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Risk of tuberculosis among contacts in a low incidence setting

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Contact investigations that are designed to identify and investigate people who have been exposed to patients with active tuberculosis (TB) are regarded an important component of TB control in low incidence settings, such as Australia [1], where the incidence of TB is 6.0/100,000 and 88% of all cases of TB occur in overseas-born people [2].

We aimed to estimate the prevalence of active TB at the time of initial screening and the subsequent incidence of TB among contacts of patients with TB living in Sydney, New South Wales (NSW), Australia.

The study population comprised all persons who were screened as contacts of patients with TB between January 2000 and December 2009 at TB clinics within the Sydney West and Sydney South West Area Health Services. Contact screening and management in this jurisdiction is guided by state policy directives. Cases of active TB among the study population were identified by linking a database containing details for all identified contacts and the NSW Notifiable Diseases Database (which includes the TB registry) using a combination of probabilistic and deterministic linkage methods [3].

TB was defined as any case that was notified as a case of active TB in the NSW Notifiable Diseases Database. TB diagnosis at initial screening (period prevalence of TB) was defined as a TB diagnosis within 90 days of the first health care contact for contact screening.

Incident cases of TB were ascertained for a period starting 90 days after the first health care contact for contact screening and continuing until 31/12/2009 or the date of diagnosis of TB, whichever was the earlier. TB incidence rates were expressed per 100,000 person-years.

In addition, we reviewed the clinical files of 293 randomly selected contacts of patients with pulmonary TB and a TST \geq 10mm who did not receive LTBI treatment in order to ascertain whether this was because it was not offered or because it was declined. For the purpose of this study LTBI was defined as a TST \geq 10mm.

The study cohort comprised 14,371 contacts of patients with TB seen at six Sydney TB clinics. A median of 3 contacts (interquartile range 2 to 5) were seen per index case. The mean age of contacts was 32.9 (SD 19.3) years, 55% were female and 56% were overseas-born. The most common countries of origin for overseas born contacts were the Philippines (12.5%), India (11.8%) and Vietnam (10.4%). Characteristics of the study population of contacts are shown in Table 1.

Overall, 14% of subjects in the cohort had missing data for TST results. However, 163 of 212 prevalent cases of TB (77%) and 16 of the 61 cases of incident cases of TB (26%) had no record of a TST.

Among the 14,371 contacts, 273 (1.9%) people were diagnosed with TB during the study period. Of those contacts who were diagnosed with TB at any time before the 31/12/2009, 212 (77.7 %) were diagnosed at the time of the initial screening. The period prevalence of TB in contacts at initial screening was 1.48% (95% CI 1.26 to 3.12%). The mean follow up period was 4.6 years (SD 2.9). The incidence of TB during the period from 90 days to 2 years after initial health care contact was 232/100,000 person-years (95% CI 174 to 309), which was 10-times higher than the incidence of TB in the overseas-born population in Australia in 2009 (22.4/100,000/year) [2]. The incidence of TB during the period from two years after initial health care contact to the 31/12/2009 was 27/100,000 person-years (95% CI 14 to 50).

Table 1 shows the period prevalence and subsequent incidence of TB stratified by age, sex, and country of birth as well as the incidence of TB stratified by TST size and preventive treatment status.

Of all contacts with at least one TST result, 35% had a TST ≥ 10 mm and were thus assumed to have LTBI. Only 9.5% of all contacts with LTBI received treatment for LTBI. Among the randomly selected sample of the cohort who were contacts of patients with pulmonary TB, had a TST ≥ 10 mm and did not receive treatment for LTBI, 95% (95% confidence interval 92% to 97%) were not offered treatment for LTBI by the treating physician.

The prevalence of active TB among contacts of patients with TB in our study was 1.48%, which is similar to findings in other high income countries from a recently published meta-analysis of the results of TB contact investigations [4]. Our study has shown that, in the majority of contacts who were ultimately diagnosed with TB, the disease was already present at the time of the screening and hence there was little opportunity to prevent these cases.

A potential limitation of this study is that a large number of subjects, especially contacts who were diagnosed with TB at initial screening (prevalent cases), had missing data for TSTs. The main reason for this is that a TST is not usually performed in patients who present with clinical features of TB. For this reason we did not attempt to assess LTBI as a risk factor for prevalent cases of TB in contacts. A further limitation of this analysis is that we have no direct evidence on out-migration for this cohort. However, these data are available for a cohort of refugees newly arrived in the Australian state of NSW between 1984 and 1994 [5]. Based on data from that cohort, we estimate that a maximum of 15% of the cohort may have left NSW during the follow-up period.

Finally, there are no genotyping data available for the prevalent and incident cases of TB in this cohort. Hence, we cannot directly estimate the proportion of these cases that are likely to have arisen as a result of exposure to the identified index case.

This study reveals that a low proportion of contacts with LTBI who attended the participating TB clinics received preventive therapy. This low proportion (9.5%) is in stark contrast to the USA where, mainly as a result of policy directives in that country in line with the goal of TB elimination in the USA [6], 74 to 79% of patients diagnosed with LTBI are commenced on treatment [7, 8]. In our cohort of contacts, low treatment rates for LTBI appeared to be mainly a consequence of physicians' reluctance to offer LTBI treatment rather than low patient uptake of treatment.

In conclusion, in a setting where more than half of all screened contacts were born overseas and the background incidence of TB is low, contacts of patients with TB have a significantly increased risk for TB compared to the general overseas-born population of Australia. Most contacts who develop active TB are diagnosed with TB at the time of the initial screening, thus efforts should be made to ensure at least one screening visit for every identified contact at risk. Few contacts receive treatment for LTBI in this study setting due to physicians' reluctance to prescribe preventive treatment.

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Author contributions

Both authors were involved in study concept and design, analysed data, revised the manuscript for important content and approved the final manuscript. CCD acquired the data, performed the statistical analysis and drafted the manuscript.

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Competing interests

No conflict of interest reported.

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Table1. TB cases among contacts by risk factor status and period of follow-up

Characteristic	Population at risk at start of contact investigation			Total TB cases		Prevalence of TB at time of initial contact screening ^a		Person-years at risk for incidence of TB 3 months to 2 years after initial screening ^b		Incidence of TB 3 months to 2 years after initial screening ^b		Person-years at risk for incidence of TB 2 years+ after initial screening ^c		Incidence of TB 2 years+ after initial screening ^c	
	N	N	%	N	% (95%CI)	Person-years at risk (persons at risk)	N	per 100,000 (95% CI)	Person-years at risk (persons at risk)	N	per 100,000 (95% CI)				
All	14,371	273	1.9	212	1.48 (1.26 to 3.12)	21,518 (14,159)	50	232 (174 to 309)	40,318 (14,109)	11	27 (14 to 50)				
Age, years, info available for n=13,444															
0-14	2,369	6	1.9	38	1.60 (1.15 to 2.22)	3,629 (2331)	6	165 (67 to 379)	6,232 (2325)	2	32 (6-129)				
15-34	5,335	128	2.4	98	1.84 (1.50 to 2.24)	7,698 (5237)	26	338 (225 to 502)	15,008 (5,211)	4	27 (9 to 73)				
≥35	5,740	99	1.7	76	1.32 (1.05 to 1.66)	8,830 (5,664)	18	204 (125 to 329)	17,362 (5646)	5	29 (11 to 71)				
Sex, info available for n= 13,600															

Male	6,125	123 ^d	2.0	102	1.67 (1.37 to 2.03)	9,131 (6,023)	19	208 (129 to 331)	17,260 (6,004)	2	12 (2 to 47)
Female	7,475	149 ^d	2.0	109	1.46 (1.20 to 1.76)	11,205 (7,366)	31	277 (191 to 398)	21,677 (7,335)	9	42 (20 to 82)
TB incidence (per 100,000) in country of birth, info available for n=12,043											
Australian-born, <10/100,000	5,357	46	0.9	39	0.73 (0.53 to 1.00)	8,033 (5318)	6	75 (30 to 171)	16,287 (5312)	1	6 (0.3 to 40)
Overseas-born, incidence <10/100,000	641	15	2.3	11	1.72 (0.90 to 3.15)	969 (630)	3	310 (80 to 982)	1,979 (627)	1	51 (3 to 327)
Overseas-born, incidence 10-99/100,000	2,800	74	2.6	59	2.11 (1.62 to 2.73)	4,240 (2,741)	14	330 (188 to 568)	8,005 (2727)	1	12 (1 to 81)
Overseas-born, incidence >100/100,000	3,245	138	4.3	103	3.17 (2.61 to 3.85)	4,763 (3,142)	27	567 (381 to 836)	8,488 (3,115)	8	94 (44 to 194)
TST size, info available for n=12,417^e											
TST ≥10 mm (including results prior to contact investigation)	4,307 ^e	N/A		N/A		6,635 (4,307)	32	482 (336 to 689)	12,679 (4,275)	9	71 (35 to 140)
TST < 10mm	8,073 ^e	N/A		N/A		12,247 (8,073)	4	33 (10 to 90)	23,269 (8,069)	0	
TST result unknown or not done	1,779 ^e	N/A		N/A		2,636 (1,779)	14	531 (302 to 913)	3,757 (1,765)	2	53 (9 to 214)

Preventive treatment, info available for n=14,159^{e)}									
All preventive treatment received	548	N/A	N/A	858 (548)	2	233 (40 to 936)	1,653 (546)	1	60 (3 to 392)
TST ≥10 mm, preventive treatment received	409	N/A	N/A	633 (409)	2	316 (55 to 1266)	1,313 (407)	1	76 (4 to 493)
TST≥10 mm, no preventive treatment received	3,942	N/A	N/A	6,002 (3,942)	30	500 (343 to 722)	11,365 (3,912)	8	70 (33 to 145)

- a) Includes all TB cases among contacts diagnosed within 90 days of the first health care contact for screening
- b) The denominator is person-years at risk. The 212 contacts who were diagnosed with TB at the time of the initial screening are excluded.
- c) The denominator is person-years at risk. The 262 contacts who were diagnosed with TB at the initial screening or within the first 2 years of follow up are excluded.
- d) One contact with TB was classified as “transgender”, thus female and male cases added only up to 272 instead of 273 cases.
- e) Only includes contacts during follow up period (without the 212 contacts who were diagnosed with TB at the time of the initial screening).