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 Asia 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.

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 Australia typically have low TB incidence, and TB is commonly known as a disease of poverty that more heavily affects developing countries.7 The Global Fund is conducting country case studies on HIV/AIDS, TB, and malaria in several developing countries, including Haiti, Pakistan, and the Philippines.7 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.8,9

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 (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 (275 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.
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. In 2015, the Sustainable Development Goal 3 included a target to end the TB epidemic by 2030, 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

---

**TABLE 1. Summary of reviewed policy**

<table>
<thead>
<tr>
<th>WHO report and strategy</th>
<th>Hong Kong Government policy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sustainable Development Goals</strong>:</td>
<td>Tuberculosis manual (2006):</td>
</tr>
<tr>
<td>End the epidemics of AIDS, TB, malaria, and neglected tropical disease by 2030</td>
<td>The objectives of TB control are to reduce morbidity and mortality, stop new infections, and prevent progression from infection to disease</td>
</tr>
<tr>
<td><strong>End TB Strategy</strong>:</td>
<td>Main components:</td>
</tr>
<tr>
<td>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</td>
<td>1. Case identification</td>
</tr>
<tr>
<td><strong>Three main pillars and components</strong>:</td>
<td>2. Effective chemotherapy</td>
</tr>
<tr>
<td>1. Integrated, patient-centred care and prevention</td>
<td>3. Treatment of LTBI</td>
</tr>
<tr>
<td>2. Bold policies and supportive systems</td>
<td>4. BCG vaccination</td>
</tr>
<tr>
<td>3. Intensive research and innovation</td>
<td>5. Health education</td>
</tr>
<tr>
<td><strong>Active case identification</strong>:</td>
<td>Active case identification among four high-risk groups:</td>
</tr>
<tr>
<td>1. Household contacts and other close contacts of smear-positive individuals</td>
<td>1. Household contacts (&lt;35) of smear-positive individuals</td>
</tr>
<tr>
<td>2. People living with HIV</td>
<td>2. People with silicosis</td>
</tr>
<tr>
<td>3. Current and former workers in workplaces with silica exposure</td>
<td>3. HIV-positive people</td>
</tr>
<tr>
<td><strong>Conditional recommendation for screening for LTBI</strong>: prisoners, health care workers, immigrants from countries with high TB burden, homeless people, and illicit drug users.</td>
<td>4. People who receive immunosuppression/TNF blockers</td>
</tr>
<tr>
<td>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.</td>
<td>BCG vaccination for newborn babies and children who reside in Hong Kong aged &lt;15 years who have not received any prior BCG vaccination. Repeated doses of BCG vaccination are generally not recommended.</td>
</tr>
<tr>
<td>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.</td>
<td>Treatment of LTBI: 6–12 month isoniazid. This has not been widely practised in Hong Kong.</td>
</tr>
</tbody>
</table>

Abbreviations: AIDS = acquired immune deficiency syndrome; BCG = Bacille Calmette–Guérin; HIV = human immunodeficiency virus; INH = isonicotinic/hydrazide; LTBI = latent tuberculosis infection; TB = tuberculosis; TNF = tumour necrosis factor; WHO = World Health Organization
in 2015. 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.31 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 reactivation44,45 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>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Size</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan-Yeung et al (2006)34</td>
<td>Cross-sectional study</td>
<td>3682</td>
<td>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.</td>
</tr>
<tr>
<td>Vynncky et al (2008)35</td>
<td>Age-structured model</td>
<td>-</td>
<td>High prevalence of TB in older individuals and high risk of TB reactivation contribute to stagnation of TB rates in Hong Kong.</td>
</tr>
<tr>
<td>Leung et al (2015)37</td>
<td>Longitudinal cohort study</td>
<td>5402</td>
<td>Immigrants have higher rates of TB incidence and drug resistance from their place of origin.</td>
</tr>
<tr>
<td>Wu et al (2008)38</td>
<td>Age-period-cohort model</td>
<td>-</td>
<td>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.</td>
</tr>
<tr>
<td>Law et al (2008)39</td>
<td>Retrospective cohort study</td>
<td>312</td>
<td>Movement of population and younger age were independent predictors of MDR-TB in Hong Kong.</td>
</tr>
<tr>
<td>Leung et al (2013)40</td>
<td>Retrospective cohort study</td>
<td>736</td>
<td>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.</td>
</tr>
<tr>
<td>Chan et al (2010)41</td>
<td>Retrospective cohort study</td>
<td>349</td>
<td>TB is 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.</td>
</tr>
<tr>
<td>Leung et al (2016)42</td>
<td>Cohort study</td>
<td>478</td>
<td>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.</td>
</tr>
<tr>
<td>Leung et al (2006)44</td>
<td>Cohort and case-control study</td>
<td>94 928</td>
<td>There was a marked contrast in disease risk between those with tuberculin reaction of &lt;15 mm compared with &gt;15 mm. In light of these findings, the existing tuberculin test screening criteria may need revision.</td>
</tr>
<tr>
<td>Lui et al (2014)45</td>
<td>Retrospective cohort study</td>
<td>467</td>
<td>Mortality of hospitalised patients with TB is high and new methods are needed to prevent delayed diagnosis and treatment.</td>
</tr>
<tr>
<td>Wong et al (2005)46</td>
<td>Retrospective cohort study</td>
<td>998</td>
<td>Patients who underwent the full course of DOTS had better outcomes. Of the study’s participants, 85.6% underwent the entire of the first 2 months.</td>
</tr>
</tbody>
</table>

**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

---

* TUBERCULOSIS ELIMINATION IN HONG KONG

---

Hong Kong Med J | Volume 24 Number 4 | August 2018 | www.hkmj.org
TB reactivation. 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.

Multidrug-resistant TB (MDR-TB) is a threat that is more likely in patients diagnosed with TB at younger ages. Extensively drug-resistant TB (XDR-TB) significantly increases household TB transmission, demonstrating a need for prolonged household surveillance. 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, while the other doubted the utility of LTBI tests in annual screening of patients with HIV because of discordant results between different tests. 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. Diagnosis of TB is still problematic, and new methods are needed to prevent delayed diagnosis and treatment, as mortality of hospitalised TB patients is still high. 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. Directly observed treatment short course has significantly decreased TB incidence, 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.

**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. The BCG vaccine was introduced to Hong Kong in April 1952; 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. Despite the higher prevalence of LTBI in institutionalised older adults in Hong Kong (68.6%) compared with their American counterparts (5.5%), Hong Kong has not followed the US policy of LTBI testing in this population. 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, the infection rate in Hong Kong’s migrant population is declining. However, MDR-TB rates are higher in migrants and younger age-groups in Hong Kong and countries with low TB burden. A systematic review also concurred with a Hong Kong study’s findings that patients with HIV had a higher risk of MDR-TB. 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. It has been postulated that in Hong Kong, XDR-TB is mainly transmitted outside the household setting because of the high population density. The Peru study’s different findings may support this idea, as the population density of Hong Kong is more than double that of Lima.

The WHO has called for improved tests to diagnose LTBI, as the current ones lack accuracy. This was echoed by findings in the study of patients with HIV by Leung et al. 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. However, Hong Kong schoolchildren are not routinely screened for LTBI. 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, 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. Other developed Asian countries have similar DOTS treatment success rates to Hong Kong. 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, 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.

Funding/support
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration
All authors have disclosed no conflicts of interest. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity. Abstract of this article was presented at Infection 2016 (13th Annual Scientific Meeting), 22 June 2016, The Chinese University of Hong Kong, Hong Kong.

References
19. Tuberculosis and Chest Service, Department of Health,


49. Stead WW, Lofgren JP, Warren E, Thomas C. Tuberculosis as an endemic and nosocomial infection among the elderly.