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CME

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# Tuberculosis in Hong Kong—patient characteristics and treatment outcome

# 香港結核病患者的特徵與治療結果

**Objectives.** To identify the general characteristics of patients with tuberculosis, and to evaluate their treatment outcomes.

Design. Retrospective study.

**Setting.** Tuberculosis and Chest Service, Department of Health, Hong Kong. **Subjects and methods.** All patients with tuberculosis registered for treatment from 1 January 1996 to 31 December 1996 were included in the study. Information was extracted from their medical records at treatment commencement and at 12 and 24 months after treatment was instigated. Data gathered included demographic data, past treatment, site of disease, case category, treatment regimen, bacteriological status, and treatment outcome.

**Results.** There were 5757 patients for analysis. Approximately one third of patients were aged 60 years or older, and 69.1% were male. Pulmonary disease alone occurred in 77.7% of patients, while both pulmonary and extrapulmonary diseases occurred in 8.6%. New patients comprised 84.6% of cases, and 16.3% had concomitant illnesses. There was excess risk of disease among patients who were male, elderly, or who had silicosis. Only 0.1% of patients were co-infected with human immunodeficiency virus infection. Among the 5757 cases evaluated, 1324 (23.0%) were new patients with a positive sputum smear, 299 (5.2%) were patients who were retreated with a positive sputum smear, and 4134 (71.8%) were new or retreatment patients with a negative sputum smear. The overall treatment completion rates at 12 and 24 months were 80.4% and 84.8%, respectively. Males and patients aged 60 years or older had lower treatment completion rates. Non-adherence, transfer to other services, and mortality among the elderly were key factors influencing treatment outcomes. Co-morbidity was associated with better case-holding, and this more than compensated for its effect on prolongation of treatment and mortality.

**Conclusions.** There was an excess risk of tuberculosis among male and elderly patients, who also had a less favourable outcome. Active screening of clearly identified risk groups may be appropriate but requires the completion of more in-depth studies and careful cost-effectiveness analyses. Further efforts with respect to case-holding are indicated to address treatment defaulting and transfer rates.

目的:確定結核病患者的一般特徵,並評估他們的治療結果。

**設計:**回顧性研究。

安排:香港衞生署胸肺科。

對象與方法:本研究包括所有在1996年1月1日至12月31日期間,登記接受治療的結核病患者。分別從病人開始接受治療,治療後12個月和24個月的醫療紀錄收 集資料,包括人口統計學數據、曾接受的治療、病發位置、病例類別、治療計劃、 細菌學狀況及治療結果。

**結果**:分析了5757名患者的病歷,患者中約三分之一年齡在60歲或以上;69.1%患者為男性。只患有肺結核的患者佔77.7%,同時患有肺和肺外結核的患者則佔8.6%。84.6%的病例是新患者,16.3%同時患有其他疾病。男性、老年和患有矽肺病的人士有較高患病風險。只有0.1%患者同時感染後天免疫缺乏病毒。在評估的5757 宗病例中,分別有1324名(23.0%)新患者及299名(5.2%)復發患者的痰抹片呈陽性,其餘4134名(71.8%)新患者及復發患者的痰抹片呈陰性。12個月和24個月的總治療完成率分別是80.4%和84.8%;男性和60歲或以上患者的治療完成率較低。患者不依時服藥、轉介以及老年死亡是影響治療結果的關鍵因素。同時患有其他疾病的結核病患者,雖然治療期一般較長及死亡率較高,但定期覆診服藥的比率卻較佳。

**結論**:男性和老人患上結核病的風險較高,其治療結果亦較為不理想。為高風險組別人士進行普查可能是適當的方法,但需 要進行更深入的研究和仔細的成本效益分析。應採取進一步措施,讓病人定期覆診和服藥,以改進治療失訪率和轉介率。

# Introduction

The notification rate for tuberculosis (TB) in Hong Kong declined significantly between 1950 and 1990. In 1995, the notification rate was at a low of 100.9/100000. Since 1996, however, there has been an increase in the notification rate—117.3/100000 in 1998 and 113.7/100000 in 2000—and the rate has since failed to decline.<sup>1</sup>

The exact reasons for the recent stagnant trend in the TB notification rate in Hong Kong are not known. In many countries, poor treatment and acquired HIV infection have been found to be the major reasons for the resurgence of TB.<sup>2</sup> In view of such observations, the World Health Organization (WHO) has recommended that directly observed treatment (DOT), short course (DOTS) is the treatment of choice for TB.<sup>3</sup> Hong Kong, however, was among one of the first places to implement DOT in the 1970s,<sup>4</sup> and this was the probable reason for the dramatic decline in the rate of TB from 1970 to the 1980s. The local prevalence of HIV infection has always been relatively low.5 While there has been an improvement in notification of TB by physicians,<sup>6</sup> it is likely that other factors are also contributing to the current elevated rates. This study was undertaken to examine the reasons for the failure of the TB rate to decline. The aim was to identify the general characteristics of patients with TB seen by the Hong Kong Government Tuberculosis and Chest Service (TB&CS), and to evaluate their treatment outcome.

# Subjects and methods

All patients registered for treatment of TB with the TB&CS (which treats approximately 80% to 90% of all notified TB patients in Hong Kong) from 1 January 1996 to 31 December 1996 were included in the study. The year 1996 was chosen because an increase in the TB notification rate was first noted in that year, and population statistics were also available through a census conducted during that year. In addition, in 1996, a set of programme forms was introduced for systematic data collection of all patients with TB managed by the TB&CS. The programme forms recorded the following information: name, date of treatment commencement, age, sex, previous treatment, site of disease (pulmonary or extrapulmonary), and other medical conditions. The forms also recorded bacteriological status before treatment, at 2 months, 6 months, and at the end of treatment, and treatment outcome at intervals after treatment commencement. Data were obtained for each patient through the completion and submission of programme forms by clinicians at the TB&CS at the start of treatment and at 12 and 24 months after the start of treatment. These data were supplemented by a review of medical records for patients with missing forms, missing information on forms, or inconsistent information between completed forms, and for all patients with extrapulmonary TB. The data were entered into the Epi-Info database (Version 6; Centers for Disease Control and Prevention, Atlanta, US) and checked for accuracy by another person. The data were then exported to the Statistical Package for the Social Sciences (Windows version 6.0; SPSS Inc., Chicago, US) and edited before analysis.

# Analysis

Definitions used in the study are outlined in the Box. They were modified slightly from those provided by the International Union Against Tuberculosis and Lung Diseases.<sup>7</sup>

Statistical analyses were carried out using Statistical Package for the Social Sciences (Windows version 6.0). Continuous variables were compared using the Student's independent samples t test. Proportions were compared using the Chi squared test. Differences were considered significant at P<0.05.

## Results

There were 5971 patients registered with the TB&CS for treatment of TB in 1996. Of these, 103 had an incorrect diagnosis, 106 had an atypical mycobacterial infection, and five received chemoprophylaxis only. The number of valid patients for the following analysis was thus 5757.

## Patient characteristics

Patient characteristics are summarised in Table 1. This shows that TB affected men more frequently than women (69.1% versus 30.9%; P<0.01) in Hong Kong. Approximately one third of patients were aged 60 years or older. The mean age of male patients was significantly older than that of female patients (50.6 years versus 43.5 years; P<0.01). The male to female ratio was higher among those aged 60 years or older than among those younger than 60 years (3.36:1 versus 1.85:1; P<0.01).

The majority of patients had pulmonary disease. Pulmonary disease alone occurred in 77.7% of patients. Extrapulmonary TB without lung involvement occurred in 13.7%, while both extrapulmonary and pulmonary diseases occurred in 8.6% of patients. Extrapulmonary disease tended to occur more commonly among women.

The majority of patients (84.6%) were new patients. There were more men than women treated for relapsed disease (15.1% versus 8.0%; P<0.01), and also more men with a history of previously defaulting treatment (2.8% versus 0.7%; P<0.01).

#### Box. Definitions used in the study

A patient with tuberculosis: patient with acid-fast bacilli visible on microscopic examination of sputum (smear-positive) or on culture if smear was negative; or in the absence of positive bacteriology, those with clinical and radiological features compatible with tuberculosis **Pulmonary patients:** patients with tuberculosis of the lungs, including those sputum smear-positive and those sputum smear-negative (provided a minimum of three sputum examinations had been performed)

Extrapulmonary patients: all other patients, including those with tuberculous pleurisy and miliary tuberculosis

#### Disease categories

New patients: patients who had never received treatment of 1 month or more in duration

Retreatment patients: all patients other than new patients, including:

Relapse patients: patients who, having previously been treated, were declared cured prior to the current episode of active tuberculosis as defined above

Treatment after defaulting: patients treated for active tuberculosis after having interrupted treatment for more than 2 months Failure of previous treatment: patients for whom, after initial treatment for smear-positive sputum, pulmonary tuberculosis remained or became positive at 5 months or later during the course of treatment

Others: all other patients who had previously received treatment

#### Treatment outcome

Treatment completed: patients who had taken the prescribed course of treatment irrespective of the sputum smear status at the completion of treatment (combining cured and treatment completed categories of the International Union Against Tuberculosis and Lung Diseases)

Transferred: patients who had been transferred to continue treatment at another centre, but the results of treatment were unknown Died: patients who died for any reason during the course of their treatment or during 24 months' follow-up

Defaulted: patients who had failed to collect medication for more than 2 consecutive months after the date of the last attendance during the course of treatment. Patients whose medications were stopped by their doctor before the completion of treatment were also regarded as defaulted

#### Table 1. Characteristics of patients with tuberculosis

	Female, n=1778 No. (%)	Male, n=3979 No. (%)	Total, n=5757 No. (%)
Age-group* (years)			
0-19	134 (7.5)	175 (4.4)	309 (5.4)
20-39	812 (45.7)	1130 (28.4)	1942 (33.7)
40-59	376 (21.1)	1143 (28.7)	1519 (26.4)
≥60	456 (25.6)	1531 (38.5)	1987 (34.5)
Mean age (SD) [years]*	43.5 (20.7)	50.6 (19.0	48.4 (19.8)
Type of case*			
Pulmonary only	1214 (68.3)	3260 (81.9)	4474 (77.7)
Extrapulmonary only	410 (23.1)	380 (9.6)	790 (13.7)
Pulmonary and extrapulmonary	154 (8.7)	339 (8.5)	493 (8.6)
Case category*			
New patients	1618 (91.0)	3254 (81.8)	4872 (84.6)
Relapse <5 years	58 (3.3)	133 (3.3)	191 (3.3)
Relapse ≥5 years	83 (4.7)	471 (11.8)	554 (9.6)
Treatment after default	13 (0.7)	112 (2.8)	125 (2.2)
Failure of previous treatment	3 (0.2)	3 (0.1)	6 (0.1)
Others	3 (0.2)	6 (0.2)	9 (0.2)
Co-morbid illness*	212 (11.9)	727 (18.3)	939 (16.3)
Diabetes*	138 (7.8)	417 (10.5)	555 (9.6)
Silicosis*	1 (0.1)	83 (2.1)	84 (1.5)
Liver disease*	12 (0.7)	83 (2.1)	95 (1.7)
Lung cancer*	4 (0.2)	58 (1.5)	62 (1.1)
Other cancers	9 (0.5)	23 (0.6)	32 (0.6)
HIV infection	1 (0.1)	5 (0.1)	6 (0.1)

\* P<0.05 for differences between male and female by Chi squared test or Student's t test

Concomitant illnesses occurred in 16.3% of all patients, and was significantly higher among men than women (18.3% versus 11.9%; P<0.01), and also in those aged 60 years or older compared with those younger than 60 years (27.8% versus 10.3%; P<0.01). Diabetes, silicosis, liver disease, and lung cancer were common concomitant medical illnesses associated with TB.

# Almost 10% of all patients with TB also had diabetes at the time of diagnosis. Of the 555 patients with diabetes, 75.1% were male, and 57.6% were aged 60 years or older. The mean age (standard deviation) for this group of patients was 60.6 years (12.4 years). Only six (0.1%) patients had documented HIV infection.

# **Treatment** outcomes

Among the 5757 patients, 1324 (23.0%) were new patients with a positive sputum smear, 299 (5.2%) were retreatment patients with a positive sputum smear, and 4134 (71.8%) were sputum smear-negative patients, including both new and retreatment patients (Table 2).

At 12 months, 80.4% of patients had completed treatment, 8% had defaulted, 3.6% had been transferred, 3.9% had died, and 4.1% were still receiving treatment. However, for retreatment patients with a positive sputum smear at treatment commencement, only 71.6% completed treatment, 10.0% defaulted treatment, 2.3% were transferred, 6.0% had died, and 10.0% were still receiving treatment. There

	New patient, smear-positive No. (%)	Retreatment patient, smear-positive No. (%)	New or retreatment patient, smear-negative No. (%)	Overall No. (%)
No. of patients	1324	299	4134	5757
At 12 months* Treatment completed Still receiving treatment Transferred	1065 (80.4) 69 (5.2) 43 (3.2) 61 (4.6)	214 (71.6) 30 (10.0) 7 (2.3) 18 (6 0)	3349 (81.0) 139 (3.4) 159 (3.8) 142 (2.5)	4628 (80.4) 238 (4.1) 209 (3.6) 222 (3.0)
Defaulted treatment	86 (6.5)	30 (10.0)	344 (8.3)	460 (8.0)
At 24 months <sup>†</sup> Completed treatment No relapse Relapse Bacteriological Clinical Lost to follow-up	1136 (85.8) 895 (67.6) 16 (1.2) 11 (0.8) 196 (14.8)	243 (81.3) 187 (62.5) 4 (1.3) 3 (1.0) 45 (15.1)	3501 (84.7) 2737 (66.2) 30 (0.7) 12 (0.3) 672 (16.3)	4880 (84.8) 3819 (66.3) 50 (0.9) 26 (0.5) 913 (15.9) 70 (1.2)
Treatment not completed Died Transferred Defaulted, not found Defaulted but retreated Treatment stopped	18 (1.4) 60 (4.5) 40 (3.0) 71 (5.4) 16 (1.2) 1 (0.1)	4 (1.3) 20 (6.7) 6 (2.0) 20 (6.7) 9 (3.0) 1 (0.3)	139 (3.4) 150 (3.6) 300 (7.3) 34 (0.8) 10 (0.2)	72 (1.3) 219 (3.8) 196 (3.4) 391 (6.8) 59 (1.0) 12 (0.2)

 $^{*}_{+}$  P<0.05 for difference in outcome at 12 months between all three groups by Chi squared test

 $^{+}$  P<0.05 for difference in outcome at 24 months between all three groups by Chi squared test

#### Table 3. Outcome of patients at 12 and 24 months according to presence of concomitant medical conditions

	Concomitant medical conditions		Overall
	Absent No. (%)	Present No. (%)	No. (%)
No. of patients	4998	759	5757
At 12 months*			
Treatment completed	3996 (80.0)	632 (83.3)	4628 (80.4)
Still receiving treatment	171 (3.4)	67 (8.8)	238 (4.1)
Transferred	207 (4.1)	2 (0.3)	209 (3.6)
Died	190 (3.8)	32 (4.2)	222 (3.9)
Defaulted treatment	434 (8.7)	26 (3.4)	460 (8.0)
At 24 months <sup>†</sup>			
Completed treatment	4179 (83.6)	701 (92.4)	4880 (84.8)
No relapse	3273 (65.5)	546 (71.9)	3819 (66.3)
Relapse			
Bacteriological	45 (0.9)	5 (0.7)	50 (0.9)
Clinical	23 (0.5)	3 (0.4)	26 (0.5)
Lost to follow-up	796 (15.9)	117 (15.4)	913 (15.9)
Died	42 (0.8)	30 (4.0)	72 (1.3)
Treatment not completed			
Died	189 (3.8)	30 (4.0)	219 (3.8)
Transferred	195 (3.9)	1 (0.1)	196 (3.4)
Defaulted, not found	367 (7.3)	24 (3.2)	391 (6.8)
Defaulted but retreated	58 (1.2)	1 (0.1)	59 (1.0)
Ireatment stopped	10 (0.2)	2 (0.3)	12 (0.2)

 $^{*}_{+}$  P<0.05 for difference in outcome at 12 months between the two groups by Chi squared test

<sup>†</sup> P<0.05 for difference in outcome at 24 months between the two groups by Chi squared test

were also significant differences in outcome between men and women, between young and elderly patients, and between those with and without co-morbidity. A total of 82.9% of female patients completed treatment compared with 79.3% of male patients (P<0.05). A greater proportion (82.7%) of patients younger than 60 years completed treatment compared with 76.0% of those aged 60 years or older (P<0.05). Mortality for those younger than 60 years was only 1.0% in sharp contrast to 9.4% for those aged 60 years or older (P<0.01). More patients with concomitant medical conditions (83.3%) completed treatment compared with those without such conditions (83.3% versus 80.0%; P<0.05) [Table 3]. At 24 months, 84.8% of all patients had completed treatment. However, only 81.3% of retreatment cases with an initial positive sputum smear had completed treatment. More female patients than male patients had completed treatment (86.8% versus 83.8%; P<0.05), as had more patients younger than 60 years (86.3% versus 81.9%; P<0.05). The difference in number of patients with concomitant medical conditions who completed treatment compared with those without such conditions was more marked (92.4% versus 83.6%; P<0.001).

Of the 4880 patients who completed treatment, 76 had a relapse of TB, and this was bacteriologically confirmed



Fig 1. Tuberculosis notification rate by sex and age in 1996

for 50 patients. Only 59 of the 450 patients who defaulted treatment were found and retreated.

# Discussion

According to the 1996 by-census, only 14.3% of the population were aged 60 years or older<sup>8</sup> while, as shown in Table 1, 34.5% of the patients with TB were in this agegroup. There was clearly an excess of elderly patients with TB seen at the TB&CS. The 1996 notification registry figures indicate a generally increasing risk of TB with age (Fig 1).<sup>1</sup> While the overall notification rate was 101.0 patients per 100 000, the notification rate was as high as 361.4 patients for those aged 75 years or older. According to data from the Census and Statistics Department<sup>9</sup> and from the TB notification registry,<sup>1</sup> there have been increasing proportions of elderly citizens within the local population, and an even more marked increase in the proportion of elderly among TB patients during the past few decades (Fig 2). In 1971, only 8.0% of patients with TB were aged 65 years or older, with 1.7% aged 75 years or older. The corresponding percentages had increased to 36.2% and 19.0%, respectively, in 2001. Since the population in Hong Kong is ageing, it is likely that elderly patients will account for an increasing proportion of the total TB caseload. This may be one of the factors accounting for the persistently high rate of TB reported in Hong Kong.

As reported in a previous paper on sex differences in TB,<sup>10</sup> men had a higher rate of TB than women in all agegroups. The male to female ratio was higher among those aged 60 years or older. Male patients aged 60 years or older constituted 26.6% of the total patient pool in this sample, a sizeable risk group.



Fig 2. Percentage of elderly among tuberculosis patients and the general population

Although this study covered only 89% (5757/6501) of all TB notifications, excluding patients managed outside the TB&CS, it may serve to highlight other potential risk factors for TB in Hong Kong residents. Silicosis is a wellknown risk factor for TB and there were 84 patients with TB and silicosis in this study. If the number of surviving patients with confirmed silicosis in Hong Kong was to be approximately 3000,<sup>1</sup> the annual risk of TB among people with silicosis was approximately 2800/100000. This figure is much higher than the overall annual notification rate of 101/100000 in 1996. However, the absolute number of patients with silico-TB was small, and these patients were unlikely to have affected the overall trend in TB rates in Hong Kong.

In this study, only six patients with TB were known to be infected with HIV. Voluntary HIV testing was offered to all patients with TB attending the TB&CS, and the uptake rate was approximately 90%. The low incidence of HIV infection in this study is supported by the results of unlinked anonymous assays periodically carried out on samples from patients attending the TB&CS. These have given the incidence of HIV infection as approximately 0.13% to 0.70% between 1990 and 2000.1 Such low incidence reflects the relatively low incidence of HIV infection in the general population. Indeed, the HIV seropositive rate among blood donors is only 5/100000,<sup>5</sup> and the incidence in the general population is likely to be well below 0.1%. These results suggest that while the risk for TB is high among patients with HIV infection, HIV infection is unlikely to have contributed to the stagnation in TB rates seen in Hong Kong during the past decade.

Table 4 shows the estimated rate of TB among patients with diabetes. Using the number of patients with TB identified with diabetes in this study and the population at risk based on local statistics,<sup>1,8,11</sup> the rate of TB for each agegroup was estimated. In 1996, 10% of all patients with TB treated in the chest clinics had diabetes. The TB rates among individuals with diabetes did not differ greatly from those among the general population, with the exception of men aged between 45 and 54 years. It should be stressed that TB patients with diabetes managed outside the TB&CS have not been included in this study. A higher prevalence of diabetes could well be found among patients managed solely inside hospitals, and thus the rate of TB among patients with diabetes may have been underestimated.

At present, the overwhelming majority of patients with TB in Hong Kong are identified through passive case finding, that is, encouraging patients with symptoms suggestive of TB to come forward for screening. An active screening programme exists mostly for examination of contacts. The finding of high-risk groups raises the question of whether active screening for TB should be extended to these groups. In a series of studies conducted between 1960 and 1973 in different parts of the world, it was shown that, even in places with active case-finding programmes, approximately 60% of sputum smear-positive patients were discovered because of their symptoms.<sup>12,13</sup> Only 20% of new patients were found through indiscriminate mass radiography alone.<sup>12</sup> This is explained by the relative rapidity with which the infection develops, with symptoms developing more rapidly than repeat screening can be accomplished.

In a survey completed by the TB&CS in 1981, the yield of patients with active TB was 10% to 15% among new clinic attendees,<sup>14</sup> well over the likely yield among any of the risk groups found in this study. Screening directed at latent infection instead of active disease may potentially give a higher yield.<sup>15</sup> However, the existing screening and treatment tools for latent TB infection are far from ideal. The tuberculin test is confounded by previous bacille Calmette-Guérin vaccination and atypical mycobacterial infection, and only about 10% of immunocompetent patients with latent TB infection ever develop the disease.<sup>16</sup> Treatment of latent TB often involves a long duration of treatment with drugs that have potential for adverse events.<sup>17</sup> These factors seriously limit the widespread application of such an approach. Therefore, passive case finding must remain one of the cornerstones of the local TB control programme, as in most other areas of the world.

Among household contacts, a regularly screened highrisk group, the yield of active TB has been in the order of 1% to 2%,<sup>1,18</sup> doubling to more than 3% at the extremes of

Age-groups (years)	No. in Hong Kong population with diabetes in 1996 <sup>11</sup>	No. with tuberculosis and diabetes in this study	Estimated No. of patients with tuberculosis among diabetic individuals in Hong Kong* (per 100 000)	No. of patients with tuberculosis in the general population of Hong Kong (per 100 000)
Male				
25-34	11164	8	72	97
35-44	34945	35	100	99
45-54	37777	79	209	150
55-64	50647	139	274	266
65-74	42141	108	256	379
Female				
25-34	8804	3	34	67
35-44	19120	15	78	56
45-54	35 403	20	57	49
55-64	51 431	28	54	58
65-74	61 061	51	84	94

\* Tuberculosis patients with diabetes treated outside the TB&CS have not been included

age for both sexes.<sup>18</sup> Among elderly people in nursing homes, a high rate of TB, in the range of 1000 to 2000/100 000, has been estimated by a previous study.<sup>19</sup> Further studies and cost-effectiveness analyses are needed to assess the role of screening programmes among such well-defined risk groups.

Chaulk and Kazandjian<sup>20</sup> reported the findings of the Public Health Tuberculosis Guidelines Panel in 1998 on treatment outcome in the US. The panel chose 27 studies for review of treatment completion for pulmonary TB and, among these, 18 had implemented DOT. They were classified into three categories. In the first category, the 12 studies based on comprehensive, patient-centred DOT strategies, such as fully supervised DOT with multiple incentives and enablers (enhanced DOT), reported the highest treatment completion rates.<sup>21-32</sup> The completion rates ranged from 86.0% to 96.5% for a variety of patient populations, including alcoholics, patients with substance abuse problems, incarcerated patients, homeless persons, and patients infected with HIV. The rate of TB relapse reported in these studies ranged from 0% to 11.5%. For the four studies of DOT in the second category, without extensive enablers and incentives, treatment completion rates ranged from 85.0% to 87.6%, and reported rates of relapse ranged from 0.8% to 4.9%.<sup>33-36</sup> For the two studies in the third category with modified DOT, supervision was used for only part of the treatment period (typically during the hospitalisation phase of therapy), and thereafter, patients were self-supervised.<sup>37,38</sup> This strategy appeared to be less effective, with treatment completion rates ranging from 78.6% to 82.6%. The first two categories included two studies of DOT from Hong Kong,<sup>31,36</sup> evaluating the treatment programme in the 1970s and 1980s.

In 1996, among patients attending the TB&CS, 80.6% completed treatment at 12 months, but 84.8% completed treatment by 24 months. Thus, the treatment completion rate in Hong Kong at 12 months, although quite reasonable, still fell somewhat short of the goal of the 85% treatment success rate at 12 months for national tuberculosis programmes recommended by the WHO for all active cases.<sup>3</sup> As shown in Table 2, the treatment default rate at 12 months was 8.0%, accounting for 40.7% (460/1129) of all unfavourable outcomes, while the transfer rate was 3.6%, accounting for 18.5% (209/1129). As patients who default treatment may remain a source of infection and also acquire drug resistance, this group may have contributed in part to the persistently high rate of TB in Hong Kong. The current DOT programme employed by the Hong Kong TB&CS uses a combination of incentives and enablers, including education for patients and their families, intermittent client-focused regimens, incentives such as money for extra nutrition, referrals to other social services, as well as the use of outreach teams and tracing of patients who default treatment. Surveillance of Mycobacterium tuberculosis drug resistance in Hong Kong during the period from 1986 to 1999 showed a significant decline in drug resistance.<sup>39</sup> The overall resistance to one or more drugs was reduced from approximately 17% to 12% for new patients and from 36% to 25% for retreatment patients, while the corresponding figures for multidrug resistance were reduced from 2.7% to 1.0% and from 15.9% to 8.3%, respectively. Notwithstanding the data presented, more in-depth studies are required to examine factors that may affect case-holding in Hong Kong among a relatively mobile population with freedom of choice in seeking medical treatment.

In this study, the mortality rate for all patients with TB at 12 months was 3.9%, accounting for approximately 20% (222/1129) of the patients with unfavourable outcome. There was also a sharp contrast in mortality rates between elderly and younger patients. As more than one third of patients were aged 60 years or older, the higher mortality rate may have contributed to the overall low treatment completion rate.

The high prevalence of co-morbidity in this study is consistent with the relatively high proportion of elderly patients. As shown in Table 3, 8.8% of patients with comorbidity were receiving treatment at 12 months compared with 3.4% of those without co-morbidity. This may reflect the more frequent need to modify the treatment regimen, either to decrease the risk of side-effects or as a result of actual side-effects. Although 4.1% of patients were still receiving treatment at 12 months, accounting for another 20% (238/1129) of patients with unfavourable outcomes at 12 months, most of these patients were eventually successfully treated as reflected by the better treatment completion rate at 24 months. It is evident from Table 3 that the lower treatment defaulting and transfer rates associated with comorbidity more than compensated for the effect of prolonged treatment and higher mortality. Indeed, the treatment completion rates seen for those with concomitant medical conditions were higher than those without co-morbidity at both 12 months and 24 months.

## Conclusion

This study found an excess of TB disease risk and a less favourable treatment outcome for elderly, male patients in Hong Kong. While consideration should be given to extending active screening programmes to such clearly identified risk groups, further studies and careful cost-effectiveness analyses are called for before implementation of such programmes is indicated on a service-wide scale. The treatment success rate seen at 12 months was reasonably good, although short of the WHO goal of 85%. More in-depth studies and efforts with respect to case-holding should also be considered to address treatment default and transfer rates.

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# References

- Hong Kong Government Tuberculosis and Chest Service. Annual Report 1971-2001.
- Dolin PJ, Raviglione MC, Kochi A. Global tuberculosis incidence and mortality during 1990-2000. Bull World Health Organ 1994;72: 213-20.
- Tuberculosis control and research strategies for the 1990s: memorandum from a WHO meeting. Bull World Health Organ 1992;70:17-21.
- Hong Kong Government Tuberculosis and Chest Service. Annual Report 1970.
- Hong Kong Advisory Council on AIDS. HIV/AIDS situation in Hong Kong. Report August 2000 to July 2001,4-5.
- Leung CC, Tam CM. Guidance notes for notification of tuberculosis. Public Health Epidemiol Bull 1999;8:36-9.
- International Union Against Tuberculosis and Lung Disease. Management of tuberculosis. A guide for low income countries. 5th ed. Paris: International Union Against Tuberculosis and Lung Disease; 2000:36-9.
- Census and Statistics Department, Hong Kong. 1996 population bycensus.
- Census and Statistics Department, Hong Kong. Annual Digest of Statistics; 2002.
- Chan-Yeung M, Noertjojo K, Chan SL, Tam CM. Sex differences in tuberculosis in Hong Kong. Int J Tuberc Lung Dis 2002;6:11-8.
- Janus ED. The Hong Kong cardiovascular risk factors 1995-1996. Hong Kong: Hospital Authority; 1997:48.
- Meijer J, Barnett GD, Kubik A, Styblo, K. Identification of sources of infection [in French]. Bull Int Union Tuberc 1971;45:5-54.
- Toman K. Mass radiography in tuberculosis control. WHO Chron 1976; 30:51-7.
- 14. Survey of patients presenting to the government chest service in Hong Kong and the effects of active tuberculosis case-finding by publicity campaigns. Hong Kong Chest Service/British Medical Research Council. Tubercle 1984;65:173-84.
- Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 2000; 49:1-51.
- Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol 1974;99:131-8.
- Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations—United States, 2001. MMWR Morb Mortal Wkly Rep 2001;50:733-5.
- Noertjojo K, Tam CM, Chan SL, Tan J, Chan-Yeung M. Contact examination for tuberculosis in Hong Kong is useful. Int J Tuberc Lung Dis 2002;6:19-24.
- Woo J, Chan HS, Hazlett CB, et al. Tuberculosis among elderly Chinese in residential homes: tuberculin reactivity and estimated prevalence. Gerontology 1996;42:155-62.
- Chaulk CP, Kazandjian VA. Directly observed therapy for treatment completion of pulmonary tuberculosis: Consensus Statement of the Public Health. JAMA 1998;279:943-8.
- Sukrakanchana-Trikham P, Puechal X, Rigal J, Rieder H. 10-year assessment of treatment outcome among Cambodian refugees with sputum smear-positive tuberculosis in Khao-I-Dang, Thailand. Tuber

Lung Dis 1992;73:384-7.

- 22. Westaway MS, Conradie PW, Remmers L. Supervised out-patient treatment of tuberculosis: evaluation of a South African rural programme. Tubercle 1991;72:140-4.
- 23. Wilkinson D. High compliance tuberculosis treatment programme in a rural community. Lancet 1994;343:647-8.
- 24. Manalo F, Tan F, Sbarbaro JA, Iseman MD. Community-based shortcourse treatment of pulmonary tuberculosis in a developing nation. Initial report of an eight-month, largely intermittent regimen in a population with a high prevalence of drug resistance. Am Rev Respir Dis 1990;142:1301-5.
- Miles SH, Maat RB. A successful supervised outpatient short-course tuberculosis treatment program in an open refugee camp on the Thai-Cambodia border. Am Rev Respir Dis 1984;130:827-30.
- Schluger N, Ciotoli C, Cohen D, Johnson H, Rom WN. Comprehensive tuberculosis control for patients at high risk for noncompliance. Am J Respir Crit Care Med 1995;151:1486-90.
- Kan GO, Zhang LX, Wu JC, Ma ZI, Liu CW, Sun FZ. Supervised intermittent chemotherapy for pulmonary tuberculosis in a rural area of China. Tubercle 1985;66:1-7.
- el-Sadr W, Medard F, Berthaud V, Barthaud V. Directly observed therapy for tuberculosis: the Harlem Hospital experience, 1993. Am J Public Health 1996;86:1146-9.
- Chaulk CP, Moore-Rice K, Rizzo R, Chaisson RE. Eleven years of community-based directly observed therapy for tuberculosis. JAMA 1995;274:945-51.
- Werhane MJ, Snukst-Torbeck G, Schraufnagel DE. The tuberculosis clinic. Chest 1989;96:815-8.
- Chan SL, Wong PC, Tam CM. 4-, 5- and 6-month regimens containing isoniazid, rifampicin, pyrazinamide and streptomycin for treatment of pulmonary tuberculosis under program conditions in Hong Kong. Tuber Lung Dis 1994;75:245-50.
- Pozsik CJ. Compliance with tuberculosis therapy. Med Clin North Am 1993;77:1289-301.
- Cowie RL, Brink BA. Short-course chemotherapy for pulmonary tuberculosis with a rifampicin-isoniazid-pyrazinamide combination tablet. S Afr Med J 1990;77:390-1.
- Cohn DL, Catlin BJ, Peterson KL, Judson FN, Sbarbaro JA. A 62dose, 6-month therapy for pulmonary and extrapulmonary tuberculosis. A twice-weekly, directly observed, and cost-effective regimen. Ann Intern Med 1990;112:407-15.
- Caminero JA, Pavon JM, Rodriguez de Castro F, et al. Evaluation of a directly observed six months fully intermittent treatment regimen for tuberculosis in patients suspected of poor compliance. Thorax 1996; 51:1130-3.
- 36. Study of a fully supervised programme of chemotherapy for pulmonary tuberculosis given once weekly in the continuation phase in the rural areas of Hong Kong. Tubercle 1984;65:5-15.
- Menzies R, Rocher I, Vissandjee B. Factors associated with compliance in treatment of tuberculosis. Tuber Lung Dis 1993;74:32-7.
- Wolde K, Lema E, Roscigno G, Abdi A. Fixed dose combination short course chemotherapy in the treatment of pulmonary tuberculosis. Ethiop Med J 1992;30:63-8.
- Kam KM, Yip CW. Surveillance of Mycobacterium tuberculosis drug resistance in Hong Kong, 1986-1999, after the implementation of directly observed treatment. Int J Tuberc Lung Dis 2001;5:815-23.