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Risk and Timing of Tuberculosis Among Close Contacts of Persons with Infectious Tuberculosis

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Abstract

Background.—The risk and timing of tuberculosis among recently exposed close contacts of patients with infectious tuberculosis are not well established.

Methods.—We prospectively enrolled patients ≥15 years of age with culture-confirmed pulmonary tuberculosis and their close contacts at 9 health departments in the United States and Canada. Close contacts were screened and cross-matched with tuberculosis registries to identify those who developed tuberculosis.

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Results.—Tuberculosis was diagnosed in 158 of 4490 contacts (4%) of 718 index patients with tuberculosis. Of tuberculosis cases among contacts, cumulative totals of 81 (51%), 119 (75%), 128 (81%), and 145 (92%) were diagnosed by 1, 3, 6, and 12 months, respectively, after the index patients' diagnosis. Tuberculosis rates among contacts were 2644, 115, 46, 69, and 25 cases per 100 000 persons, respectively, in the 5 consecutive years after the index patients' diagnosis. Of the tuberculosis cases among contacts, 121 (77%) were identified by contact investigation and 37 (23%) by tuberculosis registry cross-match.

Conclusions.—Close contacts to infectious patients with tuberculosis had high rates of tuberculosis, with most disease diagnosed before or within 3 months after the index patient' diagnosis. Contact investigations need to be prompt to detect tuberculosis and maximize the opportunity to identify and treat latent infection, to prevent disease.

Keywords

Tuberculosis; contact investigation; close contacts; epidemiology; tuberculosis rates; tuberculosis timing

Close contacts of patients with infectious tuberculosis are at increased risk of developing *Mycobacterium tuberculosis* infection and disease [1, 2]. The risk of tuberculosis in individuals with latent *M. tuberculosis* infection (LTBI) is estimated to be 5%–10% over the course of a lifetime, with approximately half of cases occurring within the first 2 years after exposure [3–5]. These rates are from studies conducted >50 years ago, however, and the precise risk and timing of disease among recently exposed close contacts despite efforts to prevent tuberculosis by LTBI treatment are not well established.

Health departments throughout the United States and Canada conduct contact investigations for all patients with infectious tuberculosis to identify and treat recently exposed individuals with active tuberculosis and LTBI and thereby prevent further transmission of *M. tuberculosis* [1, 2]. A better understanding of the risk and timing of tuberculosis among recently exposed contacts has important implications for the expected yield and optimal timing of contact investigations.

To address this knowledge gap, we conducted a prospective study of contact investigations at 9 sites in the United States and Canada. Tuberculosis registry cross-matches were conducted to identify contacts with tuberculosis diagnosed after the time of the contact investigation. We evaluated rates of tuberculosis among contacts with respect to the interval from the index cases' diagnosis.

METHODS

Close contacts of all adults aged ≥15 years with culture-positive pulmonary tuberculosis were prospectively enrolled in a multicenter study from January 2002 to December 2006 at 9 health departments (7 in the United States and 2 in Canada) in the Tuberculosis Epidemiologic Studies Consortium. Close contacts were defined as persons who had shared air space with an individual with pulmonary tuberculosis in the household or other indoor setting for >15 hours per week or >180 hours total during an infectious period, defined as

the interval from 3 months before collection of the first culture-positive sputum specimen or the date of onset of cough (whichever was longer) through 2 weeks after the initiation of appropriate antituberculosis treatment.

Contacts were screened as soon as possible after they were identified through interview of patients with tuberculosis and again 10–12 weeks after last exposure to the patient. Screening consisted of a standardized interview and tuberculin skin test (TST), with a positive TST result defined as a ≥5-mm induration. Chest radiography was performed for contacts with positive results of TST. While a standard protocol was used for conducting contact investigations, the staff at the study sites did not use a standard protocol for patient management, which included efforts to prevent secondary cases by investigation and treatment of contacts with LTBI. The Centers for Disease Control and Prevention's (CDC's) standard surveillance definitions for a reported case of tuberculosis were used for tuberculosis reporting by all study sites [6].

Contacts were cross-matched with state and provincial tuberculosis registries at the end of the enrollment period and annually for 4 years thereafter, with the exception of one study site, which cross-matched contacts annually for 2 years (the final match was in February 2011).

The timing of tuberculosis among contacts was calculated by subtracting the tuberculosis diagnosis date for each index patient from the tuberculosis diagnosis date(s) for their contact(s), and tuberculosis rates per interval were based on the number of contacts with tuberculosis diagnosed in a given interval divided by the number of observed contacts who were disease free at the start of that interval. For contacts with exposure to >1 index case, the earliest index case tuberculosis diagnosis date was used.

Tuberculosis events among contacts with disease diagnosed >30 days after the index cases' diagnosis were considered incident cases, and tuberculosis events diagnosed before or ≤30 days after the index cases' diagnosis were considered coprevalent cases.

Survival analysis (Proc Lifetest) was performed using the log-rank test to assess the effect of age group, TST size, and preventive therapy on disease-free survival of contacts. Statistically significant differences for other analyses were assessed using χ^2 or Fisher exact tests. All analyses were performed using SAS software, version 9.2 (Statistical Analysis Software Institute, Cary, NC).

Approvals for human subjects research were obtained from the CDC and all project sites.

RESULTS

Characteristics of Contacts with Tuberculosis

Tuberculosis was diagnosed in 158 of 4490 close contacts (4%) identified for 718 patients with active pulmonary tuberculosis. Demographic and clinical characteristics of the 158 contacts with tuberculosis (81 coprevalent cases and 77 incident cases) are presented in Table 1. Children 0–5 years of age represented 31% of all contacts with tuberculosis, including 36% of coprevalent cases and 26% of incident cases. Of the contacts with

tuberculosis, 121 (77%) were identified during contact investigation (including 96 of 127 with a diagnosis after the index case), and 37 (23%) were identified by registry match; disease in 77 (49%) was confirmed by culture (67% of adults and 16% of children), and disease in 81 (51%) was diagnosed on the basis of clinical criteria.

Rates, Timing, and Risk Factors for Tuberculosis

The timing of tuberculosis diagnosis among contacts in relation to the index cases' diagnosis is displayed in Figure 1. Of the contacts with tuberculosis, disease in 27 (17%), 4 (3%), and 127 (80%) was diagnosed before, on the same day as, and after, respectively, the index cases' diagnosis. Of the contacts with tuberculosis, cumulative totals of 81 (51%), 119 (75%), 128 (81%), and 145 (92%) had tuberculosis diagnosed by 1 month, 3 months, 6 months, and 12 months, respectively, after the index cases' diagnosis.

Disease-free survival curves for all enrolled contacts who remained disease free, by age group, screening skin test results, and receipt of treatment for LTBI, are presented in Figure 2. The proportion of children 0–5 years of age who remained disease free was lower than that for contacts in other age groups ($P < .001$; Figure 2A). In addition, there was a close relationship between TST size and risk of tuberculosis (Figure 2B). The risk of tuberculosis was lowest for contacts with a 0–4-mm induration (0.6%) and progressively increased as the induration diameter increased, with risks of 2.8%, 6.1%, 8.2%, and 8.9% among those with indurations of 5–9, 10–14, 15–19, and ≥20 mm, respectively ($P < .001$ for trend). Finally, the proportion of contacts who had a positive TST result and remained disease free was significantly greater among those who completed a full course of treatment for LTBI, compared with those who had a positive TST result and were not treated ($P < .001$), and was similar to the proportion with a negative TST result (Figure 2C). The proportion of contacts who remained disease free and had a positive TST result was significantly greater among those who initiated but did not complete treatment, compared with those who were not treated ($P < .001$), but was significantly less, compared with those who completed treatment ($P = .03$).

Table 2 presents tuberculosis rates among contacts, according to the interval between initiation of treatment of index cases and initiation of treatment in contacts. Tuberculosis rates among contacts were 2644, 115, 46, 69, and 25 cases/105 persons during years 1, 2, 3, 4, and 5, respectively, after the index cases initiated treatment. Two additional contacts had tuberculosis diagnosed >5 years after the index case initiated treatment (one each in years 6 and 8). Cumulative tuberculosis rates among the subset of TST-positive contacts with no treatment for LTBI (Table 3) were >5-fold higher than for all contacts (Table 2).

DISCUSSION

In a large prospective study of close contacts of patients with culture-positive pulmonary tuberculosis, we found that 4% of all close contacts had tuberculosis diagnosed and that, of these, 75% had tuberculosis diagnosed before or ≤3 months after the index cases had tuberculosis diagnosed. Our study represents an important update on the 1950s studies, which established rates of tuberculosis among contacts to be somewhat lower (1.5% over a 7-year observation period) and identified the risk of tuberculosis to be highest in the first 2

years after exposure, with 48% of all cases occurring in that period [3–5, 7]. We have shown that recently exposed close contacts have very high rates of tuberculosis. In addition, we have provided important, new evidence from the modern era to demonstrate that tuberculosis among exposed contacts is not evenly distributed over the first 2 years after exposure but, instead, that most cases occur soon after exposure and are already evident at the time of contact investigation. These findings emphasize the importance of performing contact investigations immediately after identifying index cases, as a public health measure for detecting new cases of active tuberculosis and taking steps to interrupt transmission [1, 2, 8, 9].

In the health departments participating in our study, contact investigations took anywhere from a few weeks to many months to complete. This timeline is similar to what has been reported in other settings for completing this complex, multistep process [2, 10, 11]. As a result, it is often difficult to be certain which tuberculosis cases identified at the time of contact investigation represent secondary transmission from the index case. In our study, we used ≥1 month after diagnosis of tuberculosis in the index case to distinguish incident from coprevalent tuberculosis diagnoses in contacts. Categorization of more than half of tuberculosis cases among contacts 0–5 years of age as coprevalent suggests that the true number of cases of secondary transmission may be somewhat higher than the number of cases we categorized as incident, since tuberculosis in young children is not infectious and is almost always the result of transmission from an adult index case.

Only 2 previous reports presented results separately for prevalent and incident tuberculosis, and each defined incident tuberculosis among contacts by using different intervals after the index patients' diagnosis (270 and 180 days) [10, 11]. Despite these differences in definition, tuberculosis risks in our study were higher overall (3.5% vs 1.2% and 1.5%), for coprevalent tuberculosis (1.8% vs 1.0% and 1.2%), and for incident tuberculosis (1.7% vs 0.3% and 0.3%), compared with tuberculosis risks in the 2 previous studies. The tuberculosis risks observed among contacts in this study were also higher than those reported for screening of other identified high-risk groups, including recent immigrants, refugees, and incarcerated populations [12–15], and considerably higher than those (range, 0.6%–1.5%) reported in previous studies of contact investigations conducted in the United States, Canada, and the Netherlands [2, 10, 11, 16–19].

The higher tuberculosis rates among contacts that we observed likely reflect, at least in part, the fact that our study was prospective, enabling us to use a standard structured interview to elicit contacts and track outcomes, as well as a standard definition for contact closeness, based on a high minimum number of hours of exposure (>15 hours per week) to a patient with infectious tuberculosis, whereas previous studies have reported a retrospective analysis of tuberculosis program and surveillance data and have either not used hours of exposure or used a minimal requirement (>4 total hours) to define a contact [1, 2, 10, 11, 16–18]. The considerably higher LTBI rate in our study (48%), compared with rates in other recent reports (33% in New York City [10] and 16% in Amsterdam [11]), supports the hypothesis that our study methods resulted in the evaluation of contacts with a greater likelihood of exposure, compared with those in previous studies. Conducting registry matches to identify contacts who received a tuberculosis diagnosis for 4 years (and for some contacts, up to 8

years) after the contact investigation likely also contributed to our findings. The fact that our study was conducted in the context of tuberculosis control programs and included all eligible contacts, rather than persons who were selected and provided consent for a clinical trial, may be an additional factor contributing to the higher tuberculosis rates we observed, compared with those in 1950s public health trial reports [5]. Although it is not directly stated, it is likely that those reports excluded coprevalent cases of tuberculosis, in which case our incident tuberculosis rates (1.7%) are remarkably similar to the tuberculosis rates reported over 50 years ago by Ferebee (1.5%).

More than half of all cases of tuberculosis among contacts in our study were diagnosed by 1 month and three quarters were diagnosed by 3 months after treatment initiation among index cases, suggesting that the opportunity to prevent many additional cases of tuberculosis in contacts was more time limited than previously recognized. High rates and rapid progression to tuberculosis were particularly notable among young children: among contacts 0–5 years of age, 10% developed tuberculosis, and 59% of all cases were diagnosed by 1 month and 93% by 3 months after index case diagnosis. These findings have important implications for the optimal timing, expected yield, and prevention goals of contact investigations.

Our data demonstrating that tuberculosis rates among exposed contacts are highest in the first few months after exposure and decline rapidly thereafter are consistent with those reported in a meta-analysis of 203 studies in low-medium and high-income settings by Fox et al, who found that the greatest risk of tuberculosis occurs in the year after exposure [20]. Based on our data, strategies that improve the timeliness of identifying and treating recently exposed persons would likely have the greatest effectiveness in preventing tuberculosis. However, they do not preclude the importance of screening and treatment at later time points, particularly in groups at increased tuberculosis risk, such as persons born outside the United States [21], or as part of national and global efforts aimed at tuberculosis elimination [22, 23].

Contact investigation is a complex, multistep process involving index case interview to identify contacts and multiple steps to locate, screen, and provide treatment to recently exposed individuals [1, 2]. In an analysis of data from our study evaluating contact investigation processes, the average times from index case diagnosis to initial contact screening and start of contact treatment for LTBI were 35 days and 53 days, respectively [24], and in recent reports from Amsterdam and New York, the estimated times from index case diagnosis to completion of contact investigation and initiation of preventive therapy were 180 days and 270 days, respectively [10, 11]. These reports reflect the realities of the time requirements for implementing contact investigation, and for our report, even under study conditions [24]. Although our findings emphasize the importance of initiating contact investigations as early as possible after diagnosis in a patient with infectious tuberculosis, the rapid progression to disease suggests that, even with timelier contact investigations, tuberculosis in many contacts who receive a diagnosis in the first few months after the index cases' diagnosis is unlikely to be prevented and that the number of preventable contact cases is thus relatively small. Nevertheless, contact investigations remain an important means of identifying contact cases and initiating treatment to prevent further (tertiary) transmission. Given the large resource implications of contact investigation and treatment for LTBI, cost-

benefit and cost-effectiveness analyses incorporating our new estimates of disease risk over time may be warranted.

Determining the number and proportion of tuberculosis cases among contacts that can be prevented is of importance to an assessment of the potential impact of LTBI treatment programs, as well as for sample size considerations for clinical trials. Of the tuberculosis cases among contacts in our study, 27 (17%) and 4 (3%) were detected and treated earlier than and at the same time as, respectively, detection and treatment of tuberculosis among index cases, so by definition these cases could not have been prevented through contact investigation for the index case. A further 96 cases (60% of all cases among contacts) were diagnosed after the index cases received a diagnosis but during the health department contact investigation. Thus, only the 31 cases detected after the index case by registry match—representing 20% of all cases among contacts in our study—are likely in theory to have been preventable with currently available diagnostic tests and strategies. Therefore, the rate of potentially preventable cases of tuberculosis in our population beyond those cases already prevented by traditional contact investigation was 0.7% (in 31 of 4490 contacts) over a follow-up period of up to 8 years. The rate of preventable tuberculosis cases was somewhat higher when limiting the analysis to TST-positive contacts (1.3% [20 of 1505]). Based on these findings, sample size requirements for clinical trials of preventive chemotherapeutic agents will be considerably higher than previously estimated [25]. These findings also may help explain the much lower than expected disease event rate in a recent clinical trial of preventive chemotherapeutic agents [25].

In addition to sample size considerations, the rates of tuberculosis over time among contacts in our study also have important implications for the methods, comparability of study arms, and length of follow-up for clinical trials of chemotherapeutic agents to treat LTBI. Our data demonstrate that the risk of tuberculosis in contacts following exposure varies considerably over time, with the highest risk immediately following the end of exposure and a rapid and progressive decrease in risk in the following months. Tuberculosis risks for all contacts fell from 2% (88 of 4459) in the first 3 months to 0.2% (9 of 4371) in the subsequent 3 months after index case diagnosis, for a decrease of 90%. Similarly, among the subset of TST-positive contacts who did not initiate treatment for LTBI, the risks of tuberculosis dropped from 13% (65 of 482) in the first 3 months to 2% (8 of 417) in the following 3 months, for a decrease of 85%. These findings have important implications for steps to ensure the comparability of tuberculosis risks in clinical trial study arms, suggesting the need to control not only for recent versus remote exposure, but also for time since last exposure among persons with recent exposure. In our study, 81% of all tuberculosis cases among contacts were diagnosed by 6 months and 93% by 12 months after index cases received a diagnosis. Thus, our findings suggest that it may be possible to shorten the follow-up time for patients enrolled in clinical trials, from the usual 2 years [25] to 1 year or even 6 months.

Despite a rapid decline in the risk of tuberculosis over time, higher rates of tuberculosis were observed among close contacts in our study than was expected in the general population [26] for at least 5 years after index cases' diagnosis, demonstrating that close contacts remain a high-risk population well beyond the time of exposure to an infectious case and initial contact investigation. This finding underscores the importance of educating persons who

have been exposed to a patient with infectious tuberculosis about the ongoing risk of developing tuberculosis, the symptoms of tuberculosis, and the need to seek prompt medical evaluation if symptoms occur. It also highlights the need for greater awareness on the part of the medical community about the importance of asking about past and recent contacts of patients with infectious tuberculosis and of considering tuberculosis when evaluating patients with a history of close contact to patients with infectious tuberculosis. Furthermore, this finding suggests that periodic evaluation of contacts for several years after contact investigation could be a productive activity, particularly for contacts at highest risk of tuberculosis. This strategy may be particularly important for contacts who do not initiate treatment for LTBI.

The incomplete human immunodeficiency virus (HIV) testing data for many contacts is a study limitation. Although one of our 9 project sites withdrew 2 years after enrollment ended, this is unlikely to have had much influence on our findings because the denominators used for our tuberculosis incidence rates were based on the number of contacts during a given period. Furthermore, this site had very low enrollment, so the effect on the overall tuberculosis rates among contacts is expected to be quite small, particularly since registry match data for this site were available for the first 2 years after enrollment, when tuberculosis rates are highest. Other limitations include our inability to determine with certainty the source case for contacts with tuberculosis, the possibility that tuberculosis registry matches failed to detect contacts who moved out of state or used a different name, and the fact that contacts who were treated for LTBI may have been those at highest risk for tuberculosis. Although we did not directly assess the impact of LTBI treatment on the rates and timing of tuberculosis, we present data both for all contacts and for the subset of untreated TST-positive contacts. Although the rates are somewhat higher in the latter group, the timing is quite similar. Furthermore, our findings that most secondary cases occur quite rapidly and could not have been prevented even with timely contact investigation, the fact that only one third of contacts with LTBI completed treatment [27], and evidence that most contacts who initiated treatment did so >3 months after exposure [24] (when the risk of progression to tuberculosis is already lower) suggest that the impact of LTBI treatment on the rates and timing of tuberculosis we present in this report is not expected to be large. Study strengths include the large number of contacts with tuberculosis included in our study, the use of registry matches, the long follow-up period, the prospective and protocol-driven nature of our data collection, and the ability to prospectively collect information on many epidemiologic factors, including hours of exposure.

In conclusion, our prospective study provides important new information on the risk of tuberculosis over time in recent contacts of patients with infectious tuberculosis. Our findings support the important role of contact investigation as a means of identifying and treating new cases of active tuberculosis among contacts, and they underscore the importance of rapid screening and initiation of treatment for LTBI. These findings have important implications for tuberculosis prevention efforts worldwide, as well as for the design and interpretation of clinical trials of preventive therapeutic regimens.

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***Disclaimer*.** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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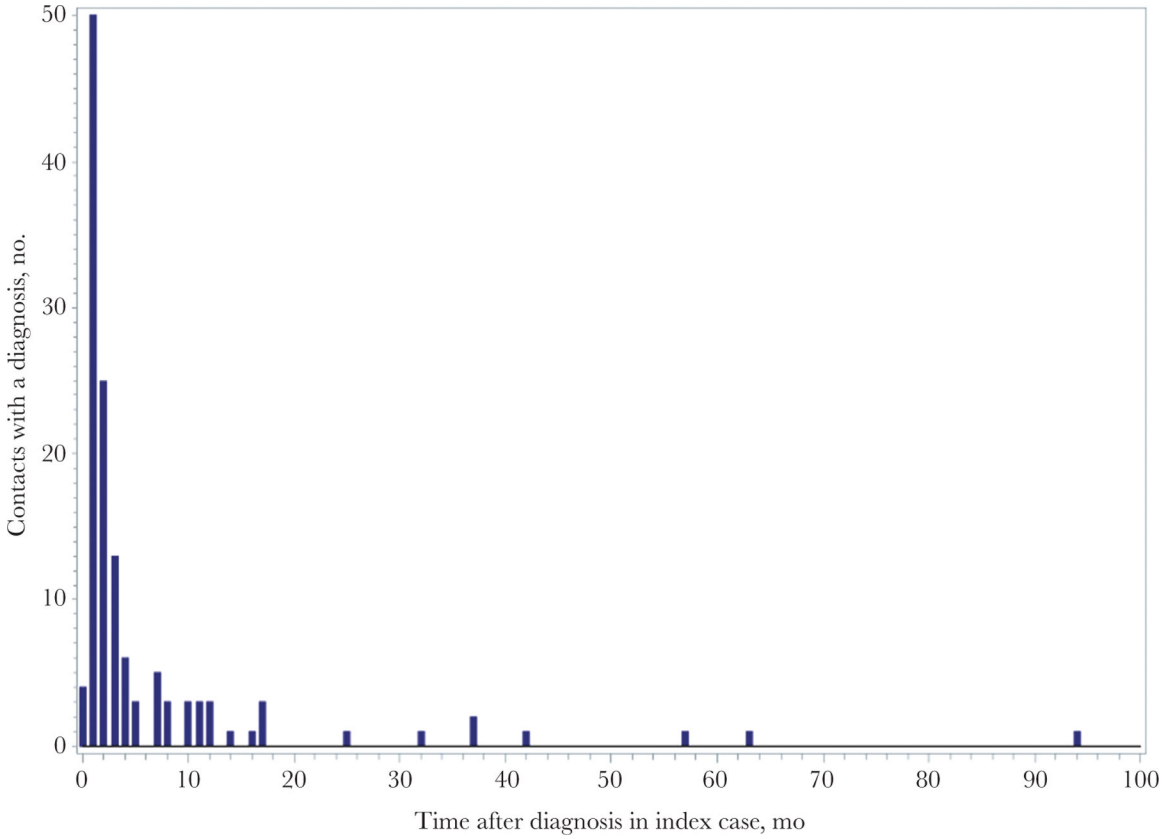

Figure 1.

Timing of tuberculosis (defined as the interval from index case treatment initiation to contact treatment initiation) among 131 contacts, by interval from index case treatment initiation; the 27 contacts in whom tuberculosis was diagnosed before the index cases received a diagnosis are excluded. Of note, tuberculosis registry matches were used to identify the diagnosis of tuberculosis among enrolled contacts after contact investigations were completed; tuberculosis registry matches were performed annually for 4 years after last site enrollment at 8 sites and annually for 2 years at one site. Since enrollment occurred over a 4-year period, contacts enrolled earlier in the study had a longer tuberculosis registry match observation period, with 100%, 94%, 76%, 55%, and 34% observed for 4, 5, 6, 7, and 8 years, respectively, after enrollment.

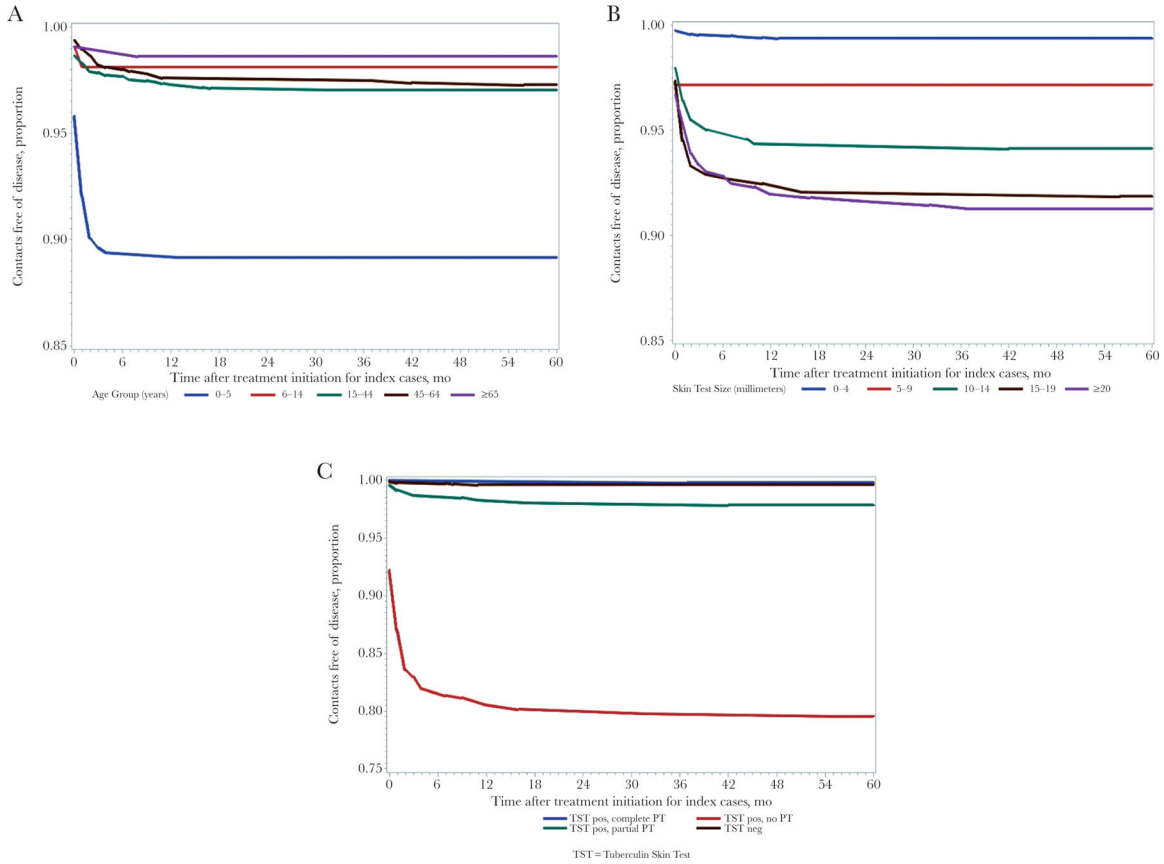

Figure 2.

Disease-free survival for 4490 contacts (158 with and 4332 without tuberculosis), by age group (*A*), screening tuberculin skin test (TST) result (*B*), and receipt of treatment for latent *Mycobacterium tuberculosis* infection (*C*). Tuberculosis registry matches were performed annually for 4 years after last site enrollment at 8 sites and annually for 2 years at 1 site. Since enrollment occurred over a 4-year period, contacts enrolled earlier in the study had a longer tuberculosis registry match observation period, with 100% and 94% observed for 4 and 5 years, respectively. Neg, negative; pos, positive; PT, preventive therapy.

Table 1.

Characteristics of 158 Contacts With a Diagnosis of Tuberculosis

Characteristic	Overall, No. (%)(n = 158)	Coprevalent, No. (%)(n = 81)	Incident, No. (%)(n = 77)
Age, y			
0–5	49 (31)	29 (36)	20 (26)
6–14	8 (5)	6 (7)	2 (3)
15–24	26 (16)	11 (14)	15 (19)
25–44	42 (27)	25 (31)	17 (22)
45–64	28 (18)	8 (10)	20 (26)
≥65	3 (2)	2 (2)	1 (1)
Sex			
Male	87 (55)	42 (52)	45 (58)
Female	71 (45)	39 (48)	32 (42)
Race			
White	9 (6)	3 (4)	6 (8)
Black	95 (60)	51 (63)	44 (57)
Asian/Pacific Islander	16 (10)	6 (7)	10 (63)
Hispanic	30 (19)	19 (23)	11 (14)
Other	8 (5)	2 (2)	6 (8)
Birthplace			
US/Canada	123 (78)	62 (77)	61 (79)
Other	35 (22)	19 (23)	16 (21)
HIV status			
Positive	4 (3)	3 (4)	1 (1)
Negative	54 (34)	24 (30)	30 (39)
Unknown	100 (63)	54 (67)	46 (60)
TST screening result			
Negative	6 (4)	3 (4)	3 (4)
Positive	115 (73)	57 (70)	58 (75)
Other[a]	37 (23)	21 (26)	16 (21)
Place of contact			
Household	115 (73)	64 (79)	51 (66)
Workplace	9 (6)	1 (1)	8 (10)
Social place	26 (16)	14 (17)	12 (16)
School	8 (5)	2 (2)	6 (8)
Means of identification			
Contact investigation	121 (77)	69 (85)	52 (68)
Registry match	37 (23)	12 (15)	25 (32)

Contacts were categorized as having coprevalent tuberculosis if disease was diagnosed before, at the same time as, or ≤1 month after the index cases' tuberculosis diagnosis and as having incident tuberculosis if disease was diagnosed >30 days after the index cases' diagnosis.

Abbreviations: HIV, human immunodeficiency virus; TST, tuberculin skin test.

[a]Not screened, partially screened, not eligible for screening, or unknown screening

Table 2.

Rates and Timing of Tuberculosis Among 4490 Contacts of Index Patients With Culture-Positive Tuberculosis, by Time Since Treatment Initiation for Index Cases

Time Since Treatment Initiation, mo[a]	Contacts With Tuberculosis, No. (Cumulative %[b])	Contacts Observed, No.	Tuberculosis Rate Among Contacts		Cumulative Tuberculosis Risk Among Contacts, %[c]
			Percentage	Events/ 10^5	
<0[d]	27 (17.1)	4490	0.60	601	0.6
0–12	118 (91.8)	4463	2.64	2644	3.2
0	4 (19.6)	4463	0.09	90	0.7
1	50 (51.3)	4459	1.12	1121	1.8
2	25 (67.1)	4409	0.57	567	2.4
3	13 (75.3)	4384	0.30	297	2.7
4	6 (79.1)	4371	0.14	137	2.8
5	3 (81.0)	4365	0.07	69	2.9
6	0 (81.0)	4362	0.00	0	2.9
7	5 (84.2)	4362	0.11	115	3.0
8	3 (86.1)	4357	0.07	69	3.0
9	0 (86.1)	4354	0.00	0	3.0
10	3 (88.0)	4354	0.07	69	3.1
11	3 (89.9)	4351	0.07	69	3.2
12	3 (91.8)	4348	0.07	69	3.2
13–24	5 (94.9)	4345	0.12	115	3.3
25–36	2 (96.2)	4340	0.05	46	3.3
37–48	3 (98.1)	4338	0.07	69	3.5
49–60	1 (98.7)	4075	0.02	25	3.5
61–72	1 (99.4)	3249	0.03	31	3.5
73–84	0 (99.4)	2293	0.00	0	3.5
85–96	1 (100)	1345	0.07	74	3.5

Tuberculosis registry matches were performed annually for 4 years after last site enrollment at 8 sites and annually for 2 years at 1 site. Since enrollment occurred over a 4-year period, contacts enrolled earlier in the study had a longer tuberculosis registry match observation period, with 100%, 94%, 76%, 55%, and 34% observed for 4, 5, 6, 7, and 8 years, respectively, after enrollment.

[a]Zero, 1–30, 31–60, 61–90, 91–120, etc. days were considered equivalent to months 0, 1, 2, 3, 4, etc.

[b] Calculated as the proportion of all contacts with tuberculosis (denominator, 158).

[c] Calculated as the proportion of all contacts observed who received a diagnosis of tuberculosis (denominator, 4490).

[d] Of 27 contacts with an interval of <0 months from index case treatment initiation to contact treatment initiation, 22, 2, 1, 1, and 1 initiated treatment 1–12, 13–24, 25–36, 61–72, and 85–96 months, respectively, before the index case.

Table 3.

Rates and Timing of Tuberculosis Among 499 Contacts With Positive Results of Tuberculin Skin Tests (TSTs) and No Treatment for Latent *Mycobacterium tuberculosis* Infection

Time Since Treatment Initiation, mo[a]	Contacts With Tuberculosis, No. (Cumulative %[b])	Contacts Observed, No.	Tuberculosis Rate Among Contacts		Cumulative Tuberculosis Risk Among Contacts, %[c]
			Percentage	Events/10^5	
<0[d]	13 (12.7)	499	2.6	2605	2.6
0–12	84 (95.1)	486	17.3	17 284	19.4
0	4 (16.7)	486	0.8	800	3.4
1	36 (60.0)	482	7.5	7469	10.6
2	21 (72.5)	446	4.7	4709	14.8
3	8 (80.4)	425	1.9	1882	15.8
4	5 (85.3)	417	1.2	1199	16.8
5	3 (88.2)	412	0.7	728	17.4
6	0 (88.2)	409	0.0	0	17.4
7	1 (89.2)	409	0.2	244	18.2
8	2 (91.2)	408	0.5	490	18.6
9	0 (91.2)	406	0.0	0	18.6
10	1 (92.2)	406	0.2	246	18.8
11	1 (93.1)	405	0.2	247	19.0
12	2 (95.1)	404	0.5	495	19.4
13–24	2 (97.1)	402	0.5	498	19.8
25–36	2 (99.0)	400	0.5	500	20.2
37–48	0 (99.0)	398	0.00	0	20.2
49–60	1 (100)	376	0.3	266	20.4
61–72	0 (100)	322	0.00	0	20.4
73–84	0 (100)	218	0.00	0	20.4
85–96	0 (100)	134	0.00	0	20.4

Tuberculosis registry matches were performed annually for 4 years after last site enrollment at 8 sites and annually for 2 years at 1 site. Since enrollment occurred over a 4-year period, contacts enrolled earlier in the study had a longer tuberculosis registry match observation period, with 100%, 96%, 85%, 64%, and 47% of contacts with positive results of TSTs observed for 4, 5, 6, 7, and 8 years, respectively, after enrollment.

[a] Zero, 1–30, 31–60, 61–90, 91–120, etc. days were considered equivalent to months 0, 1, 2, 3, 4, etc.

[b] Calculated as the proportion of all contacts with tuberculosis (denominator, 102).

[c] Calculated as the proportion of all contacts observed who received a diagnosis of tuberculosis (denominator, 499).

[d] Of the 13 contacts with an interval of <0 months from index case treatment initiation to contact treatment initiation, 12 and 1 initiated treatment 1–12 and 84–96 months, respectively, before the index case.