

Mixed methods study on elimination of tuberculosis in Hong Kong

Greta Tam *, H Yang, Tammy Meyers

ABSTRACT

Introduction: Tuberculosis (TB) commonly affects developing countries. Several developed regions in Asian still have a stagnant intermediate TB burden. Information to adequately inform TB strategies is lacking. We conducted a mixed methods study to fill this information gap in Hong Kong.

Methods: Data from the Hong Kong government were used to analyse trends of TB notification rates compared with World Health Organization (WHO) targets. A review of policy documents and literature was conducted to evaluate TB control and elimination in Hong Kong.

Results: Extrapolated trends showed that Hong Kong will be unable to meet the WHO target of a 90% drop in incidence rate by 2030. The policy review showed that the Hong Kong government has not set a clear strategy and timeline for specific goals in TB control and elimination. The literature review found that older adults are largely responsible for the

stagnant TB prevalence because of reactivation of latent TB infection, while mortality of hospitalised patients with TB is still high because of delayed diagnosis and treatment.

Conclusion: Tuberculosis incidence is currently under control in Hong Kong, but further actions are needed if the elimination targets are to be achieved. Improved diagnostic tools are required, and policies targeting latent TB infection in older adults should be implemented to achieve the WHO target by 2030.

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Introduction

Tuberculosis (TB) is a major global health burden that ranks with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) as a leading cause of death worldwide. The World Health Organization (WHO) estimated that 9.6 million people were sickened by TB and 1.5 million died as a result in 2014, with 58% of global TB cases occurring in the South-East Asia and Western Pacific regions.^{1,2} As a part of the global response to TB, the sixth Millennium Development Goal (MDG) set out to halve TB prevalence and mortality rates by 2015 compared with the 1990 baseline.³ Following significant declines in TB mortality and prevalence rates, in 2015, the third Sustainable Development Goals contained targets to end the epidemics of AIDS, TB, malaria, and neglected tropical disease by 2030.⁴ The TB target for 2030 is to reduce the number of TB deaths by 90% compared with 2015 numbers. The WHO established the End TB Strategy in 2014, aiming to reduce the TB burden by 2030 and eliminate TB entirely by 2050.^{5,6} Advanced economies such as the US and Australia⁷ typically have low TB incidence, and TB is commonly known as a disease of poverty that more heavily affects developing countries.⁸ The Global Fund is conducting country case studies on

HIV/AIDS, TB, and malaria in several developing countries, including Haiti, Pakistan, and the Philippines.⁹ No country case studies have yet been conducted in developed Asian countries/regions such as Hong Kong, Japan, Singapore, Taiwan, or South Korea, which have good health infrastructure and stable economic growth, but where intermediate levels of TB incidence persist.^{10,11}

Reaching the WHO targets in Asia will require strategies specific to TB epidemiology in this setting. However, information to adequately inform strategies is lacking. The last report of comparative data between Asian countries was published 10 years ago by the WHO.⁵ The reasons for the gap between the TB burden in Asian countries and that in their equally developed counterparts in other regions need to be understood. The TB burden in low-incidence countries is attributable mostly to immigrants.¹² In contrast, the stagnant intermediate incidence in developed Asian countries is ascribed mainly to latent TB infection in ageing populations.¹³

Compared with that of Singapore, Japan, or Western countries with similar gross domestic products, the notification rate of TB in Hong Kong is relatively high (60 per 100 000 population in 2016).^{11,14} Presently, TB is the second most common notifiable disease in Hong Kong, following chickenpox.¹⁵ The

TB notification rate in Hong Kong has declined slowly since 1995, although the notification rate only dropped below 100 per 100 000 population in 2002, and it took until 2011 for the notification rate to decline below 70 per 100 000 population.¹⁶

The present case study of the TB situation in Hong Kong highlights successful policies intended to achieve WHO goals and identifies areas for further research or intervention in gaps that could prevent attainment of these targets. This could facilitate useful comparisons with the situation in other developed Asian countries.

Methods

Secondary data analysis of publicly available data

A document review including both policy and literature was conducted. Statistics on TB notification in Hong Kong were obtained from the official website of the Tuberculosis and Chest Service, Department of Health of Hong Kong SAR Government.¹⁴ The TB notification rates were analysed in terms of immigrant status, age-group, and gender and presented in line graphs. The notification trend was extrapolated to 2030 by using Microsoft Excel's FORECAST function on the trend in the past 10 years (2005-2015).

Policy review

Existing documents from the Tuberculosis and Chest Service, Department of Health of Hong Kong SAR Government, such as the TB manual (2006),¹⁷ TB annual reports (2007-2013),¹⁸⁻²⁴ information and guidelines (2006-2015),²⁵⁻³¹ and other recommendations were obtained. Reports and strategies regarding TB control and elimination from the WHO were also reviewed to analyse how the strategy had been operationalised, how this may affect implementation of local programmes, and to identify the policy gap between the Hong Kong government's and WHO's strategies.

Literature review

Two electronic databases, PubMed and Google Scholar, were searched to identify articles related to TB control and elimination in Hong Kong. The key words 'tuberculosis' or 'TB' in combination with the terms 'Hong Kong', 'epidemiology', 'risk factors', 'prevention', 'treatment', 'Latent TB', 'MDR-TB', or 'XDR-TB' were used to search for relevant articles.

Selected publications included studies (a) carried out in Hong Kong; (b) published in the past 10 years; (c) related to TB prevalence, at-risk populations, and TB control measures/interventions in Hong Kong; (d) with full-text articles in English; (e) with no overlapping data; and (f) qualitative studies with sufficient sample size, significant results

消除香港結核病的混合方法研究

譚俊萱、楊華慧、邁耶斯

引言：結核病通常影響發展中國家，但若干亞洲發達國家及地區的結核病發率仍屬中等水平。本文採用混合方法研究以填補目前制定結核病控制策略訊息的不足。

方法：透過香港政府數據分析結核病呈報率的趨勢並與世界衛生組織的所訂目標比較，以及搜索政策回顧和文獻綜述評估香港結核病的控制和消除策略狀況。

結果：推算趨勢表明香港在2030年前無法達到世衛將發病率降低90%的目標。政策回顧也顯示香港政府沒有明確的結核病控制和消除策略及時間表。文獻綜述發現老年人的潛伏性結核病是結核病發率仍處一定水平的主因，並因診斷和治療延誤使住院結核病患者的死亡率高企。

結論：目前香港結核病的發病率已受控，惟要達到消除目標還須採取進一步行動。要在2030年前實現世衛所訂目標，當局須改善診斷工具並實施針對老年群體潛伏結核感染的政策。

($P < 0.05$), and specified outcomes/outputs.

Results

Tuberculosis notification in Hong Kong

Since 1947, a downward trend in total TB notification in Hong Kong has been observed. From 1970 to 1977, TB notification rapidly declined but remained stagnant thereafter (Fig 1). The oldest age-group (≥ 75 years) had much higher TB notification rates (Fig 2). Between 1995 and 2015, reductions in notification rates occurred in younger age-groups but increased sharply at the turn of the millennium

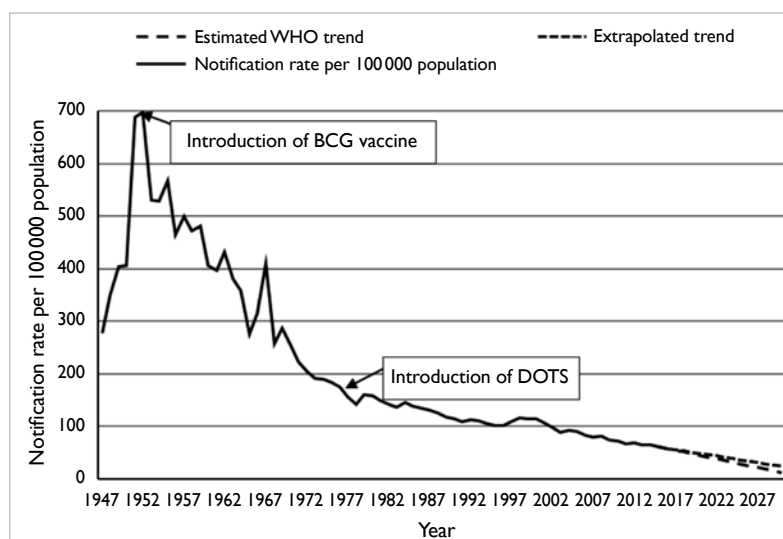


FIG 1. Notification rates of TB in Hong Kong (1947-2015) with extrapolated trend to 2030 and estimated trend according to the WHO target

Abbreviations: BCG = Bacille Calmette-Guérin; DOTS = directly observed treatment short course; TB = tuberculosis; WHO = World Health Organization

in the oldest group, whose notification rate had only gradually decreased by 2015. Notification rates in both genders showed downward trends, although men had a higher notification rate than women (data not shown).

Tuberculosis notification rates dropped rapidly after the Bacille Calmette–Guérin (BCG) vaccine was introduced in 1952, with a further decline after the introduction of directly observed treatment short course (DOTS) [Fig 1]. The incidence in 2015 had almost halved compared with that in 1990. Extrapolated trends showed that at the current rate, Hong Kong would be unable to meet the WHO target of a 90% drop in incidence rate by 2030. By then, Hong Kong’s TB notification rate is predicted to drop by only 60.2%, compared with that in 2015. The analysis shows that Hong Kong could become a low-incidence country (10 cases per 100 000 population) by 2036.

Comparison of reviewed policy between the World Health Organization and Hong Kong

A comparison between the WHO’s and Hong Kong’s TB policies is shown in Table 1.^{4,6,17,30,32,33} In 2015, the Sustainable Development Goal 3 included a target to end the TB epidemic by 2030,⁴ and the End TB Strategy aims to achieve a 90% drop in TB incidence rate and up to 95% reduction in number of TB-related deaths by 2035 compared with those

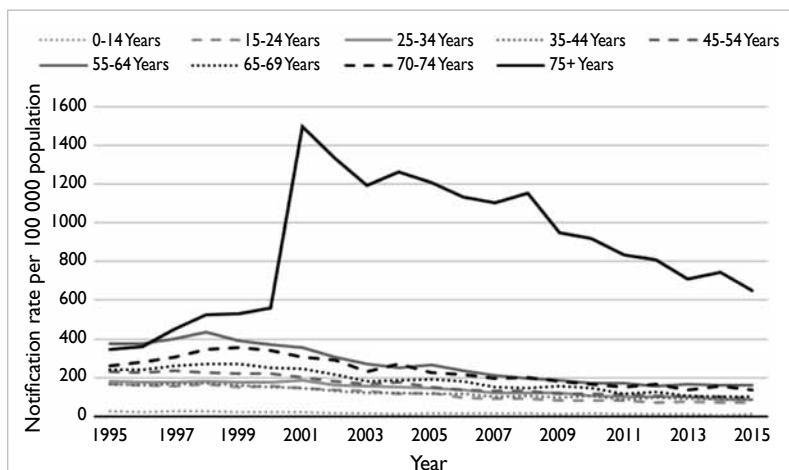


FIG 2. Notification rates of tuberculosis by age-group in Hong Kong (1995-2015)

TABLE I. Summary of reviewed policy^{4,6,17,30,32,33}

WHO report and strategy	Hong Kong Government policy
<p>Sustainable Development Goals⁴: End the epidemics of AIDS, TB, malaria, and neglected tropical disease by 2030</p> <p>End TB Strategy⁶: Up to 90% reduction in the number of TB deaths compared with 2015 and no TB-affected families facing catastrophic costs due to TB by the end of 2030</p> <p>Three main pillars and components: 1. Integrated, patient-centred care and prevention 2. Bold policies and supportive systems 3. Intensive research and innovation</p> <p>Active case identification⁶: 1. Household contacts and other close contacts of smear-positive individuals 2. People living with HIV 3. Current and former workers in workplaces with silica exposure</p> <p>Conditional recommendation for screening for LTBI: prisoners, health care workers, immigrants from countries with high TB burden, homeless people, and illicit drug users.³²</p> <p>In countries with high TB burden, a single dose of BCG vaccine should be given to all infants as soon as possible after birth. Because severe adverse effects of BCG vaccination are extremely rare even in asymptomatic, HIV-positive infants, all healthy neonates should receive BCG vaccination, even in areas in which HIV is endemic.³³</p> <p>The following treatment options are recommended for LTBI: 6-month isoniazid, 9-month isoniazid, 3-month regimen of weekly rifapentine plus isoniazid, 3-4 month isoniazid plus rifampicin, or 3-4 month rifampicin alone. For patients with HIV co-infection, 36 months of INH is recommended for those with no signs and symptoms of TB or TB-HIV co-infection.³²</p>	<p>Tuberculosis manual (2006)¹⁷: The objectives of TB control are to reduce morbidity and mortality, stop new infections, and prevent progression from infection to disease</p> <p>Main components: 1. Case identification 2. Effective chemotherapy 3. Treatment of LTBI 4. BCG vaccination 5. Health education</p> <p>Active case identification among four high-risk groups³⁰: 1. Household contacts (<35) of smear-positive individuals 2. People with silicosis 3. HIV-positive people 4. People who receive immunosuppression/TNF blockers</p> <p>Other patients at risk of developing active TB disease may also be offered similar screening after assessment on a case-by-case basis. The Hong Kong government lists one example: close contacts of smear-positive individuals aged ≥35 years.³⁰</p> <p>BCG vaccination for newborn babies and children who reside in Hong Kong aged <15 years who have not received any prior BCG vaccination. Repeated doses of BCG vaccination are generally not recommended.¹⁷</p> <p>Treatment of LTBI: 6-12 month isoniazid. This has not been widely practised in Hong Kong.¹⁷</p>

Abbreviations: AIDS = acquired immune deficiency syndrome; BCG = Bacille Calmette–Guérin; HIV = human immunodeficiency virus; INH = isonicotinylhydrazide; LTBI = latent tuberculosis infection; TB = tuberculosis; TNF = tumour necrosis factor; WHO = World Health Organization

in 2015.⁶ Yet, the Hong Kong government has not set a clear strategy and timeline for specific goals in TB control and elimination.

The WHO guidelines for management of latent TB infection (LTBI) strongly recommended that high-income and upper-middle income countries with TB incidence less than 100 per 100 000 population per year perform systematic testing and treatment of LTBI in specific groups, and Hong Kong was listed among these.³² Hong Kong follows the WHO recommendations for LTBI screening in high-risk groups. However, conditional recommendations for a number of target populations to be included in active case finding are not included in the local Hong Kong policy documents. According to the Hong Kong TB Manual, active case finding in high-risk groups was not very effective, as only 1% of active TB was found in household contacts in 2004.¹⁷

Summary of reviewed literature

We reviewed the TB literature about studies conducted in Hong Kong published in the past 10 years (Table 2).³⁴⁻⁴⁶ Thirteen published studies were included: two on older adults in old age homes, one on migrant populations, two on drug-resistant TB, two on HIV-related TB, two on primary school children, three on TB treatment outcomes, and one on TB prevalence in Hong Kong.

Among the included studies, three indicated that Hong Kong's TB prevalence rate is stagnating because of high TB prevalence in older adults and a high risk of TB reactivation^{34,35} caused by high prevalence of latent infection among older adults in old age homes.³⁶ Some immigrants come from countries with higher TB incidence and drug resistance rates, particularly mainland China. These migrants may also be at increased risk of

TABLE 2. Articles on TB in Hong Kong included in the literature review³⁴⁻⁴⁶

Study	Design	Size	Results
Chan-Yeung et al (2006) ³⁴	Cross-sectional study	3682	High prevalence of LTBI is the main cause of the high rate of active infection in old age homes. Early diagnosis and treatment are recommended.
Vynnycky et al (2008) ³⁵ *	Age-structured model	-	High prevalence of TB in older individuals and high risk of TB reactivation contribute to stagnation of TB rates in Hong Kong.
Chan-Yeung et al (2006) ³⁶	Cross-sectional study	2243	High TB prevalence in old age homes with high risks of treatment side-effects in this population.
Leung et al (2015) ³⁷	Longitudinal cohort study	5402	Immigrants have higher rates of TB incidence and drug resistance from their place of origin.
Wu et al (2008) ³⁸ *	Age-period-cohort model	-	As the Chinese migrant population decreases, reactivation rates will decrease. The effects of improved living conditions on prevalence may be subject to a time lag of several decades. DOTS adherence is an important determinant of TB incidence.
Law et al (2008) ³⁹	Retrospective cohort study	312	Movement of population and younger age were independent predictors of MDR-TB in Hong Kong.
Leung et al (2013) ⁴⁰	Retrospective cohort study	736	XDR-TB increases the risk of household transmission of TB and is mainly transmitted among lower-risk social contacts outside the household setting in Hong Kong.
Chan et al (2010) ⁴¹	Retrospective cohort study	349	TB the most common AIDS-defining illness in Hong Kong. LTBI should be treated in patients with HIV. There is a higher rate of MDR-TB in patients with HIV compared with the general population.
Leung et al (2016) ⁴²	Cohort study	478	The current utility of LTBI tests in patients with HIV-related TB in annual screenings was doubted because of discordant rates of positive results, high reversion rates, and low TB incidence.
Leung et al (2012) ⁴³	Prospective cohort study	19 383	Strong tuberculin reaction in primary school children predicted TB in adolescents.
Leung et al (2006) ⁴⁴	Cohort and case-control study	94 928	There was a marked contrast in disease risk between those with tuberculin reaction of <15 mm compared with >15 mm. In light of these findings, the existing tuberculin test screening criteria may need revision.
Lui et al (2014) ⁴⁵	Retrospective cohort study	467	Mortality of hospitalised patients with TB is high and new methods are needed to prevent delayed diagnosis and treatment.
Wong et al (2005) ⁴⁶	Retrospective cohort study	998	Patients who underwent the full course of DOTS had better outcomes. Of the study's participants, 85.6% underwent the entirety of the first 2 months.

Abbreviations: AIDS = acquired immune deficiency syndrome; DOTS = directly observed treatment short course; HIV = human immunodeficiency virus; LTBI = latent tuberculosis infection; MDR-TB = multidrug-resistant tuberculosis; TB = tuberculosis; XDR-TB = extensively drug-resistant tuberculosis

* Mathematical modelling study so no numerical sample size is included

TB reactivation.³⁷ However, TB in the migrant population is likely to decrease as migration from China is reduced and living conditions for those entering the city improve.³⁸

Multidrug-resistant TB (MDR-TB) is a threat that is more likely in patients diagnosed with TB at younger ages.³⁹ Extensively drug-resistant TB (XDR-TB) significantly increases household TB transmission, demonstrating a need for prolonged household surveillance.⁴⁰ Treatment of LTBI is recommended to control TB, especially among people with HIV. Two studies reported outcomes of treating LTBI in patients with HIV in Hong Kong, one confirming the usefulness of LTBI treatment,⁴¹ while the other doubted the utility of LTBI tests in annual screening of patients with HIV because of discordant results between different tests.⁴² Identification of children with LTBI is also useful: in a study that described the use of tuberculin tests to screen primary school children, strong tuberculin reactions (>15 mm) predicted TB in adolescence.^{43,44} Diagnosis of TB is still problematic, and new methods are needed to prevent delayed diagnosis and treatment,³⁵ as mortality of hospitalised TB patients is still high.⁴⁵ However, one Hong Kong study demonstrated that although early diagnosis and treatment are recommended, TB therapy carried a high risk of side-effects in the study population.³⁶ Directly observed treatment short course has significantly decreased TB incidence,^{38,46} although not all patients in Hong Kong completed the first 2 months of treatment, with failure to complete treatment predicting poorer outcomes than undergoing the full course.⁴⁶

Discussion

In Hong Kong's older adult population, TB accounts for the majority of the city's high burden from the disease. In Hong Kong, those aged >75 years showed an especially high TB incidence rate. Migrants and people with HIV also have higher TB prevalence but contribute significantly less to the burden than do older adults. Children with a strong purified protein derivative reaction indicating infection were more prone to develop TB in adolescence. Also, MDR-TB and XDR-TB pose a relatively rare but important threat in Hong Kong. Late or underdiagnosis results in high TB-related mortality in those who present symptoms late and require hospitalisation.

High rates of LTBI in Hong Kong have been documented in other Asian countries with low and intermediate TB burden.⁴⁷ The BCG vaccine was introduced to Hong Kong in April 1952¹⁷; therefore, by 1995, 2005 and 2015, those aged >43, >53 and >63 years, respectively, would not have been vaccinated in infancy. The higher prevalence of LTBI and active TB in old age homes compared with that in older adults living in the community is a trend shared with

other countries, including low-burden countries such as the US.⁴⁸⁻⁵⁰ Despite the higher prevalence of LTBI in institutionalised older adults in Hong Kong (68.6%)³⁶ compared with their American counterparts (5.5%),⁵¹⁻⁵⁶ Hong Kong has not followed the US policy of LTBI testing in this population.⁵⁷ Further research is needed to explore the feasibility and cost-effectiveness of screening and providing prophylaxis to older adults and other populations.

In contrast to countries with low TB burden, where infections in migrants primarily contribute to the burden,⁵⁸ the infection rate in Hong Kong's migrant population is declining.¹⁶ However, MDR-TB rates are higher in migrants and younger age-groups in Hong Kong and countries with low TB burden.^{59,60} A systematic review also concurred with a Hong Kong study's findings that patients with HIV had a higher risk of MDR-TB.^{41,61} Meanwhile, the findings on transmission of XDR-TB in Hong Kong differ from those in Peru, where household contacts reported a very high prevalence of XDR-TB.⁶² It has been postulated that in Hong Kong, XDR-TB is mainly transmitted outside the household setting because of the high population density.⁴⁰ The Peru study's different findings may support this idea, as the population density of Hong Kong is more than double that of Lima.^{63,64}

The WHO has called for improved tests to diagnose LTBI, as the current ones lack accuracy.⁶⁵ This was echoed by findings in the study of patients with HIV by Leung et al.⁴² The finding that a strong tuberculin reaction in 6-to-10-year-old schoolchildren in Hong Kong predicted TB in adolescence was reinforced by a similar study in Singapore, which is also a developed city with an intermediate TB burden.^{43,66,67} However, Hong Kong schoolchildren are not routinely screened for LTBI.³⁰ It may be advisable to extend LTBI testing to cover schoolchildren.

The high mortality of hospitalised patients with TB in Hong Kong is also seen in many other countries,^{45,68} emphasising the need for early detection and treatment. The DOTS strategy is an important cornerstone of TB treatment; however, there is room for improvement in compliance with DOTS in Hong Kong.⁴⁶ Other developed Asian countries have similar DOTS treatment success rates to Hong Kong.⁶⁹ Without improvement in medication adherence, treatment success rates are unlikely to rise.

Policy recommendations

Hong Kong reached the MDG target of reducing TB incidence, with a declining notification rate. However, according to the extrapolated trend, if improvements are not instituted, there will likely be only a 60% reduction in TB notification by 2030 compared with the 2015 baseline. To achieve the

goal of 80% reduction in TB incidence proposed by the End TB Strategy,⁷⁰ an improved supportive protocol targeting older adults with a clear timeline is needed. In addition, the Hong Kong government should consider screening high-risk groups included in the WHO's conditional recommendations. More research needs to be done to explore whether screening these groups would be beneficial.

Limitations

This study has several limitations. First, some key literature and important policies or strategies may have been missed, as no systematic review was conducted. This may have imposed error on the screening and article selection. Second, some patients that did not seek health care may have been missed by the system. Despite these limitations, this research has provided helpful suggestions and valuable insights for future research and implementation of TB-related policy.

Conclusion

The TB incidence rate is currently under control in Hong Kong, but further actions are warranted if the elimination targets are to be achieved. More accurate diagnostic tools are required, and policies targeting LTBI in older adults and children should be implemented to achieve the WHO goal by 2030.

Author contributions

Concept or design: G Tam.

Acquisition of data: H Yang.

Analysis or interpretation of data: H Yang.

Drafting of the article: All authors.

Critical revision for important intellectual content: G Tam, T Meyers.

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Declaration

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