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Passive versus active tuberculosis case finding and isoniazid preventive therapy among household contacts in a rural district of Malawi

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SUMMARY

SETTING: Thyolo district, rural Malawi.

OBJECTIVES: To compare passive with active case finding among household contacts of smear-positive pulmonary tuberculosis (TB) patients for 1) TB case detection and 2) the proportion of child contacts aged under 6 years who are placed on isoniazid (INH) preventive therapy.

DESIGN: Cross-sectional study.

METHODS: Passive and active case finding was conducted among household contacts, and the uptake of INH preventive therapy in children was assessed.

RESULTS: There were 189 index TB cases and 985 household contacts. Human immunodeficiency virus (HIV) prevalence among index cases was 69%. Prevalence of TB by passive case finding among 524 household contacts was 0.19% (191/100 000), which was significantly lower than with active finding among 461 contacts (1.74%, 1735/100 000, $P = 0.01$). Of 126 children in the passive cohort, 22 (17%) received INH, while in the active cohort 25 (22%) of 113 children received the drug. Transport costs associated with chest X-ray (CXR) screening were the major reason for low INH uptake.

CONCLUSIONS: Where the majority of TB patients are HIV-positive, active case finding among household contacts yields nine times more TB cases and is an opportunity for reducing TB morbidity and mortality. The need for a CXR is an obstacle to the uptake of INH prophylaxis.

KEY WORDS: tuberculosis; case finding; isoniazid; HIV; Malawi

THE ANNUAL RISK of developing active tuberculosis (TB) is higher in a person infected with the human immunodeficiency virus (HIV) than in a non-infected individual, ranging from 5% to 15%.[1] HIV infection also favours rapid progression from exposure to *Mycobacterium tuberculosis* to active disease, which can develop over weeks rather than years.

In Malawi, the national HIV prevalence rate is estimated at a high 9%.[3] In 2000, a country-wide survey found that 77% of new patients registered with TB were HIV-seropositive.[4]

A high frequency of TB among household contacts of index TB patients has been reported in Malawi.[5] There is also growing evidence that a significant number of new TB cases in Africa result from recent transmission and casual contact.[6,7]

Case finding in the Malawi National Tuberculosis Control Programme (NTP) has so far been limited to self-referral of symptomatic individuals to health facilities, so-called 'passive case finding'. This approach is used in household contacts of smear-positive pulmonary TB (PTB) cases. However, an 'active case finding' strategy in individual households of smear-positive TB cases might allow earlier diagnosis of TB and thus facilitate decisions for either anti-tuberculosis treatment or preventive therapy. This 'active' approach may reduce TB transmission as well as morbidity and mortality among individual patients.

Young childhood contacts of smear-positive TB cases are at a high risk for progression of latent infection to active and severe forms of disease.[8] Isoniazid (INH) prophylaxis, which reduces the risk of such progression,[9,10] is therefore recommended for all household contacts of smear-positive TB cases who are aged under 6 years and in whom active TB has been excluded. To be placed on INH, the child must first be assessed clinically and undergo chest X-ray (CXR) to rule out active TB.

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The aim of the current study was to compare 'passive' versus 'active' case finding among household contacts of smear-positive pulmonary TB cases. The measurable outcomes were 1) the number of TB cases detected (all types of TB) and 2) the proportion of children aged under 6 years who underwent TB screening and were placed on INH preventive therapy.

METHODS

Study setting and management of TB

The study was conducted between October 2001 and May 2002 in Thyolo district, a rural region of southern Malawi with a population of 450 000. The main public hospital, which registers and treats the majority of TB cases in the district, was involved in the study. All patients diagnosed with TB are registered and started on standardised anti-tuberculosis treatment according to national guidelines.[11] Drugs and investigations for TB are free of charge, and since early 1999 all TB patients also undergo voluntary counselling and HIV testing. HIV-seropositive patients are offered cotrimoxazole prophylaxis provided there are no contraindications to the medication.

Until the study, passive case finding was used for household contact tracing. In brief, index smear-positive PTB cases should be informed by the TB officer that any household contact who is symptomatic with cough should attend the hospital for investigations, and that any child aged 6 years or less should attend to receive anti-tuberculosis treatment or INH preventive treatment. Children less than 6 years of age need a CXR regardless of symptoms, according to national recommended policy.[11] A decision is made on the basis of the CXR to provide INH preventive treatment at the dose of 5 mg/kg body weight for 6 months, or start anti-tuberculosis treatment. INH preventive treatment is offered if the CXR is normal; otherwise the child receives a full course of anti-tuberculosis treatment.

Other symptoms such as fever, weight loss and lymph gland enlargement are not part of the screening protocol. Tuberculin skin testing is also not part of the screening process. It requires single-use syringes and needles, a cold chain for storage and a new visit by the patient for reading of results, and the NTP therefore feels that this is not feasible in rural Malawi. The district TB team responsible for supervising district TB activities is comprised of non-clinical staff, and depends entirely on hospital clinicians for clinical assessments and reading CXRs.

Study population and data collection

The study was a sequential assessment of passive case finding for 3 months, followed by active case finding for another 3 months, among household members of all new smear-positive TB index cases. An index case was defined as the first registered smear-positive PTB case from a household. A household contact was defined as an individual (adult or child) who was living under the same roof as the index case at the time of the visit.

Passive case finding was done as described earlier. To obtain data on the measurable outcomes, a visit was made to all households of this 3-month cohort of registered smear-positive TB patients one month after registration of the index TB case. The following information was collected into a structured proforma: the number of people living in the household at the time of the visit, the number with cough for more than 3 weeks, the number who had attended for a check up at hospital, and the number diagnosed with TB. For children aged under 6 years, data were collected on the number in whom a CXR had been performed, the number put on INH preventive therapy and the number put on anti-tuberculosis treatment.

In active case finding, a visit was conducted to all households of the next 3-month cohort of registered smear-positive TB patients one month after registration of the index TB case. This visit was used to promote actions as follows: individuals with cough for more than 3 weeks were requested to provide sputum samples on the spot and a day later, and these were taken back to the hospital for acid-fast staining and smear microscopy. All children aged under 6 years were given referral slips for CXR at the hospital. Children aged under 6 who had a cough at the time of the visit were first given a full course of a broad spectrum antibiotic (erythromycin) according to body weight. CXR was then done at least 10 days after completion of the antibiotics to try to exclude lower respiratory tract infections other than PTB.

In the active case finding cohort, CXRs were read by an experienced clinician and were systematically cross-checked by a paediatrician experienced in reading CXRs. Data were then collected on the measurable outcomes of these interventions.

The district TB register was used to identify index cases, and data for the study were collected after informed consent was obtained. An interviewer-administered questionnaire and record form were used to gather basic socio-demographic data on the index case and other information related to the study. The interviews were conducted in the local language by experienced interviewers, and the same team was used throughout the course of the study. In the case of children, either the father or mother was interviewed.

A motorcycle and fuel were made available for household visits. Individuals involved with such visits were not part of the routine district TB control team.

The study received ethical approval from the National Health Sciences Research Council of Malawi.

Statistical analysis

Data entry and analysis were done using Epi Info (Centers for Disease Control and Prevention, Atlanta, GA, USA). The number of detected cases were stan-

dardised to a population of 100 000. The level of significance was set at $P = 0.05$, and 95% confidence intervals (CI) were used throughout. The measures of risk were determined by crude odds ratio (OR).

RESULTS

Characteristics of the study population

A total of 189 smear-positive index TB cases were registered in the study, with a total of 985 household contacts. There were 102 index cases in the passive case finding cohort and 87 in the active cohort, the majority of whom resided in villages (89%) and were farmers (80%). Index cases included 85 men and 104 (55%) women, with a median age of 31 years (range 15–72) and a median educational level of 5 years' schooling (range 0–14). Ninety-one patients were married, and 98 (53%) were unmarried, divorced or widowed.

Index patients had had a cough for a median period of 60 days (range 7–210) before being diagnosed with smear-positive PTB. All index cases received pre-test counselling; 185 (98%) underwent HIV testing and received post-test counselling. HIV status was not known in four patients who had refused HIV testing. In the passive cohort, 65 (64%) of 102 index TB cases were HIV-positive, while in the active cohort 62 (71%) of 87 index cases were HIV-infected. The overall HIV infection rate among index TB cases was 69%.

Number of cases of TB detected by passive and active case finding.

Prevalence of TB by passive case finding (Figure 1) among 524 household contacts was 0.19% (191/100 000), which was significantly lower than with active finding among 461 household contacts (1.74% or 1735/100 000, OR 9.24, 95%CI 1.2–197, $P = 0.01$) (Figure 2). Eight (89%) of the nine detected cases of TB were among household contacts, where the index case was known to be HIV-positive.

INH preventive therapy in children under 6 years of age

In the passive case finding cohort, there were 126 children under 6 years of age, of whom none were referred for CXR (Figure 1). The TB team members felt that even if a CXR was available it was not worthwhile as hospital clinicians were either too busy or unavailable to interpret the findings. However, 22 (17%) children who were staying with their parents in the hospital were put on INH preventive treatment by ward nurses or clinicians without undergoing CXR.

In the active case finding cohort, there were 113 children aged under 6 years (Figure 2); all were asked to go hospital for CXR. Of these, 44 (39%) went to the hospital and underwent CXR; four had features suggestive of PTB and were put on anti-tuberculosis treatment and in 40 children the CXRs were normal. Of the 40 children who had a normal CXR and were eligible for INH preventive treatment, only 25 were started on INH treatment. Fifteen (40%) children who had actually completed the CXR screening process were asked to return for a new consultation the next day. They could not afford to spend the night in town and returned to their village. INH was not started in these children.

Of 113 children referred for CXRs, 69 (61%) did not go to the hospital, the great majority because the household member(s) could not afford the transport costs. The other reasons for not going to the hospital are given in Figure 2.

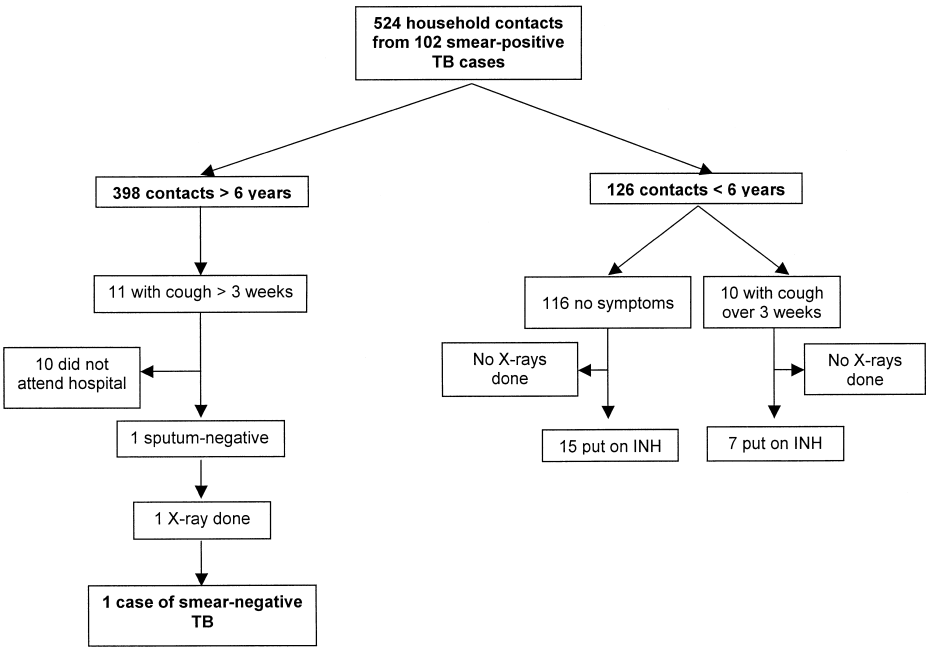

Figure 1 Passive case finding among household contacts of smear-positive tuberculosis (TB) cases.

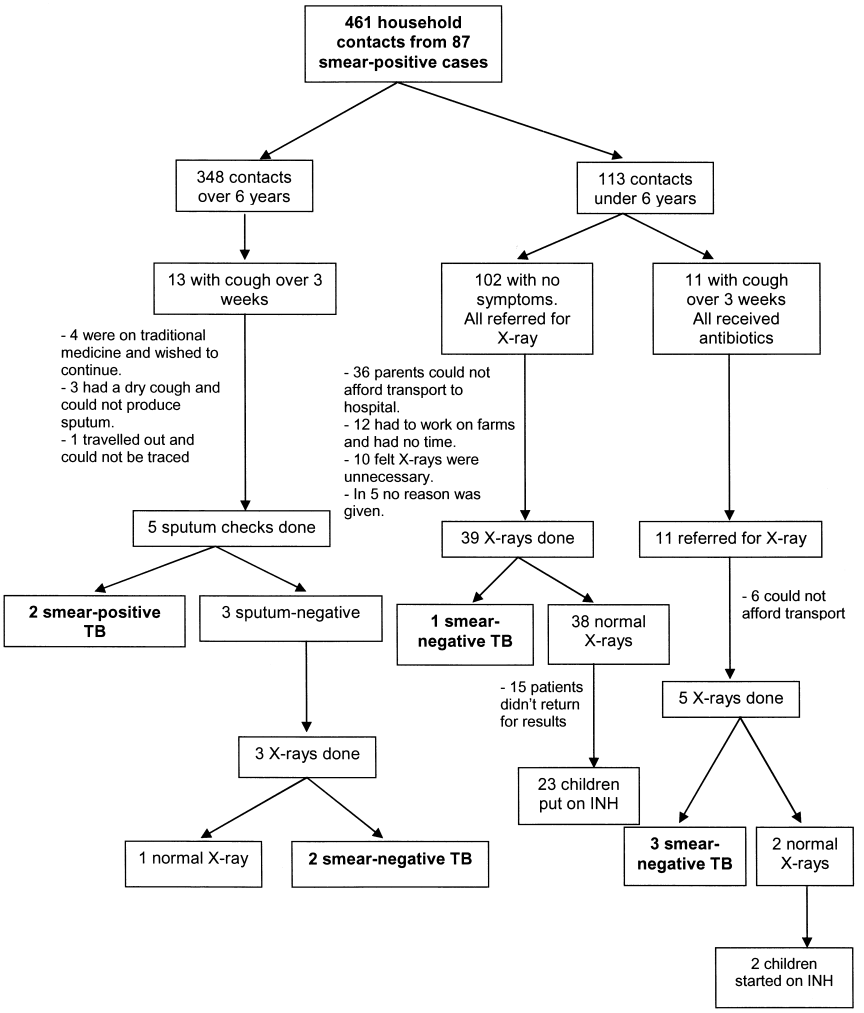

Figure 2 Active case finding among household contacts of smear-positive tuberculosis (TB) cases.

DISCUSSION

This study shows that active case finding among household contacts of smear-positive PTB cases yields a significantly higher number of TB cases than the current system of passive case finding. In children under 6 years of age, the uptake of INH preventive therapy is low, even with active case finding. Transport costs and delays in reading results associated with CXRs were obstacles for INH preventive therapy uptake.

In a rural setting where the main public hospital is far away, it is understandable that there will be individuals who will not come for screening because they are unable to afford the transport costs to hospital, might have limited time due to work on their farms, or might have sought care with traditional healers.[12] Despite this, active case detection as early as one month after registration of the index case yielded nine times more pulmonary TB cases among household contacts than passive case finding. The great majority of these cases occurred among contacts where the index cases were known to be HIV-positive. Although we do not know the HIV status of the household contacts, an HIV-positive individual in a household might imply more HIV-infected individuals within the same household, and hence more TB-susceptible individuals.[13–15] In our setting, stigma did not appear to be an obstacle to the active case research.

Most TB control programmes in sub-Saharan Africa are currently facing an epidemic of TB that has been fuelled by HIV.[3] In such contexts, active case finding in households of smear-positive TB cases who are known to be HIV-positive might be one way of targeting early case detection and treatment. Such a targeted strategy of active case finding is more likely to be sustainable in the longer term by national programmes where resources are limited. The yield of case detection might also be higher and hence be of greater benefit to TB control.

Despite the fact that routine INH preventive therapy is recommended for all childhood contacts (<6

years), the proportion of children who were eventually placed on INH preventive therapy, even with active case finding, was very low (<25% in our study). Our study identifies a number of operational problems in this respect.

First, most household members simply cannot afford to travel to hospital several times for CXRs, or are simply not convinced that screening an apparently healthy child is worthwhile. Information, education and communication campaigns targeting households of index TB cases might help improve awareness about latent TB and the importance of screening.

Second, even after completing the screening process, a considerable proportion of children (40% in our study) dropped out due to undue delays in reading CXR results. The opportunity to institute INH preventive therapy in these children was therefore missed.

The links between the TB programme and the general services are weak, and clinicians are often not available to read CXRs. It is therefore not surprising that TB officers tend to simply neglect the screening of children or leave the decision about INH preventive therapy to be made by the clinical staff on the ward. Attaching a full-time clinician in the framework of the TB programme and improving the links with the general services might prevent such undue delays.

Third, the CXR is itself an obstacle for the uptake of INH preventive therapy in our resource-poor setting. Of the children sent for CXR, 61% did not have one performed for a variety of reasons: reagents and films for radiology are expensive, machines break down frequently and good technicians are often hard to find. In the context of HIV, reading of films is also difficult, and clinicians often lack the necessary skills. The screening process is also cumbersome for the patient, as visits to hospital take time and involve additional, sometimes excessive costs. Finally, although the reason for CXR is to exclude TB, the specificity of CXR for TB diagnosis in children is low, especially in HIV-endemic regions such as Malawi.[16–18]

As long as the CXR remains an obligatory part of the screening process for TB, the uptake of INH preventive therapy in resource-poor settings and its impact in terms of TB prevention is likely to be limited. There is therefore a need to develop a more simple and rapid diagnostic test for latent TB that will help to simplify the existing algorithm and make it more patient-friendly.

TB policy makers in high HIV prevalence settings may consider a number of operational options if they are to improve the uptake of INH preventive therapy in children.

First, drop out rates for screening were very high, and among asymptomatic cases CXR revealed less than 1% of active TB cases. In contrast, the yield from CXRs in contact children with cough was high, with 27% being diagnosed with TB. It may be more practical and effective to assess childhood contacts on the basis of clinical symptoms and findings alone. Asymptomatic childhood contacts could be given INH at the same schedule (daily or intermittently) at which anti-tuberculosis treatment is given to the adult case,[19] while symptomatic childhood contacts require further evaluation. Asymptomatic contacts are followed for 6 months while on preventive therapy and if they become symptomatic during that time they can undergo further evaluation, including CXR. TB programmes in settings such as Malawi could therefore concentrate their resources on symptomatic children rather than performing CXRs for all childhood contacts.

Second, can all asymptomatic childhood contacts be placed on INH preventive therapy at home? Using such a strategy, children from households who can not afford transport costs, those with families who do not have the time to travel to hospital and those who drop out due to service delays at hospital would then benefit. In our study, this group comprises the majority (71%) of all asymptomatic children, and is currently denied access to INH preventive therapy. Monthly INH for such children could simply be given to the index TB case along with TB drugs, as long as the children remain asymptomatic. Monitoring could be reinforced with existing home-based care and community workers who are already an integral part of the TB activities in Malawi and who could become further involved in a decentralised approach.[12,20]

As such a strategy is likely to considerably increase the uptake of INH preventive therapy, it would also be useful to verify whether INH resistance is higher as a consequence. INH preventive therapy has been shown to be a useful, cost-effective intervention in HIV-positive adults.[21,22] Children of all ages who are contacts of smear-positive PTB cases are also likely to benefit. There is now a need to explore new strategies that will improve its uptake in children.

In a setting where the majority of TB patients are HIV-positive, active case finding among household contacts provides an opportunity to reduce TB morbidity and mortality. TB control programmes in countries such as Malawi must be provided with more resources if such a strategy is to become a reality. Otherwise, more household members are bound to come into contact with TB, TB case rates will continue to increase and more people will eventually die from the disease.

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RÉSUMÉ

CADRE : District de Thyolo, Malawi rural.
OBJECTIFS : Comparer le dépistage actif au dépistage passif parmi les contacts dans le même maison que des patients atteints de tuberculose (TB) pulmonaire à bacilloscopie positive en ce qui concerne 1) la détection de cas de TB et 2) la proportion d'enfants-contact âgés de moins de 6 ans qui sont placés sous chimiothérapie préventive à l'isoniazide (INH).
SCHÉMA : Etude transversale.
MÉTHODES : On a mené un dépistage passif et actif parmi les contacts au foyer et on a évalué la prise d'un traitement préventif à l'INH chez les enfants.
RÉSULTATS : Il y a eu 189 cas index de TB et 985 sujets-contact au foyer. La séroprévalence VIH parmi les cas index était de 69%. La prévalence de la TB lors du dépistage passif parmi 524 contacts au foyer était de 0,19% (191/100.000), ce qui est significativement plus faible que lors du dépistage actif parmi 461 contacts, où il atteignait 1,74% (1.735/100.000 ; P = 0,01). Parmi les 126 enfants de la cohorte passive, 22 (17%) ont reçu l'INH, alors que dans la cohorte active 25 des 113 enfants (22%) ont reçu le médicament. Le coût de transport associé au dépistage par les clichés du thorax (CXR) a été la raison majeure de la faible administration d'INH.
CONCLUSIONS : Là où la majorité des patients TB sont séropositifs pour le VIH, le dépistage actif des cas parmi les contacts au foyer ramène neuf fois plus de cas de TB et constitue une opportunité de réduction de la morbidité et de la mortalité tuberculeuses. La nécessité d'un contrôle par cliché thoracique constitue un obstacle à la prise de la prophylaxie par l'INH.

RESUMEN

CONTEXTO : Distrito de Thyolo, Malawi rural.
OBJETIVO : Comparar la detección pasiva con la detección activa en los contactos domiciliarios de los pacientes con tuberculosis (TB) pulmonar con baciloscopia positiva con respecto a 1) la detección de los casos de TB y 2) la proporción de niños contactos menores de 6 años de edad sometidos a terapia preventiva con isoniacida (INH).
DISEÑO : Estudio transversal.
MÉTODO : Se efectuó la detección pasiva y activa en los

contactos domiciliarios y se evaluó la administración de terapia preventiva con INH, en los niños.

RESULTADOS: Se estudiaron 189 casos índice y 985 contactos domiciliarios. La prevalencia de VIH en los casos índices era de 69%. Con la detección pasiva, la prevalencia de TB en 524 contactos domiciliarios era de 0,19% (191/100.000), la que es significativamente más baja que con la detección activa en 461 contactos que fue de 1,74% (1.735/100.000, *P* = 0,01). De 126 niños de la cohorte pasiva, 22 (17%) recibieron INH, mientras que en la cohorte activa, 25 de 113 niños (22%) recibieron este medicamento. El costo de transporte asociado a la radiografía de tórax (CXR) era la principal razón de la baja tasa de administración de INH.

CONCLUSIÓN: En los lugares donde la mayoría de los pacientes TB son VIH positivos, la detección activa de casos entre los contactos domiciliarios produce nueve veces más casos de TB y es una oportunidad para reducir la morbilidad y la mortalidad TB. La necesidad de CXR es un obstáculo para la administración de una terapia preventiva con INH.