S3 Fig. Serial ultrathin section array of cell 3. A total of 69 serial ultrathin sections were cut to a thickness of 55 nm. The cell profile begins in the 2nd ultrathin section and ends at the 70th ultrathin section.
(TIFF)

S4 Fig. Serial ultrathin section array of cell 4. A total of 55 serial ultrathin sections were cut to a thickness of 55 nm. The cell profile begins in the 1st ultrathin section and ends at the 55th ultrathin section.
(TIFF)

S5 Fig. Serial ultrathin section array of cell 5. A total of 63 serial ultrathin sections were cut to a thickness of 55 nm. The cell profile begins in the 2nd ultrathin section.
(TIFF)

S1 Table. Dimensional properties determined from serial ultrathin sections of cell 1.
(XLSX)

S2 Table. Dimensional properties determined from serial ultrathin sections of cell 2.
(XLSX)

S3 Table. Dimensional properties determined from serial ultrathin sections of cell 3.
(XLSX)

S4 Table. Dimensional properties determined from serial ultrathin sections of cell 4.
(XLSX)

S5 Table. Dimensional properties determined from serial ultrathin sections of cell 5.
(XLSX)

Author Contributions

Conceived and designed the experiments: HY MY. Performed the experiments: HY. Analyzed the data: HY. Contributed reagents/materials/analysis tools: HY KC AA SM. Wrote the paper: HY MY SM.

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ORIGINAL ARTICLE

Use of the QuantiFERON®-TB Gold in Tube test for screening TB contacts and predictive value for active TB

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Abstract

Background: This study estimated the incidence of progression to active tuberculosis (TB) among contacts categorized by QuantiFERON®-TB Gold in Tube (QFT-GIT) test results and investigated other risk factors related to progression to TB. *Methods:* Contacts of patients with TB were tested using QFT-GIT and were followed up every 6 months at public health centers to detect clinical progression to TB. *Results:* Analysis of a retrospective cohort revealed that, of the 625 contacts, 168 were QFT-GIT positive and 457 were negative. Of these, 10 (6%) QFT-GIT-positive and two (0.4%) QFT-GIT-negative contacts progressed to TB during the follow-up period ($p < 0.01$, statistically significant). Multivariable logistic regression analysis revealed that QFT-GIT positivity ($p < 0.01$), contact of index patients with many other positive contacts ($p < 0.01$), household contact ($p = 0.014$), and untreated latent TB infection ($p = 0.047$) were independent risk factors for progression to TB during an average follow-up period of 637 days. *Conclusions:* Progression to TB among QFT-GIT-positive contacts was higher than among QFT-GIT-negative contacts. Other independent risk factors for progression to TB were index cases with more QFT-GIT-positive contacts as well as household contacts.

Keywords: *Tuberculosis, interferon-gamma release test, infection, diseases, QFT-GIT*

Introduction

Japan is a country with an intermediate tuberculosis (TB) burden, with a case notification rate of 16.1 per 100 000 population in 2013. In countries with low to intermediate TB morbidity, including Japan, one effective control measure is the detection and treatment of contacts with latent TB infection (LTBI). Interferon-γ release assays (IGRAs) are increasingly utilized as specific tools for detection of *Mycobacterium tuberculosis* infections in suspected contacts with LTBI; the World Health Organization (WHO) recommends their use together with the tuberculin skin test [1]. The ability of IGRAs to identify individuals who will progress to active TB after recent infection has been reported in several systematic reviews and meta-analyses [2–4] that include information regarding IGRA-detected incidence rate ratios (ratio of incidence rate of TB diseases among QuantiFERON®-TB (QFT)-positive risk persons to QFT-negative risk persons) as low as 2.11. There are few reports concerning other risk factors for progression to TB during follow-up. We assessed data regarding various risk factors for progression to TB, from contacts that had been screened using the QuantiFERON®-TB Gold in Tube (QFT-GIT) test, to evaluate its usefulness in identifying those likely to progress to active TB.

Materials and methods

Study design

This study was a retrospective analysis of TB patient contacts. In Japan, public health centers are responsible for contact investigations of index TB cases that are sputum smear positive or have cavitary chest X-ray findings. The target contacts included household contacts and workplace contacts, as well as

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hospital contacts that shared a room with patients diagnosed with TB. Contact investigations included an IGRA test 2 months after index case detection and follow-up radiographic examinations when necessary. If any contacts were positive for TB infection, health center staff obtained radiographs soon after diagnosis, and if the contacts had no X-ray findings suggestive of active TB, they were advised to undergo isoniazid (INH) treatment for latent tuberculous infection (TLTBI) for 6 months to reduce the risk of TB [5], unless the index case was identified as INH-resistant. TLTBI was self-administered and adverse reactions were followed up by clinicians every month. However, some contacts refused to undergo TLTBI due to fear of adverse drug reactions. The contacts were followed up with radiographic examinations every 6 months for 2 years. Contacts considered uninfected with TB, or with unknown TB infection status, did not typically undergo TLTBI. In some health centers, staff performed follow-up radiographic examinations every 6 months for 2 years, while other centers did not perform follow-up radiographic examinations. Only those with follow-up examinations were included in the study.

Subjects

By the end of 2013, we had collected QFT-GIT test results from follow-up of contacts in 2010 and 2011. We collected information about contacts, index cases, and contact locations. Contact information included age, nationality, QFT-GIT test results, and TLTBI status. Index case information included age, radiography findings, sputum smear results, and the number of QFT-GIT-positive contacts. Contact locations were categorized as 'household,' 'job,' 'hospital,' and 'others.' Other contact locations included various categories such as church, family members living in other houses, part-time home-helpers, which were considered less direct contact than households, hospitals, and workplaces. We collected data regarding which contacts had received TLTBI and whether they had completed the treatment. Interrupted TLTBI was defined as treatment that was discontinued within 6 months for reasons other than clinical progression to TB. Information regarding the reasons for not prescribing, accepting, or for interrupting INH treatment was not always available. HIV status was not examined in either contacts or index cases. Contacts were followed up with radiographic examinations every 6 months and upon developing clinical symptoms of TB. In cases of abnormal radiography findings, TB tests were continued with bacteriological examination of sputum or gastric juice specimens or specimens obtained with fiberoptic bronchoscopy. Contacts showing progression to TB were classified as having bacillary or non-bacillary TB based on the results of either culture or polymerase chain reaction for *M. tuberculosis* with sputum or gastric juice specimens or with specimens from fiberoptic bronchoscopy. Non-bacillary TB cases were diagnosed by radiologists and pulmonologists based on chest computed tomography (CT) scan findings and slow improvement after TB treatment.

The Internal Review Board of the Tuberculosis Research Institute approved the research protocol on January 24, 2013.

QFT-GIT testing

QFT-GIT tests (Qiagen, Melbourne, Australia) were carried out in hygienic or commercial laboratories according to the manufacturer's instructions [6].

Statistical analysis

Data were compared using the chi-squared test. Kaplan–Meier analysis was performed to compare individual independent variables in progression to TB over the duration of observation. Logistic regression was used to compare independent risk factors for clinical progression to TB, including potential predictors and confounders (performed using backward selection and likelihood methods) using Excel Toukei® 2010 (Social Survey Research Information Company, Tokyo, Japan).

Results

QFT-GIT positivity among total population

Multivariate analysis of QFT-GIT positivity among 2711 subjects showed a higher likelihood of QFT positivity among older contacts (adjusted odds ratio (aOR) = 1.039; 95% confidence interval (CI) = 1.029–1.049; $p < 0.001$); index cases with a higher number of QFT-GIT-positive contacts (aOR = 1.23; 95% CI = 1.17–1.28; $p < 0.001$); index cases with sputum smear grading results (aOR = 1.13; 95% CI = 1.00–1.28; $p = 0.049$); younger index patients (aOR = 0.983; 95% CI = 0.976–0.990; $p < 0.001$); and household contacts (aOR = 3.52; 95% CI = 2.56–4.85; $p < 0.001$).

Study population

A total of 2711 contacts were examined with the QFT-GIT test from 2010 to 2011 in 72 health centers during contact investigation. We excluded 2086 contacts from the analysis. Of these, 11 were excluded

as they already had active TB diseases at the time of contact investigation and the remaining 2075 were excluded for lack of follow-up for more than 3 months. We included 625 contact cases, arising from 168 index cases, from 49 health centers in the study. There were no differences in characteristics (geographical differences or differences between urban and rural areas) between health centers that reported 625 cases included in the study and those that did not report. The proportion of inclusion was greater among QFT-GIT-positive contacts (168/341; 49%) than QFT-GIT-negative contacts (457/2368; 14%). Table I shows the QFT-GIT test results and details of the study population by categories.

Treatment of latent TB infection

In all, 107 of 168 (64%) QFT-GIT-positive contacts started INH treatment, with 88 (82%) completing the 6-month regimen. There were no factors positively related to TLTBI among QFT-GIT-positive contacts. The time at which TLTBI was stopped

Table I. Demographic characteristics of total participants and study population.

	Total		Study population	
Characteristic	*n*	QFT-GIT-positive	*n*	QFT-GIT-positive
Total	2711	341 (13%)	625	168 (27%)
Age (years)				
0–19	222	22 (10%)	38	8 (21%)
20–39	1205	101 (8%)	236	39 (17%)
40–59	1021	142 (14%)	263	78 (30%)
≥60	253	75 (30%)	87	42 (48%)
Unknown	10	1 (10%)	1	1 (100%)
Nationality				
Japanese	2478	306 (12%)	590	147 (25%)
Foreigner	85	26 (31%)	19	14 (74%)
Unknown	148	9 (6%)	16	7 (44%)
X-ray findings of index cases				
Cavitary	860	140 (16%)	210	78 (37%)
Non-cavitary	1244	124 (10%)	393	83 (21%)
Unknown	607	77 (13%)	22	7 (32%)
Sputum smear of index cases				
–	262	27 (10%)	38	19 (50%)
±	380	34 (9%)	117	17 (15%)
1+	703	89 (13%)	258	52 (20%)
2+	473	58 (12%)	116	35 (30%)
3+	434	71 (16%)	92	44 (48%)
No. of QFT-GIT-positive contacts of index cases				
0	869	0 (0%)	168	0 (0%)
1–4	1007	208 (21%)	240	126 (53%)
5–9	252	38 (15%)	198	33 (17%)
≥10	74	33 (45%)	11	6 (55%)
Unknown	508	62 (12%)	8	3 (38%)
Age of index cases (years)				
0–19	479	65 (14%)	5	3 (60%)
20–39	295	58 (20%)	106	29 (27%)
40–59	437	69 (16%)	62	33 (53%)
≥60	1219	141 (12%)	445	101 (23%)
Unknown	281	8 (3%)	7	2 (28%)
Place of contacts				
Household	547	111 (20%)	142	67 (47%)
Hospital	908	76 (8%)	264	40 (15%)
Job	610	89 (15%)	99	27 (27%)
Others	646	65 (10%)	120	34 (28%)
TLTBI				
No TLTBI	2284	133 (6%)	504	61 (12%)
No interruption	163	147 (90%)	102	91 (89%)
Interrupted	25	15 (60%)	12	9 (75%)
Others	49	39 (80%)	7	7 (100%)
No information	190	7 (4%)	0	0

QFT-GIT, QuantiFERON®-TB Gold in Tube; TLTBI, treatment of latent tuberculous infection.

varied. The duration of treatment ranged from 1 month to 5 months among the interrupted group. Of 457 QFT-GIT-negative contacts, 14 (3%) were treated with INH. The reasons for offering INH treatment to these 14 QFT-GIT-negative contacts were not available.

Follow-up and progression to clinical TB

All contacts with normal radiography findings (or those not diagnosed with TB at the time of the QFT-GIT examination) were followed up after 91–1578 days (average 637 days). The duration of the follow-up period among QFT GIT-positive and -negative contacts was 619 and 643 days, respectively. Over the follow-up period, 12 contacts were identified as having developed active TB, including 10 (83%) cases of bacillary TB. In one pair, the index case and the supposed secondary TB case were found to be identical, based on variable number tandem repeat analysis, although the remaining 11 cases were not examined by genetic fingerprinting. Among the six cases in which results of drug susceptibility tests were available, none of the *M. tuberculosis* infections was found to be resistant to INH.

Table II shows the characteristics of TB patient contacts that progressed to TB during follow-up.

Table III shows the numbers and percentages of contacts that progressed to active (including both bacillary and non-bacillary) and bacillary TB, according to QFT-GIT status and LTBI treatment. Among 168 subjects with a positive QFT-GIT result at the time of screening, 10 (6%) were diagnosed with active TB, including 8 (5%) cases of bacillary TB. Of 90 QFT-GIT-positive contacts with uninterrupted INH treatment, 1 case progressed to active TB during INH treatment (SN 11). No cases of TB developed after completion of INH. Two of the 459 (0.4%) QFT-GIT-negative contacts developed active TB during the follow-up period. The rate of progression for QFT-GIT-positive contacts (6%) was significantly greater than for negative contacts (0.4%; $p < 0.001$).

During the first and second years of follow-up, there was no difference in the incidence of clinical development to TB. This was true for both the whole group of follow-up contacts (1.0/100 and 0.7/100 person-years during the first and second years, respectively) and for QFT-GIT-positive follow-up contacts (3.3/100 and 2.8/100 person-years during the first and second years, respectively).

Table IV shows the proportion of contacts that progressed to active TB during follow-up, according to various factors. QFT-GIT-positive individuals and household contacts showed a higher risk of progression to active TB than QFT-GIT-negative and hospital contacts, respectively.

Table II. List of contacts who progressed to clinical TB during follow-up after QFT-GIT testing.

					Investigation of contacts						TLTBI index cases			
SN	Age (years)	QFT	Result	Duration of contact (days)	Duration from last contact to QFT (days)	Location	Sputum smear exam	Other bacillary	DST (INH)	VNTR	Duration from last contact to TB diseases (days)	Status	Case	X-ray findings	Sputum smear exam
1	7	>10	Positive	Unknown	14	House	Negative	Negative	Unknown	ND	979	Unknown	A	Cavitary	3+
2	8	1.73	Positive	Unknown	14	House	Negative	Positive	Unknown	ND	979	No	A	Cavitary	3+
3	42	1.93	Positive	365	0	House	Negative	Positive	Unknown	ND	98	No	B	Non-cavitary	1+
4	22	0.14	Negative	365	0	House	Negative	Positive	Susceptible	ND	303	No	B	Non-cavitary	1+
5	14	3.92	Positive	365	0	House	Negative	Positive	Susceptible	Same as index case	100	No	B	Non-cavitary	1+
6	60s	5.19	Positive	130	134	Other	Negative	Positive	Unknown	ND	448	No	C	Cavitary	2+
7	50s	>10	Positive	130	134	Other	Negative	Positive	Unknown	ND	681	No	C	Cavitary	2+
8	50s	0.05	Negative	Unknown	55	Job	Positive	Positive	Susceptible	ND	1162	No	D	Non-cavitary	Negative
9	50s	>8	Positive	308	65	Other	Unknown	Positive	Susceptible	ND	707	Interrupted	E	Non-cavitary	2+
10	40s	>10	Positive	141	137	House	Negative	Positive	Susceptible	ND	136	No	F	Non-cavitary	3+
11	40s	3.12	Positive	150	62	Job	Negative	Positive	Susceptible	ND	94	On TLTBI	G	Cavitary	3+
12	40s	0.42	Positive	90	68	House	Negative	Unknown	Unknown	ND	121	Unknown	H	Non-cavitary	±

DST (INH), drug susceptibility test result to isoniazid; Duration of contact, duration from the first TB-related symptom of index case until the last date of contact before diagnosis; Duration from last contact to QFT, duration from the last contact before diagnosis of TB of index case until QFT examination of contacts; Duration from last contact to TB diseases, duration from the last contact before diagnosis of TB of index case until diagnosis of TB of contact; ND, not done; QFT, QuantiFERON®-TB Gold in tube; SN: serial number; TB, tuberculosis; TLTBI, treatment of latent tuberculous infection; VNTR, variable number tandem repeat.

Table III. Risk of progression to active tuberculosis during follow-up by QFT-GIT results at the baseline.

QFT-GIT Status	*n*	No. (%) with active TB at follow-up (including bacillary)	No. (%) with bacillary TB at follow-up
QFT-GIT positive	168	10 (6%)	8 (5%)
With completion of TLTBI	90	0 (0%)	0 (0%)
During TLTBI	1	1	1
With interrupted TLTBI	9	1 (12%)	1 (12%)
With TLTBI but without enough information	7	2 (29%)	0 (0%)
Without TLTBI	61	6 (10%)	6 (10%)
QFT-GIT negative	457	2 (0.4%)	2 (0.4%)
With completion of TLTBI	11	0 (0%)	0 (0%)
With interrupted TLTBI	3	0 (0%)	0 (0%)
Without TLTBI	443	2 (0.5%)	2 (0.5%)
Total	625	12 (2%)	10 (2%)

QFT-GIT, QuantiFERON®-TB Gold in Tube; TB, tuberculosis; TLTBI, treatment of latent tuberculous infection.

Table V lists the variables that were independently associated with clinical progression to TB by multivariate analysis. The strongest association was positive QFT-GIT test result, with an OR of 14.9 for active TB. This finding did not take into account the effects of INH treatment in reducing the rate of progression or that most QFT-GIT-positive contacts received treatment (60%). Other calculations using numerical variables related to interferon-γ production with QFT-GIT, rather than the dichotomous positivity of QFT-GIT, also showed a significantly increased risk of TB with increasing interferon-γ production. Other independent variables associated with progression to active TB were the number of QFT-GIT-positive contacts with the index case for each contact, lack of TLTBI, and household contacts.

Figure 1 shows the proportion of cases progressing to TB by QFT-GIT status. Progression to TB occurred in both the first and second years. Kaplan–Meier analysis showed significant difference in the risk of progression to TB diseases between QFT-GIT-positive and -negative contacts at the time of examination.

Discussion

This study demonstrated that the QFT-GIT test is useful for predicting future clinical progression to TB and for targeting LTBI treatment. In our previous study [7], the proportion of QuantiFERON®-TB Gold (QFT-G)-positive individuals among contacts who developed clinical TB during the follow-up period was as low as 52%; the proportion in the current QFT-GIT study was 83% (10/12). The same calculations for bacillary cases were 57% for QFT-G and 80% for QFT-GIT. This difference might reflect the higher sensitivity of QFT-GIT compared with QFT-G for detection of TB infections that may develop into clinical disease.

We have previously demonstrated that contact with highly infectious TB cases, as well as lack of TLTBI, were factors related to increased risk of future clinical progression to TB [7]. In the present study, we have added household contact as an independent risk factor for progression to TB. One study in Poland demonstrated that close contact showed high risk of progression to TB compared with periodic contacts. Close contacts in this study included both household members and those that shared a room at work [8]. Another study in Amsterdam reported that contacts in the first ring of contact examination showed higher risk of progression to TB diseases than contacts in the second ring [9]. Guidelines in Japan recommended performing contact investigations to determine the point of contact with infectious TB cases [10]. Close contacts usually fall into three categories in Japan. The first category includes household members. The second category includes other persons who share the same air for daily life including workplace contacts. The third category includes those who share the same air in hospitals. Household members are usually the closest contacts of patients with TB. Quantification of the length of time that contacts share a room would be a better indicator of contact closeness; however, those data were not available for the present study. Another study showed longer contact periods to be a risk factor for QFT-GIT conversion but not for progression to active TB [11]. To our knowledge, this is the first study to demonstrate that differences in contact patterns influence the risk of progression to TB during the follow-up period. Hospital contacts included staff members. Hospital staff are known to be at high risk of TB in Japan, and QFT-G positivity of hospital staff was high [12]. Therefore, contacts in hospitals may have been infected earlier and the risk of progression to TB diseases may be lower than that in other contact populations.

Table IV. Univariate analysis of risk of progression to active TB.

	All		Progression to active TB			Incidence/100 person-years	
Characteristic	*n*	Person-years	*n*	%	OR	*p* value	
No. of subjects	625	1089	12	1.9%			1.1
Contact persons' information							
Age (years)							
0–19	38	66	3	7.9%	–		4.54
20–39	105	180	1	1.0%	0.11	0.1	0.56
40–59	263	467	7	2.7%	0.32	0.23	1.5
≥60	87	137	1	1.1%	0.14	0.16	0.73
Unknown	1	1	0	0.0%			0
Nationality							
Japanese	590	1028	12	2.0%	–		0
Foreigner	19	25	0	0.0%	0	–	0
Unknown	16	36	0	0.0%	0	–	0
QFT-GIT							
Negative	457	805	2	0.4%	–		0.25
Positive	168	285	10	6.0%	14.4	<0.01	3.51
FT-GIT value							
<0.1	361	632	1	0.3%			
0.1–0.35	96	173	1	1.0%	3.79	0.89	0.58
0.35–1	51	88	1	2.0%	7.2	0.59	1.14
1–3	48	78	2	4.2%	15.7	0.04	2.56
3–5	17	25	2	11.8%	48	<0.01	8
5–8	10	18	1	10.0%	40	0.05	5.68
>8	30	55	4	13.3%	55.4	<0.01	7.22
Other positive	12	21	0	0.0%			
TLTBI QFT positive							
No TLTBI	504	882	8	1.6%	–		0.91
Completed	102	172	1	1.0%	0.61	0.99	0.58
Interrupted	12	23	1	8.3%	5.64	0.52	4.31
Others	7	12	2	28.6%			17.1
No information	0	0	0				
Index persons' information							
Age (years)							
0–19	5	9	0	0.0%	–		0
20–39	36	62	2	5.6%	–		3.24
40–59	62	103	5	8.1%	1.49	0.95	4.84
≥60	445	797	5	1.1%	0.19	0.16	0.63
X-ray findings							
Cavitary	210	373	5	2.4%			1.34
Non-cavitary	393	682	7	1.8%	0.74	0.84	1.03
Unknown	22	34	0	0.0%	0	0.97	0
Sputum smear							
–	38	67	2	5.3%	1.22	0.82	2.99
±	117	210	1	0.9%	0.19	0.24	0.48
1+	258	429	3	1.2%	0.26	0.15	0.7
2+	116	209	3	2.6%	0.58	0.75	1.43
3+	92	170	4	4.3%	–		2.35
No. of QFT-GIT-positive contacts							
0	168	313	0	0%			
1–4	240	428	6	2.5%	–		1.4
5–9	198	319	4	2.0%	0.8	0.99	1.25
≥10	78	125	2	2.6%	1.03	0.7	1.6
Place of contact							
Household	142	238	7	4.9%	–		2.95
Hospital	264	472	0	0.0%	0	<0.01	0
Workplace	99	167	2	2.0%	0.4	0.41	1.2
Others	120	212	3	2.5%	0.49	0.48	1.41

OR, odds ratio; QFT, QuantiFERON®-TB Gold in Tube; TLTBI, treatment of latent tuberculous infection.

Table V. Logistic regression for the risk of progression to active tuberculosis during follow-up.

Factor	Adjusted OR (95% CI)	*p* value
QFT-GIT positivity	14.9 (2.77–80.3)	0.002
No. of QFT-GIT-positive contacts of same index case	1.33 (1.11–1.59)	0.002
Treatment of latent TB infection	0.23 (0.05–0.98)	0.047
Household contact	6.04 (1.45–25.2)	0.014

CI, confidence interval; OR, odds ratio; QFT-GIT, QuantiFERON®-TB Gold in Tube; TB, tuberculosis.

Our study has a number of limitations. The primary limitation is the large proportion of contacts that were not followed up. Because of the retrospective nature of this study, there is a potential for serious selection bias. The study population included more QFT-GIT-positive individuals, more contacts of infectious index cases with many QFT-GIT-positive contacts, and an increased proportion of older index patient contacts, than the total population. QFT-GIT positivity and index cases with large numbers of QFT-GIT-positive contacts are both factors related to an increased risk of progression to TB. Therefore, the risk of clinical progression to TB may be overestimated. The duration of observation among study cases also varies and we investigated with Kaplan–Meier method and calculated the incidence rate of TB disease. Another limitation was that since this was a retrospective cohort study of the follow-up of TB contacts in field conditions, the extent of collected information was limited and there were some missing data that could weaken the value of the study. The third limitation was the possibility of new exposures after initial QFT-GIT testing, particularly since fingerprinting was not performed for many index–contact pairs, although the risk of re-infection is not high in Japan because the annual risk of tuberculous infection is estimated to be 0.05–0.07% [13]. The index case of case SN 8 was smear negative and might be due to other infection, although no other contact history was detected. Finally, the possibility of over-diagnosis of non-bacillary TB cases during follow-up and the possibility of under-diagnosis need to be discussed, although the risk of under-diagnosis is lower, as radiography screening of the contacts in this study was performed at public health centers.

In summary, progression to TB was higher among QFT-GIT-positive contacts than QFT-GIT-negative contacts. Other independent risk factors for

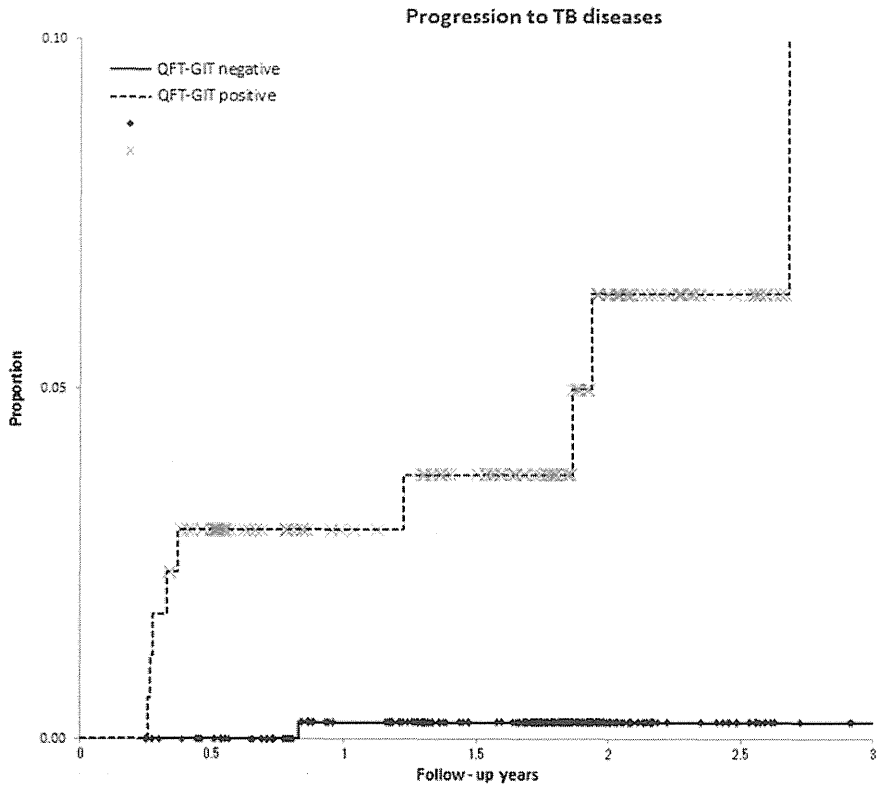

Figure 1. Progression to tuberculosis (TB) diseases. QFT-positive and -negative contacts at the time of contact examination were compared as to the proportion of progression to clinical TB during the observation period. Positive persons had a higher risk of progression to TB diseases. The Kaplan–Meier method was used to compare the risk.

progression to TB were index cases with more QFT-GIT-positive contacts and household contacts.

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