

**Strategies for Tuberculosis Control from Experiences in Manila:  
The Role of Public-Private Collaboration and of Intermittent Therapy**

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Prof. Dr. Marcel Tanner

Dekan

## DEDICATION

*In memory of Aling Tess and Mang Tony, former neighbours of mine,  
victims of tuberculosis,  
the unrestrained killer that terminates daily the lives of 5000 people.*

*With the sincere hope and plea that  
some findings and thoughts of this dissertation  
will contribute to  
reducing tuberculosis and poverty.*

“The appalling global burden of tuberculosis at the turn of the millennium, despite the availability of effective control measures, is a blot on the conscience of humankind. For developing countries, the situation has become desperate and the "cursed duet" of tuberculosis and AIDS is having a devastating impact on large sections of the global community. The vital question is, can despair be turned to hope early in the next millennium?”

John Grange and Almuddin Zumla, 1999



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## **SUMMARY**

It is estimated that 8.5 million new tuberculosis cases occurred in the year 2001 and that 1.8 million people died of TB. Operational research to improve the use of existing tools is vital. Studies in Manila, Philippines were carried out to examine TB illness experience and help seeking of TB patients. Apart from patient interviews, focus group discussions with non-affected urban poor residents and group discussions with public health care providers were carried out. The TB illness burden was found to be substantial; ill-defined suffering, such as emotional and social distress as well as social stigma, was common. Non-affected urban poor residents expressed ambivalence towards TB patients: fear of getting infected contrasted with feelings of concern and support. Interaction with the health care providers was found to be problematic. Misconceptions have the potential to increase the burden of TB. Giving health information, interpersonal skills and other aspects of clinical care need to be improved.

The patient interviews also inquired about case finding. Only 29% of the respondents had gone first to a health centre after onset of TB-related symptoms, and 53% had initially consulted a private doctor. Two-thirds of the patients (66%) had received a prescription for drugs, and 29% had purchased and taken anti-TB drugs for at least three weeks before they came to a public health centre. The health seeking delay after symptom onset was relatively short – 64% of the respondents said they went to a health facility within one month.

With these findings as a background, we examined the TB-related practices of the private practitioners and approaches to public-private collaboration and assessed the feasibility, acceptability and effectiveness of thrice-weekly therapy in comparison to daily therapy. Forty-five private practitioners of Malabon who treat adult TB

## *Summary*

patients were interviewed in their clinics. For diagnosis, most private practitioners relied on clinical presentation and result of an X-ray and 96% used X-ray as a tool to monitor treatment. Sixty percent of the respondents prescribed in accordance to international guidelines a regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol. However, over-dosage was common and length of treatment not always correct. For re-treatment cases, none prescribed the recommended re-treatment regimen. The private practitioners perceived the main reasons for patient non-adherence to be the patients' lack of finances to buy drugs and patients' perceived well-being after a certain period of treatment. Patients' lack of money was seen as the main obstacle to treatment adherence. The only case holding mechanism mentioned was occasional visits of the TB patients to the clinic. Our findings of the private practitioner's unsatisfactory quality of care and of the limitations of the public sector indicate the need for collaboration between public and private sectors. The private practitioners were therefore asked about their felt needs for additional knowledge on clinical management of tuberculosis and their views on the public TB programme and collaboration with the public health sector. And discussions with personnel of the public health centres inquired about collaboration with private practitioners. The private practitioners' most frequently mentioned needs for updated clinical knowledge were about appropriate use of sputum microscopy, how to tell patients that household contacts need a check-up, and motivating the patients to adhere to treatment. There was considerable interest to receive and follow the national TB guidelines. The main perceived problems they identified with the public TB programme were insufficient drug supply, poor quality of the TB drugs, and lack of health education. Two suggestions on how to establish public-private collaboration (mandatory referral of poor TB patients to the public TB programme and allowing private practitioners to use the governmental TB drugs) were generally welcome, but they expressed reservation concerning feasibility of the latter suggestion. The personnel of the public

### *Summary*

health centres were positive about mandatory referral of poor TB patients to the public TB programme but sceptical about allowing private practitioners to use the governmental TB drugs. Our findings suggest steps to facilitate public-private collaboration. The public programme needs to be strengthened and collaboration prioritised. Public-private collaboration has great potential to make TB care that is based on the principles of DOTS, the internationally recommended treatment strategy, accessible to more people with TB.

While our studies on the private practitioners and public-private collaboration aimed to see DOTS being used more widely, the randomised controlled trial that compared thrice weekly with daily therapy aimed to make the main tool of DOTS, namely short-course chemotherapy, more efficient and patient- as well as provider-friendly. Intermittent regimens (twice weekly and thrice weekly regimens) are recommended, but the evidence base regarding their effectiveness in comparison to daily therapy is not very strong. We carried out a randomised controlled trial: thrice-weekly therapy was randomly assigned to 10 of the 20 health centres of a municipality in Manila. All TB patients of the other 10 health centres received daily therapy. Patients were interviewed three times. Drug susceptibility tests were performed. A total of 806 patients (451 under thrice-weekly and 355 under daily therapy) were interviewed shortly after treatment start. 18.5% were re-treatment cases. Multidrug-resistant TB was found among 2% of the new and 26% of the previously treated patients. Under thrice-weekly therapy, directly observed therapy in the health centres was more common than when treatment was daily. Thrice-weekly therapy was more popular among patients and health personnel and resulted in savings of about 40% of the cost of drugs. There were also some disadvantages of thrice-weekly therapy compared to daily therapy: gastro-intestinal disturbances were reported more frequently. And sputum conversion rate assessed after two months of

### *Summary*

treatment was lower (74% vs. 81%;  $p = 0.03$ ). Treatment outcome was similar, but treatment failure and default due to side effects was more common among those treated thrice weekly ( $p = 0.08$  and  $p = 0.04$ , respectively). In a multivariate model, adverse treatment outcome (failure and relapse) was not associated with mode of treatment ( $p = 0.7$ ). In the light of the potential benefits of intermittent therapy, its equivalence to daily therapy should be established more firmly and if confirmed, fully thrice-weekly therapy should be used more widely.

Our research indicated approaches of how to improve TB control in terms of more appropriate practices in the private sector, better access to proper TB care, and more efficient and patient-friendly use of treatment. Resources and commitment for further operational research and for pilot projects are needed to further test and implement outlined approaches to public-private collaboration and to clarify the role of intermittent therapy.

## **ZUSAMMENFASSUNG**

Es wird geschätzt, daß im Jahr 2001 rund 8,5 Millionen neue Tuberkulosefälle aufgetreten und 1,8 Million Leute an Tuberkulose (TB) gestorben sind. Angewandte Forschung, die das Ziel hat, den Einsatz der bestehenden Instrumente zu verbessern, ist sehr wichtig. In Manila, Philippinen wurden Studien durchgeführt, um TB-Krankheitserfahrungen (‘TB illness burden’) und das Suchen nach Gesundheitsdienstleistung (‘help seeking’) von TB Patienten zu erfassen. Abgesehen von einer Befragung von TB Patienten wurden ‚Focus Group Discussions’ mit nicht-erkrankten städtischen armen Bewohnern und Gruppendiskussionen mit öffentlichen Gesundheitsversorgern durchgeführt. Es wurde gefunden, daß die TB-Krankheitsbelastung erheblich ist. Schwer zu definierendes Leiden, wie emotionale und soziale Not und soziales Stigma, war verbreitet. Nicht-erkrankte städtische arme Bewohner drückten Ambivalenz gegenüber TB-Patienten aus: Furcht vor dem infiziert Werden stand im Kontrast zu Gefühlen der Anteilnahme und Hilfsbereitschaft. Die Interaktion mit den Versorgern des Gesundheitsdienstes wurde als problematisch empfunden. Mißverständnisse haben das Potential, die TB-Krankheitsbelastung zu erhöhen. Das Vermitteln von Gesundheitsinformationen, Kompetenz im Umgang mit Patienten und andere Aspekte der klinischen Versorgung müssen verbessert werden.

Die Patienteninterviews untersuchten auch den Prozess der Identifizierung der Krankheit (‘case finding’). Nur 29% der Antwortenden waren nach dem Ausbruch von Symptomen, die mit TB in Verbindung standen, zuerst zu einem öffentlichen Gesundheitszentrum gegangen und 53% hatten zuerst einen Arzt im privaten Sektor aufgesucht. Zweidrittel der Patienten (66%) hatten eine Verordnung für Medikamente und 29% hatten TB-Medikamente für mindestens drei Wochen eingenommen, bevor sie zu einem öffentlichen Gesundheitszentrum gingen. Die Verzögerung der Suche nach Gesundheitsdienstleistung (‘help seeking delay’) war eher gering; 64% der Antwortenden sagten, daß sie innerhalb eines Monats zu einer Gesundheitseinrichtung gegangen waren.

## *Zusammenfassung*

Mit diesen Befunden als Hintergrund untersuchten wir sich auf TB beziehende Handhabungen der Ärzte im privaten Sektor und Ansätze zur Zusammenarbeit des öffentlichen und privaten Sektors ('public-private collaboration'). Wir untersuchten auch die Machbarkeit, Akzeptanz und Wirksamkeit der dreimal-wöchentlichen Therapie im Vergleich zur täglichen Therapie. In Malabon befragten wir 45 Ärzte des privaten Sektors, die erwachsene TB-Patienten behandeln, in ihren Kliniken. Für die Diagnose verliessen sich die meisten Ärzte des privaten Sektors auf die klinische Erscheinung und auf das Resultat einer Röntgenschirmbilduntersuchung; 96% benutzten Letzteres, um die Behandlung zu überwachen. Sechzig Prozent der Antwortenden verschrieben in Übereinstimmung mit den internationalen Richtlinien eine Behandlung, die aus Isoniazid, Rifampicin, Pyrazinamide und Ethambutol bestand. Jedoch war Überdosierung verbreitet und die Länge der Behandlung nicht immer korrekt. Für schon zuvor behandelte Fälle verschrieb niemand die empfohlene Wiederholungs-Therapie. Die Ärzte im privaten Sektor empfanden, daß die Hauptgründe für die Nichtbefolgung der Therapie von Seiten der Patienten der Mangel an Geld für das Kaufen der Medikamente und die von den Patienten empfundene Gesundung nach einer Weile der Behandlung sind. Der Geldmangel der Patienten wurde als das Haupthindernis zur Befolgung der Therapie gesehen. Die einzige Massnahme, die Therapietreue zu fördern, bestand darin, den TB Patienten von Zeit zu Zeit in die Klinik zu bitten. Unsere Befunde, daß die Dienstleistung der Ärzte im privaten Sektor von unbefriedigender Qualität war und daß der öffentliche Sektor an Grenzen stiess, deuten auf die Notwendigkeit der Zusammenarbeit zwischen dem öffentlichen und dem privaten Sektor. Die Ärzte im privaten Sektor wurden folglich gefragt, welches ihre Bedürfnisse nach zusätzlichen Wissen betreffend klinischer Handhabung der Tuberkulose waren und was ihre Ansichten über das öffentliche TB Programm und die Zusammenarbeit mit dem öffentlichen Sektor des Gesundheitswesens waren. Und Diskussionen mit dem Personal der öffentlichen Gesundheitszentren erörterten die Zusammenarbeit mit den Ärzten des privaten Sektors. Passender Gebrauch von Sputummikroskopie, wie man Patienten erklärt, daß Haushaltkontakte eine Gesundheitsüberprüfung benötigen und das Motivieren von Patienten, die Therapie korrekt zu befolgen, wurden am häufigsten erwähnt in Bezug auf Bedürfnisse nach zusätzlichem klinischen Wissen. Es gab beträchtliches Interesse, die nationalen TB-Richtlinien zu erhalten und zu befolgen. Als Hauptprobleme des öffentlichen TB-

## *Zusammenfassung*

Programms wurden unzulängliche Versorgung mit TB-Medikamenten, unbefriedigende Qualität der TB-Medikamenten und Mangel an Gesundheitsausbildung („health education“) erwähnt. Zwei Vorschläge, wie man Zusammenarbeit zwischen dem öffentlichen und dem privaten Sektor erreichen könnte (obligatorisches Weiterleiten von armen TB-Patienten an das öffentliche TB-Programm und den Ärzten des privaten Sektors erlauben, TB-Medikamente der Regierung zu verwenden) waren im Allgemeinen willkommen, aber Vorbehalte hinsichtlich der Machbarkeit des zweiten Vorschlages wurden formuliert. Das Personal der öffentlichen Gesundheitszentren war positiv eingestellt gegenüber obligatorischem Weiterleiten von armen TB-Patienten an das öffentliche TB-Programm, aber skeptisch gegenüber dem Vorschlag, den Ärzten des privaten Sektors die Verwendung von TB-Medikamenten der Regierung zu erlauben. Unsere Befunde führen zu Vorschlägen, wie Zusammenarbeit zwischen dem öffentlichen und dem privaten Sektor gefördert werden kann. Das öffentliche TB-Programm muß gestärkt und die Zusammenarbeit eine Priorität werden. Die Zusammenarbeit zwischen dem öffentlichen und dem privaten Sektor hat grosses Potential, die Behandlung von TB, welche auf den Grundsätzen von DOTS (der international empfohlenen Behandlungsstrategie) beruht, mehr Patienten zugänglich zu machen.

Während unsere Untersuchungen über die Ärzte des privaten Sektors und über eine Zusammenarbeit zwischen dem öffentlichen und dem privaten Sektor zum Ziel hatte, DOTS zu umfassenderer Anwendung zu bringen, hatte die randomisierte kontrollierte Studie zum Ziel, einen Bestandteil von DOTS, nämlich die 6-bis 8-Monate dauernde Chemotherapie, effizienter und gebrauchsfreundlicher (sowohl für Patienten als auch für das Gesundheitspersonal) zu machen. Die Studie verglich ein Behandlungsschema, bei der die Medikamenteneinnahme nur dreimal pro Woche stattfindet („thrice-weekly therapy“) mit täglicher Behandlung („daily therapy“). Nicht-tägliche Behandlungsschemen („intermittent therapy“), sei es zweimal oder dreimal pro Woche, werden empfohlen, aber die vorhandene Evidenz betreffend ihrer Wirksamkeit im Vergleich zu täglicher Medikamenteneinnahme ist nicht sehr robust. Wir führten eine randomisierte kontrollierte Studie durch: dreimal-wöchentliche Therapie („thrice-weekly therapy“) wurde nach dem Zufallsprinzip 10 der 20 Gesundheitszentren eines Stadtbezirkes in Manila zugewiesen. Alle TB-Patienten der anderen 10

## *Zusammenfassung*

Gesundheitszentren empfangen tägliche Therapie. Die Patienten wurden dreimal interviewt. Die TB Bazillen in den Sputa wurden in Bezug auf Medikamentenresistenz getestet. Insgesamt wurden 806 Patienten (451 unter dreimal-wöchentlicher Therapie und 355 unter täglicher Therapie) kurz nach dem Beginn der Behandlung interviewt. 18,5% waren schon früher mindestens einmal wegen TB behandelt worden. Zwei Prozent der Patienten, die erstmals TB hatten, und 26% der schon zuvor behandelten Patienten hatten TB Bazillen, die zumindest gegen Isoniazid und Rifampicin resistent waren („multidrug-resistent TB“). Mit dreimal-wöchentlicher Therapie war in den Gesundheitszentren durchgeführtes Beobachten der Medikamenteneinnahme häufiger als mit täglicher Therapie. Dreimal-wöchentliche Therapie war unter Patienten und dem medizinischen Personal populärer und ergab Einsparungen von ungefähr 40% der Medikamentenausgaben. Es gab auch einige Nachteile der dreimal-wöchentlichen Therapie verglichen mit täglicher Therapie: gastro-intestinale Störungen wurden häufiger gemeldet. Und nach zwei Monaten der Behandlung war ein Sputum, in dem sich noch immer TB-Bazillen mit dem Lichtmikroskop finden liessen, häufiger (26% im Vergleich zu 19%;  $p = 0.03$ ). Der Ausgang der Behandlung war ähnlich, aber erfolglose Behandlung und das Abbrechen der Therapie wegen Nebenwirkungen waren häufiger mit der dreimal-wöchentlichen Therapie ( $p = 0,08$  und  $p = 0,04$ , beziehungsweise). In einem multivariaten Modell war ein nachteiliger Ausgang der Behandlung (erfolglose Behandlung und Rückfall) nicht mit dem Modus der Behandlung assoziiert ( $p = 0,7$ ). Angesichts der potenziellen Vorteile der nicht-täglichen Behandlungsschemen sollte seine Gleichwertigkeit zur täglichen Therapie eingehender untersucht werden und (falls die Gleichwertigkeit bestätigt ist) durchgehend dreimal-wöchentliche Therapie verbreiteter eingesetzt werden.

Unsere Forschung wies auf Strategien für eine bessere Bekämpfung der TB auf drei Ebenen hin: Bessere Handhabungen im privaten Sektor, besserer Zugang zu korrekter Behandlung der TB und effizienterer und patientenfreundlicherer Gebrauch der Medikamente. Mittel und echter Einsatz für weitere angewandte Forschung und für Pioniersprojekte sind nötig, um die erwähnten Strategien für eine Zusammenarbeit zwischen dem öffentlichen und dem privaten Sektor weiter zu testen und einzusetzen und um die Rolle der nicht-täglichen Behandlungsschemen zu klären.



## *Abbreviations*

### **ABBREVIATIONS**

AFB	Acid-fast bacilli
AIDS	Acquired immunodeficiency syndrome
BCG	Bacille Calmette-Guérin
DOT	Directly observed therapy (close supervision of drug intake)
DOTS	DOTS is WHO-backed, broadly promoted strategy to control TB. It has five key elements.
E	Ethambutol
FGDs	Focus group discussions
g	gram
GDF	Global TB Drug Facility
H	Isoniazid
HC	Health centre
HIV	Human immunodeficiency virus
IUATLD	International Union Against Tuberculosis and Lung Disease
MDR-TB	Multidrug-resistant TB
M	Million
mg	milligram
NGO	Non-governmental organisation
NTP	National tuberculosis control programme
P	Pyrazinamide
PAS	Para-aminosalicylic acid
PZA	Pyrazinamide
R	Rifampicin
S	Streptomycin

*Abbreviations*

sm+	Sputum smear-positive
TB	Tuberculosis
TDR	UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases
UNDP	United Nations Development Programme
WHO	World Health Organization

***PART I: Introduction and overview***

**Motivation for the thesis and overview**

**The burden of tuberculosis**

**The control of tuberculosis in the world**

**Tuberculosis and its control in the Philippines**

**Goal and objectives of the dissertation**

**Study areas and data collection methods**



## **CHAPTER 1: BACKGROUND**

### **1.1. Motivation for the thesis and overview**

In 1997 and 1998 operational research on tuberculosis (TB) control was carried out in Malabon and to a lesser degree also in Navotas, two municipalities of Metro Manila, Philippines. The main components were:

1. An evaluation of the public TB programme of Malabon. This included questionnaires for health centre staff and community health volunteers. Countless encounters with people responsible for TB control (the range was from the municipal TB co-ordinator to the community health volunteers) were part of this evaluation.
2. Extensive patient interviews (319 patients were interviewed) that covered topics such as health seeking behaviour, treatment adherence (Auer, 1998), the socio-emotional burden of having TB, and stigma.
3. Focus group discussions with poor urban residents. Chapters 4 and 5 presents parts of the findings from the health provider questionnaires, the patient interviews, and the focus group discussions.
4. Record reviews and interviews with public health providers and with TB patients from Malabon and from Navotas regarding DOT (directly observed therapy).

Three findings became important for the development of further research:

One, as presented in Chapter 5, it was found that more than half of the TB patients being treated in the public health centres had made use of private practitioners (66% had received a prescription for drugs, and 29% had purchased and taken anti-TB drugs for at least three weeks before they came to a public health centre).

Two, availability of TB drugs in the health centres was not always guaranteed.

Three, proper DOT (daily supervision of drug intake) was hard to implement. The burden for the patients and/or for the health providers could be substantial.

Also, a review of the international literature made clear that intermittent therapy (thrice-weekly or twice-weekly intake of drugs) resulted in reduced costs for buying drugs and suggested that it was effective, facilitating treatment supervision, and of advantage to patients and providers.

This led to the conviction that the two following approaches have considerable potential to improve TB control and TB care:

- One, collaboration between the private practitioners and the public health providers would significantly reduce the burden of having TB, mainly by simplifying the health seeking process and by making proper treatment more likely.
- Two, intermittent therapy would enable the government to treat more TB patients with the same amount of money earmarked for TB drugs, would facilitate proper implementation of DOT and would reduce the burden of treatment, especially DOT, for patients and providers.

## *Chapter 1: Background*

Thus, further research in Manila was carried out as a PhD project. The main goal of the project is to contribute to the development of more effective strategies for TB Control. One part of the research project looks at the TB-related practices of the private practitioners of Malabon and at approaches to public-private collaboration. The other part compares thrice-weekly with daily therapy in the public health centres of Taguig, another municipality of Metro Manila.

While the two parts do not have obvious links apart from their common goal to find a more effective and efficient approach to TB control, it can be argued that the second part facilitates the goal of the first part, namely public-private collaboration. If the public health providers use a more efficient and more attractive treatment approach (and the hypothesis is that intermittent therapy is more efficient and patient- as well as provider-friendly) then collaboration with the private practitioners, for instance timely referral of private patients with limited financial resources to the health centres, is more likely. The better the public TB programme works, the more willing people with TB are to get treated in public health clinics and the easier facilitation of public-private collaboration is.

After first giving an overview of the burden of tuberculosis in the world, and outlining as well as critically discussing the internationally recommended treatment approach, this thesis then reports some of the findings of the work of 1997 and 1998 (Chapters 4 and 5) that help to understand the TB patient. This understanding lays a ground for aspiring to improve TB control. The findings of the two tested strategies to improve TB control are then presented. First the findings regarding public-private collaboration and then the findings from the randomised controlled trial that compares thrice-weekly with daily therapy in the public health centres of Taguig.

## **1.2. The burden of tuberculosis**

### **1.2.1. Public health indicators**

*"The conquest of the 'Great White Plague', undreamt of less than ten years ago,  
is now virtually within sight."*

and

*"... the ancient foe of man, known as consumption, the great white plague, tuberculosis,  
or by whatever other name, is on the way to being reduced to a minor ailment of man.  
The future appears bright indeed, and the complete eradication of the disease is in sight."*

Selman A. Waksman, co-discoverer of streptomycin, in his Nobel Lecture 1952  
and in his book of 1966 "The Conquest of Tuberculosis" (Waksman, 1952 and 1966)

*"Tuberculosis currently kills three million people a year. Unless immediate action is  
taken it will claim more than 30 million lives during the coming decade. The disease is  
out of control in many parts of the world."*

Hiroshi Nakajima in 1993, then the Director-General of the WHO (Nakajima, 1993)

\* \* \*

In the nineteenth century, TB was responsible for nearly one in ten deaths in Europe (Preston *et al.*, 1972, cited in Murray *et al.*, 1990). Another estimate is that in the middle of the nineteenth century, TB accounted for 15-20% of all deaths in industrialised countries. In many countries of the South, particularly in sub-Saharan Africa, TB had not yet spread widely and was mostly confined to urban areas. It is further estimated that in



the mid-1800's, TB killed 1.9 million people per year, more than half of these deaths occurring in Europe and North America (Dubos & Dubos, 1952, cited in Kochi, 1994).

Over the next 150 years, the TB mortality rate in Europe, North America and Oceania declined from more than 300 per 100,000 to 1-2 per 100,000 and the absolute number of people dying of TB declined from more than one million to less than 50,000 in spite of a more than tripling of the population. In the countries of the South, the death rate declined from more than 100 to less than 50 per 100,000. But because of a more than fivefold population increase and poorly implemented TB control programmes, the absolute number of TB deaths increased from less than one million to 2.7 million in 1992 (Kochi, 1994). The estimate for 1995 was that 3 million people died of tuberculosis globally and that 8.9 million new cases of tuberculosis occurred (WHO, 1996). It is further estimated that 98% of TB mortality and 95% of the new cases of TB occur in the so-called developing countries (WHO, 2001, p. 29).

A paper of 1994 stated that without improvement of treatment, 3.5 million people were expected to die of tuberculosis in the year 2000 (Dolin *et al.*, 1994). For 1997, it was estimated that 1.87 million TB deaths and 7.96 million new cases of TB occurred in the world (Dye *et al.*, 1999) and an estimated 1.66 million people died of TB in the year 2000 (WHO, 2001a). This much lower figure compared to the expected number of 3.5 million is mostly due to more accurate estimates (some assumptions about TB case fatality rates were altered - Dye *et al.*, 1999) but partly also due to the effects of a growing implementation of the DOTS strategy (see chapter 1.3.1. regarding DOTS). For instance, it is estimated that the successful implementation of the DOTS strategy in India

has prevented the death of 200,000 people, mostly in the years 1999 to 2001 (Khatri & Frieden, 2002).

In terms of global burden of disease (expressed in DALYs - disability-adjusted life years lost), it is estimated that in 1990, TB ranked seventh (Murray & Lopez, 1997) and in the year 2000 TB tenth (WHO, 2002). In the year 2001, an estimated 2.5% of the global burden of disease was due to TB (WHO, 2002a).

### **1.2.2. Economic indicators**

The economic impact of TB can be severe. Studies in Asian countries such as Thailand (Kamolratanakul *et al.*, 1999), Bangladesh (Croft & Croft, 1998) and India (Rajeswari *et al.*, 1999; Nair *et al.*, 1997) and in African countries such as Uganda (Saunderson, 1995), Zambia (Needham *et al.*, 1998; Needham & Godfrey-Faussett, 1996), Malawi (Pocock *et al.*, 1996), Sierra Leone (Gibson *et al.*, 1998) and Tanzania (Wyss *et al.*, 2001) revealed that before and during treatment substantial patient costs often occur, direct and indirect costs. For instance, the study in Bangladesh (Croft & Croft, 1998) found that by the time the TB patients had registered for treatment at an NGO, the mean financial loss per patient was US \$ 245.-. Approximately half of this loss was due to loss of income, and most of the other half was spent for drugs.

In most low- and middle-income countries, more than 75% of the TB patients are in the economically active age group of 15 to 54 years (Murray, 1996, p. 212). Thus, loss of family income due to a case of TB is often severe. It is estimated that on average, TB causes three to four months of lost work time and lost earnings of 20 to 30% of the

annual household income. And for families of persons who die of TB, about 15 years of income are lost due to the premature death of the TB patient (Stop TB, 2000). Most of the indirect costs of having tuberculosis are difficult to assess and quantify. For instance, a study in South India found that 11% of 276 children of TB patients had discontinued school and 8% took up some form of employment as a result of the burden of their father's or mother's TB (Rajeswari *et al.*, 1999). And another study in South India found that female TB patients reported a 50% reduction in household work, and two-thirds felt they were not able to attend adequately to the needs of their children (Ramachandran *et al.*, 1997). Direct costs can also be substantial. For instance, in Thailand, out-of-pocket expenditure for the diagnosis and treatment of TB in the private sector accounts for over 15% of annual income for households already below the poverty line (Kamolratanakul *et al.*, 1999). And in Mumbai (Bombay) it was found that almost 10% of the income was used for travel expenses even though these patients had to come to the clinic twice a month only (Chakraborty *et al.*, 1995). The study in South India (Rajeswari *et al.*, 1999) gives the following overview in terms of the various costs: the proportion of various costs in relation to the annual family income was 13% for direct costs, 26% for indirect costs, 40% for total cost, and 14% for debts.

In terms of macroeconomics, it is estimated that the burden of TB results in an economic toll of US \$ 12 billion from incomes of the world's poorest communities every year (Stop TB, 2002). It follows that using money for TB control is a good investment for a government. A study in India from the mid-1990's illustrates this. It found that projected incremental costs to the Indian government for successful DOTS implementation throughout India are of the order of US \$ 200 million per year compared

to the tangible economic benefits of at least US \$ 750 million per year (WHO, 1997). This is true for all low - and middle-income countries: for each dollar invested in DOTS, the expected return in increased economic output is more than 3.5 dollars (Stop TB, 2002). Eliminating TB is a way of putting back billions of dollars into the national economies of poorer countries.

All these figures demonstrate that the burden of disease due to tuberculosis is huge. This is a tragic paradox since effective and cheap therapy has been available for decades. This paradox indicates a dramatic failure to use medical advances for the wider benefit of humankind, as the quotes at the beginning of this chapter also suggest.

### **1.2.3. The burden of illness**

In addition to the impact of TB indicated by its morbidity, mortality and DALY burden, and economic indicators, TB produces immense suffering that must be characterised in other ways, though it is strongly linked to the other indicators of the burden of TB. TB not only brings sickness and death but also causes emotional distress and relational strain within families and communities. TB has an awesome capacity to disrupt lives and families. Even within their families TB patients may experience being feared or ostracised, as studies revealed in India (Nair *et al.*, 1997), Pakistan (Khan *et al.*, 2000; Liefoghe *et al.*, 1995), Kenya (Liefoghe *et al.*, 1997), and Mexico (Herrera *et al.*, 1971, cited in Rubel & Garro, 1992). In the study in Mexico, 52% of hospitalised but eventually discharged TB patients were no longer accepted in their families. And in the study in Pakistan the risks of not getting married and of divorce due to TB were seen to be greater for female than for male patients (Liefoghe *et al.*, 1995).

## *Chapter 1: Background*

Stigma is an important aspect of the social and emotional suffering from tuberculosis; chapter 4 explores the experience of stigma and its meaning. The following case study illustrates the heavy burden of illness of TB in a place where strong stigma is attached to tuberculosis. The case study is a shorter version of the original case study presented by Rangan and Uplekar (1999).

Sharda, a mother of four, living in Western India, felt weak and tired and was troubled by cough. She visited the local private doctor who treated her with some cough mixtures, tonics and antibiotics for one and a half months. He later told her to get a check-up in the nearby town or at the local public health centre. However, over the next few months, Sharda had no further check-up and her physical condition deteriorated. Her mother-in-law then told her to go home to her own mother for treatment and rest. There, a neighbour was a health worker of the public health centre who told Sharda's mother that the sputum should be examined. This worried the family since usually only TB patients had their sputum examined. Giving sputum would result in having the whole neighbourhood talk about Sharda's health. Therefore, Sharda went to a reputed private doctor in a city. This doctor diagnosed TB and explained the need to take drugs for 6 to 8 months. The family refused to believe that Sharda had TB. Two other doctors were consulted before the diagnosis TB was accepted. It was clear that Sharda's TB had to be kept secret from her in-laws and husband. Otherwise, she would never be accepted back. When the private treatment no longer was possible due to lack of money and after a failed trial to get healed at a traditional healer Sharda started treatment in the public health centre and managed to complete treatment thanks to her brother's prodding.

A letter was sent to Sharda's husband, and the husband, together with the elder children, came to Sharda's place. He wanted to take her home but his mother was sceptical and refused to accept her due to her TB, although now cured. Since the husband did not want his family to be ostracised because of having Sharda among them, he went home without her.

A month later Sharda was informed that her husband had decided to get re-married. Devasted, Sharda lost all interest in life and two months later developed cough and fever. TB was diagnosed. However, Sharda refused treatment.

### **1.3. The control of tuberculosis in the world**

#### **1.3.1. DOTS - the recommended control strategy**

The last major improvement in treatment of tuberculosis occurred in the late 1960's/early 1970's with the introduction of rifampicin and pyrazinamide, which made highly efficacious and effective 6- to 9-month-long treatment possible (Fox *et al.*, 1999) and paved the way for so-called short-course chemotherapy<sup>1</sup>. However, this cost-effective tool - one of the most cost-effective health interventions of all (De Jonghe *et al.*, 1994; World Bank, 1993; Jamison & Mosley, 1991) - was not used at all or was not used effectively in many countries all over the 1970's and 1980's. An important step towards the end of an irresponsible neglect of tuberculosis and its control<sup>2</sup> was made in 1991 when Arata Kochi, then the Chief Medical Officer of the Tuberculosis Unit of the WHO (World Health Organisation) in Geneva, published an article. The title of this article - hailed as a classic public health paper (Sbarbaro, 2001) - was "The global tuberculosis situation and the new control strategy of the World Health Organization" (Kochi, 1991). In the same year, the World Health Assembly adopted the new control strategy (WHO, 1991). However, the outline of this new control strategy was not very clear and another two years passed until the WHO took the unprecedented step of declaring tuberculosis a global emergency (WHO, 1993) and clearly propagated a treatment strategy (WHO, 1994).

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<sup>1</sup> The first-line anti-TB drugs were introduced in the following years: streptomycin in 1944, thioacetazone in 1946, isoniazid in 1952 (but first synthesised in 1912! - Bloom & Murray, 1992; Meyer & Mally, 1912, cited in Rieder, 2002), pyrazinamide in 1952, ethambutol in 1961, and rifampicin in 1966 (Rieder, 2002).

<sup>2</sup> Three expressions of this neglect (reported in Klautt, 1998) were: One, in 1986, the British government closed the TB unit of the British Medical Research Council (a major player in the development of short-course chemotherapy). Two, in 1988, WHO had only one medical officer responsible for tuberculosis at its Geneva headquarters. Four decades earlier, WHO had had nearly fifty medical staff assigned to address TB in its European regional office alone. Three, in 1990, only 0.03% of foreign aid (16 million US \$) went to TB control in the developing countries although TB was responsible for 26% of avoidable adult death in the so-called developing world (Murray *et al.*, 1990).

The strategy was called DOTS for the first time in 1994 by the WHO (WHO, 2001, p. 37).

Based on decades of experience with various approaches to TB control that saw vertical approaches to TB control and waves of integration (Raviglione & Pio, 2002) DOTS has evolved and proven it can be implemented in all kinds of settings. It makes good use of the existing health services but at the same time specific key functions and central technical staff that also exercise supervisory function are an integrated part of a national TB programme that is based on DOTS.

DOTS<sup>3</sup> has five key components:

1. Political commitment to sustained TB control activities
2. Case detection by sputum smear microscopy among symptomatic patients self-reporting to health services ('passive case finding')
3. Standardised treatment regimen of six to eight months for at least all confirmed sputum smear positive cases, with directly observed therapy (DOT) for at least the initial two months of treatment (DOT should be for the whole length of treatment if rifampicin is being used for the whole length of treatment)
4. Free, reliable (i.e. regular and uninterrupted) supply of high-quality anti-TB drugs
5. A standardised recording and reporting system that allows the assessment of treatment results for each patient and for the TB control programme overall.

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<sup>3</sup> Until recently, DOTS stood for 'Directly Observed Treatment, Short-course'. However, in the year 2002 it was decided to see DOTS as a pure brand name, i.e. to no longer see it as an acronym for 'directly observed treatment, short-course'. When being seen as an acronym, DOTS gives undue emphasis to just one of the five elements of DOTS, namely to DOT, the only element of DOTS that is controversial (Lancet correspondence, 2001).

## Chapter 1: Background

The strategy was developed based mainly on experiences of the IUATLD (International Union Against Tuberculosis and Lung Disease) in the late 1970s and early 1980s (Enarson, 1991; Rouillon, 1991). The countries were Tanzania and then other African countries, and Nicaragua (WHO, 2001, p. 37). A key person was Dr. Karel Styblo (1921 - 1998), then the scientific director of the IUATLD. He used a managerial approach and introduced the so-called short-course chemotherapy in poor settings, thereby reducing treatment from up to 18 months to 6 to 8 months. Close supervision of the patient was emphasised. Later on, the term DOT was formed (DOT means a representative from the health care system watches the patient swallowing his or her medicines, be it in the health facility, in the patient's home or somewhere else, e.g. in the workplace). However, the concept of patient supervision comes from the 1950's and early 1960s: in places as diverse as Hong Kong, Madras (today called Chennai) and London it was concluded that direct supervision of therapy was needed (Humphries, 1995; Bayer & Wilkinson, 1995). The principle of DOT has also been known in Russia since the 1950s (Perelman, 2000; Rabuhin, 1960, cited in Heifets & Iseman, 2002). And in Cuba, tuberculosis treatment by DOT was started in 1970 (Gonzalez *et al.*, 1994). In other words, the principle of DOT was developed decades before the DOTS strategy was developed. It is also noteworthy that a TB programme with all the elements of DOTS was implemented in the whole of Chile in 1984. This happened at least partly due to visits of Karel Styblo (Farga, 1999).

In early 1997, WHO declared DOTS to be a "breakthrough in tuberculosis control that will make it possible to save millions of lives" (Kochi, 1997). This announcement caused concern among tuberculosis frontline workers and leading TB researchers (Brown



1997; Grange & Zumla, 1997). It was felt that the difficulties in expanding DOTS and the limits of DOTS in the light of new threats, e.g. HIV/AIDS and multidrug-resistant tuberculosis (MDR-TB<sup>4</sup>), were underestimated. A report published in 1999 illustrated that WHO had been too optimistic. The report found that 37 of 85 examined "DOTS countries" had treatment success rates of below 70% and that none of the 22 high-burden countries (the 22 countries that worldwide account for 80% of all new TB cases) achieved WHO targets for TB control (Netto *et al.*, 1999). And a paper published in late 1998 stated: "Without greater efforts to control tuberculosis, the annual incidence of the disease is expected to increase by 41% (95% confidence interval: 21 - 61%) between 1998 and 2020." (Dye *et al.*, 1998).

It became clear that the WHO targets for the year 2000, namely to detect 70% of smear-positive cases and cure at least 85% of the detected cases, could not be reached. Achieving these targets for the year 2005, the new goal, remains a formidable challenge. Without considerable *acceleration* of progress, the targets, specifically a 70% case detection under DOTS, will be reached by 2013 only (WHO, 2002b). Still, progress has been made: in the end of the year 2001, 61% of the world's population lived in parts of countries providing DOTS; 155 countries were implementing DOTS, notifying 1.2 million smear-positive cases (and 1.2 million smear-negative cases) under DOTS.

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<sup>4</sup> MDR-TB is defined as resistance to at least rifampicin and isoniazid, the two most powerful drugs. Its treatment often lasts 2 years, is very expensive and the medications often cause side effects. The recent development of the so-called DOTS-Plus strategy slowly makes treatment for some MDR-TB cases possible in low-resource settings.

However, these 1.2 million represent only 32% of the estimated global total (WHO, 2003). With an additional 143,000 cases detected by DOTS programmes in 2001 (WHO, 2003), the rate of progress in case finding in 2001 was not significantly faster. The average progress from 1994 to 2000 was a mean annual increment of 133,000 smear-positive cases (WHO, 2002b). But globally, DOTS programmes must recruit an extra 360,000 smear-positive cases each year to reach 70% case detection by the end of 2005 (WHO, 2003). It was also found that in the year 2000, DOTS programmes successfully treated 82% of all registered new smear-positive cases. Only one of the 22 high-burden countries, namely Vietnam, reached targets of case detection and cure (WHO, 2003).

### **1.3.2. Challenges in TB control and responses to them**

In early 1998, WHO organised a meeting of health experts in London (WHO, 1998). This meeting identified six principle constraints to TB control, namely:

1. Financial shortages
2. Human resource problems
3. Organisational factors
4. Lack of a secure supply of quality anti-TB drugs
5. Public information gaps about the danger of TB
6. Lack of political will to develop and sustain effective TB programmes.

Lack of political will was identified as the most fundamental constraint. However, in the past few years, this will has strengthened. The increased funding is one expression of this: external financing for TB control in low-income countries (including bank loans) totalled only US \$ 16 M in 1990, but increased to US \$ 190 M in the year 2000

(Raviglione & Pio, 2002). The WHO is the leading agency in a movement called 'Global Partnership to Stop TB' (often called the "Stop TB Partnership", "Stop TB Initiative" or "Stop TB") that was launched in November 1998. The 'Global Partnership to Stop' is a global coalition of partners to accelerate social and political action to stop the spread of tuberculosis and to mobilise more resources for this. The goal is to expand, adapt and improve strategies to control and eliminate TB. The targets are:

- By 2005: 70% of people with infectious TB will be diagnosed, and 85% cured
- By 2010: The global burden of TB disease (deaths and prevalence) will be reduced by 50% (compared with 2000 levels)
- By 2050: The global incidence of TB disease will be less than 1 per million population.

Two important events organised by the Stop TB Initiative were the 'Ministerial Conference on Tuberculosis and Sustainable Development', held in Amsterdam, March 2000 (WHO, 2000), resulting in the "Amsterdam Declaration to Stop TB" (WHO 2000a), and the first so-called *Stop TB Partners' Forum* in Washington, October 2001 (WHO, 2001b), resulting in the "Washington Commitment to Stop TB" (WHO, 2001c). Ministers of health and finance from 20 of the 22 high-burden countries were present in Amsterdam. The 'Amsterdam Declaration' highlighted the magnitude and seriousness of the global epidemic and outlined the ways to curb this epidemic. It called for accelerated expansion of control measures and for increased political commitment and financial resources to reach the targets for global TB control by 2005. In May 2000, a World Health Assembly resolution of the WHO restated this call.

The *Stop TB Partners' Forum* in Washington, hosted by the World Bank, reported on progress since the Amsterdam Conference and discussed ways to accelerate efforts to reach targets for TB control by 2005. The "Washington Commitment to Stop TB" renewed the goal that all people with TB have access to effective care. Care of patients with drug-resistant tuberculosis, enhancing collaboration between TB and HIV/AIDS programmes, and establishing close public-private sector collaboration were specifically mentioned. A commitment to co-ordinate effective across-border action, emphasising that the health sector alone cannot control TB, was also made. Specific goals for the end of the year 2001 and for the end of 2002 were made and the targets of the Stop TB Initiative upheld. Also, the 'Global Plan to Stop TB' (WHO, 2001) was launched. This plan can be seen as the framework of all the activities co-ordinated by the Stop TB Initiative. The plan lays out what needs to be done to control, and eventually eliminate, TB in the world. It describes the strategies and mechanisms to achieve this and what these accomplishments will cost. It estimates the five-year cost of TB control to be US\$ 9.3 billion (6.2 billion of this for DOTS expansion). The estimated funding gap between resources currently available or pledged and the amount required is roughly US\$ 4.5 billion. The recently established 'Global Fund to Fight AIDS, TB and Malaria' is expected to help close the funding gap. The new estimates in the latest WHO report indicate this. It is now estimated that for the period 2001 to 2005, the total funding gap for national TB control programmes is only 0.2 billion US dollars. There may be an additional shortfall of at least 0.9 billion US dollars due to deficiencies in staff and infrastructure (WHO, 2003).

Advocacy, resource mobilisation and co-ordination are basic functions of the 'Global Partnership to Stop TB'. Six working groups are being co-ordinated. The working groups focus on:

- DOTS expansion ([http://www.stoptb.org/Working\\_Groups/DOTSExpansion/default.asp](http://www.stoptb.org/Working_Groups/DOTSExpansion/default.asp))
- TB and HIV/AIDS ([http://www.stoptb.org/Working\\_Groups/TBHIV/default.asp](http://www.stoptb.org/Working_Groups/TBHIV/default.asp))
- MDR-TB ([http://www.stoptb.org/Working\\_Groups/DOTS.Plus.htm](http://www.stoptb.org/Working_Groups/DOTS.Plus.htm))
- Development of new vaccines ([http://www.stoptb.org/Working\\_Groups/TB.Vaccines.htm](http://www.stoptb.org/Working_Groups/TB.Vaccines.htm))
- Development of new diagnostics ([http://www.stoptb.org/Working\\_Groups/TB.Diagnostics.htm](http://www.stoptb.org/Working_Groups/TB.Diagnostics.htm))
- Development of new drugs (<http://www.tballiance.org/home.cfm>)

And another initiative of the 'Global Partnership to Stop TB' is *The Global TB Drug Facility* (GDF), launched in March 2001 (<http://www.stoptb.org/GDF>). It is a global purchasing and distribution mechanism to expand access to, and availability of, high-quality TB drugs to facilitate global DOTS expansion.

The various initiatives co-ordinated by Stop TB are a step forward and increase the likelihood that significant progress in TB control will occur in the years to come. Still, these developments do not necessarily mean that the identified constraints, especially the constraints regarding human resources and organisational aspects, are now being addressed comprehensively. Also, even if the search for new vaccines, diagnostic tool and drugs turns out to be successful, there remains a huge challenge, namely to see these new tools being made fully accessible for the poor and marginalised.

To see progress in the actual expansion of DOTS, the following main constraints that have recently been identified (WHO, 2002b) need to be addressed:

- Lack of qualified staff and management skills
- Shortage of laboratory equipment
- Decentralisation of health services
- Absence of collaboration between TB and HIV programmes
- An unregulated private sector
- Poor access to health services (partly due to war).

The problem of poor access is of great importance, and not just regarding TB control. It indicates that more fundamental issues also deserve a close look. A recent critical review (Jaramillo, 1999) identified four fundamental problems of DOTS: One, the cost for TB patients of diagnosis and treatment can be substantial even when the diagnostic procedures and drugs are free. Two, poor education on TB of TB patients and the stigma attached to TB hamper case finding and treatment. Three, preventive therapy (commonly 6 to 9 months of isoniazid) is not being provided in most low- and middle-income countries. Four, long-term political commitment is unlikely since it becomes difficult to obtain political support over many years, especially when the incidence of TB starts to decrease. As the incidence goes down, concern about TB also decreases, causing the so-called U-shaped curve of concern (Reichman, 1991), i.e. support follows the incidence of TB. An even more fundamental critique in Jaramillo's review is that the understanding of traditional epidemiology regarding causality is reductionistic, neglecting social, economic and political issues. Jaramillo then presents as an illustration of a reductionistic understanding the view that the epidemic of multi-drug resistant tuberculosis is a consequence of (i) failure of health care providers to give adequate

treatment and (ii) failure of patients to adhere to treatment. Section 5 of chapter 1.3.3. discusses access to DOTS.

In many places, the most severe challenge to successful TB control is the HIV/AIDS pandemic. As of December 2002, 42 million people were living with HIV/AIDS (UNAIDS/WHO, 2002). Escalating tuberculosis case rates over the past decade in many sub-Saharan African countries and in parts of Southeast Asia are largely attributable to the HIV epidemic (Bleed *et al.*, 2000). Since the mid-1980's, annual case notification rates have risen up to fourfold in many African countries (WHO, 2001d). In the WHO African Region, an average of 38% of new TB cases are HIV-positive (Corbett *et al.*, 2003). In 2000, nine percent of all new TB cases were attributable to HIV infection, but the proportion was much greater in the WHO African Region (31%) and some high-income countries (e.g. 26% in the United States). It is estimated that globally 11 million adults were co-infected with TB and HIV in 2000 (Corbett *et al.*, 2003).

### **1.3.3. Limitations of DOTS**

#### **1. Diagnosis**

A limitation of DOTS is that diagnosis is based on sputum microscopy (reviewed in Jochem & Walley, 1999), a cumbersome procedure that has low sensitivity (see e.g. Levy *et al.*, 1989). Its low sensitivity means that at least half of all TB cases cannot be detected by sputum microscopy, namely sputum smear-negative cases and extrapulmonary cases that make up an estimated 55% of all cases in the so-called developing countries (Murray *et al.*, 1990). In countries with a strong presence of

HIV/AIDS, this percentage may be even higher. Still, WHO expects that in DOTS programmes 45-60% of all cases are smear-positive (WHO, 2002b). In the year 2000, only 42% of the TB cases notified by the 202 countries that reported to WHO and 44% of all estimated TB cases that occurred in the year 2000 in the 22 high-burden countries were smear-positive. In DOTS areas, the rate was higher, namely 52% (WHO, 2002b). It follows that for approximately half of all TB cases, diagnosis cannot be made with sputum microscopy, and it is not uncommon that only smear-positive patients receive free treatment. The importance of smear-negative cases is sometimes underestimated: while clearly less infectious than smear-positive cases (Rieder, 1999, p. 21) smear-negative cases also contribute to transmission of TB bacilli. For instance, a study in the USA suggested that in San Francisco, smear-negative but culture-positive cases were responsible for about 17% of TB transmission (Behr *et al.*, 1999). And without treatment, a considerable proportion of smear-negative cases will turn smear-positive after some time (Fox, 1988). A study in Hong Kong found that 63% of 283 smear-negative patients judged to have active tuberculosis who were not given treatment turned culture-positive within 30 months (Hong Kong Chest Service/ Tuberculosis Research Centre, Madras/ British Medical Research Council, 1981). Sputum microscopy is cumbersome and giving sputum is perceived by some patients to be embarrassing (see chapter 4). Also, sputum microscopy may have a negative yield in spite of acute illness of the one who gave sputum. Thus, emphasising smear microscopy often has the undesired effects of alienating patients and discouraging private practitioners to collaborate with the public TB programme. The diagnostic process can be long; for instance, a study in Ho Chi Minh City, Vietnam found that 14% of the patients had not been finally diagnosed six to eight weeks after first attending a DOTS facility (Lönnroth *et al.*, 2001). And a study in



Malawi found that among 499 TB symptomatics who were asked to give sputum samples, only 37% submitted the prescribed three specimens and collected the results of the examination (unpublished data from Squire and colleagues, cited in Jochem & Walley, 1999). For patients whose initial three sputum specimens are found to be negative, lengthy procedures are often prescribed, causing the diagnostic part of DOTS to act as a deterrent. The low sensitivity of sputum microscopy has the paradoxical effect that delayed health seeking may be better for the patient since at an early stage of disease, the likelihood to have smear-negative TB (and thus miss diagnosis) is higher (Lönnroth, 2000, p. 78).

## 2. Treatment regimens

This writer believes that there should be a stronger evidence base in terms of which regimens are most cost-effective and patient-friendly. For instance, two common regimens are: (i) using rifampicin for the initial two months only and then having a maintenance phase of six months of isoniazid and ethambutol; and (ii) a six-month regimen using rifampicin throughout the length of treatment. Some years ago there was some inconclusive debate about the equivalence of effect of these two regimens (Rieder *et al.*, 2001; Mathew & Santha, 2000; Long & Scalcini, 2000; Long & Scalcini, 1999), though the arguments against the eight-month regimen were rather convincing. Only very recently has clear evidence emerged that (i) is inferior to (ii) (WHO, 2003a). Also, as discussed in chapter 6, it is not clear if using ethambutol as a fourth drug is really needed and if yes whether it should be used for two months only (as recommended in DOTS programmes) or for six months (as prescribed by many private practitioners). And while intermittent therapy has been used for decades, most modes of intermittent therapy (e.g.

intermittent therapy from the start of treatment) have not been tested in clinical trials, as admitted in a WHO workshop of October 1995 (WHO, 1996a, p. 6). In view of the considerable potential advantages of intermittent therapy their non-inferiority versus daily regimens should be tested rigorously and intermittent therapy promoted strongly if found to be equivalent to daily therapy.

The standardised treatment regimens may also miss the need to consider prolonging treatment for certain patients. It is interesting to note that the new TB treatment guidelines of leading American anti-TB organisations now recommend to consider extension of treatment for patients with cavitation on the initial chest X-ray (ATS/CDC/IDSA, 2003, p. 609). Embracing such new recommendations is important not only for clinical reasons but also for convincing sceptical private practitioners that DOTS really is "best practice".

There are also doubts if the so-called re-treatment regimen (for patients with previous anti-TB treatment for at least one month) is needed (Connolly *et al.*, 1999; Wilkinson *et al.*, 1998). One may also argue that for re-treatment patients it would be more cost-effective to get drug resistance results (though this is a lengthy procedure and not possible in many rural areas) than to automatically give them the re-treatment regimen. In other words, a stronger case should be made for making drug susceptibility testing available to a much larger number of TB patients.

### 3. Implementation of DOT (directly observed therapy)

An important task is to find ways to increase patient adherence to treatment, and DOT<sup>5</sup> is seen as the main approach. However, there are at least five potential problems with DOT: (i) a conceptual problem leading to a narrow focus; (ii) a lack of evidence of the effect of DOT; (iii) a lack of appreciation of the potential burden of receiving treatment under DOT. DOT may make continuation of treatment difficult; (iv) DOT may set into motion a selection process; and (v) DOT may act as a deterrent.

One, there is a conceptual problem (as a recent review has pointed out - Ogden *et al.*, 1999). Seeing DOT as the answer to increase compliance<sup>6</sup> implies that patient beliefs and behaviour are the main barriers to good compliance. Insensitive implementation of DOT may also suggest that *controlling* the patient is the key to success, rather than *supporting* and *enabling* the patient (Coker, 1999; Porter & Ogden, 1997). There is growing evidence that poor accessibility and quality of care and financial as well as social constraints of the patients are the main culprits of non-compliance [see (iv) of this discussion of DOT]. Focussing on DOT may thus lead to a neglect of other determinants of a successful TB programme and lead away from looking at the larger issues.

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<sup>5</sup> DOT is implemented in various ways: (i) health facility-based DOT, meaning the patient comes to the health facility for each drug intake; (ii) someone from the health system (often community health workers) is responsible for observation of treatment which means that either the health worker goes to the patient's house or the patient goes to the health worker's house. (iii) a household member of the TB patient is given the task to act as treatment observer ('family DOT').

<sup>6</sup> The term compliance is more general and more often used than the term 'adherence'. In this thesis the term 'adherence' is preferably used. The term 'compliance' is associated with obeying, submitting and deferring to instruction and indicates a power gap between the caregiver and the receiver. It also somehow implies that the caregiver delivers information clearly and that any failure to comply is thus the fault or problem of the patient. Acknowledging the importance of establishing a patient-provider relationship that is based on partnership, a move from 'compliance' to 'concordance' has been suggested (Royal Pharmaceutical Society of Great Britain, 1997, cited in Fox, 1997 and in Mullen, 1997). See also Trostle (1988) who critically looks at the term 'compliance' and postulates it should be re-conceptualised.

Two, there is no clear evidence of what the contribution of DOT *per se* is to improved programme outcome (Volmink & Garner, 2003). So far, the results of four controlled trials have been published. In the study in Pakistan (Walley *et al.*, 2001) and in the first of the two studies in South Africa (Zwarenstein *et al.*, 1998) DOT was not found to contribute to better programme outcome while in Thailand (Kamolratanakul *et al.*, 1999a), more patients under DOT (it was mainly family DOT) compared to patients under self-administered treatment completed treatment. The second study in South Africa showed a trend (the sample size was small) toward better treatment outcome with supervision performed by lay health workers (Zwarenstein *et al.*, 2000). Even though these trials do not clearly show that DOT furthers treatment completion, it needs to be stressed that carefully implemented DOT makes sure that while the patient is under treatment the drugs are taken properly. Thus, trials examining the effect of DOT should not only look at completion of treatment but also at development of drug resistance. The primary outcome of interest should be development of drug resistance while on treatment. In other words, the main assumed benefit of DOT is avoiding the creation of drug resistance. There is some evidence from observational studies supporting this assumption (Trébuq *et al.*, 1999; Chaulk *et al.*, 1995). Unfortunately, none of the four randomised controlled trials looking at the effect of DOT on patients with active TB had as an outcome of interest emergence of drug resistance.

Three, the burden of DOT can be heavy. Rigid DOT may actually make adherence to treatment more difficult. Health facility-based DOT implies that the patient has to come to the health facility daily (less often if treatment is intermittent). Clearly, this can be a heavy burden for a substantial proportion of patients. A study from

Pakistan illustrates this: all 36 respondents in a study in Pakistan complained of the fatigue and weakness induced by each visit to the health facility (Khan *et al.*, 2000). Also, an important consideration is that social stigma may lead to non-compliance (mentioned in a review of Hudelson, 1996 and found in various studies, e.g. in a study in Vietnam: Johansson *et al.*, 1999). Social stigma towards TB patients often makes DOT highly problematic since frequent walks or trips to the health centre or regular visits by the treatment observer to the patient's house may make concealment of the illness impossible. Such concern has been found in a qualitative study in Thailand (Ngamvithayapong *et al.*, 2001). And a study in Kerala, India revealed that 27% of TB patients being treated in a DOTS programme were not being treated under DOT. Twenty-eight percent (15/53) of them stated social stigma as the reason for not being under DOT (Balasubramanian *et al.*, 2000).

Four, DOT may cause a selection process. Such selection process can be of two kinds. Under the pressure to reach certain targets, health care providers may be tempted to keep 'problematic patients' out of the DOTS programme. It may thus happen that patients that do not seem willing or able to comply with DOT (which are normally those in greatest need) are not accepted in a DOTS programme. Such an unfortunate selection process has been documented in India (Singh *et al.*, 2002). Also, rigid DOT (especially daily health facility-based DOT) may set in motion another selection process: for the poorest and most vulnerable section of society it may make continuation of treatment impossible (Ogden *et al.*, 1999; Hurtig *et al.*, 1999). In focus group discussions in Vietnam, it was said that some patients have no choice but to discontinue treatment and return to work (Johansson *et al.*, 1999). In a study in Pakistan the twelve interviewed

treatment defaulters all mentioned financial constraints as the major factor leading to default (Khan *et al.*, 2000). Another interesting finding comes from a study of a DOTS programme in Malaysia, where 23 non-compliant patients were interviewed: more than half of the respondents (55%) stated the reason for non-compliance was inability to spend money for the transportation cost. And 17% stated more generally that they were unable to get transport. Family DOT was the second most often mentioned suggestion on how to improve the TB programme (O'Boyle *et al.*, 2002).

Five, DOT may act as deterrent. The more demanding a programme, the smaller its acceptability for the patient; DOT may thus deter patients from making use of DOTS (Heymann *et al.*, 1998). Studies from Ho Chi Minh City in Vietnam indicate that the features of the public TB programme that are unattractive for the patients, e.g. DOT, are a reason why even an extremely well functioning DOTS programme (such as the one in Vietnam) is not accessed by all TB symptomatics (Lönnroth *et al.*, 2001a; Lönnroth *et al.*, 1998). A narrative from Manila illustrates this dynamic. A neighbour of mine came from a private doctor who had given her a prescription for TB treatment. Her reaction to my suggestion of having her sputum examined at the local health centre was: "I don't want to go there because when you get treatment there, then you have to go to the health centre every day."

This critical look at DOT does not imply that DOT should be abandoned. Rather, it points to a key issue: how must DOT be implemented so that the patients perceive DOT as a *supportive* rather than *punitive* element? How can one make sure that DOT is characterised by the "development of intense personal bonds between patients and those

who care for them" (Sbarbaro, 1997) or "free, respectful and convenient treatment" (Khatri & Frieden, 2002a)? What determines if DOT is a means towards establishing clear communication and co-operation or towards making the patient the passive recipient of advice and treatment? It is clear that a TB control programme must create a service culture that motivates the patient to adhere to treatment (Wares & Clowes, 1997). But more operational research to clarify the role of DOT and the most appropriate forms of DOT is needed. A report from a South African study where the patients could choose what kind of supervision they wanted (Kironde & Meintjies, 2002) and a recent review article of Macq and colleagues (2003) present welcome explorations of the perceptions of DOT and the various forms of DOT. It is also important to explore the gap between 'theory' and 'practice': similar to the study in Kerala (Balasubramanian *et al.*, 2000) a recent study in Thailand found that the actual DOT practice often differs from the one initially assigned (Pungrassami *et al.*, 2002; Pungrassami & Chongsuvivatwong, 2002). This raises the question of to what extent burdensome forms of DOT (burdensome for patients and/or health providers) are watered down and whether it might be better to promote less rigid forms of DOT that are then implemented more willingly and faithfully. In the discussions about DOT, less dogmatism would be welcome. For instance, brilliant but less than fully-balanced argumentation<sup>7</sup> may incorrectly suggest that family DOT is not acceptable (Frieden & Sbarbaro, 2002). On the other hand, in my perception the Cochrane review on DOT for TB patients (Volmink & Garner, 2003) concluded prematurely that DOT and self-administered treatment have a similar effect on success of

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<sup>7</sup> The findings referred to from Thailand (Pungrassami *et al.*, 2002) were misinterpreted. And the findings referred to from Nepal (Mathema *et al.*, 2001) are from a study with potentially severe selection bias.

treatment. Also, reading the Cochrane review and then the papers of the quoted studies suggests that the reviewers did not give due weight to some findings of the reviewed studies that indicated there was a benefit of DOT.

Operational research should also explore other ways of supervising drug intake. For instance, an interesting question is whether medication monitors can be used to reduce the number of patients who need labour-intensive DOT. The patients not under DOT would then have self-administered but monitored treatment. The patients whose medication monitors show that regular drug intake is not taking place can then be put under special care (i.e. DOT and enablers, as well as incentives for regular drug intake). A recent study from Haiti indicates that such medication monitors are feasible and cost-effective (Moulding & Caymittes, 2003; Moulding & Caymittes, 2002).

Whatever the focus of operational research regarding DOT is, it must not lead to placing the onus of treatment completion primarily on the patient and thereby diverting attention from the system or environment that disables the patient from completing treatment. Rather, it should incorporate the social, political, economic, and cultural dimensions of tuberculosis control. Farmer's assertion "throughout the world, those least likely to comply are those least able to comply" remains valid (Farmer, 1997).



4. The role of the health worker

The World Health Organization has identified the neglect of human resource development as one of the main constraints to rapid expansion of DOTS (WHO, 2002c). Being part of a DOTS programme is not an easy task for a health worker. Having good medical and managerial abilities is not enough. In the light of the emotional distress often being caused by TB, the stigma attached to tuberculosis, and the need of prolonged and regular but unpleasant drug intake, a health worker should have strong interpersonal skills, showing empathy and genuine care (Porter & Ogden, 2002; Grange, 1999; Grange & Festenstein, 1993). Being able to give patients support requires that the health care providers have enough own emotional strength. Health care providers may feel the need to shield themselves against emotional engagement or invasion (Van der Walt & Swartz, 2002). A South African TB patient who was herself a trained nurse explained the impersonal approach of her treatment observer as follows: "Nurses prefer to avoid involvement with the patient. I don't think it is because of the germs. I think that they lack the emotional strength to provide the support that patients need. They are not prepared to acknowledge the person behind the folder. They prefer to deal with the disease rather than with the human being." (Van der Walt & Swartz, 2002). And a study in South Africa found that the crucial factors in terms of acceptability of a health facility are the emphatic dimensions (friendliness, good communication, encouraging, listening) (Westaway & Wolmarans, 1993). An illustration of the power of kindness was recently given through a case study in Ghana, where the kindness of the health provider at initiation to treatment brought the young female TB patient to tears. The patient completed DOTS treatment despite difficulties in attending the clinic (Lawn, 2000). Another example is a patient in Colombia with MDR-TB who was actually thankful to have tuberculosis; the positive experience of the presence of people that provide support and show genuine concern was

so powerful (Ernesto Jaramillo, personal communication, January 2003). It is fundamental that in the efforts to progress in the fight against the diseases of poverty, a central part be given to strengthening the health services and the health workers (Brugha & Walt, 2001). A recent report assessing the impact of 'Health Workers for Change' workshops in seven settings found that the findings from all seven settings indicated that overall health system development is essential for improved service provision including quality of care (Onyango-Ouma *et al.*, 2001). The welcome emphasis on the diseases of poverty, namely HIV/AIDS, TB and malaria, brings the danger that strengthening the health services and the health providers is neglected (Verheul & Rowson, 2002). In the words of The Lancet: "Sustainable primary care must be the first ambition of any global fund for health." (Editorial in the Lancet, 2001). Strengthening primary care must include ways of enabling the health worker to be more patient-friendly, such as appropriate training in interpersonal skills and offering better remuneration. Also simple measures such as increased training and supervision of health providers can improve the outcome of a TB programme, as has been shown in places such as Malawi (Kelly, 2001) and Korea (Jin *et al.*, 1993).

#### 5. Access to DOTS

In spite of considerable progress in expanding DOTS over the last few years, only 28% of the estimated TB cases were treated in DOTS programmes at the end of 2001 (WHO, 2003). Physical availability of DOTS does not mean that a DOTS programme is being accessed. A major reason for the low use of DOTS programmes is that a large proportion of people with TB symptoms seek care and get treatment in the private sector. The recent emphasis of WHO to bring DOTS to the private sector and establish public-private collaboration (WHO, 2001e) is thus highly warranted. Another

reason for non-use of DOTS may be the economic and social vulnerability of large sections of the population. For instance, a study in Vietnam found the main reasons for delay in help seeking were: (i) economic constraints, (ii) poor quality of health services, such as inadequate attitudes of the health care providers; and (iii) fear of social isolation (Johansson *et al.*, 2000). Thus, reaching out to the private sector should be complemented with a growing awareness that DOTS needs to engage more with the strong political, social, economic and cultural dimensions of tuberculosis and its control (Gandy & Zumla, 2002; Ogden *et al.*, 1999; Hurtig *et al.*, 1999; Rangan & Uplekar, 1999; Farmer, 1997). Gandy and Zumla (2002) dare state: "The DOTS strategy is approaching the limits of what can be achieved without more fundamental changes in public health policies as part of a wider programme to tackle poverty and social inequality." The large-scale forces that hinder rapid progress in reducing sickness and death must be exposed and addressed. The recent "Expanded DOTS Framework for Effective Tuberculosis Control" of the WHO (WHO, 2002d) seems to take this into account. Different sectors of society should be asked to become partners in the fight against TB. Health professionals are among those whose voices should be heard at all levels - Rudolf Virchow (1821 - 1902) argued that physicians must be the "natural attorneys of the poor" (cited in Farmer, 1999). Roughly one hundred years later, the Lancet discussed the social and public health dimension of epidemiology. This discussion affirmed that the study of social causes of disease is an important epidemiological goal and that speaking out for social betterment and human rights has its place (Rothman *et al.*, 1998; Lancet Editorial, 1997).

#### **1.4. Tuberculosis and its control in the Philippines**

In 2001, the Philippines ranked 9<sup>th</sup> for the estimated incidence rate of all TB cases among the 22 high-burden countries and the estimated incidence rate was 297 per 100,000 (WHO, 2003, p. 10). The percentage of multi-drug resistant TB among new cases of TB was estimated to be 3.2%, and it is estimated that only 0.4% of TB cases are harbouring HIV (WHO, 2003, p. 103).

Up to 1954, TB was the leading cause of death in the Philippines, and up to 1984 TB was number two (Philippine Department of Health, 1988, p. 2). In 1998, tuberculosis was the sixth leading cause of mortality; the mortality rate was 38.3 per 100,000 inhabitants, resulting in 28,041 reported TB deaths (Philippine Department of Health, 2003). Estimates say that TB killed approximately 65,000 people in the Philippines in the year 2001 (Peabody *et al.*, 2003) which translates into approximately 180 Filipinos dying of TB every day.

In 1997, a national prevalence survey regarding TB was performed (Tropical Disease Foundation 1997 and Tupasi *et al.*, 1999). The main findings were:

- Approximately 18% of the surveyed population older than 19 years were considered TB symptomatics and would have been qualified for case finding as defined in the national TB programme.
- Only 57% of these symptomatic respondents took action: 32% self-medicated, 12% consulted a private practitioner, 7.5% a public health facility, 4.5% a (mostly private) hospital and 2% a traditional healer.

- The prevalence of active TB was 42/1000 population. The corresponding rate for culture-positive TB was 8.1/1000 and for smear-positive TB 3.1/1000.
- The annual risk of infection was 2.3% (the annual rate of infection was 2.5% in the 1981-1983 national tuberculosis prevalence survey; Philippine Department of Health, 1984). Also when comparing other figures of the two prevalence surveys only a minimal decrease of tuberculosis since 1983 can be found.
- Among respondents of urban poor areas of Metropolitan Manila and two other cities (a sub-sample of the surveyed population), the rate for culture-positive TB was 12.4/1000 and for smear-positive TB 5.6/1000, and the annual rate of infection was 6.5% (Tupasi *et al.*, 2000).

The TB control programme (called NTP) was initiated in 1968, became nationwide in 1978 and was strengthened in 1986. The same year saw the introduction of short-course chemotherapy. The devolution/decentralisation of the health services in the early 1990's complicated full implementation of the NTP. An external evaluation done in 1993 revealed the following constraints: (i) an inadequate budget for drugs; (ii) poor quality of the diagnostic process; (iii) irregular programme supervision and monitoring; and (iv) poor patient adherence to treatment (Philippine Department of Health, 1993; Philippine Department of Health, 2001, p. 2).

The Philippines adopted the DOTS strategy in 1995, and since July 1996, DOTS has been increasingly implemented. By the end of 2001, 95% of the population had access to DOTS (WHO, 2003, p. 103). In 2001, 107,133 TB cases were notified, 59,341 of them new smear-positive, representing 58% of the estimated total of new smear-positive cases (WHO, 2003), p. 196). Access is limited in some remote areas and in areas of conflict/war. To increase the case detection rate, implementing DOTS in all

governmental hospitals, stronger social mobilisation and collaboration with the private sector is planned. Several efforts are already being implemented, and PhilCAT (Philippine Coalition Against Tuberculosis; a broad and very active umbrella organisation; Roa & Romulo, 2000) is spearheading most of these initiatives.

Treatment outcome in the 1999 cohort is encouraging: 87% of the enrolled new smear-positive TB patients had successful treatment (70% were 'cured' and 17% 'completed treatment'). Only 6% defaulted; 3% transferred-out; 3% died; and 2% were treatment failures (data are from a presentation given by a staff of the Manila Department of Health, Center for Infectious Diseases). And in the 2000 cohort of new smear-positive patients, 88% had successful treatment (WHO, 2003, p. 103). However, it should be noted that it is possible that reported rates of successful treatment are too high, as was found in Malabon (Auer, 1998a).

Constraints are mainly seen in the following areas: (i) procurement and distribution of the anti-TB drugs; (ii) maintaining the quality of DOTS in view of a small number of the central TB staff and insufficient monitoring; (iii) uncertainty regarding commitment of local government units (WHO, 2002b, p. 104) and from a presentation given by a staff of the Manila Department of Health, Center for Infectious Diseases). Finances are also a constraint: the budget for the years 2001 to 2005 amounts to US \$ 109.3 million, and the funding gap was estimated to be 25.2 million. The main areas with a funding gap are diagnosis and activities to increase case detection and cure rates (WHO, 2002b, p. 104). For the year 2003, the NTP budget is US \$ 9.1 million, and 36% of this amount is allotted for drugs. The funding gap for the year is expected to be US \$ 5.8 million (WHO, 2003, p. 104).

## **CHAPTER 2: GOAL AND OBJECTIVES**

### **2.1. Overall goal**

To contribute to more effective and more efficient control of tuberculosis in resource-limited settings.

### **2.2. Objectives**

1. To assess TB illness experience in Manila from the perspective of TB patients, non-affected urban poor residents and health providers
2. To establish the health seeking behaviour and perceived causes of tuberculosis of TB patients in Malabon, Metro Manila
3. To assess how the private practitioners of Malabon diagnose and treat tuberculosis
4. To establish the views of the private practitioners of Malabon regarding public-private collaboration in TB control
5. To outline approaches for collaboration between the private practitioners and the public TB programme in Malabon
6. To assess feasibility, acceptability, and effectiveness of fully intermittent TB therapy (thrice-weekly) compared to daily TB therapy.

## CHAPTER 3: STUDY AREAS AND DATA COLLECTION METHODS

### 3.1. Study areas

The studies took place in Metropolitan Manila ("Metro Manila"), a conglomerate of cities and municipalities that had approximately 11 million inhabitants in the year 2000 (United Nations Population Division, 2000). Roughly one third of Metro Manila's population is living in poor areas (slums and squatter areas).

Malabon (now called Malabon City; up to the year 2000 it was a municipality) had approximately 400,000 inhabitants in 1999. It is located in the north-west of Metro Manila and compared to the other cities of Metro Manila it is less highly developed and urbanised. Due to various demolitions of squatter areas the population size of Malabon has decreased in recent years. Malabon has 23 public health centres and approximately 50 private practitioners that treat TB patients.

Taguig is situated in the south-east of Metro Manila along the big lake *Laguna de Bay*. With an average annual population growth rate of 4.5% during the period 1995-2000 it is the fastest growing area in Metro Manila (National Statistics Office, 2000). Taguig had 520,000 inhabitants in the year 2001, served by 20 public health centres. Most people live in urban areas, some in semi-urban areas.



### **3.2. Overview of data collection methods**

Chapters 4 and 5 present findings from a survey among TB patients of Malabon. These patients, interviewed in their houses, had received anti-TB treatment in the public health centres of Malabon. Chapter 4 includes findings from a survey among the public health care providers of Malabon, using a self-administered questionnaire and findings from focus group discussions (FGDs) carried out among non-affected local residents in three urban poor areas of Metro Manila, one belonging to Malabon, and two to Quezon City, the largest city of Metro Manila. Chapter 5 also made use of patient narratives.

Chapters 6 and 7 present the main findings from our survey among the private practitioners of Malabon who were interviewed in their clinics. Chapter 7 also includes findings from group discussions with the public health care providers of Malabon.

Chapter 8 presents the main findings from a randomised controlled trial in Taguig that compared daily with thrice-weekly therapy. The main source of data were the patient interviews; each patient was interviewed twice while on treatment and once shortly after the end of treatment. Other data used were health centre records and laboratory records. In addition, chapter 8 includes findings from group discussions with the public health care providers of Taguig.

***PART II: Understanding the patient:  
TB illness experience and help seeking***

**TB illness experience from patient, provider and community perspectives  
in Manila, Philippine**

**Health seeking and perceived causes of tuberculosis among patients in  
Manila, Philippines**



**TB ILLNESS EXPERIENCE FROM PATIENT, COMMUNITY AND PROVIDER PERSPECTIVES IN MANILA, PHILIPPINES**

*Running title: TB illness experience: three perspectives*

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## **TB illness experience from patient, community and provider perspectives in Manila, Philippines**

### **ABSTRACT**

Recognising the nature of the severe illness burden of tuberculosis and its implications for TB care are important steps to better TB control. We aimed to establish how TB patients experience their illness and its treatment, how non-affected urban poor residents perceive TB patients and why TB carries stigma. We also examined the patient-health care provider relationship. Our methods were: (i) interviews with 319 TB patients of public health centres of Malabon, Metropolitan Manila; (ii) three focus group discussions with non-affected urban poor residents of Metropolitan Manila; and administration of questionnaires to health care providers of Malabon.

Having TB commonly resulted in feelings of sadness, guilt, embarrassment, fear of dying, loss of self-esteem, and feeling ostracised. An index of stigma was established. In a multivariate analysis, six factors were found to be associated with high stigma score, e.g. having TB for at least the second time; having separated the eating utensils due to having TB; and *not* having been found by active case finding.

Behavioural changes of the TB patients were: separating eating utensils; reducing or abstaining from sexual activities; sleeping separately; and reducing tobacco and alcohol consumption.

Non-affected urban poor residents expressed ambivalence towards TB patients: fear of getting infected contrasted with feelings of concern and support. Non-affected people saw fear of infecting others as the major reason why TB patients feel embarrassed and withdraw from people. It was also found that the term 'weak lungs' is often being used as a euphemistic expression for TB.

Health care providers tended to blame the patient and to give inappropriate health education messages.

The illness burden is substantial. Misconceptions have the potential to increase the burden of TB. The findings suggest aspects of clinical care that need improvement, such as giving health information and interpersonal skills.

*Keywords:* pulmonary tuberculosis, illness experience, stigma, cultural epidemiology, TB control, Philippines

## **INTRODUCTION**

In terms of the burden of disease, the economic burden, and the burden of illness, tuberculosis (TB) is a top priority for international health. Approximately 16 million people have the disease at any time (Dye *et al.*, 1999) and there were an estimated 8.5 million new TB cases in 2001 (WHO, 2003). Almost two million people die of this disease every year (Dye *et al.*, 1999).

The economic burden of TB is substantial. Indirect costs are especially important since more than 75% of those sick with TB belong to the economically productive age group 15 to 54 years (Murray, 1996). Studies suggest that on average three to four months of work time are lost (Stop TB, 2000). For the families of those who die from the disease, there is a loss of about 15 years of income resulting from the premature death (Stop TB, 2000). The impact of TB on difficult-to-measure economic activities of many women must also be considered. For instance, in South India, female TB patients reported a 50% reduction in household work and two thirds reported that they were not able to adequately attend to the needs of their children (Ramachandran *et al.*, 1997). Additional costs, both monetary and psychological, may result from stigma and discrimination against those with TB and members of their households.

In 2001, the Philippines ranked 9<sup>th</sup> for the estimated incidence rate of all TB cases among the 22 high-burden countries that worldwide account for 80% of all new TB cases, and the estimated incidence rate was 297 per 100,000. It was estimated that only 0.4% of the TB cases were co-infected with HIV (WHO, 2003). In 1998, tuberculosis was the sixth leading cause of mortality; the reported mortality rate was 38.3 per 100,000 inhabitants (Philippine Department of Health, 2003).

#### *Chapter 4: TB illness experience: three perspectives*

Apart from physical symptoms and death, TB brings emotional suffering as well as disrupted lives, families, and communities. Its treatment may adversely affect the patient's daily and social life.

Social stigma is an important aspect of the illness experience identified with TB. Stigma was characterised by Goffman (1963) as the situation of the individual denied full social acceptance. Various forms of stigma exist in most cultures (Rubel & Garro, 1992), also in the Philippines (Nichter, 1994). Marginalised or weaker segments of a community may be especially vulnerable to stigma (Uplekar & Rangan, 1999). Findings from focus group discussions in Pune, India (Morankar *et al.*, 2000) and Vietnam (Johansson *et al.*, 1999) suggest that stigma affects women more than men. This differential stigma may partly explain why in many countries, women experience more barriers than men in accessing health services (Uplekar *et al.*, 2001).

The severe and far-reaching illness burden of TB and the problematic interactions between health care providers and TB patients may well be major reasons why only 28% of global TB cases are currently identified and treated in DOTS programmes (WHO, 2003). DOTS is the broadly promoted strategy to control TB which had been implemented by 155 countries in the year 2001 (WHO, 2003). New insights that shed light on the rationale for patient behaviour that is problematic or undesired from the point of view of a control programme are needed.

This study was performed to elucidate TB illness experience to make a contribution in clarifying ill-defined and hidden suffering, outlining policy for promoting appropriate help seeking, including the needed support for patients, and identifying barriers to

*Chapter 4: TB illness experience: three perspectives*

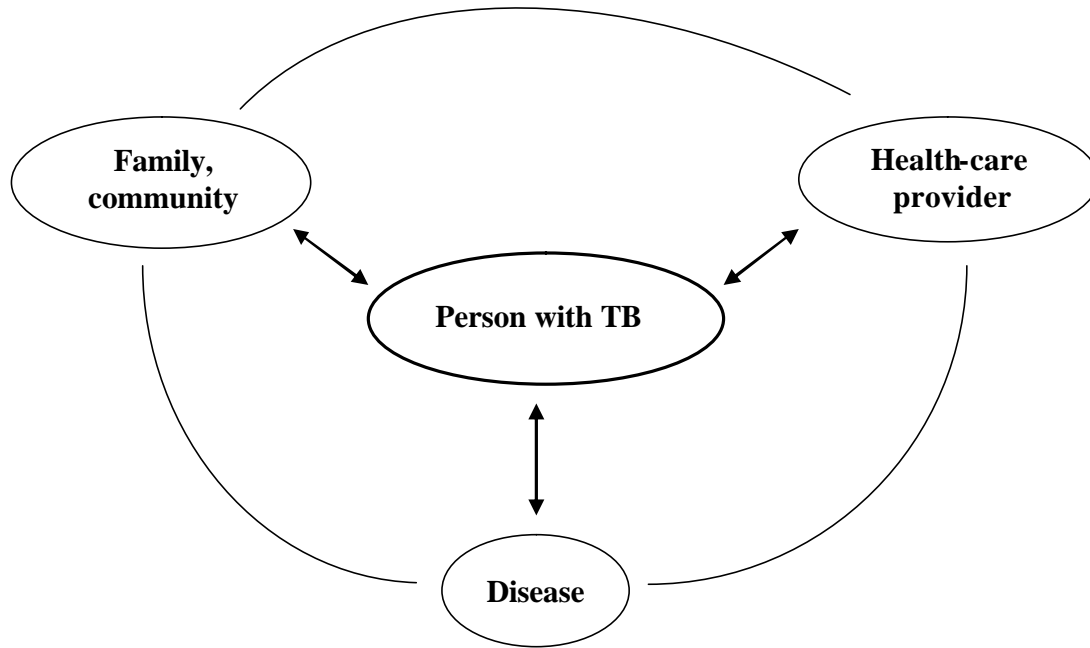
effective treatment. The paper examines the nature of the illness burden from three vantage points: the TB patient, the community (i.e. poor urban residents without TB), and health care providers. We examined the suffering coming from the personal distress of having TB and its social implications. The views of the community clarify the context of TB illness experience and social stigma. Consideration of the relationship between patients and providers shows how this relationship may also contribute to patients' distress. Our approach in this study is guided by the principles of cultural epidemiology. Cultural epidemiology provides an approach integrating frameworks and methods from epidemiology and anthropology to characterise illness experience from the perspective of affected people, meanings of illness and illness-related behaviour (Weiss, 2001). Figure 4.1 outlines this conceptual framework. Focussing on illness experience indicates the importance of other complementary contexts accounting for the quality and effectiveness of health systems for TB control. These include consideration of political and socio-economic constraints and limited resources for public health. Our study aimed at identifying key features of TB-related illness experience. These include patients' personal accounts of the illness and illness meanings (as suggested by consideration of the semantics for specifying TB), attention to the impact of social responses and illness-related stigma, the experience of treatment for TB, and the nature of interactions between patients and providers.



Figure 4.1

## ILLNESS EXPERIENCE OF PEOPLE WITH TUBERCULOSIS

### A) The Actors



### B) The Features

#### *Somatic impact:*

- Signs and symptoms
- Side effects of drugs
- Propagation of TB bacilli into the air

#### *Psychological impact:*

- Anxiety, sadness
- Loss of self-esteem
- Feelings of guilt
- Self-perceived stigma

#### *Social impact:*

- Enacted stigma
- Strained relationships
- Changes in lifestyle
- Health system and provider interactions

## **METHODOLOGY**

### 1. Introduction and setting

Research in Metro Manila included semi-structured interviews with former TB patients treated in public health centres of Malabon, a municipality of Metro Manila, focus group discussions with non-affected community members of three urban poor areas of Metro Manila, and administration of questionnaires to the health care providers of the 23 public health centres of Malabon. Roughly one third of Malabon's 400,000 inhabitants belongs to the poor. Metro Manila had around 11 million inhabitants in the year 2000 (United Nations Population Division, 2000).

Consent for the study was obtained from the municipal health office of Malabon and from the Department of Health in Manila. The patients were free to refuse an interview.

### 2. The patient interviews

To characterise illness experiences, including the context of treatment, 319 patient interviews were administered. These 319 patients, all smear-positive, had received treatment in the public health centres of Malabon.

The interviews inquired about the experience of symptoms of TB and focussed on key illness experience and treatment experience.

The semi-structured interview was administered to these former patients in their homes at a point 1 to 16 months after the end of treatment. This instrument, consisting of 131 questions, was written in the Filipino language (Tagalog), and it was developed

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through a process of peer review and pre-testing (see Annex). Experience of the first author (CA) with four years of prior residence in impoverished urban areas of Metro Manila and fluency in Tagalog facilitated the development and administration of the research instrument. Culturally appropriate interactions with respondents, informed by extensive local experience of the principal investigator (CA) and the other interviewers, helped to ensure conscientious responses and valid data.

Sixty-one questions were self-administered. The remaining questions were answered in an interview at a subsequent visit to the respondents. We decided upon this approach because answering the entire questionnaire in a single-session interview would have required about 50 minutes, and we were reluctant to come to people's homes and request this much time. We also expected that some of the more personal questions would be answered more candidly if the respondent could answer these questions privately. Questions for self-report were closed and simple. Other questions that required more careful explanation were administered by an interviewer. Twelve questions were open-ended. Interviewers administered the entire interview to patients who had difficulty reading or understanding the self-report questions (approximately seven patients), or who preferred having an interviewer for the whole questionnaire (approximately 50% of the sample).

A total of 812 sputum smear-positive patients who were registered in the records of the 23 health centres of Malabon between 1 January 1996 and 31 July 1997 were identified. All had been treated in a non-DOTS programme in the governmental health centres. Finding these former patients, however, proved to be difficult; only 319 (39%) could be found and interviewed.

### 3. Focus group discussions (FGDs)

Three focus group discussions among non-affected lay people living in poor urban areas considered social and emotional effects of having TB and ideas about people with TB, including stigma. They also prompted discussion of the expression 'weak lungs' (*mahina ang baga*) which is widely used for TB. The FGDs were tape-recorded and transcribed for analysis.

The FGDs were held in the participants' communities in non-medical settings. In all three groups, the participants knew each other by their first names. All the participants knew the first author at least casually. Each discussion group consisted of nine participants, selected by convenience sampling. None of the participants had TB at the time of the FGD. However, some of the participants had had TB in the past. Two groups consisted of women and men of various ages. The third group was very homogeneous, consisting of young men with a history of drug abuse from various urban poor areas of Metro Manila who were in a Christian 'rehabilitation programme'. Thus, in this focus group, the role of vices possibly received undue emphasis. Apart from this, we believe the statements of the FGDs are generally representative for the urban poor population of Metro Manila.

### 4. The health care provider questionnaires

Various health care providers of the 23 health centres, namely 21 physicians, 25 nurses, 23 midwives and 35 barangay health workers (health volunteers with a basic training) received and filled in self-administered questionnaires. These questionnaires contained questions concerning the TB patient and apart from the physicians' questionnaire, they also specifically addressed the interaction between the TB patient and the health care providers.

5. Statistical analyses

All data derived from the questionnaires were processed using Epi Info software package (version 6.04). For statistical analysis, Epi Info, STATA and SAS were used. Categorical data were compared using Pearson's Chi-square test ( $X^2$ ).

Our questionnaires had seven items suggesting stigma-related social distress. These items were feeling embarrassed about giving sputum, feeling embarrassed about having TB, feeling ostracised due to having TB, a loss of self-worth, guilt about having TB, feeling depressed about having TB, and fear of dying. We combined these items additively with equal weight to create an index of stigma, and validated this index with the Cronbach's alpha statistic (Cronbach, 1951), using the SAS statistical programme. This analysis indicated one item inconsistent with the others: dropping feeling embarrassed about giving sputum improved alpha from 0.721 to 0.735. This index of stigma was then correlated to various variables, and the non-parametric Kruskal-Wallis equality of populations rank test was used to compare the resulting means. For the variable age, Spearman's non-parametric correlation was used. The variables with p-values below 0.20 ( $n = 15$ ) were used for the linear regression. All the variables with  $p < 0.15$  were included in a multivariate regression model (154 observations, stepwise backward regression, verifying the distribution of residuals was close to normal). STATA statistical software was used (Stata Corporation, 1999).

## **RESULTS**

After briefly describing the sample of TB patients, we focus on their personal illness experience and complement the findings with qualitative data from the FGDs. The section on community attitudes towards TB patients is based on findings from the FGDs. A section on TB illness semantics sheds further light on TB and its stigma. We also present the patients' views on the health centre personnel and end with data from questionnaires for the health care providers.

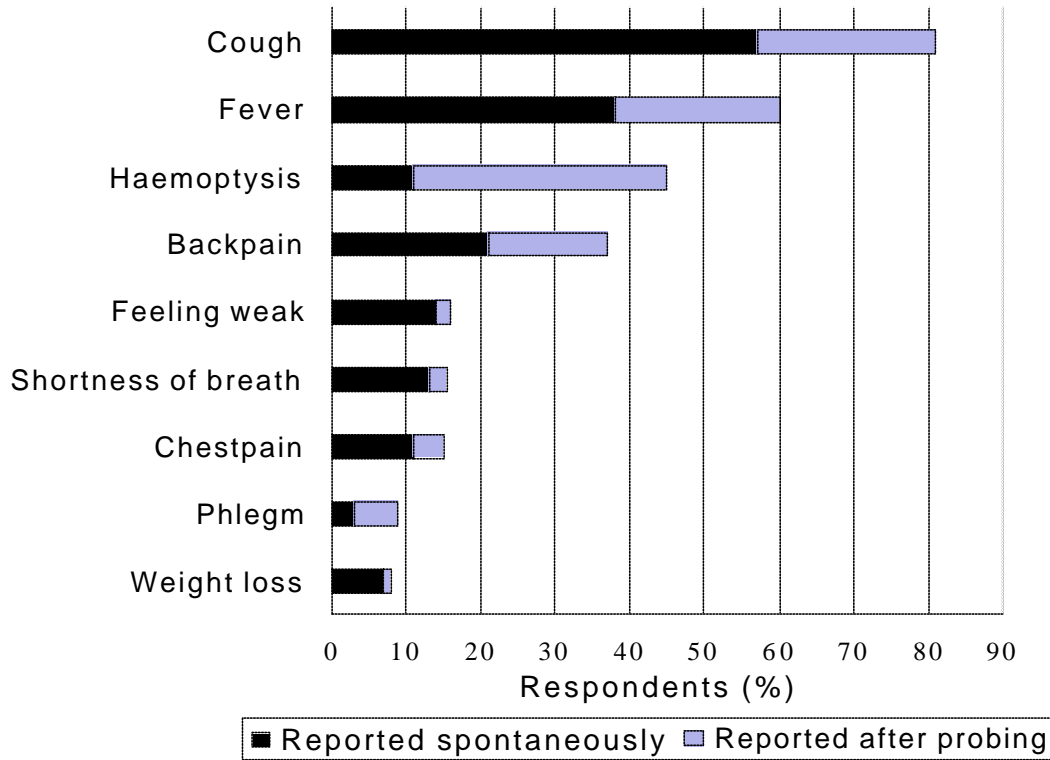
### **A) Findings from the patient survey and the FGDs**

#### Sample characteristics of the TB patients

We interviewed 319 patients. Most were male (70%). The mean age was 43.8 years; 4% were younger than 20 years of age, and 5% were older than 70 years. Most (82%) were in the 15 to 59 year age group. Eighty-seven percent identified themselves as poor (31% chose 'rather poor', 49% 'poor' and 7% 'very poor'). About a quarter of the sample (27%) reported having previously had TB. Sixty-eight percent of the respondents reported that they had completed their treatment.

Figure 4.2 presents the clinical symptoms of the respondents at the point when they became aware of their illness. The most common symptoms were cough (81%), fever (60%), haemoptysis (44%), and backpain (37%).

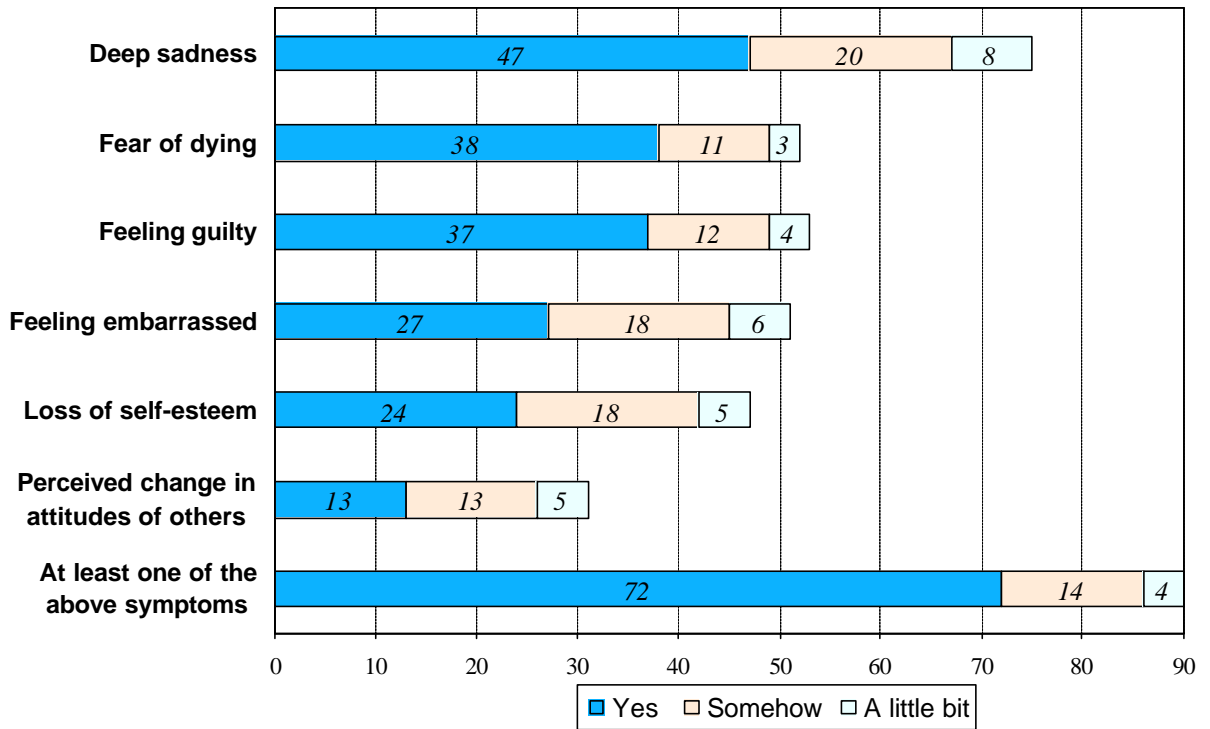
**Figure 4.2: Recalled symptoms at illness onset (n = 319)**



Illness experience: emotional impact

The patients were asked how finding out they had TB had affected their emotional state. The following feelings were 'definitely' or 'somehow' reported: sadness by 67% of the respondents, fear of dying by 49%, feeling guilty by 49%, feelings of embarrassment by 45%, loss of self-esteem by 41%, and feeling ostracised by 26%. The vast majority (86%) experienced at least one of these various forms of emotional distress. Figure 4.3 presents details.

**Figure 4.3: Symptoms of TB-Related Emotional Distress after Learning Diagnosis (percentage; n = 319)**



The following quotes from the FGDs illustrate the social dimension of the emotional distress:

- "A TB patient feels very depressed. He is ill-tempered and irritable, especially if he feels being detested." (mother, approximately 45 years old)
- "What must not be said is: 'Gosh, maybe we get infected through you!' Someone with TB is in a pitiful state and maybe after having heard you say this he will take poison to kill himself." (mother, approximately 50 years old)



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TB is a stigmatised disease. The following quotes from the FGDs illustrate that TB sufferers may have a 'spoiled' or 'marked' identity, causing them to feel *mahiya* (the Filipino *mahiya* means embarrassed, ashamed, shy):

- "This state of feeling embarrassed goes on for months. For some months you don't go out of your house. And if you do go out, then only for a short time. Unlike when you are normal, then you are outside very often. I experienced this when I was sick [with TB]; I was embarrassed. I only left our house when I had to do something important. Then you are back in your house and there you think about your difficult situation." (father, approximately 30 years old who had TB some years ago)
- "A TB patient has self-pity. He thinks he is not entitled or worth to meet other people." (mother, approximately 45 years old)

For one quarter of the respondents feelings of embarrassment occurred also during the diagnostic process: 25% said giving sputum was embarrassing (7% clearly, 13% somewhat, and 5% slightly embarrassing). The section 'community attitudes' discusses stigma from the perspective of the non-affected person.

In a bi-variate analysis, being male was found to be significantly associated with having a higher index of stigma (Kruskal-Wallis equality of populations rank test:  $p = 0.03$ ,  $X^2 = 4.6$ ). Looking at the single items in the index of stigma, it was found that feeling ostracised and/or embarrassed was more common among men: 29% of the men reported feeling ostracised, compared with 18% of women ( $X^2 = 4.32$ ,  $p = 0.04$ ). And 49% of the men reported feeling embarrassed, compared with 35% of women ( $X^2 = 5.57$ ,  $p = 0.02$ ). Among the single respondents, feeling embarrassed was not more common among men: 55% of these men felt embarrassed and 58% of these women felt embarrassed;  $p = 0.8$ ). Young people were more likely to suffer from feelings of embarrassment than older people ( $X^2 = 10.66$ , with 4 degrees of freedom;  $p = 0.03$ ).

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In a multiple regression analysis, the following six patient features were shown to be associated with a higher index of stigma: fearing that the TB illness might come back (fear of relapse) ( $p < 0.001$ ); having TB for at least the second time ( $p = 0.002$ ); believing TB was a dangerous illness ( $p = 0.004$ ); *not* having been found by active case finding (active case finding was only done in urban poor areas) ( $p = 0.005$ ); having separated their eating utensils due to their TB illness ( $p = 0.009$ ); and having been a tobacco smoker before anti-TB treatment was started ( $p = 0.048$ ). Also, increasing age was found to be marginally associated with lower index of stigma ( $p = 0.09$ ). These seven factors explained 40% of the variance of the index of stigma (model R-squared).

Fears of falling sick again with TB persisted after completing treatment for 80% (for 50% this fear was 'definite', for 23% 'somewhat' and for 7% 'small'). One reason for this might be that only 26% felt 'fully healed' and 16% felt 'almost healed' at the time of interview (6% were not sure, 38% felt 'not really healed' and 14% felt clearly not healed). However, even among those who felt 'fully healed' or 'almost healed' at the time of the interview, 66% reported concern about relapse.

#### Impact on lifestyle

Respondents reported effects of TB on eating, sleeping, sexual activity, and what they called '*vices*' (mainly smoking tobacco and regularly drinking alcohol). Behavioural changes in these four areas of life were recommended, mainly in order to reduce the risk of infecting others with TB, but also to increase the chance of full recovery. Table 4.1 summarises behavioural changes in lifestyle.

Table 4.1: Behavioural changes while under treatment (n = 319)

Treatment-related behavioural changes	Number of respondents	%
Separate eating utensils:	172	54%
For up to 1 month only	20	6%
For more than 1 but less than 6 months	51	16%
For 6-12 months	61	19%
Up to the time of the interview	38	12%
Time span unclear	2	1%
Slept separately:	73	23%
For at least 6 months	44	14%
Reduced or renounced sexual activities:	57 (27% of 210*)	
For at least 6 months	33 (16% of 210)	

\* Only 210 of the respondents were married.

The advice of health workers influenced many of these behavioural changes. Fifty-one percent of the 172 respondents who separated their eating utensils from others in the household said that they were told to do so by health centre personnel (based on misconception that TB bacilli are spread through eating utensils). In the FGDs, the supposed role of eating utensils in spreading TB was mentioned at least twice in each group. Reflecting this widely held view, a 45-year-old woman explained: "If the one who has TB very often talks to you that's okay. But if he eats and uses your eating utensils, then you need to boil them in water before using these eating utensils he used."

Twenty-seven percent of the 73 respondents who said they slept separately reported that they were told to do so by health centre personnel.

Thirty-nine percent of the 57 married respondents who reduced or stopped sexual activities reported that they were told to do so by health centre personnel. In only one FGD was renouncing sexual activities mentioned, but not because of concern about contagion. The group considered exhausting activities, such as sexual intercourse, were not allowed for TB patients. A discussant in one FGD, however, said that TB bacilli could be transmitted through seminal fluid. Another FGD suggested another view, that TB is not transmitted by sexual intercourse. In the third FGD, sex was not mentioned.

Having TB can also bring about lifestyle changes that positively affect one's state of health such as reducing tobacco and alcohol consumption. Such behavioural changes can be expected to follow from a popular view, reported in patient interviews and the FGDs, that vices cause TB (see also Auer *et al.*, 2000). Seventy-one percent of the smokers said they stopped smoking while under treatment, and at the time of the interview, 45% still had not resumed smoking. And 85% of those consuming alcohol no longer drank while on treatment. At the time of the interview, 41% still had not resumed consuming alcohol. In all three FGDs, participants referred to such vices at least four times. For instance, a father (approximately 35 years old) explained: "It's in their lungs. Most of the old people, when they were still young, took alcoholic drinks on an empty stomach. This lowered their resistance. Then smoking came and too heavy consumption of alcoholic drinks."

Fifty-four percent of those who had smoked before TB was diagnosed suffered from feelings of guilt but only 43% of those who had *not* smoked before their diagnosis suffered from feelings of guilt ( $X^2 = 4.11$ ,  $p = 0.04$ ). There was no such association for alcohol consumption, however.

Experience of treatment

The interview inquired about the perceived effects of medication and side effects. It also considered the length of treatment and consequences of incomplete treatment. Respondents were also asked how long they considered themselves contagious once regular treatment started.

Generally, the respondents expressed confidence in the medication. More than one-third (35%) were 'very confident' about the curing effect of the treatment, 56% 'confident', 6% 'rather confident', and 1% 'not confident'. Three respondents (1%) were uncertain.

Nine percent of the 319 respondents reported experience of considerable side effects, and 21% reported minor side effects. Approximately one-third of the respondents (35%) feared side effects (7% reported 'strong fear', 14% 'considerable fear', and 14% 'some fear').

Most respondents (84%) acknowledged a need for treatment for a period of six months; 11% expressed some doubts, 3% strong doubts, and 2% were uncertain. And 97% stated that non-completion of treatment would have negative consequences.

Whereas length of treatment and consequences of non-completion were well known, there was widespread lack of knowledge about the duration of contagiousness once regular treatment started. Only 24% said, in accordance with biomedical knowledge, that they remained contagious up to one month. Most (56%) did not know how long they would remain contagious. Ten percent said they would be contagious for two to three months; and another 10% said it would be even longer; and 10% did not consider TB contagious at all.

Community attitudes: social impact and the stigma of tuberculosis

The FGDs with non-affected laypersons explored the social and stigma dimensions of the illness experience. FGD participants indicated that patients feel embarrassed about being contagious and that the contagious nature of TB causes others to avoid TB patients. The same discussants, however, recognised the need to support the TB patients. Self-perceived stigma was seen to be more prevalent than enacted stigma.

The following quotes illustrate how feeling embarrassed or ashamed (*mahiya*) mainly arises from concern about being infectious:

- "I think if I had TB, I would feel embarrassed to meet other people. Because they would be in a pitiful state if they get infected because I have TB. I probably would stay on my own, because I have TB. I would no longer meet others." (male, approximately 20 years old)

Being contagious may mean that people avoid a TB patient. The following typical FGD quote illustrates this: "What the people think about someone with TB is: 'Oh, this one has a sickness. Let us not approach him!' This is how the people's thinking always is." (mother, approximately 50 years old). However, the basic attitude people have towards someone with TB is ambivalent; feelings of concern and compassion combat with the fear of getting infected. A 25-year-old man explained this as follows: "It depends who the TB patient is for you. Of course, if it is someone dear to you then it may really be your desire to serve him. (...) Even though you are afraid. But you need to serve him. Because he trusts in you. It is your responsibility."

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In close relationships, 'acceptance' of the TB patient seems to be the rule. Still, it was stated in all three FGDs that TB patients are generally feared/avoided. It was also expressed (once in one FGD and three times in the other two FGDs) that TB patients are sometimes detested or feel detested (the Filipino word - *pinandirian* - can be translated as being detested, abhorred, loathed, disgusted):

- “Some TB patients say that they merely have ‘weak lungs’, because they fear their friends no longer come to them. They fear being detested. That is why they lie so that the people don’t stay away from them.” (male, approximately 25 years old)
- "I think we must give ‘special treatment’ to TB patients. What should not happen is that when we see a TB patient then we seem to detest him. (...) I know of a case when a TB patient killed himself. He was detested.“ (father, approximately 35 years old)

And in an informal one-to-one interview, a young lady from another urban poor area said: "Having TB is like having AIDS!"

One FGD discussed the question whether the TB patients are really ostracised or being avoided and detested or incorrectly *perceive* discrimination. Considering whether there was any legitimate basis for feeling ostracised, the discussants made the following points:

- “No, because the TB patient gets healed.” (mother, approximately 50 years old)
- “No. It is in yourself only, you see. And if you are strongly embarrassed, then the people will inquire about you: “Why is he so embarrassed?”. So instead that the people don’t find out [your illness] they find it out all the more.” (female, approximately 20 years old).

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In another FGD, too it was stated that it is only in the patient himself. Another participant reinforced this by saying: “It is only self-pity.” On the other hand, all three FGDs mentioned that TB patients are being avoided.

The FGDs discussed whether or not someone who had had TB in the past has a reduced chance of getting married. It was found that having had TB does not reduce, or only minimally reduces the chances of getting married. Still, two reasons were given why young men might have a reduced chance. One, TB is a sickness strongly associated with vices which makes the man less attractive. Two, having had TB may cast doubts on the man’s capability to act as successful breadwinner. On the other hand, in one FGD it was said that the young man was less disadvantaged than the young lady because in the courting process it is the man who is active.

#### Illness semantics: the expression ‘weak lungs’ (*mahina ang baga*)

Words clearly indicate the nature of the social response and stigma. This section examines the impact of the name given to the illness tuberculosis. Most of our interviewed TB patients did not call their illness 'TB'. When asked whether their illness had been 'TB', 'illness in the lungs' (*sakit sa baga*) or 'weak lungs' (*mahina ang baga*), only 23% stated 'TB'. 'Illness in the lungs' was used by 37%, and 'weak lungs' by 34% (1.3% of the respondents said their illness was 'cough', and 2% were uncertain).

The findings of the FGDs suggest that the term 'weak lungs' has three kinds of meanings. First, the literal meaning: a person with 'weak lungs' is more prone to getting sick, especially to sicknesses of the respiratory tract. But 'weak lungs' is not or not yet a



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disease. Someone with a negative chest X-ray may still have 'weak lungs'. Secondly, it refers to an illness less severe than TB: a minimal chest X-ray finding may be considered to be 'weak lungs'. Having 'weak lungs' is also seen to be a risk factor for developing TB, as this FGD quote illustrates: “From 'weak lungs' to TB is a step-to-step process. But some have directly TB.” (male, approximately 20 years old). However, there was one participant (male, approximately 25 years old) who said that 'weak lungs' was more severe than TB arguing that it can be a general, chronic condition. Thirdly, 'weak lungs' is frequently used as a euphemistic expression for TB. Doctors and TB patients use 'weak lungs' to avoid the embarrassing and/or frightening term TB:

- “Some use the expression 'weak lungs'. They have TB, but they say they have 'weak lungs'.” (mother, approximately 50 years old)
- “If your 'inner strength' is not so strong, then the doctors say you have 'weak lungs'. They will not tell you directly that you have TB. If the doctor is your friend he will not tell you directly. He may think: ‘O my poor friend, I know his character; he may be depressed. I'll just say: You have 'weak lungs'; just take these vitamins<sup>1</sup>.”  
(mother, approximately 50 years old)

In short, our findings from the patient interviews and the FGDs illustrate the partly severe undefined and hidden burden of TB and the social dynamics enforcing this burden.

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<sup>1</sup> Some doctors call isoniazid, and some even the whole anti-TB treatment, ‘vitamins for the lungs’ (*bitamina sa бага*) (see also Easton, 1998; Nichter, 1994).

## **B) Patient and health care provider perceptions**

A substantial component of illness experience results from the interaction between patients and the health system. We examined these interactions from both patient and provider perspectives.

The patients were asked to grade their experiences with the personnel of the health centres in terms of three indicators of received quality of service. Most stated that the competence of the personnel, the personnel's explanation given to them and their kindness were of a good standard. A minority perceived their competence, their explanations, and/or their friendliness to be unsatisfactory (16%, 16%, and 11%, respectively). These perceptions did not differ among male and female patients, nor did they differ among different age groups. However, when comparing respondents who rated themselves to be relatively well off with those who felt they belonged to the poor or very poor, those better off were more sceptical: 22% of those who felt to be better off were not satisfied with the competence of the personnel while only 13% of those who rated themselves to be poor or very poor were not satisfied ( $X^2 = 4.03$ ,  $p = 0.04$ ). Those patients who had initially consulted a private doctor were not less satisfied with the health centre personnel compared to those who had initially consulted the health centre, a hospital or a traditional healer. Nor was there any evidence that those with a high educational level were more critical. However, those who did not feel fully healed (at the time of the interview) were more sceptical about the competence of the staff: 20% of those who did not feel fully healed were not satisfied with the competence of the health centre personnel while only 7% of those who felt fully healed were not satisfied ( $X^2 = 6.8$ ,  $p = 0.009$ ). The corresponding rates were similar when those who had not completed treatment were compared with those who had completed treatment (26% vs. 12%;  $X^2 = 8.98$ ,  $p = 0.003$ ).

The health centre staff (69 physicians, nurses and midwives) and 35 barangay health volunteers were asked what caused patients to prematurely stop treatment. Patients getting fed up or lazy was the most common response. Especially among the barangay health volunteers, this was seen as an important reason (mentioned by 49%). Side effects was the second most common response (mentioned by 30%). Table 4.2 presents details.

Table 4.2: Patients' reasons for dropping out of treatment, according to health care providers

Reasons stated	Patients' reasons for dropping out of treatment, according to health care providers			
	Physicians (n = 21)	Nurses and midwives (n = 48)	Barangay health workers (n = 35)	Total of all three groups of providers (n = 104)
Patients get lazy or fed up	19%	27%	49%	33%
Side effects	43%	35%	14%	30%
Patients feel cured	24%	29%	23%	26%
Treatment not available	29%	15%	26%	21%
Patients lack knowledge	19%	8%	3%	9%
Patients run out of money	0%	4%	14%	7%
Patients are hard-headed	5%	6%	6%	6%

In another part of the questionnaire where the physicians, nurses and midwives were asked to grade features of case holding in terms of being a problem or not, patients not realising the importance of completing treatment was seen as the most prominent problem; it was mentioned by 76% (48/63).

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Nine of the 35 barangay health volunteers (26%) stated it was hard to make follow-up visits to the TB patients, half of them felt it was 'somehow hard', and 14% felt it was easy. Half of them (51%) explained that many of their TB patients were hot-headed, and 37% perceived many of their TB patients to be ill-tempered. One fourth (23%) felt that their TB patients got angry easily. Other traits mentioned were over-sensitive, lazy and shy. Positive traits of TB patients were not mentioned. And only 29% of the barangay health volunteers felt that their TB patients' knowledge on TB was sufficient. Similarly, merely 37% stated that only *few* of their TB patients have inappropriate beliefs about TB.

Information about TB given to patients commonly mentioned that it is a contagious disease. However, a substantial proportion of the health care providers (35% of the physicians, 64% of the nurses and midwives, and 59% of the barangay health volunteers) said they would tell their TB patients that they were still contagious for *more* than one month once treatment had started. Other common advice given by the nurses, midwives and barangay health volunteers was to tell their TB patients to stop or at least reduce smoking, to separate eating utensils and to eat nutritious food. Ninety-six percent of the 48 nurses and midwives give these three kinds of health advice. And 81% (39/48) recommend stopping or at least reducing use of alcohol. Seventy-three percent (35/48) tell their TB patients to sleep separately. The only other advice mentioned by more than 30% (namely by 69%) was to encourage others in the patient's household to get a check-up.

The barangay health volunteers gave similar advice. More than half of them encouraged the patients to eat nutritious food, stop vices (alcohol, smoking, illegal drugs), separate eating utensils, and reduce or stop sexual activity.

In short, a small proportion of patients was not content with the personnel in the health centres and the health care providers tended to blame patients. Also, some health advice was based on misconceptions.

## **DISCUSSION**

This study examines aspects of the illness burden that complement more commonly cited aspects of disease burden. It considers the intangible costs of fear, diminished self-worth, depression, and social distress, as well as the role of the health care providers, factors that also affect help seeking and treatment adherence. We found that illness-related and treatment-related changes of behaviour have two main purposes. One, to avoid infecting others, and two to hasten recovery. The degree of infectiousness of TB is commonly overestimated and the ability of the drugs to make a TB patient non-infectious is underestimated. This results in medically unjustifiable responses, such as a prolonged avoidance of the patients towards other people and of the people towards the patients, thereby maintaining stigma and contributing to the burden of illness.

### Stigma

We found that the TB patient's perception of being ostracised/avoided (self-perceived stigma) is stronger than the actual ostracism (enacted stigma). The self-perceived stigma (an individual's sense of 'spoiled' or 'marked' identity) may be stronger than the enacted stigma (the degree and ways how others devalue someone with TB and disqualify her or him from full social acceptance). Other studies in the Philippines have also shown that TB is a stigmatised disease (Nichter, 1994; Ortega *et al.*, 1991; Sarmiento, 1990; Philippine Department of Health, 1984). In a rural area, the informants stated that people thought having TB was something 'shameful' or 'a bad mark to the family' (Nichter,

1994). Nichter's study also showed that the term 'weak lungs' is mainly used to avoid the stigma-loaded term 'TB'. Similarly, another study in the Philippines found that only 13% of a sample of TB patients under treatment labelled their illness as 'TB' (Valeza *et al.*, 1992). Avoiding the term 'TB' or 'tuberculosis' is common: in Vietnam (Johansson *et al.*, 1996) and in Colombia (Jaramillo, 1998), the terms 'lung disease' and 'illness of the lungs' (*enfermo de los pulmones*), respectively are used.

It is interesting that those found by active case finding had a lower index of stigma. In Malabon, active case finding basically consisted of microscopists going through urban poor areas and openly inviting people with cough for more than one or two weeks to give a sputum sample. It is thus not surprising that people that tend to feel stigmatised are not willing to positively respond to such an invitation that is given in the midst of their community. The DOTS approach does not recommend active case finding. But in the light of the low DOTS detection rates, there is reason to consider active case finding. Recently, Murray and Salomon (1998) argued for using active case finding. Our findings indicate that those TB patients most strongly affected by stigma may not be reached with active case finding that is not sensitive to the impact of stigma.

We also found a strong association between stigma and separating eating utensils. The FGDs showed that the fear of spreading the disease is an important reason for feeling embarrassed, and thus, those suffering from stigma may want to do something practical to reduce their feeling of powerlessness and fear. However, the activity of separating eating utensils does *not* reduce the chance of spreading the disease. The cumbersome practice to separate eating utensils (and in many cases also to boil them in water) has the potential to aggravate stigma and the feelings of alienation and guilt, and narratives of TB patients we have confirm this. It is also illustrated by the comment of a private doctor who said: "Filipinos are sensitive when it comes to separating eating utensils." We believe it is not

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advisable to recommend a stigma-enhancing and ineffective activity; inaccurate and imprecise knowledge, specifically the wrong assumption that burdensome practices need to be done for a prolonged time, may also lead to denial and fatalism. This may result in not doing the few measures that are medically justified to avoid the spread of TB and to hasten recovery.

Care must be taken to distinguish between medically justified and necessary behavioural changes that are to be promoted (e.g. "don't cough openly during the early weeks of treatment") and unnecessary behavioural changes that come from an inappropriate and stigma-driven understanding (e.g. "don't mix with people while on treatment"). In this, it is healthy to acknowledge the tension between wanting to avoid behavioural changes that increase stigma (e.g. sleeping separately) and the obligation to avoid the risk of spreading TB. What complicates the matter is that treatment does not have the same effect on all patients. For instance, for most patients it is correct to state that after two to four weeks of regular treatment, his or her disease is no longer contagious. But in the light of the fact that multidrug-resistant TB (MDR-TB) is not uncommon (a recent study in another part of Metro Manila found that 7% of TB patients treated in public health centres had MDR-TB; report forthcoming. See also chapter 8), it might not be advisable to tell the patients that after some weeks of treatment contagion no longer is an issue. This is a difficult trade-off: is it justified to tell TB patients to be concerned for up to one year about spreading their disease when for at least 90% their concern is no longer justified after some weeks of treatment? Since the risk of MDR-TB is much higher in previously treated patients a sensible compromise may be to tell all previously treated patients to be conscious about the danger of spreading their disease for a prolonged time.

We found that previously treated TB patients suffer more under stigma. The added stigma among previously treated TB patients may be a reason why in some studies (e.g.

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Santha *et al.*, 2002; Zwarenstein *et al.*, 1998) previously treated TB patients were found to be under a high risk of not completing treatment. It is interesting to note that in the study of Zwarenstein and colleagues (1998), clinic-based DOT seemed to discourage re-treatment patients from completing treatment while in another study in South Africa clinic-based DOT worked quite well for re-treatment patients (Kironde & Meintjies 2002). In our study, the patients were not under directly observed therapy (DOT). Several studies have indicated that implementing DOT in areas where social stigma is pronounced can be problematic (Singh *et al.*, 2002; Ngamvithayapong *et al.*, 2001; Balasubramanian *et al.*, 2000). A recent review concluded that stigma is a reason for non-completion of treatment (Thomas, 2002). Clearly, there is a lack of understanding about the role of stigma and its potential for complicating TB care, e.g. adherence to treatment. The role and relationship of the four factors (i) stigma, (ii) appropriate knowledge and health education, (iii) infectivity, and (iv) mode of treatment supervision need to be further explored.

#### Validity of the findings

In view of the size and diversity of Metro Manila, there are of course limitations of how widely we may generalise findings. Several additional points in that regard should be considered.

Only 39% of the 812 known smear-positive TB patients could be found and interviewed. Many patients moved back to the province. Others could not be found due to inadequate addresses in the health centre records. The bias was probably less of a factor than the low percentage (39%) indicates, because many of the patients came from rural areas, and they were likely to have been in Malabon only for their treatment. Consequently, we interviewed more than 39% of the affected persons residing in Malabon.



Refusal to be interviewed constitutes only a minimal potential bias since only ten former patients declined to be interviewed.

Recall bias may be a limitation of the study, inasmuch as patients were interviewed retrospectively (1 to 16 months after the end of treatment). Social desirability bias also needs to be considered. Thus, in spite of having related to the interviewees in an informal and culturally appropriate way, the proportion of patients reporting distressful emotions is probably an underestimate. In addition, we found only 29% stated to have perceived their illness as 'very serious' or 'serious'; this seems to be an underestimation in the light of the finding that 49% reported fear of dying. It should be kept in mind that reported indicators of stigma seem to be significantly lower for disease-affected respondents compared to the non-affected, as a study in Africa among patients of onchocercal skin disease showed (Vlassoff *et al.*, 2000). This point also needs to be considered regarding the FGDs: the participants were non-affected urban poor residents, not TB patients.

#### Implications for TB control

The substantial emotional and social burden of TB makes it especially important that health care providers give accurate, relevant and appropriate information in an empathic, empowering and encouraging way. The social and emotional implications of health advice must carefully be considered. Several areas of specific concern arise from the results.

First, health education among the health care providers and the general population should address misconceptions to fasten the case finding process, support case holding, and reduce stigma. For instance, the misperception that using eating utensils of a

#### *Chapter 4: TB illness experience: three perspectives*

TB patient is a way of getting TB is prevalent among the public, the public health care providers, and among private practitioners of Malabon (report forthcoming). It is important that the health care providers refrain from unnecessary and burdensome health education messages. On the other hand, the importance of completing treatment must be emphasised. Other medical advice given to minimise the spread of TB, such as avoiding open coughing, sleeping separate from others and not having sex are justified while the TB patient is still infectious. However, we found that only one fourth of the interviewed patients knew that being contagious persists up to one month only once proper treatment has started and that many health care providers overestimated the length of being contagious. In the light of stigma, it is important to correctly inform the patient that this burdensome state of being contagious does not last long (however, as discussed, in settings with high rates of MDR-TB this is not true). It should also be considered that sleeping separately may not be possible in crowded living conditions and may increase the self-perceived stigma. Avoiding sex while on treatment may aggravate the intangible burden (i.e. it can create emotional and relational stress).

Secondly, correct terms to specify tuberculosis should be used, even though Filipino culture may encourage euphemisms. Telling TB patients that they merely have 'weak lungs' is misleading and may contribute – especially in the long term – to the spread of TB. Using the term 'weak lungs' may also promote self-medication and default from treatment by undermining appreciation of the serious nature of the illness. And the fact that 'weak lungs' can refer to TB as well as to acute respiratory infection further complicates treatment.

Thirdly, the health care providers should specifically address the patients' fear of dying and of experiencing a relapse. It should be explained that when being fully adherent to treatment, the chance of recovery is very high and the likelihood of relapse very small. The term 'weak lungs' may contribute to fear. Inasmuch as the term 'weak lungs' is also used for respiratory illnesses (Nichter, 1994), former TB patients who develop an acute respiratory infection may interpret this as a sign that TB ('weak lungs') is recurring.

Fourthly, the health care providers also need to be aware that gender plays a role. In our study, men seemed to be more prone than women to suffer from feeling embarrassed and ostracised, suggesting a need for special sensitivity towards men, especially since in the Philippines, most health centre personnel are female. Findings from studies in other countries suggest that women, especially unmarried women, are more affected by social stigma than men (Khan *et al.*, 2000; Rangan & Uplekar, 1999; Hudelson, 1999; Liefoghe *et al.*, 1995). Our finding that among the single respondents, women were slightly more likely to feel embarrassed than men also highlights the vulnerability of unmarried women.

Finally, patient support within the family and if possible also the community should be strengthened to reduce the adverse emotional and social impact of TB. An encouraging finding comes from a rural area of India where the support for the patient in the case holding process consisted not only of a family member as 'treatment partner' but also of a former TB patient and of the immediate neighbourhood of the TB patient. It was observed that TB largely lost its stigma over time (Schüth, 1998). This suggests that with innovative approaches, stigma can be reduced.

## **ACKNOWLEDGEMENTS**

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**HEALTH SEEKING AND PERCEIVED CAUSES OF TUBERCULOSIS AMONG PATIENTS IN MANILA, PHILIPPINES**

*Running title: Health seeking of TB patients in Manila*

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## **Health seeking and perceived causes of tuberculosis among patients in Manila, Philippines**

### **SUMMARY**

Inefficient case finding is an important stumbling block to successful control of tuberculosis (TB). Multiple health seeking may account for delayed case finding. Health seeking behaviour, health seeking delay, perceived causes, and perceived quality of care related to TB were studied in interviews with 319 sputum smear-positive TB patients. The patients were treated in 22 governmental health centres of Malabon, a municipality of Metro Manila, Philippines. Only 29% of the respondents had gone first to a health centre after onset of TB-related symptoms, and more than half (53%) had initially consulted a private doctor. A chest X-ray was obtained for nearly everyone (97%). Two-thirds of the patients (66%) had received a prescription for drugs, and 29% had purchased and taken anti-TB drugs for at least three weeks before they came to a governmental health centre. Concerning community interactions, 36% said they knew at least one person who had been treated for TB without success. The health seeking delay after symptom onset was relatively short – 64% of the respondents said they went to a health facility within one month. Case studies illustrate the rationale for health seeking and explain delayed initiation of appropriate treatment for many patients. Findings underscore the need for and indicate approaches to health communication for improved control of TB. Our findings from interview narratives also suggest that improved interpersonal skills of health centre staff and co-ordination between the private doctors and the health centres may substantially improve services for TB patients.

*Keywords:* pulmonary tuberculosis, health seeking, health providers, perceived causes of TB, Philippines

## INTRODUCTION

Control strategies for TB involve two components: case finding and case holding. Currently, *active case finding*, i.e. attempts to screen populations at large or to target specific populations, is much less widely used than *passive case finding* (i.e. only those who come to the health facilities are screened and diagnosed) (Murray, 1994, pp. 603-4). Effective control requires case finding at an early stage of illness, both for the welfare of the patient and to minimise spread of the disease and development of drug resistance. Also, the case finding process should entail no more than minimal financial costs for the patient. Most TB patients are poor, and any money they may be required to spend for diagnosis and case finding may ultimately compromise case holding, that is, their ability to remain in treatment.

Many people with symptoms of tuberculosis first approach a private doctor (Pathania *et al.*, 1997; Valeza *et al.*, 1991). A process of multiple and varied help seeking that may be called ‘shopping’ for diagnosis and treatment thereby begins. Typically, poor patients end up in public health services, mainly because they cannot pay for prolonged care in the private sector (Nair *et al.*, 1997). Moving from one provider to another often delays the diagnosis and the start of treatment, and thus increases the likelihood of developing multi-drug resistant TB, and it often involves considerable costs to patients. Several reasons may lead to this ‘shopping’: (i) the felt need of the patients to explore alternative providers, especially when symptoms persist or re-appear; (ii) lack of trust in the public health services; (iii) sub-optimal health services, and (iv) financial constraints that require patients to shift from more expensive providers they see initially to others they can afford.

A body of literature documents how effective health seeking and case finding are influenced by the health system, community, family, and other personal issues (Pathania *et al.*, 1997; Rubel & Garro, 1992). Personal issues include the ways people experience their symptoms and illness, perceived causes and experiences with the health care system. A survey among TB patients of public health centres of Malabon, a municipality in Metro Manila, Philippines, examined these factors, considering how they may contribute to multiple health seeking and delayed treatment. The respondents’ experiences and perceptions about TB, their health seeking behaviour, health seeking delay and possible

determinants of this delay were established. Two case studies illustrate how these factors operate.

In 1997, the rate of TB cases registered in the health centres of Malabon was 325 per 100,000 inhabitants. There was a functional TB program operating but the DOTS strategy (*Directly Observed Treatment, Short-course*; the widely promoted strategy to control TB, now being used in more than 100 countries) (WHO, 1998a) had not yet been implemented. Twenty-three governmental health centres operate in Malabon, all of them offering TB services. At the time of the study, three of these health centres had laboratory facilities for sputum examination, and there were six teams of health workers engaged in active case finding and sputum microscopy in the low-income areas of Malabon.

## **METHODOLOGY**

Patients were surveyed in Malabon, an urban municipality of Metro Manila with approximately 360,000 inhabitants in 1996. A total of 812 sputum smear-positive (sm+) patients who were registered in the records of 22 of the 23 health centres between 1 January 1996 and 31 July 1997 were identified. One health centre did not have sm+ patients during the study period. Finding these former patients, however, proved to be difficult; only 319 (39%) could be found and interviewed.

A semi-structured interview, which included questionnaire items for self-report, was administered to former patients in their home at a point 1 to 16 months after the end of treatment. This interview-questionnaire of 131 questions, written in the Filipino language (known locally as Tagalog), was developed through a process of peer review and pre-testing (see Annex). Experience of the first author (CA), who had already spent four years residing in impoverished urban areas of Metro Manila and was fluent in Tagalog, facilitated the development and administration of the research instrument. Culturally appropriate interactions with respondents, informed by extensive local experience of the principal investigator (CA) and the other interviewers, helped to ensure honest responses and valid data.



Sixty-one questions were self-administered. The remaining questions were answered in an interview at a subsequent visit to the respondents. We decided upon this approach because answering the entire questionnaire in an interview would have required about 50 minutes, and we were reluctant to come to people's homes and request this much time for an interview. We also expected that some of the more personal questions would be answered more honestly if the respondent could complete the questionnaire in the absence of the interviewer. Questions for self-report were closed and simple (e.g. marital status, number of people in the patient's household), and they were self-administered. Other questions that required more careful explanation were administered by an interviewer. Twelve questions were open-ended. Interviewers administered the entire interview to patients who had difficulty reading (approximately five patients) or understanding the self-report questions, or who preferred having an interviewer (approximately 50% of the sample).

The interview included questions regarding the patient (e.g. marital status, education, socio-economic status). It also inquired about the emotional impact of having TB, about perceived quality of care received in the health centres and details about case finding and case holding. Perceived causes of tuberculosis were also explored. Consequently, the patients were asked to explain in general why someone may get TB ('health beliefs'), and they were also asked how they acquired TB in their own particular case ('explanatory models of one's own illness episode'). For the general case, they were asked to classify thirteen presented potential causes into 'definite causes', 'probable causes' or 'not causes' of TB. These potential causes were selected from a review of the literature and through ethnographically sensitive interaction with urban poor residents and TB patients over an extended time. Regarding causes of TB patients' own illness, only eight potential causes were presented to the respondents and the possible answers were 'yes or 'no'. Some causes that were included among response options for the question about why someone may get TB – such as drying sweat on the back, sleeplessness, and exposure to dust or chemicals – were not presented in this item regarding patients' own illness.

All data derived from the questionnaires were processed using Epi Info software package (version 6.04, USD Inc., Stone Mountain, GA, USA).

## RESULTS

### The sample

Among the respondents 70% were male, and 80% were between 20 to 60 years of age; 87% considered themselves to be poor. About a quarter of the sample (27%) reported having previously had TB, and so for them, the interview was not dealing with their first personal experience with TB.

What people know or perceive about TB when they are not yet affected is an important determinant of their health seeking. TB was found to be a well-known disease. Nearly everyone (84%) knew somebody who had had TB, and a quarter of the sample (27%) had a close friend or relative with the disease. A few more (28%) reported that when they first came for treatment, there was someone else with TB in their household. More than half (52%) knew someone who had died of it, and many knew people who had been in treatment, either successfully (57%) or unsuccessfully (36%).

Table 5.1 indicates respondents' ideas about the perceived dangerousness and risk of acquiring TB before becoming ill with TB. Approximately 20% of the respondents had considered TB to be only slightly dangerous or a harmless disease and 15% did not consider themselves vulnerable to TB.

**Table 5.1: Perceived dangerousness of TB and perceived risk of acquiring TB (n = 319)**

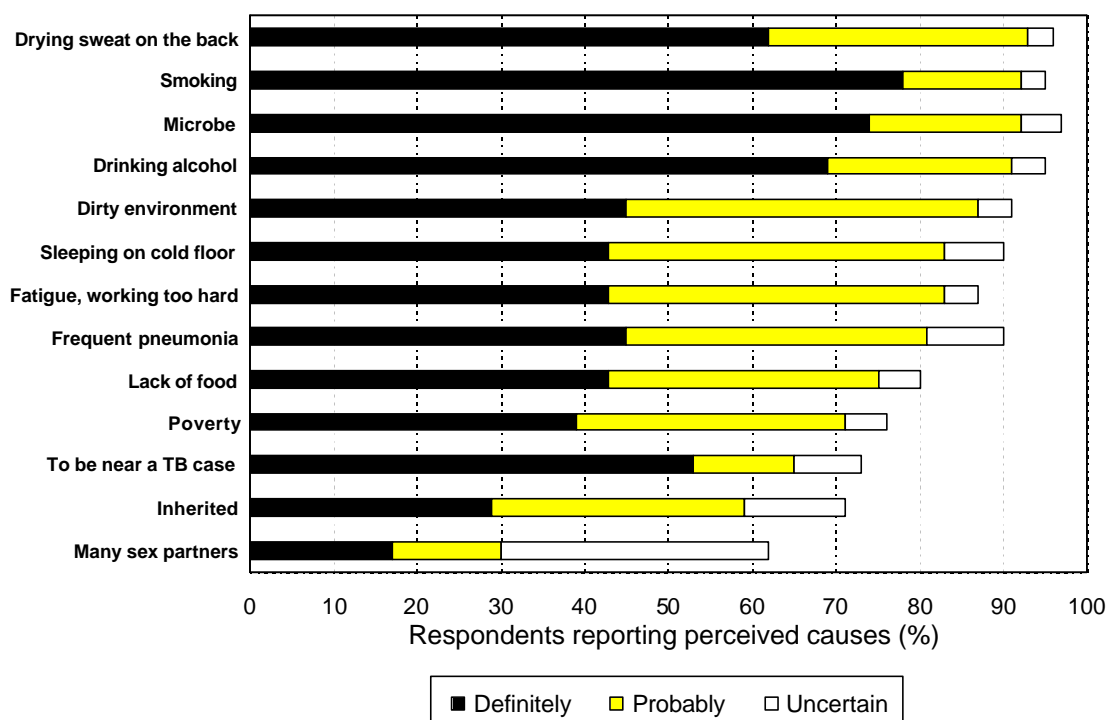
<b>Dangerousness of TB</b>	<b>Number</b>	<b>Percentage</b>
Really dangerous	177	55%
Quite dangerous	75	24%
Slightly dangerous	18	6%
Not dangerous	44	14%
Don't know	5	2%
<b>Perceived risk of acquiring TB</b>	<b>Number</b>	<b>Percentage</b>
Could get TB easily	144	45%
May get TB	114	36%
Probably would not get TB	30	9%
Definitely would not get TB	19	6%
Don't know	12	4%

Seventeen percent stated not to have known or to have been unsure whether their condition could be treated effectively (be it with drugs of Western medicine or in other ways).

Perceived causes

Perceived causes help to explain the meaning of a problem, whether it is considered a medical problem or a particular disease, and the implications based on cultural, familial, and personal background. Perceived causes may influence health seeking behaviour and treatment delay. Figure 5.1 presents the perceived causes of TB in general. The responses are summarised in order of the frequency of reports as definite or possible. Sweat drying on one’s back, followed by smoking, microbe, and drinking alcohol were the most frequently reported definite or possible cause of TB in general. A higher proportion of men than women considered ‘often smoking’ to be a definite or probable cause for someone getting TB (94% of the men vs 86% of the women;  $C^2 = 5.5$ ,  $p = 0.02$ ). Sex differences among respondents reporting ‘often drinking alcohol’ were similar; 94% of the men and 84% of the women considered this to be a definite or probable cause for getting TB ( $C^2 = 7.3$ ,  $p = 0.007$ ). On the other hand, fewer men than women reported fatigue or overwork to be a definite or probable cause for acquiring TB (80% of the men vs 91% of the women;  $C^2 = 5.3$ ,  $p = 0.02$ ).

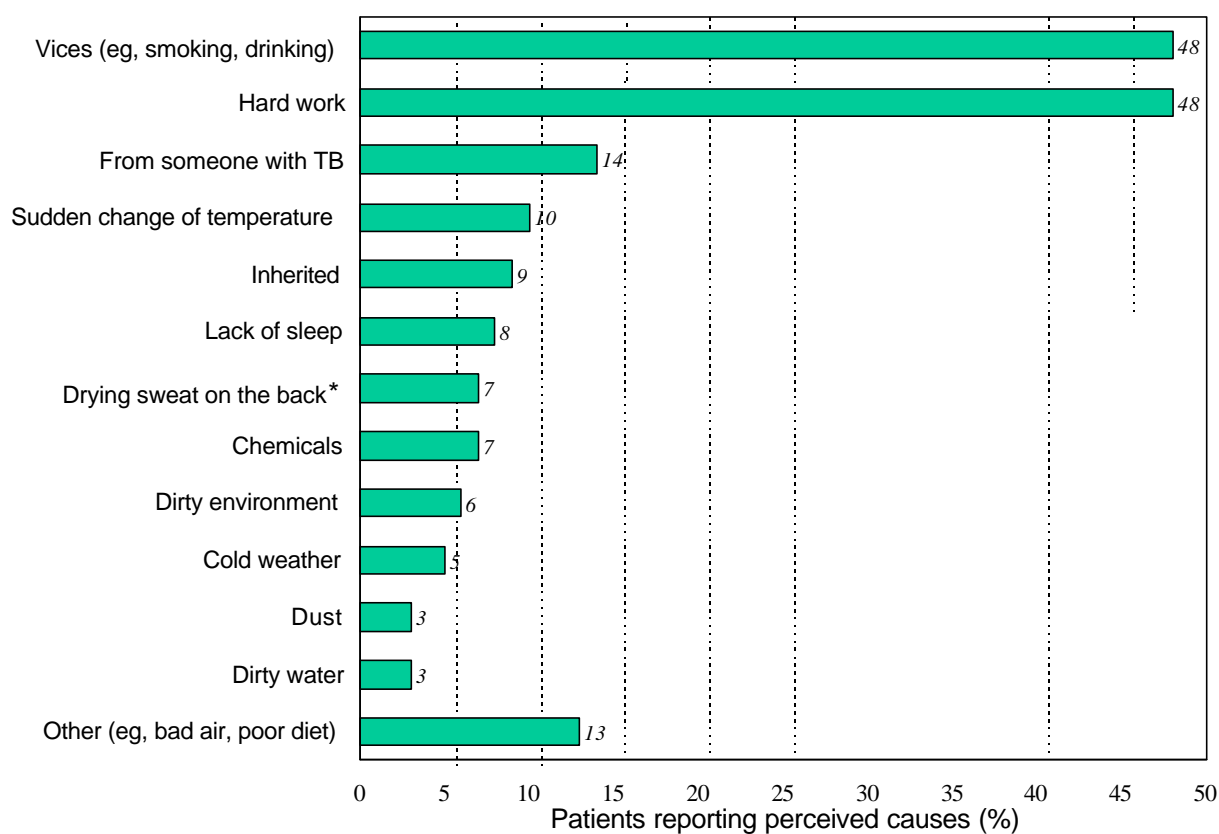
**Figure 5.1: Perceived causes of TB in general (n = 319)**



A subgroup of 216 patients was asked about the spread of TB, and notably, 12% did not recognise it to be contagious: 7% said it was not, and 5% said it was 'rather not' contagious.

Figure 5.2 summarises perceived causes reported by patients to explain how they themselves acquired TB. Sixty-two percent of the respondents gave more than one answer. Many emphasised a moral aspect of vulnerability: vices and hard work were mentioned much more frequently than mechanistic causes, such as person-to-person transmission.

**Figure 5.2: Perceived causes of patients' TB (n = 319)**



\* This was not presented which may explain why it was not mentioned more often.

Self-blame appeared to play a role among men. They were more likely than women to report ‘vices’ as the perceived cause of their own TB (64% vs 12%;  $C^2 = 72.7$ ,  $p < 0.0001$ ). On the other hand, men were less likely than women to identify hard work as the cause for their own TB (44% vs 57%;  $C^2 = 4.6$ ,  $p = 0.03$ ), as they did for explaining the causes of TB generally.

### Health seeking

About two-thirds of patients (69%) had been told by someone to have a medical check-up for their symptoms. This advice came from a spouse (18%) or a relative or someone else in their household for 59% of the sample. Table 5.2 indicates that in many cases (53%) a private doctor was the first health care provider approached for treatment. Less than one-third of the respondents first approached a health centre. Only nine respondents (3%) reported consulting a traditional healer (*albularyo*) first, although three additional respondents mentioned they saw a traditional healer at a later point.

**Table 5.2: Health facility first approached for help (n = 319)**

First health facility approached	Number	Percentage
Private doctor	170	53%
Health centre (HC)	91	29%
Hospital	40	13%
Traditional healer ( <i>albularyo</i> )	9	3%
Diagnostic centre	4	1%
Non-governmental organisation	3	1%

In addition, one respondent went first to a company doctor and one respondent did not answer this question.

Almost two-thirds of the respondents (63%) stated that before they were sick with TB, they had never been to the health centre (HC). Forty-five percent of those patients who had used the HC before falling sick with TB went to the HC first after initial symptoms of TB, compared with only 19% of those who had not yet used the HC when they fell sick with TB ( $C^2 = 24.6$ ,  $p < 0.0001$ ).

According to guidelines for TB control in the Philippines, the HCs should not routinely request X-rays. However, 97.5% of the respondents—all of them with a record of being smear-positive—stated they had a chest X-ray; only eight patients did not have the unnecessary X-ray. Since none of the HCs has X-ray equipment, this means that all but eight patients went to at least two health care providers for diagnostic procedures.

The following case study indicates that impolite health centre personnel may be an important reason for consulting private doctors. It also indicates that for many patients and health care providers, chest X-rays may be preferable to sputum examinations.

Case study 1: Health worker's attitudes and diagnostic priorities

Bong (a pseudonym), a single man from a squatter area who had had TB twice in the past seven years, developed symptoms suggesting TB. One morning he coughed up blood-streaked sputum, and later that same morning he presented the sputum sample to the nearby health centre to have it examined. They didn't accept it, however, and told him to come back the following day. This he did, bringing his blood-streaked sputum sample from the previous day and another early morning sputum sample of the current day. The health worker received him rudely, asking, "Why do you bring a sputum sample?" After Bong explained, the health worker accepted only one of the samples, and with obvious disgust she smeared some of it on a slide, holding the slide far away from her. Bong was discouraged. When he returned to the health centre, he was told that his sputum sample was negative. He was not told to give a second sputum sample, but was advised to get a chest X-ray.

Consulting a private doctor was more likely to result in a diagnosis on the spot. The diagnosis was made at the clinic for 94% of the 170 patients who first went to a private doctor, but only for 84% of those who first went to the HC ( $\chi^2 = 6.0$ ,  $p = 0.01$ ). Among those initially not diagnosed at the HC, the diagnosis was made by a private doctor or at a hospital.

The cost of treatment was not considered appropriately for many patients. Two-thirds of the patients (66%) received a prescription for drugs; 21% of these 209 persons receiving prescriptions said they had not been told by their private doctor or at the hospital that anti-TB medication was available free of charge in the HCs. In our total sample, 57% (n

= 182) reported purchasing anti-TB drugs before they came to the HC, and 29% had been taking them for at least three weeks before they came to the HC. These 182 patients were nevertheless smear-positive when they underwent sputum microscopy at the HC. Table 5.3 provides additional details.

**Table 5.3: Duration of TB treatment before coming to the health centre (n = 319)**

Weeks of prior treatment	Number and percentage of patients		
	Number	Percentage	Cumulative %
More than 4 months	6	2%	2%
3 - 4 months	13	4%	6%
Approximately 2 months	18	6%	12%
3 - 4 weeks	56	18%	29%
1 - 2 weeks	61	19%	48%
Less than one week	28	9%	57%
None	137	43%	100%

#### Delayed health seeking

The delay from first awareness of symptoms to beginning treatment is a matter of considerable public health interest. Table 5.4 summarises the lag time from reported symptom onset to first health seeking at a health care facility. The median lag time was one month, and the inter-quartile range was half a month to two months. Twenty percent of the 302 respondents had had symptoms for at least three months before they approached a health facility.

**Table 5.4: Lag time from onset of symptoms to first health seeking (n = 302\*)**

Lag time (health seeking delay)	Number and percentage of patients		
	Number	Percentage (of 302)	Cumulative %
More than 6 months	25	8%	8%
5 to 6 months	16	5%	14%
3 to 4 months	20	7%	20%
1 to 2 months	35	12%	32%
Between half a month and one month	90	30%	62%
Up to half a month	116	38%	100%

\* Seventeen respondents are not included (eleven respondents did not have symptoms and for six respondents the degree of delay was not clear)

The emotional impact of TB on health seeking delay was considered. Reactions such as sadness, fear of dying, guilt, embarrassment, and loss of self-esteem were not associated with increased health seeking delay. Among those who felt ostracised because of their TB, however, 41% had had a lag time longer than four weeks, compared with only 29% for those who did not say they felt ostracised ( $C^2 = 3.9$ ,  $p = 0.05$ ).

Among other possible determinants of health seeking delay, we examined perceived dangerousness of TB and perceived susceptibility when not yet sick with TB, and knowing at least one person who was treated unsuccessfully for TB. None of these three factors were associated with health seeking delay. We also examined the perceived causes of TB and none of them were associated with health seeking delay, neither perceived causes for TB in general, nor perceived causes of patients' own illness.

Among eight additional factors that were considered (age, sex, marital status, self-perceived impoverishment, having or not having been at the HC before getting sick with TB, degree of education, employment status, and having or not having TB for the *first* time), only marital status was significantly associated with health seeking delay. Among those without a marital partner only 24% had a lag time longer than four weeks, compared with 36% for those with a marital partner ( $C^2 = 4.3$ ,  $p = 0.04$ ).

The patients were asked what they felt contributed to the delay. The two most frequent responses were that the symptoms were considered harmless and the cost of medical care too high (Table 5.5).

**Table 5.5: Frequency of reasons reported for delayed health seeking (n = 228\*)**

Reasons for delay	Persons reporting	Percentage (of 228)
Illness considered harmless	135	59%
Lack of money	51	22%
Symptomatic person was working	16	7%
Self-treatment considered sufficient	9	4%
Other reasons	29	13%

\* Those patients with a short delay were not asked. There were 228 patients who were asked and gave an answer. A patient could mention more than one reason.



Difficulty staying in treatment appears to result from dissatisfaction with care and the search for acceptable alternatives. The experience of the following patient indicates how the perceived inferior quality of care may motivate patients to seek other providers.

Case Study 2: 'Shopping' for health care by a dissatisfied health centre patient

Juan (a pseudonym) is 48 years old, married, and ill with a new case of TB. When he was troubled by chest symptoms he purchased antipyretics and amoxicillin without consulting a health care provider. After approximately three weeks of unremitting symptoms he went to a HC where his sputum was examined. Although the HC records showed he had a positive sputum smear, Juan said no one told him the results of his sputum examination. The HC, which had run out of anti-TB drugs when Juan came for help, asked Juan to get an X-ray. Juan bought drugs for two months, but it is not known what kind of anti-TB drugs he bought. Then he went to a private doctor for an X-ray, which was positive for TB. Juan was given a prescription and bought the prescribed drugs. Although he could go back to work one month after having started to take these drugs, he could no longer afford to purchase these drugs after three months.

Juan mentioned he was discouraged at the HC because often there was no physician present, and he was told to come back the next day. He also felt the HC staff had not given him sufficient information or an adequate explanation of his condition. At the time of interview Juan felt his TB was clearly not yet healed.

## **DISCUSSION**

One fifth of the patients had symptoms for at least three months before they approached a health facility. The median lag time from symptom onset to starting treatment was only four weeks, but this figure is somewhat misleading because a certain proportion of the respondents was found through active case finding. Because records are unreliable, the precise number of these patients is unknown, and although the median lag time underestimates the problem, the magnitude of this underestimate is unclear. Treatment delays in our study are similar to those of a previous study in the Philippines (Valeza *et al.*, 1991), which found 32% of 180 urban respondents had a delay of at least two months (compared to 30% in this study), and 16% had a delay of at least six months (compared to 12% in this study).

Our study did not show a relationship between any perceived causes of TB and delayed health seeking, and the role of several other anticipated predictors of delayed health seeking remained unsubstantiated. These included the idea that TB is not dangerous, not feeling personally at risk, and lack of awareness of person-to-person transmission. The absence of such relationships is consistent with studies suggesting that fear does not necessarily motivate health seeking (Leventhal, 1965, cited in Toledo *et al.*, 1979). The tendency to minimise the severity and dangerousness of TB may also reflect a coping mechanism, rather than long-standing ideas about the disease or a lack of information. Consequently, health educational efforts should not overstate or over-dramatise the issue, as this could reinforce stigma and denial, thereby further delaying help seeking.

Our data showing 29% of respondents went first to the HC, compared with 53% who went first to a private doctor, is consistent with other studies in the Philippines. A study by Valeza and colleagues (1991) in several other regions of the country found that 52% of 571 TB patients had also approached a private doctor first. Several factors may explain the use of services other than public health centres first: People expect private providers to be more effective, more easily accessible, more sympathetic and more likely to respect privacy than governmental health care providers (Pathania *et al.*, 1997). They appear to maintain this view despite contradictory evidence, as was found in India where research showed a large number of private providers offer poor services for TB patients (Uplekar & Shepard, 1991; Uplekar & Rangan, 1996). It is not just that private practitioners are perceived as better. There is also a lack of awareness that HCs even provide services for TB, or an overall low regard based on the poor reputation of HCs.

Our findings support these explanations and raise additional questions: almost half of the patients who had used the HC for something else before falling sick with TB went to the HC first when they sought help for symptoms of TB, compared with only one-fifth of those who had not used the HC before their TB illness. Prior use encouraged, rather than discouraged, further use. Could this be taken as evidence that HCs are better liked than their reputation suggests? A study examining that question in India found that people generally ascribed a poor attitude to HC staff. However, when Indian TB patients who had used both the private and the public sector providers were asked to compare the two, they said the behaviour of the public doctors was better (Uplekar & Rangan, 1996, p. 24).

It seems the way most health providers, public and private, relate to their patients needs to be improved. The study by Uplekar and Rangan showed health education was a low priority for providers and received little more than scant attention. Patients received only “a series of across-the-desk instructions, which the patient could rarely comprehend.” (Uplekar & Rangan, 1996, p. 54). In South America as well, research in Cali, Colombia, revealed that the communication skills of most health workers were also poor (Jaramillo, 1998).

Recognition of the importance of the quality of the initial patient counselling needs to become a higher priority. Anecdotal evidence indicates that there are health providers whose TB patients all complete treatment (Sumartojo, 1993). An empathic and respectful style of listening and interacting with patients is essential. This enables patients to speak frankly, which in turn helps the health care provider to appreciate the problems that confront their patients. Giving priority to such values in the clinical interaction engenders mutual respect that contributes to development of an effective therapeutic alliance, especially important to support the six-month-long course of treatment for TB. Patients and clinicians who consider each other partners with a shared goal, to cure TB, are more likely to foster a clinical relationship conducive to effective treatment. Although it is easy to find examples of troubled doctor-patient relationships, identifying solutions is more challenging (Rubel & Garro, 1992; Zwarenstein, 1999). Nevertheless, there are success stories (see e.g. Steyn *et al.*, 1997), and it is important to learn from them.

Another reason why private doctors are so attractive may be that for chest-related symptoms patients want an X-ray, and many private doctors rely heavily on chest X-rays. For example, data from Korea show that 75% of 224 cases diagnosed with tuberculosis in facilities other than health centres relied exclusively on X-ray findings (Mori *et al.*, 1992).

The cost of case finding to patients is often considerable. A study in rural Africa found that approximately half the monetary costs and majority of the time lost from work and other social costs are incurred before diagnosis (Saunderson, 1995). A study in Thailand found the pre-diagnostic out-of-pocket expenditures to be similar or higher than the post-diagnostic out-of-pocket expenditures (Kamolratanakul *et al.*, 1999). Ways to reduce these costs are needed. It is crucial that the case finding process entails only minimal expenses for the patient so that she or he can bear the cost of treatment that follows. Minimal case finding expenses not only reduce financial barriers to treatment; they also facilitate a positive

attitude towards the health provider. Other benefits of efficient case finding include reduced transmission of the TB bacilli, less likely development of drug resistance, less physical and mental suffering; and reduced likelihood of incomplete recovery.

Most TB patients buy the prescribed anti-TB drugs when they come from the private doctor. Buying anti-TB medication, rather than receiving it free at the HC, not only aggravates the financial hardships of the poor, it often results in incomplete and/or irregular intake of drugs (Nichter, 1994). Better public-private collaboration and innovative approaches to improving interactions between the public and private health providers need to be developed (Brugha & Zwi, 1999). Policy should be implemented that requires private doctors to refer patients who lack the financial means to complete treatment on their own. A reliable supply of high-quality anti-TB drugs in the health centres is of course essential for such a policy to be effective.

Several factors may have compromised the validity of our data. Since patients were interviewed 1 to 16 months after the end of treatment, recall bias may have been a factor. Only 39% of the 812 known sm+ TB patients could be found and interviewed. Many patients moved back to the province, and inadequate addresses for others in the health centre records made it impossible to find them. Consequently, there may have been a selection bias. This was probably less of a factor than the low percentage indicates, because many of the patients came from rural areas, and they were likely to have been in Malabon only for their treatment. Consequently, we reached a larger proportion of the affected persons residing in Malabon. Only ten former patients declined to be interviewed; thus, refusal to be interviewed constitutes only a minimal potential bias.

Our findings clarify important aspects of treatment delay for TB in the Philippines and relevant issues in the doctor-patient relationship require attention for improved TB control. With the implementation of DOTS and consideration of alternative strategies for implementing control measures, it is hoped that these insights may be useful and that they may form policy in the Philippines and comparable regions.

## CONCLUSION

The urgent need to foster co-ordination and collaboration between the private and the public health providers is clear. In addition, several findings of this study suggest that improved health communication is an important supporting element in case finding, both general information about TB, perhaps making better use of television and radio, and tactful individual health communication in health facilities.

This study found that the family plays an important role in health seeking. This is as expected in the Philippines where the family remains an important source of support. Health communication to promote health and prevent illness should be conveyed to more than one person in the family. Our finding that 28% of respondents reported someone else with TB in their household when they themselves came for a medical check-up underscores the importance of “family-based” health communication. Encouraging the public to always be accompanied by a family member when seeking health care and enabling community health workers to adequately convey health communication messages to the families in their houses are two approaches to strengthen family-based health communication. Two kinds of educational materials may act as enabler: Culturally sensitive materials that the health worker can give to the patients and materials for the health workers themselves. The latter was produced in the Philippines: so-called cue cards were developed for the health providers dealing with TB patients. These cue cards contained the key words of the ten essential messages that need to be conveyed to TB patients (Valeza *et al.*, 1990).

Overuse and inappropriate use of X-rays, and failure to examine sputa in accordance with current policy indicate the need to update skills and practice of private practitioners and HC staff.

Clearly, health communications alone are insufficient for adequate control of TB. They cannot reduce lag time to treatment unless health services are available, affordable, and acceptable. There is no substitute for competent, efficient and patient-oriented personnel who effectively engage patients in a productive treatment alliance, and of course, medicines must be readily available. Efforts to promote the DOTS strategy must account for the human aspect of clinical interactions. The technical and organisational aspects of TB control should not detract from appreciation of the human aspects of treatment and control strategies.

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***PART III: Strategies for improving TB control: the role of private practitioners and intermittent therapy***

**Diagnosis and management of tuberculosis by private practitioners in Manila, Philippines**

**Public-private collaboration for TB control in Manila, Philippines: views from both sectors**

**Feasibility, acceptability and effectiveness of fully thrice-weekly intermittent TB therapy compared to daily TB therapy in public health centres in Manila, Philippines**





**DIAGNOSIS AND MANAGEMENT OF TUBERCULOSIS BY PRIVATE PRACTITIONERS IN MANILA, PHILIPPINES**

*Running title: TB-practices of private practitioners in Manila*

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## **Diagnosis and management of tuberculosis by private practitioners in Manila, Philippines**

### **ABSTRACT**

**Setting:** Private for-profit health care providers are prominent in the health system of the Philippines.

**Objectives:** To examine the practices of the private practitioners in Malabon, Metropolitan Manila, Philippines, concerning diagnosis and treatment of TB.

**Design:** Forty-five private practitioners of Malabon who treat adult TB patients were interviewed.

**Results:** For diagnosis, most private practitioners relied on the clinical presentation and result of an X-ray. Only 13% of the respondents routinely also ask for sputum examination. Ninety-six percent used X-ray as a tool to monitor treatment.

Sixty percent of the respondents prescribed a regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol. Except for rifampicin, over-dosage was common. For re-treatment cases, none prescribed the WHO-recommended re-treatment regimen.

The private practitioners perceived the main reasons for patient non-adherence to be the patients' lack of finances to buy drugs and patients' perceived well-being after a certain period of treatment. Patients' lack of money was seen as the main obstacle to compliance. The only case holding mechanism mentioned was occasional visits of the TB patients to the clinic.

**Conclusion:** Private practices for diagnosis and treatment of TB typically deviate from guidelines. The quality of care among private practitioners needs improvement. Innovative strategies are required.

*Keywords:* private practitioners, tuberculosis, diagnosis, treatment, Philippines

## INTRODUCTION

Private for-profit health providers play an important role in most countries of the world, especially in Asian countries (Brugha & Zwi, 1999a). In India, 50 to 80% of the tuberculosis (TB) patients first seek professional help from a private health provider (Pathania *et al.*, 1997). And in urban Pakistan 80% of the patients being treated in the public TB programme had first sought help from private practitioners (Marsh *et al.*, 1996).

Shortcomings in the diagnosis and/or treatment of TB by private providers have been reported in various countries. Such shortcomings include failure to use sputum microscopy, inappropriate treatment regimens, failure to properly educate patients and a lack of case holding mechanisms.

In the Philippines, 50% of the total health expenditures consists of out-of-pocket expenditures (WHO, 2000b). A nationwide tuberculosis survey in the Philippines found that in response to symptoms of TB, most sought no professional help: 43% of the respondents took no action, 32% self-medicated, 12% consulted a private practitioner, 8% a public health centre, 4% a hospital, and 2% a traditional healer (Tupasi *et al.*, 2000a). Recent research in Malabon, Metropolitan Manila, Philippines showed that 53% of the TB patients treated in public health centres had gone to a private practitioner as their first health seeking action, and 66% of the patients had received a prescription for drugs before getting treated at the public health centres (Auer *et al.*, 2000). A survey across the Philippines among family physicians revealed misunderstandings in the area of transmission and inadequate prescriptions, especially for re-treatment cases (Manalo *et al.*, 1998).

It is important to establish the deficiencies of the practitioners' knowledge and practices so that these deficiencies can be addressed and the principles of the DOTS strategy made known. Also, assisting the private practitioners to adhere to the principles of DOTS not only benefits their patients but also enhances collaboration between the private and public sectors.

Our study aimed to determine diagnostic and treatment practices for TB, including case holding mechanisms, among private practitioners in Malabon, Metro Manila with reference to accepted standards of TB care.

## **METHODS**

We surveyed 45 private for-profit practitioners who treat TB in Malabon, Metro Manila. Malabon had approximately 400,000 inhabitants in 1999. The public health sector consists of 23 health centres providing TB care. Although the DOTS strategy was implemented in May 1999, not all elements of the DOTS strategy were functioning satisfactorily by the end of 2000.

Our survey aimed to interview all private practitioners with adult TB patients. Private practitioners were identified by actively searching for private clinics and by asking health centre staff to identify private practitioners in the catchment areas of their health centres. Most private practitioners (41) were interviewed in 1999; four were interviewed in early 2000.

The interview questionnaire, was pre-tested and reviewed with several doctors. There was an almost even mix of closed and open-ended questions. The interview lasted approximately fifty minutes, on average, and was performed in the doctors' clinics in the absence of patients and clinic staff.

## **RESULTS**

### The private practitioners

None of the 45 identified private practitioners refused to be interviewed. Four additional private practitioners that also had adult TB patients, identified subsequently, were not interviewed. It is estimated that at least 90% of Malabon's adult TB patients of 1999 that approached a private practitioner went to these 45 private practitioners. Of these 45 private practitioners (25 male and 20 female), 22 (49%) were less than 41 years old, 9 (20%) were between 41 and 50 years old, and 14 (31%) were between 51 and 81 years old.

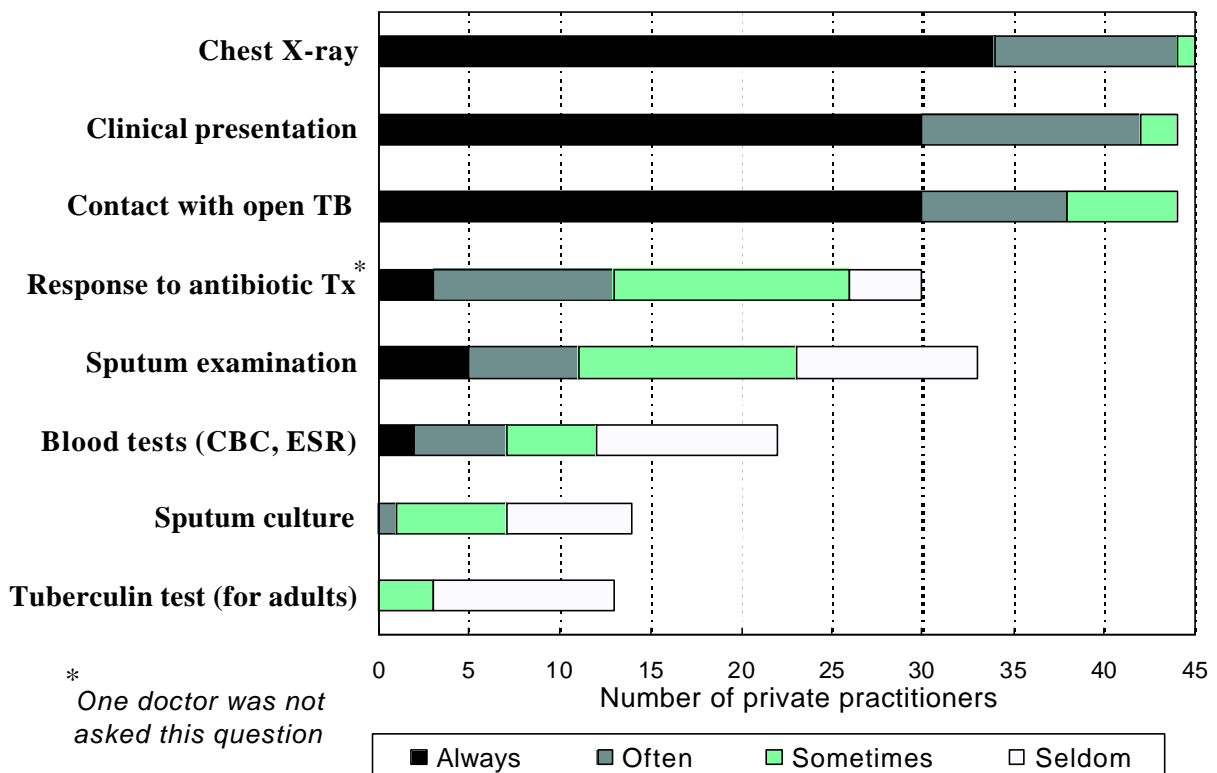
These 45 private practitioners estimated they saw a total of 3,530 adult TB patients in the previous year. Based on this estimate, the rate of TB patients who consult private practitioners in Malabon is approximately 880 per 100,000 inhabitants. According to the private practitioners' estimates, only 1.6% of their TB patients had extra-pulmonary TB.

For most private practitioners (61%), less than 10% of their total number of patients were adult TB patients. A quarter (25%) of the private practitioners stated that 10 to 15% of their total number of patients were adult TB patients. And 14% stated that at least 20% of their total number of patients were adult TB patients. Eighty percent of the respondents characterised the economic status of at least 80% of their TB patients as poor.

Diagnostic process

Contrary to DOTS principles, almost all respondents (93%) relied on the clinical presentation and result of an X-ray to decide whether or not to start anti-TB treatment. Only six respondents (13%) said they routinely also asked for sputum examination (microscopy). Nineteen (42%) said that in some cases they would also ask for a sputum examination in addition to an X-ray. Two respondents reported they used X-ray only ‘when considered necessary’. One of them mainly relied on the clinical presentation and the other one on sputum microscopy. Figure 6.1 presents the answers of the respondents when specifically asked about the role of various diagnostic tools.

**Figure 6.1: Diagnostic tools used by private practitioners to diagnose TB (n = 45)**



Of those respondents who did not always use X-ray (n = 11; 24%), only one reported 'often' using sputum examination, and three reported to 'sometimes' use sputum examination. The remaining 7 (16%) rely on the signs and symptoms and on the question of whether the patient had been in contact with someone with open TB. In addition, one of the 7 also 'always' considers the response of the TB suspect to antibiotic treatment.

Most respondents thought chest X-ray was a tool with high specificity, i.e. the reliability of X-ray findings was believed to be high. The question, asked to only 39 of the 45 private practitioners, was if a chest X-ray that is considered "positive for TB" by one radiologist is also considered "positive for TB" by another, independent radiologist. Fifty-six percent (22/39) believed interpersonal discrepancy in X-ray interpretation happened in only 1 to 5% of the cases; 26% expected an interpersonal discrepancy in 10% of the cases, and 15% in 15 to 20% of the cases. The remaining respondent expected an interpersonal discrepancy in 25% of the cases.

Thirty-eight percent of the respondents (17/45) had own X-ray equipment. Their responses about diagnosing TB patients were not different from the responses of those without own X-ray equipment.

### Monitoring treatment

Use of X-ray was also popular as a tool to follow-up or monitor treatment: all except two respondents used X-ray to monitor response to treatment. Most (60%) asked for only one follow-up X-ray (normally at the end of treatment) and 27% asked twice for follow-up X-ray (normally after two or three months and at the end of treatment). Nine percent asked once, twice or three times for a follow-up X-ray during treatment.

Only 20% of the private practitioners reported using follow-up sputum examinations for some or all of their TB patients, even though two-thirds stated that follow-up sputum examinations for monitoring treatment are ‘important’ (53%) or ‘essential’ (13%).

### Treatment

The private practitioners were asked what they normally prescribed to a patient with far-advanced tuberculosis, weighing 45 kg. Table 6.1 presents their responses. Twenty-seven respondents (60%) prescribed a quadruple regimen, consisting of isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E), but only 15 (33%) prescribed this quadruple regimen for six months. Of these 15, only 4 (9%) prescribed 2HRZE / 4HR (meaning: H, R, Z, and E for the first two months of treatment, and then H and R for another four months). Eight (18%) prescribed 2HRZE / 4HRE, and the remaining three (7%) prescribed Z for more than two months. Eleven (24%) prescribed triple therapy consisting of HRZ, but only 6 (13%) of them prescribed 2HRZ / 4HR, the regimen endorsed up to the middle of the 1990’s by the Philippine National Tuberculosis Control Programme (NTP). Based on WHO recommendations, the main regimens used in the NTP are: (i) 2HRZE / 4HR for smear-positive patients and smear-negative patients who do not have minimal TB, as judged by a chest X-ray; and (ii) 3HRZES<sup>1</sup> / 1HRZE / 5HRE for previously treated patients.

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<sup>1</sup> S = streptomycin



*Chapter 6: TB-practices of private practitioners in Manila*

Tables 6.2 and 6.3 present the duration of treatment and the dosage, respectively. While 58% (26/45) of the respondents reported prescribing R and also H for six months and 64% (29/45) prescribe Z for two months, only 11% (5/45) prescribe E for two months. As to dosing for a patient weighing 45 kg, 91% (41/45) prescribed the recommended 450mg for R (480mg in one case), 16% (7/45) the recommended 300mg for H (320mg in one case), 11% (5/45) the recommended 1000mg for Z, and 29% (13/45) the recommended 800mg for E.

An operational formulation of acceptable treatment accepted a somewhat longer course of treatment than WHO-recommended regimens. (This is in accordance with the latest TB treatment guidelines of leading American anti-TB organisations that now recommend to consider extension of treatment for patients with cavitation on the initial chest X-ray - ATS/CDC/IDSA, 2003, p. 609.) If we define an acceptable regimen as either HRZE for 6 to 9 months with PZA for not more than 3 months and with acceptable dosages (Rifampicin 450 or 600mg, isoniazid of not more than 400mg, PZA of not more than 1500mg and Ethambutol of less than 1200mg), or HRZ/HR for 6 to 9 months with PZA for not more than 3 months and acceptable dosages, then half of the respondents (47%) prescribed acceptable regimens.

**TABLE 6.1:**  
**Private practitioners prescribing various treatment regimens for far-advanced TB (n = 45)**

Regimen	Number of months prescribed for each drug					Respondents prescribing this regimen	
	Isoniazid	Rifampicin	PZA	Ethambutol	Streptomycin	N	%
1. According to WHO/NTP guidelines							
1.1.	6	6	2	2	-	4	9
2. Acceptable deviation from guidelines						17	38
2.1.	6	6	2	6	-	8	18
2.2.	6	6	3	3	-	1	2
2.3.	6-9	6	2	6	-	1	2
2.4.	6-9	6-9	2	6-9	-	1	2
2.5.	6	6	2	-	-	6	13
3. Problematic deviation from guidelines (treatment longer than recommended)						13	29
3.1.	6	6	4	6	-	1	2
3.2.	6	6	6	2	-	1	2
3.3.	6-12	6-12	2	6-12	-	1	2
3.4.	6-12	6-12	6-12	6-12	-	1	2
3.5.	8	8	6	3	-	1	2
3.6.	9	9	9	9	-	1	2
3.7.	12	12	2	6-12	-	1	2
3.8.	12	12	2	12	-	1	2
3.9.	12	12	2-4	2-12	-	1	2
3.10.	18	18	6	18	-	1	2
3.11.	6-12	6-12	6-12	-	-	2	4
3.12.	6-12	6-12	-	-	6-12	1	2
4. Problematic deviation from guidelines (treatment shorter than recommended)						7	16
4.1.	4	4	4	4	-	1	2
4.2.	3-6	3-6	2	3-6	-	1	2
4.3.	<6	<6	<6	-	-	3	7
4.4.	3-6	3-6	-	-	-	2	4
5. Other problematic deviation from guidelines						4	9
5.1.	6	6	6	-	1	1	2
5.2.	6	6	2	6	3	1	2
5.3.	6	6	6	6	2	1	2
5.4. <sup>1</sup>	6-12	6-12	2-3	3-6	-	1	2

<sup>1</sup> Apart from isoniazid, rifampicin, PZA and ethambutol, this regimen included a fifth drug for the initial two to three months of treatment. This fifth drug was specified as a “third generation drug”.

**TABLE 6.2: Prescribed duration of treatment for each of the four main drugs for far-advanced TB (n = 45)**

<u>Specified duration</u>	<u>Isoniazid &amp; Rifampicin</u> <sup>1</sup> (used by all respondents)	<u>Pyrazinamide</u> (used by 42 respondents)	<u>Ethambutol</u> (used by 30 respondents)
1-12 months:	-	-	3
2 months:	-	<b>29</b> <sup>2</sup>	<b>5</b> <sup>2</sup>
2-4 months:	-	5	-
3-4 months:	-	-	4
4 months:	1	-	-
3-6 months:	4	1	-
6 months:	<b>25</b> <sup>2,3</sup>	5	10
6-9 months:	5	-	-
6-12 months:	4	2	7
12 months:	3 <sup>4</sup>	-	1
18 months:	1	-	-

<sup>1</sup> Forty-three used these two drugs for the same duration. One used 6 months of H and 6-9 months of R, and one used 12 months of H and 6 months of H.

<sup>2</sup> Duration recommended by WHO.

<sup>3</sup> 25 used 6 months of H and 6 months of R. In addition, one used 6 months of H and 6-9 of R.

<sup>4</sup> Three used 12 months of H and 12 months of R. In addition, one used 12 months of H and 6 months of R.

**TABLE 6.3: Prescribed dosage for each of the four main drugs for patients weighing 45 kg with far-advanced TB (n = 45)**

Kind of drug	Rifampicin (used by all respondents)	Isoniazid (used by all respondents)	Pyrazinamide (used by 42 respondents)	Ethambutol (used by 30 respondents)				
Dosage			none	3	none	15		
	240 mg	1 <sup>1</sup>	160 or 200 mg	2	200 mg	1	400 or 500 mg	9
	450 mg	<b>40</b> <sup>2</sup>	300 mg	<b>6</b> <sup>2</sup>	500 mg	1	600 mg	1
	480 mg	1	320 mg	1	1000 mg	<b>5</b> <sup>2</sup>	800 mg	<b>13</b> <sup>2</sup>
	600 mg	3	300-400 mg	3	1500 mg	33	1000 mg	6
			400 mg	30	2000 mg	2	1200 mg	1
			500 or 600 mg	3				

<sup>1</sup> Number of respondents who mentioned this dosage.

<sup>2</sup> Dosage recommended by WHO.

The private practitioners were also asked about their re-treatment regimen, that is what they prescribe for a patient who previously had anti-TB treatment for at least 2 months. Twenty-seven respondents (60%) stated they prescribed the same regimen for new cases and for re-treatment cases. Fifteen (33%) prescribed a weaker regimen (less drugs and/or shorter duration of treatment), and only one respondent prescribed a stronger regimen. Two respondents said they referred such patients to a specialist or for drug susceptibility testing. None prescribed the recommended regimen.

For treating patients with multidrug-resistant TB, none of the private practitioners mentioned an adequate regimen.

Prescribing vitamins was common: 32 (71%) 'always' prescribed vitamins, and 12 (27%) 'sometimes' prescribed vitamins, and one private practitioners did not prescribe vitamins. Only three private practitioners prescribed tonics.

Twenty-five (56%) of the 45 respondents had their own drug supply or their own pharmacy from which they assumedly supplied drugs to their TB patients.

### Patient education

Only 40% of the private practitioners told their TB patients clearly that they had tuberculosis ('TB' or 'tuberculosis' were the used terms), and 27% used 'TB'/'tuberculosis' and/or a euphemism, such as 'weak lungs' (*mahina ang baga* in Filipino) 'illness in the lungs' (*sakit sa baga*), and 'spot in the lungs' (*espot sa baga* or *tama sa baga*). One third (33%) used only euphemistic expressions.

Health educational priorities for the private practitioners included: (i) providing information about treatment and/or the importance of compliance (reported by 62%); (ii) recommending ways to prevent infecting others (62%, including eight respondents who advised patients to use separate eating utensils); (iii) promoting intake of nutritious food (40%); (iv) recommending to stop risk behaviours, mainly smoking and drinking alcohol (27%); and (v) explaining the importance of adequate rest (20%).

More than two thirds (71%) reported they had no health education materials; 18% said they usually have, and 11% said they sometimes have such materials (mostly leaflets). Most said they would definitely (84%) or possibly (11%) like to have such materials.

Effective health education to patients requires accurate knowledge among health care providers, but this was a problem. Misconceptions among the providers about infectivity were common: almost two thirds of the respondents (62%) said that using the eating utensils of a sputum smear-positive TB patient is a risk for getting infected. And 36% said there was a risk that someone gets infected from fomites in bedsheets, cloths of a smear-positive patient.

#### Case holding mechanisms

Apart from occasional visits of the TB patient to the clinic no case holding mechanisms were mentioned. Most private practitioners (58%) stated to ask for a clinic visit *monthly*, 13% for a clinic visit *more frequently than once a month*, and 29% for a clinic visit *less frequently than once a month*.

When the private practitioners were asked if their TB patients complied with this request, approximately half of them (47%) estimated that 75% to 100% of their TB patients complied. One fourth (27%) estimated that 40% to 70% of their TB patients follow this request. And 20% estimated that 10% to 35% of their TB patients follow this request (three private practitioners did not respond to this question).

The respondents were asked what they would do when a TB patient did not appear for the next appointment. Almost two-thirds (62%) indicated no follow-up for defaulters. Table 6.4 presents the reported defaulter actions.

**TABLE 6.4: Follow-up specified by private practitioners when a TB patient misses a scheduled clinic visit (n = 45)**

Action done by the private practitioner	Number	Percentage
Thought about this problem but has not yet found a mechanism or system to do something	20	44%
Calling those TB patients who have a telephone	10	22%
None (arguing that it is up to the patient to come back)	8	18%
Reminding TB patients through relatives or neighbours the private practitioners happen to meet	6	13%
Visiting those TB patients living near the clinic (by clinic staff or by the private practitioner)	2	4%
Reminding the patient when happening to meet him/her (e.g. in church)	1	(2%)

Note: Of the 45 respondents, three gave two answers and one was a non-respondent.

#### Perceived patient adherence to treatment

The private practitioners were asked what they believed was the percentage of their patients who regularly took treatment up to completion of treatment. Sixteen percent of the respondents were very optimistic: they estimated 90 to 95% of their TB patients correctly and regularly took their medication up to completion of treatment. And 29% estimated 75 to 85% of their TB patients were adherent. Thirty-eight percent estimated between 30 and 70% of their TB patients were adherent, and 4% estimated only 2 to 5% of their TB patients were adherent. The remaining 13% felt they could not respond because of insufficient caseload.

The two main reasons by which they explained patient non-adherence were lack of finances to continue to buy drugs (mentioned by 91% of the respondents) and feeling improved enough that further treatment seemed unnecessary to patients (76%). About half of the respondents (49%) mentioned patients lacked awareness of the importance of adherence to treatment. Patients getting lazy or fed up, and patients experiencing adverse reactions were each mentioned by 36% of the respondents.

## DISCUSSION

### Validity of the findings

We did not attempt to verify the answers of the private practitioners with observations or by consulting patients. Consequently, some of the findings probably reflect the *knowledge* of the private practitioners more accurately than their *practices*. Various studies have found a gap between the private practitioners' knowledge of what to prescribe and their actual practice while treating patients, for instance in treatment of tuberculosis in Karachi (Thaver *et al.*, 1998). And research in India revealed discrepancies between reported diagnostic and treatment practices of the private practitioners and what their patients actually followed (Uplekar *et al.*, 1998). Any problems identified through self-report are likely to be an underestimate of problems in practice.

The interviewer of the private practitioners (the first author) was not an official part of the public TB programme, but the introduction of the questionnaire made it clear that the interviewer had links to the public TB programme. Thus, the answers of the respondents may have been incorrectly too much in accordance with the TB guidelines of the Department of



Health. A good example is sputum microscopy. Since most private practitioners know that sputum examinations are the main diagnostic procedure in the public TB programme, there probably was a tendency to overstate the use of sputum microscopy. Such discrepancy was documented in a study in India (Uplekar *et al.*, 1998). In short, social desirability bias and reluctance to admit outdated practices may have resulted in findings too much in line with Department of Health and WHO recommendations.

Recall bias together with social desirability bias and over-diagnosis of TB may explain the rate of 880 per 100,000 inhabitants, as estimated by the respondents. This rate is extremely high, and it does not include the TB patients treated in the public sector. It is estimated that in the Philippines the 1998 incidence rate was 307 per 100,000 (WHO, 2000c). Even if we assume that Malabon is especially heavily affected by the TB epidemic, it is clear that our respondents overestimated the number of TB patients in their practice.

#### Deficiencies in the diagnostic process and in monitoring of treatment

Over-reliance of chest X-ray for diagnosis and monitoring treatment with corresponding under-use of sputum examination was common.

There are several reasons why X-ray is preferred over sputum examination: (i) easier process and faster result when opting for X-ray; (ii) sputum microscopy - if not undergone in a public TB programme - generally entails higher expenditures for the patients than X-ray. (iii) Due to the low sensitivity of sputum microscopy, the value of sputum microscopy is questioned. (iv) Poor reputation of sputum microscopy, also because giving sputum is strongly associated with having TB (Rangan & Uplekar, 1999). (v) Over-estimation of the

reliability of chest X-ray. (vi) A substantial proportion of private practitioners has their own X-ray facility (38% in this setting).

The three reasons mentioned first (and in areas where stigma is a major problem also the fourth reason) are valid concerns. However, a higher awareness of the limitations of X-ray and a clearer appreciation of the advantages of sputum microscopy may well create a higher demand for sputum microscopy among private practitioners. Improving the knowledge of the private practitioners regarding X-ray radiology and sputum examination may thus bring changes. Probably more important is to provide easy access to high-quality sputum examination, for instance by simple referral procedures for the private practitioners' TB symptomatics to public facilities performing sputum examinations. But this exposes private patients to the public system which both patients and private providers may resist.

Few respondents used follow-up sputum examinations for monitoring of treatment. Requesting patients to undergo X-ray while on treatment was much more popular. Follow-up chest X-rays are generally not recommended (WHO, 1997a; Mangura & Reichman, 1999). However, it can be useful for bacteriologically negative cases (Gordin *et al.*, 1989), and for such cases it is generally recommended, also in the Philippines (Task Force on Tuberculosis, 2000). The main problem is that at three months of treatment, an unimproved X-ray finding is not uncommon (Gordin *et al.*, 1989) and is not a matter of concern. But it may result in inappropriate changes in treatment (e.g. prolonged treatment) and cause unnecessary anguish in the patient.

### Issues in treatment

Although most private practitioners (60%) knew the recommended quadruple drug combination, they were not prescribing it correctly. For new cases there was a tendency to over-prescribe. And TB patients with previous treatment of TB were almost always treated inappropriately (not long enough and not with a fivefold regimen). The following paragraphs look at these issues in more detail. We also examine the evidence-base of the WHO-recommended regimens since successfully winning the private practitioners over for the DOTS strategy somehow implies that the regimens used by the DOTS strategy are based on available evidence.

We found that in terms of dosing and duration of usage of each drug, most private practitioners did not follow the recommendations. Using ethambutol for six months was common and some experts recommend this for areas where resistance to isoniazid (such as the Philippines) is common. It is also promoted by many drug companies. A randomised controlled trial comparing 2HRZE/4HR with 2HRZE/4HRE among TB patients with strains resistant to isoniazid would be helpful.

The role of ethambutol is not only unclear regarding its use during the maintenance phase of treatment; there is also no convincing evidence that it is needed during the first two months of treatment. A recent meta-analysis did *not* find differences in treatment outcome between three and four drugs, except for adverse reactions (more frequent with four drugs) and compliance rates (higher with four drugs; some studies used streptomycin instead of ethambutol) (Task Force on Tuberculosis, 2000). We found only three studies comparing three with four drugs in which data on isoniazid resistance were available. Two studies did

not find that treatment response to three or four drugs correlated with initial isoniazid resistance (however, the sample sizes were small) (Yu *et al.*, 1996; Yu *et al.*, undated). In the third study, twice-weekly therapy was compared, and the dosages were rather low. Adding six months of ethambutol was found to improve the treatment response (Tuberculosis Research Centre, 1997). Large trials addressing the question of whether adding ethambutol to a triple regimen is advantageous should be performed.

It must be considered that adding ethambutol has several disadvantages: One, using ethambutol increases the financial and logistic burden for TB programmes and is a financial burden for private patients. Two, ethambutol is associated with severe ocular side effects. Three, the use of ethambutol may result in decreased treatment adherence either directly due to increased number of tablets to be taken or indirectly due to side effects. Four, addressing the deficiencies of the private practitioners should be done by presenting *evidence-based* treatment recommendations. The public programmes and WHO lose credibility when a recommended regimen has no solid evidence base.

On the other hand, there is clear evidence that using pyrazinamide for more than two months is not useful (Singapore Tuberculosis Service/British Medical Research Council, 1979; Singapore Tuberculosis Service/British Medical Research Council, 1981). For TB with drug resistance, a longer course of pyrazinamide might provide some benefit though we do not know of studies supporting this view. In the Philippines, the prescription sheet of a quadruple fixed dose combination recommends an intensive phase of treatment for three months. The drawbacks of added toxicity, of more likely non-compliance due to a high number of tablets that need to be swallowed for a longer time and of an increased financial

burden need to be balanced with the unlikely benefit of using pyrazinamide for more than two months.

The inadequate prescription habits of the private practitioners for re-treatment cases are of concern. The regimens mentioned by the respondents may leave a rather high percentage of previously treated TB patients uncured and aggravate drug resistance. Some research, however, questions whether this may be as serious as it seems, inasmuch as some research suggests re-treatment patients may be treated with the regular regimen used for new patients (Wilkinson *et al.*, 1998; Connolly *et al.*, 1999). Especially for re-treatment cases with pan-susceptible TB bacilli, the re-treatment regimen is most likely not needed. On the other hand, for patients with multi-drug resistant TB (MDR-TB), the re-treatment regimen is inadequate (Kimerling *et al.*, 1999; Farmer, 1999a). Only the availability of a test that would determine the resistance pattern within a few days would be the way out of the unfortunate reality that for many patients the re-treatment is either unnecessarily high-powered or lacks potency. Still, for re-treatment cases, the conventional drug susceptibility test should be performed if possible. Treatment can then be adjusted once the resistance pattern is known. This requires rethinking policy and then assuring such policy may be implemented in the public TB programmes and among private practitioners.

Another practice that imposes risk for development of drug resistance is the almost complete absence of case holding mechanisms. This absence of case holding mechanisms - a common feature of private TB care (WHO, 2001e) - is a threat to the health of the patients and a public health threat.

Ways to assist the private practitioners to improve care

The findings of this survey call for remedial actions. What can easily be implemented and logically follows from our findings is to provide the private practitioners with appropriate health education materials. They appear willing to use such materials. However, health education materials alone normally do not increase adherence to treatment (Haynes *et al.*, 2002).

To change the private practitioners' practices, simple dissemination of information, e.g. through seminars, is not expected to be effective (Oxman *et al.*, 1995). More promising are multifaceted approaches, combining e.g. practice visits, using local opinion leaders (Thomson O'Brien *et al.*, 2002), and patient-mediated interventions to reduce the pressure on the private practitioners that comes from the patient demands (Kamat, 2001; Schwartz *et al.*, 1989). Assisting the private practitioners to optimise their prescription practices should be relatively easy, especially if participation of the influential pharmaceutical companies and a commitment to evidence-based medicine can be brought about. The big challenge is to see effective case holding mechanisms established for TB patients treated in the private sector. Operational research that explores the role of incentives and disincentives, including legislation and regulation is needed. The option of re-certification (i.e. renewal of the license to practice depends on fulfilling certain standards) should be discussed. Measures to promote case holding should be evaluated and refined continuously. Processes that enable and encourage private practitioners to meet as peers in order to find effective case holding mechanisms suitable to them and their patients need to be found. However, efforts among the private sector alone will be of limited value. Communication as well as collaboration between the private and public health sector is crucial in the search for effective TB control.

## **CONCLUSION**

This study showed that there is room for improvement in the diagnosis of TB among private practitioners of Malabon. Although the private practitioners need more accurate knowledge, the main challenge is to find patient-friendly mechanisms that will enable the private practitioners to diagnose TB correctly and efficiently.

With respect to proper treatment, most private practitioners know the correct quadruple drug combination but they do not know how to prescribe them in accordance with recommended policy. There is a tendency to over-medicate new patients, and TB patients with previous treatment of TB are almost always under-medicated. Findings indicate needs for improved diagnostic and treatment practices of private practitioners in Metro Manila. These results are also consistent with findings from other studies that highlight the importance of public-private collaboration among global and national priorities for TB control.

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**PUBLIC-PRIVATE COLLABORATION FOR TB CONTROL IN MANILA,  
PHILIPPINES: VIEWS FROM BOTH SECTORS**

*Running title: Public-private collaboration for TB control in Manila*

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## **Public-private collaboration for TB control in Manila, Philippines: views from both sectors**

### **SUMMARY**

In the Philippines, many TB patients are treated by private practitioners. Questions about the private practitioner's quality of care and efficiency of service as well as limitations of the public sector suggest needs for improved collaboration between public and private sectors.

This study examines the private practitioners' felt needs for additional knowledge on clinical management of tuberculosis and their views on the public TB programme and collaboration with the public health sector. It also examines the views of the public health centre personnel about the private practitioners, their own TB programme, and public-private collaboration.

Forty-five private practitioners were interviewed. Group discussions with personnel of the public health centres inquired about collaboration with private practitioners.

The private practitioners' most frequently mentioned needs for updated clinical knowledge were about appropriate use of sputum microscopy, how to tell patients that household contacts need a check-up, and motivating the patients to adhere to treatment. There was considerable interest to receive and follow the national TB guidelines.

The main perceived problems they identified with the public TB programme were insufficient drug supply, poor quality of the TB drugs, and lack of health education. Two suggestions on how to establish public-private collaboration (mandatory referral of poor TB patients to the public TB programme and allowing private practitioners to use the governmental TB drugs) were generally welcome, but they expressed reservation concerning feasibility of the latter suggestion. The personnel of the public health centres were positive about mandatory referral of poor TB patients to the public TB programme but sceptical about allowing private practitioners to use the governmental TB drugs.

Our findings suggest steps to facilitate public-private collaboration and the need for specific human resources. The public programme needs to be strengthened and collaboration prioritised.

*Keywords:* tuberculosis, DOTS, private practitioners, public-private collaboration, Philippines

## **INTRODUCTION**

Private for-profit health providers play an important role in most countries of the world (Brugha & Zwi, 1999, p. 168). For the 22 countries that account for 80% of all new tuberculosis (TB) cases in the world, the out-of-pocket expenditures expressed as percentage of the total health expenditures range from 23% (Russia) to 91% (Cambodia) (Uplekar *et al.*, 2001). In most other countries as well, people with tuberculosis from all levels of socio-economic status make use of the private health care sector (Uplekar, 1999). It is estimated that in India, 50 to 80% of the TB patients first seek professional help from a private health provider (Pathania *et al.*, 1997). And a survey in Ho Chi Minh City, Vietnam found that about half of the patients being treated in the public TB programme had initially chosen a private health provider and that there was no significant association between socio-economic status and use of private providers (Lönnroth *et al.*, 2001). On the other hand, other studies in Asia found that the level of utilisation of private providers increases with socio-economic status (Yesudian, 1994; Aljunid & Norhassim, 1992; Ministry of Health Malaysia, 1988).

Recent research in Malabon, Metro Manila, Philippines revealed that 53% of the TB patients treated in public health centres had gone to a private practitioner as their first health seeking action and 66% of the patients had received a prescription for drugs (Auer *et al.*, 2000). The patient survey in Malabon also found that there was no association between self-perceived degree of poverty of patients and either the public or private status of their commonly approached health provider or whether they received a prescription for TB drugs during help seeking. Nor could an association be found between self-perceived degree of poverty and having or not having bought TB drugs for at least two weeks (unpublished survey data).

In general, the following makes the private providers attractive in comparison to the public health sector: (i) easier accessibility (sometimes geographically and often in terms of clinic hours); (ii) shorter waiting periods; (iii) a more stable doctor-patient relationship; (iv) more considerate staff attitudes; (v) a greater degree of confidentiality; and (vi) more reliable availability of staff and drugs (Brugha & Zwi, 1999a, p. 171; Swan & Zwi, 1997; Aljunid, 1995). Also, making use of private practitioners may not be much more expensive than making use of public facilities; even when using public health facilities, there are often considerable costs that are mainly hidden. Common hidden costs are wasted trips to public facilities due to irregular drug supplies, donations at the public facility, and opportunity costs due to long hours of travelling to and waiting in public facilities, especially when DOT (directly observed therapy) is health facility based.

The common notion is that the private sector provides better services than the public sector (Lönnroth *et al.*, 1998). However, evidence suggests that the services offered in the private sector are often poor (Swan & Zwi, 1997; Aljunid, 1995). A review at WHO found undue emphasis on chest X-ray for diagnosis, neglect of sputum examinations (for diagnosis and monitoring of treatment), inappropriate drug prescriptions and little or no recording of case data were common problems in the private sector (WHO, 2001e, p. 24). Studies in Malaysia (Hooi, 1994) and in South India (Rajeswari *et al.*, 2002) showed patients who first visited private providers had longer health system delays (i.e. delay in the health seeking process that is due to the provider) than those who first went to government health facilities. Another study in India found that TB patients preferred the behaviour of public over private doctors in clinical consultations (Uplekar & Rangan, 1996, p. 24).

Failure to establish public-private collaboration may result in various problems. First, it may prolong the health-seeking phase. This often worsens the clinical condition and increases the likelihood of developing drug resistance. It also furthers transmission of the TB bacilli and aggravates the negative emotional and social consequences of having TB. In addition, it aggravates the financial repercussions of having TB and burdens the health services. Second, inadequate treatment is more likely to happen from inappropriate prescriptions, the patients' financial incapacity to buy the drugs as prescribed, and a weak or non-existing case holding mechanism. Third, establishing a diagnosis by the public sector (which relies heavily on sputum microscopy) is less sensitive if TB patients have already consumed anti-TB drugs. Negative sputum smears believed to be due to previous intake of anti-TB drugs have been identified as a problem by public health providers in Malabon, Metro Manila (Auer, 1998a). Fourth, patients may be less willing to accept the medications given in the public health services since the patients were accustomed to the anti-TB drugs prescribed by their private practitioners that differed from those at the public health centre. Fifth, since private practitioners generally do not report on their TB patients, any assessment of the epidemiological situation of tuberculosis in a country, e.g. the national TB case detection rate, remains inaccurate.

The last few years have seen a growing international interest in collaboration between the private and the public health sector. The important role of the private sector and the need to include the private sector in disease control strategies are increasingly being acknowledged. A recent WHO consultation in Geneva discussed strategies for public private sector collaboration and highlighted the need to develop and assess such collaborative approaches (WHO, 2001e). And the latest WHO document on DOTS even states that

involving private health care providers is imperative (WHO, 2002d). Also in the Philippines, there has been a call to establish collaboration between the private and public sector in tuberculosis control (Tupasi *et al.*, 2000, Tupasi *et al.*, 2000a; WHO, 2001f, p. 69). In 1999, the gross national product per capita in the Philippines was US \$ 1020.-, life expectancy 69 years, and infant mortality rate 31 per 1000 live births<sup>1</sup>, and 27% of the population lived with an income of below 1 US \$ a day (UNICEF, 2002). The population size was 76.5 million in May 2000 (National Statistics Office, 2002). In 2001, the country ranked 9<sup>th</sup> in the world for the estimated incidence rate of all TB cases. The annual estimated incidence rate for the year 2001 was 297 per 100,000 and the percentage of multi-drug resistant TB among new cases of TB was estimated to be 3.2%. By the end of 2000, 90% of the population had access to DOTS, the internationally promoted strategy to control TB which had been implemented by 155 countries in the year 2001. One year later, DOTS coverage reached 95% of the population (WHO, 2003). For many years already, the private sector has been strong in the Philippines. For instance, a Ministry of Health report of 1981 stated that 59% of the physicians was entirely engaged in private practice and that among the remaining 41%, nearly all did some private practice part-time (Roemer, 1991, p. 301).

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<sup>1</sup> However, according to the Philippine government, infant mortality rate was only 17.3 per 1000 live births (figure for 1998). <[http://www.doh.gov.ph/data\\_stat/html/infant\\_10.htm](http://www.doh.gov.ph/data_stat/html/infant_10.htm)>, accessed on Sept. 11, 2002.

Various questions should be considered to facilitate establishing effective collaboration. One set of questions is addressed to private practitioners, such as the common deficiencies among private practitioners and how these deficiencies can be addressed. Important questions regarding the public TB programme are what the public sector can offer to facilitate collaboration and how the public programme can increase its capacity in anticipation of the increased workload as a result of successful collaboration with the private sector. Other key questions are what local mechanisms that can facilitate collaboration are already in place and what are the complex influences which determine patient behaviour?

We aimed to examine the perceived need for public-private collaboration, the attitudes towards collaboration, existing collaborative efforts (if any), and problems to expect. Thus, we surveyed forty-five private for-profit practitioners of Malabon to examine knowledge and practices regarding diagnosis and treatment of TB (report forthcoming), as well as their perceived needs regarding further information on TB and its control. Their views on collaboration with the public health sector and on suggestions how such collaboration could look like were also established. Here we present the findings relevant to collaboration between the private and public sector. Also presented are findings regarding public-private collaboration from group discussions with health personnel of public health centres of Malabon.

## **METHODS**

### 1. The setting

The study was performed in Malabon, a municipality of Metro Manila with approximately 400,000 inhabitants in 1999. Roughly one third of Malabon's population belongs to the urban poor. The public health sector consists of 23 health centres (and a hospital where TB patients are not typically treated); it adopted DOTS in May 1999, but not all elements of the DOTS strategy were functioning satisfactorily by the end of 2000. In addition to TB care in the public sector, a large number of licensed private practitioners also treat patients with TB. None of their clinics are located in urban poor areas. There is one NGO that has a TB treatment programme. It operates through a local church in an urban poor area. Traditional healers are common in Malabon, but rarely consulted for tuberculosis (Auer *et al.*, 2000).

### 2. The survey among the private practitioners

Our survey aimed to interview all private practitioners that have adult TB patients. These private practitioners were identified by actively searching for private clinics and by asking health centre staff to identify private practitioners in the catchment areas of their health centres. Most private practitioners (41) were interviewed in 1999; four were interviewed in early 2000.



The interview questionnaire, containing 100 items, was pre-tested and reviewed with several physicians. There was an almost even mix of closed questions and open-ended questions. The interview lasted approximately fifty minutes on average, and it was performed in the doctors' clinics without the presence of patients and clinic staff. The interview elicited information about clinical practice with respect to diagnosis, treatment, case holding, case notes, and TB surveillance. The interview asked about ideas concerning infectiousness of TB and provider-perceived needs and ways of updating knowledge about TB. The survey also inquired about perceived quality of the public TB programme, its strengths and weaknesses, and suggestions for collaboration with the public TB programme.

### 3. Group discussions with health personnel of the public health centres of Malabon

Seven health centres broadly representative of the whole sample of 23 health centres, were selected by convenience sampling. The number of participants at each ranged from two to five. Most of the 28 participants were physicians, nurses, or midwives; and three were community health volunteers (locally known as *barangay health workers*).

The facilitator of the group discussions (CA) who was known to the health centre staff from extensive prior participatory research among them, made use of an interview guide to systematically cover the points of the research agenda. The main topics of discussion were the relative strengths and weaknesses of the private practitioners and the public health centres. Consideration of specific suggestions for public-private collaboration concluded the discussion. Detailed notes from the discussions were maintained by the facilitator.

#### 4. Ethical approval

The study received clearance from a review body of the Department of Health Manila. This review body is part of the office of 'Essential National Health Research'. The municipal health office of Malabon welcomed the study. Also, a committee of the Swiss Tropical Institute that reviews study proposals regarding ethical issues approved the study.

## **RESULTS**

### **A) Survey of private practitioners**

This section first presents priorities of the respondents regarding their need for updated knowledge of TB and its control. We then examine their views about the public TB services, and their attitude towards collaboration with the public TB programme.

#### Felt need for more knowledge

The respondents were asked to comment on twelve common elements of TB control and any need for more information about them (Table 7.1). The top items mentioned were (i) appropriate use of sputum microscopy; (ii) how to tell patient that household contacts need a check-up; and (iii) motivating the patient to adhere to treatment.

We presented the same 12 elements of TB control and asked the private practitioners to comment on the need for improved practices of Metro Manila's private practitioners in general in reference to these 12 elements of TB control. Interestingly, two items regarding diagnosis that were perceived to be top items (first and fourth) in terms of own need for

more information, namely 'Appropriate use of sputum microscopy' and 'Accurate reading of X-ray films' then ranked only seventh and eighth, respectively.

**Table 7.1: Perceived information needs of private practitioners of Malabon (n = 45)**

Ranking of the twelve items presented to the private practitioners (in descending order of felt need to get information)	More information needed?		
	<i>Yes</i>	<i>Possibly</i>	<i>No</i>
Appropriate use of sputum microscopy	58%	20%	20%
How to tell patient that household contacts need a check-up (tracing household contacts)	56%	18%	22%
Motivating the patient to adhere to treatment	56%	29%	13%
How to deal with side effects	53%	27%	16%
Accurate reading of X-ray films	53%	27%	16%
Patient health education about TB	53%	31%	13%
Monitoring patient during treatment	53%	24%	20%
Length of treatment period	53%	22%	22%
Informing relatives of patient about TB	47%	24%	22%
Correct dosing of drugs	42%	16%	40%
Standard treatment	36%	31%	31%
Appropriate use of X-ray	33%	27%	36%

*Note: Not all respondents answered to all items (thus, some percentages may not add up to 100%).*

When asked how they update skills for clinical management of TB, the following points were mentioned by at least 44% of the respondents: various meetings (seminars, conventions, scientific meetings), professional literature (periodicals and journals), educational leaflets and brochures, and inputs from the medical representatives of pharmaceutical companies. When asked how they would like to receive more information, they typically acknowledged of all of them except medical representatives of pharmaceutical companies. Only three respondents (7%) valued such advice.

The following three findings indicate that most respondents were not properly updated on TB control. First, only eleven respondents (24%) more or less accurately knew what the acronym DOTS stands for. Second, only one doctor knew what the acronym PhilCAT stands for (PhilCAT: Philippine Coalition Against Tuberculosis; a broad and very active umbrella organization; Roa & Romulo, 2000). Third, only five respondents could explain what intermittent therapy is.

Although DOTS was not yet well-known, respondents expressed interest in receiving and following the TB guidelines (based on DOTS) of the Department of Health: 62% expressed much willingness to follow these guidelines, and 33% expressed some willingness. There was also a widespread interest to attend continuing medical education meetings sponsored by the Department of Health: 51% were "very much interested", and 44% "quite interested". One chose not to respond and one responded with no interest to attend. A third (32%) wanted such meetings once a year, 39% wanted it twice a year and 30% thrice a year.

#### Case notes and reporting by private practitioners

Nearly half of the respondents (47%) were clearly discontented and 29% somewhat discontented with the available tool they were using for case notes. Most of the practitioners expressed their interest in having a recording tool similar to the treatment card of the public health centres. Only one respondent said he gave his TB patients a 'treatment card' for recording drug intake. Most respondents (78%) expressed clear interest and 16% some interest in using a treatment card for their patients.

Even though 82% of the private practitioners knew that TB is a notifiable disease, none of them had a reporting system.

Forty percent indicated a clear willingness to receive reporting forms and send these reports regularly to the near-by public health centre or to the Municipal Health Office, 53% indicated some willingness, and 7% no willingness.

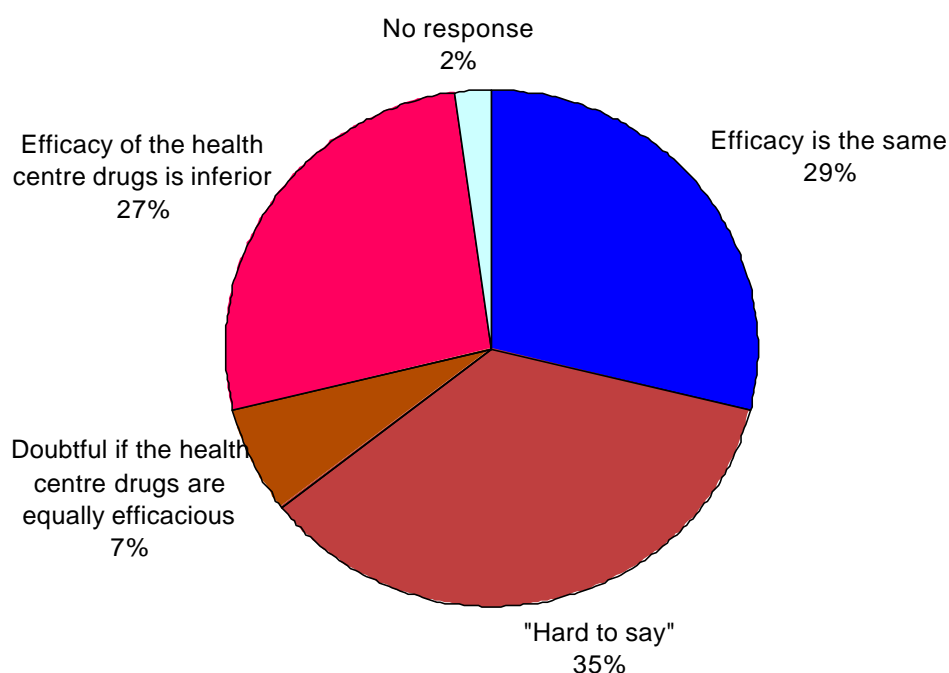
#### Perceived quality of the public TB programme

The private practitioners identified the following problems with the public TB programme: (i) insufficient treatment supply (mentioned by 67%); (ii) lack of health education (22%); (iii) poor quality of the TB drugs (18%); (iv) insufficient follow-up and monitoring of patients under treatment (11%); and (v) insufficient funding of the programme (9%).

They also discussed problems among the personnel of the public health centres, whom they thought lacked motivation and dedication (mentioned by 24%); failed to educate patients (20%); and were open for corruption (7%). When specifically asked about weaknesses of the public TB programme, the main concerns were insufficient drug supply and poor health education, followed by a lack of commitment and motivation of the personnel, lack of funding and poor quality of the drugs and/or treatment. When specifically asked regarding the quality of the TB drugs used in the health centres, only 30% of the respondents stated that the TB drugs in the health centres were as effective as the TB drugs of multinational companies. Figure 7.1 presents detail.

**Figure 7.1: Private practitioners' perceptions of inferiority of TB drugs in the public health centres (n = 45)**

Private practitioners' response to the question of whether the TB drugs used in the health centres are as efficacious as the TB drugs of multinational companies



#### Attitude towards public-private collaboration

The private practitioners were asked to comment on two approaches to collaboration between them and the public TB programme. They were asked to consider the idea of making referral of poor patients to the public health centres compulsory. The most commonly stated *advantage* was availability of free treatment, mentioned by 76% of the respondents. Other advantages were infrequently acknowledged: 16% mentioned it would curb the spread of TB; 11% mentioned it would facilitate patient health education; and 7% mentioned it would make compliance/completion of treatment more likely. The main perceived *problems* of this idea

were that treatment is not always available at the health centres, a concern mentioned by 36% and that the quality of drugs and/or treatment may be poor (20%). Table 7.2 presents more perceived problems.

**Table 7.2: Problems expected by private practitioners of Malabon from compulsory referral of poor patients to the public health centres (n = 45)**

Perceived main problem when referral of poor patients to the public health centres is compulsory	Frequency of response	
	Number	Percentage
Treatment is not always available at health centre	16	36%
Quality of drugs/treatment may be poor	9	20%
Some patients may not like to be referred to the health centre	7	16%
Some private doctors may dislike losing patients and income	4	9%
The health centres may not have the capacity for more patients	4	9%
Follow-up of patients is inadequate at the health centres	3	7%
Smear-negative patients may not be accepted at health centre	3	7%
Patients may not receive enough information about good treatment	2	4%
Some patients don't trust the TB drugs of the health centres	2	4%

*Note: Multiple responses were possible.*

To make the question more immediate, the respondents were asked what would be disadvantageous for them if this idea was implemented. Three-fourth (74%) stated implementing this idea would *not* be disadvantageous for them. Only three (7%) said their income would go down. Other unwelcome consequences were mentioned by only one respondent each: (i) the income from the private practitioner's drugstore would go down; (ii) miscommunications with the patients would occur; and (iii) private practitioners would be unable to monitor patients' treatment and treatment outcome. When the respondents were

more specifically asked what would be the *financial* repercussions for them, there were four kinds of answers. One, 27% of the respondents said there would be no effect. Secondly, 27% of the respondents said their income would go down or would go down minimally but they would not mind the financial loss. Thirdly, 14% of the respondents said their income would go down only minimally. Fourthly, 32% of the respondents said their income would go down.

When asked if it would be a good idea to give the private practitioners a certain amount of money for each referred TB patient, 20% answered positively. Forty-one percent felt this was not needed or not realistic. And 39% were negative towards it.

The respondents were also asked whether they had referred some of their patients to the public health centres during the twelve months before the interview. Most (83%) said they had referred TB patients; 11% of the respondents had referred between 30 and 100; 31% between seven and twenty; and 33% between one and five patients.

Forty-four respondents were asked if they normally mention to the patients that there are free anti-TB drugs available at the health centres; all respondents said they did. Fifty-five percent of them, however, mentioned this to their poor TB patients only, and 45% claimed to mention this to all their TB patients.

The second idea presented to them was that the private practitioners could avail of TB drugs from the health centres for their patients *if* they had a case holding mechanism and sent reports to Malabon's health office. Nearly three-fourth (73%) endorsed the idea (29% felt this was a "very good idea" and 44% felt this was "quite a good idea"). A minority



(18%) felt it was not a good idea, and 9% were not certain. While many approved of this idea, doubts about its feasibility were common: 5% felt this idea could be "very easily", and 29% felt it could be "quite easily" put into practice. A fifth (20%) said it was hard to comment on this, and 27% felt it was not easy but possible. For 20% it was definitely not easy.

We wanted to know if there were already existing relationships with personnel from the public health centres. The question was if private practitioners met at least one health centre staff once every three months. One third (33%) affirmed this. Seven of these 15 respondents said they met health centre staff more frequently or more than only one person from the health centres.

## **B) Group discussions with personnel from the public health centres**

The findings from the group discussions present perceived strengths and weaknesses of both public and private providers and the views of the participants regarding the two suggested approaches to public-private collaboration in TB control.

### Perceptions about private practitioners

The participants identified both strengths and weaknesses. Among the strengths, they discussed: (i) the consultation and diagnostic process proceed fast; (ii) their clinics are nice, have complete facilities and are open in the evenings and on week-ends; (iii) the physicians themselves deal with the patients (unlike in the health centres were often, the nurses and/or midwives deal with the patients); (iv) the drugs are from transnational companies; (v) they choose the best treatment; and (vi) some of the private practitioners are specialists.

They also considered a number of weaknesses: (i) the diagnostic process is too fast, leading to a neglect of sputum examination; (ii) when the X-ray does not show clear signs of TB, there is a temptation to declare the patient has minimal TB so that there is treatment and thus income; (iii) weak treatment monitoring (e.g. no DOT); (iv) weak recording; (v) some are not up-to-date regarding TB and its control; e.g. DOT not known to them; (vi) some are strongly money-oriented and lack concern for the patients; and (vii) low awareness regarding the TB programme in the health centres.

When the participants were asked what they believed the private practitioners think about the health centres, only one positive statement was made, namely that the private practitioners refer patients to the health centres and therefore seem to have some trust in the health centres. Other expressed perceptions were negative: the private practitioners: (i) have low regard for the health centres; (ii) underestimate the capacity of the health centres; (iii) think the health centre physicians lack knowledge and training and that the health centre lacks equipment; (iv) consider the processes of the health centres to be slow; and (v) do not trust the drugs of the health centres.

The participants saw themselves and their health centres in a better light. They consider the health centre personnel to be well trained, updated and capable and also felt their diagnostic processes (mainly sputum examinations) were quite fast now. They also mentioned that treatment is available "these days", that health education and DOT is being done, and that the TB services are free of charge. They also felt that their approach to the patients is personal; most patients would be known to the staff. Still, they mentioned some weaknesses, namely a lack of manpower and unreliable supply of slides and drugs, as well as

some slowness in certain processes; e.g. the drugs may not yet be ready when the sputum examination result is known. Finally, they acknowledged that some health centres tend to be crowded.

Attitude towards two proposals for public-private collaboration

The participants were asked to comment on two suggestions for enhancing collaboration: compulsory referral of poor patients and access to TB drugs for private practitioners in return for clear measures to improve case holding and reporting. They generally felt compulsory referral was a good idea, but saw the following problems on the side of the private practitioners: the private practitioners; (i) may not be able to find out if a patient really is poor; (ii) do not ask for sputum examinations; (iii) may lack knowledge regarding the public TB programme; and (iv) may not be willing to refer patients, i.e. to 'lose' patients. The participants also mentioned the need to have a proper process for this referral scheme and that their health centres may sometimes lack the needed TB drugs.

The participants were more sceptical about the second idea presented to them, i.e. that the private practitioners could avail of TB drugs from the health centres for their patients *if* they had a case holding mechanism and sent reports to Malabon's health office. In only one health centre was there a positive comment, namely that this would mean a reduced burden for the health centres. In another health centre a comment was that for this to happen it would be important to have standard treatment in the health centres *and* in the private clinics. Interestingly, one participant recalled that some years back (when there were lots of TB drugs available), such a scheme had actually been in place for an NGO working in two places of Malabon.

They saw the following problems on the side of the private practitioners: the private practitioners may feel like employees of the public programme; may sell the TB drugs; would still ask for a consultation fee; and have weak case holding mechanisms, e.g. no direct observation. From the health centre side they saw two problems: first, the health centre physicians may feel offended because this scheme suggests that the health centre physicians can't be trusted to take care of the TB patients. And second, there would be confusion about case records and reporting.

## **DISCUSSION**

### Limitations of the study

The interviewer of the private practitioners (the first author) was not an official part of the public TB programme, but the introduction of the questionnaire made it clear that the interviewer had links to the public TB programme. Thus, the answers of the private practitioners may have been incorrectly too positive about the public TB programme and about collaboration with the public TB programme. Such social desirability bias is very likely to occur when respondents are directly being interviewed one-to-one.

No formal efforts were made to counteract this bias. However, an informal way of verification of the findings was that all the interviewed private practitioners were visited several times after the interview. These visits strengthened the impression that approximately half of the respondents were genuinely interested in public-private collaboration.

Another limitation is that no attempts were made to verify answers of the private practitioners. For instance, it was not checked with the corresponding public health centres if a private practitioner really referred people with symptoms of TB to them.

#### Prospects for public-private collaboration in Malabon

The following encountered perceptions and characteristics of the private practitioners were found to be potential stumbling blocks in establishing public-private collaboration:

- Perceived lack of availability of anti-TB drugs in the health centres
- Lack of trust in the efficacy of the anti-TB drugs of the health centres
- The treatment regimens used in the public health centres are questioned
- Partly a lack of trust in the commitment of the health centre staff
- Loss of income feared if referral to health centres is frequent
- No record keeping
- Poor or non-existing case holding mechanisms among private practitioners.

Another complication was the lack of unity in the Medical Society of Malabon/Navotas, which is factionalised in two distinct groups.

Nevertheless, some degree of public-private collaboration is already on-going: most private practitioners refer TB patients to the public centres and there is some experience of a past scheme where the public TB programme provided TB drugs to an NGO. And our survey found that at least half of the respondents were open to public-private collaboration. A recent telephone survey across the Philippines found an even higher proportion of private practitioners being willing to collaborate with the public TB programme. However, most of

them wanted to be financially rewarded for this (Portero & Rubio, 2003). In Malabon, we found:

- Most private practitioners expressed a need to receive further information about TB and its control and a desire to get updated on the public TB programme
- Many also indicated a willingness to report to the public health sector
- They also expressed their willingness to follow the guidelines of the public TB programme, i.e. to follow a standard diagnostic and treatment procedure
- There was awareness that the financial demands of private TB treatment are a real threat to treatment adherence
- Half of the private practitioners stated that frequent referral of their TB patients to the health centres would either not affect their income or it would not bother them
- Most liked the idea of having access to the public TB drugs, and one third believed such a scheme could be developed easily or quite easily

#### Moving towards public-private collaboration: next steps

Our findings suggest the following avenues should be pursued to achieve better public-private collaboration:

##### *a) A referral system*

Most private practitioners in Malabon already refer TB patients, commonly those who are obviously poor. An official referral letter and a commitment of the public programme to let the private practitioner know the outcome of treatment of the referred patients would make this referral mechanism more acceptable. Similar efforts to provide feedback to the private practitioners on each patient referred proved important in a public-

private collaboration TB project in Hyderabad, India (Murthy *et al.*, 2001). Other options need to be explored, such as: (i) mechanisms that facilitate a regular visit of the referred patient to the private practitioner, e.g. every two months; (ii) incentives for referring patients, e.g. receiving TB health education materials from the public health sector when TB patients are referred; and (iii) strengthening the awareness of the private practitioners regarding the dangers of incomplete treatment and the costs of full private TB treatment. A daily six-month-regimen costs at least Peso 4000.-. This corresponds roughly to the monthly cash-on-hand income of low-income earners. Ethical standards of care in some places, like Nairobi, require private practitioners to make their patients sign an agreement that states the patient has chosen private care knowing about the free public TB programme (WHO, 2001e, p. 56).

Experience of New York City demonstrates that success is possible: strengthening the public TB programmes and actively informing and educating the private practitioners resulted in a four-fold increase in referrals from the private sector (Fujiwara *et al.*, 1996, cited in Uplekar *et al.*, 2001a). On the other hand, in a public-private collaborative TB project in Kathmandu, Nepal, where the public sector had very limited capacity to engage with the private sector, very few patients were referred from the private to the public sector (Hurtig *et al.*, 2002).

While it is not in the short-term financial interest of private practitioners to refer patients, it may well be in their long-term interest. Private practitioners in two places in India participating in a public-private collaboration TB project expressed their belief that if they work with the public TB programme and offer free services to patients, these patients

and their families may stay with their practice for treatment of other health problems (Uplekar *et al.*, 2001a). Similarly, properly informing their patients about the cost of TB treatment and the free services of the public TB programme may provide a strong and welcome sign of genuine concern and thus make the private practitioner more popular. But it may also enhance stigma, and practitioners need to be careful to explain the rationale for referral, so that referral is not perceived as an indication of a low, undesirable status of TB.

*b) Helping the private practitioners improve their practices*

The expressed desire for more information and the willingness to follow the governmental TB guidelines should motivate the public sector to provide seminars to improve clinical expertise of private practitioners. Disseminating evidence-based information to private practitioners is the first step (Mills *et al.*, 2002). However, it must be kept in mind that seminars alone are seldom effective (Thomson O'Brien *et al.*, 2002a). Academic detailing has been suggested as a more promising approach (Thomson O'Brien *et al.*, 2002b). This approach, however, is highly labour-intensive. For instance, in Karachi, an intervention to improve the performance of private practitioners included academic detailing that required two physicians to visit the private practitioners eight times (Thaver & Harpham, 1997). Academic detailing should be accompanied by other measures, such as mobilising local opinion leaders (Thomson O'Brien *et al.*, 2002) and patient-mediated interventions.



*c) Tools to enhance public-private collaboration*

Various tools and forms routinely used in the public sector for recording, reporting and health education should be adapted for private clinics. For instance, adapted reporting forms should be given to the private practitioners and the private practitioners should be contacted regularly (best by phone or in person) by personnel from the public health system to gather the needed data. Evidence suggests that only actively telephoning private practitioners works (Aljunid, 1995).

*d) Making free drugs available to the private practitioners*

A careful assessment of the experience of an earlier strategy for a public TB programme to provide TB drugs to an NGO may provide valuable lessons. Based on this, discussions between the public health sector and the private practitioners should be held on how to establish a mechanism that makes public TB drugs available to the private practitioners who fulfil certain conditions. Of course, careful co-ordination with the central office of the national TB programme to ask for the needed supply of drugs and for full authorisation is fundamental for this.

Recently a public-private collaborative project has started in Delhi, giving private practitioners access to free public TB drugs. These private practitioners have informed the community through prominent boards in their clinics that they can get free TB medication (Uplekar *et al.*, 2001a).

Other steps to strengthen public-private collaboration

A well-running public TB programme is a prerequisite for public-private collaboration. Special attention is needed to ensure prompt diagnosis and a reliable drug supply, and to develop a patient-friendly implementation of supervision of treatment. Continuous training and empowerment of the health centre personnel with reference to recently published principles (WHO, 2002c) to ensure technical capability and interpersonal skills are crucial. Where needed and possible, health centres should be renovated and their equipment upgraded. Human capacity needs to be set free to work on establishing public-private collaboration. Public physicians should be released from clinical responsibilities to ensure the smooth running of the DOTS programme and to liaise with the private sector. It is crucial that the public sector has the capacity and resources to engage with the private sector, as experience with a public-private collaboration TB project in Kathmandu showed (Hurtig *et al.*, 2002).

The public TB programme should offer evening seminars for the private practitioners to respond to the expressed needs and willingness of the private practitioners and issues of diagnosis and treatment that need improvement. It is crucial that these seminars be of high quality. Of great help would be if a well-known chest physician could be won over to become a part in this public-private collaboration endeavour. A key ingredient in the successful public-private collaboration TB project in Hyderabad (Murthy *et al.*, 2001) is the

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<sup>2</sup> In May 2000, a dinner-seminar for the public and the private practitioners was organised by the Swiss Tropical Institute in co-ordination with the health office of Malabon to give an update on TB control and to give a first stimulus regarding public-private collaboration. A well-known chest physician was the key speaker. The attendance of the meeting was fair. Some months later, the health office of Malabon organised a dinner-seminar for the private practitioners to present the public TB programme and discuss public-private collaboration. Attendance was satisfactory. However, the quality of the meeting was not high. At a second meeting, performed approximately eight months later, only three private practitioners were present and the quality of the meeting was poor.

fact that the hospital physician who visits the private practitioners is a well-known and well-respected chest physician (KJR Murthy, personal communication, February 2000). The seminars could also serve as a first forum to discuss practical issues regarding collaboration. To facilitate the taking of the steps toward collaboration, the creation of a local committee that is composed of representatives of the public and the private sector may be helpful. Such a committee should have the local knowledge and insights to develop practical approaches to collaboration. It would also have an important role to play to guide on-going implementation and evaluation of public-private collaboration initiatives. This committee could also decide whether measures to understand the local situation better are needed.

Another option that should be considered is to have an NGO serve as intermediary between the public TB programme and the private practitioners. This approach has been implemented in Kathmandu, Nepal (Hurtig *et al.*, 2002) and Chennai, India (Balambal, 2001).

It is also important to address the expressed concerns of private practitioners and the public health care providers. This should be done in collaboration with the central office of the national TB programme. These concerns encompass issues such as: (i) the lack of trust in the public TB drugs; (ii) the lack of trust in the DOTS regimens; (iii) the over-reliance on chest X-rays. Of great help is that through the efforts of PhilCAT, national comprehensive guidelines for TB control are now available in the Philippines. PhilCAT has also recently drafted a document regarding a unified strategy of TB control for government agencies and the private sector (Task Force on Tuberculosis, 2000). The challenge remains of effectively disseminating these materials through some of the mechanisms suggested above.

Seminars and academic detailing will hopefully create a strong demand from the private practitioners to have their patients with symptoms of TB undergo sputum examinations. Mechanisms for free sputum examinations performed by the public sector for private patients need to be considered and developed in collaboration with the central office of the national TB programme.

To improve public knowledge of TB and evoke appropriate responses, health education activities targeting the general population, especially the low-income groups, are needed. Mass media campaigns have been effective (Jaramillo, 2001; Grilli *et al.*, 2002). In an advanced stage of public-private collaboration, the health educational activities should proceed through active and innovative collaboration with private practitioners.

## **CONCLUSION**

Our study identified obstacles to public-private collaboration but also indicated the potential value of public-private collaboration. More information about the private practitioners is needed, especially perceived incentives and disincentives for the private practitioners with respect to public-private collaboration. Local communities, like Malabon, will benefit from a stakeholder analysis. On the other hand, it is no longer appropriate to wait for more information; the time has come to proceed with public-private collaboration. Suggested measures should be continuously evaluated and revised as indicated.

The support of NGOs, research institutions, and funding agencies to support public-private collaboration must be actively cultivated.

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**FEASIBILITY, ACCEPTABILITY AND EFFECTIVENESS OF FULLY THRICE-WEEKLY INTERMITTENT TB THERAPY COMPARED TO DAILY TB THERAPY IN PUBLIC HEALTH CENTRES IN MANILA, PHILIPPINES**

*Running title: Thrice-weekly vs. daily TB therapy*

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*Working paper*

**Feasibility, acceptability and effectiveness of fully thrice-weekly intermittent TB therapy compared to daily TB therapy in public health centres in Manila, Philippines**

**ABSTRACT**

**Introduction:** Intermittent therapy makes supervision of treatment more feasible for patients and providers, and it reduces the costs for drugs by up to 50%. Intermittent therapy regimens are recommended, but the evidence base is not very strong.

**Objectives:** To compare the feasibility, acceptability, and effectiveness of thrice-weekly and of daily therapy in a public health care setting.

**Methods:** Randomised controlled trial; thrice-weekly therapy was randomly assigned to 10 of the 20 health centres of a municipality in Manila. All TB patients of the other 10 health centres received daily therapy. Patients were interviewed three times. Drug susceptibility tests were performed.

**Results:** 806 patients (451 under thrice-weekly and 355 under daily therapy) were interviewed shortly after treatment start. 18.5% were re-treatment cases. Multidrug-resistant TB was found among 2% of the new and 26% of the previously treated patients.

Under thrice-weekly therapy, DOT in the health centres was more common than when treatment was daily (32% vs. 21%). Thrice-weekly therapy was more popular among patients and health personnel and resulted in savings of about 40% of the cost of drugs.

There were also some disadvantages of thrice-weekly therapy compared to daily therapy: difficulty swallowing the pills as well as nausea were reported more frequently (16% vs. 11% and 30% vs. 21%, respectively). And sputum conversion rate assessed after two months of treatment was lower (74% vs. 81%;  $p = 0.03$ ). Treatment outcome was similar, but treatment failure and default due to side effects was more common among those treated thrice weekly ( $p = 0.08$  and  $p = 0.04$ , respectively). In a multivariate model, adverse treatment outcome (failure, relapse) was not associated with mode of treatment.

**Conclusion:** In the light of the potential benefits of intermittent therapy, its equivalence to daily therapy should be established firmly and if confirmed, fully thrice-weekly therapy should be used more widely.

*Keywords:* tuberculosis, intermittent regimens, acceptability, effectiveness, randomised controlled trial

## INTRODUCTION

Tuberculosis continues to be one of the most devastating diseases in the world. It is estimated that 8.5 million new TB cases occurred in the year 2001 (WHO, 2003) and that 1.8 million people died of TB in the year 2000 (Corbett *et al.*, 2003). As these two figures indicate, effective treatment of tuberculosis remains a major problem even though powerful drugs have been available for half a century now.

### Short-course chemotherapy: the backbone of tuberculosis control

The last major improvement in the treatment of tuberculosis occurred in the late 1960's/early 1970's with the introduction of rifampicin and pyrazinamide, which made highly efficacious and effective 6- to 9-month-long treatment possible (Fox *et al.*, 1999) and paved the way for so-called short-course chemotherapy. However, this cost-effective tool - one of the most cost-effective health interventions of all (Murray *et al.*, 1991; World Bank, 1993) - has not been used widely. With the recent implementation of the DOTS strategy progress has been made (DOTS: the broadly promoted strategy to control TB which had been implemented by 155 countries in the year 2001; WHO, 2003). Still, a rapid acceleration of progress in the expansion of DOTS is needed to reach the WHO-targets of a global case detection rate of 70% and a successful treatment rate of at least 85% by the year 2005 (WHO 2001f, p. 5). More human and financial resources need to be mobilised (Floyd *et al.*, 2002). And a more cost-effective, patient- and health provider-friendly implementation of DOTS must be explored and pursued rigorously; the available interventions must be delivered better (Remme *et al.*, 2002). Since no new diagnostic tools or anti-TB drugs can be expected in the years to come, there is a need to sharpen the existing tools.



Intermittent therapy

Using intermittent therapy (drugs are taken only twice or three times a week with generally increased dosages) may be such a way of enhancing the effectiveness of DOTS. It has the potential to make supervision of treatment (DOT - directly observed therapy) more feasible for patients and for health providers. Indeed, a review from 1980 (Sbarbaro, 1980) even stated that *daily* directly observed therapy was not viable and that intermittent therapy was an effective approach for overcoming non-adherence to treatment. Another advantage of intermittent therapy is that it reduces the costs for drugs by up to 50% (see table 2 in Van Gorkom *et al.*, 2001). There is also evidence that severe side effects occur less often (Tuberculosis Research Centre, 1997; Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council, 1989; Hong Kong Chest Service/British Medical Research Council, 1981; Hong Kong Chest Service/British Medical Research Council, 1976; Tempel *et al.*, 1950).

While daily treatment is common, various treatment schemes with intermittent therapy were and are being used. Intermittent regimens after an initial intensive phase of daily therapy were already studied in the early 1950s (Fox, 1971). For instance, a report on an intermittent regimen with streptomycin and isoniazid was published in 1954 (Mackey-Dick, 1954, cited in Sbarbaro, 1980). In some areas, intermittent therapy is used after two (or three) months of daily treatment, for instance in Sulawesi, Indonesia (Becx-Bleumink *et al.*, 1999) and Peru (Suarez *et al.*, 2002). In other places, twice-weekly therapy is used after an initial phase of several weeks of daily therapy, for instance in the USA (Cohn *et al.*, 1990; Sterling *et al.*, 1999) and in South Africa (Davies *et al.*, 1999). Twice-weekly therapy from day one of treatment has also been used (Caminero *et al.*, 1996). Fully thrice-weekly

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therapy from day one of treatment is being used in India (Khatri & Frieden, 2002) and in Myanmar (National Tuberculosis Programme Myanmar, 2000) in all DOTS areas. And in large parts of China, treatment every other day (i.e. 3.5 times per week) from day one of treatment is being used (China Tuberculosis Control Collaboration, 1996). Intermittent regimens are recommended, e.g. by the British Thoracic Society (British Thoracic Society, 1998), the American Thoracic Society (ATS/CDC/IDSA, 2003) and the World Health Organization (WHO, 1997a). The latter endorsed intermittent therapy in 1974 (WHO, 1974) but does not encourage the use of twice-weekly therapy, mainly due to the fact that a missed dose represents a big fraction (50%) of the total number of weekly treatment doses (WHO, 1997a, p. 26). With the occurrence of rifapentine, once-weekly regimens during the maintenance phase are being tested now (Benator *et al.*, 2002; Tam *et al.*, 2002).

#### Rationale for the study

Observational studies have shown intermittent therapy to be effective (Khatri & Frieden 2002; Connolly *et al.*, 1999; El Sadr *et al.*, 1998; Cao *et al.*, 1998; Yan *et al.*, 1996; Chaisson *et al.*, 1996; Neher *et al.*, 1996; China Tuberculosis Control Collaboration 1996; Alwood *et al.*, 1994; Hong Kong Chest Service/British Medical Research Council, 1991. See also WHO, 1997b for an overview). However, a few studies had less good results, e.g. one from Malawi (Harries *et al.*, 2001) and two from India (Tuberculosis Research Centre, 1997, Datta *et al.*, 1993). A recent Cochrane review (Mwandumba & Squire, 2002) concluded that larger randomised trials are warranted. The review found only one randomised trial that properly compared intermittent therapy (it was thrice-weekly therapy from day one of treatment) with daily therapy (Hong Kong Chest Service/British Medical Research Council 1981. This study in Hong Kong indicated a possibility of an increased

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relapse rate with intermittent therapy. There are also some concerns that with intermittent therapy there might be a higher likelihood of development of drug resistance while on treatment (Mitchison & Dickinson, 1971). However, to our knowledge this potential danger has not been documented, and in a study in mice bacterial resistance to isoniazid appeared to develop at a slower rate in the mice treated intermittently (Bloch, 1961, cited in Sbarbaro, 1980). And a recent review only mentioned once-weekly but not twice-weekly or thrice-weekly treatment as a risk factor for the development of drug resistance (Mitchison, 1998). Considering the established and potential advantages of intermittent therapy, non-inferiority of intermittent therapy compared to daily therapy should be tested thoroughly and if confirmed, intermittent therapy should be used widely. In 1998, WHO identified a "profound neglect of research relevant to tuberculosis control activities". Cost-effectiveness analyses and alternative ways of delivering the DOTS strategy were found to be among the priority areas of research (WHO, 1998b). And in 2002, the Special Programme for Research and Training in Tropical Diseases (TDR) of UNDP/World Bank/WHO stated that the first TB research priority is health policy and systems research to promote a wider use of DOTS, and to make better use of existing tools (TDR, 2002). In view of the enormity of the tuberculosis problem and due to the fact that every year, millions of TB patients are being treated, clarifying which regimens are most appropriate and efficient must be a high priority.

## **METHODS**

### Setting

The study took place in Taguig. Taguig is an urban and partly semi-urban municipality of Metropolitan Manila, Philippines; it had 520,000 inhabitants in the year 2001, served by twenty public health centres whose catchment area populations ranged from 150

6,500 to 96,000. Most of the twenty health centres have an own physician; some health centres share a physician with another health centre. All health centres have at least one nurse and one midwife. Sputum microscopy is being done in four health centres, and quality assurance measures are in place. With the exception of one health centre, the patients can submit their sputum specimens in their local health centre.

DOTS was introduced in Taguig in late 1996. DOTS was generally implemented well in Taguig and Taguig was recommended by the Philippine Department of Health as an area where research can be performed. A physician and a nurse act as the 'TB co-ordinators'. They both also serve as local staff in a health centre.

#### Randomisation and patients

Randomisation took place at the level of health centres (cluster randomisation; randomisation at the level of the patients would not have been feasible). Stratified random sampling was performed: among the ten health centres with the highest number of TB patients in the year 1999 and in the first half of 2000, five were randomly allocated to thrice-weekly therapy. The same was done for the remaining ten health centres. Starting November 13, 2000 all newly enrolled TB patients of the public sector in Taguig were either given daily therapy or thrice-weekly therapy, depending on whether their health centre was allocated daily therapy or thrice-weekly therapy. However, in all the 20 health centres, failure cases were given daily therapy. The trial lasted until the end of December 2002.

All patients whose initial sputum examination (at least one of the three specimens) was positive for acid-fast bacilli (AFB) on sputum microscopy or whose sputum sample showed growth for *Mycobacteria* on culture were included in the study (patients in whose

sputum only one acid-fast bacillus or one colony on culture was found were included in the study). Failure cases were excluded from analysis. No other exclusion criteria were applied.

Before being initiated to treatment, the patients were asked by the health centre staff regarding previous treatment. However, the patient interviews revealed that many patients classified as 'new patients' had actually had previous anti-TB treatment for at least one month. The health centres of such patients were then informed and advised to shift the patient to the re-treatment regimen.

Follow-up sputum examinations were done two, four and five months after initiation to treatment for new patients and three, five, and seven months after initiation to treatment for patients under re-treatment (according to the national guidelines). The samples of the first follow-up sputum examination and of the last follow-up sputum examination of patients included in the study underwent culturing. In addition, the samples of other follow-up sputum examinations that were AFB-positive also underwent culturing.

#### Diagnostic procedures

Patients with symptoms of tuberculosis had to submit three sputum examinations: two on-the-spot samples and one early-morning sample. Staining was with Ziehl Neelsen. If only one sample was found positive, the patient usually had to submit another three sputum samples. AFB-positive samples and AFB-negative samples of patients who had at least one cavity on their chest X-ray were stored in cool temperatures (in styropore boxes with pieces of ice). Several times a week, the sputum samples (but not more than two per patient) were brought for culturing to the 'TB Research Laboratory' of the Philippine General Hospital, located in nearby Manila City. There, AFB microscopy was done by the concentrated

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technique and each sample underwent decontamination process by the 4% NaOH procedure (Petroff's Method) and was inoculated to a solid medium (Löwenstein Jensen) and to a liquid medium (7H9 broth). Reading of cultures for growth was done every week until the eighth week of incubation and even extended up to twelve weeks when necessary.

Drug susceptibility tests were performed in the 'Mycobacteriology Unit' of the Institute of Tropical Medicine in Antwerp, Belgium, a supranational reference centre for susceptibility testing of tuberculosis drugs. In the 'TB Research Laboratory' in Manila, growth from cultures was transferred to screw cap tubes with 7H9 broth once a month. At the time of dispatch to Antwerp (which is approximately every two months) the vials were brought by airfreight to Antwerp. However, during the first seven months of the trial the samples were transported from Manila to Antwerp using skimmilk. Due to a high rate of contamination this kind of medium was no longer used; instead, 7H9 broth was used.

In Antwerp, culture re-growth on Löwenstein-Jensen medium was done. Drug susceptibility testing was performed according to the proportion method of Canetti *et al.* (1969). The antibiotics tested were isoniazid (H), rifampicin (R), ethambutol (E), streptomycin (S) and para-aminosalicylic acid (PAS). Approximately 10% of the samples also underwent drug susceptibility testing in Manila, also according to the proportion method. In Manila, the drugs tested were H, R, E, S, and pyrazinamide (Z). Drug resistance of pyrazinamide was examined with the disc submerge method.

Follow-up of patients after treatment

To increase the likelihood of finding the relapse cases, all patients who completed treatment were asked to submit a sputum sample five, ten and fifteen months after the end of treatment. Only few patients followed this request. Thus, attempts were made to visit the patients in their homes five, ten and fifteen months after the end of their treatment to ask them to submit a sputum sample. In addition, patients who had some indication that they were treatment failures were also visited in their homes after the end of treatment. All the sputum samples that turned out to be positive for AFB underwent culturing. Culturing was done with *all* the sputum samples submitted fifteen months after the end of treatment.

Definitions referring to treatment outcome

*Completion of treatment:* The third patient interview provided information about whether or not the patient had completed treatment. When the patient stated not to have completed treatment but the patient's record in the health centre was 'completed treatment' the statement of the patient was accepted as more accurate. On the other hand, when the patient stated to have completed treatment but according to the patient's record in the health centre the patient had *not* completed treatment, then the health centre record was accepted as more accurate. Treatment was considered to be completed if at least 22 of the prescribed 24 weeks of treatment (or 30 of the 32 prescribed weeks of treatment for patients on the re-treatment regimen) were taken.

The following was considered to be a *failure case*:

- The third follow-up sputum smear examination (at 5 or 7 months of treatment) was at least +1 (more than 10 AFB per 100 microscopy fields) and the corresponding culture result was not negative.
- The third follow-up sputum examination (at 5 or 7 months of treatment) was only scanty positive (less than 10 AFB per 100 microscopy fields) or negative but sputum microscopy and/or culture in the 'TB Research Laboratory' was positive *and* the patient clearly still had signs and symptoms of tuberculosis.
- The third follow-up sputum examination (at 5 or 7 months of treatment) was culture-positive with more than 10 colonies *and* the patient clearly still had signs and symptoms of tuberculosis or - when the patient could no longer be re-visited after the third interview - the patient did not feel fully healed at the third interview.

The same criteria applied for *relapse cases* with the difference that the sputum positivity was at least two months after the end of treatment. In addition, patients who (after at least two months after the end of their treatment) were accepted as re-treatment cases in one of the health centres of Taguig were also considered to be relapse cases.

### Treatment

In the health centres with thrice-weekly therapy, new cases (and those classified as new cases) received 2 H<sub>3</sub>R<sub>3</sub>Z<sub>3</sub>E<sub>3</sub>/4H<sub>3</sub>R<sub>3</sub> (meaning: H, R, Z, and E for the first two months of treatment, and then H and R for another four months) and re-treatment cases received 2 H<sub>3</sub>R<sub>3</sub>Z<sub>3</sub>E<sub>3</sub>S<sub>3</sub>/1 H<sub>3</sub>R<sub>3</sub>Z<sub>3</sub>E<sub>3</sub>/5H<sub>3</sub>R<sub>3</sub>E<sub>3</sub>. Patients with "minimal TB" received a weaker regimen.



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The patients of the other ten health centres received the same regimens but with *daily* drug intake. The dosages for patients under thrice-weekly therapy were as follows:

- a) with a bodyweight of up to 50kg: 600mg H, 450 mg R, 1500mg Z, 1200mg E, 1g S
- b) with a bodyweight of more than 50kg: 600mg H, 600 mg R, 2000mg Z, 1600mg E, 1g S.

The dosages for patients under daily therapy were as follows:

- c) with a bodyweight of up to 50kg: 300mg H, 450 mg R, 1000mg Z, 800mg E, 1g S
- d) with a bodyweight of more than 50kg: 450mg H, 450 mg R, 1500mg Z, 1200mg E, 1g S.

In addition, the physicians of the health centres were advised to adjust dosages for patients weighing less than 35kg, especially for patients weighing less than 30kg.

All drugs were provided in single tablets (rifampicin is in capsule form). Thus, patients under thrice-weekly therapy had to swallow nine or twelve tablets, respectively, depending on their bodyweight. For patients under daily therapy, the corresponding figures were six and nine tablets, respectively. Except for ethambutol, the drugs were given in blister packs for those under daily therapy. For those under thrice-weekly therapy, a small plastic bag with the medication good for one day was prepared.

Interviewing of patients

All AFB-positive patients were interviewed three times (almost all of them in their homes): during the first month of treatment (in exceptional cases also later), after approximately two months of treatment, and shortly after the end of treatment. AFB-

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negative patients that turned out to have a positive culture were commonly interviewed twice only: after approximately two months of treatment and shortly after the end of treatment.

### Discussions with health providers

Informal group discussions were held in four health centres where thrice-weekly therapy was given and in one health centre where daily therapy was given. The topic was a comparison of the daily and the thrice-weekly treatment approach, especially in terms of the advantages and disadvantages.

### Ethical considerations

The study received clearance from a review body of the Department of Health Manila. This review body is part of the office of 'Essential National Health Research'. And the Municipal Health Office of Taguig agreed to have the study performed in Taguig. On October 27, 2000, a 'Memorandum of Agreement' was signed with the Municipal Health Office of Taguig. Among other things, this document defined the responsibilities and stated ethical guidelines. In addition, a committee of the Swiss Tropical Institute that reviews study proposals in terms of ethical issues approved the study.

### Data management and statistical analysis

All data derived from the questionnaires were processed using Epi Info software package (version 6.04, USD Inc., Stone Mountain, GA, USA). Two of the authors did the encoding, and one of them (CA) re-checked the encoding of all the questionnaires.

Statistical analysis was performed using Chi-Square or Fisher's exact test (two-tailed) for categorical factors. Treatment outcome was analysed using the intention-to-treat approach (Newell, 1992). There were some exceptions: several patients were not included in the analysis since they had a mix of daily and thrice-weekly therapy, for instance, a patient who – in spite of being in a health centre with daily therapy - first took treatment thrice weekly, then daily treatment, and then shifted back to thrice-weekly therapy. Multivariate logistic regression analysis was performed to account for the effect of possible confounders. STATA statistical software was used (Stata Corporation, 1999). Seven variables were included in the multiple regression analysis (596 observations, stepwise backward regression).

## **RESULTS**

### The study population

We here present the findings from data of 806 patients that were interviewed shortly after initiation of treatment in the health centre (73% were interviewed within the first three weeks of treatment; mostly in the second or third week of treatment). We also make use of some data gathered from 668 patients at the second interview (at two months of treatment) and from 465 patients at the third interview (shortly after the end of treatment). The fieldwork of this study has not yet been completed, and data from approximately 900 patients will be reported at a later stage.

Majority (72%) were male, and 18.5% of the 806 patients had had previous anti-TB treatment for at least four weeks. For 333 of the 806 patients (41%), results from drug

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susceptibility tests were available; 68% of the tested patients had strains susceptible to all tested drugs. Table 8.1 presents more data. Twenty-two percent of the new patients (58/260) and 39% of the re-treatment cases (27/69) had resistance to isoniazid (for 4 patients their status regarding previous anti-TB treatment was not clear; one of them had resistance to isoniazid). Multidrug-resistant tuberculosis (MDR-TB) was found in 7% of the patients (23/333); 2% of the new patients (5/260) had MDR-TB, and 26% of the re-treatment cases (18/69) had MDR-TB.

**TABLE 8.1: Drug resistance pattern before start of treatment at the health centre**

	<i>All patients</i> ( <i>n</i> = 806)	<i>Patients under</i> <i>thrice-weekly therapy</i> ( <i>n</i> = 451)	<i>Patients under</i> <i>daily therapy</i> ( <i>n</i> = 355)	<i>p-value</i> <sup>1</sup>
With results from drug susceptibility test:	41% (333/806)	44% (200/451)	37% (133/355)	0.05
Among those with results:				
No resistance found	68% (228/333)	65% (130/200)	74% (98/133)	0.09
Any drug resistance	32% (105/333)	35% (70/200)	26% (35/133)	0.09
Any drug resistance other than MDR-TB	25% (82/333)	29% (57/200)	19% (25/133)	0.04
Resistance to isoniazid	26% (85/333)	26% (52/200)	25% (33/133)	0.8
MDR-TB <sup>2</sup>	7% (23/333)	6.5% (13/200)	7.5% (10/133)	0.7

<sup>1</sup> Comparing patients with thrice-weekly therapy with patients with daily therapy.

<sup>2</sup> Two percent of the new patients and 26% of the previously treated patients had MDR-TB.

Comparison of the two treatment arms

Table 8.2 presents the frequency distribution of baseline data among those treated thrice weekly and among those treated daily. The two patient groups differed statistically significantly for four patient features. We also attempted to assess the quality of care provided in the health centres, comparing the health centres giving thrice-weekly therapy with those giving daily therapy. We looked at the perceived skill and kindness of the health centre personnel and the perceived sufficiency of explanation received. There were no clear differences between those treated daily and those treated thrice-weekly. Slightly more patients under thrice-weekly therapy were discontent with the perceived skill of the health centre personnel compared to patients under daily therapy (9% vs. 6%;  $p = 0.1$ ). One of the researchers, the public TB co-ordinator and one research assistant graded the 20 health centres according to how they perceived the quality of the services in these 20 health centres. This assessment did not find differences between the two groups of health centres. Also, no difference was found in the extent of delay between sputum examination and initiation to treatment between the two groups of health centres. Nor was there a difference in the proportion of patients who were wrongly put on treatment for new cases (10% vs. 12%) or who received a non-recommended dosage (12% vs. 9%). However, in the last interview at the end of treatment, more patients under thrice-weekly therapy compared to those under daily therapy stated to have received complete treatment all the time (95% vs. 89%;  $p = 0.01$ ).

**TABLE 8.2: Baseline data among those treated thrice weekly and those treated daily**

	<i>Patients under thrice-weekly therapy (n = 451)</i>	<i>Patients under daily therapy (n = 355)</i>	<i>p-value</i>
Bodyweight below 35kg:	4.9% (22/448)	9.0% (32/355)	0.02
High self-perceived degree of poverty ('poor', 'very poor'):	49.5% (181/366)	58.2% (173/297)	0.02
Male and no job:	22.7% (102/450)	17.7% (63/355)	0.09
High degree of sputum positivity (+3 <sup>1</sup> )	20.5% (91/443)	19.6% (68/347)	0.7
Patients having co-morbidity:			
Asthma	3.3% (15/449)	4.5% (16/355)	0.4
Hypertension	4.0% (18/449)	1.1% ( 4/355)	0.01
Diabetes	5.6% (25/449)	5.1% (18/355)	0.8
X-ray finding:			
No X-ray or result ill-defined or not known	50.6% (228/451)	59.2% (210/355)	0.01
Non-cav. TB	50.7% (113/223)	57.2% ( 83/145)	0.1
TB w/ at least one cavity	49.3% (110/223)	42.8% (62/145)	0.2
Previous anti-TB treatment for a least 4 weeks:	18.3% (81/442)	18.6% (66/354)	0.9
Haemoptysis: (before treatment started)	53.7% (241/449)	46.0% (163/354)	0.03

<sup>1</sup> More than 10 acid-fast bacilli per microscopy field in at least 20 fields.

**Note:** In addition, our analysis did not indicate significant association between the mode of treatment (daily or thrice weekly) and other factors, such as sex, age group, civil status, level of attained education, degree of health seeking delay, presence of BCG scar, having stopped treatment more than once during the first two months due to feeling bad, and having had anti-TB treatment for at least one week before coming to the health centre (with an interruption of anti-TB treatment of not more than nine days before treatment was started in the health centre).

Experience of treatment

How treatment is experienced has an impact on the treatment completion rate. One of the important features of treatment is the occurrence of side effects (adverse reactions to the anti-TB drugs). The patients were asked shortly after initiation to treatment and after two months of treatment regarding side effects they might experience. Reporting side effects was more common among those treated thrice weekly (Table 8.3 presents details). Also more common among patients under thrice-weekly therapy was difficulty swallowing the drugs (Table 8.4).

Proper health facility-based DOT (directly observed therapy taking place in the health centre) was much more common among those treated thrice weekly (32% vs. 21%;  $p = 0.0008$ ). Other factors did not differ in the two treatment groups, for instance self-reported missing and forgetting of drug intake. Table 8.4 presents details about how treatment was experienced.

**TABLE 8.3: Frequency of occurrence of common side effects in the two treatment arms, as reported by the patients at two points in time**

A) Rate of patients who reported side effects when asked some weeks after the start of treatment (806 patients were interviewed):

	<i>Patients under thrice-weekly therapy (n = 451)</i>	<i>Patients under daily therapy (n = 355)</i>	<i>p- value</i>
Any kind:	44% (198/448)	36% (128/355)	0.02
Feeling dizzy:	22% ( 97/449)	19% ( 67/355)	0.3
Nausea/vomiting:	14% ( 64/449)	11% ( 38/355)	0.13
Joint pains:	0.9% ( 4/448)	1.1% ( 4/355)	0.7 <sup>1</sup>
Signs of jaundice:	0.4% ( 2/448)	0.6% ( 2/353)	1.0 <sup>1</sup>
After probing: Clearly feeling nauseous while taking the drugs:	30% (134/449)	21% ( 74/355)	0.004

B) Rate of patients who reported side effects when asked at two months into treatment (668 patients were interviewed):

	<i>Patients under thrice-weekly therapy (n = 367)</i>	<i>Patients under daily therapy (n = 301)</i>	<i>p- value</i>
Any kind:	53% (196/367)	38% (113/300)	< 0.0001
Feeling dizzy:	27% (100/366)	19% ( 58/300)	0.02
Nausea/vomiting:	19% ( 71/366)	13% ( 38/300)	0.02
Joint pains:	1.6% ( 6/367)	2% ( 6/300)	0.7
Signs of jaundice:	0% ( 0/367)	1% ( 3/300)	0.09 <sup>1</sup>

<sup>1</sup> Fisher's exact test, 2-tailed.



**TABLE 8.4: Experience of treatment in the two treatment arms**

	<i>Patients under thrice-weekly therapy (n = 451)</i>	<i>Patients under daily therapy (n = 355)</i>	<i>p- value</i>
Rate of patients who stated to have definite difficulty swallowing the drugs	16% (72/447)	11% (38/353)	0.03
Rate of patients who expressed a strong or very strong fear regarding side effects at the start of treatment:	13% ( 56/443)	9% ( 33/350)	0.15
Mode of treatment supervision:			
Health-facility based DOT:	32% (143/451)	21% (75/355)	0.0008
Partial health-facility DOT <sup>1</sup> :	38% (172/451)	25% (90/355)	0.0001
Health volunteer DOT:	2% ( 9/451)	5% (17/355)	0.03
Family DOT <sup>2</sup> :	17% (78/451)	26% (92/355)	0.003
Self-administered treatment:	11% (49/451)	23% (81/355)	< 0.0001
Rate of patients who reported more than two days of missed treatment during the first two months of treatment:	8% (28/365)	9% (28/302)	0.5
Rate of patients who had stopped treatment more than once during the first 2 months of treatment due to feeling bad:	4% (14/366)	3% (8/300)	0.4
Rate of patients who reported having forgotten treatment more than twice during treatment (6 or 8 months of treatment):	5% (12/251)	8% (16/205)	0.2
Rate of patients who expressed limited trust in the effect of treatment	6% (16/259)	6% (12/205)	0.9
Rate of patients who felt fully healed after the end of treatment	70% (179/255)	72% (147/203)	0.6

<sup>1</sup> Commonly health-facility based DOT for up to one month only or administration of medication in the health centre for some drugs only (e.g. for streptomycin only).

<sup>2</sup> A family member of the patient (or a close friend) has the responsibility to make sure and observe the patient's treatment intake.

Popularity of the two treatment approaches

The first 429 patients were asked what kind of treatment (daily or thrice weekly) they would prefer if they had the choice. Five of them stated to not have a preference. Most (86%) stated they would have chosen the treatment they actually had. However, 8% of the patients under thrice-weekly therapy preferred daily therapy (20/236) and 21% of the patients under daily therapy (39/188) preferred thrice-weekly therapy ( $p = 0.0003$ ).

When asked for the reason(s) for their preference, most (140/255) of those who were happy with their thrice-weekly therapy ( $n = 216$ ) or would have chosen thrice-weekly therapy ( $n = 39$ ) mentioned that thrice-weekly therapy allowed them to have days without drug intake ("days of rest"). Also commonly mentioned was that compared to daily therapy, thrice-weekly therapy was easier or less tiring ( $n = 64$ ), resulted in less transportation costs ( $n = 22$ ), and saved time or interfered less with the duty of work ( $n = 15$ ).

Common comments of those who were happy with their daily treatment ( $n = 149$ ) or would have chosen daily treatment ( $n = 20$ ) were that - compared to thrice-weekly therapy - daily therapy (i) made forgetting drug intake less likely ( $n = 49$ ); (ii) was more effective ( $n = 47$ ); (iii) was a good routine ( $n = 37$ ); and (iv) meant a lower number of tablets had to be swallowed ( $n = 35$ ).

Among the health centre personnel, the following was expressed in all four health centres that had thrice-weekly therapy and where group discussions were held: (i) thrice-weekly therapy results in reduced workload for the staff; (ii) the patients are content with thrice-weekly therapy. In one health centre it was said that some of their patients who had previously had daily therapy stated to prefer the current thrice-weekly therapy; (iii) a

preference for thrice-weekly therapy if the personnel themselves was in need of treatment of TB. Also, in three of the four health centres it was stated that with thrice-weekly treatment it is realistic to expect the patients to come to the health centre for drug intake. In one health centre it was pointed out that since on Tuesdays and Thursday there were no TB patients in their health centre, these two days with a reduced workload allowed them to make home visits of defaulting patients.

Disadvantages were also mentioned: in three health centres, it was said that under thrice-weekly therapy the patients have to swallow a larger number of tablets. Patients may feel like vomiting was said once. In one health centre, preparing and giving of drugs was perceived to be less easy than when blister packs are available (no blister packs were available for thrice-weekly therapy).

In the group discussion in the health centre with daily therapy, the advantages of thrice-weekly therapy were seen as follows: (i) patients have to go to the health centre less often; (ii) the health centre personnel is exposed to contagious TB patients only three times a week; and (iii) the patients have days of rest from treatment. But there were concerns that with thrice-weekly therapy forgetting drug intake might happen more frequently and that the number of tablets to be ingested was higher. All participants wanted daily therapy in case they themselves needed anti-TB treatment; the reason stated was that with daily therapy the number of tablets to be ingested was lower.

Interestingly, no one mentioned the reduced expenditures for drugs that go with intermittent therapy. We calculated that in comparison to daily therapy, thrice-weekly therapy resulted in savings of approximately 40% of the cost of drugs.

Sputum conversion rate

An important indicator of the effect of treatment is the so-called sputum conversion rate at two months (or three months for re-treatment cases) of treatment. We found that the sputum conversion rate was lower for the patients treated thrice weekly when looking at sputum microscopy. When looking at the results of culturing, no difference was found. Table 8.5 presents the data. Drug resistance pattern, previous treatment, mode of treatment supervision and self-reported missing of drug intake were not found to act as confounders.

Having had previous treatment was marginally associated with non-conversion of sputum: 30% of those previously treated were still positive while only 22% of the new TB patients were still positive ( $p = 0.06$ ). Missing drug intake was also associated with non-conversion of sputum (37% vs. 22%;  $p = 0.02$ ). Cavities on a chest X-ray were not found to be associated with non-conversion of sputum (26% vs. 20%;  $p = 0.3$ ).

After four months (or five months for re-treatment cases) of treatment, sputum examinations were generally performed in Taguig only. Only 3% (12/349) of those under thrice-weekly therapy and 2% (6/263) of those under daily therapy were still positive ( $p = 0.4$ ).

**TABLE 8.5: Sputum conversion rates after two months (or three months for re-treatment cases) of treatment (n = 598<sup>1</sup>)**

*a) According to mode of treatment*

	<i>Patients under thrice-weekly therapy (n = 341)</i>	<i>Patients under daily therapy (n = 257)</i>	<i>p-value</i>
Sputum still positive <sup>2</sup>	26% (89/341)	19% (48/257)	0.03
Sputum still positive, only results from Taguig considered	9% (32/341)	7% (18/257)	0.3
Sputum still culture-positive <sup>3</sup>	15% (29/196)	16% (19/117)	0.7
Sputum still positive <sup>2</sup> , only new patients included	24% (68/278)	18% (38/212)	0.08
Sputum still positive <sup>2</sup> , only patients with fully sensitive strains included	23% (24/106)	17% (12/71)	0.35

*b) According to mode of treatment and mode of treatment supervision*

	<u>Sputum still positive<sup>2,4</sup></u>		
	<i>Thrice-weekly therapy</i>	<i>Daily therapy</i>	<i>Both groups combined</i>
Patients under health centre-DOT	27% (34/124)	20% (12/ 61)	25% (46/185)
Patients under less strict forms of supervision	25% (44/175)	17% (22/132)	21% (66/307)
Patients under self-administered treatment	26% (11/ 42)	20% (12/ 60)	23% (23/102)

<sup>1</sup> Sputum samples of patients who had at least one week of anti-TB treatment prior to starting anti-TB treatment at the health centre and whose treatment interruption before starting treatment at the health centre did not exceed 9 days were not included (n = 77).

<sup>2</sup> Be it AFB-positive in Taguig and/or in the 'TB Research Laboratory' and/or positive on culture.

<sup>3</sup> Not all sputum samples underwent culture since in the laboratories of Taguig not all sputum samples were set aside for dispatch to the 'TB Research Laboratory'.

<sup>4</sup> No significant differences were found between the three forms of treatment supervision.

Treatment outcome

Treatment outcome could be established for 705 patients. Treatment failure was slightly more common with thrice-weekly therapy (3% vs. 1%;  $p = 0.08$ ), indicating that thrice-weekly therapy might be inferior to daily therapy. Also, among patients treated thrice weekly, adverse reactions to drugs were statistically significantly more frequently stated as reason to stop treatment. Table 8.6 presents the results in detail. To control for confounding, we included six factors whose distribution was not similar in the two treatment groups in our multivariate logistic regression model. The explanatory factors were (apart from mode of treatment) a bodyweight of less than 35 kg, a high or very high self-perceived degree of poverty, being male and jobless, suffering from hypertension, having had haemoptysis before the start of treatment and discontentment with the skills of the health centre personnel. One factor was shown to be marginally *inversely* associated with adverse treatment outcome (relapse, failure), namely a high or very high self-perceived degree of poverty ( $p = 0.08$ ). Mode of treatment was clearly not associated with adverse treatment outcome ( $p = 0.7$ ).

Development of drug resistance while on treatment

It is important to examine whether intermittent therapy makes development of drug resistance while on treatment more likely. Excluding patients with resistance to more than two drugs at start of treatment, comparison of the drug resistance patterns at two points of time (commonly at start of treatment and two or five months later) has so far been possible for 29 patients. Five of 21 patients under thrice-weekly therapy and one of 8 patients under daily therapy developed drug resistance ( $p_{\text{Fisher's exact test; 2tailed}} = 0.6$ ). Twenty of these 29 patients were pan-sensitive at start of treatment. For eight of these 20 patients there was no result of the drug susceptibility test at start of treatment but since the result of the drug

susceptibility test at a later stage of treatment was pan-sensitivity to all drugs, it was concluded that no development of drug resistance had occurred (assuming that the same strain was in the sputum sample at both points of time). Patients with resistance to more than two drugs at start of treatment were not included in this analysis.

**TABLE 8.6: Treatment outcome (n = 705<sup>1</sup>)**

	<i>Of the 393 patients under thrice-weekly therapy</i>	<i>Of the 312 patients under daily therapy</i>	<i>p-value</i>
Successful treatment (87% of them were confirmed cured)	71% (280/393)	75% (234/312)	0.3
Defaulted /Transferred-out <sup>2</sup>	23% (90/393)	20% (62/312)	0.3
Defaulted due to side effects	5% (19/393)	2% (6/312)	0.04
Relapse	2% ( 7/393)	1% ( 4/312)	0.8 <sup>3</sup>
Failure	3% (11/393)	1% (3/312)	0.08
Failure, relapse combined (‘adverse treatment outcome’)	5% (18/393)	2% ( 7/312)	0.1
Died while on treatment	1% ( 5/393)	3% ( 9/312)	0.13

<sup>1</sup> In addition to these 705 patients, a further 28 patients (17 under thrice-weekly therapy and 11 under daily therapy) completed treatment but their third follow-up sputum examination was scanty positive (e.g. microscopy was only scanty positive and culture was negative or microscopy was negative and on culture only few colonies grew) and as of mid-March 2003, no clear indices as to whether these patients were healed or treatment failures emerged. These 28 patients can be called 'potential failures'. Most of these 28 patients who are culture-negative are probably healed, as recent studies indicate (Tuberculosis Research Centre, 2002; Al-Moamary *et al.*, 2000; Vidal *et al.*, 1996).

<sup>2</sup> We decided not to differentiate between default and transferred-out since it was often difficult to find out if a patient had properly transferred out or left Taguig without proper notice at the health centre. A common reason for default was to have left Taguig. According to the assessment of the health centre staff, the proportion of people who are not permanent residents of Taguig is higher on an average in the health centres with thrice-weekly therapy compared to the health centres with daily therapy.

<sup>3</sup> Fisher's exact test, 2-tailed.

## DISCUSSION

### Limitations of the study

Several factors may have affected the internal validity of this study. Since the patients were interviewed prospectively, recall bias is not expected to have occurred, but social desirability bias needs to be considered. Thus, in spite of efforts to relate to the interviewees in an informal and culturally appropriate way, some answers may not accurately reflect the patients' experiences. For instance, self-report about missing drug intake is known to be unreliable, underestimating the true incidence of missing drug intake (recently reviewed by Gorin & Stone, 2001 and found in many studies, e.g. Mwinga *et al.*, 2002; Meissner *et al.*, 2002; Chaisson *et al.*, 2001). Since we had to rely on patient self-report (we did not attempt to monitor intake of treatment, e.g. through urine testing) we have no accurate data regarding regularity and completeness of treatment intake. Although it cannot be excluded, we do not believe that underreporting of missing drug intake was more common in one treatment group compared to the other treatment group.

Our figure that 86% of the respondents preferred the mode of treatment they had is probably an overestimate: it is culturally expected that many respondents chose not to express discontentment with the free treatment they had. The greater popularity of thrice-weekly therapy compared to daily therapy may thus be more pronounced than our data suggest.

Our ability to compare our two treatment groups regarding factors that may influence outcome of treatment was limited. For instance, we had results of drug susceptibility tests for only 41% of our patients, and 54% of our patients had no chest X-ray or the result of



their chest X-ray was ill-defined (e.g. 'Koch's infection') or not known. Thus, we did not include the results of drug susceptibility tests or those of chest X-rays in our logistic regression analysis. Having cavities in the lungs is a risk factor for adverse treatment outcome (ATS/CDC/IDSA, 2003; Benator *et al.*, 2002; Oursler *et al.*, 2002; Sonnenberg *et al.*, 2001). Also, rigorous medical check-ups regarding co-morbidity are beyond the scope of what can be done in public health centres; we had to rely on self-report of the patients. We have no idea about HIV co-infection. It is believed that in the Philippines, TB patients are rarely co-infected with HIV (WHO estimates that in 2001, only 0.4% of adult TB patients were co-infected with HIV in the Philippines - WHO, 2003, p. 103).

We also had to rely on self-report regarding occurrence of side effects. In addition, the health centre personnel also asked their TB patients about side effects. But there was no thorough professional assessing (including laboratory test) of occurrence of side effects.

A point of contention can be the definition of failure and relapse cases. In view of the logistical limitations, we used non-stringent definitions. In several studies in special TB study sites, definitions were more stringent, e.g. repeated culture positivity with a growth of at least 10 or 20 colonies per culture (Tuberculosis Research Centre, 1997; Hong Kong Chest Service/British Medical Research Council, 1981). Other studies required one positive culture with more than 10 colonies (Bechan *et al.*, 1997). In other places, culture examination was not used to determine failure or relapse, one smear-positive follow-up sputum examination being sufficient to become a relapse case (Cao *et al.*, 1998). A review summarised the variations as follows: "Some studies required mycobacteriologic confirmation of failure, whereas others require only clinical evidence of failure or lack of response to therapy" (El-Sadr *et al.*, 2001). Since the number of cases with adverse treatment outcome is low but crucial, variations in definition of failure and relapse can make a decisive difference.

Also important is to know whether a relapse case is due to endogenous reactivation or exogenous re-infection. DNA fingerprinting techniques (e.g. restriction fragment length polymorphism - Cohn & O'Brien, 1998) can be used to make this differentiation. We have not used DNA fingerprinting (as of April 2003). Exogenous re-infection in relapse cases appears to be more common than was believed some years ago (De Boer *et al.*, 2003; De Viedma *et al.*, 2002; Caminero *et al.*, 2001; Van Rie *et al.*, 1999). In failure cases, exogenous re-infection seems to be rare (Sonnenberg *et al.*, 2000).

We did a cluster randomisation which has two disadvantageous effects. First, the two groups to be compared (in our case those treated thrice weekly and those treated daily) should be similar in terms of factors that may influence outcome of treatment. Such similarity is potentially less likely with cluster randomisation. Our multivariate analysis accounted for this. Secondly, cluster randomisation reduces the statistical power of the study (Campbell & Grimshaw, 1998). We did not account for the effect of clustering in our analysis which potentially overstates the found differences (i.e. p-values become too small). On the other hand, our sample size – though relatively large – can easily result in type II errors (existing differences are not detected), also because we used intention-to-treat analysis (Sommer & Zeger, 1991; Rubin, 1998; both cited in Fergusson *et al.*, 2002). With a treatment outcome available for 705 patients (with slightly more having thrice-weekly therapy than daily therapy), we have - when choosing a 95% probability that the found difference presents a true difference - a statistical power of only 50% to detect an almost double difference in adverse treatment outcome (failure and relapse cases) between the two treatment groups, e.g. an adverse treatment outcome in 4% of those treated daily and 7.7% in those treated thrice weekly.

### *Chapter 8: Thrice-weekly vs. daily TB therapy*

Another limitation is that it was not possible to perform the trial in such a way that the investigators and those analysing the data would be blinded concerning mode of treatment of the patients.

#### Advantages of intermittent therapy

This study identified several advantages of thrice-weekly therapy over daily therapy. One, proper treatment supervision (DOT) is more feasible. In Taguig it meant that the patients who took all treatment in the health centres (which is the ideal situation according to WHO and the Philippine Department of Health) had to go to the health centre only three times a week, not five times a week, resulting in a reduced burden for patients and providers. The reduced work load of the health workers may lead health workers to invest more efforts (e.g. defaulter tracing) in achieving high treatment completion rates among their TB patients. Home visits to defaulting patients can be successful (Chee *et al.*, 2000; Baily *et al.*, 1974). Secondly, this reduction in the number of visits to the health facility also means that the likelihood that TB is transmitted to other people in the health facilities is reduced. Using thrice-weekly therapy may thus contribute to prevention of tuberculosis among health workers and also among users of health facilities, especially in places where health facilities are crowded. Thirdly, the cost reduction in terms of purchase of drugs is substantial. If thrice-weekly therapy were used all over the Philippines, the National TB Programme would save US \$ 1.32 million each year; this would result in a budget reduction of 15% (infrastructure costs of shared staff and shared facilities not considered). (Calculation is based on figures presented in the latest WHO report on TB - WHO, 2003, p. 104.) Fourthly, thrice-weekly therapy is more popular among patients and also among providers. In the light of the distressing TB illness experience, treatment schemes that make treatment less

burdensome and more appealing to patients are crucial. Using a more popular treatment scheme may well result in more people with TB symptoms making use of the public facilities, thereby increasing the DOTS case detection rates.

#### Disadvantages of intermittent therapy

At two (or three) months of treatment, more patients under thrice-weekly therapy were still sputum-positive compared to patients under daily therapy. Such a difference could not be found when we looked at positivity on culture, suggesting that for many patients the acid-fast bacilli still released at two months of treatment were no longer viable and thus no longer contributed to the spread of TB. Our findings suggest that with thrice-weekly therapy it might take longer to stop a smear-positive TB patient from propagating viable TB bacilli. However, this was not found in a study where the sputum conversion rate at 1 month of treatment was known: In a study in Hong Kong (Hong Kong Chest Service/British Medical Research Council, 1981) culturing was done at 1 and 2 months of treatment. At 1 month of treatment, 53% of those treated thrice weekly and 51% of those treated daily ( $p = 0.6$ ) were culture-negative. At 2 months of treatment the corresponding rates were 89% and 94%, respectively ( $p = 0.09$ ).

Patients under thrice-weekly therapy had to swallow a rather high number of pills (up to twelve pieces), and side effects (especially gastro-intestinal complaints) were commoner among them compared to those under daily therapy. This is in conformity with other studies comparing daily with intermittent therapy (Tuberculosis Research Centre, 1997; Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council, 1989; Hong Kong Chest Service/British Medical Research Council, 1981). It is of concern that among those treated thrice weekly, default from treatment due to

side effects was significantly commoner than among those treated daily. Using fixed-dose combination-tablets would reduce the number of pills to be swallowed and probably also the incidence of gastro-intestinal disturbances. However, the fixed-dose combination tablets available these days are not well fitted for intermittent therapy use (isoniazid would be under-dosed) and WHO does not recommend intermittent treatment with fixed-dose combination tablets (WHO/STOP TB, 2002).

In contrast to what could be expected from the literature review (Tuberculosis Research Centre, 1997; Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council, 1989; Hong Kong Chest Service/British Medical Research Council, 1981; Hong Kong Chest Service/British Medical Research Council, 1976) we did not find arthralgia and jaundice or hepatic reactions to be less common among those with intermittent therapy.

A problem of intermittent therapy is that a missed dose represents a bigger fraction of the total treatment. Concerns that thrice-weekly therapy might make forgetting drug intake more likely were not confirmed by our study.

#### The effectiveness of intermittent therapy

There are a number of observational studies that found thrice-weekly therapy from day one of treatment to be effective (Cao *et al.*, 1998; Chaisson *et al.*, 1996; China Tuberculosis Control Collaboration 1996<sup>1</sup>; Yan *et al.*, 1996; Neher *et al.*, 1996). A recent

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<sup>1</sup> In China, intermittent therapy is given every other day, i.e. 3.5 times per week.

review comparing observational studies with randomised controlled trials indicates that evidence found from observational studies can be very robust (Concato *et al.*, 2000). Well-designed observational studies merit careful consideration (Ioannidis *et al.*, 2001). Still, randomised controlled trials should be used to create a stronger evidence base and to demonstrate the comparative advantages and disadvantages of intermittent and daily therapy.

We know of only one study performed with smear-positive patients that compared thrice weekly with daily therapy in a randomised controlled trial with mode of treatment (daily or intermittent) as the only difference of the regimens to be compared (Hong Kong Chest Service/British Medical Research Council, 1981). In this study in Hong Kong, 399 patients were included for analysis of treatment outcome. The same drugs as in Taguig were used. However, pyrazinamide and ethambutol were used throughout treatment. Five of those under thrice-weekly therapy and one of those under daily therapy had a relapse ( $p$ -value = 0.12). Similar to this study in Hong Kong, our study has not clearly answered the question whether thrice-weekly therapy is of equivalence to daily therapy. With our results we can argue that thrice-weekly therapy is not inferior to daily therapy (the  $p$ -value for mode of treatment as an explanatory variable for adverse treatment outcome was 0.7 in the multivariate logistic regression model). However, the bivariate analysis suggests there is a trend indicating intermittent therapy to be inferior to daily therapy. In countries with large number of TB patients small differences in the proportion of TB patients with adverse treatment outcome translate into thousands of additional relapse and failure cases when the regimen that is slightly inferior is chosen. These patients are not only in need of re-

treatment, but continue to spread tuberculosis, and a substantial proportion of them may spread drug-resistant strains.

An interesting finding is that in the multivariate model, a high degree of self-perceived poverty was shown to be *inversely* marginally associated with adverse treatment outcome ( $p = 0.08$ ). More detailed studies would be needed to determine whether belonging to the very poor really does not hamper the chances of full recovery. In any case, apart from pursuing the search for the best possible use of existing tools, other issues being intrinsically linked to tuberculosis, such as poverty, need to be addressed urgently.

## CONCLUSION

We believe that due to the potentially grave consequences of having more failure and relapse cases, using fully thrice-weekly therapy is warranted only if there is stronger evidence of its non-inferiority compared to daily therapy. It is hoped that our final report with treatment outcome from almost 900 patients will allow a firmer conclusion. Randomised controlled trials with larger sample sizes are needed; such trials should be carried out using fixed-dose combination tablets. Also, in view of the low sputum conversion rate we found after two months of treatment under thrice-weekly therapy, such trials should include a third treatment arm for patients taking two weeks of daily therapy before shifting to intermittent therapy.

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***PART IV: General Discussion and Conclusion***



## **CHAPTER 9: GENERAL DISCUSSION AND CONCLUSION**

### **9.1. Key findings**

Chapters 4 and 5 of this thesis described the illness experience of TB patients and their search for treatment. We found the TB illness burden to be substantial; ill-defined suffering, such as emotional and social distress as well as social stigma, was common and has considerable potential to complicate TB care. What significantly increases the burden of having TB is the widely found inefficient health seeking behaviour. Based on the knowledge gained, two approaches with considerable potential to make care of TB patients more effective and efficient were examined: to expand DOTS by introducing it to the private sector and establishing public-private collaboration, and to make treatment more efficient by using intermittent therapy. Thus, we wanted to know the diagnostic and treatment practices of private practitioners and their views towards public-private collaboration. Various aspects of the health seeking behaviour found in Malabon and various findings from our survey among the private practitioners strongly suggest that successful public-private collaboration offers the following benefits:

1. Shortened case finding for people with symptoms of TB
2. Considerable financial savings for patients over the course of diagnosis and treatment
3. Improved diagnosis and treatment by private practitioners
4. Stronger motivation for the public care providers to offer friendly and competent TB care
5. Better epidemiological data for the local TB epidemic due to less non-reporting of cases
6. Less drug resistance since inadequate treatment and repeated interruption of anti-TB treatment are less likely to occur.
7. Fewer people wrongly treated for TB, since sputum microscopy is more accurate than chest X-rays.

## *Chapter 9: General Discussion and Conclusion*

In our comparison of daily with thrice-weekly therapy in public health care clinics we found thrice-weekly therapy to be feasible, attractive to patients and providers, and effective but could not remove doubts about non-inferiority to daily therapy (see chapter 9.4.). We identified the following benefits of intermittent therapy:

1. Treatment is less burdensome for patients and providers
2. Increased likelihood of properly supervised treatment
3. Reduced cost of needed TB drugs
4. Reduced emotional distress since intake of drugs – an act that has the unpleasant connotation of not being in the normal state of health – occurs not daily but only three times a week. And for patients who want to keep their illness a secret this goal is easier to achieve.
5. Increased utilisation of the public TB programme since intermittent therapy is more popular than daily therapy.

### **9.2. Methodological considerations**

#### *a) Internal validity*

We used carefully designed interview catalogues for our patient survey to identify help seeking and TB illness experience. Focus group discussions and a survey among the health care providers of Malabon yielded additional information about TB illness experience. However, as discussed more precisely in each of the chapters, our research had several limitations. More attention to qualitative data from the study of patients would have been useful to clarify quantitative findings. With a stigmatized disease such as TB, social desirability bias may be a problem, and the patient interviews in Malabon were performed retrospectively, so recall bias also needs to be considered. Thus, the validity of the index of stigma may not be very high (chapter 4). We believe our findings regarding help seeking and perceived causes of tuberculosis (chapter 5) are less prone to

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have reduced validity. Unlike questions referring to sensitive personal issues such as emotional distress and social consequences of having TB, questions regarding help seeking and causes of TB are answered more candidly.

The main limitation in the survey among the private practitioners is that some of the findings are more likely to reflect *knowledge* rather than *actual practices* and that due to social desirability bias some findings may overestimate the willingness of the private practitioners for public-private collaboration.

Since the interviews in Taguig were carried out prospectively and less sensitive topics were covered we believe the internal validity of the patient findings in Taguig is high. An exception may be the issue of self-report on regularity of drug intake. A literature review and also our field experiences make it clear that some patients overstate regularity and completeness of their drug intake (Gorin & Stone, 2001). In spite of drug resistance being common in Taguig, we found adverse treatment outcome in only 3.5% of our patients. This low rate indicates that adherence to treatment was high. Thus, we do not believe that underreporting of missing of drug intake was substantial and that it strongly affected the internal validity of our study in Taguig.

#### *b) External validity*

To what degree can we generalise our findings for the whole of the Philippines and for other countries? Other studies from Manila and the Philippines have similar findings regarding health seeking behaviour (Tupasi *et al.*, 2000a; Valeza *et al.*, 1991), while findings regarding perceived causes of tuberculosis are more heterogeneous: our results are only partly similar to results from three studies in or near Metro Manila (Tiglao & Tempongko, 1991; Ortega *et al.*, 1991; Cure TB Foundation, 1991). However,

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it must be considered that several years have passed between these three studies and our patient survey in Malabon. Beliefs may change over time and become more congruent with medical knowledge. This may well have happened in the Philippines: The national TB programme in the Philippines has become stronger in the mid-1990's. The general population has thus been exposed to health information about TB.

Other studies of TB in the Philippines have emphasised the role of stigma (Nichter, 1994; Aresta, 1994; Ardales & Castel, 1992; Ortega *et al.*, 1991; Sarmiento, 1990). Some findings indicate that the effects of stigma can be far-reaching. For instance, in a study in a rural setting, Ardales and Castel (1992) encountered several patients who tried to keep their illness from their family members. In other countries, a large number of studies have found similar aspects of TB illness experience, including social stigma (Rangan & Uplekar, 1999).

The results of our survey among the private practitioners of Malabon are similar to a recent survey performed among private practitioners in five settings in and near Metro Manila<sup>1</sup>. In a recent telephone survey across the Philippines the private practitioners' deficiencies in diagnostic and treatment practices were similar but appeared more pronounced, and a worrying finding was that more than three quarters of the private practitioners did not agree with the national TB programme. More than half (53% of the 1355 respondents) did not agree with the policy that diagnosis was based on sputum smear microscopy (Portero & Rubio, 2003).

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<sup>1</sup> Results were presented in Manila in 2002 but are not or not yet published: "Current Trends in TB Management by Private Physicians in the Philippines: A Survey in Five Private Health Settings". Philippine Coalition Against Tuberculosis (PhilCAT) and Centers for Disease Control and Prevention, Atlanta, USA.

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Our studies were all performed within Metro Manila, a highly urbanised setting. The nationwide TB prevalence survey in the Philippines of 1997 showed that compared to other urban centres of the Philippines, TB is less common (i.e. lower rate of culture positivity as well as sputum smear positivity) in Metro Manila. When excluding Metro Manila, TB was found to be more common in urban areas compared to rural areas (Tupasi *et al.*, 1999). It is hard to know if our findings can be generalised for rural areas in the Philippines. In some aspects, the form and quality of family life and social networks differ in urban and rural areas, and thus, TB illness experience may be different in rural areas. Studies from India suggest that in rural areas TB illness experience may be less distressing: rejection of the TB patients by their families was less common in rural than in urban areas (Ramachandran *et al.*, 1997), and children discontinuing school as a result of parental TB was also less common in rural areas (Rajeswari *et al.*, 1999).

Health seeking behaviour may be less prolonged in rural areas due to a limited availability of health care providers. Establishing public-private collaboration in rural areas may prove more challenging, depending on the social dynamics prevailing in a rural place. The nationwide telephone survey of Portero and Rubio (2003) in the Philippines did not mention any rural-urban differences in their findings. Neither in the Philippines nor elsewhere have we heard of public-private collaboration initiatives in rural areas.

Several of our findings regarding health seeking and public-private collaboration are also valid for other countries, for instance an inefficient case finding process, diagnostic and treatment deficiencies among the private practitioners, and the existence of starting points for establishing public-private collaboration (Uplekar *et al.*, 2001a).

How would thrice-weekly therapy work in other settings? As discussed, several observational studies have found thrice-weekly therapy to be effective. We believe that generally our results in Taguig have a high external validity. However, in areas strongly affected by the HIV/AIDS pandemic, the situation may be different, as a study in Malawi suggested (Harries *et al.*, 2001). Also, it is important that intermittent therapy be used only in settings where TB programmes work well. Good case holding mechanisms are important: under intermittent therapy missing of drug intake is more likely to have adverse consequences than under daily therapy (since a missed dose represents a larger fraction of the whole treatment). Due to the virtual non-existence of case holding mechanisms in the private sector concerns have been expressed about the effect of the recent occurrence of drug formulations for intermittent therapy in India (WHO, 2001e).

### **9.3. Recommendations for public health action**

#### *a) for TB programmes generally*

The findings from the study of TB illness experience (Chapter 4) and the case studies presented in Chapter 5 illustrate the importance of giving correct, appropriate and patient-centred health advice. Clear guidelines from the central TB office and training of the health care providers should address the knowledge level, attitude, and skills of the health care providers. Consequently, misperceptions, such as the supposed need to separate eating utensils while on anti-TB treatment, need to be exposed and rectified. Training of TB health workers needs to make more explicit the balance of appropriate public health interests to prevent spread and the interests of preventing unwarranted social exclusion. Higher priority in the training of health care providers is needed to promote empathy for the TB patient and relating to the patient in such a way to enhance dignity, feelings of self-worth and emotional resilience of the patient. Such empathy



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results, among other things, in giving health advice in an appropriate way. Attitudes and skills are often intertwined. Based on changed attitudes, communication skills of the health care providers can be improved. This includes the ability to maintain a balance between making clear how to avoid contagion and minimising the emotional burden and stigma of TB. Improving the skills of the health care providers must be supported by a wider effort from national governments and the international community to end the neglect of human resource development, as discussed in Chapter 1, section 3.3.

Our findings also suggest that case holding can be strengthened by involving the family of the patient. Emphasizing to the patients and their families that TB can be cured when treatment is taken correctly and completely also has the potential to reduce stigma and its adverse effects. By facilitating support for the patient, the often distressing experience of having TB and undergoing treatment becomes much more manageable which has great potential for decreasing drop-out rates.

Our research experience raised important questions about the relationship of policy and practice. We found in Taguig that contrary to the guidelines of the TB programme, a substantial proportion of TB patients was not receiving treatment under DOT. Our research in Malabon from the year 2001 (not reported in this thesis) also found considerable non-compliance with the principle of direct observation of treatment. Studies in Thailand and India have also found this (Pungrassami *et al.*, 2002; Balasubramanian *et al.*, 2000). Rather than insisting on a strict form of treatment supervision that is then not widely implemented<sup>2</sup>, the local health authorities and those

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<sup>2</sup> The new 'Manual of Procedures' for the TB programme of the Philippine Department of Health (Philippine Department of Health, 2001) recommends daily DOT for the whole length of treatment (and no longer for the intensive phase of treatment only). Talking with people from the Department of Health responsible for the control of TB, I indicated that since daily DOT for two (or three) months apparently cannot be implemented fully, this new recommendation will probably not be followed. There was a shrugging of shoulders and the remark that WHO wanted this new emphasis on longer DOT. Wide gaps between what guidelines stored in offices and on desks state and what is actually happening in the field are problematic.

responsible for the implementation of the DOTS strategy need to take note of this non-adherence and develop guidelines that facilitate a feasible decision-making regarding which form of treatment supervision is most appropriate for each TB patient. Important factors that need to be considered when deciding on the mode of treatment supervision are: distance from the patient's home to the health facility; degree and quality of the relationship between the patient and the health facility (based on former visits to the health facility); the kind of work and working hours of the patient; work load at home (for some mothers with several small children, health facility-based DOT may not be feasible); physical and mental condition of the patient, including degree of self-perceived stigma; and degree of support in the patient's household.

*b) regarding public-private collaboration*

It is crucial that investments are made in the public sector for additional human resources to deal with public-private collaboration. At the central level, a person should be employed to handle policy issues related to public-private collaboration, develop indicators and a system that allows monitoring and supervision, and coordinate with local programmes (at district, city, or municipal level). At the local level, the health workforce has to be increased. On the one hand, establishing public-private collaboration is labour-intensive and on the other hand, successful public-private collaboration may significantly increase the demand for the public TB programme. The physician in charge of a local TB programme should be released from clinical responsibilities to be able to perform frequent supervision in the public health facilities to ensure that each health facility implements DOTS well and does its part needed to establish and maintain public-private collaboration. This public TB physician should have an assistant to perform regular basic

tasks that are part of public-private collaboration, such as visiting the local private practitioners (e.g. for gathering their records to inform the public sector on patient load in the private sector and on the number of patients referred to the public health facility), ensuring proper functioning of logistic aspects (e.g. availability and distribution of TB drugs once a system has been set up that allows the private practitioners to make use of public TB drugs), and organising seminars and meetings. The public TB physician should be a member of a local committee that facilitates public-private collaboration.

*c) regarding intermittent therapy*

Our findings do not warrant drastic recommendations. Since we do *not* have strong evidence of non-inferiority of intermittent therapy compared to daily therapy with the results available now we do not recommend a shift from daily to intermittent therapy. Our results suggest a trend towards inferiority of thrice-weekly therapy in terms of treatment outcome. Since this is only a trend, we do not recommend programmes using intermittent therapy to change to daily regimens. Programmes using intermittent therapy regimens should be especially aware of the importance of regular drug intake and of rigid evaluation of treatment outcome.

**9.4. Recommendations for further research**

A clear understanding of the patients and their behaviour is fundamental. What aspects of illness experience are particularly burdensome and what aspects of the illness burden are amenable through interventions that can easily be implemented in public TB programmes? In some places, enough is already known about the health seeking behaviour and the knowledge, attitude and practices of the general population regarding

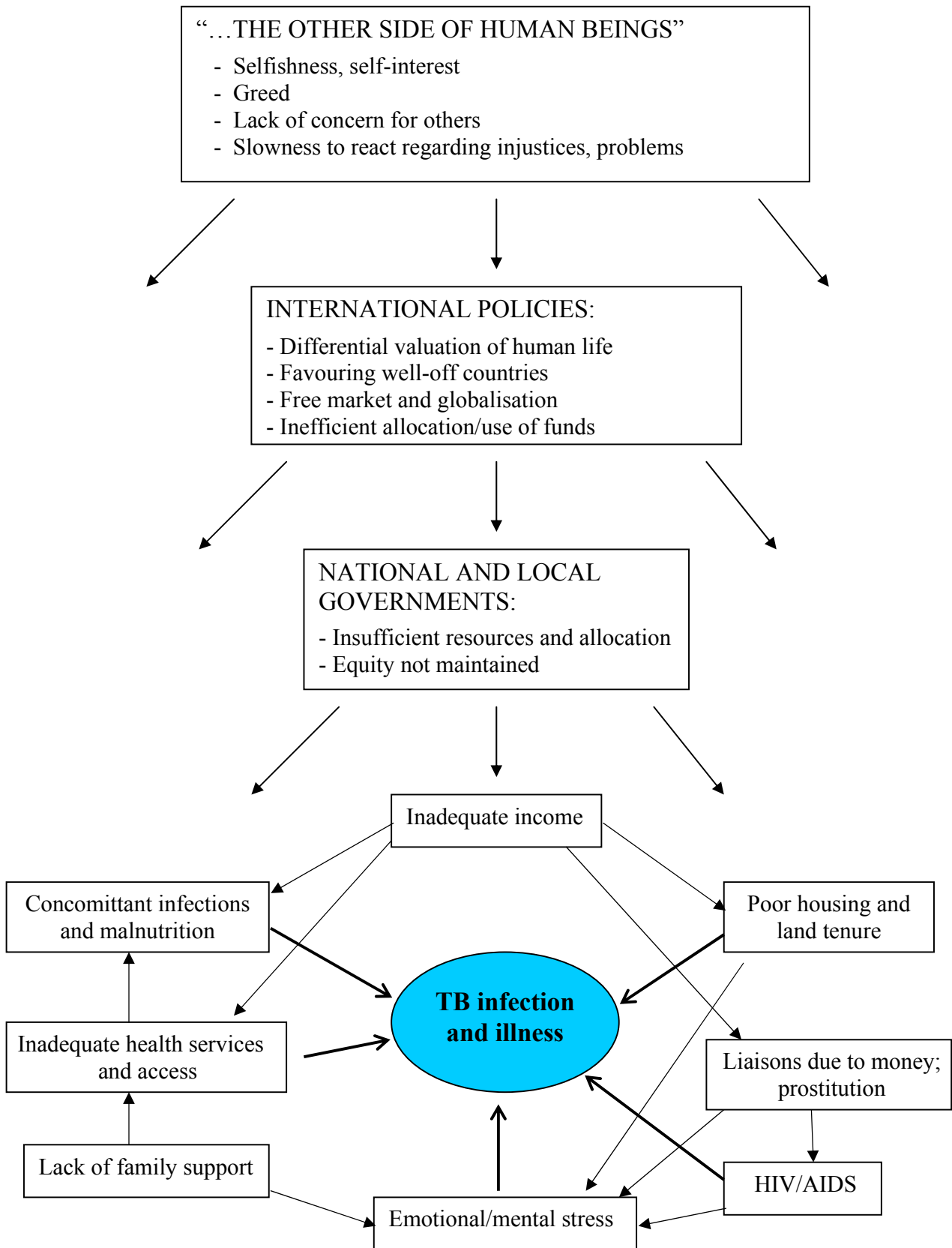
### *Chapter 9: General Discussion and Conclusion*

TB. In other places, patient interviews and focus group discussions are needed to document these behaviours and the underlying attitudes, beliefs and experiences. The approach of cultural epidemiology facilitates generation of accurate knowledge. In-depth studies about health seeking behaviour, especially the switching of patients between private and public providers and their motives for doing so may provide further important insights and help identify the complex influences that determine patient behaviour. Patient behaviour should be explored on several levels: psycho-social and economic factors at the patient level; factors in the community and locality of the patient (focussing on the availability of health services, including folk healers); actors at the national level, such as existence and enforcement of laws related to health, availability of health insurance schemes, and health policies of the government; activities of and level of influence of pharmaceutical companies (such as advertising and promoting activities, sponsoring of medical meetings, and level of support for efforts to establish public-private collaboration<sup>3</sup>); and international factors, such as trade liberalisation, globalisation and enforcement of structural adjustment programmes. Figure 9.1 gives an indication of the different levels and serves as an aid to keep the wider picture of TB in mind.

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<sup>3</sup> The Philippine Coalition Against Tuberculosis (PhilCAT), a driving force in public-private collaboration in the Philippines, has several large pharmaceutical companies among its members.

**Figure 9.1: The context and causal web of tuberculosis**



## *Chapter 9: General Discussion and Conclusion*

An area of research relevant to treatment (be it daily or intermittent) and how the patient experiences it, arises from the study in Taguig. Our finding that the mode of treatment supervision did not influence the sputum conversion rate is interesting. The question arises what kind of treatment supervision is needed and what the determinants of successful treatment supervision are. We did not in detail look at the factors that determined what kind of treatment supervision a TB patient received. One factor clearly was that in certain health centres the health care providers were more serious in following the concept of DOT than in other health centres. Also, narratives strongly indicate that in most health centres the TB patients have a kind of ‘bargaining power’, meaning that less rigid forms of treatment supervision are considered and negotiated when the patient expresses apprehension towards health facility-based treatment intake. In other words, the kind of treatment supervision a patient has is often a result of a negotiating process between the health care provider and the patient. This process also occurs in other places (Macq *et al.*, 2003). Operational research should be carried out to create a stronger evidence base of the effects of the various modes of treatment supervision that result from such negotiating processes. Operational research may also be needed to finetune guidelines for the health care providers on how to go through such a process of negotiation.

Operational research is needed to find ways of how to implement public-private collaboration. Additional support for such research is required. Finding ways of establishing public-private collaboration for TB control may also encourage valuable public-private collaboration for other diseases. Our survey in Malabon established common deficiencies among Malabon’s private practitioners. Such surveys need to be

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carried out in other geographical areas where public-private collaboration is envisioned. These surveys and the questionnaires for them can be less elaborate than the one we performed in Malabon. The question of how identified deficiencies can be addressed is more difficult to answer; studies adopted to the local context have to address this question. Linked to this question are other questions referring to the private practitioner: What are the complex influences that determine provider behaviour? (E.g. what motivates the private practitioners apart from profit-maximisation? What encourages the private practitioners to collaborate with the public sector?) What kind of levers can be used to improve the practices of the private practitioners?

Concerning the public TB programme, important questions are: What can the public sector learn from the private sector? What can the public sector offer to facilitate collaboration? How can the public sector be strengthened sufficiently so that the general public and the private practitioners trust in it? Focus group discussions with public and private health care providers as well as in-depth interviews with some key informants (e.g. physicians who work in both sectors) are useful tools to find answers to such questions.

Other key questions are: What local mechanisms are already in place that can be used to facilitate collaboration? What kind of local mechanisms need to be put in place to facilitate collaboration? What kind of regulative mechanisms can realistically be put in place and enforced long-term? Who/what are the key local people and institutions whose support is needed? This last question indicates that a stakeholder analysis (Brugha & Varvasovszky, 2000) can be useful. A stakeholder analysis provides insights into the current and future organizational environment of a locality, leading to a deeper

### *Chapter 9: General Discussion and Conclusion*

understanding on how organizational changes can facilitate public-private collaboration in TB control. For instance, it clarifies the role a local medical society can play in establishing public-private collaboration and the steps the public health sector can undertake to strengthen health-related public-private relationships. A stakeholder analysis yields information about the relevant actors, i.e. it contributes to an increased understanding of the behaviour and intentions of private practitioners and the public providers and of the interrelations between the two kinds of health care providers. It also clarifies the influence and resources various stakeholders of a locality outside the health sector have (e.g. religious organisations) and how these can be tapped to facilitate public-private collaboration.

To establish public-private collaboration, research and public health action should go hand-in-hand. Findings from surveys (for instance regarding the practices of the private practitioners) should immediately be translated into remedial action. Thus, the research activities leading to public-private collaboration should involve the local players, i.e. health care providers from the public and the private sector. These local health care providers know best how remedial action can be implemented in their setting. A useful approach for such research is *Research-Action-Capacity Building (Recherche Action Formation* in French) to further the participation of these people and use their own experiences and creativity as an asset. *Research-Action-Capacity Building* sees research and action as two connected elements of one entity, stimulates a process of on-going exchanges between the various players, and sees social change as the ultimate purpose (Wyss *et al.*, 2002). Public-private collaboration is often aided by social change and its successful implementation is an indicator of social change.



Our study showed intermittent therapy to have several advantages (compared to daily therapy). But since there is a lack of solid evidence that intermittent therapy is not inferior to daily therapy, further randomised controlled trials with a large statistical power comparing daily with intermittent therapy are warranted. Our concern stems not so much from considerations about limited external validity than from the fact that only much larger sample sizes would ensure that small differences in effectiveness are detected. It is vital that intermittent regimens are really non-inferior to daily regimens. Box 9.1 illustrates how using a slightly less effective regimen can significantly affect individual and public health (calculations with figures from India, the country with the largest number of TB cases in the world, were used - Khatri & Frieden, 2002).

**Box 9.1: Hypothetical calculations of the detrimental effect of using a slightly less effective regimen – the example of India**

It is expected that in some years, DOTS reaches 100% of India's population. This means around 1.4 million TB cases will be treated under DOTS every year. Assuming an adverse treatment outcome (failure and relapse cases) among 5% of new smear-positive patients, 3% of new smear-negative patients, and 8% of re-treatment patients when using thrice-weekly therapy and an adverse treatment outcome among 3% of new smear-positive patients, 1% of new smear-negative patients, and 6% of re-treatment patients when using daily therapy results in 24,800 excess cases of pulmonary TB cases each year when thrice-weekly instead of daily therapy is used. If 4% of these excess cases turn out to have MDR-TB, then thrice-weekly therapy produces an excess number of 992 cases of MDR-TB each year in India under this scenario.

For the calculations, we assumed that 39% are new smear-positive patients, 31% new smear-negative patients, and 18% re-treatment patients (and the remaining ones patients with extrapulmonary tuberculosis), based on the report by Khatri and Frieden (2002). The rates for adverse treatment outcome are partly based on the figures given for failure cases in Table 4 of Khatri and Frieden (2002). Observational studies of thrice-weekly therapy show that the rates here assumed are conservative. For instance, Cao and colleagues (1998) in China found an adverse treatment outcome rate of 6.4% for 306 new patients and of 22.7% for 343 re-treatment patients. Another report from China (China Tuberculosis Control Collaboration, 1996) found a failure rate of 3.1% among 55,213 new patients and a failure rate of 10.2% among 57,629 re-treatment patients. And 3.2% of 4,037 patients that were followed-up became relapse cases (the relapse rate was not differentiated according to new or re-treatment patient).

## **9.5. Conclusion**

With the goal to contribute to better TB care in the world, this thesis examined several aspects of TB illness experience and two approaches to enhance DOTS. The survey in Malabon to establish TB illness experience and clarify aspects of help seeking and treatment provided insights that served as a sound basis for our efforts to reach private practitioners and establish a bridge between the private and the public sector, and to study intermittent therapy. Other research more rooted in basic science, invigorated by new money available for such research, provides cautious optimism that at the end of this decade, better diagnostic tools and new drugs making shorter therapy and treatment of highly resistant forms of tuberculosis possible will be available (Perkins & Kritski, 2002; Crabb, 2002; Freire & Roscigno, 2002; Young, 2001). Identifying and then applying such new tools could greatly simplify TB control. In the meantime, the challenge is to find ways to work more efficiently with what is available, and this is the contribution of this thesis. The thesis indicated the significant benefits that can result from bringing DOTS to the private sector and establishing public-private collaboration. A clear awareness of the need and benefits of public-private collaboration is needed to face the formidable challenges of establishing public-private collaboration in TB control. Additional resources, people on the ground dedicated to the task, and operational research to identify feasible approaches in various settings are required.

While public-private collaboration results in a wider use of sound principles of TB care, our study on intermittent therapy focussed on sharpening the main tool of DOTS, namely short-course chemotherapy. All possible means to make DOTS more efficient and convenient to patients and health care providers need to be pursued.

### *Chapter 9: General Discussion and Conclusion*

Intermittent therapy has considerable potential in this connection. Forty years ago, Canetti said: "On an international scale, among the efforts that are necessary to accomplish the eradication of tuberculosis, there is one absolute priority; the *perfecting of chemotherapeutic methods adapted to conditions of 'developing' countries*. In realising this objective, the 'developed' countries can give 'developing' ones considerable help." (Canetti, 1962; emphasis added). There still is considerable room for perfecting therapy based on drugs available for more than 30 years. At the same time, it needs to be stressed that while using intermittent therapy instead of daily therapy can substantially improve TB care, better chemotherapy alone does not result in progress. Many aspects of TB care need improvement and many facets of treatment need to be considered. Our discussion in Chapter 1 on the limitations of DOTS highlights this reality. The growing support for TB control and research working towards controlling TB and the emerging awareness of the global community for the need of an all-embracing approach in confronting TB give rise to hope that this decade will see progress.

## References

### REFERENCES

- Aljunid S (1995). The role of private medical practitioners and their interactions with public health services in Asian countries. *Health Policy and Planning* 10: 333-49.
- Aljunid SM, Norhassim I (1992). Utilization of health facilities by the Malays of Kuala Selangor. *Journal of UKM Medical Faculty* 14 (1): 43-52.
- Al-Moamary MS, Black W, Bessuille E, Elwood RK, Vedal S (2000). The significance of the persistent presence of acid-fast bacilli in sputum smears in pulmonary tuberculosis. *Chest* 116 (3): 726-731.
- Alwood K, Keruly J, Moore-Rice K, Stanton DL, Chaulk CP, Chaisson RE (1994). Effectiveness of supervised, intermittent therapy for tuberculosis in HIV-infected patients. *AIDS* 8 (8): 1103-1108.
- Ardales V, Castel M (1992). *An Evaluation of the National Tuberculosis Program in Western Visayas*. Research & Development Office, West Negros College, Bacolod City, October 1992. Copy received from the 'Essential National Health Research', Department of Health, Manila, Philippines.
- Aresta RB (1994). *Factors Influencing the Low TB Case Finding Rate and Patient Acceptance Rate of the Short Course Chemotherapy in Cagayan and Isabela*. Cagayan State University, Tuguegarao, Cagayan. Copy received from the 'Essential National Health Research', Department of Health, Manila, Philippines.
- ATS (American Thoracic Society)/CDC (Centers for Disease Control and Prevention)/IDSA (Infectious Diseases Society of America) (2003). Treatment of Tuberculosis. *American Journal of Respiratory and Critical Care Medicine* 167 (4): 603-662.
- Auer C (1998). Factors associated with non-compliance with anti-TB treatment in Manila, Philippines. *International Journal of Tuberculosis and Lung Disease* 2 (11; Suppl. 2): S349.
- Auer C (1998a). *Evaluation of the National Tuberculosis Control Program in Malabon, Metropolitan Manila and Determination of Patient Factors Related to Tuberculosis – An Extended Summary*. TB Control Service, Department of Health, Santa Cruz, Manila, Philippines and Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland.
- Auer C, Sarol J, Tanner M, Weiss MG (2000). Health seeking and perceived causes of tuberculosis among patients in Manila, Philippines. *Tropical Medicine and International Health* 5 (9): 648-656.
- Baily GVJ, Rupert Samuel GE, Nagpaul DR (1974). A concurrent comparison of an unsupervised self-administered daily regimen and a fully supervised twice weekly-regimen of chemotherapy in a routine outpatient treatment programme. *Indian Journal of Tuberculosis* 21 (3): 152-167.
- Balambal R (2001). Profile of DOT providers in the private sector. *Indian Journal of Tuberculosis* 48: 73-75.
- Balasubramanian VN, Oommen K, Samuel R (2000). DOT or not? Direct observation of anti-tuberculosis treatment and patient outcomes, Kerala State, India. *International Journal of Tuberculosis and Lung Disease* 4 (5): 409-413.
- Bayer R, Wilkinson D (1995). Directly observed therapy for tuberculosis: history of an idea. *Lancet* 345: 1545-1548.

## References

- Bechan S, Connolly C, Short GM, Standing E, Wilkinson D (1997). Directly observed therapy for tuberculosis given twice weekly in the workplace in urban South Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 91 (6): 704-707.
- Becx-Bleumink M, Djalamuddin S, Loprang F, de Soldenhoff R, Wibowo H, Aryono M (1999). High cure rates in smear-positive tuberculosis patients using ambulatory treatment with once-weekly supervision during the intensive phase in Sulawesi, Republic of Indonesia. *International Journal of Tuberculosis and Lung Disease* 3 (12): 1066-1072.
- Behr MA, Warren SA, Salamon H, Hopewell PC, Ponce de Leon A, Daley CL, Small PM (1999). Transmission of Mycobacterium tuberculosis from patients smear-negative for acid-fast bacilli. *Lancet* 353: 444-449.
- Benator D, Bhattacharya M, Bozeman L, Burman W, Cantazaro A, Chaisson R, *et al.* (2002). Rifapentine and isoniazid once a week versus rifampicin and isoniazid twice a week for treatment of drug-susceptible pulmonary tuberculosis in HIV-negative patients: a randomised clinical trial. *Lancet* 360 (9332): 528-534.
- Bleed D, Dye C, Raviglione M (2000). Dynamics and control of the global tuberculosis epidemic. *Current Opinion in Pulmonary Medicine* 6: 174-179.
- Bloch H (1961). Intermittent isoniazid therapy for mice. *American Review of Respiratory Diseases* 84: 824-836.
- Bloom BR, Murray CJL (1992). Tuberculosis: Commentary on a Reemergent Killer. *Science* 257: 1055-1064.
- British Thoracic Society (1998). Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. Joint Tuberculosis Committee of the British Thoracic Society. *Thorax* 53 (7): 536-548.
- Brown P (1997). TB claims slammed as 'dangerous'. *New Scientist*, April 19: 4.
- Brugha R, Varvasovszky Z (2000). Stakeholder analysis: a review. *Health Policy and Planning* 15 (3): 239-246.
- Brugha R, Walt G (2001). A global health fund: a leap of faith? *British Medical Journal* 323: 152-154.
- Brugha R, Zwi AB (1999) Sexually transmitted disease control in developing countries: the challenge of involving the private sector. *Sexually Transmitted Infections* 75: 283-385.
- Brugha R, Zwi A (1999a). *Tuberculosis Treatment in the Public and Private Sectors - Potential for Collaboration*. In: Porter JDH & Grange JM (eds), *Tuberculosis: An Interdisciplinary Perspective* (pp. 167-192). London: Imperial College Press.
- Caminero JA, Pavon JM, Rodriguez de Castro F, Diaz F, Julia G, Cayla JA, Cabrera P (1996). Evaluation of a directly observed six month fully intermittent treatment regimen for tuberculosis in patients suspected of poor compliance. *Thorax* 51: 1130-1133.
- Caminero JA, Pena MJ, Campos-Herrero MI, Rodriguez JC, Afonso O, Martin C, Pavon JM, *et al.* (2001). Exogenous reinfection with tuberculosis on a European island with a moderate incidence of disease. *American Journal of Respiratory & Critical Care Medicine* 163 (3 Pt 1): 717-720.

## References

- Campbell MK, Grimshaw JM (1998). Cluster randomised trials: time for improvement. *British Medical Journal* 317: 1171-1172.
- Canetti G (1962). The Eradication of Tuberculosis: Theoretical Problems and Practical Solutions. *Tubercle* 43: 301-321.
- Canetti G, Fox W, Khomenko A, Mahler HT, Menon NK, Mitchison DA, *et al.* (1969). Advances in techniques of testing mycobacterial drug sensitivity, and the use of sensitivity tests in tuberculosis control programmes. *Bulletin of the World Health Organization* 41 (1): 21-43.
- Cao JP, Zhang LY, Zhu JQ, Chin DP (1998). Two-year follow-up of directly-observed intermittent regimens for smear-positive pulmonary tuberculosis in China. *International Journal of Tuberculosis and Lung Disease* 2 (5): 360-364.
- Chaisson RE, Clermont HC, Holt EA, Cantave M, Johnson MP, Atkinson J, *et al.* (1996). Six-month supervised intermittent tuberculosis therapy in Haitian patients with and without HIV infection. *American Journal of Respiratory & Critical Care Medicine* 154 (4 Pt 1): 1034-1038.
- Chaisson RE, Barnes GL, Hackman J, Watkinson L, Kimbrough L, Metha S, *et al.* (2001). A randomized, controlled trial of interventions to improve adherence to isoniazid therapy to prevent tuberculosis in injection drug users. *The American Journal of Medicine* 110 (8): 610-615.
- Chakraborty AK, Rangan S, Uplekar M (1995). *Urban Tuberculosis Control: Problems and Prospects*. Mumbai: The Foundation for Research and Community Health.
- Chaulk CP, Moore-Rice K, Rizzo R, Chaisson R (1995). Eleven years of community-based directly observed therapy for tuberculosis. *Journal of the American Medical Association* 274 (12): 945-951.
- Chee CB, Boudville IC, Chan SP, Zee YK, Wang YT (2000). Patient and disease characteristics, and outcome of treatment defaulters from the Singapore TB control unit--a one-year retrospective survey. *International Journal of Tuberculosis and Lung Disease* 4 (6): 496-503.
- China Tuberculosis Control Collaboration (1996). Results of directly observed short-course chemotherapy in 112,842 Chinese patients with smear-positive tuberculosis. *Lancet* 347 (8998): 358-362.
- Cohn DL, Catlin BJ, Peterson KL, Judson FN, Sbarbaro JA (1990). A 62-dose, 6-month therapy for pulmonary and extrapulmonary tuberculosis. A twice-weekly, directly observed, and cost-effective regimen. *Annals of Internal Medicine* 112 (6): 407-415.
- Cohn DL, O'Brien RJ (1998). The use of restriction fragment length polymorphism (RFLP) analysis for epidemiological studies of tuberculosis in developing countries. *International Journal of Tuberculosis and Lung Disease* 2 (1): 16-26.
- Coker R (1999). Public health, civil liberties, and tuberculosis. *British Medical Journal* 318: 1434-1435.
- Concato J, Shah N, Horwitz RI (2000). Randomized, controlled trials, observational studies, and the hierarchy of research designs. *New England Journal of Medicine* 342 (25): 1887-1892.
- Connolly C, Reid A, Davies G, Sturm W, McAdam KP, Wilkinson D (1999). Relapse and mortality among HIV-infected and uninfected patients with tuberculosis successfully treated with twice weekly directly observed therapy in rural South Africa. *AIDS* 13 (12): 1543-1547.

## References

- Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC, Dye C (2003). The Growing Burden of Tuberculosis. Global Trends and Interactions With the HIV Epidemic. *Archives of Internal Medicine* 163: 000-000. To be published in May 2003.
- Crabb C (2002). A new TB drug by 2010 – or sooner? *Bulletin of the World Health Organization* 80 (6): 518-519.
- Croft RA, Croft RP (1998). Expenditure and loss of income incurred by tuberculosis patients before reaching effective treatment in Bangladesh. *International Journal of Tuberculosis and Lung Disease* 2 (3): 252-254.
- Cronbach LJ (1951). Coefficient alpha and the internal structure of tests. *Psychometrika* 16, 297-334.
- Cure TB Foundation (1991). *Survey on Knowledge, Attitude and Practices on Tuberculosis in Barangay Singkamas, Makati*. Cure TB Foundation, Makati City, Philippines.
- Datta M, Radhamani MP, Selvaraj R, Paramasivan CN, Gopalan BN, Sudeendra CR, Prabhakar R (1993). Critical assessment of smear-positive pulmonary tuberculosis patients after chemotherapy under the district tuberculosis programme. *Tubercle and Lung Disease* 74: 180-186.
- Davies G, Connolly C, Sturm AW, McAdam KPWJ, Wilkinson D (1999). Twice-weekly, directly observed treatment for HIV-infected and uninfected tuberculosis patients: cohort study in rural South Africa. *AIDS* 13: 811-817.
- De Boer AS, Borgdorff MW, Vynnycky E, Sebek MM, van Soolingen D (2003). Exogenous re-infection as a cause of recurrent tuberculosis in a low-incidence area. *International Journal of Tuberculosis and Lung Disease* 7 (2): 145-152.
- De Jonghe E, Murray CJL, Chum HJ, Nyangulu DS, Salomao A, Styblo K (1994). Cost-effectiveness of chemotherapy for sputum smear-positive pulmonary tuberculosis in Malawi, Mozambique and Tanzania. *International Journal of Health Planning and Management* 9: 151-181.
- De Viedma DG, Marin M, Hernangomez S, Diaz M, Ruiz Serrano MJ, Alcala L, Bouza E (2002). Tuberculosis recurrences: reinfection plays a role in a population whose clinical/epidemiological characteristics do not favor reinfection. *Archives of Internal Medicine* 162 (16): 1873-1879.
- Dolin PJ, Raviglione MC, Kochi A (1994). Global tuberculosis incidence and mortality during 1990-2000. *Bulletin of the World Health Organization* 72: 213-220.
- Dubos R, Dubos J (1952). *The white plague. Tuberculosis, man and society*. Little, Brown and Company, Boston.
- Dye C, Garnett GP, Sleeman K, Williams BG (1998). Prospects for worldwide tuberculosis control under the WHO DOTS strategy. *Lancet* 352: 1886-1891.
- Dye C, Scheeles S, Dolin P, Pathania V, Raviglione MC (1999). Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. *Journal of the American Medical Association* 282: 677-686.
- Easton A (1998). Tuberculosis controls in Philippines have failed so far. *British Medical Journal* 317: 557.
- Editorial in the Lancet (2001). A global health fund: heeding Koch's caution. *Lancet* 358: 1. 202

## References

- El-Sadr WM, Perlman DC, Matts JP, Nelson ET, Cohn DL, Salomon N, *et al.* (1998). Evaluation of an intensive intermittent-induction regimen and duration of short-course treatment for human immunodeficiency virus-related pulmonary tuberculosis. *Clinical Infectious Diseases* 26 (5): 1148-1158.
- El-Sadr WM, Perlman DC, Denning E, Matts JP, Cohn DL (2001). A review of efficacy studies of 6-month short-course therapy for tuberculosis among patients infected with human immunodeficiency virus: differences in study outcomes. *Clinical Infectious Diseases* 32 (4): 623-632.
- Enarson DA (1991). Principles of IUATLD Collaborative Tuberculosis Programmes. *Bulletin of the International Union Against Tuberculosis and Lung Disease* 66: 195-200.
- Farga V (1999). The origins of DOTS. *International Journal of Tuberculosis and Lung Disease* 3 (2): 175-176.
- Farmer PE (1997). Social scientists and the new tuberculosis. *Social Science & Medicine* 44 (3): 347-358.
- Farmer P (1999). *Infections and inequalities – the modern plagues*. University of California Press, Berkeley, Los Angeles, London.
- Farmer P (1999a). Managerial successes, clinical failures (editorial). *International Journal of Tuberculosis and Lung Disease* 3 (5): 365-367.
- Fergusson D, Aaron SD, Guyatt G, Hébert P (2002). Post-randomisation exclusions: the intention to treat principle and excluding patients from analysis. *British Medical Journal* 325: 652-654.
- Floyd K, Blanc L, Raviglione M, Lee JW (2002). Resources required for global tuberculosis control. *Science* 295 (5562): 2040-2041.
- Fox R (1997). Are you a commander or a guide? *Journal of the Royal Society* 90: 242-243.
- Fox W (1971). General considerations in intermittent drug therapy of pulmonary tuberculosis. *Postgraduate Medical Journal* 47: 729-736.
- Fox W (1988). Tuberculosis case-finding and treatment programmes in the developing countries. *British Medical Bulletin* 44 (3): 717-737.
- Fox W, Ellard GA, Mitchison DA (1999). Studies on the treatment of tuberculosis undertaken by the British Medical Research Council Tuberculosis Units, 1946-1986, with relevant subsequent publications. *International Journal of Tuberculosis and Lung Disease* 3 (10; Suppl.): S231-S279.
- Freire M, Roscigno G (2002). Joining forces to develop new weapons against TB: together we must. *Bulletin of the World Health Organization* 80 (6): 429.
- Frieden T, Sbarbaro JA (2002). The slippery slope of sloppy DOTS (editorial). *International Journal of Tuberculosis and Lung Disease* 6 (5): 371-372.
- Fujiwara PI, Cook SV, Osahan SS, Frieden TR (1996). Working with the private medical sector: Improvements in tuberculosis control. *Tubercle and Lung Disease* 77 (S2). 72-75.
- Gandy M, Zumla A (2002). The resurgence of disease: social and historical perspectives on the 'new' tuberculosis. *Social Science & Medicine* 55: 385-396.



## References

- Gibson N, Boillot F, Jalloh H (1998). The cost of tuberculosis to patients in Sierra Leone's war zone. *International Journal of Tuberculosis and Lung Disease* 2 (9): 726-731.
- Goffman E (1963). *Stigma*. Prentice-Hall Inc., Englewood Cliffs, New Jersey, USA.
- Gonzalez E, Armas L, Alonso A (1994). Tuberculosis in the Republic of Cuba: Its possible elimination. *Tubercle and Lung Disease* 75: 188-194.
- Gordin FM, Slutkin G, Schecter G, Goodman PC, Hopewell PC (1989). Presumptive diagnosis and treatment of pulmonary tuberculosis based on radiographic findings. *American Review of Respiratory Diseases* 139 (5): 1090-1093.
- Gorin AA, Stone AA (2001). *Recall biases and cognitive errors in retrospective self-reports: A call for momentary assessments*. In: Baum A, Revenson T, Singer J (eds), *Handbook of health psychology* (pp. 405-413), Mahwah, NJ: Erlbaum.
- Grange JM (1999). DOTS with a SMILE. *International Journal of Tuberculosis and Lung Disease* 3 (4): 360.
- Grange JM, Festenstein F (1993). The human dimension of tuberculosis control. *Tubercle and Lung Disease* 74: 219-222.
- Grange JM, Zumla A (1997). Making DOTS succeed. *Lancet* 350: 157.
- Grange JM, Zumla A (1999). Paradox of the global emergency of tuberculosis. *Lancet* 353 (9157): 996.
- Grilli R, Ramsay C, Minozzi S (2002). Mass media interventions: effects on health services utilisation (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
- Harries AD, Gausi FK, Kwanjana JH, Nyirenda TE, Salaniponi FML (2001). Is oral intermittent initial phase anti-tuberculosis treatment associated with higher mortality in high HIV-prevalent areas in sub-Saharan Africa? *International Journal of Tuberculosis and Lung Disease* 5 (5): 483-485.
- Haynes RB, McDonald H, Garg AX, Montague P (2002). Interventions for helping patients to follow prescriptions for medications (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2002. Oxford: Update Software.
- Heifets L, Iseman MD (2002). Leo Tolstoy, TB in Russia, and American perceptions (editorial). *International Journal of Tuberculosis and Lung Disease* 6 (11): 939-941.
- Herrera M. *et al.* (1971). Problemática sociológica del enfermo tuberculoso internado en hospitales de estancia prolongada. *Salud Publica de Mexico XIII*: 749-762.
- Heyman SJ, Sell R, Brewer TF (1998). The Influence of Program Acceptability on the Effectiveness of Public Health Policy: A Study of Directly Observed Therapy for Tuberculosis. *American Journal of Public Health* 88: 442-445.
- Hong Kong Chest Service/British Medical Research Council (1976). Adverse reactions to short-course regimens containing streptomycin, isoniazid, pyrazinamide and rifampicin in Hong Kong. *Tubercle* 57 (2): 81-95.

## References

- Hong Kong Chest Service/British Medical Research Council (1981). Controlled trial of four thrice-weekly regimens and a daily regimen all given for 6 months for pulmonary tuberculosis. *Lancet* i (8213): 171-174.
- Hong Kong Chest Service/British Medical Research Council (1991). Controlled trial of 2, 4, and 6 months of pyrazinamide in 6-month, three-times-weekly regimens for smear-positive pulmonary tuberculosis, including an assessment of a combined preparation of isoniazid, rifampin, and pyrazinamide: Results at 30 months. *American Review of Respiratory Diseases* 143: 700-706.
- Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council (1981). A study of the characteristics and course of sputum smear-negative pulmonary tuberculosis. *Tubercle* 62: 155-167.
- Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council (1989). A controlled trial of 3-month, 4-month, and 6-month regimens of chemotherapy for sputum-smear-negative pulmonary tuberculosis. Results at 5 years. *American Review of Respiratory Diseases* 139 (4): 871-876.
- Hooi LN (1994). Case-finding for pulmonary tuberculosis in Penang. *Medical Journal of Malaysia* 49 (3): 223-230.
- Hudelson P (1996). Gender differentials in tuberculosis: the role of socio-economic and cultural factors. Review article. *Tubercle and Lung Disease* 77: 391-400.
- Hudelson P (1999). *Gender Issues in the Detection and Treatment of Tuberculosis*. In: Porter JDH & Grange JM (eds), *Tuberculosis: An Interdisciplinary Perspective* (pp. 339-355). London: Imperial College Press.
- Humphries M (1995). Tuberculosis: history of directly observed therapy. *Lancet* 346: 380.
- Hurtig AK, Pande SB, Baral SC, Newell J, Porter JDH, Bam, DS (2002). Linking private and public sector in tuberculosis treatment in Kathmandu Valley, Nepal. *Health Policy and Planning* 17 (3): 78-89.
- Hurtig AK, Porter JD, Ogden JA (1999). Tuberculosis control and directly observed therapy from the public health/human rights perspective. *International Journal of Tuberculosis and Lung Disease* 3 (7): 553-560.
- Ioannidis JPA, Haidich AB, Lau J (2001). Any casualties in the clash of randomised and observational evidence? *British Medical Journal* 322: 879-880.
- Jamison DT, Mosley WH (1991). *Evolving Health Sector Priorities in Developing Countries*. Washington DC: World Bank.
- Jaramillo E (1998). Pulmonary tuberculosis and health-seeking behaviour: how to get a delayed diagnosis in Cali, Columbia. *Tropical Medicine & International Health* 3 (2): 138-144.
- Jaramillo E (1999). Encompassing treatment with prevention: the path for a lasting control of tuberculosis. *Social Science & Medicine* 49: 393-404.
- Jaramillo E (2001). The impact of media-based health education on tuberculosis diagnosis in Cali, Colombia. *Health Policy and Planning* 16 (1): 68-73.
- Jin BW, Kim SC, Mori T, Shimao T (1993). The impact of intensified supervisory activities on tuberculosis treatment. *Tubercle and Lung Disease* 74: 267-272.

## References

- Jochem K, Walley J (1999). *Tuberculosis in high-prevalence countries: current control strategies and their technical and operational limitations*. In: Porter JDH & Grange JM (eds), *Tuberculosis: An Interdisciplinary Perspective* (pp. 123-165). London: Imperial College Press.
- Johansson E, Diwan VK, Huong ND, Ahlberg BM (1996). Staff and patient attitudes to tuberculosis and compliance with treatment: an exploratory study in a district in Vietnam. *Tubercle and Lung Disease* 77: 178-183.
- Johansson E, Long NH, Diwan VK, Winkvist A (1999). Attitudes to compliance with tuberculosis treatment among women and men in Vietnam. *International Journal of Tuberculosis and Lung Disease* 3 (10): 862-868.
- Johansson E, Long NH, Diwan VK, Winkvist A (2000). Gender and tuberculosis control - perspectives on health seeking behaviour among men and women in Vietnam. *Health Policy* 52 (1): 33-51.
- Kamat VR (2001). Private practitioners and their role in the resurgence of malaria in *Mumbai* (Bombay) and *Navi Mumbai* (New Bombay), India: serving the affected or aiding an epidemic? *Social Science & Medicine* 52 (6): 885-909.
- Kamolratanakul P, Sawert H, Kongsin S, Lertmaharit S, Sriwongsa J, Na-Songkhla S, *et al.* (1999). Economic impact of tuberculosis at the household level. *International Journal of Tuberculosis and Lung Disease* 3 (7): 596-602.
- Kamolratanakul P, Sawert H, Lertmaharit S, Kasetjaroen Y, Akksilp S, Tulaporn C, *et al.* (1999a). Randomized controlled trial of directly observed treatment (DOT) for patients with pulmonary tuberculosis in Thailand. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 93 (5): 552-557.
- Kelly PM (2001). Local problems, local solutions: improving tuberculosis control at the district level in Malawi. *Bulletin of the World Health Organization* 79 (2): 111-117.
- Khan A, Walley J, Newell J, Imdad N (2000). Tuberculosis in Pakistan: socio-cultural constraints and opportunities in treatment. *Social Science & Medicine* 50: 247-254.
- Khatri GR, Frieden TR (2002). Controlling Tuberculosis in India. *New England Journal of Medicine* 347 (18): 1420-1425.
- Khatri GR, Frieden TR (2002a). Rapid DOTS expansion in India. *Bulletin of the World Health Organization* 80 (6): 457-463.
- Kimerling ME, Kluge H, Vezhnina N, Iacovazzi T, Demeulenaere T, Portaels F *et al.* (1999). Inadequacy of the current who re-treatment regimen in a central Siberian prison: treatment failure and MDR-TB. *International Journal of Tuberculosis and Lung Disease* 3 (5): 451-453.
- Kironde S, Meintjies M (2002). Tuberculosis treatment delivery in high burden settings: does patient choice of supervision matter? *International Journal of Tuberculosis and Lung Disease* 6 (7): 599-608.
- Klaudt K (1998). *The Political Causes and Solutions Of the Current Tuberculosis Epidemic*. In: *The Politics of Emerging and Resurgent Infectious Diseases*. MacMillan.
- Kochi A (1991). The global tuberculosis situation and the new control strategy of the World Health Organization. *Tubercle* 72: 1-6.

## References

- Kochi A (1994). Tuberculosis: Distribution, Risk Factors, Mortality. *Immunobiology* 191: 325-336.
- Kochi A (1997). Is DOTS the Health Breakthrough of the 1990s? *World Health Forum* 18 (3/4): 225-232.
- Lancet Editorial (1997). Putting public health back into epidemiology. *Lancet* 350: 229.
- Lancet, correspondence (2001). Direct observation for tuberculosis treatment. *Lancet* 358: 420-422.
- Lawn SD (2000). Tuberculosis in Ghana: social stigma and compliance with treatment. Letter. *International Journal of Tuberculosis and Lung Disease* 4 (12): 1190-1191.
- Leventhal H (1965). Fear Communications in the Acceptance of Preventative Health Practices. *Bulletin of New York Academy of Medicine* 41: 1144.
- Levy H, Feldman C, Sacho H, van der Meulen H, Kallenbach J, Koornhof H (1989). A reevaluation of sputum microscopy and culture in the diagnosis of pulmonary tuberculosis. *Chest* 95 (6): 1193-1197.
- Liefoghe R, Michiels N, Habib S, Moran MB, De Muynck A (1995). Perception and social consequences of tuberculosis: a focus group study of tuberculosis patients in Sialkot, Pakistan. *Social Science & Medicine* 41 (12): 1685-1692.
- Liefoghe R, Baliddawa JB, Kipruto EM, Vermeire C, De Muynck AO (1997). From their own perspective. A Kenyan community's perception of tuberculosis. *Tropical Medicine and International Health* 2 (8): 809-821.
- Long R, Scalcini M (1999). Is the treatment of WHO Category I tuberculosis with 2HRZE/6HE a defensible practice? *International Journal of Tuberculosis and Lung Disease* 3 (9): 747-748.
- Long R, Scalcini M (2000). More on the question of optimal chemotherapy in the presence of isoniazid resistance. *International Journal of Tuberculosis and Lung Disease* 4 (9): 890-894.
- Lönnroth K, Thuong LM, Linh PD, Diwan VK (1998). Risks and benefits of private health care: exploring physicians' views on private health care in Ho Chi Minh City, Vietnam. *Health Policy* 45: 81-97.
- Lönnroth K (2000). *Public Health in Private Hands – Studies on private and public tuberculosis care in Ho Chi Minh City, Vietnam*. PhD dissertation. Department of Social Medicine, Göteborg University, and Nordic School of Public Health, Göteborg, Sweden.
- Lönnroth K, Thuong LM, Linh PD, Diwan VK (2001). Utilization of private and public health-care providers for tuberculosis symptoms in Ho Chi Minh City, Vietnam. *Health Policy and Planning* 16 (1): 47-54.
- Lönnroth K, Tran TU, Thuong LM, Quy HT, Diwan V (2001a). Can I afford free treatment?: Perceived consequences of health care provider choices among people with tuberculosis in Ho Chi Minh City, Vietnam. *Social Science & Medicine* 52 (6): 935-948.
- Mackey-Dick J (1954). Nursing the tuberculous. *Lancet* ii: 44-45.
- Macq JCM, Theobald S, Dick J, Dembele M (2003). An exploration of the concept of directly observed treatment (DOT) for tuberculosis patients: from a uniform to a customised approach. *International Journal of Tuberculosis and Lung Disease* 7 (2): 103-109.

## References

- Manalo MF, Pineda AV, Montoya JC (1998). Knowledge, attitudes and practices for tuberculosis among Filipino family physicians: a comparative analysis by practice setting and location. *Philippine Journal of Microbiology and Infectious Diseases* Jan-Mar: 6-12.
- Mangura BT, Reichman LB (1999). Periodic chest radiography: unnecessary, expensive, but still pervasive. *Lancet* 353: 319-320.
- Marsh D, Hashim R, Hassany F, Hussain N, Iqbal Z, Irfanullah A *et al.* (1996). Front-line management of pulmonary tuberculosis: an analysis of tuberculosis and treatment practices in urban Sindh, Pakistan. *Tubercle and Lung Disease* 77: 86-92.
- Mathema B, Pande SB, Jochem K, Houston RA, Smith I, Bam DS, McGowan, Jr JE (2001). Tuberculosis treatment in Nepal: a rapid assessment of government centers using different types of patient supervision. *International Journal of Tuberculosis and Lung Disease* 5 (10): 912-919.
- Mathew R, Santha T (2000). The treatment of WHO Category I tuberculosis with 2HRZE/6HE is indeed defensible. *International Journal of Tuberculosis and Lung Disease* 4 (9): 795.
- Meissner PE, Musoke P, Okwera A, Bunn JEG, Coulter JBS (2002). The value of urine testing for verifying adherence to anti-tuberculosis chemotherapy in children and adults in Uganda. *International Journal of Tuberculosis and Lung Disease* 6 (10): 903-908.
- Meyer H, Mally J (1912). Über Hydrazinderivate der Pyridincarbonsäuren. *Monatshefte für Chemie und verwandte Teile anderer Wissenschaften* 23: 393-414.
- Mills A, Brugha R, Hanson K, McPake B (2002). What can be done about the private health sector in low-income countries? *Bulletin of the World Health Organization* 80: (4): 325-330.
- Ministry of Health Malaysia (1988). *National health and morbidity survey (1986-87). Overview of findings and recommendations*. Kuala Lumpur: Ministry of Health.
- Mitchison DA (1998). How drug resistance emerges as a result of poor compliance during short course chemotherapy for tuberculosis. *International Journal of Tuberculosis and Lung Disease* 2 (1): 10-15.
- Mitchison DA, Dickinson JM (1971). Laboratory aspects of intermittent drug therapy. *Postgraduate Medical Journal* 47: 737-741.
- Morankar S, Suryawanshi N, Kudale A, Deshmukh D, Patil O, Rangan S (2000). *Social Stigma in Tuberculosis*. In: Thakur AK (ed.), *Recent Trends in Tuberculosis and Chest Diseases* (pp. 1-50). Patna, India: Bihar TB Association.
- Mori T, Shimao T, Jin BW, and Kim SJ (1992). Analysis of case finding process of tuberculosis in Korea. *Tubercle and Lung Disease* 73: 225-231.
- Moulding TS, Caymittes M (2002). Managing medication compliance of tuberculosis patients in Haiti with medication monitors. *International Journal of Tuberculosis and Lung Disease* 6 (4): 313-319.
- Moulding TS, Caymittes M (2003). The use of medication monitors to evaluate compliance among tuberculosis patients in Haiti. In reply (letter). *International Journal of Tuberculosis and Lung Disease* 7 (1): 98-99.
- Mullen PD (1997). Compliance becomes concordance. *British Medical Journal* 314: 691-692.

## References

- Murray CJL (1994). *Issues in Operational, Social, and Economic Research on Tuberculosis*. In: *Tuberculosis: Pathogenesis, Protection, and Control* (pp. 583-622). Bloom BR (ed), American Society for Microbiology, Washington, DC 20005.
- Murray CJL (1996). *Epidemiology and demography of tuberculosis*. In: Timaeus IM, Chackiel J, Ruzieka L (eds), *Adult Mortality in Latin America* (pp. 199-216). Oxford: Clarendon Press.
- Murray CJL, Lopez AD (1997). Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 349: 1436-42.
- Murray CJL, Salomon JA (1998). Expanding the WHO tuberculosis control strategy: rethinking the role of active case-finding. *International Journal of Tuberculosis and Lung Disease* 2 (9; Suppl. 1), S9-S15.
- Murray CJL, Styblo K, Rouillon A (1990). Tuberculosis in developing countries: burden, intervention and cost. *Bulletin of the International Union Against Tuberculosis and Lung Disease* 65: 6-24.
- Murray CJL, DeJongue E, Chum HJ, Nyangulu DS, Salomao A, Styblo K (1991). Cost effectiveness of chemotherapy for pulmonary tuberculosis in three sub-Saharan African countries. *Lancet* 338: 1305-1308.
- Murthy KJR, Frieden TR, Yazdani A, Hreshikesh P (2001). Public-private partnership in tuberculosis control: experience in Hyderabad, India. *International Journal of Tuberculosis and Lung Disease* 5 (4): 354-359.
- Mwandumba HC, Squire SB (2002). Fully intermittent dosing with drugs for treating tuberculosis in adults (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
- Mwinga A, Nunn A, Ngwira B, Chintu C, Warndorff D, Fine P, *et al.* (2002). Mycobacterium vaccae (SRL172) immunotherapy as an adjunct to standard antituberculosis treatment in HIV-infected adults with pulmonary tuberculosis: a randomised placebo-controlled trial. *Lancet* 360 (9339): 1050-1055.
- Nair DM, George A, Chacko KT (1997). Tuberculosis in Bombay: new insights from poor urban patients. *Health Policy and Planning* 12 (1): 77-85.
- Nakajima H (1993). Tuberculosis: a global emergency. Editorial. *World Health*, 46<sup>th</sup> Year, No. 4, July-August 1993, page 3. World Health Organization, Geneva, Switzerland.
- National Statistics Office (2000). *Philippine National Census 2000 – Highlights*. National Statistics Office, Republic of the Philippines, Manila, Philippines.  
[http://www.census.gov.ph/census2000/c2khighlights\\_final.html](http://www.census.gov.ph/census2000/c2khighlights_final.html), accessed on February 16, 2003.
- National Statistics Office (2002). National Statistics Office, Republic of the Philippines, Manila, Philippines. [www.census.gov.ph](http://www.census.gov.ph), accessed on September 11, 2002.
- National Tuberculosis Programme Myanmar (2000). *Tuberculosis - A Guideline for General Practitioners*. December 2000, Ministry of Health Myanmar.
- Needham DM, Godfrey-Faussett P (1996). Economic barriers for tuberculosis patients in Zambia [letter]. *Lancet* 348: 134-135.

## References

- Needham DM, Godfrey-Faussett P, Foster SD (1998). Barriers to tuberculosis control in urban Zambia: the economic impact and burden on patients prior to diagnosis. *International Journal of Tuberculosis and Lung Disease* 2 (10): 811-817.
- Neher A, Breyer G, Shrestha B, Feldmann K (1996). Directly observed intermittent short-course chemotherapy in the Kathmandu valley. *Tubercle and Lung Disease* 77 (4): 302-307.
- Netto EM, Dye C, Raviglione MC, for the Global Monitoring and Surveillance Project (1999). Progress in global tuberculosis control 1995-1996, with emphasis on 22 high-incidence countries. *International Journal of Tuberculosis and Lung Disease* 3 (4): 310-320.
- Newell DJ (1992). Intention-to-treat analysis: implications for quantitative and qualitative research. *International Journal of Epidemiology* 21 (5): 837-841.
- Ngamvithayapong J, Yanai H, Winkvist A, Saisorn S, Diwan K (2001). Feasibility of home-based and health centre-based DOT: perspectives of TB care providers and clients in an HIV-endemic area of Thailand. *International Journal of Tuberculosis and Lung Disease* 5 (8): 741-745.
- Nichter M (1994). Illness Semantics and International Health: the Weak Lungs/TB Complex in the Philippines. *Social Science & Medicine* 38: 649-663.
- O'Boyle SJ, Power JJ, Ibrahim MY, Watson JP (2002). Factors affecting patient compliance with anti-tuberculosis chemotherapy using the directly observed treatment, short-course strategy (DOTS). *International Journal of Tuberculosis and Lung Disease* 6 (4): 307-312.
- Ogden J, Rangan S, Uplekar M, Porter J, Brugha R, Zwi A, Nyheim D (1999). Shifting the paradigm in tuberculosis control: illustrations from India. *International Journal of Tuberculosis and Lung Disease* 3 (10): 855-861.
- Onyango-Ouma W, Laisser R, Mbilima M, Araoye M, Pittman P, Agyepong I, *et al.* (2001). An evaluation of *Health Workers for Change* in seven settings: a useful management and health system development tool. *Health Policy and Planning* 16 (Suppl. 1): 24-32.
- Ortega AR, Meniado MV, Tobias MC (1991). *Comparative Study on the Knowledge, Attitudes, and Practices on Tuberculosis in Low Income Groups in a Rural and Urban Community in the Philippines*. Philippine Council for Health Research and Development (PCHRD), Bicutan, Taguig, Metro Manila, Philippines, April 1991.
- Oursler KK, Moore RD, Bishai WR, Harrington SM, Pope DS, Chaisson RE (2002). Survival of patients with pulmonary tuberculosis: clinical and molecular epidemiologic factors. *Clinical Infectious Diseases* 34 (6): 752-759.
- Oxman AD, Thomson MA, Davis DA, Haynes RB (1995). No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *Canadian Medical Association Journal* 153 (10): 1423-1431.
- Pathania V, Almeida J, Kochi A (1997) *TB Research. TB Patients and Private For-Profit Health Care Providers in India*. Global TB Programme of the World Health Organisation, Geneva, Switzerland: Publication WHO/TB/97.223.
- Peabody J, Tan CAR, Luck J, Leyco EA (2003). *Measuring the burden of disease and economic consequences of tuberculosis in the Philippines*. Final Report. Philippine Tuberculosis Initiatives for the Private Sector (Philippine TIPS). West Tower, Philippine Stock Exchange Building, Ortigas, Metro Manila, Philippines.

## References

- Perelman MI (2000). Tuberculosis in Russia. *International Journal of Tuberculosis and Lung Disease* 4 (12): 1097-1103.
- Perkins MD, Kritski AL (2002). Diagnostic testing in the control of tuberculosis. *Bulletin of the World Health Organization* 80 (6): 512-513.
- Philippine Department of Health (1984). *National Tuberculosis Prevalence Survey in the Republic of the Philippines (1981 - 1983)*. National Institute of Tuberculosis, Manila, Philippines.
- Philippine Department of Health (1988). *Manual of the National Tuberculosis Control Program*. TB Control Service, Department of Health, Manila, Philippines.
- Philippine Department of Health (1993). *External Evaluation (March 1993)*. Conducted by the WHO. TB Control Service. Department of Health, Manila, Philippines.
- Philippine Department of Health (2001). *Manual of Procedures for the National Tuberculosis Control Program, 2001*. Department of Health, Manila, Philippines.
- Philippine Department of Health (2002). [http://www.doh.gov.ph/data\\_stat/html/mortal\\_98.htm](http://www.doh.gov.ph/data_stat/html/mortal_98.htm), accessed on November 15, 2002.
- Philippine Department of Health (2003). Health Indicators - Leading Causes of Mortality. [http://www.doh.gov.ph/data\\_stat/html/mortal\\_98.htm](http://www.doh.gov.ph/data_stat/html/mortal_98.htm), accessed on February 16, 2003.
- Pocock D, Khare A, Harries AD (1996). Case holding for tuberculosis in Africa: the patients' perspective [letter]. *Lancet* 347: 1258.
- Porter JDH, Ogden JA (1997). Ethics of directly observed therapy for the control of infectious diseases. *Bulletin Institute Pasteur* 95: 117-127.
- Porter JDH, Ogden JA (2002). Commentary on 'the resurgence of disease: social and historical perspectives on the 'new' tuberculosis'. *Social Science & Medicine* 55: 397-398.
- Portero JL, Rubio M (2003). Private practitioners and tuberculosis control in the Philippines: strangers when they meet? *Tropical Medicine and International Health* 8 (4): 329-335.
- Preston SH, Keyfitz N, Schoen R (1972). *Cause of death: life tables for national populations*. New York: Seminar Press.
- Pungrassami P, Chongsuvivatwong V (2002). Are health personnel the best choice for directly observed treatment in southern Thailand? A comparison of treatment outcomes among different types of observers. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 96: 695-699.
- Pungrassami P, Johnson SP, Chongsuvivatwong V, Olsen J, Sorensen HT (2002). Practice of directly observed treatment (DOT) for tuberculosis in southern Thailand: comparison between different types of DOT observers. *International Journal of Tuberculosis and Lung Disease* 6 (5): 389-395.
- Rabuhin AE (1960). *Treatment of tuberculosis*. Third edition (in Russian). Moscow: Medgiz.



## References

- Rajeswari R, Balasubramanian R, Muniyandi M, Geetharamani S, Thresa X, Venkatesan P (1999). Socio-economic impact of tuberculosis on patients and family in India. *International Journal of Tuberculosis and Lung Disease* 3 (10): 869-877.
- Rajeswari R, Chandrasekaran V, Suhadev M, Sivasubramaniam S, Sudha G, Renu G (2002). Factors associated with patient and health system delays in the diagnosis of tuberculosis in South India. *International Journal of Tuberculosis and Lung Disease* 6 (9): 789-795.
- Ramachandran R, Balasubramanian R, Muniyandi M, Shanmugham G, Xavier T, Venkatesan P (1997). *Economic impacts of tuberculosis on patients and family*. Tuberculosis Research Centre, Indian Council of Medical Research, Chennai, South India.
- Rangan S, Uplekar M. (1999). *Socio-Cultural Dimensions in Tuberculosis Control*. In: Porter JDH & Grange JM (eds), *Tuberculosis: An Interdisciplinary Perspective* (pp. 265-281). London: Imperial College Press.
- Raviglione MC, Pio A (2002). Evolution of WHO policies for tuberculosis control, 1948-2001. *Lancet* 359: 775-780.
- Reichman LB (1991). The U-shaped curve of concern. *American Review of Respiratory Diseases* 144 (4): 741-742.
- Remme J, Blas E, Chitsulo L, Desjeux P, Engers H, Kanyok T, *et al.* (2002). Strategic emphases for tropical diseases research: a TDR perspective. *TRENDS in Microbiology* 10 (10): 435-440.
- Rieder HL (1999). *Infection with tubercle bacilli*. In: *Epidemiologic Basis of Tuberculosis Control*. First edition. International Union Against Tuberculosis and Lung Disease, Paris, France.
- Rieder HL (2002). *Essential Drugs*. In: *Interventions for Tuberculosis Control and Elimination*. First edition. International Union Against Tuberculosis and Lung Disease, Paris, France.
- Rieder HL, Arnadottir T, Trébuq A, Enarson DA (2001). Tuberculosis treatment: dangerous regimens? *International Journal of Tuberculosis and Lung Disease* 5 (1): 1-3.
- Roa CC, Romulo RLC (2000). *Coalition Building for TB Control: the Philippine Experience*. In: Reichman LB, Hershfield ES (eds), *Tuberculosis - A Comprehensive International Approach*. Lung Biology in Health and Disease. Vol 144, pp. 525-552, 2<sup>nd</sup> Edition. Marcel Dekker Inc., New York.
- Roemer MI (1991). *National health system of the world. Volume 1: The countries*. New York: Oxford University Press.
- Rothman KJ, Adami HO, Trichopoulos D (1998). Should the mission of epidemiology include the eradication of poverty? *Lancet* 352: 810-813.
- Rouillon A (1991). The Mutual Assistance Programme of the IUATLD. Development, contribution and significance. *Bulletin of the International Union Against Tuberculosis and Lung Disease* 66: 159-172.
- Royal Pharmaceutical Society of Great Britain (1997). *From compliance to concordance: towards shared goals in medicine taking*. London, Royal Pharmaceutical Society.
- Rubel AJ, Garro LC (1992). Social and Cultural Factors in the Successful Control of Tuberculosis. *Public Health Reports* 107 (6): 626-636.

## References

- Rubin DB (1998). More powerful randomization-based p-values in double-blind trials with non-compliance. *Statistics in Medicine* 17 (3): 371-385.
- Santha T, Garg R, Frieden TR, Chandrasekaran V, Subramani R, Gopi PG, *et al.* (2002). Risk factors associated with default, failure and death among tuberculosis patients treated in a DOTS programme in Tiruvallur District, South India, 2000. *International Journal of Tuberculosis and Lung Disease* 6 (9): 780-788.
- Sarmiento AG (1990). *Operational Assessment of the Case Finding and Treatment Aspects of the Strengthened National Tuberculosis Control Program*. Department of Health, Manila, Philippines.
- Saunderson PR (1995). An economic evaluation of alternative programme designs for tuberculosis control in rural Uganda. *Social Science & Medicine* 40 (9): 1203-1212.
- Sbarbaro JA (1980). Public health aspects of tuberculosis: supervision of therapy. *Clinics in Chest Medicine* 1 (2): 253-263.
- Sbarbaro JA (1997). Directly Observed Therapy - Who is Responsible? *Clinics in Chest Medicine* 18 (1): 131-133.
- Sbarbaro J (2001). Kochi's tuberculosis strategy article is a "classic" by any definition. *Bulletin of the World Health Organization* 79 (1): 69-70.
- Schüth T (1998). DOTS implementation by an NGO (SHIS) in two rural districts of West Bengal, India. *International Journal of Tuberculosis and Lung Disease* 2 (11; Suppl 2), S363.
- Schwartz RK, Soumerai SB, Avorn J (1989). Physician motivations for nonscientific drug prescribing. *Social Science & Medicine* 28 (6): 577-582.
- Singapore Tuberculosis Service/British Medical Research Council (1979). Clinical trial of six-month and four-month regimens of chemotherapy in the treatment of pulmonary tuberculosis. *American Review of Respiratory Diseases* 119: 579-85.
- Singapore Tuberculosis Service/British Medical Research Council (1981). Clinical trial of six-month and four-month regimen of chemotherapy in the treatment of pulmonary tuberculosis: the results up to 30 months. *Tubercle* 62: 95-102.
- Singh V, Jaiswal A, Porter JD, Ogden JA, Sarin R, Sharma PP, *et al.* (2002). TB control, poverty, and vulnerability in Delhi, India. *Tropical Medicine & International Health* 7 (8): 693-700.
- Sommer A, Zeger SL (1991). On estimating efficacy from clinical trials. *Statistics in Medicine* 10 (1): 45-52.
- Sonnenberg P, Murray J, Shearer S, Glynn JR, Kambashi B, Godfrey-Faussett P (2000). Tuberculosis treatment failure and drug resistance—same strain or reinfection? *Transactions of the Royal Society of Tropical Medicine and Hygiene* 94 (6): 603-607.
- Sonnenberg P, Murray J, Glynn JR, Shearer S, Kambashi B, Godfrey-Faussett P (2001). HIV-1 and recurrence, relapse, and reinfection of tuberculosis after cure: a cohort study in South African mineworkers. *Lancet* 358 (9294): 1687-93.
- Stata Corporation (1999). *Stata Statistical Software: Release 6.0*. College Station: Stata Press.

## References

- Sterling TR, Alwood K, Gachuhi R, Coggin W, Blazes D, Bishai WR, Chaisson RE (1999). Relapse rates after short-course (6-month) treatment of tuberculosis in HIV-infected and uninfected persons. *AIDS* 13: 1899-1904.
- Steyn M, van der Merwe N, Dick J, Borchers R, Wilding RJ (1997). Communication with TB patients; a neglected dimension of effective treatment? *Curationis* 20 (1): 53-56.
- Stop TB (2000). *The economic impacts of tuberculosis*. World Health Organization, Geneva, Switzerland, WHO/CDS/STB/2000.5.
- Stop TB (2002). *Stop TB, fight poverty*. The campaign diary. World TB Day 24 March 2002. World Health Organization, Geneva, Switzerland.
- Suarez PG, Floyd K, Portocarrero J, Alarcon E, Rapiti E, Ramos G, *et al.* (2002). Feasibility and cost-effectiveness of standardised second-line drug treatment for chronic tuberculosis patients: a national cohort study in Peru. *Lancet* 359: 1980-1989.
- Sumartojo E (1993). When Tuberculosis Treatment Fails. A Social Behavioral Account of Patient Adherence. *American Review of Respiratory Diseases* 147: 1311-1320.
- Swan M, Zwi A (1997). *Private practitioners and public health: close the gap or increase the distance*. London: London School of Hygiene and Tropical Medicine.
- Tam CM, Chan SL, Kam KM, Goodall RL, Mitchison DA (2002). Rifapentine and isoniazid in the continuation phase of a 6-month regimen. Final report at 5 years: prognostic value of various measures. *International Journal of Tuberculosis and Lung Disease* 6 (1): 3-10.
- Task Force on Tuberculosis (2000). Philippine Practice Guidelines Group in Infectious Diseases. *Pulmonary Tuberculosis: Clinical Practical Guidelines*. PPGG-ID Philippine Society for Microbiology and Infectious Diseases and Philippine College of Chest Physicians. No. 116, 9<sup>th</sup> Avenue, Cubao. Quezon City 1109, Philippines.
- TDR (2002). *Strategic Direction for research on Tuberculosis*. A 2-page information sheet given on the 4<sup>th</sup> World Congress on TB (3-5 June 2002, Washington DC, USA). See also Remme *et al.* (2002).
- Tempel CW, Hughes FJ, Mardis RE, Towbin MN, Dye WE (1950). Combined intermittent regimens employing streptomycin and paraaminosalicylic acid in the treatment of pulmonary tuberculosis. *Transactions of the Ninth Streptomycin Conference, Veterans Administration*, p. 36.
- Thaver IH, Harpham T (1997). *Private practitioners in the slums of Karachi: professional development and innovative approaches for improving practice*. In: Bennett S, McPake B & Mills A (eds), *Private Health Providers in Developing Countries: Serving the public interest?* (pp. 71-81). London and New Jersey: Zed Books Ltd.
- Thaver IH, Harpham T, McPake B, Garner P (1998). Private practitioners in the slums of Karachi: what quality of care do they offer? *Social Science & Medicine* 46 (11): 1441-1449.
- Thomas C (2002). A literature review of the problems of delayed presentation for treatment and non-completion of treatment for tuberculosis in less developed countries and ways of addressing these problems using particular implementations of the DOTS strategy. *Journal of Management in Medicine* 16 (4-5): 371-400.

## References

- Thomson O'Brien MA, Oxman AD, Haynes RB, Davis DA, Freemantle N, Harvey EL (2002). Local opinion leaders: effects on professional practice and health care outcomes (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
- Thomson O'Brien MA, Freemantle N, Oxman AD, Wolf F, Davis DA, Herrin J (2002a). Continuing education meetings and workshops: effects on professional practice and health care outcomes (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
- Thomson O'Brien MA, Oxman AD, Davis DA, Haynes RB, Freemantle N, Harvey EL (2002b). Educational outreach visits: effects on professional practice and health care outcomes (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
- Tiglao TV, Tempongko MSB (1991). People's perception of tuberculosis. *Philippine Journal of Public Health* January-December: 37-38.
- Toledo JR, Hughes H, Sims J (1979). Management of non-compliance to medical regimen: a suggested methodological approach. *International Journal of Health Education* 22 (4): 232-241.
- Trébuq A, Anagonou S, Gninafon M, Lambregts K, Boulahbal F (1999). Prevalence of primary and acquired resistance of Mycobacterium tuberculosis to antituberculosis drugs in Benin after 12 years of short-course chemotherapy. *International Journal of Tuberculosis and Lung Disease* 3 (6): 466-470.
- Tropical Disease Foundation (1997). *Final Report - 1997 National Tuberculosis Prevalence Survey*. Submitted 5 December 1997. Tropical Disease Foundation, Makati Medical Center, 2, Amorsolo St, Makati City 1200, Philippines.
- Trostle JA (1988). Medical compliance as an ideology. *Social Science & Medicine* 27 (12): 1299-1308.
- Tuberculosis Research Centre (1997). A controlled clinical trial of oral short-course regimens in the treatment of sputum-positive pulmonary tuberculosis. *International Journal of Tuberculosis and Lung Disease* 1 (6): 509-517.
- Tuberculosis Research Centre (2002). Shortening short course chemotherapy: a randomised clinical trial for treatment of smear positive pulmonary tuberculosis with regimens using ofloxacin in the intensive phase. *Indian Journal of Tuberculosis* 49: 27-38.
- Tupasi TE, Radhakrishna S, Rivera AB, Pascual MLG, Quelapio MID, Co VM, *et al.* (1999). The 1997 Nationwide Tuberculosis Prevalence Survey in the Philippines. *International Journal of Tuberculosis and Lung Disease* 3 (6): 471-477.
- Tupasi TE, Radhakrishna S, Quelapio MI, Villa ML, Pascual ML, Rivera AB, *et al.* (2000). Tuberculosis in the urban poor settlements in the Philippines. *International Journal of Tuberculosis and Lung Disease* 4 (1): 4-11.
- Tupasi TE, Radhakrishna S, Co VM, Villa ML, Quelapio MI, Mangubat NV, *et al.* (2000a). Bacillary disease and health seeking behavior among Filipinos with symptoms of tuberculosis: implications for control. *International Journal of Tuberculosis and Lung Disease* 4 (12): 1126-1132.
- UNAIDS/WHO (2002). *AIDS epidemic update, December 2002*. Joint United Nations Programme on HIV/AIDS (UNAIDS) World Health Organization. Geneva, Switzerland.
- UNICEF (2002). *The State of the World's Children 2001*. UNICEF, New York, USA.

## References

- United Nations Population Division (2000). *World Urbanization Prospects: The 1999 revision*. New York. UN.
- Uplekar M (1999). *Involving the private medical sector in tuberculosis control: practical aspects*. In: Porter JDH & Grange JM (eds), *Tuberculosis: An Interdisciplinary Perspective* (pp. 193-212). London: Imperial College Press.
- Uplekar MW, Shepard DS (1991). Treatment of private general practitioners in India. *Tubercle* 72: 284-290.
- Uplekar M, Rangan S (1996). *Tackling TB: The Search for Solutions*. Mumbai, The Foundation for Research in Community Health.
- Uplekar M, Juvekar S, Morankar S, Rangan S, Nunn P (1998). Tuberculosis patients and practitioners in private clinics in India. *International Journal of Tuberculosis and Lung Disease* 2 (4): 324-329.
- Uplekar MW, Rangan S, Weiss MG, Ogden J, Borgdorff MW, Hudelson P (2001). Attention to gender issues in tuberculosis control. *International Journal of Tuberculosis and Lung Disease* 5 (3): 220-224.
- Uplekar M, Pathania V, Raviglione M (2001a). Private practitioners and public health: weak links in tuberculosis control. *Lancet* 358: 912-916.
- Valeza FS, Mantala MJ, Lofranco V, *et al.* (1990). *Operations Research to Improve Delivery of TB Information to Patients by Nurses and Midwives*. TB Control Service, Department of Health, Manila, Philippines.
- Valeza FS, Lagahid JY, Hernandez AM, *et al.* (1991) PART I (pp. 1-34): *Health Facilities' Delay and Total Delay in the Diagnosis and Treatment of Tuberculosis*. PART II (pp. 35-66): *Study on the Factors Influencing Compliance on Treatment in Tuberculosis of Short Course Chemotherapy*. TB Control Service, Department of Health, Manila, Philippines.
- Valeza F, Mantala M, Blumenfeld S (1992). Application of systems analysis to identify service quality problems in the Philippine National Tuberculosis Control Program. *Philippine Journal of Public Health* (Jan.-Dec.): 38-43.
- Van der Walt HM, Swartz L (2002). Task orientated nursing in a tuberculosis control programme in South Africa: where does it come from and what keeps it going? *Social Science & Medicine* 54: 1001-1009.
- Van Gorkom J, Van Cleeff M, Becx-Bleumink M, Veen J (2001). Short-course instead of long-course chemotherapy for smear-negative patients in sub-Saharan Africa. *International Journal of Tuberculosis and Lung Disease* 5 (1): 4-11.
- Van Rie A, Warren R, Richardson M, Victor TC, Gie RP, Enarson DA, *et al.* (1999). Exogenous reinfection as a cause of recurrent tuberculosis after curative treatment. *New England Journal of Medicine* 341 (16): 1174-1179.
- Verheul E, Rowson M (2002). Where is health? Editorial. *Tropical Medicine and International Health* 7 (5): 391-394.

## References

- Vidal R, Martin-Casabona N, Juan A, Falgueras T, Miravittles M (1996). Incidence and significance of acid-fast bacilli in sputum smears at the end of antituberculous treatment. *Chest* 109 (6): 1562-1565.
- Vlassoff C, Weiss M, Ovuga EBL, Eneanya C, Nwel PT, Babalola SS, *et al.* (2000). Gender and the stigma of onchocercal skin disease in Africa. *Social Science & Medicine* 50 (10): 1353-1368.
- Volmink J, Garner P (2003). Directly observed therapy for treating tuberculosis (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003.
- Waksman SA (1952). Streptomycin: background, isolation, properties, and utilization. Nobel Lecture of 12 December 1952. <http://www.nobel.se/medicine/laureates/1952/waksman-lecture.pdf>
- Waksman SA (1966). *The Conquest of Tuberculosis*. Berkeley and Los Angeles: University of California Press.
- Walley JD, Khan MA, Newell JN, Khan MH (2001). Effectiveness of the direct observation component of DOTS for tuberculosis: a randomised controlled trial in Pakistan. *Lancet* 357: 664-669.
- Wares DF, Clowes CI (1997). Tuberculosis in Russia [letter]. *Lancet* 350: 957.
- Weiss MG (2001). Cultural epidemiology: an introduction and overview. *Anthropology and Medicine* 8 (1 - Special issue): 5-29.
- Westaway MS, Wolmarans L (1993). Acceptability of the Tuberculosis Service: Scale Development. *International Journal of Epidemiology* 22 (3): 543-547.
- WHO (1974). *WHO Expert Committee on Tuberculosis. Ninth Report*. WHO Technical Report Series No 552. Geneva, Switzerland: World Health Organization.
- WHO (1991). *Forty-fourth World Health Assembly. Resolution and Decisions*. Resolution WHA 44.8. Geneva, Switzerland: World Health Organization. WHA44/1991/REC/1.
- WHO (1993). Tuberculosis: a global emergency. *World Health Forum* 14: 438.
- WHO (1994). WHO Tuberculosis Programme: *Framework for Effective Tuberculosis Control*. Geneva, Switzerland: World Health Organization. WHO/TB/94.179.
- WHO (1996). *The World Health Report 1996. Fighting disease, Fostering development*. Geneva, Switzerland: World Health Organization.
- WHO (1996a). *Tuberculosis Control Workshop Report and Revision of "Treatment of Tuberculosis; Guidelines for National Programmes"*. Geneva, Switzerland: World Health Organization. WHO/TB/96.199.
- WHO (1997). The potential economic benefits of the DOTS strategy against TB in India. Geneva, Switzerland: World Health Organization. WHO/TB/96.218.
- WHO (1997a). *Treatment of Tuberculosis: Guidelines for National Programmes*. Geneva, Switzerland: World Health Organization. WHO/TB/97.220.
- WHO (1997b). *Tuberculosis Control; the DOTS Strategy*. Geneva, Switzerland: World Health Organization. WHO/TB/97.228.

## References

- WHO (1998). Global Tuberculosis Programme: *Report of the ad hoc Committee on the Tuberculosis Epidemic*. London, March 17-19, 1998. Geneva, Switzerland: World Health Organization. WHO/TB/98.245.
- WHO (1998a). *WHO Report on the Tuberculosis Epidemic 1998*. Geneva, Switzerland: World Health Organization. WHO/TB/98.247.
- WHO (1998b). Global Tuberculosis Research Initiative. First meeting of the WHO/GTB working group on operational, health systems and health policy research on tuberculosis control. 15-17 June, 1998. Geneva, Switzerland: World Health Organization.
- WHO (2000). *Report from the Ministerial Conference on TB & Sustainable Development*, Amsterdam, 22-24 March 2000. Geneva, Switzerland: Stop TB Partnership, World Health Organization. WHO/CDS/STB/2000.6. See also: <http://www.stoptb.org/conference/5sessions.pdf>
- WHO (2000a). *Amsterdam Declaration to Stop TB*. Geneva, Switzerland: Stop TB Partnership, World Health Organization. Publication WHO/CDS/STB/2000.6. See also: <http://www.stoptb.org/conference/decla/pdf>
- WHO (2000b). *Health Systems: Improving Performance*. The World Health Report 2000. Geneva, Switzerland: World Health Organization.
- WHO (2000c). *Global Tuberculosis Control. WHO Report 2000*. Geneva, Switzerland: World Health Organization. WHO/CDS/TB/2000.275.
- WHO (2001). *The Global Plan to Stop Tuberculosis*. Geneva, Switzerland: Stop TB Partnership, World Health Organization. WHO/CDS/STB/2001.16. See also: <http://www.stoptb.org/GPSTB/default.asp>
- WHO (2001a). *The World Health Report 2001. Mental Health: New Understanding, New Hope*. Geneva, Switzerland: World Health Organization.
- WHO (2001b). *The Report: "Highlights: First Stop TB Partners' Forum"*, Washington Doctors, 22-23 October 2001. Geneva, Switzerland: Stop TB Partnership, World Health Organization. WHO/CDS/STB/2001.14b. See also: <http://www.stoptb.org/Forum/Documents/STBhighlights.pdf>
- WHO (2001c). *Washington Commitment to Stop TB*. Geneva, Switzerland: Stop TB Partnership, World Health Organization. WHO/CDS/STB/2001.14a. See also [http://www.stoptb.org/Forum/Documents/WashCommitm\\_Eng12Dec.pdf](http://www.stoptb.org/Forum/Documents/WashCommitm_Eng12Dec.pdf)
- WHO (2001d). *Global Tuberculosis Control. WHO Report 2001*. Geneva, Switzerland: World Health Organization. WHO/CDS/TB/2001.287.
- WHO (2001e). *Involving Private Practitioners in Tuberculosis Control: Issues, Interventions and Emerging Policy Framework*. Geneva, Switzerland, World Health Organization. WHO/CDS/TB/2001.285.
- WHO (2001f). *Global DOTS Expansion Plan*. Geneva, Switzerland: World Health Organization. WHO/CDS/STB/2001.11.
- WHO (2002). *Global Burden of Disease 2000: Version 2 methods and results*. Global Programme on Evidence for Health Policy Discussion Paper No. 50. Geneva, Switzerland: World Health Organization.

## References

- WHO (2002a). *The World Health Report 2002. Reducing Risk, Promoting Healthy Life*. Geneva, Switzerland: World Health Organization.
- WHO (2002b). *Global Tuberculosis Control: Surveillance, Planning, Financing. WHO Report 2002*. Geneva, Switzerland, WHO/CDS/TB/2002.295.
- WHO (2002c). *Training for Better TB Control: Human Resource Development for TB Control*. Geneva, Switzerland: World Health Organization. WHO/CDS/TB/2002.301.
- WHO (2002d). *An Expanded DOTS Framework for Effective Tuberculosis Control*. Geneva, Switzerland: Publication WHO/CDS/TB/2002.297. Also published in *International Journal of Tuberculosis and Lung Disease* 2002; 6(5): 378-388.
- WHO (2003). *Global Tuberculosis Control: Surveillance, Planning, Financing. WHO Report 2003*. Geneva, Switzerland: World Health Organization. WHO/CDS/TB/2003.316.
- WHO (2003a). *Treatment of Tuberculosis. Guidelines for National Programmes*. Third edition. Geneva, Switzerland: World Health Organization. To be printed in May 2003 (received in electronic form on December 16, 2002).
- WHO/STOP TB (2002). *Frequently asked questions about the 4-drug fixed-dose combination tablet recommended by the World Health Organization for treating tuberculosis*. Geneva, Switzerland: World Health Organization. WHO/CDS/STB/2002.18.
- Wilkinson D, Bechan S, Connolly C, Standing E, Short GM (1998). Should we take a history of prior treatment, and check sputum status at 2-3 months when treating patients for tuberculosis? *International Journal of Tuberculosis and Lung Disease* 2 (1): 52-55.
- World Bank (1993). *World Development Report 1993: investing in health*. Oxford: Oxford University Press.
- Wyss K, Kilima P, Lorenz N (2001). Costs of tuberculosis for households and health care providers in Dar es Salaam, Tanzania. *Tropical Medicine and International Health* 6 (1): 60-68.
- Wyss K, N'Diekhon Y, Jeannée E (2002). *Research-Action-Capacity Building: A Potential Instrument for New Practices in the Field of Urban Environmental Management and Public Health*. In: Flury M & Geiser U (eds), *Local Environmental Management in a North-South Perspective. Issues of Participation and Knowledge Management* (pp. 79-90). vdf Hochschulverlag AG an der ETH Zürich, Zürich/Singen.
- Yan S, Ye H, Lin S (1996). [Effects of intermittent short-course chemotherapy under full-course supervision on the treatment of smear positive pulmonary tuberculosis.] [Article in Chinese] *Zhonghua Jie He He Hu Xi Za Zhi* 19 (2): 104-106.
- Yesudian CAK (1994). Behaviour of the private sector in the health market of Bombay. *Health Policy and Planning* 9 (1): 72-80.
- Young DB (2001). A post-genomic perspective. *Nature Medicine* 7 (1): 11-13.
- Yu C *et al.* (1996). Comparison of triple (2RHZ/4RH) versus quadruple (2RHZE/4RH) drug treatment for tuberculosis in the Philippines: a multi-center study. *Tubercle and Lung Disease* 77: 132.



### References

Yu CY, Carlos GN, Guiuan E (undated, but must have been in 1998 or 1999). *Technical report: comparison of triple (2RHZ/4RH) versus quadruple (2RHZE/4RH) drug treatment for tuberculosis in the Philippines: a multi-center study*. Philippine Council for Health Research and Development (PCHRD). Bicutan, Taguig, Metro Manila, Philippines.

Zwarenstein (1999). Directly observed treatment for tuberculosis. Authors' reply. *Lancet* 353: 147-148.

Zwarenstein M, Schoeman JH, Vundule C, Lombard CJ, Tatley M (1998). Randomised controlled trial of self-supervised and directly observed treatment for tuberculosis. *Lancet* 352: 1340-1343.

Zwarenstein M, Schoeman JH, Vundule C, Lombard CJ, Tatley M (2000). A randomised controlled trial of lay health workers as direct observers for treatment of tuberculosis. *International Journal of Tuberculosis and Lung Disease* 4 (6): 550-554.

**ANNEX: PATIENT QUESTIONNAIRE (used in Malabon)**

QUESTIONNAIRE

HC: \_\_\_\_\_

GHC \_\_\_\_

Number: \_\_\_\_\_

GNO \_\_\_\_

Re-Treatment? \_\_\_\_\_

GRETX \_\_\_\_

UHNP? \_\_\_\_\_

GUHNP \_\_\_\_

*This is a questionnaire about how one of the programs of the health centers can be improved. Your honest answers are very valuable and will help to improve one program of the health centers. We are **not** from the government. This questionnaire is part of a study performed by a student of the College of Public Health, UP Manila.*

*Please try to give truthful answers. It is not bad or embarrassing if your answer is "I don't know" or "I can't remember" since we need to find out what the people know and what they do not yet know in order to improve the program.*

*Christian Auer, student of the College of Public Health, UP Manila*

**KINDLY ONLY ANSWER THOSE  
QUESTIONS WRITTEN IN BOLD  
AND LARGE LETTERS**

a) General

1. Gender \_\_\_\_\_

GSEX \_\_\_\_

(1=male, 2=female)

2. Age \_\_\_\_\_

GAGE \_\_\_\_

3. **Your civil status in the first half of 1996?**

GCS \_\_\_\_

- Not yet having a partner (=)1)
- Having a partner then (=)2)
- I have a partner but she or he was absent in the first half of 1996 (=)3)
- I had a partner but we are separated (=)4)
- Widowed (=)5)

4. **Since when have you been living in this place?**

\_\_\_\_\_ GAREA \_\_\_\_

5. **Generally**, do you more often go to a private doctor or to a health center?

PRIVORHC \_\_\_\_

- to a health center (=)1)
- to a private doctor (=)2)
- To both (private doctor and health center) (=)3)
- Other: \_\_\_\_\_ (=)4,5)

6. **What are common serious illnesses of people aged 13 years and older in this place?**

GCOMDIS \_\_\_\_

- If possible, mention three illnesses: 1. \_\_\_\_\_  
2. \_\_\_\_\_  
3. \_\_\_\_\_

7. In your opinion, when a person is sick, can he or she do a lot to become healthy again or only a little bit?

GCONTROL \_\_\_\_

- Really a lot (=)1)
- A lot (=)2)
- Quite a bit (=)3)
- A little bit (=)4)
- Almost nothing (=)5)
- I don't know (=)8)

b) Case finding

*The following questions (Nos 9 to 32) are regarding the time span when you first noticed that your health was not fine up to the time when it became clear what your illness was. Therefore, try to remember what you did when your symptoms began.*

**8. In your opinion, what was the illness you had last year?**

FSAKIT \_\_\_\_

- "Sicknees on the lungs" (=1)
- "Weak lungs" (=2)
- TB (=3)
- Other; what? \_\_\_\_\_ (=4)
- I don't know (=8)

**9. When you were not yet sick on your lungs did you then consider TB to be a dangerous disease?**

FDANGER \_\_\_\_

- Yes, really dangerous (=1)
- Yes, somewhat dangerous (=2)
- Only slightly dangerous (=3)
- No. Not dangerous (=4)
- I don't know (=8)

**10. When you were not yet sick on your lungs did you believe that you could get sick on your lungs?**

FTBGET \_\_\_\_

- Yes, really (=1)
- Yes, somewhat (=2)
- Not really (=3)
- Definitely not (=4)
- I don't know (=8)

Annex: Patient questionnaire

11. Before getting sick on your lungs, did you believe then that there exists an effective cure for TB? FCURE \_\_\_\_
- \_\_\_ Yes, really (=1)
  - \_\_\_ Yes, I thought it probable (=2)
  - \_\_\_ Rather not (=3)
  - \_\_\_ Definitely not (=4)
  - \_\_\_ I don't know/ I can't remember (=8)

12. If yes, what was the cure according to your believe **at that time**? FCUREANO \_\_\_\_

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13. What was the **very first** thing you did when you got concerned about your symptoms? FFIRST \_\_\_\_
- \_\_\_ Self-treatment **SHOW IT AND PROBE!!** (=1)
  - \_\_\_ Asked advice at relatives/family/friends (=2)
  - \_\_\_ Asked advice at the relatives/family/friends and then got self-treatment (=3)
  - \_\_\_ Went to a folk healer (*albularyo*) (=4)
  - \_\_\_ Went to a health center (=5)
  - \_\_\_ Went to a private doctor (=6)
  - \_\_\_ Other: \_\_\_\_\_ (=7)

14. **Did someone invite you or tell you to have a medical checkup?** FENCOUR \_\_\_\_
- \_\_\_ Yes (=1)
  - \_\_\_ No (=0)
  - \_\_\_ I can't remember (=8)

15. **If yes: Who?** \_\_\_\_\_ FENCWHO \_\_\_\_
- (E. g. health center staff, someone from your house, neighbour)

Annex: Patient questionnaire

16. Where did it become clear what your illness was? FDIAGWO

- At the health center (=1)
- At the private doctor (=2)
- At both (health center and private doctor) (=3)
- Somewhere else: \_\_\_\_\_ (=4)

IF APPLICABLE:

17. If at the private doctor: Did the private doctor tell you that you can get treatment for sickness on the lungs at the health center? FDRSABIHC \_\_\_\_

- No (=0)
- No, I don't think so (=1)
- Yes, I think so (=2)
- Yes (=3)
- I don't know (=8)

18. What was the result or what came up at the first check-up you had? \_\_\_\_\_ FFIRSANO \_\_\_\_  
(X-ray? Prescription? Buying drugs for how long? ....)

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19. After that, did you still go somewhere else or do something else? FTHENGO \_\_\_\_

20. What were the symptoms that made you go to check for sickness on the lung? FSYMP \_\_\_\_

1. \_\_\_\_\_

2. AFTER PROBING: \_\_\_\_\_

HEMOPTYSIS? \_\_\_\_\_

Annex: Patient questionnaire

21. Approximately, how many weeks or months did you first have symptoms before you went to a private doctor or health center (or NGO)? FTIME \_\_\_\_

\_\_\_\_\_

IF APPLICABLE:

22. What was the reason for your waiting to get a check-up? FDISCOU \_\_\_\_  
Or in other words: Why did you wait for \_\_\_\_\_ before having a check-up?

\_\_\_\_\_

23. How many times had you gone to the health center before you got sick on your lungs? FMANY \_\_\_\_

Around \_\_\_\_\_ times

24. **Did you undergo a sputum test, an X-ray, both or even something else?** FHOWDIA \_\_\_\_

- Sputum test only (=1)
- X-ray only (=2)
- Both (sputum test and X-ray) (=3)
- Something else: \_\_\_\_\_ (=4, 5 evt)  
(Write down here what)
- I can't remember (=8)

25. If you had a sputum test: What was the result of the sputum test?? SPUTEST \_\_\_\_

- (*PROBE!!*)
- positive (=1)
  - negative (=0)
  - I can't remember (=8)

26. Is giving of sputum embarrassing?

FSPUEMB \_\_\_\_

- \_\_\_ No (=0)
- \_\_\_ I little bit (=1)
- \_\_\_ Somehow yes (=2)
- \_\_\_ Yes (=3)
- \_\_\_ I don't know (=8)

27. Was there someone with sickness on the lungs in your household during the time when you went for a check-up?

FHHSICK \_\_\_\_

- \_\_\_ No (=0)
- \_\_\_ Yes (=1)
- \_\_\_ I can't remember (=8)

28. How many people who had had sickness on the lungs or had sickness on the lungs did you know of during the time when you went for a check-up??

FHADTB \_\_\_\_

Around \_\_\_\_\_ people.

29. How many of them are your relatives or close friends? Around \_\_\_\_

FHADTBRF \_\_\_\_

30. How many people who had sickness on the lungs **and** who were treated successfully did you know of during the time when you went for a check-up??

FTREAT \_\_\_\_

Around \_\_\_\_\_ people.

31. How many of them are your relatives or close friends? Around \_\_\_\_

FTREATRF \_\_\_\_

32. How many people had died ***of TB*** did you know of during the time when you went for a check-up??

FDIED \_\_\_\_

Around \_\_\_\_\_ people.

33. How many of them are your relatives or close friends? Around \_\_\_\_

FDIEDRF \_\_\_\_



c) Case holding

*The following questions refer to the time when you were treated, i.e. they refer to the time span when your illness was clearly diagnosed up to the end of treatment. Therefore, try to remember what you did while you were taking medications.*

34. **When the result of the sputum examination came out, were you then told that your disease was contagious?** HINFEC \_\_\_\_

- Yes (=1)
- Yes, I think so (=2)
- I do not think so (=3)
- No (=4)
- I can't remember (=8)

35. **Were you also told how to prevent that other would get infected?** HPREV \_\_\_\_

- Yes (=1)
- Yes, I think so (=2)
- No (=3)
- I do not think so (=4)
- I can't remember (=8)

IF APPLICABLE:

36. If yes: What were you told? \_\_\_\_\_ HPRWHAT \_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

37. **For how long must TB be treated?** HLENGTH \_\_\_\_

For around \_\_\_\_\_ months

Annex: Patient questionnaire

38. When the result of the sputum examination became known were you then immediately treated or did you have to wait? HTXWAIT \_\_\_
- I was immediately treated (=0)
  - I had to wait for \_\_\_\_\_ (1=1 wk, 2=2wks, ect)
  - I can't remember (=8)

IF APPLICABLE:

39. If treatment was not yet available at the health center when the result of the sputum examination came out, what did you do then? HHCGAWA \_\_\_
- I really just waited (=1)
  - I bought treatment even though it was incomplete (=2)
  - I bought treatment. And it was complete. (=3)
  - I was looking for treatment somewhere else and I succeeded. (=4)
  - I was looking for treatment somewhere else but in vain. (=5)
  - Something else; what? \_\_\_\_\_ (=6)
  - I can't remember (=8)

40. When the result of the sputum examination became known were you then told that the other members of your household should have a check-up at the health center? HHHCOME \_\_\_
- No (=0)
  - Yes (=1)
  - Yes, all of them. (=2)
  - Yes, those with symptoms (cough, fever, weight loss etc.) (=3)
  - I can't remember (=8)

Comment: \_\_\_\_\_

41. **Was there someone in your household that got sickness on the lungs after you had been diagnosed?** HHHTBAF \_\_\_
- Yes (=1)
  - No (=2)
  - I can't remember (=8)

*Annex: Patient questionnaire*

42. How much is the transportation fee from your house to the health center? (both ways) HTRSP \_\_\_\_

\_\_\_ None, because I just walked to the health center (0=none, 1= up to P 5,  
\_\_\_ Pesos 2=P 6-10, 3=P 11-15,  
4= 16 plus)

43. How many minutes does it take to go to the health center (one way)? TIMEHC \_\_\_\_

Around \_\_\_\_\_ minutes

44. How many minutes did you have to wait in the health center to get your medication? HHCWAIT \_\_\_\_

\_\_\_ Around \_\_\_\_\_ minutes  
\_\_\_ It depended, varied: \_\_\_\_\_

45. Was there someone who picked up the medication from the health center for you? HPICKUP \_\_\_\_

\_\_\_ Yes (0=no, 1=yes, mw/bhw,  
\_\_\_ No 2=yes, relat., 3=friend,  
\_\_\_ I can't remember 4=k'bahay, 5=other)

If yes: Who? \_\_\_\_\_

46. Did it happen that sometimes the medications were not complete when you went to the health center to get them? HNOTCOMP \_\_\_\_

\_\_\_ No (=0)  
\_\_\_ It happened; around \_\_\_\_\_ times (=1,2,3...)  
\_\_\_ It happened, but I can't remember how many times (=55)  
\_\_\_ I can't remember (=88)

Annex: Patient questionnaire

IF APPLICABLE:

47. What did you do if there was no medication or incomplete medication at the health center? HDOTHEN \_\_\_\_
- The medication was always complete (=9)
  - There was nothing I could do but wait. This meant that my treatment was interrupted.. (=1)
  - I bought medication even though incomplete. (=2)
  - I bought medication. And it was complete. (=3)
  - I was successfully looking for medication somewhere else. (=4)
  - I was looking for medication somewhere else. But I had no success. (=5)
  - Something else? If yes: what? \_\_\_\_\_ (=6, 7)
- 
- I can't remember (=8)

48. Did you have to show the empty 'blister pack' of the medication when you went to the health center to get your medication? HBLIPACK \_\_
- No (=0)
  - Yes, but only in the beginning (=1)
  - Yes, but not always (=2)
  - Yes, always (=3)
  - I can't remember (=8)

49. How did you help yourself in order not to forget to take your daily medication? (reminders, clues) HCLUES \_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_

50. For how many months did you take your medication? For \_\_\_\_ months HTXMOS \_\_\_\_
- If for less than 6 months: Why did it happen that you did not finish six months? \_\_\_\_\_
- \_\_\_\_\_

Annex: Patient questionnaire

51. **Did you take your medication daily during the months of being on medication?** HTXDAILY \_\_\_\_

- Yes, during all the months of taking my medication (=1)
- Yes, but only during the first few months (=2)
- Not really. There were months when I took my medication daily, but there were also months with interruption(s) (=3)
- Almost every month there were interruption(s) (=4)
- Every month there were interruption(s) (=5)
- Something else: \_\_\_\_\_ (=6)

52. In your opinion, if we compare the TB drugs that can be bought in the drug stores with those that we get in the health centers: which ones are better? Or are they the same? HDRUGSEF \_\_\_\_

- They are the same (=0)
- Those in the drug stores are better (=1)
- \_\_\_\_\_ (=2)
- I don't know (=8)

53. Were you asked in the health center whether you experienced side effects? HSIDEEFA \_\_\_\_

- No (=0)
- Only once (=1)
- Around \_\_\_\_\_ times (=2, 3, 4...)
- I can't remember (=8)

54. Was it only one person who gave you the medication in the health center? HONEGAVE \_\_\_\_

- No. different ones (=0)
- Mostly (=1)
- Often (=2)
- Always (=3)
- I can't remember (=8)

- 55. Did you experience side effects when you were taking your TB medication?** HSIDEEF \_\_\_\_
- No (=0)
  - Yes, but only in the beginning. And it was harmless (=1)
  - Yes, but it was harmless (=2)
  - Yes. (=3)
  - Yes. And I had to change my medication (=4)
  - Yes. And I had to stop my medication (=5)
  - I can't remember (=8)
- 
56. Did you sometimes stop taking your medication because you felt unwell? HBAD \_\_\_\_
- Quite frequent (=1)
  - Only sometimes (=2)
  - Seldom (=3)
  - No (=4)
  - I can't remember (=8)
- 
57. It is rather difficult to take medication every day, isn't it. Probably it happened to you that you forgot to take your daily drugs. Did this happen? How frequent? HFORGOT \_\_\_\_
- No (=0)
  - Around once a month (=1)
  - Twice or three times a month (=2)
  - Around once a week (=3)
  - More than once a week (=4)
  - Something else: \_\_\_\_\_ (=5)
  - I can't remember (=8)
- 
58. Did it happen that for more than two weeks you could not take your medication? (i.e. your treatment was interrupted for more than two weeks?) HTXMISS \_\_\_\_
- No (=0)
  - Yes, but only once (=1)
  - Yes, \_\_\_\_ times (=2, 3, 4...)
  - I can't remember (=8)

Annex: Patient questionnaire

59. After how many weeks or months of taking your medication regularly did you feel well again? HFEEL \_\_\_\_  
(1=after 1week, 2=after 2wks etc.)

After \_\_\_\_\_

60. Was there someone who encouraged you to keep on taking your medication? HENCOUR \_\_\_\_  
\_\_\_ Yes (1=yes)  
\_\_\_ No (0=no)

If yes: Who? \_\_\_\_\_ (2= MW/BHW, 3=relative, 4=friend, 5=k'bahay, 6=other)  
(e.g. someone in your household, a neighbour, a health worker)

61. If yes: How important was this encouragement for you to continue to get and take your medication? HENCHHELP \_\_\_\_  
\_\_\_ Definitely not important (=0)  
\_\_\_ A little bit important (=1)  
\_\_\_ Quite important (=2)  
\_\_\_ Important (=3)  
\_\_\_ Really important (=4)  
\_\_\_ I don't know (=8)

**What can you say about the personnel in the health center *during the time of getting your medication?***

62. Were they competent? HHCSKIL \_\_\_\_  
\_\_\_ Yes, really competent  
\_\_\_ Yes, competent (1=no, 2=somehow, 3=quite,.....)  
\_\_\_ Somehow competent  
\_\_\_ A little bit competent  
\_\_\_ Not competent

63. Did they explain you well?

HHCEXPL \_\_\_\_

- Yes, really well
- Yes, well
- Somehow well
- A little bit well
- Not well

64. Were they kind to you?

HHCKIND \_\_\_\_

- Yes, really kind
- Yes, kind
- Somehow kind
- A little bit kind
- Not kind

65. What did they tell you in the health center why you had to come and get medication for six months?

HTOLD \_\_\_\_

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66. What can happen to someone who has TB if his or her time of medication is stopped too early? (*PROBE!*)

HTXSTOP \_\_\_\_  
(1= he won't get cured,  
2=he'll die 3= ...  
[not now])

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*Annex: Patient questionnaire*

67. When you started to have medication - meaning to say ***after*** the result of the sputum examination came out - how many times more did you have to give sputum?  
In other words: Apart from your giving sputum at the beginning of your treatment how many times more did you give sputum ? **PROBE!!** HSPUTUM \_\_\_\_

- No more (=0)
- No more, but X-ray after \_\_\_\_ months (=1)
- Only once; after \_\_\_\_\_ months (=2)
- Twice (=3)
- Three times (=4)
- Four time or more (=5)
- I can't remember (=8)

68. **Did it happen to you that someone asked you to give him or her medication?** HASKED \_\_\_\_

- No (=0)
- Seldom (=1)
- From time to time (=2)
- Quite often (=3)
- Really often (=4)
- I can't remember (=8)

69. **If it happened: Did you give medication to those who asked you?** HGAVE \_\_\_\_

- No, because no-one asked me (=9)
- No (=0)
- Seldom; around \_\_\_\_\_ times (=1)
- From time to time; around \_\_\_\_ times (=2)
- Quite often; around \_\_\_\_ times (=3)
- Really often (=4)
- I can't remember (=8)

Annex: Patient questionnaire

70. If a TB patient starts to take medication regularly: For how many days or weeks or months more will he or she still be contagious? HINFDAY \_\_\_\_

For around \_\_\_\_\_ I don't know

.....

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d) Social effects

71. **Did you have a job before you had sickness on the lungs?** ASOK \_\_\_\_

- Yes (=1)
- Only in between (=2)
- No (=0)

72. **If yes: What kind of job did you have then?** PJOBANO \_\_\_\_

I was employed as a \_\_\_\_\_ (=...)

I had my own work: \_\_\_\_\_ (=...)

73. To those with a job: What was the effect of your illness on your job? SJOB \_\_\_\_

- It had no effect (=0,
- I interrupted my work for \_\_\_\_\_ (weeks or months) (=1,2,3,4,....)
- I stopped my work up to now. (=44)
- I lost my job, but found a new one after \_\_\_\_\_ (weeks or months) (=55)
- I lost my job and hav enow job up to now (=66)
- Something else: \_\_\_\_\_ (=77)

(Write down what)

**To those with a job:**

74. **Did the six months of getting medication become an obstacle for your work?** HCONFL \_\_\_\_

- No, because I didn't have a job then . (=9)
- No (=0)
- Only a little bit (=1)
- Yes, somehow (=2)
- Yes (=3)

75. **Were you the only one in your household who had an income before you fell sick on the lungs?** SBREADW \_\_\_\_

- Yes, I only (=1)
- Yes, but not only I had an income (=2)
- No-one counted on my income because it was small (=3)
- I did not earn (=4)

76. **Did you - because of your sickness on the lungs - have separate eating utensils?** SEATAFF \_\_\_\_

- Yes (=1)
- No (=2)
- I can't remember (=3)

77. **If yes: for how long?** SEATLONG \_\_\_\_

Mga \_\_\_\_\_ (1= ≤1 mo., 2= ≤ 2mos...)

78. **If you had separate eating utensils: Who told you to do this?** SEATWHO \_\_\_\_

\_\_\_\_\_  
 (e.g. Someone in your household, neighbour, health worker) (1=mw/BHW, 2=relat. 3=friend, 4=k'bahay, 5=other)

79. **Did you - because of your sickness on the lungs - change your way of sleeping? (for instance: you slept on your own)** SSLEAFF \_\_\_\_

- \_\_ Yes (=1)
- \_\_ No (=2)
- \_\_ I can't remember (=8)

80. **If yes: What kind of change?** \_\_\_\_\_ SLEANO \_\_\_\_

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81. **If there was change: for how long?** SSLELONG \_\_\_\_  
For around \_\_\_\_\_ (1= $\leq 1$  mo., 2= $\leq 2$ mos.etc)

82. **If there was change: Who told you to change?** SSLEWHO \_\_\_\_  
\_\_\_\_\_  
(e.g. Someone in your household, neighbour, health worker)  
(1=mw/BHW, 2=relat.  
3=friend, 4=k'bahay,  
5=other)

83. **If you are married or have a partner : Did you - because of your sickness on the lungs - change your marital life?** SSEAFF \_\_\_\_

- \_\_ Yes (=1)
- \_\_ No (=2)
- \_\_ I can't remember (=8)

84. **If yes: What kind of change?** \_\_\_\_\_ SSEANO \_\_\_\_

---

85. **If there was change: for how long?** SSELONG \_\_\_\_  
For around \_\_\_\_\_ (1= $\leq 1$  mo., 2= $\leq 2$ mos.etc)

**86. If there was change: Who told you to change?**

SSEWHO \_\_\_\_

---

(e.g. Someone in your household, neighbour, health worker)

**87. In your opinion, who from or what from did you get your sickness on the lungs?**

SWHFROM \_\_\_\_

SHOW IT!!

- From the dirty environment
- From the dirty water
- From too heavy work
- From cold wheather
- From sudden change of temperature
- Inherited
- From vices
- From something else: \_\_\_\_\_
- From someone who had TB

If from someone: Who from did it come?

- from a household member
- from a friend
- from a neighbour
- from a work-mate
- from someone else
- I don't know who it came from
- I don't know

Annex: Patient questionnaire

In your opinion, what are the reasons why someone gets TB?

Hand it over and tell the patient that this is not regarding him/her	<u>Is not a reason</u>	<u>Is somehow</u> <u>a reason</u>	<u>Is really a</u> <u>reason</u>	<u>I don't know</u>	
88. Fatigue, too hard work ('overwork')	1	2	3	8	TBWORK ___
89. Dirty environment	1	2	3	8	TBDIRT ___
90. Lack of food	1	2	3	8	TBFOOD ___
91. Poverty	1	2	3	8	TBPOV ___
92. Microbe	1	2	3	8	TBMICROB ___
93. There is often drying sweat on the back	1	2	3	8	TBPAWIS ___
94. He is close to someone with TB	1	2	3	8	TBCATAO ___
95. Inherited	1	2	3	8	TBMANA ___
96. He had already often had pneumonia	1	2	3	8	TBPULM ___
97. He is often drinking alcohol	1	2	3	8	TBALAK ___
98. He is often smoking	1	2	3	8	TBZIGI ___
99. He has many 'sex partners'	1	2	3	8	TBSEX ___
100. He is often sleeping on cold floor	1	2	3	8	TBCOLD ___

101. **When you found out that you had TB: were you then very sad or in other words very depressed?**

- \_\_\_ No (= $0$ )
- \_\_\_ A little bit (= $1$ )
- \_\_\_ Somewhat yes (= $2$ )
- \_\_\_ Yes (= $3$ )
- \_\_\_ I can't remember (= $8$ )

102. **Were you afraid to die when you found out that you had TB?** SDIE \_\_\_\_

- No (=0)
- A little bit (=1)
- Somewhat yes (=2)
- Yes (=3)
- I can't remember (=8)

103. **Did you feel that your self-worth or self-esteem became smaller when you found out that you had TB?**

- No (=0)
- A little bit (=1)
- Somewhat yes (=2)
- Yes (=3)
- I can't remember (=8)

104. **Did you feel embarrassed or ashamed when you found out that you had TB?** SHIYA \_\_\_\_

- No (=0)
- A little bit (=1)
- Somewhat yes (=2)
- Yes (=3)
- I can't remember (=8)

105. **Did you feel kind of sinful when you found out that you had TB?** SGUILT \_\_\_\_

- No (=0)
- A little bit (=1)
- Somewhat yes (=2)
- Yes (=3)
- I can't remember (=8)

106. **In your opinion, were there some people who changed their attitude towards you when they heard that you had sickness on the lungs?** SBAD \_\_\_\_

- No (=0)
- A little bit (=1)
- Somewhat yes (=2)
- Yes (=3)
- I don't know (=8)

107. **Did you feel that some people avoided you when you had TB?** SOSTRA \_\_\_\_

- No (=0)
- A little bit (=1)
- Somewhat yes (=2)
- Yes (=3)
- I don't know (=8)

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e) Personal items

108. **How many persons were living in your household while you were taking?** PPEOPLE \_\_\_\_

\_\_\_\_\_ person

109. **How big was the monthly income of all those together who had an income in your household before you got sick on your lungs?** PINCOME \_\_\_\_

- less than P 3000 (=1)
- less than P 4000: (=2)
- between P 4000 and 6000 (=3)
- between P 6000 and 8000 (=4)
- between P 8000 and 10,000 (=5)
- between P 10,000 and 14,000 (=6)
- more than P 14,000 (=7)
- It's hard to say / I don't know (=8)



110. **In your opinion, to what group of people does your family belong?** PPERCPOV \_\_\_\_

- quite rich (=1)
- not rich, but a good income (=2)
- has a bit more than just needed (=3)
- quite poor (=4)
- poor (=5)
- very poor (=6)
- I don't know (=8)

111. **How often did you go to church in 1996?** PCHURCH \_\_\_\_

- very seldom (=1)
- around once every second month (=2)
- around once a month (=3)
- around twice a month (=4)
- around once a week (=5)
- more than once a week (=6)
- I don't know (=8)

112. **Normally, in which church do you go?** PRELI \_\_\_\_

- in the Catholic Church (=1)
- in a Protestant church (=2)
- in a "born-again" church (=3)
- in the "Iglesia ni Cristo" church (=4)
- in another church; what kind? \_\_\_\_\_ (=5)
- it depends (=6)

113. **What kind of education did you have?** PEDUC \_\_\_\_
- None (=0)
  - Elementary school (=1)
  - Graduate of elementary school (=2)
  - High School (=3)
  - graduate of High School (=4)
  - Vocational training (=5)
  - Graduate of a vocational training (=6)
  - College level (=7)
  - College graduate (=8)
  - Post-graduate (=9)

114. **Do you feel that your TB is now totally healed?** PHEALED \_\_\_\_
- No (=0)
  - Not really (=1)
  - Yes, almost (=2)
  - Yes, fully healed (=3)
  - I don't know (=8)

115. **Are you afraid that your TB might come back?** PFEAR \_\_\_\_
- No (=0)
  - A little bit (=1)
  - Somehow yes (=2)
  - Yes, I am really afraid (=3)
  - I don't know (=8)

116. Was it the first time when you had sickness on the lungs in 1996? PTBULIT \_\_\_\_
- PROBE!!
- Yes, the first time
  - No; it was the \_\_\_\_\_ time.

117. **Did you *smoke* before you got diagnosed?** PSMKBEF \_\_\_\_

<input type="checkbox"/> No	(=0)
<input type="checkbox"/> From time to time	(=1)
<input type="checkbox"/> Often	(=2)
<input type="checkbox"/> Always and quite heavily	(=3)

118. **And while you got medication, did you smoke?** PSMKTX \_\_\_\_

<input type="checkbox"/> No	(=0)
<input type="checkbox"/> From time to time	(=1)
<input type="checkbox"/> Often	(=2)
<input type="checkbox"/> Always and quite heavily	(=3)

119. **And now, do you smoke?** PSMKNOW \_\_\_\_

<input type="checkbox"/> No	(=0)
<input type="checkbox"/> From time to time	(=1)
<input type="checkbox"/> Often	(=2)
<input type="checkbox"/> Always and quite heavily	(=3)

120. **Did you drink *alcohol* before you got diagnosed?** PALCBEF \_\_\_\_

<input type="checkbox"/> No	(=0)
<input type="checkbox"/> From time to time	(=1)
<input type="checkbox"/> Around once a week	(=2)
<input type="checkbox"/> More than once a week	(=3)

121. **And while you got medication?** PALCTX \_\_\_\_

<input type="checkbox"/> No	(=0)
<input type="checkbox"/> From time to time	(=1)
<input type="checkbox"/> Around once a week	(=2)
<input type="checkbox"/> More than once a week	(=3)

122. And now, do you drink *alcohol*?

PALCNOW \_\_\_\_

- No (=0)
- From time to time (=1)
- Around once a week (=2)
- More than once a week (=3)

g) Re substudy 3

**What can you say about the giving of explanations of the health center staff to you?**

123. Were the explanations sufficient

CCSAPAT \_\_\_\_

- Yes, very sufficient (=1)
- Yes, sufficient (=2)
- Only somehow sufficient (=3)
- Not sufficient (=4)
- I don't know (=8)

124. Were the explanations clear (easy to understand)?

CCCLEAR \_\_\_\_

- Yes, very clear (=1)
- Yes, clear (=2)
- Only somehow clear (=3)
- Not clear (=4)
- I don't know (=8)

125. Was it easy to remember the explanations?

CCEASY \_\_\_\_

- Yes, very easy (=1)
- Yes, easy (=2)
- Only somehow easy (=3)
- Not easy (=4)
- I don't know (=8)

126. Was your belief or trust in the drugs (that they were effective) firm while you were receiving medication?

CCDRUGS \_\_\_\_

SHOW IT AND PROBE!

- Yes, very firm (=1)
- Yes, firm (=2)
- Only somehow firm (=3)
- No. It was small (=4)
- I don't know (=8)

127. Was your belief that treatment was lacking if it did not last six months strong while you were receiving medication?  
(Or in other words that treatment was really needed for six months?)

CCSIXMOS \_\_\_\_

SHOW IT AND PROBE!

- Yes, very strong (=1)
- Yes, strong (=2)
- Only somehow strong (=3)
- No. It was weak (=4)
- I don't know (=8)

*Annex: Patient questionnaire*

128. Was your sickness very serious or dangerous in your view when you started to get medication? CCGRABE \_\_\_\_

- SHOW IT AND PROBE!
- Yes, very serious (=1)
  - Yes, serious (=2)
  - Only somehow serious (=3)
  - No (=4)
  - I don't know (=8)

129. Were you afraid of the 'side effects' while being on medication? CCSIDEF \_\_\_\_

- SHOW IT AND PROBE!
- Yes, very much afraid (=1)
  - Yes, I was afraid (=2)
  - I was only somehow afraid (=3)
  - No, I was not afraid (=4)
  - I don't know (=8)

130. Do you know of someone who was not healed of his or her TB even though he or she was receiving medication? If yes: How many do you know? CCDIGALI \_\_\_\_

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131. If yes: Why were they not getting well? \_\_\_\_\_ CCWHY \_\_\_\_

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## CURRICULUM VITAE

### 1. Personal data:

Name: AUER Christian  
Date and place of birth: 14 June 1963, Basel, Switzerland  
Nationality: Swiss Civil status: married  
Address: Bruderholzstr. 26, 4103 Bottmingen, Switzerland; phone: ++41 61 421 03 71  
Languages: German, English, Filipino, French, (Spanish)

### 2. Education and experience

1970 – 1975 Primary School  
1975 - 1982 High School, Matura B (Latin)  
1983 - 1989 University of Basel: Studies mainly in zoology, botany, medical microbiology and medical biochemistry  
1987 Final examination in medical microbiology and biochemistry  
1988 First part of diploma (MSc): - biology of invertebrates  
- phytomedicine  
- ecological plantphysiology  
May 1988 - July 1989 Second part of diploma: MSc in medical zoology with a thesis on the health problems of children living in a squatter area of Manila, Philippines.  
Title: "Health problems (especially intestinal parasitoses) of children living in Smokey Mountain, a squatter area of Manila, Philippines."  
The MSc thesis project included a 4-month stay in Manila (fieldwork)  
June 1994 - March 1998: Studies at the College of Public Health, University of the Philippines Manila for a Master of Science in Epidemiology (in Public Health). The thesis was carried out in co-operation with the Swiss Tropical Institute.  
Title: "Evaluation of the National Tuberculosis Control Program in Malabon, Metro Manila and Determination of Patient Factors Related to Tuberculosis."

### 3. Employment and Activities:

From September 1989 to March 1990 I was working as a scientific assistant at the Swiss Tropical Institute, Department of Public Health & Epidemiology. During this time I was mainly occupied with analysing data from a rural Tanzanian district hospital.

From September 1990 up to June 1996 (the last two years of it not full-time) I was with a Christian NGO that is working holistically among the urban poor of Metro Manila, Philippines. It is the policy of this NGO that its members not only work with the urban poor but also live with them. This made me live in three different urban poor areas of Metro Manila. I am still a member of this NGO.

May 19 to June 5, 1992 I attended a course at the College of Public Health, University of the Philippines Manila called "Applied epidemiology in health care".

Since early 1997, I have been doing research in Metro Manila, performing a TB patient survey and looking at the effectiveness of the implementation of DOTS (directly observed treatment, short-course), supported by the Swiss Tropical Institute.

Since May 1999 I have been working as a doctoral student of the Swiss Tropical Institute (Department of Public Health & Epidemiology) in Metro Manila. Title of the thesis: "*Strategies for Tuberculosis Control from Experiences in Manila: The Role of Public-Private Collaboration and of Intermittent Therapy*".

Member of: - International Union Against Tuberculosis and Lung Disease (IUATLD)  
- Philippine Coalition Against Tuberculosis (PhilCAT)

## Curriculum Vitae

### 4. Publications:

Auer Ch. (1990). Health Status of Children Living in a Squatter Area of Manila, Philippines with Particular Emphasis on Intestinal Parasitoses. *Southeast Asian J Trop Med Public Health*; 21, 289-300.

Auer Ch. & Tanner M. (1990). Childhood Vaccination in a Squatter Area of Manila, Philippines: Coverage and Providers. *Soc Sci Med*; Vol. 31, No. 11, 1265-1270.

Auer Ch. & Tanner M., Intestinal Parasites in Children of Smokey Mountain, a Squatter Area of Manila, Philippines. Residential Meeting of the Royal Society of Tropical Medicine and Hygiene, Cambridge, England, July 1990.

Duncan M & Auer Ch (1995). View from the Slums of Asia - the Experience of a Christian Missionary Group. In: *Urban Health in Developing Countries - Progress and Prospects*. Edited by Trudy Harpham and Marcel Tanner. Earthscan.

Auer Ch. (1998). Factors Associated With Non-Completion of Anti-TB Treatment in Manila, Philippines. *International Journal of Tuberculosis and Lung Disease (Abstract Book) 2 (11)*; November, Suppl. 2, S349.

Auer Ch, Tanner M, Sarol J, Weiss MG (2000). Health seeking and perceived causes of tuberculosis among patients in Manila, Philippines. *Tropical Medicine & International Health*; 5 (9), 648-656.

Auer Ch, Montejo L, Lagahid J, Roa CC, Ang CF, Van Deun A, Tanner M, Weiss MG (2002). Randomized controlled trial of daily vs. thrice-weekly anti-TB therapy in public health centres of Manila, Philippines. *International Journal of Tuberculosis and Lung Disease (Abstract Book) 6 (10)*, Suppl. 1, S149.

### 5. Presentations at Scientific Meetings:

1989: Auer Ch. & Tanner M., Childhood Vaccination in a Squatter Area of Manila: Coverage and Providers. Presented at the Eleventh International Conference on the Social Sciences and Medicine.

Auer Ch. & Tanner M., Intestinal Parasitoses in Children of Smokey Mountain, a Squatter Area of Manila, Philippines. Presented at the annual meeting of the Swiss Society of Tropical Medicine and Parasitology.

1990: Auer Ch., Intestinal Parasitoses in Children of Smokey Mountain, a Squatter Area of Manila, Philippines. Presented at ZOOLOGIA 90, annual conference of the Swiss Zoological Society.

Auer Ch. & Tanner M., Intestinal Parasitoses in Children of Smokey Mountain, a Squatter Area of Manila, Philippines. Presented at the residential meeting of the Royal Society of Tropical Medicine and Hygiene.

1998: Auer Ch., Factors associated with non-completion of anti-tuberculosis treatment among TB patients of Manila, Philippines. Presented at the annual meeting of the Swiss Society of Tropical Medicine and Parasitology.

Auer Ch., Factors associated with non-completion of anti-TB treatment in Manila, Philippines. 29<sup>th</sup> World Conference of the IUATLD Global Congress on Lung Health.

1999: Auer Ch. TB and Private Doctors in Manila. Monday afternoon seminar at the Liverpool School of Tropical Medicine. Liverpool, September 27, 1999.

2000: Auer Ch. TB and the private sector – Perspectives from the Philippines. Conference of the tb.net (“Power, Poverty and TB”), Kathmandu, Nepal, February 23 to 25, 2000.

2001: Auer Ch. Private doctors and TB patients in Malabon, Metro Manila - Results of a survey among 45 private doctors. Conference of the Eastern Region of the IUATLD, Manila, Philippines, March 2001

Auer Ch. Health seeking and perceived causes of tuberculosis among patients in Manila, Philippines. Conference of the Eastern Region of the IUATLD, Manila, Philippines, March.

Auer Ch. Acceptability of thrice-weekly TB therapy in comparison to daily TB therapy in the public health centers of Taguig, Metro Manila. Conference of the Eastern Region of the IUATLD, Manila, Philippines, March.



## *Curriculum Vitae*

2002: Auer Ch., Montejo L., Lagahid J., Ang C., Van Deun A., Tanner M., Weiss MG. Randomized Controlled Trial of Daily vs Thrice-Weekly anti-TB Therapy in Public Health Centres of Manila, Philippines. Washington DC, USA, June 2002.

Auer Ch., Montejo L., Lagahid J., Ang C., Van Deun A., Tanner M., Weiss MG. Randomised Controlled Trial of Daily vs Thrice-Weekly anti-TB Therapy in Public Health Centres of Manila, Philippines. Presented at the annual meeting of the Swiss Society of Tropical Medicine and Parasitology.

During my studies in Basel, I attended lectures and courses given by the following lecturers:

W. Arber, C. Baroni Urbani, B. Betschart, K.A. Bienz, T. Boller, B. Bruderer, R. Brun, A. Degrémont, P. Duelli, H. Durrer, E. Ebert, P. Erb, A. Erhardt, S. Fallab, T.A. Freyvogel, W. Galluser, W. Gehring, U. Gisi, R. Guggenheim, T. Harpham, H. Hecker, G. Hutton, L. Jenni, C. Kessler, K.M. Leisinger, Ch. Lengeler, R.L. Marr, J. Meyer, J. Nüesch, B. Obrist, W. Pankow, G.-R. Plattner, U. Rahm, H.F. Rowell, W. Rudin, G. Schatz, V. Schmid, P. Schmid-Hempel, M. Schuster, F.J. Schwinn, D.G. Senn, H. Sigel, T. Smith, S.C. Stearns, H-R. Striebel, Ch. Tamm, M. Tanner, P. Vounatsou, M.G. Weiss, M. Wall, N. Weiss, A. Wiemken, H. Zoller, J. Zinsstag, A. Zumstein.