Tuberculosis and Special Situations:
An Annotated Bibliography

Emanuele Pontali
Jai P. Narain

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# Acronyms and Abbreviations Frequently Used in the Text

- AIDS  Acquired Immune-Deficiency Syndrome
- AFB  Acid Fast Bacilli
- ARI  Annual Risk of Infection
- ARTI  Annual Risk of Tuberculosis Infection
- BCG  Bacillus Calmette-Guerin
- CI  Confidence Interval
- DNA  Deoxyribo Nucleic Acid
- DOT  Directly Observed Treatment
- DOTS  Directly Observed Treatment Short-Course
- E  Ethambutol
- FDC  Fixed Dose Combination
- H  Isoniazid
- HCW  Health Care Worker
- HIV  Human Immunodeficiency Virus
- IEC  Information Education Communication
- IUATLD  International Union Against Tuberculosis and Lung Diseases
- MDR  Multi-Drug Resistant
- MSF  Mèdicines Sans Frontière
- M. tuberculosis  Mycobacterium tuberculosis
- NGO  Nongovernmental Organization
- NTP  National Tuberculosis Programme
- OR  Odds Ratio
- PPD  Purified Protein Derivative
- R  Rifampicin
- S  Streptomycin
- SEA  South-East Asia
- SEARO  South-East Asia Regional Office
- TB  Tuberculosis
- USD  United States Dollar
- WHO  World Health Organization
- Z  Pyrazinamide
1. **INTRODUCTION**

The worldwide implementation of the Directly Observed Treatment Short-course (DOTS) strategy aims to achieve better global control of the tuberculosis pandemic. This strategy is now starting to show important achievements. However, in many of the countries, National Tuberculosis Programme (NTP) managers and other personnel working in tuberculosis control sometimes face difficulties or obstacles that seem beyond the DOTS strategy.

This bibliography collection is mainly drawn from the medical literature recently published in English. Whenever possible, examples are taken from the experiences of Member Countries of the South-East Asia (SEA) Region of WHO or from neighbouring countries in Asia. Since many of these challenges are encountered in SEA Region, it provides opportunities for Member Countries to learn from each other’s experience.

This bibliography is intended as a resource for NTP managers and for other personnel working in TB control and includes the following: DOTS in the workplace, private sector and NGOs’ involvement in tuberculosis control, tuberculosis and gender, HIV infection and TB, tuberculosis control in prisons, in immigrants, in refugees and in conflict situations, the use of fixed dose combinations of anti-tubercular drugs and the socio-economic impact of tuberculosis.

We hope that this bibliography will be found useful, and look forward to receiving comments for improvement.
2. TUBERCULOSIS CONTROL AND DOTS IN THE WORKPLACE


The study-evaluated adherence to anti-tubercular treatment among patients working in a mining site where DOTS programme had been introduced by the mining medical service. In the medical stations of the mining site, TB patients collected their drugs daily and their attendance was recorded by nurses and countersigned by patients. Availability of drugs and accessibility to health care centres did not present any problem.

Authors established non-compliance with treatment by testing urine samples from TB patients for rifampicin and isoniazid drug metabolites. They then compared the results from urine tests with attendance data from registers.

All patients who were on TB treatment during the week 26 June to 6 July 1995 formed the study population; 270 patients were evaluated in five medical stations.

There was high discrepancy between the two sources: prevalence of non-compliance from urine tests was 14.6 ± 3.3%, while non-compliance established on the basis of attendance in the same period of time was only 0.2%.

In conclusion, the evaluation of non-compliance with TB treatment through surveillance procedures (registers) underestimated the actual size of the problem and supervision of patient treatment was poor.

Actually, a few of these medical stations were understaffed and this probably prevented nurses from actual supervision at the moment of drug administration, i.e. they probably did not watch patients swallowing their doses.

The main lesson learnt was that the DOTS strategy could be employed in the workplace. However, adequate staff is needed to effectively run the programme.

The study evaluated the frequency of clusters of patients with TB pulmonary cases in a gold-mining community (28,522 men). South African gold miners have among the highest rates of tuberculosis in the world; in particular, in this community the incidence was about 1 300 per 100 000 population each year. HIV seroprevalence was estimated to be 21% in 1995.

All patients with culture-positive pulmonary TB (448) in 1995 were considered; IS6110 DNA fingerprints were made in 434 of them. In the end, 371 patients were valuable; 248 (67%) of them were categorized into 62 clusters. Most clusters included from 2 to 7 patients; two bigger clusters were present: the first included 43 patients, while the second included 20 patients.

Many risk factors possibly associated with the clustering phenomena were identified: TB category (new, recurrent, treatment failure), age, years working in the mining site, actual mine of working and accommodation, years spent underground, HIV status, number of CD4+ cells in HIV-infected, drug resistance, living in South Africa, education, alcohol consumption, smoking, changes in chest radiograph and sputum smear. Strong associations (p=0.005) were found with treatment failure (supporting the notion that patients who failed treatment were sources rather than secondary cases) and with duration of employment in the mines. Room-based transmission in dormitories (1609 rooms, 18 men per room) accounted for 12% of clustered patients. Other direct links (working together, being friends, same village of origin) were identified for 19% more clustered patients. Other clusters (29/62) were identified as occurring at a single mine. In the end there were only 15% of clustered patients with no documented “bridge” to others within the cluster.

The authors estimated that at least 50% of TB cases among mining workers were caused by ongoing transmission within the mining community. This happened despite TB control activity: active case finding, contact tracing, treatment regimen tailored on drug sensitivity, initial treatment in the hospital, then DOT treatment in the clinics and a cure rate of 86% in new cases.

In conclusion, in special settings as this one, characterized by high incidence of TB and HIV, crowded living and working arrangements, silica
dust exposure, and a high prevalence of chronic and recurrent cases of tuberculosis, targets proposed by WHO for TB control are not enough to interrupt transmission of TB.

In this context, a few problems were identified: patients failing treatment were a significant source of infection in the working community, dormitories accounted for more than 10% of clustered patients (crowded living) and ongoing transmission within the community was responsible for at least 50% of cases.

The possible interventions are: improvement of living conditions and of working arrangements that may increase the impact of control activities on TB transmission, and the availability of second-line treatment that could help in interrupting transmission from “treatment failures” in this particular setting.


The study evaluated the risk factors associated with Mycobacterium tuberculosis infection following occupational exposure in health care workers (HCWs) in Chiang Rai Hospital, northern Thailand. In this area, a recent resurgence of TB, largely attributed to the emergence of the HIV epidemic, is present.

The assumption that HCWs are already infected in areas with high TB prevalence has never been proved, and it caused underestimation of HCW’s risk of being infected following occupational exposure.

The study was performed during February and March 1996. Of 1,229 hospital employees, 911 participated in the study and underwent tuberculin skin testing (TST) by using the Mantoux intradermal injection method (5 PPD units). Of them, 623 (68%) had ≥ 10 mm induration, and 322 (35%) ≥ 15 mm induration. They also had to answer a questionnaire aimed at evaluating predictive factors for TST positivity in relation to their work.
Regardless of whether the $\geq 10$ mm or the $\geq 15$ mm TST cut-off was used, a significantly increased risk of \textit{M. tuberculosis} infection was observed to be associated with employment in the hospital for at least one year or with occasional or frequent direct patient contact (69\% vs. 50\% with the 10 mm cut-off and 36\% vs. 17\% using the 15 mm cut-off).

In conclusion, preventive interventions are needed to reduce HCWs’ risk for \textit{M. tuberculosis} infection from occupational exposure also in an area where tubercular infection has high prevalence in general population. Similar risk assessments in other areas of the developing world are needed.
3. TUBERCULOSIS CONTROL AND THE PRIVATE SECTOR


The study evaluated the involvement of private practitioners in tuberculosis control in the urban area of Lalitpur in the Kathmandu Valley - Nepal. They conducted a door-to-door survey among private practitioners working in the area in the period January-April 1998. Physicians were asked to complete a questionnaire; 43/59 (73%) returned it. Thirty-nine (93%) of them were treating TB patients in their clinics. A high number of cases was followed in the private sector: 97 patients were started on treatment during the previous month, in comparison to the approximately 650 patients who are treated annually in the public sector in the same area.

Notwithstanding that 52% of physicians employed internationally or nationally recommended regimens, 14 different combinations were used. None of the doctors gave treatment under supervision.

A positive note emerged from the fact that 85% of the doctors regularly referred TB patients to governmental or NGOs clinics. However, the main reason for this was the patients’ inability to afford treatment; less frequently, this happened because of diagnostic difficulties, need for hospital admission or suspect of multi-drug resistance.

These findings made NTP of Nepal stop neglecting the private sector and start looking for new forms of collaboration. The problems on which to focus were: the wide variety of employed anti-TB combinations (no standardization) and lack of treatment supervision.

In conclusion, knowledge of how private practitioners treat TB patients should be known to NTPs and collaboration in order to obtain uniformity of action and especially of therapeutic regimens should be started.
Tuberculosis and Special Situations: An Annotated Bibliography


The authors conducted a nationwide survey in the Philippines in 1997 among the general population aged 20 years or more to evaluate the health-seeking behaviour of symptomatic patients with tuberculosis. They interviewed 2 358 symptomatic patients. Only 25.4% of them had consulted a health care provider: 11.8% a private practitioner (PP), 7.5% the public health clinic (PHC), 4.4% a hospital (mainly private) and 1.7% a traditional healer. Among the 76 bacillary patients, an equal proportion (17.1% for each group) had consulted a PP or the PHC, and 8% had consulted a hospital.

The study identified the main reasons for patients’ attendance of PPs as fear of stigmatisation and their perception of the inferior quality of care in PHC.

In consideration of this study and of other reports, private-public collaboration was hence started by the Philippines NTP. So, the NTP would now provide training to PPs and free and uninterrupted supply of anti-TB drugs.

Recruitment of private sector was started by the Philippine Coalition Against Tuberculosis (PhilCAT), an alliance of all governmental and nongovernmental anti-TB organizations.

Examples of private-public collaboration obtaining encouraging results already exist in the Philippines, as the hospital-based DOTS clinic initiated by the Tropical Disease Foundation and the Makati Medical Centre (from private sector), in collaboration with the Department of Health and the local government unit, Barangay San Lorenzo.

However, a few problems were identified: patients with TB do not trust public health services for fear of stigmatization and because of perception of poor quality of services.

In conclusion, IEC interventions for TB are necessary in order to reduce stigma general population should be targeted by IEC interventions aimed to diffuse knowledge of successful strategies (as DOTS) available in public health services, and private-public collaboration appears useful, necessary and feasible.

This paper analyses the relationship between the private sector and public health in relation to tuberculosis control. Private Practitioners (PPs) treat a substantial proportion of TB cases in the world. About 50% of such patients in India are treated – partly or completely – in the private sector. These cases alone account for a sixth of the world’s TB burden. However, a similar situation is present in other high prevalence countries. Furthermore, many studies showed that PPs treat patients belonging to all socioeconomic classes and that they frequently deviate from the recommended TB management practices.

There are many barriers to overcome to reach a good public-private collaboration in TB care. Within the national TB programmes can be found: ideological opposition, lack of information on the private sector, preoccupation with strengthening and expansion of the national TB programme, prejudices about the profit motive and the behaviour of PPs, weak or absent regulatory mechanisms, absence of precedents and little evidence on replicability of them.

While within the private sector can be found: inadequate training and lack of information, technical doubts about national TB programmes guidelines, low priority to public health functions (also not remunerative), infrastructural limitations to performance of “public health” tasks such as defaulter retrieval, doubts about quality of care within the national TB programmes, poor organization and challenging liaison and interactions.

However, many successful experiences of involvement of PPs in national TB programmes exist. They can be found in low prevalence countries such as The Netherlands and the USA (New York City), in moderate prevalence countries such as Egypt (Cairo), Morocco (Casablanca), Republic of Korea and the Syrian Arab Republic, and in high prevalence countries such as DR Congo (Kinshasa), India (Hyderabad, Chennai, Jamnagar, Delhi), Kenya (Nairobi) and The Philippines (Manila).

In conclusion, notwithstanding many obstacles and difficulties, it is crucial and possible to involve PPs in TB control activities. Each country can use the reported experiences to develop its own strategy (a few are suggested in the paper) to cope with this aspect of TB control.

Private practitioners are de facto primary health care providers in much of India and other developing countries. Their involvement in TB control programme is crucial to avoid unnecessary delays in the diagnosis of TB. A poor section of Hyderabad (state of Andhra Pradesh, India) was selected for this pilot project. A microscopy centre was established in a non-profit hospital, then a hospital physician visited all private practitioners (allopathic and non-allopathic), encouraging them to refer suspect cases of TB to the hospital.

In September 1995, the project started with a population coverage of 100,000. After diagnosis, patients were addressed for treatment to the trust hospital itself or to 30 conveniently located privately run small hospitals. Following the initial success, in October 1998, the project expanded to cover a population of 500,000.

In the initial phase of the project, all physicians working in the area (92) agreed to participate and more than 80% of them referred at least one patient. After expansion, again all physicians working in the area (358) agreed to participate and almost 60% of them referred at least one patient.

Interestingly, in this project, the proportion of female patients enrolled was significantly higher than that of neighbouring government DOTS service in the same city.

Private practitioners working in the small hospitals provided space and staff for treatment observation without any compensation; they found that doing so did not interfere with their routine work. In addition, being considered as an official centre increased their status in the community, and care of intercurrent illness during or after the full course of anti-TB treatment may have increased their patient population and earnings.

Reasons for the successful involvement of private practitioners may be found in the specific feedback on each patient referred (diagnosis and treatment) and in the fact that patients continued to consult their private practitioner for health problems other than TB (clients were not lost!).
In conclusion, this is a successful example that collaborative efforts between private practitioners and the public sector are feasible and can achieve good results. Contrary to general belief, private practitioners are willing to collaborate with Government-run programmes. Clearly definition of roles and expectations, and frequent communication appeared to be crucial for success. Furthermore, involvement of private practitioners in TB control makes it possible to increase the number of reported female patients.


In 1998, a private registered society of Chennai (India) - Advocacy for Control of Tuberculosis (ACT) - started a project concerning provision of DOTS in the private sector following the guidelines of the National TB Programme. ACT identified private practitioners of Chennai willing to participate (20) and the laboratory technicians associated with them; then, ACT trained these two groups. When a patient was diagnosed with TB, he/she and the practitioner identified together a drug provider (DP), who was subsequently trained and supervised by ACT. In the period between December 1998 and November 1999, 130 tuberculosis patients were treated following this model.

Characteristics of 97 DPs of these patients were evaluated through an interview. Most of them (86%) were chosen by patients: 34% were family members, 35% were neighbours, 20% were friends and 11% were ex-patients (mainly identified by practitioners). In most of the cases (79%), drugs were given in patients’ houses; other places included DPs’ houses and DPs’ work place. Almost all (97%) said that DOT was used to ensure regular treatment and they all were well aware of their responsibilities, although they did not always adhere correctly to them.

Though the number of DPs’ and the duration of the study were limited, their performance demonstrates that DOT can be provided in private sector. No specific criteria seem needed for the choice of DPs and informal training is adequate; however, frequent monitoring of DPs, as done by ACT staff, is essential.
4. **TUBERCULOSIS AND NGO's**

Central TB Division - Directorate General of Health Services - Ministry of Health and Family Welfare - India. Involvement of Nongovernmental Organizations in the Revised National Tuberculosis Control Programme.

The Revised National Tuberculosis Control Programme (RNTCP) of India has acknowledged the importance of a greater involvement of NGO's in TB control and has subsequently issued guidelines for this purpose.

They based NGO's' involvement and integration within the RNTCP on these principles:

1. Involved NGO's must follow all principles of the RNTCP;
2. If an NGO is already providing satisfactory services in TB control in RNTCP areas, it should not be displaced by new, parallel structures established by the RNTCP.

RNTCP would also provide training for staff and volunteers of involved NGO's.

They issued the various schemes under which NGO's collaboration would be established:

1. Health education and community outreach (including IEC activities, counselling to patients and families, retrieval of defaulters)
2. Provision of directly observed treatment
3. In-hospital care for tuberculosis disease
4. Microscopy and treatment centre
5. TB unit model

They also provided guidelines for NGO's on how to apply to participate in RNTCP and on what they could expect from RNTCP.

This can be considered a model of how political commitment on NGO's' involvement translates into practical instruments.

In conclusion, systematic involvement of NGO's by NTPs is possible, even in very large countries, and guidelines for integration (to avoid overlapping of activities) of NGO's in NTP should be developed.

The Britain-Nepal Medical Trust (BNMT) is an NGO that - at the time of this study – was assisting the Government of Nepal in tuberculosis services in eight hill/mountain districts with populations of between 100 000 and 300 000.

Home visiting of patients who are late for appointments by “default chasers” (DCs) is believed to be a key element in the success of the BNMT’s tuberculosis programme. This study aimed at defining the home visiting process and to assess the inputs necessary to conduct such a service.

DCs visited – usually on foot – patients already under treatment who missed an appointment or any TB suspect that did not return for a smear result if it was positive.

For a total of 205 considered patients, 37 home visits for 29 cases were performed (one every 5.5 new smear positive patients registered). Where DC action was carried for the first time during a treatment episode, 84.7% returned to treatment at least for one time. Only six patients required more than one visit: four required two visits and two needed three visits. The median time for the DC to reach a patient’s home was three hours. For the majority of cases, walking was the only method of transport available.

The median delay from the missed appointment to the home visit was three days, while the median time from the start of treatment to the missed appointment was 88 days.

In conclusion, almost one-third of registered new smear-positive patients will require a home visit at some stage, either to inform them of their diagnosis (16%) or to perform patient retrieval (14%).

This activity proved to be necessary and useful to avoid both primary and secondary default of patients.

In 1968, the Indonesian Association Against Tuberculosis (PPTI) was established as an NGO. Since then, it has always supported the Indonesian government in combating tuberculosis.

In December 1997, in collaboration with the Japan Anti-Tuberculosis Association (JATA), PPTI started a DOTS implementation project in two of its clinics located in Jakarta City.

Since the beginning, the collaboration with government and the results were excellent. In the first year, the cure rate of new smear positive cases was 83% (success rate 87%) and defaulters were less than 5%. Satisfactory, although less brilliant results were observed in re-treatment cases: among them cure rate was 57.5% and success rate was 78%.

The “contract system”, an innovative strategy to improve adherence to treatment was used in the programme: every patient had to sign a kind of contract to underline his/her willingness to complete treatment. Food incentives were also used.

In conclusion, NGO involvement in NTPs is useful and can be successful, development of partnerships is useful to sustain and strengthen NGOs’ interventions, and innovative approaches and strategies can be developed with NGO’s.


Self Employed Women’s Association (SEWA) is an NGO that, in February 1999, entered into an agreement with the local (Ahmedabad, India) District TB Control Society to provide TB control services in an area of the town with a population of 500 000 on a pilot basis.

The project was located in a large slum, with a highly mobile population, where few health care facilities were available. They operated two microscopy centres and one sputum collection centre. Sixty DOTS treatment centres
operated by volunteers were also established. In these latter centres, the activities included treatment of patients in the centre or at home or in the workplace, late-patients tracing, counselling for patients and for their families, health education about TB for patients and for the community.

Since the beginning of the project, more than 800 patients have started anti-TB treatment.

This is a successful example of effective collaboration between a National TB Programme and an NGO, and of its feasibility.

In conclusion, NGOs can operate in special situations, as in slums, at least as efficiently as “official” health services, and innovative approaches as treatment at home or in the workplace can be easily experimented by NGOs.
5. TUBERCULOSIS AND GENDER


The study investigated the TB case detection process in Nepal in relation to gender in order to identify differences between men and women; in particular, it examined delays in TB diagnosis and health care seeking behaviour of men and women.

The investigation was conducted in the Nawalparasi district (population: 185,000), a rural area in the plain where DOTS was already in place. Subjects included in the study were new cases of TB who began to receive DOT from December 1997 to June 1999. Data were obtained from registration documents and face-to-face interviews with the patients using a questionnaire. The interviewers had been specifically trained and they knew Nepali, English and some of the dialects of the area.

The delay in case detection was measured as the time from the onset of symptoms to the diagnosis of TB. Two components constituted the total delay: patient’s delay (the period from the onset of symptoms to the first visit to any kind of health care provider), and health care provider’s delay (the period between the first visit and the diagnosis of TB).

During the study time, 265 men and 125 women were enrolled, but only 238 men and 98 women were actually interviewed because of death or default.

Significantly more women (35%) than men (15%) did visit a traditional healer at some time prior to their TB diagnosis (p= 0.001). Traditional healers were more convenient and familiar for women (fear of stigma if seen in public health services? Less time for travelling?).

Women had a significantly longer total delay than men did (p= 0.034): the median total delay was 2.3 months for men and 3.3 months for women. Patient’s delay did not differ by sex. Women had a longer health care provider’s delay than men if they had visited a traditional healer first (p= 0.03). However, the delay did not differ by sex when they visited private health care provider or government medical establishments first.
In conclusion, in order to reduce such women’s delay in such a context, a possible approach could be the training of traditional healers in suspecting TB and promptly addressing patients to referral government centres.

A similar analysis could be useful in other districts or in other countries to investigate if an analogous gender-related delay is present and identify its causes.


This study explores the perspectives of tuberculosis patients on which factors influenced their health seeking behaviour, with special reference to gender differentials in terms of delays in health seeking. In 1996, a multidisciplinary research team carried out 16 focus group discussions. The study was conducted in four districts in Vietnam, both in the south and north of the country and in urban and rural areas. Qualitative analysis of data was performed following general principles of modified grounded theory technique. Participants in the focus groups described the main factors as contributing to delay in health seeking. These were fear of social isolation, economic constraints and inadequate staff attitudes and poor quality of health services.

The main contributing to delay among men was described as fear of individual costs of diagnosis and treatment. Staff attitudes and quality of health service facilities were described as not always corresponding to people's expectations of appropriate health services.

Women saw themselves and were seen by others as being more sensitive to poor service conditions and staff attitudes than men are. A typical feature of the described health seeking behaviour of men was that they neglected symptoms until the disease reached a serious stage, by which time they tended to go directly to public health services. Women, on the other hand, were described as having a tendency to seek out private services and practise self-medication before seeking care at public services.

In conclusion, health workers need to better understand gender and social aspects of tuberculosis control, particularly aspects that influence the likelihood for achieving equity in diagnosis and cure.

This study aimed at assessing gender differences in access to tuberculosis diagnosis and treatment outcome in Bangladesh. The female-to-male ratio in the country is 0.95. Information on the age and sex of a sample of patients in 1997 was collected from outpatient registers and tuberculosis laboratory and treatment registers in 59 thanas (where basic primary health care units are) in three administrative divisions in Bangladesh (Dhaka, Rajshahi and Sylhet).

The female-to-male ratio in the study population was 0.79 (ranging from 0.49 to 0.91) among 42,877 outpatients with respiratory complaints, 0.51 among 5,665 tuberculosis suspects undergoing sputum smear microscopy, 0.36 among 869 tuberculosis suspects with positive sputum smears, and 0.35 among 5,632 patients registered for tuberculosis treatment. Treatment was successful (patient cured or treatment completed) in 86% of female and 84% of male patients.

In conclusion, women in Bangladesh appear to have less access to public outpatient clinics than men, and if they present with respiratory symptoms they are less likely to undergo sputum smear examination. This discrepancy is progressively higher for older people, reaching the highest level (0.34 and 0.18 respectively) in those aged 65 years or more. If examined, women are less likely to be smear-positive than men are. No gender bias was observed in tuberculosis treatment outcome.

However, further research exploring sex differences in the incidence of respiratory conditions, identifying constraints among women in the access to outpatient clinics and verifying the quality of sputum submitted by women for examination is needed.


The study evaluated the socioeconomic consequences of TB in Vietnam with special reference to gender differentials concerning social stigma and isolation. It was conducted in four districts (rural and urban areas) both in the south and north of the country.
Sixteen focus group discussions were carried out with men and women, TB patients and participants without TB. Data were analyzed using modified grounded theory technique.

Generally, the participants had good knowledge about TB. However, knowledge and practice were not closely related in the sense that most non-TB participants perceived that TB could be successfully cured, while patients were seriously shocked (especially women) when they were told that they had TB.

The economic burden of having TB was of great concern especially for male patients. They had to leave jobs and/or increase health expenditures.

On the other hand, female patients were mainly worried about the social consequences of the disease. Both in the family and the community, isolation could be subtle, but it could also be obvious (divorce because of TB) and had the tendency to continue much longer than medically justified. In fact, unmarried persons with TB or unmarried children of parents with TB may face difficulties in getting married even after years.

In conclusion, information on stigma and isolation due to TB and gender differences is important for understanding patient dynamics and its effects on the disease. TB control programmes need a better understanding of the gender differences in attitudes and beliefs to improve case-detection and treatment outcome, and to reduce the social impact of the disease.


The study explores the causes for lower tuberculosis notification rates among women, in particular if they are due to a reduced access to the health care, especially diagnostic services, for women.

Age- and sex-specific tuberculosis prevalence rates of smear-positive tuberculosis cases were obtained from TB prevalence surveys reported to WHO or published in the literature. Age- and sex-specific notification rates from the same countries in 1996 were used.
Prevalence data and notifications from 29 surveys in 14 countries were used. Notification rates varied strongly among countries, but the female/male ratio was below 1 and decreased with increasing age in almost all them. The female/male (F/M) prevalence ratios were less than 0.5 in surveys in the South-East Asia and Western Pacific Regions, and approximately 1 in the African Region.

In most countries the F/M sex ratio in prevalent cases was similar or lower than that in notified cases, suggesting that F/M differences in notification rates may be largely due to epidemiological differences and not to differential access to health care. However, available data are limited, as the prevalence surveys in Africa were carried out many years ago, and in Asia, notification rates may be distorted by a large private sector with deficiencies in notification.
6. TUBERCULOSIS AND HIV


The study reports about the results of three tuberculin surveys performed in Tanzania from 1983 to 1998 and their relation with the ongoing HIV epidemic.

In Tanzania tuberculosis is highly prevalent, but a national TB control programme is in place since 1979 and cure rate of new smear-positive cases increased from 55% in 1980 to 80% in 1990. The notification rate of smear-positive TB increased from 38/100 000 population (1983-1987) to 69/100 000 (1993-1997) and most of this increase is attributed to the HIV epidemic.

The three rounds of tuberculin surveys were carried out in the 20 regions of mainland Tanzania in 1983-87 (Round I), 1988-1992 (Round II) and 1993-1998 (Round III). Fifty-nine out of 94 districts were randomly selected. In the round 1, 2 and 3 the total number of children tested and read was 67 412, 76 370 and 102 74 respectively.

Among children without BCG scar, ARTI for the three rounds was 1.1%, 1% and 0.9% respectively using the 17-mm cut-off and 1.4%, 1.6% and 1.6% respectively based on the 10-mm criterion. Similar changes were present among children with BCG scar, ARTI for the three rounds was 2.1%, 1.1% and 1% respectively using the 17-mm cut-off and 3.4%, 2.8% and 2.3% respectively based on the 10-mm criterion.

Data show that, despite a substantial increase in notification rates of smear-positive TB in adults, ARTI in children in Tanzania was stable over the period 1983-1998. On the opposite end, in Kenya, with a TB and HIV epidemics similar to the Tanzanian situation, the increase in notification rates was accompanied by a proportional increase in ARTI (Odhiambo JA et al. Am J Publ Health 1999; 89: 1078-1082).

The authors suggest that these differences could be justified by the earlier strengthening of the National TB Programme in Tanzania, i.e. the improved TB control contained the impact of the HIV epidemic on TB transmission over the same period.

The study evaluated the frequency of recurrence or of relapse of TB in a population with high level of coinfection with HIV in New York City, USA.

Being the optimal duration of tuberculosis treatment for persons infected with human immunodeficiency virus (HIV) still debated, authors evaluated the risk of TB recurrence with the anti-TB regimens presently employed.

A cohort of 4,571 culture-positive drug-susceptible TB patients who received at least 24 weeks of standard four-drug anti-tubercular treatment was assessed to determine the incidence of tuberculosis relapse. Incidence of relapse in patients coinfected with HIV was compared with that in HIV-negative patients.

TB "recurrence" was defined as having a positive culture < 30 days after the last treatment date and "relapse" as having a positive culture at least 30 days after the last treatment.

Patients infected with HIV were more likely than those who were uninfected to have recurrence or relapse (2.0 vs. 0.4 per 100 person-years, P < .001).

Patients infected with HIV who received < or = 36 weeks of treatment were more likely than those who received more than 36 weeks to have a recurrence (7.9% vs. 1.4%, P < .001).

In conclusion, clinicians should be aware of the possibility of recurrence of tuberculosis 6-9 months after the start of treatment.

Furthermore, the authors suggest that in similar settings, sputum evaluation to ensure cure or assessment three months after completion of treatment should be performed among persons infected with HIV who have received the shorter regimen.

The study, carried out in Hlabisa health district, a rural district of South Africa, compared success rates of anti-TB treatment among HIV-infected and uninfected patients. The cohort included 529 TB patients who accepted to receive HIV-testing and to be enrolled in the study; of these, 304 (58%) were HIV-infected. Patients received daily anti-TB therapy in hospital for the first 2-3 weeks (HRZE) and then twice weekly in the community (but always supervised) until two months, after which HR was continued twice weekly in the community until six months.

At six months, among new patients (416), outcomes among the HIV-infected and uninfected were similar (discontinuation 17% in both groups; cure 70% in HIV-infected and 74% in HIV-uninfected), except for death, which was significantly more frequent among HIV infected (6% vs. 2%; p=0.03).

In conclusion, HIV-infected patients can be successfully treated with DOT anti-TB regimens. However, excess mortality among HIV-infected patients is present despite successful treatment. So, if it appears important to treat HIV-infected patients for TB, it is also necessary to further investigate the causes of high mortality among them (most probably due to other HIV-related opportunistic infections) in order to identify possible and effective interventions.


The study, undertaken in Hlabisa health district, a rural district of South Africa compared rates of relapse and mortality among HIV-infected and uninfected patients with culture-positive pulmonary TB successfully treated with DOT. The cohort evaluated had been previously treated with daily anti-TB therapy in hospital for the first 2-3 weeks (HRZE) and then twice weekly in the
community (but always supervised) until two months, after which HR was continued twice weekly in the community until six months. The study considered all cured patients, so 403 persons were followed for a mean of 1.2 years; of these, 215 (53%) patients were HIV infected. During the follow-up period, 19 patients (5%) relapsed. The rate of relapse was similar among HIV-infected (3.9%) and HIV-uninfected (3.6%) patients. The probability of relapse at 18 months was estimated as 5% in both groups. However, mortality was increased fourfold among the HIV-infected patients: 17.8 and 4.4 deaths per 100 person-years of observation (p < 0.0001).

In conclusion, an acceptable low relapse rate was observed after DOT treatment, irrespective of HIV status; this result is in line with what was observed by another study performed in Zaire (Perriens et al. N Engl J Med 1995; 332: 779-784). Excess mortality among HIV-infected patients is present despite successful anti-TB treatment.

So, it is worthwhile to treat HIV-infected patients for TB, in order to reduce the spread of TB infection in the community, to improve their health (they are cured and with low relapse rate) and probably to prolong their life, although mortality among them remains very high despite successful treatment.


The study evaluated the presence of HIV complications in TB patients and determined whether there was enough care and treatment for them. It was a cross-sectional study carried out in all 43 hospitals in Malawi that register and treat TB patients. This study was done in the context of an HIV epidemic heavily affecting TB patients; in fact a nationwide survey of TB patients in the first six months of 2000 found a 77% HIV sero-prevalence rate. Of 1,416 adults with TB, 861 (61%) had HIV complications, 627 (44%) patients had received no ward round, and of 1,142 patients who had been on anti-tuberculosis treatment for more than 7 days, 294 (26%) had not had a clinical review. Of patients with HIV complications, only 139 (16%) were receiving treatment.
In conclusion, HIV complications in TB patients in Malawi are frequent and there is a lack of regular care and treatment of them.

Actually, there is need for increased attention to patients with the double infection in all the countries with a high TB burden and where HIV prevalence is high or is increasing. Early treatment of HIV complications could have a positive impact on HIV-related mortality of TB patients.


The authors performed two meta-analysis in reply to: evaluations of different clinical studies to determine the risk of transmission of TB from patients coinfected with HIV.

To assess if the relative infectiousness of patients with tuberculosis is enhanced by coinfection with HIV, data from six studies including 1 240 health care workers who had contact with TB patients were analyzed.

The overall rates of tuberculin skin test conversion were similar regardless of HIV positivity of TB patients (odds ratio [OR], 1.04; 95% CI, 0.23-1.84).

However, when they analyzed only three studies about TB transmission during hospital outbreaks of multidrug-resistant *Mycobacterium tuberculosis*, rates of skin test conversion were higher among contacts of HIV-positive index cases (OR, 2.85; 95% CI, 1.85-3.85; *P* = .0002).

A second meta-analysis included data from 11 studies including 10 714 household contacts of TB patients. Prevalence of both skin test positivity (OR, 0.45; 95% CI, 0.20-1.03) and active disease (OR, 1.17; 95% CI, 0.78-1.56) were similar regardless of HIV positivity of index cases.

In conclusion, these data suggest that tuberculosis patients with HIV infection are not intrinsically more infectious to their contacts than are HIV-negative TB patients.
7. **TUBERCULOSIS CONTROL AND IMMIGRANTS**


The study evaluated the effectiveness of a DOT programme in a population of Vietnamese immigrants living in Santa Clara County in California, USA. Vietnamese immigrants accounted for 103/296 (35%) of TB cases reported per ethnicity in the county and ranked number one among all ethnic groups.

The authors compared completion of treatment rates, relapse rates and time to sputum conversion between two groups of Vietnamese TB patients. One group was treated under DOT, the other one under non-DOT. Each group included 25 patients with only pulmonary TB (positive culture) who had completed treatment between 31 December, 1994 and 31 December, 1997. The two groups were similar, although a higher rate of drug resistance (7 patients vs. 2) was present in the DOT group.

Completion rate was higher in the DOT group (100% vs. 84%) and relapse rate was lower in DOT group (0 vs. 8%); however, differences were not statistically significative. Time to sputum conversion was significantly shorter (4.7 weeks vs 10.3; p< 0.05) in the DOT group.

Despite all the differences in culture, health beliefs, and health practices, the Vietnamese TB patients appeared to benefit from DOT programme. This programme apparently provided sufficient support and encouragement to complete TB treatment in this population of immigrants. These results provide evidence of the feasibility of DOT in immigrants.

In conclusion, DOT programmes can be successfully implemented among immigrants and, notwithstanding the small size of the cohorts, DOT significantly shortened time to sputum conversion (earlier interruption of *M. tuberculosis* circulation).

The study evaluated the prevalence of tuberculosis infection and the incidence of active TB among 191 Tibetan immigrants coming from India or Nepal. Immigrants arrived in Minnesota (USA) between 1992 and 1994. Most of them (54%) were not born in Tibet, but in India or in Nepal. They had lived for a mean of 23 years (2-36 years) in India or Nepal before traveling to USA.

Almost all (98%) had a positive tuberculin skin test; so, prevalence of tubercular infection was significantly higher among them (p<0.001 for each group) than among Vietnamese, Hmong or Russian refugees living in Minnesota. This probably reflected the prolonged interim staying in northern India of most of them; actually, it is known that tuberculosis is a leading cause of mortality among Tibetans in northern India.

Incidence of active TB (16 cases; 8.4%) was again significantly higher (all groups, p<0.005) than in Vietnamese, Hmong or Russian refugees. Only six cases were detected during initial screening evaluation in Minnesota, one had been diagnosed in India before departure, while the other nine were detected after a mean of 19 months from arrival.

Of the 15 tested strains, six were resistant to at least one drug, 3 of them were MDR. A previous history of TB while still in Asia was significantly (p=0.02) associated with a higher risk of MDR TB.

This study raises specific questions regarding TB prevention in this particular population in terms of incidence of TB infection, chemoprophylaxis and screening of immigrants/refugees coming from Asia and especially from countries with high TB prevalence.

In conclusion, high incidence of TB infection in refugees is not always present and it may depend on their history before arrival in the host country, screening immigrants/refugees for TB at arrival is not always enough, a prolonged follow up is probably needed (two years?) and evaluation of cost-effectiveness of chemoprophylaxis should be assessed for different populations of immigrants/refugees.

The study evaluated the feasibility of directly observed preventive therapy for TB and the adherence to it among illegal immigrants living in northern Italy, in the period between April 1996 and October 1997.

Illegal immigrants were foreign-born persons with no residence permit and limited access (emergency interventions only) to public medical care services.

Participants were randomized to receive either supervised isoniazid at a dose of 900 mg twice weekly for six months (A), unsupervised isoniazid at a dose of 900 mg twice weekly for six months (B), or unsupervised isoniazid at a dose of 300 mg daily for six months (C).

A total of 208 patients were randomised in the three groups. The proportions completing the 26-week regimen were 7.3, 26, and 41% in arms A, B, and C, respectively. Most of the patients (127/156; 81.4%) who did not complete treatment were simply lost to follow-up.

Subjects in group A had a significantly lower probability of completing treatment than participants in group C (p=0.001) or in group B (p=0.006). Also mean time to dropout was significantly shorter (3.8 weeks) for subjects in group A compared with persons in group B (6 weeks) and group C (6.2 weeks) (p=0.003).

Adherence to IPT was very low in these cohorts, and extremely low in the supervised group.

The authors suggest that probably illegal immigrants had difficulties in reporting regularly to health services to collect their drug doses and they probably need different, innovative strategies for TB control. In their opinion, an outreach system of drug delivery within the community would be useful, but it would be a labour-intensive strategy so requiring political commitment and adequate resources.

The authors reply to comments about a previous paper they published on the same journal on Vietnamese immigrants in Denmark (Wilcke JTR, Poulsen S, Askgaard DS, Enevoldsen HK, Rönne T, Kok-Jensen A. Tuberculosis in a cohort of Vietnamese refugees after arrival in Denmark 1979-1982. Int J Tuberc Lung Dis 1998; 2: 219-224).

They discuss about the possible policy for TB control in the different immigrant groups in a given country: passive case-finding, chest X-ray screening, chemoprophylaxis, tuberculin skin test.

They conclude that in order to choose one of these strategies a few questions have to be answered first:

- What is the individual long-term TB risk in the cohort?
- What is the risk of transmission of \( M. \) tuberculosis causing TB to other immigrants and to the indigenous population?
- What is the best cost/benefit ratio obtained in the different immigrants groups with the different interventions?

Who will pay for prophylactic measures and/or for the lack of them?


The objective of the study was to estimate the effect of tuberculosis screening among recent immigrants on the severity of disease at diagnosis and on the duration of the infectious period. Pulmonary tuberculosis cases among immigrants detected through screening were compared with those detected passively, using information from the Netherlands Tuberculosis Register.

Immigrants from highly endemic countries diagnosed with culture-positive pulmonary tuberculosis within 30 months after arrival in The Netherlands, 1993 through 1998 were considered. The outcome measures of the study were the severity of disease (smear-positive disease, hospitalisation and case fatality) and the duration of symptomatic period.
A total of 882 bacteriologically confirmed tuberculosis patients from highly endemic countries had been in The Netherlands less than 30 months; they were detected through screening (454), or passively (368). Compared with patients detected passively, patients found through screening were less often sputum smear-positive (OR 0.5, 95% CI 0.3-0.8) and less often hospitalised (OR 0.2, 95% CI 0.1-0.2). Those detected through screening had a shorter symptomatic period.

Screening is estimated to have reduced the infectious period by approximately 33%.

In conclusion, the screening programme detected cases earlier, resulting in fewer hospital admissions, shorter duration of symptoms and therefore probably reducing tuberculosis transmission.
8. TUBERCULOSIS AND PRISONS


The study evaluated the results of and the difficulties arising from a pilot programme of DOTS in the Central Penitentiary Hospital of Baku, Azerbaijan.

The pilot programme was implemented in two wards of the above mentioned hospital and the outcome for patients admitted to treatment between June 1995 and October 1997 was considered. The study evaluated 467 patients; only 357 of them completed the treatment, while 51 (11%) died and 59 (13%) defaulted (because of judicial or medical reasons). A susceptibility test was performed on the cultures from 131 of them. A high prevalence of resistance to first-line anti-TB drugs was observed: only 21% of patients had strains of M. tuberculosis sensitive to all antibiotics, and 23% of individuals had multidrug resistant strains. Overall, sputum conversion rate was only 42%, but ranging from 10-29% (multidrug resistant strains) to 61% (fully sensitive strains). The overall cure rate was of 54% despite excellent compliance.

Operational constraints were observed: convincing staff to directly observe patients while swallowing TB drugs (lack of adequate motivation), premature release or transfer of prisoners, late identification of cases with consequent high death rate, and advanced disease. Moreover, the authors support the idea that, in populations like this one, second-line drugs should be available and employed, but only at the condition of a very strict adherence.

In conclusion: the presence of highly resistant TB strains in prisons is important not only to affected prisoners themselves, but also the risk for their inmates, for prison staff and for their families should be considered, especially in consideration of possible diffusion to the general population.

It is necessary to evaluate the rate of drug-resistance in prison populations or whenever a TB programme would achieve low cure rates despite high-level adherence. Active case finding in prisons could help in early detection, so reducing circulation and improving outcome. Anti-TB treatment should “follow” patients when they are transferred (DOTS in all prisons) or released (referred to DOTS centres).
In 1998, results from a survey assessing the prevalence of new smear-positive TB cases among prisoners in Bangkok showed tuberculosis to be a major health problem in Thai prisons. The survey revealed that TB prevalence observed among prisoners (1226 cases per 100,000 persons) was almost 20 times higher than the national average.

In the same year, the Department of Communicable Diseases, in collaboration with the Medical Service Division of the Department of Corrections of the Ministry of the Interior, started a pilot DOTS programme for TB control in 11 prisons in Bangkok. Despite a high prevalence of TB/HIV coinfection among prisoners (65%), the programme worked well; so, it was used as a model for DOTS implementation in provincial prisons.

The programme involved 16 of the 125 provincial prisons of Thailand and was carried out by the Tuberculosis Division in collaboration with the Department of Corrections, the Regional Communicable Diseases Control Office and the Provincial Health Office.

Notwithstanding the strong commitment of institutions and of the involved staff, at the provincial level, the programme did not go as smoothly as in Bangkok. Two major problems were identified:

1. Difficulty in carrying out sputum examination in prisons where no TB Zonal centre existed, or where they were too far from microscopy centre, or when provincial hospitals were unable to handle the extra-load of sputum samples sent from prisons.

2. After release of patients from prisons before end of treatment, they were virtually all lost at follow up and did not continue their treatment.

Subsequently, improvements in sputum examination (e.g. establishing microscopy centres in prisons) and in patient referral to provincial hospitals after release were planned.

This is an example of how many institutions of the same country may cooperate in implementing TB control in one of the most difficult settings: prisons. It is to be underlined how they achieved these results: they started with a pilot project to evaluate feasibility, then a progressive implementation with the necessary adjustments due to the met difficulties followed.

The study presents a very special situation occurring in a Siberian (Russia) prison; results from this experience highlight the necessity of a deep involvement of the entire prison system of a country in order to guarantee countrywide success of the DOTS strategy.

Colony 33 (a TB referral prison in central Siberia) has 750 beds and over 1 300 patients, and it has being supported by MSF (Médecins Sans Frontière) since 1995. WHO-DOTS programme has been implemented in the Colony. The majority (79%) of prisoners transferred to Colony 33 has already received prior non-standardized Russian-based therapy with one to four anti-TB drugs given for intermittent periods of time. Due to this situation, MSF/Colony 33 medical policy is to start all newly admitted patients on WHO Category 2 therapy (2EHRZS/1EHRZ/5HER) under a strict system of direct observation using only imported medicines (to guarantee quality and constant availability).

Notwithstanding this aggressive policy, treatment outcomes for 210 initially smear-positive patients treated with Category 2 therapy (June 1996 - March 1997) were: cured 46%, completed treatment 6%, treatment failure 35%, death 4%, transfer out 6%, default 0%. Non-compliance and drug quality could not be blamed for these poor results.

Subsequently (December 1997-March 1998), drug susceptibility testing was performed for new DOTS patients to evaluate the level of initial resistance as a possible explanation for poor treatment outcome. The finding for 164 consecutive patients showed an initial resistance rate for isoniazid of 66% and an initial MDR rate (H + R) of 22.6%. Only 25% of patients were sensitive to all drugs tested.

These results proved that even WHO Category 2 regimen could be inadequate for this population. This created an immediate problem to properly treat these patients with expensive second-line anti-TB drugs in order to cure them and to prevent diffusion of MDR strains in the community after release of patients from prison.
The second issue is the urgent need to prevent new prisoners being poorly treated in the prison system. This underlines the need to expand DOTS to the very periphery of the incarceration system, especially given the length of time detainees spend in jails where TB exposure is high. It will be also important to create liaisons with DOTS treatment centres outside the prison system together with a systematic referral system in order to prevent interruption of treatment by released prisoners.


Results from a survey on the status of TB control in prison systems of a few countries of the Asia-Pacific Region are presented. A questionnaire was administered to the Ministries of Health of all 26 countries of Western Pacific Region (WPR) of WHO; only 15 of them (57%) returned the questionnaire. Unfortunately, answers were from five medium-size countries and 10 from small-size countries, so accounting for only 4% of the population of the Region.

The results are nevertheless important, as this was the first attempt to assess health care services within prison systems as they relate to tuberculosis control.

Among the various findings, it was reported that in 13 (86%) countries prison health services notified TB cases to national authorities and only 4 of 9 responders stated they followed the national guidelines for TB control. However, only 2/15 countries had a specific section on TB control in prisons in their national guidelines.

In 92% of cases, treatment regimens were consistent with those used by the NTP. Anti-TB treatment was always directly observed for its entire duration in 11 countries.

Released prisoners were transferred to the NTP to complete their treatment in 10 countries.

In conclusion, results from this survey are encouraging, because in many countries TB control in prisons was linked to the NTP, although better coordination is still necessary. In particular, systematic referral of released prisoners to NTP services for treatment completion has to be improved.
9. **TUBERCULOSIS CONTROL IN CONFLICT SITUATIONS**


The author presents his own experience of support of a TB control project in Malange (Angola) as an MSF (Médecins Sans Frontière). In September 1998 the town of Malange (420 000 inhabitants, including refugees) was quiet, although surrounded by minefields and with many difficulties in access to supplies and food.

The tuberculosis situation was alarming and the Government-run control programme was functioning imperfectly. Laboratory examination of sputum was not anymore routinely performed. Patients came to hospital to pick their treatment once a fortnight during intensive phase and once a month during the continuation phase, and sometimes they had to buy rifampicin in local market due to shortage; patients were often not recorded. Moreover, at least 50% of the 500 patients registered in hospital in 1997 were recorded as defaulters; only 4% of patients were recorded as having completed treatment.

So, the new programme focused on implementing laboratory facilities (and training of technicians), on prevention of defaulting (weekly education sessions and early tracing of defaulters) and on strict DOT. Motivation of both staff and patients gave surprisingly good results.

Unfortunately, after five months, the programme had to be interrupted because open war broke out and evacuation of expatriates became inevitable.

However, although in a situation of uncertainty positive results were achieved. Reduction of defaulting and high commitment of patients (till final deterioration of war situation, they kept coming to take treatment in between the bombardments) were obtained. Nearly 90% of the first cohort 95 patients (one third of whom were refugees) managed to complete the first phase of treatment; only four patients defaulted. Of the original sputum positive patients, 91% were sputum negative at the end of the initial phase.

In conclusion, the implementation of TB programmes with fairly good results can be obtained also in countries where war or civil unrest are present, although many difficulties have to be faced and resolved.

The study compared treatment results before and after introduction of short-course (SC) tuberculosis chemotherapy in Nicaragua and tried to identify factors affecting the same results. In 1984, an eight-month chemotherapy regimen for smear-positive pulmonary TB was introduced in Nicaragua.

The authors performed a retrospective record review to compare treatment results before and after introduction of SC chemotherapy. They also collected information on support services and programme administration, availability of hospital beds for tuberculosis patients, access to health services and the economic and war situation in the two periods. The overall success rate improved by 39% after the introduction and the implementation of SC chemotherapy, in spite of evidence of a deteriorating economy and escalation in civil war. A success ratio of 71% was achieved, so the authors estimated that between 80 and 90% of registered cases stopped transmitting TB. As it could be expected, the best results were obtained in the treatment of previously untreated patients with eight-month chemotherapy and in retreatment of relapses. The worst results were obtained in retreatment of defaulters.

The analysis of the findings by region suggested that SC chemotherapy was important, but not enough by itself to guarantee success. Other factors likely influenced treatment results: commitment by health authorities in guaranteeing personnel and hospital beds, training of personnel, and supervision of service delivery.

In conclusion, the introduction of SC chemotherapy achieved good results in TB control in spite of poverty and war. Government commitment and simultaneous improvement in supportive services and programme management are important and crucial aspects to be considered when introducing SC chemotherapy in low-income countries.

The study tried to determine the effect of irregular TB treatment due to an armed conflict in Guinea-Bissau, West Africa. In June 1998, a civil war broke out in Guinea-Bissau. The capital city, Bissau, was the main fighting zone with a large part of inhabitants fleeing. With the breakdown of the health care system, patients in treatment for TB were forced to abandon medication at least temporarily. A TB surveillance system was in place since 1996 in four suburban areas of Bissau.

The authors conducted a retrospective cohort analysis among 101 patients with TB who received irregular or no treatment during the civil war (war cohort [WC]; June -December 1998) and 108 patients with TB who received treatment 12 months earlier (peace cohort [PC]; June -December 1997). An additional comparison of 42 patients who had completed treatment before June 1998, and 69 patients who had completed treatment before June 1997 was performed. The study evaluated mortality rates, comparing by irregular (WC) vs. regular (PC) access to treatment, by intensive vs. continuation phase of treatment, and by those who had previously completed treatment for TB.

The results showed that irregular treatment was associated with an increased mortality rate. The mortality rate ratio (MR) was 3.12 (95% CI, 1.20-8.12) in the WC, adjusting for age, sex, HIV infection, residence and length of treatment. Each additional week of treatment before the war started increased probability of survival by 5% (95% CI, 0%-10%). In the intensive phase of treatment, the adjusted MR was 3.30 (95% CI, 1.04-10.50) and in the continuation phase it was 2.26 (95% CI, 0.33-15.34). Increased mortality among the WC was most marked in HIV-infected patients, who had an adjusted MR of 8.19 (95% CI, 1.62-41.25). Mortality was not increased in HIV-positive or HIV-negative patients who had completed TB treatment when the war started.

In conclusion, interruption of treatment had a profound impact on mortality among patients with TB during the war in Guinea-Bissau. Regular treatment for TB was associated with significantly improved survival for HIV-infected individuals. Therefore, in situations of emergency, e.g. during conflicts, it is extremely important to ensure availability of TB drugs.

During wartime, civilian populations usually experience a drop in caloric intake and starvation, disruption of housing, and a diminution in availability of medical services. This is what actually happened in El Salvador during its 1980-92 civil war, particularly among the 20% of the population (over one million) who were displaced ("desplazados").

A tuberculin survey among "desplazados" to estimate the annual risk of infection and the incidence of smear positive pulmonary TB prior to and during the war was done. The study was conducted in July 1992 in 12 repopulated communities in San Vincente, a rural province. This region has been a zone of conflict throughout the 12-year war; many communities had been abandoned and repopulated by returning refugees after the end of the war. A total of 1,001 persons were tested, but only 878 of them returned for reading. Overall, 21.2% of the non-BCG vaccinated had significant tuberculin reaction (≥ 10 mm), equivalent to an ARI of 2.3%. The trend in the ARI was upward in the latter six years, stable over the first 6 years, and was downward prior to the war years. The estimated incidence of smear positive TB among “desplazados” was 125 per 100,000 or three times the reported rate for El Salvador.

In conclusion, conditions of war are associated with a rapid increase in morbidity and mortality from TB, which appears to result in increased transmission among populations most severely affected by war. This increased transmission will result in an increased morbidity and mortality for many years, underscoring the need for improved TB control in the post-war period in countries that have been devastated by war, civil war included.


The study evaluated the modifications of the proportion of smear-positive TB cases in the Hospital of Kiremba, Burundi during the period 1992-1995. The hospital was located at 10 km from the Burundi-Rwanda border
and its patient population consisted of both rural and urban residents of Burundi and – since early 1994 – Rwandan refugees. The authors compared hospital admissions in two periods: 1992-1993 and 1994-1995. During observation time, total hospital admissions declined from 8,050 to 3,112, but sputum smear-positive (AFB +) pulmonary TB cases increased from 148 (1.8% of total hospital admissions) to 167 (5.4%) \( (p< 0.0001) \). The AFB positivity rates in tested patients were relatively stable during the first three years (7.1%, 8%, and 9.5%), but almost doubled in 1995 (16.9%). TB associated with HIV infection dropped from 20% of TB cases to 6%.

On the basis of the proportion of TB cases per total hospital admissions and on the AFB positivity rate in 1992-1993, the authors found 107 excess TB cases in the second biennium. Rwandan refugees significantly contributed to this excess: 58 cases (54.2%). However, 47 of the remaining excess cases were Burundian from a same rural area near the border. This area was crossed daily by refugees, but also by soldiers, so forcing inhabitants to stay out of their houses and far from their fields, causing under-nourishment and poor living conditions.

In conclusion, even in an area of Africa with high prevalence for HIV, new TB cases can dramatically increase not for HIV, but for an acute worsening of living conditions of population due to political instability and/or conflicts.
10. **TUBERCULOSIS IN REFUGEES**


The diagnosis and control of TB in refugee camps presents unique challenges because of their inherent instability, refugee mobility, overcrowding, poor socioeconomic conditions, and limited resources for food and medicines. Early detection and timely treatment of pulmonary TB cases (especially smear positive ones) will render them non-infectious, interrupting airborne transmission, and curtail spread of disease.

The study evaluated referral times of Vietnamese refugees with a confirmed diagnosis of TB from clinics in two stable refugee camps in Hong Kong in 1992. The referral time was defined as the number of days between the first referral date to the clinics in the refugee camps and the date of the first consultation at which TB was diagnosed. Three clinics (two run by NGOs and one by Government) serving about 15,000 refugees in the two camps were considered. The study evaluated 97 TB cases (64.7% with pulmonary TB); their median referral time was 18 days (range 0-417). No difference in referral time was observed comparing males and females or for the different clinical forms of TB. Thirty-nine (40%) patients were referred within 10 days; of these, 18 were referred the same day. Only 16 (16.5%) patients had a referral time longer than 90 days. The main difference between patients with early and late referral was that the latter group had been visited more often at the clinics in the camps before TB diagnosis.

In conclusion, median referral times appear “acceptable” (i.e. within one month), but worryingly some patients had long delays associated with multiple clinic consultations. So, as in “normal” settings, the physician’s delay in suspecting TB significantly delays proper treatment. The authors conclude that their findings support the use of a simple, but effective diagnostic strategy for early detection of TB cases in refugee camps, i.e. the use of the WHO case definition (a productive cough >3 weeks or haemoptysis, and significant weight loss).

The study evaluated the results of the TB control programme based in the Tibetan Delek Hospital (TDH) in Dharamsala, run for the Tibetan refugees living in Northern India. This programme was primarily based on passive case finding and sputum testing, serving both Tibetan refugee settlements and Indian communities.

The study reviewed the results of the programme in the period from 1985 to 1992, i.e. before introduction of the DOTS strategy. So, treatment was 12-month long and unsupervised.

The main differences identified for smear-positive pulmonary cases were a higher default rate (47.3% vs. 10.7%, for Indians and Tibetans respectively) and a lower cure rate (43.2% vs. 80.1%) for Indian patients (especially males).

Authors suggest that the reason for the better performance observed among Tibetan refugees could be due to the presence in their communities of Tibetan health workers, living close to patients, and being regularly supervised by staff of TDH. They supported patients and took necessary action if patients discontinued their treatment or missed coming for taking medicines at TDH.

In conclusion, these results support the feasibility of DOTS programmes in refugee camps, where community involvement for patients’ support and for monitoring can be more easily obtained.


The study evaluated the treatment outcome of sputum smear-positive tuberculosis cases recruited in refugee camps in Ngara district (Tanzania). Six camps for Rwandan and Burundian refugees were considered. Moreover, many refugees came from areas with a high HIV prevalence.
The study included patients treated between January 1995 and December 1999. The Tanzania NTLP (National TB/Leprosy Programme), in collaboration with health NGOs working in the camps, started a TB control programme following the Tanzania national guidelines. A nurse directly observed patients taking drugs throughout the course of treatment.

Of 546 patients with smear-positive tuberculosis who were notified in the programme, 363 (66.5%) had completed treatment and were bacteriologically cured after seven months, 10.9% had died (most of them within the first two months of treatment), 7.1% had defaulted and 14.5% had transferred out. Sputum conversion after the two-month intensive phase was 88%, and increased to 99% after seven months of chemotherapy.

In conclusion, these data suggest that it is possible for tuberculosis control programmes to perform successfully in refugee settings.


Croatia gave shelter to more than half a million displaced persons and refugees from Croatia and Bosnia-Herzegovina during the civil war. This study compared the incidence of pulmonary TB among displaced persons and residents attending a referral pulmonary diseases and TB hospital in Klenovnik in 1992.

During the observation period, 271 refugees were admitted to the hospital; 46.1% of them had a discharge diagnosis of pulmonary TB. In the same time, only 21.3% of the other 2503 patients admitted to the hospital had pulmonary TB.

TB is known to be associated with poor living conditions and these refugees and displaced persons experienced such poor conditions in the war zones before they were forced to leave their homes.

The authors conclude that doctors dealing with refugee problems should keep in mind the possibility of TB when taking care of these special populations.

The study aimed to evaluate the feasibility of TB treatment in refugee camps. In fact, tuberculosis control among displaced persons is fraught with difficulties to ensure adherence of patients to treatment for a prolonged period of time.

In the Khao-I-Dang camp (Thailand) for Cambodian refugees an approach with daily, directly observed treatment throughout the course of nine months duration was chosen to address the problem. In the period from April 1981 to December 1990, 2 039 patients were enrolled into the programme. Of them, 929 had sputum smear-positive tuberculosis. The programme showed the following results: 5% died, 75.5% completed treatment and were bacteriologically cured (71.7% within six months, 3.8% within nine months), none failed bacteriologically, 19.2% were transferred to another camp where continuation of treatment was guaranteed, and only 0.4% discontinued treatment. Day-to-day adherence was of more than 98%. The choice to give DOT helped also in preventing the sale of valuable drugs on the thriving markets.

In conclusion, TB control was feasible even in these conditions of poverty and of mobile population. The approach to TB control in this refugee camp was very effective in cutting the chain of transmission of tuberculosis in a highly mobile population and in reducing substantially unnecessary morbidity and mortality.
11. TUBERCULOSIS AND SOCIOECONOMIC IMPACT


The study objective was to determine direct and indirect costs for patients affected by tuberculosis. All adult tuberculosis patients who completed treatment between August 1996 and February 1997 at 16 randomly selected government health care facilities in Thailand were interviewed using a structured questionnaire (673 patients were interviewed).

Information was obtained on direct and indirect patient costs before and after diagnosis, and on financing methods and changes in household consumption patterns. All results were stratified for three levels of patient household income: above national average, below national average but above the poverty line, and below the poverty line.

Illness-related costs particularly affected patients with incomes below the poverty line (153 patients). In this group, average out-of-pocket expenditures for the disease amounted to more than 15% of annual household income, while incomes were reduced by 5% due to illness-related effects.

Expenditures were most frequently financed from household savings or transfer payments from community members and relatives. However, 11.8% of patient households took out bank loans, and 15.9% sold part of their property.

After diagnosis, more than 80% of all patients had out-of-pocket expenditure for travel to hospital and more than 35% had the same for food when going to hospital.

In conclusion, low case detection and treatment completion rates for tuberculosis patients may partly be due to the inability of poor patients to cope with the economic consequences of diagnosis and treatment. The authors suggest that the strict enforcement of an existing government policy of free care, further decentralization of services to reduce travel costs and work absences, and social security payments for patients undergoing treatment could improve the performance of the NTP.

and


The studies report an investigation performed at the Chest Clinic, Lusaka University Teaching Hospital, Zambia. The authors conducted in-depth interviews over a nine-week period with adult in-patients and outpatients registering with new pulmonary TB. Interviews were completed by 202 patients. Before the onset of the disease, 64% of them normally worked, but 31% stopped their work due to tuberculosis.

In seeking diagnosis, patients incurred a mean total cost equivalent to 127% of their mean monthly income (USD 59); direct expenditures represented 60% of this cost. In addition, patients lost, on average, 18 working days prior to diagnosis.

The median (mean) diagnostic delay was 8.6 (9) weeks, and was significantly associated with the following factors: female sex, lower education, more than six instances of health-seeking encounters, outpatient diagnosis of tuberculosis, and visiting a private doctor or traditional healer. Women were probably more vulnerable because of their heavy workload, combined with lack of mobility, independence and financial resources, and with fear of stigma.

In conclusion, the economic burden of tuberculosis on patients creates barriers to prompt diagnosis, especially for women. Important economic barriers include transportation expenditure, cost of 'special food', and lost income. These barriers may be reduced through interventions reducing the number of health encounters, travel distances and duration of illness before diagnosis. Decentralization of public TB care and improved integration with private sector health providers may also reduce diagnostic delay.

The study investigated the socioeconomic impact of TB on affected men and women, and on their families. The main objectives of the study were: 1) to assess the expenditure involved in TB diagnosis and treatment and its effects on patients' families; 2) to estimate the loss of income caused by the loss of working hours due to active disease and/or its sequelae. The investigation included 304 patients (184 males, 120 females) receiving treatment from private Practitioners (PVT) in Chennai city or attending government (GH) and NGO hospitals/clinics situated in Chennai city and two rural districts (Kancheepuram and Thiruvellore, Tamil Nadu State, South India).

Expenditure assessment included direct (DIR) and indirect (IND) costs. DIR: consultation fees and money spent on investigations and drugs (medical expenditure - ME); money spent on travel, lodging, special food and for persons accompanying the patients (non-medical expenditure - NME). IND: loss of wage and decreased earning ability due to illness, or long-term disability necessitating change of work were included.

The mean total DIR in the three different types of health facilities (GH, NGO, and PVT) was 38.5 USD, 48.5 USD and 253 USD, respectively. The mean DIR incurred by rural and urban patients were 38 USD and 79 USD, respectively. Overall average was 58.5 USD (ME: 34 USD and NME: 24.5 USD). IND were calculated only for the employed patients and were respectively 109 USD, 121 USD and 115.5 USD (overall average 112.5 USD). IND were nil in 46%, 54% and 52% of patients attending the three health facilities.

Total costs attributable to TB for GH, NGO and PVT patients were 147.5 USD, 169.5 USD and 368.5 USD, respectively. The average total cost was 171 USD.

Due to the high cost of being affected by TB, 67% of rural and 75% of urban patients borrowed money on account of the disease. The average debt incurred as a result of the disease was 40 USD for rural and 79 USD for urban patients.
The overall evaluation of direct, indirect and intangible costs shows that uncontrolled TB is a very important source of poverty and loss of development for affected people.

In conclusion, direct costs for TB care were very high in private sector, but also costs for patients attending government and NGO's services were not negligible. Cost assessment of TB should be performed in every country, to be used as an instrument to advocate for allocation of resources from Governments, NGO's and international organizations.


The study investigated the socioeconomic impact of parental pulmonary TB on children. The cohort examined is the same presented in Rajeswari R et al, in this same section. The main objective of the study were: 1) to assess the impact of social, economic and demographic factors of TB patients on their children; 2) to assess the impact of TB in women on child care functions; 3) to evaluate the impact of parental TB on children's education. In all, 276 children (aged 6-16 years) of 167 TB parents were studied.

Child caring on the part of mothers fell from 64% to 35% among rural females and from 74% to 33% in urban females. Moreover, 58% of TB mothers expressed inability to feed their children, to take care of their daily needs and their education.

The impact of parental disease on children caused discontinuation of school for 11% of them (8% rural, 13% urban). Furthermore, 8% of the children took up employment to support the family. In 34% of cases, parents could not buy adequate food or clothing or books for their children because of the loss of income due to TB.

In conclusion, TB in mothers affected the entire household (and especially children) because of loss of their earnings outside the household and because of the reduced routine household activities.

This study is a simulated estimate of the socioeconomic impact of tuberculosis on the household of a rickshaw puller living in Chittagong, Bangladesh.

It is known that illness reduces the earning capacity and increases the risk of families with ill members to drift down the social and economic ladder. This is especially true in the case of illness affecting the person with the highest or only income of the household. In this study, the authors present a simulation model of how a poor rickshaw puller in Bangladesh copes with TB.

They first analyzed the various coping mechanisms that are set in motion when the patient starts to suffer from tuberculosis; then, the impact on household assets, income and food intake were also evaluated. The simulation model was then used to analyze the effects on puller’s household of a specific health intervention, namely the Directly Observed Treatment Short Course (DOTS). They tested three different models of DOTS strategy in which the patient is asked a financial contribution, no money at all or simply a deposit for the duration of the treatment.

It is evident from the model that DOTS (all strategies) offers positive improvements of the overall well-being of the household by restoring the working capacity of the rickshaw puller in one treatment course and minimizing loss of income. Assets and food consumption would be preserved significantly more in the presence of DOTS, rendering the household both financially and physically less vulnerable. The probability of death of the sick rickshaw puller is also significantly reduced, improving the household’s welfare over the long run.
12. FIXED DOSE COMBINATIONS (FDCs) FOR TUBERCULOSIS CONTROL


This is a review aimed to support the use of fixed-dose combinations (FDCs) of anti-TB drugs.

Major advantages of FDCs are the simplified treatment and drug management, and the reduced probability of monotherapy. Actually, using FDCs, the number of tablets to be taken daily can be reduced to as few as three or four for the whole course of treatment from the 9-16 (intensive phase of treatment) or 3-9 (continuation phase) tablets when using single-drug formulations.

Use of FDCs may improve the patient’s compliance with treatment (reduced number of tablets) and limit prescription mistakes by simplifying the calculation of dosages.

Using FDCs requires fewer drug formulations, thus making it easier to calculate the drug needs. Since fewer drug formulations are needed, orders, shipments and distribution are simplified, and the efficiency of the TB drug supply system is improved.

The recommended strength of FDC formulations of essential anti-TB drugs has been clearly identified and a weight-related dosage schedule for all treatment phases and for both adults and children has been prepared.

However, a critical issue about FDCs is their quality, and especially the bioavailability of its components, rifampicin in particular. If adequate quality standards are not achieved, the use of FDCs could increase rather than decrease the rate of rifampicin resistance among TB patients. When buying FDCs from manufactures, quality assurance procedures should be put in place to buy only good-quality FDCs.

Other inconveniences are the increased size of tablets (improvements in pharmaceutical technology could help), the higher price in comparison to the sum of the individual single-drug tablets (a decrease is foreseen when there will be a higher demand in the markets) and the necessity to keep limited stocks of single-drug tablets for the treatment of patients experiencing adverse events.

This is a review of the advantages in employing fixed-dose combinations (FDCs) of anti-TB drugs; it also identifies the necessary institutional passages necessary to fully implement to use of FDCs in national TB programmes.

The essential advantage of FDCs is:
- Prevention of monotherapy and selection of bacilli strains resistant to isoniazid/rifampicin.

Other operational advantages are:
- Prevention of mistakes in drug prescription and drug dosage
- Simplified/standardized chemotherapy regimens
- Facilitated health education and compliance of patients
- Improved acceptance by patients and health workers
- Prevention of shortages of individual drug supplies
- Improved drug handling and delivery
- Facilitated quantification of needs for programme managers

However, national regulations should recommend stocking small quantities of separate formulations only in medical institutions that are capable of managing individual cases of drug intolerance and toxicity.

The review identifies also the responsibilities of the following “players” for the implementation of quality FDCs anti-TB drugs:
- International players: WHO; producers and suppliers of anti-TB drugs; aid development institutions
- National players: the NTP manager; the National TB Advisory Committee; the National Drugs and Therapeutics Committee; the National Drug Regulatory Authority; the Procurement Office; the Legislative Office; the Financing Office; the office responsible for inspection of stocks and distribution; the Pharmacovigilance Network.

Fixed-dose combinations (FDCs) of anti-TB drugs have been used for years, although they always represented a fraction of the total used antitubercular drugs. Since 1998, WHO and IUATLD started to promote the use of FDC tablets for first-line treatment of TB in all TB programmes.

A few advantages justify the promotion of FDCs: simplicity of treatment, decrease in prescription and administration errors, improved compliance, simplification of drug management.

On the opposite side, there are a few problems: bioavailability of rifampicin is affected in combination tablets, a reserve of single-drug forms should remain available for patients who experience drug reactions and have to replace FDCs.

The authors review the advantages and constraints of FDCs use in national TB programmes and underline that FDCs should not be seen as an alternative to the DOTS strategy, but, rather, as a major benefit for these programmes.