommended doses according to the body weight of the patient (*14*). Patients were followed until the end of treatment, and cohort outcome analysis was carried out according to IUATLD guidelines (*14*).

In 1991, an examination of case holding was undertaken. This entailed cohort analysis of TB patients and a detailed audit of the WHO DOTS strategy for TB control. The technical elements of the DOTS strategy are as follows:

- passive case detection using smear microscopy;
- short-course chemotherapy, directly observed at least in the intensive phase;
- an uninterrupted supply of drugs;
- a reporting and recording system to allow evaluation of the programme (*2*).

Supervision and training at all levels of the programme are explicit requirements of a successful TB control programme. All the elements of the programme were reviewed, possible areas for improvement were identified, and several simple, low-cost interventions were undertaken.

The intervention

A practical training course was arranged for the hospital TB assistant. He was sent to accompany an experienced district health officer in an adjoining district for 6 weeks of on-the-job training as a health surveillance assistant. Other TB staff from the NGO hospital were also included in NTP educational activities. A system was devised to accurately record as many details regarding each patient's address as possible. For example, urban patients' addresses included the township or suburb name and the name of a nearby prominent landmark such as a church, school, medical clinic, shop, or tavern. The addresses of rural patients included the district and traditional authority (subdistrict) names in addition to the village name and the name of the village headman. Further identification was made by identifying the closest larger settlement, school, or medical clinic. Supervision at all levels of the programme, especially at the treatment unit, was improved. Formal and informal links were established and sustained by the formation of a district TB committee at which all parties were represented. Weekly meetings between the hospital TB assistant and the municipal health department led to more efficient follow-up of defaulters. Cohort outcome analysis was improved by the appointment of a well-trained and enthusiastic regional TB officer.

Definitions of outcomes

The treatment outcome categories used in this study were defined as follows:

- *died:* death during TB treatment due to any cause;
- *treatment failure (smear-positive):* smear-positive after 8 months of TB treatment;
- *cure:* proven sputum smear-negative after 8 months of TB treatment;
- *treatment completed (smear not done):* finished 8 months of TB treatment but cure not documented by sputum smear examination;
- *treatment success:* proven cure plus those completing treatment and clinically well;
- *default:* failed to complete treatment (and not included in any other category);
- *transfer out:* transferred to another TB treatment unit and no further information obtained (and not included in any other category);
- *cure rate (survivors):* proven sputum smear-negative after 8 months of TB treatment as a proportion of those surviving at the end of treatment.

All other rates were calculated as a proportion of the entire cohort.

Data entry and analysis used EpiInfo 5.01 software (*17*). Confidence intervals at the 95% level were determined by the approximate, test-based method. Fisher's exact test was used to calculate *P*-values when an expected frequency was <5.

Results

Cure rate, Mzuzu, 1990–91

TB cure rates in Mzuzu in 1990–91 were extremely low (see Table 1). In all patients, the cure rate was 24%. In those surviving to the end of treatment, the rate was 29%. But cure rates are merely a summary outcome measure for case-holding activities, and

Table 1. **Treatment outcome of new sputum smear-positive pulmonary TB patients in Mzuzu, Malawi**

Outcome[a]	No. "before"[b] (*n* = 42)	No. "after"[c] (*n* = 143)	Relative risk	*P*-value
Died	7 (17)[d]	36 (25)	1.5; *0.7, 3.1*[e]	0.3
Transferred out[f]	8 (19)	6 (4)	0.2; *0.1, 0.6*	0.001
Defaulted[g]	7 (17)	2 (1)	0.1; *0.0, 0.3*	<0.001
Smear not done	10 (24)	2 (1)	0.1; *0.0, 0.3*	<0.001
Smear positive	–	6 (4)	NA[h]	0.3[i]
Cure	10 (24)	91 (64)	2.7; *1.5, 4.7*	<0.001
Treatment success	20 (48)	93 (65)	1.4; *1.0, 1.9*	0.04
Cure (survivors)	10 (29)	91 (85)	3.0; *1.8, 5.1*	<0.001

[a] See Methods for definitions of treatment outcomes.

[b] 1 April 1990–30 September 1991 (18 months).

[c] 1 November 1991–31 May 1993 (17 months).

[d] Figures in parentheses are percentages.

[e] Figures in italics are 95% confidence intervals.

[f] Transferred to another treatment unit and not in another category.

[g] Defaulted and not included in other categories.

[h] NA = not applicable

[i] Fisher's exact test.

more detailed analysis is required to elicit the underlying reasons for low case-holding rates.

An audit of case-holding activities revealed several problems (see Table 1). There was a high death rate during treatment, possibly related to coinfection with HIV. Mzuzu TB patients were a highly mobile population. As a result of poor communication between TB treatment units within the Malawi NTP, there was no information about the outcome of treatment for one in five patients. The defaulter rate was high. One in four patients who completed treatment had no proof of cure, indicating poor adherence to NTP protocols. There were no proven treatment failures in this cohort — perhaps due to the low number of follow-up sputum examinations performed. Alternatively, this may indicate a low level of drug resistance, as has been found in other Malawian studies (*18*).

Evaluation of the NTP in Mzuzu

The TB control programme in Mzuzu was compared with the WHO DOTS strategy for successful TB control in high-prevalence countries. Underlying problems were identified in the Mzuzu programme, and action was taken to improve the situation (see Table 2). The main problems identified in case holding were as follows:

- a fragmented TB control programme;
- inadequate training and supervision of the hospital TB assistant;
- suboptimal recording of patients' addresses;
- nonadherence to NTP protocols for follow-up of patients transferred out to other treatment units and for sputum collection at the completion of treatment.

Table 2. **TB control in Mzuzu, 1991: programmatic problems identified and interventions for improvement**

DOTS strategy	Problem	Solution
Case detection	Low rate of sm + PTB[a]	Sputum smears for all patients with chronic cough
Drug supply	Remote regional store Separate from regional pharmacy	Relocated to Mzuzu Link with pharmacy
Recording/ reporting	Lack of training of hospital TB assistant Inaccurate patient addresses Poor interhospital communication	Short practical training Cross-tabulation system Post and phone contacts
Training	Lack of formal training for NGO staff[b]	Staff included in NTP training[c]
Supervision	Poor at all levels	Increased frequency and intensity of supervision
Evaluation	Reporting only	Investigation and action

[a] sm + PTB = Sputum smear-positive pulmonary TB.

[b] NGO = Nongovernmental organization.

[c] NTP = National TB control programme.

Programmatic improvements

The formal upgrading of the skills of the hospital TB assistant built on his considerable personal attributes of commitment to TB control, capacity for hard work, and standing in the local community. His enhanced understanding of public health led to improvements in recording and reporting systems that were especially evident in improved defaulter tracing. The new model for TB control in Mzuzu involved improved coordination and collaboration at the local level, which replaced the previously rigid administrative structure. The quarterly evaluation of TB control in Mzuzu by the regional TB officer was expanded from mere recording of a cure rate to include investigation of problems and action to rectify them.

Cure rate, Mzuzu, 1992–93

After the changes in TB control were introduced, there were statistically significant falls in default rates, and proof of cure increased markedly. Table 1 shows a comparison of outcomes for TB patients in the period before and after the interventions to improve TB control in Mzuzu.

Patients remained mobile, but information on treatment outcomes from other treatment units also improved significantly. The result was a statistically significant improvement in cure rate (proven sputum smear negativity at the end of treatment: 64% versus 24%, $P < 0.001$) and treatment success (proven cure or successful treatment completion without proof of cure: 65% versus 48%, $P = 0.04$). In those surviving to the end of treatment, patients were three times more likely to be cured after the intervention (85% versus 29%, $P < 0.001$).

Discussion

This study examined TB control in a peripheral district within the Malawi NTP. Using cohort analysis of smear-positive pulmonary TB patients, the reasons for a low cure rate were elucidated, and local solutions were implemented to address these problems, with a spectacular rise in the cure rate within 1 year. The comparison of pre- and post-1991 TB control in Mzuzu was a "before-and-after study", and thus assumptions of causality should be guarded. However, the magnitude of the improvement in the cure rate in Mzuzu is such that an examination of the possible causes for this improvement are worthwhile.

Case finding

A total of 143 sputum smear-positive patients were identified in the 17-month period following the intervention compared with only 42 in the 18 months prior to the intervention. This rise was partly due to an increase in the caseload of TB patients and partly to improved case detection, with an increased proportion of sputum-positive cases (data not shown).

Cure rates

The conventional way to examine cure rates is the approach advocated by IUATLD and WHO (*14, 19*). All smear-positive pulmonary TB patients who present during a specified period are assessed as a cohort. The cure rate is defined as those with demonstrated smear negativity at the end of the treatment period expressed as a proportion of the total number of smear-positive patients who commenced the treatment. Deaths during treatment, treatment failure (sputum positivity), and failure to complete treatment therefore all affect cure rates defined in this way.

The alternative definition of cure used in this study is the demonstration of sputum negativity at the end of TB treatment in those subjects surviving to the end of treatment. This definition has been used in studies that have examined the effect of HIV on the response to therapy of TB patients (*20–24*). Cure rates by this definition are unaffected by mortality rates during TB treatment.

Which definition of cure is the more valid measure of TB control? This depends on which question is being asked. If the question is "How successful is the treatment regimen at rendering and keeping TB patients non-infectious?", the "cure in survivors" definition is the more appropriate. From a public health point of view, this is arguably the most important issue in TB control. If the question is "How many patients are retained by the programme, successfully complete treatment, and have bacteriological evidence of cure?", the IUATLD/WHO definition is the more appropriate. De Cock has argued that, in the era of high death rates in HIV-coinfected TB patients, counting deaths as treatment failures leads to an underestimate of the success of TB control programmes and unnecessary levels of demoralization among TB programme staff (*25*). As Nunn et al. have observed, it appears that community confidence in a TB control programme is badly affected when people see friends and family dying during TB treatment, even if these deaths are largely due to other, HIV-related illnesses (*16*).

Default rates are another important indicator of programme effectiveness and need to be quantified alongside mortality and cure or treatment success rates. The current IUATLD/WHO definition of cure is perhaps too blunt an instrument. When used as a single measure of programme efficacy, many of these other important issues are obscured. This makes it difficult to address problems when they occur.

Local problems, local solutions

In the present study the arrival of three committed and enthusiastic people at the regional, district, and hospital levels who were prepared to cooperate and work to improve the situation, together with suitable training for the TB assistant, raised the cure rate among patients who completed treatment to over 85%. This improvement was not due to any change in the treatment regimen or death rates, and was unlikely to be due to a decrease in HIV coinfection during the study period. By ensuring that sputum samples were collected when patients completed TB treatment, the proven cure rate (WHO/IUATLD definition) was doubled. Sputum smear results were gathered by direct contact (by telephone or in person during the routine visit of the regional TB officer) with other treatment units to which St John's Hospital patients had been transferred, and the cure rate was increased by 44%. Finally, more accurate recording of addresses facilitated the better follow-up of patients and probably contributed to the marked decrease in default rates. In short, there was local analysis of local problems and the formulation of local solutions. There were no revolutionary, unorthodox, or expensive interventions. We simply attempted to do the simple things better, to follow the guidelines more closely, and to cooperate between the various sectors involved in TB control, particularly at the local level in Mzuzu. The Mzuzu cohort study was the catalyst for change (*13*). Frequent evaluation, training, supervision, and encouragement at all levels of the programme were the crucial elements for sustained improvement in cure rates. De Cock (*25*) as well as Harries et al. (*26*) have noted that simple and often "unmeasurable" factors such as intersectoral collaboration, interest on the part of influential people, enthusiasm, and hard work are often the key to success in TB control programmes. The Mzuzu experience confirms that these elements, coupled with a dispassionate evaluation of a district TB control programme, can indeed lead to improved public health outcomes.

Conclusions

Despite a high HIV prevalence among TB patients in sub-Saharan Africa, high rates of cure are achievable using the usual TB treatment protocols. Simple, inexpensive programmatic interventions can quickly and dramatically improve TB case holding at the district level. The solutions outlined here may not be generalizable, but the method employed may be successfully applied to other situations. Further research is needed to elucidate the ways in which local solutions to local problems, within the framework of WHO guidelines, can lead to improved TB control at district level in high-prevalence countries. ■

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Résumé

A problèmes locaux, solutions locales : l'amélioration de la lutte contre la tuberculose au niveau du district au Malawi

Objectif Examiner les causes du faible taux de guérison au niveau du district obtenu par un programme de lutte contre la tuberculose et formuler, mettre en œuvre et évaluer des interventions en vue d'améliorer la situation.

Méthodes L'étude a été réalisée à Mzuzu (60 000 habitants), où l'incidence annuelle de la tuberculose pulmonaire à frottis positif était de 160 pour 100 000 et la séroprévalence du virus de l'immunodéficience humaine (VIH) de 67 % parmi les malades atteints de tuberculose. Il existe un service de traitement de la tuberculose mais plusieurs organisations sont actives dans ce domaine. On a examiné les activités de prise en charge des cas, identifié les possibilités d'amélioration et mis en œuvre des interventions.

Résultats En 1990–1991, le taux de guérison était de 24 % parmi les cas à frottis positif (29 % parmi les survivants à la fin du traitement). Parmi les problèmes identifiés figuraient une dispersion du programme de lutte contre la tuberculose, une insuffisance de la formation et de la supervision, une insuffisance de l'enregistrement de l'adresse des malades, et le non-respect des protocoles du programme national de lutte contre la tuberculose. Des mesures correctrices ont été prises et en 1992–1993, le taux de guérison est passé à 68 % (risque relatif (RR) = 2,85 ; intervalle de confiance (IC) à 95 % : 1,63–4,96) et à 92 % parmi les survivants à la fin du traitement (RR = 3,12 ; IC 95 % : 1,84–5,29). Il est donc possible d'obtenir des taux de guérison élevés malgré la forte prévalence du VIH.

Conclusion Des interventions programmatiques locales simples et peu coûteuses peuvent améliorer considérablement la prise en charge des cas de tuberculose. Cette étude montre la nécessité d'une évaluation, d'une formation et d'une supervision à tous les niveaux du programme.

Resumen

Problemas locales, soluciones locales: mejora de la lucha contra la tuberculosis a nivel distrital en Malawi

Objetivo Determinar las causas de la baja tasa de curación observada a nivel distrital en un programa de lucha contra la tuberculosis (TB), y formular, ejecutar y evaluar una intervención para mejorar la situación.

Métodos El entorno del estudio fue la localidad de Mzuzu (60 000 habitantes), donde la incidencia anual de TB pulmonar con frotis positivo era de 160 por 100 000, y la seroprevalencia del virus de la inmunodeficiencia humana (VIH) entre los pacientes de TB, del 67%. Existe una unidad de tratamiento de la TB, pero hay también otras organizaciones que combaten esta enfermedad. Se llevó a cabo un examen de las actividades de seguimiento de casos, se identificaron posibles ámbitos de mejora, y se intervino en ellos.

Resultados En 1990–1991, la tasa de curación fue del 24% entre los casos con frotis positivo (29% entre los sobrevivientes al final del tratamiento). Entre los problemas identificados cabe citar la fragmentación del programa de lucha antituberculosa; una formación y supervisión inadecuadas; las deficiencias del registro de las direcciones de los pacientes; y la inobservancia de los protocolos del programa nacional de lucha contra la TB. Todos estos problemas fueron abordados, y en 1992–1993 la tasa de curación aumentó al 68% (riesgo relativo (RR) = 2,85 (IC95%: 1,63-4,96)), y al 92% entre los sobrevivientes al final del tratamiento (RR = 3,12 (IC95%: 1,84-5,29)). Por consiguiente, se pueden lograr tasas de curación altas pese a la elevada prevalencia de infección por el VIH.

Conclusión Es posible mejorar espectacularmente el seguimiento de los casos de TB mediante intervenciones programáticas locales, sencillas y de bajo costo. Este estudio demuestra que es necesario implantar sistemas de evaluación, formación y supervisión a todos los niveles del programa.

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