

# A Probabilistic Transmission Model to Assess Infection Risk from *Mycobacterium Tuberculosis* in Commercial Passenger Trains

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The objective of this article is to characterize the risk of infection from airborne *Mycobacterium tuberculosis* bacilli exposure in commercial passenger trains based on a risk-based probabilistic transmission modeling. We investigated the tuberculosis (TB) infection risks among commercial passengers by inhaled aerosol *M. tuberculosis* bacilli and quantify the patterns of TB transmission in Taiwan High Speed Rail (THSR). A deterministic Wells-Riley mathematical model was used to account for the probability of infection risk from *M. tuberculosis* bacilli by linking the cough-generated aerosol *M. tuberculosis* bacilli concentration and particle size distribution. We found that (i) the quantum generation rate of TB was estimated with a lognormal distribution of geometric mean (GM) of 54.29 and geometric standard deviation (GSD) of 3.05 quantum/h at particle size  $\leq 5 \mu\text{m}$  and (ii) the basic reproduction numbers ( $R_0$ ) were estimated to be 0.69 (0.06–6.79), 2.82 (0.32–20.97), and 2.31 (0.25–17.69) for business, standard, and nonreserved cabins, respectively. The results indicate that commercial passengers taking standard and nonreserved cabins had higher transmission risk than those in business cabins based on conservatism. Our results also reveal that even a brief exposure, as in the bronchoscopy cases, can also result in a transmission when the quantum generation rate is high. This study could contribute to a better understanding of the dynamics of TB transmission in commercial passenger trains by assessing the relationship between TB infectiousness, passenger mobility, and key model parameters such as seat occupancy, ventilation rate, and exposure duration.

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**KEY WORDS:** Airborne transmission; modeling; passenger trains; probabilistic risk assessment; tuberculosis

## 1. INTRODUCTION

Airborne transmission is known to be a route of infection for diseases. Tuberculosis (TB)

transmitted in indoor overcrowded settings, such as hospital buildings, commercial airliners, and passenger trains/buses, is a typical example of airborne infection.<sup>(1–7)</sup> TB remains a leading cause of death worldwide, killing an estimated 3 million people annually and an estimate of one-third of the world's population is infected with tuberculosis bacilli (World Health Organization (WHO), 2006; [www.who.int/tb/publications/2006/en/index.html](http://www.who.int/tb/publications/2006/en/index.html)). All TB outbreaks have been associated with cough-generating procedures,<sup>(8)</sup> bronchoscopy,<sup>(9)</sup> endotracheal intubation and suctioning,<sup>(10)</sup> open abscess irrigation,<sup>(11)</sup> and autopsy.<sup>(12)</sup>

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TB infection is caused by inhalation of *Mycobacterium tuberculosis* bacilli in a droplet nucleus form with a diameter  $\leq 5 \mu\text{m}$ .<sup>(13)</sup> Droplet nuclei settle slowly and are airborne for several hours. The spread of TB in indoor environments is strongly influenced by the number of infected airborne droplet nuclei and the viability of the *M. tuberculosis* bacilli. Thus, it is recognized that TB outbreaks occurred under crowded living conditions with prolonged close exposure to an infectious person ([www.sciencedaily.com/releases/1999/02/990201072734.htm](http://www.sciencedaily.com/releases/1999/02/990201072734.htm)).

Based on one case report, 21 of 60 hospital staff (35%) became infected while working on a ward that housed an undiagnosed TB patient for seven hours.<sup>(14)</sup> Kenyon *et al.*<sup>(15)</sup> indicated a transmission of multidrug-resistant TB during a long airplane flight. Miller *et al.*<sup>(16)</sup> estimated the risk of TB transmission aboard an aircraft by conducting a contact investigation of passengers. Moore *et al.*<sup>(3)</sup> provided the findings to support the limited transmission of TB from a potentially highly infectious passenger to other persons during extended train and bus travel. These researchers<sup>(3,15,16)</sup> performed follow-up tuberculin skin tests (TSTs) for systematically screening passengers, which is the most easy and quick test method for TB infection.<sup>(3)</sup> Nicas,<sup>(17)</sup> Ko *et al.*,<sup>(5)</sup> and Jones *et al.*<sup>(7)</sup> characterized the relationships among the TB infection, dose, and risk, and estimated the efficacy of different respiratory protective devices based on a predictable mathematical modeling. Ko *et al.*<sup>(5)</sup> employed a steady-state four-compartment model to predict TB transmission in a commercial aircraft. Recently, Jones *et al.*<sup>(7)</sup> used a quantitative microbial risk assessment framework to model the spatiotemporal variability of exposure to *M. tuberculosis* bacilli and the infection risk also predicted in a Boeing 747-400 aircraft. Thus, the TB risk assessment in commercial passenger transport vehicles is worth studying. Little is known, however, about the relationship among overcrowding, exposure duration, and risk of infection in commercial passenger trains.

The incidence and mortality rates of TB infection in Taiwan are 74.6–62.0 (per 1,000,000) and 5.7–3.3 (per 1,000,000) from 2002 to 2008, respectively (Taiwan CDC). Last year, Taiwan High Speed Rail (THSR) transported nearly 3 million passengers per month during January 2007 to May 2009. There are eight stations situated from northern to southern Taiwan, namely, Taipei Banciao, Taoyuan, Hsinchu, Taichung, Chiayi, Tainan, and Zuoying stations, respectively. THSR also plays a key role in traveling,

entertainment, and commercial use in the Taiwan region. Hence, the objective of this article is to characterize the risk of infection from airborne *M. tuberculosis* bacilli exposure in commercial passenger trains based on a risk-based probabilistic transmission modeling. We investigated the TB infection risks among commercial passengers by inhaling aerosol *M. tuberculosis* bacilli and quantified the patterns of TB transmission in THSR.

In this present research, the cough-generated aerosol *M. tuberculosis* bacilli concentration and particle size distribution were linked to estimate the infectious risks for susceptible hosts in THSR. This study provided an opportunity to get insights into the pattern of TB transmission and its potential control measures for plausible scenarios occurring in THSR. This study also could contribute to a better understanding of the dynamics of TB transmission in commercial passenger trains by assessing the relationship between TB infectiousness, passenger mobility, and key model parameters such as seat occupancy, ventilation rate, and exposure duration.

## 2. MATERIALS AND METHODS

### 2.1. Aerosol Tuberculosis Concentration

A valuable data set was obtained from the experiment based on Fennelly *et al.*<sup>(18)</sup> These data represent the unique opportunity to examine the linkage between experimental aerosol TB concentrations and particle size distribution per infectious person. Fennelly *et al.*<sup>(18)</sup> first quantified the aerosol concentration and size distribution of emission characteristics of *M. tuberculosis* bacilli from TB patients by the Anderson sampler for culturing cough-generated aerosols and estimating the infectivity simultaneously.

Briefly, (1) the subject was instructed to cough into the tubing for five minutes or for as long as he/she was comfortable while the author sampled the air from the chamber with both impactors and recorded the cough frequency. While the subject rested after the first session of coughing, the plates were replaced with fresh plates and were removed and labeled; (2) three experimental tests were conducted including sputum smear grades, sputum culture (CFU), and culturable cough-generated aerosols (CFU) for 16 subjects; and (3) particle size distributions of aerosols culturable TB were collected by Anderson impactors during the first day of each subject. Here

the size ranges were divided into 0.65–1.1, 1.1–2.1, 2.1–3.3, 3.3–4.7, 4.7–7.0, and >7.0  $\mu\text{m}$ .

Based on the relationship between experimental aerosol TB concentrations and particle size distribution per infectious person, this study adopted the software Table Curve 2D (Version 5.01 2002, SYSTAT Software Inc., Richmond, CA, USA) to perform the curve fitting for estimating the average aerosol culturable TB concentration based on the experimental results. We also use the Kolmogorov-Smirnov (K-S) test to perform the goodness of fit of distribution. The particle size diameters  $\leq 5 \mu\text{m}$  were also considered to define and quantify the infectious quantum generation rates of aerosol TB. The Monte Carlo simulation was performed to quantify the quantum generation rate by using Crystal Ball software (Version 2000.2, Decisioneering, Inc., Denver, CO, USA).

## 2.2. Exposure Factors

In this study, we were interested in the infection risk from commercial passengers' occupancy in THSR. Each train had 12 cabins in which the numbers of 1–5 and 7–10, 6, and 11–12 were standard, business, and nonreserved cabins, respectively. On average, the ticket prices were nearly 1.6 and 0.9 times the business and standard to nonreserved cabins, respectively. Moreover, there were on average 66, 86, and 80 seats in standard, business, and nonreserved cabins, respectively. Based on the cabin-dependent seat utilization percentages in THSR, the risk of infection for susceptible host would be estimated.

Exposure factors affecting the TB transmission included ventilation, population numbers in ventilation room, exposure duration, and quantum generation rate of the infected TB patient. This study assumed that the ventilation values were 3 air changes per hour (ACH) in THSR. This study ignored the loss/contributed ventilation by commercial passengers on board or off the train. Besides, the population numbers in business, standard, and nonreserved cabins were estimated by the seat utilization percentages times the total seat numbers in that specific cabin. Exposure duration was quantified by the average distance of total commercial passengers taken as the average kilometers per person. The Monte Carlo simulation was performed to quantify the uncertainty of exposure factors by using Crystal Ball software (Version 2000.2, Decisioneering, Inc., Denver, CO, USA).

## 2.3. Risk of Infection and Basic Reproduction Number

In dealing with indoor TB transmission, one usually employs the well-known deterministic Wells-Riley mathematical model to account for the probability of infection risk from *M. tuberculosis bacilli*.<sup>(1,4–6,19–22)</sup>

Riley *et al.*<sup>(23)</sup> made two assumptions to quantify the indoor respiratory infections. The first assumption implies that an infectious droplet nucleus has an equal chance of being anywhere within a building's airspace. The second assumption implies that the quantum generation rate and the outdoor air supply rate remain constant with time. We used the Wells-Riley mathematical equation<sup>(19)</sup> to estimate the transmission potential of aerosol TB in THSR:

$$P = \frac{D}{S} = 1 - \exp \left\{ -\frac{Iqpt}{Q} \left( 1 - \frac{V}{Qt} \left[ 1 - \exp \left( -\frac{Qt}{V} \right) \right] \right) \right\}, \quad (1)$$

where  $P$  is the probability of infection for susceptible population,  $S$  is the number of susceptible individuals,  $D$  is the number of infected cases among  $S$  individuals susceptible,  $I$  is the number of sources of infection,  $q$  is the quantum generation rate of TB concentration (quanta/h) considering a best-fitted distribution of the experimental database,  $p$  is the pulmonary ventilation rate of susceptible individuals ( $\text{m}^3/\text{h}$ ),  $t$  is the exposure duration (hours),  $Q$  is the fresh air supply rate that removes the infectious aerosol per unit of time ( $\text{m}^3/\text{h}$ ), and  $V$  is the volume of the ventilated space ( $\text{m}^3$ ).

To model the respiratory infection risk, we incorporated  $I = 1$  and  $S = n - 1$  into Equation (1) to estimate the basic reproduction number ( $R_0$ ) for quantifying the average number of successful secondary infection cases generated by a typical primary infected case within an entirely susceptible population as:

$$R_0 = (n - 1) \times P, \quad (2)$$

where  $n$  represents the total number of individuals in the ventilation airspaces. The cabin-specific  $R_0$  values can then be estimated by using Equation (2).

$R_0$  is defined as the average number of successful secondary infection cases generated by a typical primary infected case in an entirely susceptible population.<sup>(24)</sup> Average  $R_0$  of 1 means that the disease is in endemic equilibrium within the population.

Date	Category	Stations	Seat Utilization (%)		
			Standard Cabin	Business Cabin	Nonreserved Cabin
2009/08/14	Weekend	Taichung–Zuoying	55	29	38
2009/08/14	Weekend	Taichung–Taipei	66	12	45
2009/08/16	Weekend	Taipei–Taichung	66	12	54
2009/08/19	Weekday	Taichung–Taipei	61	50	66
2009/08/19	Weekday	Taipei–Taichung	48	18	58

**Table I.** Investigation of the Actual Seat Utilization in THSR Among Five Practices

### 3. RESULTS

#### 3.1. Cabin-Dependent Seat Utilization

Cabin-dependent seat utilization percentages are changeable scenarios due in part to the weekday, weekend, or nonpreferential/preferential prices periods. Experiment investigations were randomly chosen: one train on Wednesday, Friday, and Sunday from Taichung to Taipei, Taichung to Zuoying, and Taipei to Taichung during the periods from August 14 to 19, 2009, respectively. Table I represents the cabin-dependent occupant seats and estimates the seat utilization. The seat utilization was higher in standard cabins than in nonreserved and business cabins, respectively, with a geometric mean (GM) of 57.49%, 50.56%, and 19.61% and a geometric standard deviation (GSD) of 1.26, 1.27, and 1.76 for standard, nonreserved, and business cabins.

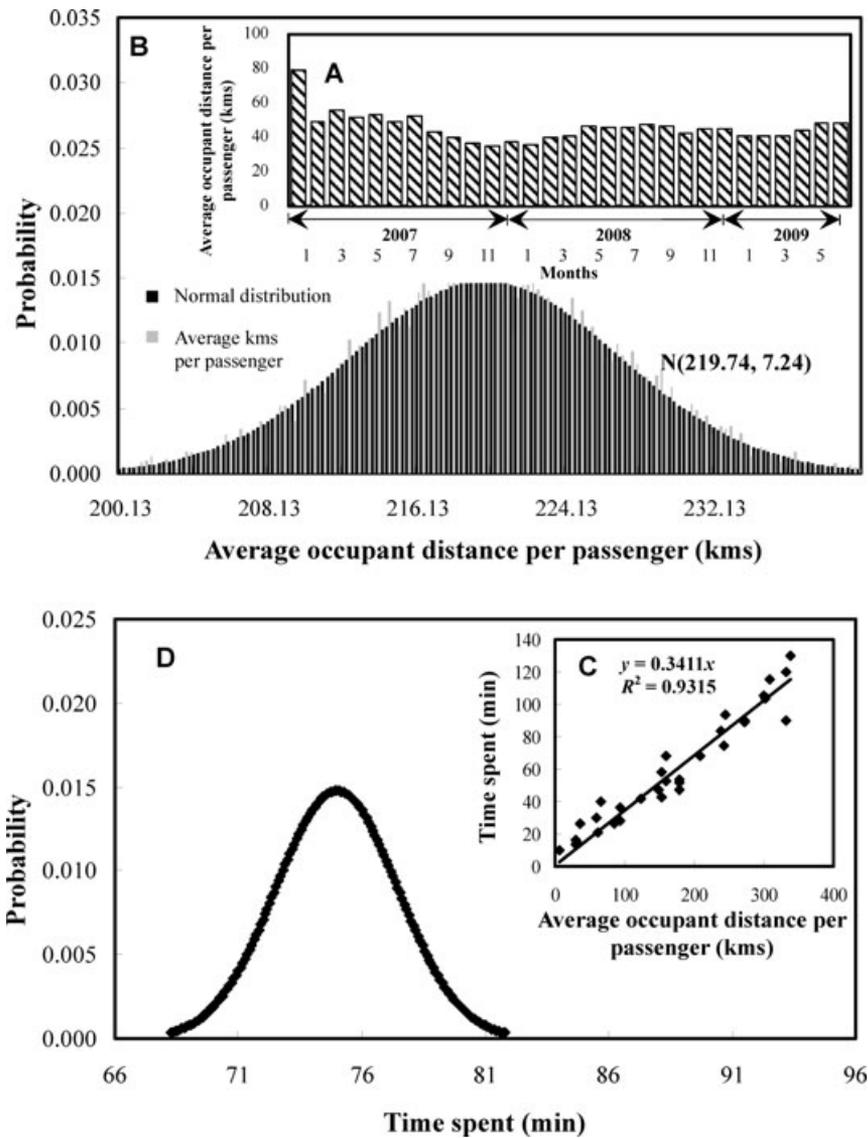
#### 3.2. Exposure Duration

Fig. 1A shows the monthly average occupant distance (km) per passenger for the period from January 2007 to May 2009. Results indicated that the average distance per passenger was 226.86 and 214.96 km in 2007 and 2008, respectively. Fig. 1B shows that the normal distribution best describes the average occupant distance per passenger with a mean of 219.74 km and a standard deviation of 7.24. Moreover, in order to estimate the exposure duration per commercial passenger, we used the relationship between the average occupant distance per passenger and time spent in THSR and a good correlation was found ( $R^2 = 0.93$ ) (Fig. 1C) where  $R^2$  means the coefficient of determination of the linear regression. Fig. 1D shows the probability distribution of time spent for a commercial passenger, indicating that the highest probability was given at 74 minutes.

#### 3.3. Estimated Tuberculosis Generation Rates

Figs. 2A–D show the relationship between the particle size diameter and aerosol culture (CFU) of the tested subjects with five-minute sampler time adopted from Fennelly *et al.*<sup>(18)</sup> The best-fitting equation ( $R^2 = 0.91$ – $0.99$ ) is presented in Table II for three subjects based on Figs. 2A, 2B, and 2D, respectively. Fig. 2A shows that the highest cultural TB concentration was 633 CFU where 309 CFU (49%) and 572 CFU (90%) were isolated from 1.1–2.2  $\mu\text{m}$  and 0.65–3.3  $\mu\text{m}$  in aerodynamics diameter. For two other test subjects, the aerosol culture concentration of 3 and 4 CFU had higher TB concentration in 0.65–1.1  $\mu\text{m}$  (Fig. 2B) and 1.1–4.7  $\mu\text{m}$  (Fig. 2D), respectively. The particle size distribution of cough-generated aerosol was slightly larger, with a mode in 1.1–2.1  $\mu\text{m}$  in aerodynamic diameter (Fig. 2C). These results implied that cough-generated culturable aerosol shows high variability for each subject (Figs. 2A–D).

The size-dependent quantum generation rates ( $q$ ) were estimated by averaging the fitted equation (Table II) from the particle size-dependent aerosol TB concentration. The unit transfer from aerosol culture to quantum generation rates (quanta/h) was adopted from Jones *et al.*,<sup>(7)</sup> which gives the assumption that 1 CFU is equal to 1 quantum, and the sampler time was divided into five minutes simultaneously. We averaged the size-dependent quantum generation rate (Fig. 2E), which corresponds to the median value of 6 droplet diameter range for the Anderson sampler, such as 0.875 (0.65–1.1  $\mu\text{m}$ ), 1.6 (1.1–2.1  $\mu\text{m}$ ), 2.7 (2.1–3.3  $\mu\text{m}$ ), 4 (3.3–4.7  $\mu\text{m}$ ), 5.85 (4.7–7.0  $\mu\text{m}$ ), and 8.5  $\mu\text{m}$  (we assume that  $> 7 \mu\text{m}$  is expressed as 7–10  $\mu\text{m}$  diameter) (Figs. 2A–D). A Monte Carlo simulation was used based on Fig. 2E to describe the probability distribution of quantum generation rate by using a lognormal distribution with  $\text{GM} = 54.29$  and  $\text{GSD} = 3.05$  (Fig. 2F).



**Fig. 1.** (A) Monthly average occupant distance (km) per passenger for the period from January 2007 to May 2009. (B) Probability density functions of average occupant distance (km) per passenger by Monte Carlo simulation. The black and gray color columns express the fitted normal distribution and 10,000 time simulations, respectively. (C) Correlation analysis between the occupant distance per passenger and time spent. (D) Probability density function of time spent per passenger per time.

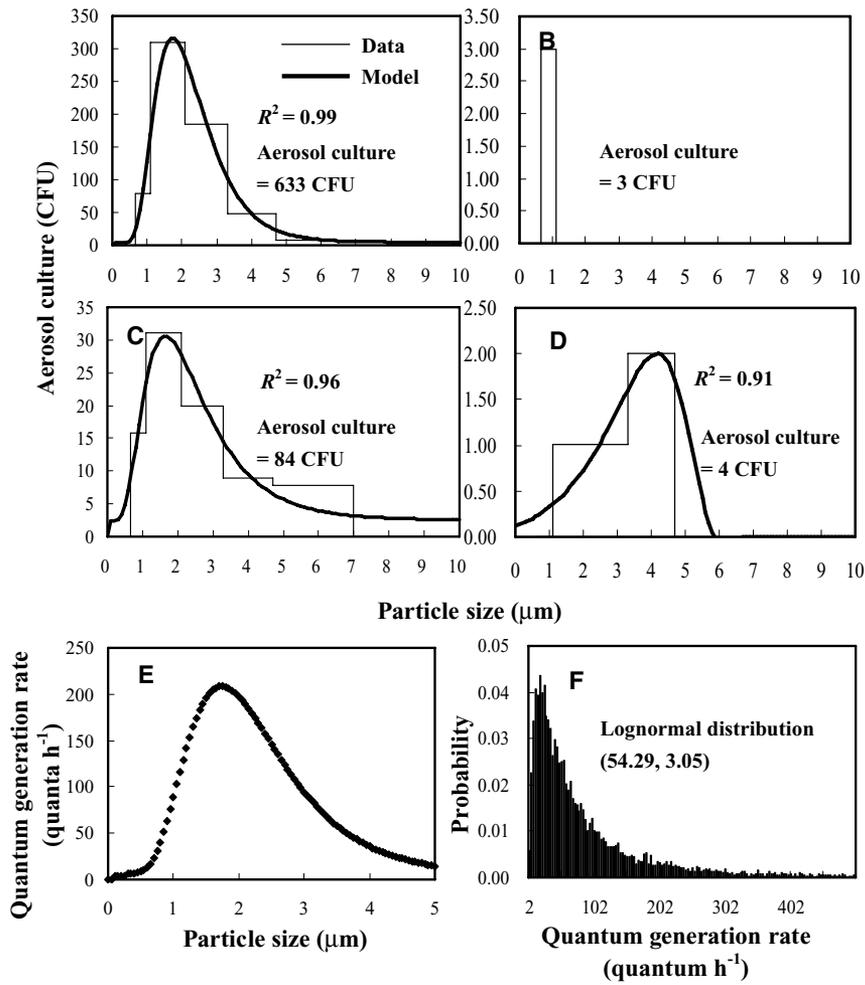
### 3.4. Risk of Infection and the Basic Reproduction Number

This study used a set of estimated values for the number of individuals in the ventilated airspace ( $n$ ), the volume of the shared airspace ( $V$ ), exposure time ( $t$ ), and fresh air supply rate ( $Q$ ) to characterize the risk of infection from TB in commercial passenger trains (Table III). The result indicated that the box and whisker plots of median with 95% CI of infection risks ( $P$ ) were estimated to be 0.059 (0.007–0.42) for all cabins (Fig. 3A). On the other hand, basic reproduction numbers ( $R_0$ ) were estimated to be 0.69 (0.06–6.79), 2.82 (0.32–20.97), and 2.31 (0.25–17.69) for business, standard, and nonreserved cabins, re-

spectively (Fig. 3B). Therefore, from a conservative point of view, the results revealed that commercial passengers taking standard and nonreserved cabins had higher transmission risk than those in the business cabins.

### 3.5. Sensitivity Analysis for Quantum Generation Rates

We fitted a Wells-Riley mathematical model to quantum generation rates data in the THSR environment. Fig. 4 shows the risk of infection and  $R_0$  in three cabins associated with the exposure time and quanta modeling, in which the curves are derived for



**Fig. 2.** (A)–(D) The relationship between the particle size diameter and aerosol culture (CFU) of the four experimental test subjects with five-minute sampler time, as adopted from Fennelly *et al.*<sup>(18)</sup> Histogram plot expressed the original data source of size-dependent culture CFU concentration and the line presents the best-fitted equation with highest correlation coefficient. (E) Size-dependent average quantum generation rate. The estimation process was described in Section 1. (F) The lognormal distribution of quantum generation rate with GM = 54.29, GSD = 3.05.

Individual	Fitted Equations	$R^2$
Aerosol culture concentration in Fig. 3A	LN (4.283, 312.2, 1.746, 1.773, 1.656) <sup>a,c</sup>	0.99
Aerosol culture concentration in Fig. 3C	LN (2.498, 28.02, 1.649, 0.532) <sup>b,c</sup>	0.96
Aerosol culture concentration in Fig. 3D	LN (−0.0918, 2.090, 4.159, 2.816, 0.586) <sup>a,c</sup>	0.91

<sup>a</sup>  $LN(a, b, c, d, e) = a + b \exp(-\ln 2 \ln(1 + (x - c)(e^2 - 1)/(de))^2 / \ln(e)^2)$ .

<sup>b</sup>  $LN(a, b, c, d) = a + b \exp(-0.5(\ln(x/c)/d)^2)$ .

<sup>c</sup> LN represents lognormal distribution with geometric mean (GM) and geometric standard deviation (GSD).

THSR-related parameters at five levels of infectivity ( $q$ ). Fig. 4 presents the simulated results of parameter point estimates. The curve shows that more exposure time would have increased risk of infection and  $R_0$  (Fig. 4). On average  $q = 1.25$  for TB patient; the curve shows that  $R_0$  were estimated to be 0.048, 0.20, and 0.16 over a 130-minute exposure for business, standard, and nonreserved cabins, respectively. At  $q = 250$ , an extraordinary TB exposure that occurred

during an intubation and bronchoscopy, the curve predicts that  $R_0$  were estimated to be 6.63, 26.89, and 21.89 over a 130 minutes exposure for business, standard, and nonreserved cabins, respectively. Hence, under the environmental parameters of THSR modeling, quantum generation rate of the specific TB patient would predict the level of  $R_0$ . Even a brief exposure, however, as in the bronchoscopy cases, can also result in a transmission when  $q$  is high.

**Table II.** Optimal Fitted Equations of Particle-Size-Dependent and Aerosol Culture (CFU) for Three Tested Subjects

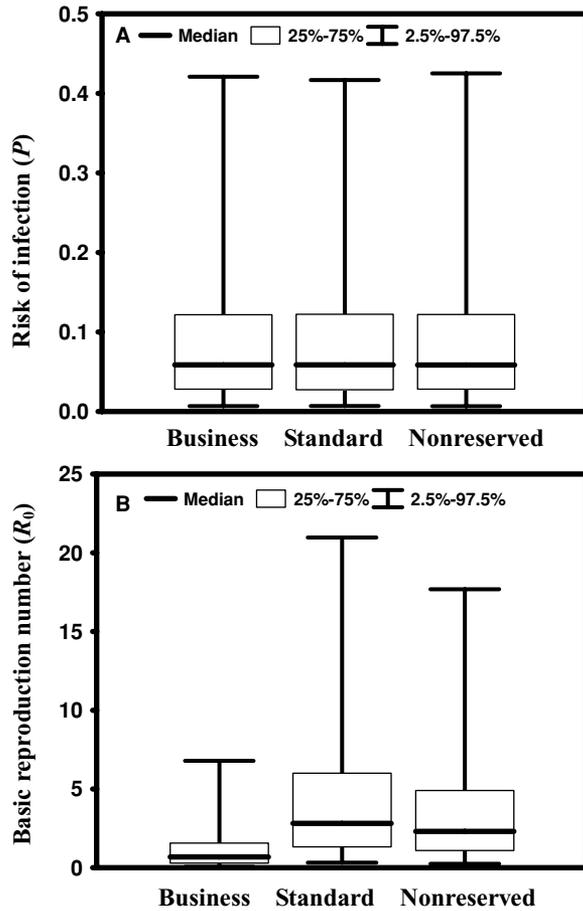
**Table III.** Input Parameters Used in the Wells-Riley Mathematical Equation

Symbols	Meaning	Value
$n$ (ind)	People in the ventilated airspace	Business: $66 \times \text{LN}$ (19.61%, 1.76) <sup>a</sup> Standard: $86 \times \text{LN}$ (57.49%, 1.26) <sup>a</sup> Nonreserved: $80 \times \text{LN}$ (50.56%, 1.27) <sup>a</sup>
$I$ (ind)	Number of infectors	1
$V$ (m <sup>3</sup> )	Volume of the shared airspace	$25 \times 3.38 \times 3.65 = 308.43$ <sup>a</sup>
$t$ (h)	Exposure time	$N$ (1.25, 3.95) <sup>a</sup>
$p$ (m <sup>3</sup> /h)	Pulmonary ventilation rate of susceptible individuals	$N$ (0.465, 0.20) <sup>a,c</sup>
$Q$ (m <sup>3</sup> /h)	Fresh air supply rate	22,224 <sup>b</sup>
$q$ (quanta/h)	Quantum generation rate	$\text{LN}$ (54.49, 3.05) <sup>c</sup>

<sup>a</sup> $N$  and  $\text{LN}$  represent the normal distribution with mean and standard deviation ( $SD$ ) and lognormal distribution with geometric mean ( $GM$ ) and geometric standard deviation ( $GSD$ ), respectively.

<sup>b</sup>We assumed that the fresh air supply rate = 3 ACH in THSR.

<sup>c</sup>Adopted from ICRP.<sup>(25)</sup>



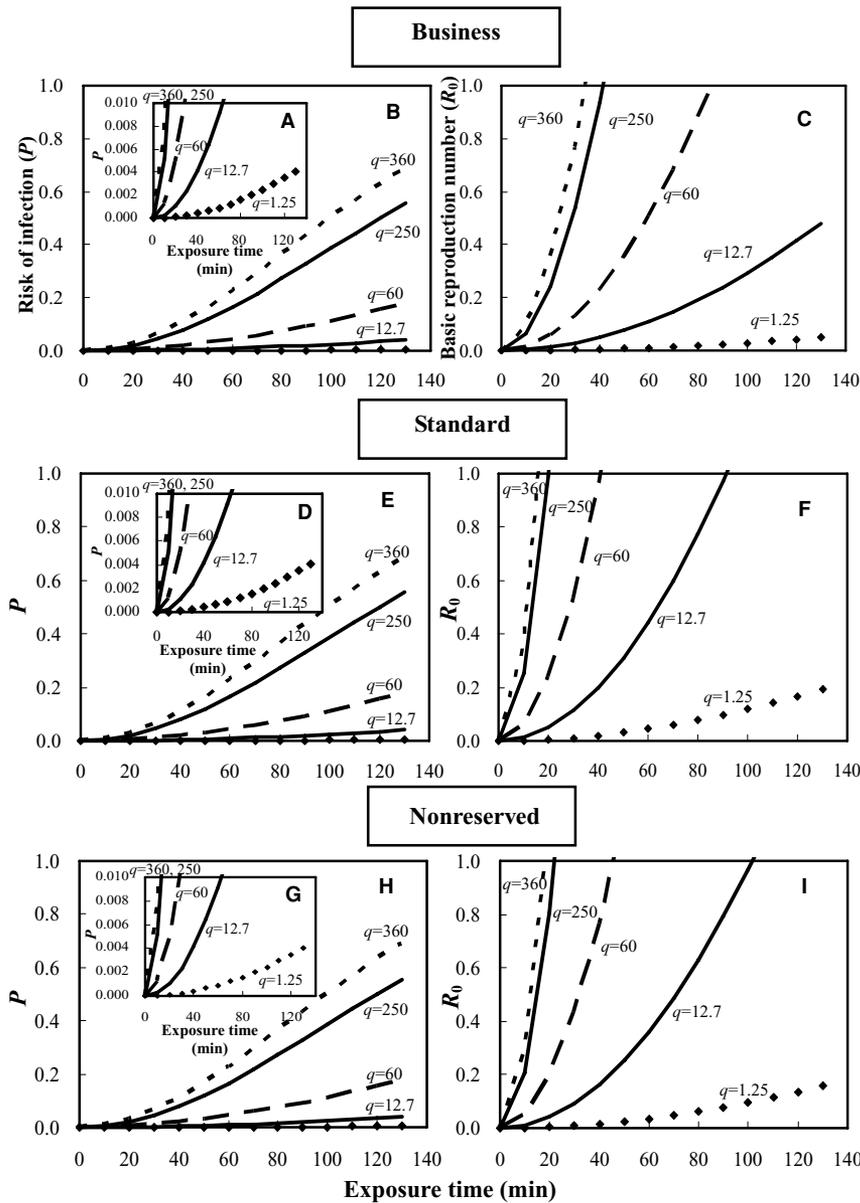
**Fig. 3.** Box whisker plots illustrated the (A) risk of infection and (B) basic reproduction number of business, standard, nonreserved cabins, respectively. These predictions are estimated by a Wells-Riley mathematical equation (Equations (1) and (2)) with parameter inputs (Table II) where the distributions were used by Monte Carlo simulation.

#### 4. DISCUSSION

This study revealed the exposure factors estimation that may affect the infection risk of TB in commercial passenger exposure. This study also integrated the cough-generated aerosol TB concentration and particle size to estimate the infectious risks for susceptible host in THSR.

The overall infectivity of any airborne pathogen is as much dependent on the immunological state of the susceptible individuals as the physical and biological characteristics of the agent; it is impossible to directly measure the quanta present in any outbreak.<sup>(4)</sup> Hence, based on the excellent research by Fennelly *et al.*,<sup>(18)</sup> it is clear that the infectiousness estimation of cough-generated aerosols of TB is a valuable application for mathematical modeling for estimating the risk of infection. The size distributions suggested that most of the viable particles in these cough-generated aerosols were immediately respirable.<sup>(18)</sup> Hence, we used these characteristics to estimate the quantum generation rates by averaging four test individuals.

On the other hand, we also collected the quantum generation rates of TB outbreak and determined those values by epidemiological models. Table IV presents quantum generation rate data for TB outbreaks that have been analyzed and reported by several researchers. Table IV indicates that there is a wide range of quantum generation rates associated with the various TB outbreaks. The quantum generation rates ranged from 1.25 to 30,840, indicating that the various sources of bronchoscopy-related outbreak, jet irrigation of abscess outbreak, autopsy, and intubation-related outbreak. Based on the different



**Fig. 4.** The risk of infection and the basic reproduction number at various levels of exposure time and infectivity ( $q = 1.25, 12.7, 60, 250, \text{ and } 360$  quanta/h) modeling in (A)–(C) business, (D)–(F) standard, and (G)–(I) nonreserved cabins, respectively. (A), (D), and (E) are enlarged figures for (B), (E), and (H), respectively. Point estimates were used in these figures with  $Q = 926 \text{ m}^3/\text{day}$ ,  $p = 11.16 \text{ m}^3/\text{day}$ ,  $V = 308.43 \text{ m}^3$  and  $I = 1$  in modeling.

scenario of TB infection risk, we think that our results indicate that quantum generation rate emitted by the TB patient is the most critical parameter in risk modeling. As in the discussion in Fig. 4, no matter which cabin you take in THSR, the significant infection risk ( $R_0 > 1$ ) will occur only for emission rates greater than 12.7 quanta/h. If we take THSR from the start station (Taipei) to the last station (Zuoying), it takes not more than 130 minutes. According to the TB outbreak news and literature review, the long-term exposure to *M. tuberculosis* bacilli seems an indicator for risk quantification. Hence, we think

the factor of quantum generation rate will contribute more than exposure time for risk estimations. Exposure/risk controls would be warranted unless there is a very small likelihood that a person with infectious TB is on the train.

There are several limitations to this study. Most subjects were studied during sputum-induction procedures. Therefore, the aerosols culturable TB data may not be representative of most patients with pulmonary TB, especially those in whom the disease caused by drug-susceptible bacilli has been newly diagnosed.<sup>(18)</sup> The small number of subjects limited

**Table IV.** Quantum Generation Rate Data for TB

Description	Reported Quanta per Hour	Reference
Average TB patient	1.25 <sup>a</sup>	Riley <i>et al.</i> <sup>(23)</sup>
Laryngeal case of TB	60 <sup>a</sup>	Riley <i>et al.</i> <sup>(23)</sup>
Bronchoscopy-related outbreak	250 <sup>a</sup>	Catanzaro <sup>(9)</sup>
Bronchoscopy-related outbreak	360 <sup>b</sup>	Catanzaro <sup>(9)</sup>
Intubation-related outbreak	30,840 <sup>b</sup>	Haley <i>et al.</i> <sup>(10)</sup>
Outbreak related to jet irrigation of abscess	2,280 <sup>b</sup>	Hutton <i>et al.</i> <sup>(11)</sup>
Outbreak in office building	12.7 <sup>a</sup>	Nardell <i>et al.</i> <sup>(13)</sup>
Autopsy outbreak	5,400 <sup>b</sup>	Kantor <i>et al.</i> <sup>(12)</sup>

<sup>a</sup>Estimated by Nardell *et al.*<sup>(13)</sup>

<sup>b</sup>Estimated by Gammaitoni and Nucci.<sup>(1)</sup>

the statistical power to assess sources of variability in aerosol production. Otherwise, the inherent limitations of the Wells-Riley airborne infection model make a number of assumptions such as conditions being in steady state and infection being a one-hit process. This study also did not take into account the fact that a susceptible person located closer to an infectious source was more likely to become infected than one who was far away.

The proposed Wells-Riley mathematical equation also did not account for the deposition or settling from the droplet particles from the air.<sup>(6)</sup> The assumption of nonuniform mixing in the Wells-Riley equation could produce heterogeneous exposures in the cabin. For example, the infectious aerosols were never being completely mixed in indoor environment because of the ventilation variability, and the higher concentration usually close to the infectious sources. However, Ko *et al.*<sup>(5)</sup> still adopt the Wells-Riley equation to estimate the TB transmission. On the other hand, Beggs *et al.*<sup>(4)</sup> review the alternative epidemiological models including the mass action (MA) model,<sup>(26)</sup> Riley, Murphy, and Riley's (RMR) model,<sup>(27)</sup> and Gammaitoni and Nucci's (GN) model.<sup>(1)</sup> Here, the RMR model had the same concept of the quanta of infection and reflected the exponential behaviors of airborne infections in confined spaces as the Wells-Riley equation.

The risk of infection from M. Tuberculosis in commercial passengers was characterized in this study. The results indicated that  $R_0$  were estimated to be 0.69 (0.06–6.79), 2.82 (0.32–20.97), and 2.31 (0.25–17.69) for business, standard, and nonreserved cabins, respectively. The average  $R_0$  was estimated to be 1.94 in THSR associated with the input parameter

$q$  with a lognormal distribution of  $GM = 54.29$  and  $GSD = 3.05$  quantum/h together with environmental and exposure factors. This study suggested that the exposure levels of TB emission infectivity in THSR were a major determinant for the transmission risks.

In conclusion, by integrating the experimental particle size distribution, quantum generation rate, and Wells-Riley mathematical model, we achieved that (i) cough-generated aerosol TB concentration and particle size could be linked to estimate the quantum generation rate and (ii) a quantitative framework was developed for understanding the risk of infection and  $R_0$  for TB infection in THSR commercial passengers based on the epidemiological modeling.

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