Passive Smoking and Tuberculosis

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Background: Increasing evidence has incriminated active smoking as a causal factor for tuberculosis (TB). However, the effect of secondhand tobacco smoke exposure on TB has not been similarly elucidated.

Methods: A cohort of 15 486 female never-smokers aged 65 to 74 years and living with their surviving husband were enrolled at 18 Elderly Health Centers in Hong Kong from 2000 to 2003 and followed up prospectively through linkage with the territory-wide TB notification registry and death registry for TB and death until December 31, 2008, using an identity card number as a unique identifier. The relationship between passive smoking and the development of TB was assessed with adjustment for other baseline characteristics.

Results: Passive exposure to secondhand tobacco smoke in the household was independently associated with obstructive lung disease (odds [OR], 1.43; 95% confidence interval [CI], 1.16-1.77) and diabetes mellitus (OR, 1.13; 95% CI, 1.02-1.26) at baseline and with the development of both active TB (hazard ratio [HR], 1.49; 95% CI, 1.01-2.19) and culture-confirmed TB (HR, 1.70; 95% CI, 1.04-2.80) on prospective follow-up after potentially confounding background variables were controlled for. Passive smoking accounted for 13.7% of active TB and for 18.5% of culture-positive TB in this cohort.

Conclusions: Similar to active smoking, passive exposure to secondhand tobacco smoke in the household also predisposes to the development of TB. Increased emphasis should therefore be put on tobacco control in national TB programs.

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THE ASSOCIATION BETWEEN smoking and tuberculosis (TB) was investigated as early as 1918.[1] In recent years, active smoking has been shown to be associated with TB after a series of potential confounders were controlled for in a prospective cohort in Hong Kong.[2,3] Active smoking has also been associated with TB infection[4,5] and mortality,[6-9] albeit with more heterogeneous effect sizes and/or lesser degrees of certainty.[10-12] Indoor cigarette smoke is a major source of indoor air pollution. Passive smokers are exposed to similar toxic substances as active smokers, though at different concentration ranges. However, only limited data are available to support the association between secondhand smoke exposure and TB,[13-17] and the existing evidence is insufficient for any definite conclusion. Use of biomass fuel, another major source of indoor pollution in developing areas, has also been associated with TB disease,[18-20] but, like passive smoking, it is not easy to disentangle the direct effect of biomass fuel amid a myriad of potential confounders.

See Invited Commentary at end of article

In Hong Kong, the Elderly Health Service provides a community-based health maintenance program to the elderly through 18 centers.[2] For each person on enrollment, a trained nurse administers a standardized questionnaire, collecting information on the Hong Kong identity card number and sociodemographic variables, including passive exposure to cigarette smoke in the same household. The questionnaire is followed by history taking, medical examination by a family physician, and chest x-ray examination, arranged as needed. These key variables are entered into a structured database using the Hong Kong identity card number as the unique identifier, and they are regularly checked for completeness. Notification of TB disease has been a statutory requirement in Hong Kong since the 1940s. The territory-wide computerized TB notification registry is kept under the Tuberculosis and Chest Service, again using the Hong Kong identity card number as the unique identifier. A well-functioning statutory death registration system is also in place, and the identity card number, date of death, and certified causes are entered into a computerized death registry. With the availability of these databases, a prospective cohort study was conducted to look at the association between passive smoking and TB in Hong Kong.

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METHODS

A cohort of individuals who enrolled at the 18 Elderly Health Centers from January 1, 2000, to December 31, 2003, was retrospectively assembled. The date of enrollment, name, sex, age, identity card number, smoking status, passive exposure to tobacco smoke in the same household, alcohol use, language spoken, education level, marital status, housing situation, working status, public means–tested financial assistance status, body mass index, coexisting medical conditions, hospital admission within 1 year, recent weight loss of 5% or more within 6 months, and activity of daily living scores (possible range, 7-21, from total independence to total dependence) were retrieved from the baseline health assessment database of the Elderly Health Service. Only women younger than 75 years who were married but not widowed, separated, or divorced at baseline were included in the present analysis. All persons with active TB, a suspected malignant neoplasm, or a significant weight loss of 5% or more in the past 6 months at baseline were excluded. The database was then cross-matched prospectively with the TB notification registry and the death registry using the identity card number as identifier, supplemented by name and age, from enrollment to December 31, 2008. The duration of follow-up was defined as the period from enrollment to the date of notification of TB, death, or December 31, 2008, whichever came first. Information on date of TB notification and bacteriological status was retrieved from the TB registry. The diagnosis and clinical information of all identified TB cases, including contact with other TB cases in the same household, were verified by reviewing the medical records retrieved from the chest clinics and other relevant sources as well as the public health records of the Tuberculosis and Chest Service.

A never-smoker was defined as a person who had never smoked as much as 1 cigarette a day or the equivalent for the duration of 1 year. A passive smoker was defined as a person who lived with 1 or more smokers in the same household at baseline. A regular drinker and a social drinker were defined as persons who drank on 4 or more days per week and on 3 or fewer days per week, respectively. An ex-drinker was a regular or social drinker who had stopped drinking. A never-drinker was defined as a person who had never been a regular or social drinker. Hypertension, diabetes mellitus, and cardiac and cerebrovascular diseases were defined as the corresponding physician-diagnosed conditions, and the updated diagnoses after the screening at enrollment were used in the analysis. Obstructive lung disease was defined as physician-diagnosed chronic obstructive pulmonary disease or asthma. An active case of TB was defined as disease proved by isolation of *Mycobacterium tuberculosis* or, in the absence of bacteriological confirmation, as disease diagnosed on clinical, radiologic, and/or histologic grounds together with an appropriate response to anti-TB treatment.

Univariate analysis was first performed to analyze the relationship between passive smoking and other baseline variables and to compare the incidence rates of TB among different subgroups. Fisher exact and χ^2 tests were used as appropriate for categorical variables, and 1-way analysis of variance was used for numerical variables. These univariate analyses were followed by multiple logistic regression for cross-sectional analysis and Cox proportional hazards modeling in prospective follow-up analysis, with adjustment for all relevant potential confounders. Potential multicollinearity was considered. The proportional hazards assumption of the Cox model was assessed by inspection of the log minus log curve. The attributable risk was derived by applying the adjusted hazard ratios (HRs) to a modified version of the Levin formula[21]: population attributable risk of a factor = 1 – (rate in the unexposed population/rate in the total population). A 2-tailed *P* value of .05 was considered statistically significant. The study was approved by the Ethics Committee of the Department of Health of Hong Kong.

RESULTS

A total of 15 888 female never-smokers aged 65 to 74 years who were married and living with a surviving husband were recruited into the Elderly Health Service from January 1, 2000, to December 31, 2003. Seventy-four individuals with preexisting malignancies, 320 with weight loss of 5% or more in the last 6 months, and 8 who died within 91 days of enrollment were excluded, leaving 15 486 subjects for analysis.

The background characteristics of the cohort, stratified by passive exposure to cigarette smoke in the household, are shown in **Table 1**. The data were more than 99.9% complete for the variables listed. The vast majority (98.5%) were ethnic Chinese who spoke the Cantonese dialect. The mean activities of daily living score of 7.01 was close to the lowest (total independence). Passive smoking was significantly associated with younger age, lower education level, living in public housing, not being a never-drinker, higher body mass index, obstructive lung disease, and diabetes mellitus. However, some of the differences between groups were very small (eg, age), and the low *P* values could have arisen from a large study population. No significant association was found for Cantonese-speaking, public social security assistance, hypertension, heart disease, cerebrovascular disease, hospital admission within 1 year, and activities of daily living scores. **Table 2** summarizes the results of cross-sectional multiple logistic regression analyses of the risk factors for obstructive lung disease and diabetes mellitus. Only sociodemographic factors were entered as predictor variables in the cross-sectional analyses because factors related to current health status could be affected by the outcome variables themselves. Passive smoking remained a risk factor for both conditions at baseline after the relevant background sociodemographic variables were controlled for.

The mean (SD) duration of follow-up of the entire cohort, as counted from 91 days after enrollment to notification of TB, death, or December 31, 2008, whichever came first, was 2691 (508) days. A total of 124 TB cases were identified from the territory-wide TB registry, 7 of which were excluded because of a wrong diagnosis after review of the medical records. Of the remaining 117 active TB cases, their mean (SD) duration of follow-up was 1433 (879) days. Eighty-three persons (70.9%) had pulmonary involvement alone, 24 (20.5%) had extrapulmonary involvement alone, and 10 (8.5%) had both. Fifteen persons (12.8%) had a history of treatment, and 102 (87.2%) represented new cases. Overall, 69 cases (59.0%) were culture confirmed. Only 5 of the 117 active TB cases (4.3%) involved a history of contact with a patient with TB in the household: 2 cases within 2 years and 3 cases more than 2 years earlier. Among the 117 active TB cases, there were no significant differences between individuals with and without passive exposure to cigarette smoke in the household in the percentages of new cases (89.2% vs 86.3%; $P = .66$), culture-confirmed cases (64.9% vs 56.3%; $P = .38$), and exposure to TB in the household (2.7% vs 5.0%; Fisher exact test, $P > .99$). None of the patients with confirmed TB was known to be infected with human immunodeficiency virus (HIV). Twenty-three of the patients with confirmed TB (19.7%) died after a median of 312 days (range,

Table 1. Baseline Background Characteristics of Never-Smoking Married Women in the Study Cohort

Variable	No. (%) Overall (n=15 486)	Not Exposed (n=11 687)	Passive Smoking (n=3799)	*P* Value[a]
Age, mean (SD), y	68.7 (2.6)	68.8 (2.6)	68.6 (2.6)	<.001
Cantonese speaking	15 260 (98.5)	11 517 (98.5)	3743 (98.5)	.93
Education				<.001
Postsecondary	470 (3.0)	399 (3.4)	71 (1.9)	
Secondary	1820 (11.8)	1511 (12.9)	309 (8.1)	
Primary	5455 (35.2)	4274 (36.6)	1181 (31.1)	
No formal	2862 (18.5)	2119 (18.1)	743 (19.6)	
Illiterate	4879 (31.5)	3384 (29.0)	1495 (39.4)	
Housing				<.001
Public	5693 (36.8)	4054 (34.7)	1639 (43.1)	
Private, rented	586 (3.8)	432 (3.7)	154 (4.1)	
Private, owned	8729 (56.4)	6821 (58.4)	1908 (50.2)	
Other	478 (3.1)	380 (3.3)	98 (2.6)	
On public assistance	1290 (8.3)	951 (8.1)	339 (8.9)	.13
Alcohol use				.006
Never	12 940 (83.6)	9832 (84.1)	3108 (81.8)	
Ex-drinker	577 (3.7)	414 (3.5)	163 (4.3)	
Social	1823 (11.8)	1330 (11.4)	493 (13.0)	
Regular	146 (0.9)	111 (0.9)	35 (0.9)	
BMI, mean (SD)	24.7 (3.6)	24.6 (3.6)	25.0 (3.6)	<.001
Obstructive lung disease[b]	414 (2.7)	281 (2.4)	133 (3.5)	<.001
Hypertension	6326 (40.8)	4739 (40.5)	1587 (41.8)	.18
Heart disease	1702 (11.0)	1273 (10.9)	429 (11.3)	.49
Cerebrovascular disease	275 (1.8)	204 (1.7)	71 (1.9)	.62
Diabetes mellitus	2209 (14.3)	1624 (13.9)	585 (15.4)	.02
Hospital admission within 1 y	1647 (10.6)	1223 (10.5)	424 (11.2)	.23
Activities of daily living, mean (SD)[c]	7.01 (0.26)	7.01 (0.27)	7.01 (0.22)	.47

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a] Probability for the null hypothesis of no difference: passive smoking vs not exposed.
[b] Chronic obstructive pulmonary disease or asthma.
[c] Activities of daily living scores (7 totally independent, 21 totally dependent).

Table 2. Background Predictors of Obstructive Lung Disease and Diabetes Mellitus in Cross-Sectional Analysis by Multiple Logistic Regression[a]

Predictor Variable	Obstructive Lung Disease OR (95% CI)	*P* Value	Diabetes Mellitus OR (95% CI)	*P* Value
Age, y	1.02 (0.99-1.06)	.22	1.04 (1.02-1.05)[b]	<.001
Cantonese speaking	1.70 (0.63-4.60)	.30	0.92 (0.64-1.33)	.66
Education		.05		.01
Postsecondary	0.98 (0.51-1.88)		0.63 (0.46-0.88)[b]	
Secondary	0.88 (0.60-1.27)		1.06 (0.91-1.24)	
Primary	1 [Reference]		1 [Reference]	
No formal	1.03 (0.77-1.38)		0.93 (0.81-1.06)	
Illiterate	1.35 (1.06-1.71)[b]		1.06 (0.94-1.18)	
Housing		.19		.97
Public	1 [Reference]		1 [Reference]	
Private, rented	0.57 (0.29-1.12)		0.94 (0.74-1.21)	
Private, owned	1.08 (0.87-1.34)		0.99 (0.90-1.09)	
Other	0.74 (0.39-1.41)		1.01 (0.78-1.32)	
On public assistance	1.89 (1.40-2.53)[b]	<.001	1.15 (1.04-1.28)[b]	.04
Alcohol use		.07		<.001
Never	1 [Reference]		1 [Reference]	
Ex-drinker	0.92 (0.56-1.54)		1.25 (1.00-1.55)[b]	
Social	0.61 (0.42-0.89)[b]		0.58 (0.49-0.69)[b]	
Regular	0.72 (0.23-2.28)		0.42 (0.22-0.81)[b]	
Passive smoking	1.43 (1.16-1.77)[b]	.001	1.13 (1.02-1.26)[b]	.02

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Age, Cantonese speaking, education, housing, on public assistance, alcohol use, and passive smoking were entered as predictor variables in the multiple logistic regression analysis.
[b] $P<.05$ compared with reference subgroup.

0-2307 days), but only 3 of all such deaths (13.0%) were attributable to TB. Passive smokers had a higher risk (0.26% vs 0.11%; $P=.04$) of developing TB, with subsequent death for all causes, in comparison with those not so exposed. However, the difference failed to reach statistical significance when only TB-related deaths were considered (0.026% vs 0.017%; Fisher exact test, $P=.57$).

Table 3 summarizes the incidence rates of both active TB and culture-confirmed TB by passive smoking status. Higher rates of active TB (132 vs 93 per 100 000 person-years; relative risk [RR], 1.43; $P=.07$) and culture-confirmed TB (86 vs 52 per 100 000 person-years; RR, 1.64; $P=.04$) were observed between those passively exposed to cigarette smoke within the household and those not exposed. Very consistent RRs were observed after exclusion of TB cases within the first year (1.37 for active TB and 1.54 for culture-positive TB, $P=.14$ and $P=.11$, respectively) and re-treatment TB cases (1.47 for active TB and 1.66 for culture-positive TB, $P=.07$ and $P=.06$, respectively), although the *P* values fell short of statistical significance with the reduced sample sizes.

Table 4 shows adjusted HRs of various factors for both active TB and culture-confirmed TB in an overall Cox proportional hazards analysis. Passive smoking significantly increased the risk of both active TB (adjusted HR, 1.49; $P=.04$) and culture-confirmed TB (adjusted HR, 1.70; $P=.04$) after adjustment for other potential confounding factors. The **Figure** shows the hazard curves for passive smokers and nonpassive smokers in the Cox analysis for the entire follow-up period. Using the prevalence of passive smoking and its adjusted HRs for active TB and culture-positive TB as derived, 13.7% (95% confidence interval [CI], 0.3%-27.9%) of active TB cases and 18.5% (95% CI, 1.3%-36.9%) of culture-positive cases within the cohort were attributable to passive exposure to tobacco smoke within the household.

COMMENT

To our knowledge, this is the first prospective cohort study to demonstrate a significant and independent association between passive smoking and TB. Passive exposure to tobacco smoke within the household was found to be an independent predictor of the development of both active TB and culture-confirmed TB among a cohort of never-smoking married women aged 65 to 74 years af-

Table 3. Incidence Rates of Active Tuberculosis (TB) and Culture-Confirmed TB by Baseline Characteristics

Passive Smoking	Follow-up, Person-years	No. of Cases	Incidence (95% CI)[a]	RR (95% CI)	*P* Value
Active TB					.07
No	86 137	80	93 (74-116)	1 [Reference]	
Yes	27 943	37	132 (93-183)	1.43 (0.97-2.10)	
Overall	114 081	117	103 (85-123)	NA	
Culture-confirmed TB					.04
No	86 137	45	52 (38-70)	1 [Reference]	
Yes	27 943	24	86 (55-128)	1.64 (1.00-2.70)	
Overall	114 081	69	60 (47-77)	NA	

Abbreviations: CI, confidence interval; NA, not applicable; RR, relative risk.
[a] Rate per 100 000 person-years.

Table 4. Cox Proportional Hazards Analysis of Risks of Active and Culture-Confirmed Tuberculosis (TB)[a]

	Active TB		Culture-Confirmed TB	
Variable	Adjusted HR[b] (95% CI)	*P* Value	Adjusted HR[b] (95% CI)	*P* Value
On public assistance	2.03 (1.22-3.35)	.006	2.52 (1.38-4.63)	.003
Passive smoking	1.49 (1.01-2.19)	.05	1.70 (1.04-2.80)	.04
Body mass index	0.87 (0.83-0.92)	<.001	0.87 (0.81-0.94)	<.001
Hospital admission	1.60 (0.98-2.63)	.06	2.06 (1.14-3.72)	.02

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Passive smoking and all variables as listed in the first column of Table 1 were entered as predictor variables into the initial models; under the backward conditional approach, age, Cantonese speaking, education, housing, alcohol use, obstructive lung disease, hypertension, heart disease, cerebrovascular disease, and diabetes mellitus, all with a *P* value above .10, were removed.
[b] All HRs were mutually adjusted for each other.

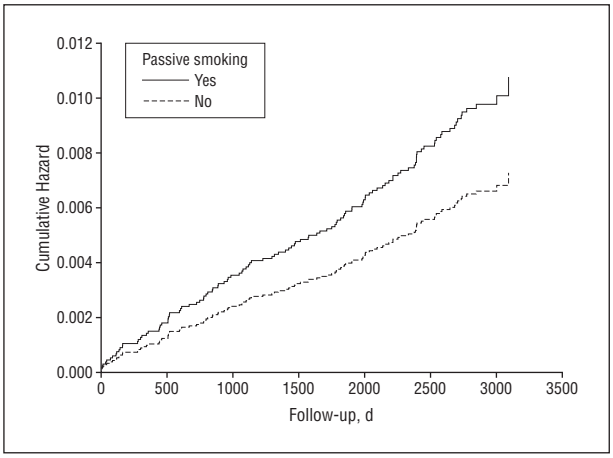

Figure. Cumulative hazards for active tuberculosis with respect to passive smoking after adjustment for potentially confounding variables by Cox proportional hazards analysis.

ter a series of potential confounders were controlled for. Passive smoking accounted for 13.7% of active TB cases and 18.5% of culture-positive TB cases in this cohort.

At baseline, passive smoking was also found to be independently associated with obstructive lung disease (odds ratio [OR], 1.43; 95% CI, 1.16-1.77) and diabetes mellitus (OR, 1.13; 95% CI, 1.02-1.26) (Table 2). A very similar effect size (OR, 1.48; 95% CI, 1.18-1.85) was reported between passive smoking and chronic obstructive lung disease in a recent cross-sectional analysis in China.[22] Two prospective cohort studies, one in Japan[23] and another in the United States,[24] also found an association between passive smoking and glucose intolerance or diabetes mellitus, even though their effect sizes of 1.35 and 1.81 were somewhat higher than those observed in this study.

Very scanty data were previously available on the relationship between passive smoking and TB.[13-17] In a community survey among children in South Africa, living in the household with at least 1 smoking adult was associated with a positive tuberculin skin test result in univariate analysis, but the association was lost after adjustment for age, presence of a patient with TB in the household, average household income, and clustering at the household level.[14] In any case, the tuberculin skin reaction is not specific and could be affected by BCG vaccination and other cross-reactions. Very limited data are available on active smoking and TB infection using a more specific interferon gamma release assay,[25] but data are still pending with regard to passive smoking. Clinically manifest disease is perhaps less elusive than latent TB infection, as the isolation of *M tuberculosis* from clinical specimens generally provides unequivocal evidence for the presence of the disease. In an unmatched case-control study among household TB contacts in Spain, passive smoking was associated with pulmonary TB (adjusted OR, 5.39) after adjustment for age and socioeconomic status.[15] A dose-response relationship was also observed between the risk of active pulmonary TB developing immediately after infection and the number of cigarettes smoked daily by adults in the household. Mean detectable urinary cotinine concentrations were also significantly different between diseased contacts and nondiseased contacts. In 2 hospital-based case-control studies in Thailand, passive smoking at home[21] and outside the home[22] was associated with a 9.31-fold and a 3.13-fold risk of TB, respectively. However, there might be difficulties in the control of multiple confounders in these small-scale case-control studies.[23] Furthermore, the observed effect sizes were also exceptionally large, substantially higher than those reported for active smoking[2,3,10-12] and in sharp contrast with the modest effect size reported between passive smoking and lung cancer.[26]

In this study, the moderate effect sizes of passive smoking (1.49 for active TB and 1.70 for culture-confirmed TB), as compared with the figures of 2.63 and 2.80, re-

spectively, for current active smoking in a similar recent cohort,[2] might be more compatible with the relative exposure levels. The relatively small effect size might also partly explain why it has previously proved so difficult to establish such a relationship in a prospective study. Although passive smoking might exert a smaller effect than active smoking at an individual level, a much bigger impact might be expected at the population level because everyone breathing the same air could be affected, smokers and never-smokers alike. Indeed, passive smoking accounted for 13.7% of active TB cases in this cohort, while active smoking, current or previous combined, only contributed to 8.6% of active TB cases among elderly women in Hong Kong.[2] The figures for passive smoking in this study could well be underestimates, as allowance has not been made for past or other sources of passive exposure among the reference group.

This study is community based. In the original design of the program admission questionnaire, a passive smoker was defined as an individual who lived with 1 or more smokers in the same household at baseline. No further details of exposure source or intensity were available, and 1 limitation is that we could not examine the dose-response relationship. To maximize the chance of detecting an association, we focused on a homogeneous group of never-smoking, married, community-living women aged 65 to 74 years. Limiting the study to this particular group would be expected to maximize the chance of exposure to a living smoking spouse, to avoid confounding by active smoking, to minimize the effects of other comorbidities, and to give a reasonable yield of TB cases on follow-up. Persons with suspected malignant neoplasms or a significant weight loss of 5% or more in the past 6 months at baseline were also excluded. With the prospective design, the exclusion of events in the first 91 days after recruitment, and a considerable period of follow-up, the possibility of reverse causality would be effectively minimized. The risk differential between passive smokers and those not so exposed also persisted throughout the whole period of follow-up (Figure).

Incomplete case ascertainment could be a cause of concern. The cohort was followed up through a territory-wide notification registry, which captured TB cases all over Hong Kong. The presence of a good health care infrastructure, the statutory requirement for all adult citizens to carry the identity card, a statutory TB notification system, and widespread use of the identity card number as a unique identifier were important factors that facilitated the current study. Undernotification remains a problem for all notifiable diseases. However, the cohort was already under the care of a service in the Department of Health and had ready access to the chest clinics in the same department for free TB treatment. In a local audit of TB notifications, the undernotification rate was only 3% in the chest clinics even before the introduction of specific improvement measures.[27] Because we examined the differences between subgroups in this cohort, there should be good internal validity.

In this study, a passive smoker was defined as an individual who lived with 1 or more smokers in the same household at baseline. A territory-wide Thematic Household Survey conducted in 2000 found that 21.8% of men 60 years or older were current daily smokers.[28] This percentage was rather similar to the 25% passive smoking rate among the married elderly women in this cohort. Selectively, mortality might still have occurred among some of the heaviest male smokers, but this would lead to an underestimate of the association between passive smoking and TB. No information was available about the tuberculin status or the newer interferon assays because such screening was not regularly performed. The sensitivity of the tuberculin skin test has been shown to be affected by advanced age,[29] while insufficient information is available for the new interferon release assays.[25] With the significant past burden of TB,[30] a high percentage of latent TB infection is expected among our elderly cohort. A previous study in Hong Kong reported a tuberculin reactivity rate (≥10 mm) of 68.6%, in the absence of recent contact history, among residents of nursing homes after 2-stage tuberculin skin testing.[31] Overcrowding could have been a potential confounder by facilitating the transmission of TB. Although overcrowding was not examined as a separate variable, attempts were made to control for type of housing and other important social determinants of living conditions, such as education level and public assistance. None of the patients with TB in our cohort was found to be HIV positive on voluntary HIV screening, which was regularly offered to all patients with TB in the Hong Kong Tuberculosis and Chest Service. Such results concur with the low HIV prevalence (<1%) found by unlinked anonymous HIV assays.[29] In contrast to communities with a high HIV prevalence, HIV is unlikely to confound the relationship between passive smoking and TB in Hong Kong.

As active smoking has been shown to increase the risk of TB, the association between passive smoking and TB could have arisen indirectly from increased exposure to TB within the same household. However, as in other high TB incidence areas, only a small percentage of patients with TB in Hong Kong could be traced to a probable contact source.[31] Most of the exposure probably occurred unrecognized outside the family setting, especially when the TB notification rate was as high as 700 per 100 000 population in the middle part of the last century. In 2006, among 2153 notified patients with TB who were older than 60 years, only 3.3% gave a history of contact with another TB case.[31] In the cohort described in this article, only 5% of the patients with TB gave a history of contact with a TB case in the household either within or over 2 years during the case investigation after notification. With such a low figure, TB contact in the household would be grossly insufficient to account for the observed association between passive smoking and TB. Furthermore, there was no significant difference in such contact exposure between individuals who were passively exposed to tobacco smoke and those who were not. Therefore, the weight of evidence is in support of a direct effect of passive smoking on TB risk rather than indirectly through increased TB risk among active smokers.

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INVITED COMMENTARY

Secondhand Smoke and Infectious Disease in Adults

A Global Women's Health Concern

Secondhand smoke is a major cause of disease, including lung cancer and coronary heart disease in adults and lower respiratory illness, middle ear disease, and asthma in children. Because the prevalence of smoking is much higher in men than in women, secondhand smoke disproportionately harms women. The scope of harm to women caused by secondhand smoke is both illustrated and widened by this study by Leung and coworkers. The investigators studied never-smoking married women in China, a country where 60% of men smoke compared with only 4% of women. They found that women who were exposed to secondhand smoke in the home were significantly more likely to develop tuberculosis (TB) than women who were not exposed.

The strengths of Leung and coauthors' study are that it included a large cohort of generally healthy women aged 65 to 74 years on entry into the study along with mandatory TB reporting over a period of 4 to 8 years. Approximately 25% of these women were exposed to secondhand smoke from at least 1 smoker in the home. None had evidence of TB or recent weight loss before the study began. Among the 15 486 women, there were 117 cases of TB, 87% of which were new cases (ie, no history of treatment of TB). A total of 15.9% of the TB cases were culture confirmed; the rest were diagnosed on clinical criteria. There was no relationship between the development of TB and exposure to TB from other household members. The odds ratio (OR) for the development of active TB in relationship to secondhand smoke was 1.49 (95% confidence interval, 1.01-2.19). This compares with an OR of 2.63 in a previously published study of active cigarette smoking and TB in the same population. Importantly, the attributable risk