Building and Environment xxx (2012) 1–10

Contents lists available at SciVerse ScienceDirect

Building and Environment

journal homepage: www.elsevier.com/locate/buildenv

Modeling the impact of control measures on tuberculosis infection in senior care facilities

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ARTICLE INFO

Article history:
Received 29 June 2012
Received in revised form
30 July 2012
Accepted 8 August 2012

Keywords:
Tuberculosis
Transmission
Senior care facilities
Control measures
Modeling
Indoor air quality

ABSTRACT

Tuberculosis (TB) is among the top ten causes of death worldwide. The impacts of potential control measures on TB infection in senior care facilities are poorly understood in Taiwan region. The purpose of this paper was to assess the impacts of potential control strategies for reducing the risk for TB infection among elderly in senior care facilities and to provide the suggestions for sound TB infection control measures that should be implemented in all senior care facilities with aged people suspected of having infectious TB. We proposed an integrated-level mathematical model, incorporating the TB transmission dynamics, the Wells–Riley mathematical equation, and the competing-risks model to quantify the potential spread of TB bacilli in senior care facilities. We found that individuals living in hospital-based nursing homes had much higher exposure to TB than those in long-term and domiciliary care facilities. We showed that the proposed combinations of engineering control measures (e.g., ventilation and ultraviolet germicidal irradiation) with personal protection (e.g., surgical mask) guarantee the provision of a reliable control strategy to decrease the transmission potential and spread rate of TB bacilli aerosols in senior care facilities in that the efficacies range from 45 to 90%. The introduction of appropriate TB transmission control measures may decrease TB annual incidence in senior care facilities by as much as 76–90% of tuberculin skin test (TST) conversion. Our study implicated that sound TB infection control measures, including diagnosis and prompt treatment of infectious cases should be prioritized.

1. Introduction

Tuberculosis (TB) is among the top ten causes of death worldwide and the number of new cases is continuous to grow. Approximately one-third of world's population is infected with TB bacilli with nearly 8.8 (range: 8.5–9.2) million new cases of TB in 2010 and an estimated 1.1 (range: 0.9–1.2) million deaths from TB in the same year [1]. Thus, TB is more prevalent in the world today than at any other time [2].

TB infection is caused by inhalation of *Mycobacterium tuberculosis* bacilli in a droplet nucleus form with a diameter less than 5 μm [3,4]. All TB outbreaks have been associated with cough-generating procedures [5], and other medical examination and treatment such as bronchoscopy [6], endotracheal intubation and suctioning [7], open abscess irrigation [8], and autopsy [9]. Emergence of strains resistant to multiple drugs has led to situations where treatment is no better than before the discovery of antibiotics [10]. Diagnosis of TB remains a major barrier to control of the disease because the standard method, the acid-fast smear using sputum, does not become positive until a few months after transmission occurs [11]. Culture-based techniques are more sensitive, but still take weeks to obtain results [12].

Recent recommendations to reduce TB infection risk in health care facilities are to use engineering control measures such as improved ventilation systems, use of ultraviolet germicidal irradiation (UVGI), recirculated high-efficiency particulate air (HEPA) filter, and adoption of N95 respirators [13–17]. Drug resistance emphasizes the urgency for implementing such measures to control the spread of *M. tuberculosis* aerosol, which would also benefit reduction of patient-to-patient transmission in health care facilities. 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. Droplet nuclei settle slowly and becomes airborne lasted for several hours. Thus, it is recognized that TB outbreaks occurred under crowded living conditions with prolonged close exposure to an infectious person (http://www.sciencedaily.com/releases/1999/02/990201072734.htm).

In Taiwan the incidence and mortality rate of TB infection are 62.0–74.6 (per 100,000 population) and 3.3–5.7 (per 100,000 population) in the period 2002–2008, respectively [18]. The cluster

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http://dx.doi.org/10.1016/j.buildenv.2012.08.008

infections in senior care facilities were occasionally reported in Taiwan, there were 6, 5, and 6 reported cases in January, April, and June, respectively, in 2006. Tsai et al. [19] indicated that the annual TB incidence from senior care facilities was 810 (per 1000 population) in Taipei City during the period 2004–2006, which was almost 15.5 times higher than in the general population during the same time.

We adopted a simple well-developed TB transmission model [20,21] to investigate the population dynamics of TB in indoor environments. The TB epidemic model captures five-group dynamics of susceptible, latently infected, infectious TB, noninfectious TB, and recovered and is referred to as the SLTR model. These approaches provide a predictive ability to describe the potential transmission dynamics in an indoor environment. We employed the Wells–Riley mathematical model of airborne infection [22–24] to estimate the exposure concentrations in indoor environments where cases of inhalation of airborne infection occurred based on reported epidemiological data and epidemic curves, and basic reproduction number (R_0) and its variability in a shared indoor airspace.

Here a competing-risks theory [25–27] is employed to account for the impact of different enhanced measure efficacies from both engineering controls and respiratory protection on the airborne infection risk. The competing-risks model is a probabilistic model by which the dynamics of interplay among different enhanced engineering control-measure strategies can be described. The inclusion of competing risks in the model recognized the fact that an individual might gain substantial benefits in risk reduction of airborne infection from many different control measures including technological controls at the source (by surgical masking and treatment booths), environmental controls (by ventilation, air filtration and ultraviolet germicidal irradiation), and receptor controls (by respiratory protection via respirators) [13,28–30].

The impacts of potential control measures on TB infection in senior care facilities are poorly understood in Taiwan region. Moreover, research on the effects of TB control measures has evaluated largely independently of one another. In this paper, we proposed an integrated-level mathematical model, incorporating the SLTR transmission dynamics, the Wells–Riley mathematical equation, and the competing-risks model to quantify the potential spread of TB bacilli in senior care facilities in Taiwan region. Modeling the impact of the indoor air-based control measures of the combination of the potential engineering controls and public health interventions was assessed.

The purpose of this paper was twofold: (1) to assess the impacts of potential control strategies for reducing the risk of infection from airborne *M. tuberculosis* bacilli exposure among elderly in senior care facilities and (2) to provide the suggestions for sound TB infection control measures that should be implemented in all senior care facilities with aged people suspected of having infectious TB.

2. Materials and methods

2.1. Study data

A valuable dataset were obtained from the experiment based on Fennelly et al. [31]. 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. [31] 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, the subject was instructed to cough into the tubing for 5 min or for as long as was comfortable while the air samples were drawn from the chamber with both impactors and recorded the cough frequency. While the subject rested after the first session of coughing, the plates and reloaded with fresh plates were be removed and labeled. Three experimental tests were conducted including sputum smear grades, sputum culture, and culturable cough-generated aerosols for 16 subjects. Particle size distributions of culturable aerosols were collected by Anderson impactors during the first day of each subject. 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 m. Based on the relationship between experimental aerosol TB concentrations and particle size distribution per infectious person, the average culturable TB aerosol concentration can be estimated. Here, the particle size diameters 5 μm were considered to define and quantify the infectious quantum generation rates of aerosol TB [3,4].

In this study, three different settings of senior care facilities were selected to be the study populations and indoor environments: (i) long-term care facilities, (ii) domiciliary care facilities, and (iii) hospital-based nursing homes. Here we used five major control measures including (i) general ventilation (GV), (ii) advanced ventilation (AV), (iii) surgical mask (M), (iv) UVGI, and (v) HEPA. The assigned combinations of control strategies include (i) GV + M, (ii) GV + M + UVGI, (iii) GV + M + HEPA, and (iv) GV + M + UVGI + HEPA.

2.2. Indoor TB transmission model

The essential features of the SLTR TB transmission model are depicted in Fig. 1. Briefly, (i) two certain types of TB were modeled: primary progressive TB (i.e., fast TB) and latently infected TB caused by endogenous reactivation or exogenous reinfection (i.e., slow TB), (ii) a case may be spontaneously cured at a cure rate and move into the recovered noninfection state *R*, and (iii) an individual in the recovered state may either relapse with equal probability into infectious or noninfectious TB or may never relapse and die of other causes at background mortality rate.

The system of ordinary differential equations corresponding to Fig. 1 can be described as follows [20],

$$\frac{dS(t)}{dt} = N\delta - (\lambda + \mu)S, \tag{1}$$

$$\frac{dL(t)}{dt} = (1 - p_n)\lambda S - (v + \mu)L, \tag{2}$$

$$\frac{dT_i(t)}{dt} = p_n p_f \lambda S + p_s v L + \omega R - (\mu + \mu_T + c)T_i, \tag{3}$$

$$\frac{dT_n(t)}{dt} = p_n(1 - p_f)\lambda S + (1 - p_s)vL + \omega R - (\mu + \mu_T + c)T_n, \tag{4}$$

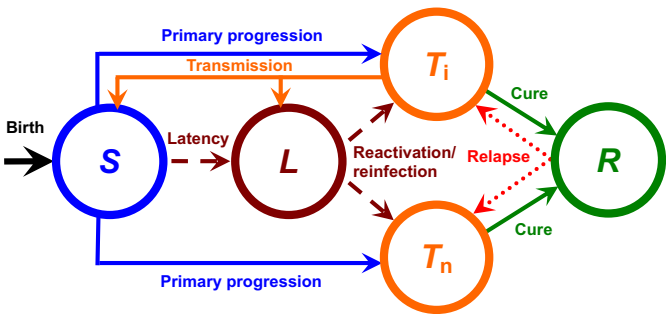

Fig. 1. Schematic of the susceptible-latently infected-active tuberculosis-recovered (SLTR) model describing TB population transmission dynamics in the present study.

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$$\frac{dR(t)}{dt} = cT_i + cT_n - (2\omega + \mu)R, \quad (5)$$

$$N(t) = S(t) + L(t) + T_i(t) + T_n(t) + R(t), \quad (6)$$

where $N(t)$, $S(t)$, $L(t)$, $T_i(t)$, $T_n(t)$, and $R(t)$ are the number of total population size, susceptible, latently infected, infectious, non-infectious, and recovered at time t, δ is the birth rate (yr^{-1}), $\lambda = T_i\beta$ is the force of infection (yr^{-1}) where β is the transmission rate ($person^{-1}\ yr^{-1}$), μ is the background mortality rate (yr^{-1}), p_n is the probability of new infections that develop progressive primary active TB within one year, ν is the progression rate from latency to active TB ($person^{-1}\ yr^{-1}$), p_f is the probability of developing fast infectious TB, p_s is the probability of developing slow infectious TB, ω is the relapse rate to active TB for recovered TB cases ($person^{-1}\ yr^{-1}$), μ_T is the TB caused mortality rate ($person^{-1}\ yr^{-1}$), and c is the TB cure rate ($person^{-1}\ yr^{-1}$).

2.3. Integrated-level analysis

In dealing with indoor TB transmission, one usually employed the well-known deterministic Wells–Riley mathematical model to account for the probability of infection risk from *M. tuberculosis* bacilli. Riley et al. [32] 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 [22] to estimate the transmission potential of aerosol TB in care facilities,

$$P = \frac{D}{S} = 1 - \exp\left\{-\frac{Iqpt}{Q}\left(1 - \frac{V}{Qt}\left[1 - \exp\left(-\frac{Qt}{V}\right)\right]\right)\right\}, \quad (7)$$

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^{-1}) considering a best fitted distribution of the experimental database, p is the pulmonary ventilation rate of susceptible individuals ($m^3\ h^{-1}$), t is the exposure duration (h), Q is the fresh air supply rate that removes the infectious aerosol per unit of time ($m^3\ h^{-1}$), and V is the volume of the ventilated space (m^3).

We adopted the concept of a competing-risks model [25–27] to account for prioritizing the impact of different enhanced engineering control measures against respiratory infections. We link the competing risks model and Wells–Riley equation to estimate the reduction of potential infectious force of R_0. Based on the competing-risks model, we derive an optimal R_0 by incorporating the effectiveness of engineering control measures such as UVGI, HEPA filter, air exchange rate, and respiratory protection into a Wells–Riley-based R_0 model [22,23]. When we consider an initial $I = 1$ and $S = N - 1$, the optimal R_0 can be estimated as [22,24,33],

$$R_0 = (N-1) \times P = (N-1)\left\{1 - \exp\left[-\left(\frac{Iqtp(1-\eta_s)}{Q + Q_r\eta_r + h_u V}\right)(1 - \exp(-(h + h_r\eta_r + h_u)t))\right]\right\}, \quad (8)$$

where N is the total number of individuals in the ventilation airspaces, Q_r is the airflow rate through a recirculated HEPA filter ($m^3\ h^{-1}$), η_s is the efficiency of a respiratory protection device used by a susceptible person (dimensionless), η_r is the single-pass removal efficiency for *M. tuberculosis* bacilli passing through the recirculated HEPA filter (dimensionless), h is the air exchange rate (h^{-1}), h_r is the air exchange rate through a recirculated HEPA filter (h^{-1}), and h_u is the inactivation rate of *M. tuberculosis* bacilli due to UVGI (h^{-1}).

To understand the relationship between the infectiousness of TB and contact rate, the SLTR TB transmission model was linked to the Wells–Riley equation to estimate the transmission parameter (β) based on the $R_0 - \beta$ relationship developed by Blower et al. [20] as,

$$\beta = \frac{R_0\mu}{N\delta}\left(\frac{1}{AB + AC + DE}\right), \quad (9)$$

in that $A = 1/(\mu + \mu_T + c)$, $B = p_n p_f$, $C = p_s(1 - p_n)\nu/(\nu + \mu)$, $D = 1/(\mu + \mu_T + c)((\mu + \mu_T + c) - ((2\omega c)/(2\omega + \mu)))$, $E = (p_n + ((1 - p_n)\nu/\nu + \mu))(\omega c/2\omega + \mu)$, and R_0 can be calculated from equation (8). Here R_0 can be analogized to R_0^{total} quantifying the transmission potential of *M. tuberculosis* due to the subepidemic driven by primary progression (R_0^{fast}), reactivation/reinfection (R_0^{slow}), and relapse ($R_0^{relapse}$) as $R_0^{total} = R_0^{fast} + R_0^{slow} + R_0^{relapse}$ [20].

Here we used the prevalence of positive tuberculin skin test (TST, %) conversion as a predictor to assess efficacy of potential control measures under different exposure scenarios [34],

$$\%TST = \left(1 - \frac{S_\infty}{S_0}\right) \times 100,\ R_0 > 1, \quad (10)$$

where S_0 is the initial susceptible individuals and S_∞ is the equilibrium susceptible individuals and can be estimated as $S_\infty = N/R_0$ at a certain control measure setting [35].

2.4. Model parameterization, uncertainty analysis, and simulation scheme

The total population size and volume of the ventilated space in long-term care and domiciliary care facilities were adopted from the establishment standards provided by Taiwan Social Affairs [36]. Wang and Tzeng [37] have recently provided a valuable data of the total population size and volume of the ventilated space in two hospital-based nursing homes in Taiwan. Furthermore, the average time they investigated that senior residents spent in public spaces can be used to estimate TB exposure duration [37]. The breathing rate of elders was estimated based on Taiwan Health Promotion [38].

The rate of airborne particles are removed from an enclosed space by ventilation is usually expressed as the number of air changes per hour (ACH). A minimum ACH of 4 h^{-1} is recommended by CDC for TB in resident gathering areas [14]. Ko et al. [39] revealed that the ACH of additional ventilation was 6 h^{-1}. CDC [14] also indicated that the airflow rate of HEPA filter should be increased to 12 ACH or more and the particle-removal efficiency ranged from 90 to 95%. Therefore, we used fixed values of 4 ACH, 6 ACH, and 12 ACH for GV, AV, and HEPA filter, respectively. The efficiency of surgical mask in preventing the inhalation of droplet nuclei with a diameter

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of 1–5 μm is 50% with a face-seal leakage of 0%–20%. Hence, the overall protection efficiency of surgical mask can be calculated by a function of $Z = (X - XY/100)$, where Z is the protection efficiency (%), X is the filter efficiency (%), and Y is the face-seal leakage (%) [34]. Xu et al. [40] conducted three experiments to evaluate the efficacy of an UVGI system for inactivating airborne *Mycobacteria* and the results showed that the average inactivation rate for UVGI was 12 ± 1.3 h^{-1}.

The likely values of key parameter in the SLTR model can be parameterized based on available TB data provided by Taiwan CDC data (http://www.cdc.gov.tw/english/index.aspx), Taiwan tuberculosis control report [41], Department of Statistics, Ministry of the Interior, ROC (Taiwan) [42], and otherwise based on data adopted from the literature [20,43–45]. TB caused mortality rate and relapse rate were estimated based on Taiwan CDC database. Age-specific background mortality rates were provided by Department of Statistics, Ministry of the Interior, ROC (Taiwan) [42]. TB cure rate of elders was estimated by annual TB cure rate in the period 2004–2008 provided by Taiwan tuberculosis control report [41] times the odds ratio for the effect of age on TB cure rate in Taiwan [45]. The odds ratio was estimated to be 0.706 (0.352–1.413) by Wang et al. [45]. Thanks to Vynnycky and Fine [43] and Dye et al. [44], they have provided age-specific TB parameters of the probability of new infections that develop TB within a year and the probability of developing fast infectious TB. Our TB population dynamic model was adopted from Blower et al. [20]. Thus, the probability of developing slow infectious TB and progression rate from latency to active TB were estimated based on Blower et al. [20].

Table Curve 2D package (AISN Software Inc., Mapleton, OR, USA) and Statistica® (version 9, Statsoft, Inc., Tulsa, OK, USA) were used to perform model fitting techniques and statistical analyses for estimating the average aerosol culturable TB concentration based on the experimental results. A Monte Carlo (MC) technique was implemented to quantify the uncertainty concerning quantum generation rate and all model parameters, except ACH of GV, AV, and HEPA filter. We used the Kolmogorov–Smirnov (KS) statistics to optimize the goodness-of-fit of distributions. A MC simulation was also performed with 10,000 iterations to generate 2.5- and 97.5-percentiles as the 95% CI for all fitted models. The Crystal Ball® software (Version 2000.2, Decisioneering, Inc., Denver, Colorado, USA) was employed to implement MC simulation. The SLTR model simulations were performed by using Berkeley Madonna 8.0.1 (Berkeley Madonna was developed by Robert Macey and George Oster of the University of California at Berkeley).

3. Results

3.1. Estimated *M. tuberculosis* aerosol generation rate

We used a lognormal (LN) function to optimal fit the published data [31] to obtain the likelihood distribution of particle size-dependent culturable aerosols in colony forming unit (CFU) (Fig. 2a, c, e, Table 1). Fig. 2a shows the highest cultural TB concentration was 633 CFU in that 309 CFU (49%) and 572 CFU (90%) were isolated from 1.1 to 2.2 μm and 0.65–3.3 μm in aerodynamics diameter, respectively. The particle size distribution of cough-generated aerosol was slightly larger, with a mode in 1.1–2.5 μm in aerodynamic diameter (Fig. 2c). For another one test subject, the culturable aerosol concentration of 4 CFU had higher TB concentration in 1.1–4.7 μm (Fig. 2e). These results also indicated that cough-generated culturable aerosols showed high variability for each subjects.

The probability distributions of quantum generation rate for each tested subject can be obtained from our fitted distributions of particle size-dependent aerosol TB concentration performed by MC simulation (Fig. 2b, d, f, Table 1). The unit conversion from culture aerosol in CFU to quantum generation rate (quanta h^{-1}) was followed by 1 CFU = 0.0218 quantum [46] in that the sampling time interval was 10 min. We summarized data by pooling subject-specific fitted size-dependent quantum generation rate distributions with particle size 5 μm (Fig. 2a, c, e) to obtain a weighted mean size-dependent quantum generation rate (Fig. 2g). The averaged probability distribution of quantum generation rate can also be obtained based on Fig. 2g, resulting in a LN distribution with a geometric mean (gm) of 4.26 quanta h^{-1} and a geometric standard deviation (gsd) of 2.81 (Fig. 2h).

3.2. Control measures impacts

Table 2 gives the essential input parameter values (likelihood and point estimates) used to estimate facility- and control measure-specific R_0 values based on equation (8). We used equation (8) together with the adopted engineering control measures of enhancing air exchange rate ($h = 6$ h^{-1}), surgical masking ($\eta_s = 45 \pm 3.1\%$), UVGI system ($h_u = 12 \pm 1.3$ h^{-1}), and HEPA filtration ($h_r = 12$ h^{-1} and $\eta_r = 92.51 \pm 1.29\%$) (Table 2) or their potential combinations to estimate the optimal R_0 for three senior care facilities (Fig. 3a). Given the R_0 estimates, we can further calculate the transmission rate (β) followed by equation (9) with the adopted input parameter values listed in Table 3 (Fig. 3b).

Our results indicated that R_0 values can be reduced from general ventilation system by incorporating the certain combinations of control measure such as enhancing the efficiencies of recirculation air filter capacity, respiratory protection by using surgical masks, and UVGI system (Fig. 3a). For long-term care and domiciliary care facilities, R_0 values can be reduced from 0.532 (95% CI: 0.059–4.672) and 0.310 (0.033–2.846) by GV to 0.043 (0.005–0.396) and 0.025 (0.003–0.222) by GV + M + UV + HEPA, respectively. On the other hand, for hospital-based nursing homes, R_0 values can also be reduced from 1.039 (0.114–9.177) by GV to 0.084 (0.010–0.714) by GV + M + UV + HEPA. Moreover, the transmission rates were also reduced one-order of magnitude (from $\sim 10^{-2}$ to $\sim 10^{-3}$ person^{-1} yr^{-1}) for study senior care facilities by increasing the certain combinations of proposed control measures (Fig. 3b).

Our results also demonstrated that individuals living in hospital-based nursing homes had much higher exposure to TB than those in long-term care and domiciliary care facilities, indicating individuals living in nursing homes had the potential to infect many more individuals than the other two care facilities. Generally, from a conservative point of view, combinations of control measures GV + M + UV can almost reduce R_0 to less than 1 for long-term care and domiciliary care facilities, but not that for nursing homes (Fig. 3a). Taken together, our results revealed that the proposed combinations of engineering control measures with personal protection guarantee the provision of a reliable control strategy to decrease the transmission potential and spread rate of *M. tuberculosis* aerosols in senior care facilities in that the efficacies range from 45 to 90%.

To assess the impacts of various control measures on the dynamics of active TB cases, we simulated the SLTR model (equations (1)–(6)) with the input parameter values listed in Table 3. Fig. 4a–c shows the simulated 5-yr time-course proportions of active TB epidemic in three senior care facilities when the proposed control measure strategies were implemented. Here we measure the overall effectiveness of the proposed control measure strategies by the percentage of active TB cases averted with respect to the baseline simulation where GV was used. The results showed that GV + M can achieve 18%, 46%, and 7%, respectively, of active TB cases averted in long-term care, domiciliary care, and nursing home

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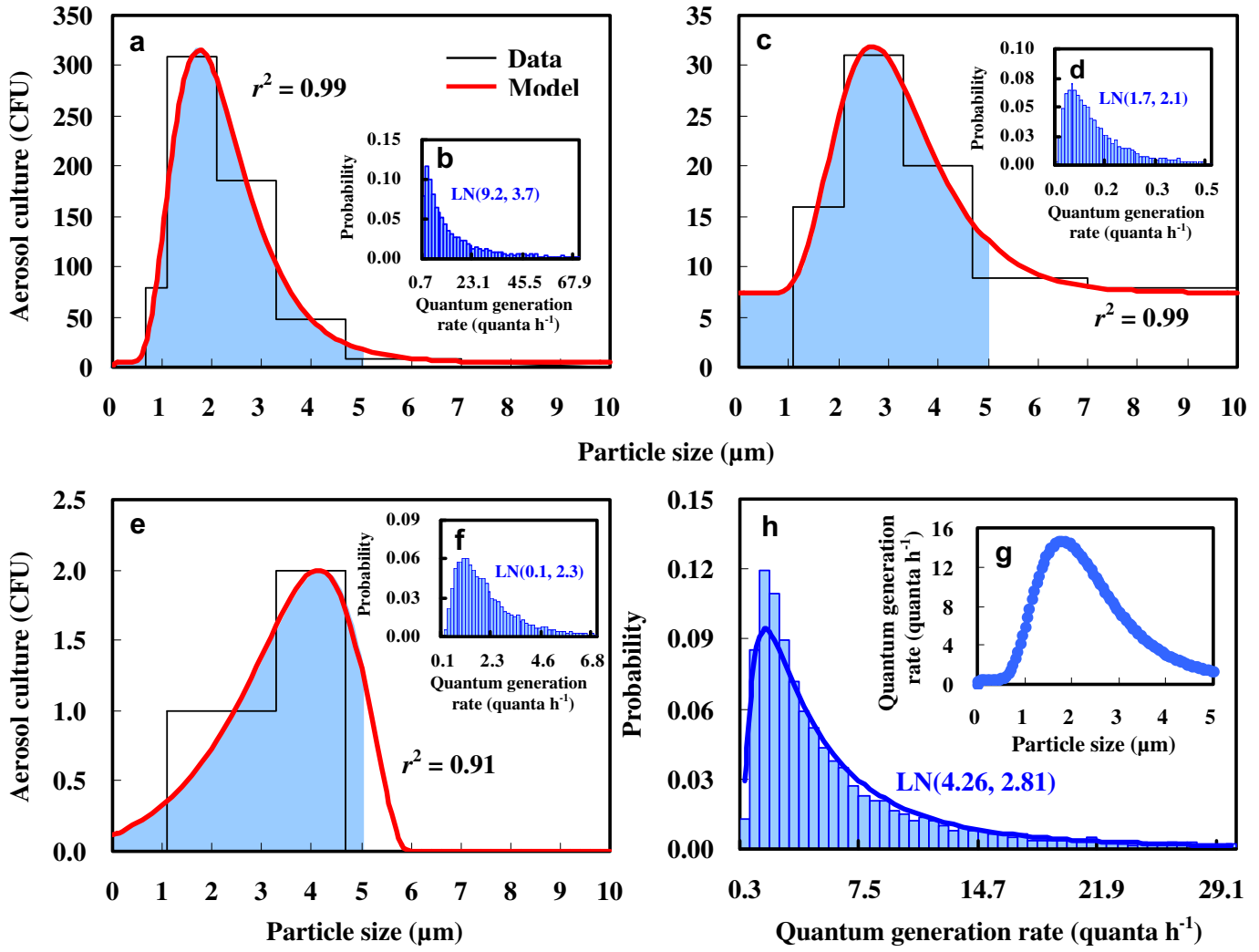

Fig. 2. (a), (c), and (e) The relationship between the particle size diameter and aerosol culture (CFU) of the three experimental test subjects adopted from Fennelly et al. [31]. The shaded region represents that *Mycobacterium tuberculosis* bacilli in particles size ≤5 μm are capable of reaching the alveoli to initiate infection. (b), (d), and (f) Probability distributions of quantum generation rate for each tested subject. (g) Weighted mean size-dependent quantum generation rate. (h) The lognormal distribution of quantum generation rate with gm = 4.26, gsd = 2.81.

facilities (Fig. 4d). However, when GV + M + UV was implemented, the over effectiveness can be achieved nearly 90% of active TB cases averted (Fig. 4d).

Fig. 5 shows the predicted percentage of TST conversions occurred in three senior care facilities during the initial period when different proposed control measures were adopted. The predicted % TST conversions of the baseline simulation where GV was used were 30.5% (95% CI: 1.88–80.79%), 20.19% (1.04–60.23%), and 43.18% (3.63–93.13%), for long-term care, domiciliary care, and nursing home facilities, respectively. Our results indicated that when GV + M was adopted, the median reducing rates of % TST conversions were estimated to 35%, 40%, and 29% compared to the baseline predictions, for long-term care, domiciliary care, and nursing home facilities, respectively (Fig. 5). However, combinations of control measures GV + M + UV was projected to avert 84%, 90%, and 76% TST conversions in long-term care, domiciliary care, and nursing home facilities, respectively (Fig. 5). The results also showed that GV + M + UV and GV + M + HEPA had the same capacities for reducing % TST conversions (Fig. 5).

Table 1
Optimal fitted lognormal (LN) functions for particle size-dependent culturable aerosol distribution obtained from published experimental data [31].

Culturable aerosols data	Fitted equations	r^2
Subject during sputum induction (Fig. 2a)	LN (4.283, 312.2, 1.746, 1.773, 1.656)[a]	0.99
Subject during voluntary coughing (Fig. 2c)	LN (7.391, 24.578, 2.669, 0.356)[b]	0.99
Subject during sputum induction (Fig. 2e)	LN (−0.0918, 2.090, 4.159, 2.816, 0.586)[a]	0.91

[a] $\mathrm{LN}(a,b,c,d,e) = a + b\exp(-\ln 2 \ln(1 + (x-c)(e^2-1)/(de))^2/\ln(e)^2)$.
[b] $\mathrm{LN}(a,b,c,d) = a + b\exp(-0.5((x/c)/d)^2)$.

4. Discussion

4.1. Quantum generation estimation

A quantum represents the average infectious source strength (or infectious dose) of infectious individuals [47]. It is difficult, if not impossible, to measure directly the quanta present in any outbreak [48]. Fennelly et al. [31] had implicated that the infectiousness estimation of cough-generated aerosols of TB could be served as a valuable application in mathematical modeling based on the

Table 2
Input parameters used in Wells–Riley equation and competing-risks model to estimate basic reproduction number (R_0) varied with different control measures ($N(a, b)$ denotes the normal distribution with mean a and sd b and LN(a, b) denotes the lognormal distribution with gm a and gsd b).

Parameters	Symbol/unit	Distribution/point value		
		Long-term care	Domiciliary care	Nursing home
Wells–Riley equation				
Total population size	N (ind)	N (161, 38)[a]	N (138, 33)[a]	N (177, 32)[b]
Volume of the airspace	V (m^3)	LN (1010.89, 1.34)[a]	LN (1522.90, 1.33)[a]	LN (595.94, 1.29)[b]
Exposure duration[b]	t (h)		LN (9.61, 1.26)	
Breathing rate[c]	p (m^3 h^{-1})		N (0.35, 0.05)	
Number of infectors	I (ind)		1	
Quantum generation rate[d]	q (quanta h^{-1})		LN (4.26, 2.81)	
Control measures				
Ventilation				
Air change per hour of GV[e]	h (h^{-1})		4	
Air change per hour of AV[e]	h (h^{-1})		6	
Fresh air supply rate through GV[f]	Q (m^3 h^{-1})	LN (4043.87, 1.34)	LN (6077.61, 1.29)	LN (2366.68, 1.33)
Fresh air supply rate through AV[f]	Q (m^3 h^{-1})	LN (6096.9, 1.30)	LN (9129.64, 1.30)	LN (3580.91, 1.29)
Surgical mask				
Efficiency of a respiratory protection[g]	η_s (%)		N (45.0, 3.1)	
UVGI				
Inactivation rate of infectious droplet nuclei due to UV[h]	h_u (h^{-1})		N (12.0, 1.3)	
HEPA filtration				
Air change per hour of HF[e]	h_r (h^{-1})		12	
Fresh air supply rate through HF[f]	Q_r (m^3 h^{-1})	LN (12,073.73, 1.34)	LN (18,289.42, 1.33)	LN (7153.76, 1.29)
Removal efficiency through HF[e]	η_r (%)		N (92.51, 1.29)	

[a] Establishment standards of large-size facilities adopted from Department of Social Affairs, Ministry of the Interior, ROC (Taiwan) [36].
[b] Estimated based on Wang and Tzeng [37].
[c] Estimated based on Bureau of Health Promotion, Department of Health, ROC (Taiwan) [38].
[d] See Table 1 and Fig. 2.
[e] Adopted from CDC [14].
[f] Air supply rate (m^3 h^{-1}) = air change per hour × volume of space (m^3).
[g] Adopted from Gammaitoni and Nucci [34].
[h] Adopted from Xu et al. [40].

relationship between particle size-dependent and aerosol culture (CFU) of TB patients. Fennelly et al. [31] suggested that most of the viable particles in the cough-generated aerosols were immediately respirable, implicating that the quantum generation rates could be estimated by averaging the test individuals.

We also collected the quantum generation rates of TB outbreak and determined those values by epidemiological models, indicating 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 the various sources of bronchoscopy-related outbreak, jet irrigation of abscess outbreak, autopsy, and intubation-related outbreak. Our estimated quantum generation rate of 3.89 (95% CI: 0.74–38.70 quanta h^{-1}) was consistent with the measured value of 1.25 quanta h^{-1} of average TB patient [3].

Most subjects were studied during sputum-induction procedures. Therefore, these data may not be representative of most patients with pulmonary TB, especially of those in whom the disease caused by drug-susceptible bacilli has newly diagnosed [31]. The small number of subjects limited our statistical power to assess sources of variability in aerosol production. Furthermore, the estimated source strength already included the dynamics of microbial growth or decay, loss of infectivity, and appropriate particle size to reach alveoli [39]. Lack of replication [49] and significant decay in the air for *M. tuberculosis* [50] would imply that the effective source strength would always be less than the actual number of released microorganisms from TB patient.

4.2. Uncertainty and limitations

Parameter estimates always links with uncertainty and variability. As with any modeling study, quality of the results depends on the input data. In the present study, data gaps are the major limitation of the model, the limited datasets used in Well–Riley equation, competing-risk model, and SLTR model may pose the greatest sources of uncertainty.

Variation in quantum generation estimates spans several orders of magnitude that can also induce the model variability. In addition, TB exposure duration is also an important factor in the TB transmission, with the risk of infection increasing with exposure time. Ice [51] indicated the residents lived in nursing home spent an average 41.40% (9.94 h) of a day to contact more than three persons. Pruchno and Rose [52] found that the average durations of the day not in bedroom and bathroom were 6.4 h in nursing home, 10.90 h in assisted living facility, and 9.40 h in the community with the support of home health services, respectively. Our estimated exposure duration of 9.60 (95% CI: 7.16–11.19 h) was similar to that of Ice [51] and Pruchno and Rose [52]. Thus, the potential of the improvement on the model predictions can best be realized in combination with larger sets of epidemiological data. For small sets of epidemiological data large uncertainties remain.

Beggs et al. [48] reviewed a number of epidemiological models have been used to determine the quanta of infection associated with outbreaks of TB. There included the mass action (MA) model [53], Riley, Murphy, and Riley's (RMR) model [54], and Gammaitoni and Nucci's (GN) model [34]. Here, the RMR model had the same concept as the Wells–Riley equation. There are some inherent limitations of Wells–Riley equation, for example assuming well-mixed airspace and steady-state conditions. The Wells–Riley equation also did not account for deposition or settling from droplet particles from the air [55]. However, there are several reports of use of the Wells–Riley equation to estimate the risk of TB infection [3,39,56].

Brooks-Pollock et al. [57] demonstrated the effect of age structure on the prevalence of infection, disease, R_0, and the projected impact of control interventions. In Taiwan, the incidence rate of TB

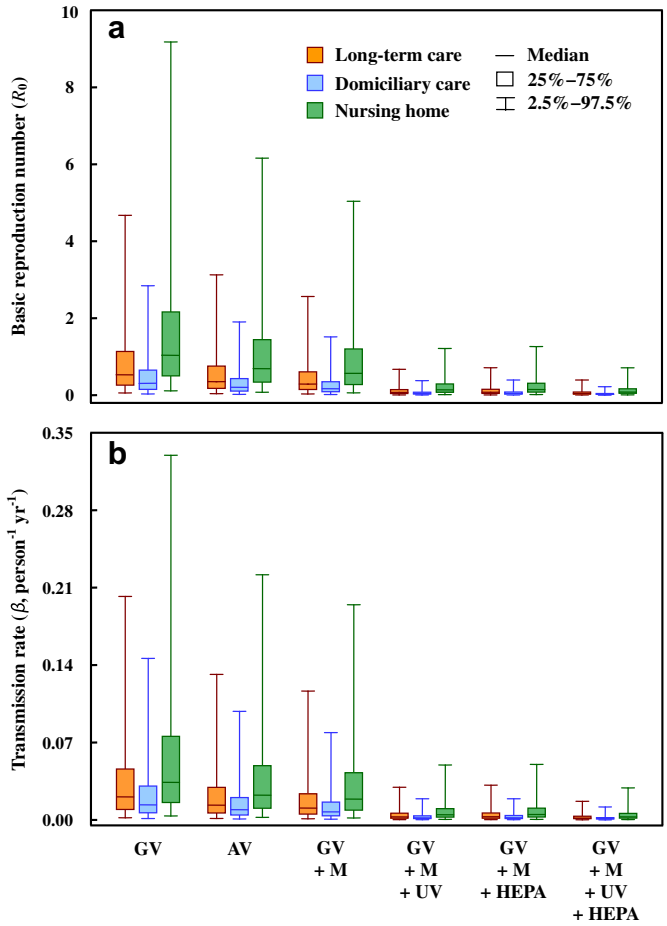

Fig. 3. The box and whisker plot illustrated the (a) basic reproduction number and (b) transmission rate for long-term care facility, domiciliary care facility, and nursing home with multiple engineering control measures.

Table 3
Input parameters used in SLTR model to estimate transmission rate (β) varied with different control measures ($N(a, b)$ denotes the normal distribution with mean a and sd b and LN(a, b) denotes lognormal distribution with gm a and gsd b).

Parameters	Symbol/unit	Distribution/point value
Probability of new infections that develop TB within a year[a]	p_n	LN (0.12, 1.45)
Probability of developing slow infectious TB[b]	p_s	N (0.78, 0.11)
Probability of developing fast infectious TB[c]	p_f	N (0.57, 0.04)
Progression rate from latency to active TB[b]	ν (person^{-1} yr^{-1})	N (0.00392, 0.0007)
Background mortality rate[d]	μ (person^{-1} yr^{-1})	LN (0.084, 1.487)
TB caused mortality rate[e]	μ_T (person^{-1} yr^{-1})	N (0.066, 0.016)
Cure rate[f]	c (person^{-1} yr^{-1})	N (0.469, 0.028)
Relapse rate[e]	ω (person^{-1} yr^{-1})	LN (0.0035, 1.44)
Recruitment rate[g]	π (person yr^{-1})	Long-term care: LN (12.91, 1.60) Domiciliary care: LN (11.21, 1.60) Nursing home: LN (14.65, 1.55)
Initial population size[h]	N_{max} (ind)	Long-term care: 256 Domiciliary care: 220 Nursing home: 257

[a] Estimated based on 0.0866 (0.0817–0.0905) for age >20 years old [43] and 0.14 (0.08–0.25) for age >15 years old [44].
[b] Estimated based on Blower et al. [20].
[c] Estimated based on 0.60 (0.5–0.65) for age >15 years old [44].
[d] Estimated based on Department of Statistics, Ministry of the Interior, ROC (Taiwan) [42].
[e] Estimated based on Taiwan CDC data.
[f] Estimated based on Taiwan tuberculosis control report [41] and Wang et al. [45].
[g] $\pi = N\mu$.
[h] See Table 2.

rises with age, among all new patients, 53% were aged ≥65 years [41]. These researches developed age-structured compartmental model to describe population dynamics of TB [43,44,57]. Age-specific parameter values appeared in the SLTR model is not easily to be parameterized in Taiwan due to data limitation. To compensate these predicaments, we may adopt published data related to age-specific risks of developing active TB together with our study results to improve model predictability. Moreover, there are few studies for estimating age-specific parameters directly or indirectly for population dynamic model, except Vynnycky and Fine [43] and Dye et al. [44]. The data sources of parameters were adopted from England and Wales and Netherlands by Blower et al. [20], Vynnycky and Fine [43], and Dye et al. [44]. However, there are several researches cited their studies for examining the population dynamics of TB in different countries, such as South African [58], China [59], Brazil [60], and Hong Kong [61].

4.3. Control measure implications

Our study found that individuals living in hospital-based nursing homes had much higher exposure to TB than those in long-term care and domiciliary care facilities. From parametric study, the transmission potential quantified by R_0 is calculated by the number of susceptible (S) and the infection probability (P) shown in equation (8) that revealed that overcrowding has a particularly strong influence on the spread of infection. Beggs et al. [48] also clearly demonstrated the considerable influence of airspace volume and the level of occupancy density on TB infection rate. Nursing home has the largest total population size but the smallest airspace volume than other two facilities.

In addition, most elders enter senior care facilities due to failing health with numerous chronic, comorbid conditions, and multiple functional deficits. It is also important to consider the immune system that is affected by age, coinfections, chronic diseases, and physical and psychological condition [62]. The senior people with low immune may increase susceptibility to TB infection and progression to disease. Particularly, the highest infection risk in nursing homes, which services to senior patients with long-term chronic diseases and in need of nursing care compare to the lowest infection risk in domiciliary care facilities, which services to senior citizens who can take care of themselves for daily life but without care takers [36].

We showed that the average reducing rates of % TST conversions were 84%, 90%, and 76% when GV + M + UV was implemented compared to the baseline predictions, for long-term care, domiciliary care, and nursing home facilities, respectively. We also showed that UVGI and HEPA had the same capacities when combined with GV + M for reducing % TST conversions. The median of TST conversion for GV were 30.50%, 20.19%, and 43.18% in long-term care, domiciliary care, and nursing home, respectively. Chang et al. [63] reported that 26 of 115 residents (22.6%) had TST conversion in nursing home in Southern Taiwan and indicated that the results were likely to be an underestimation. The TST conversions were 46.3% in old age home residents in Hong Kong [64] and 52.6% in nursing home in Japan [65], respectively.

In this study, the effectiveness are showed as the order of GV + M + UV = GV + M + HEPA > GV + M. Gammaitoni and Nucci

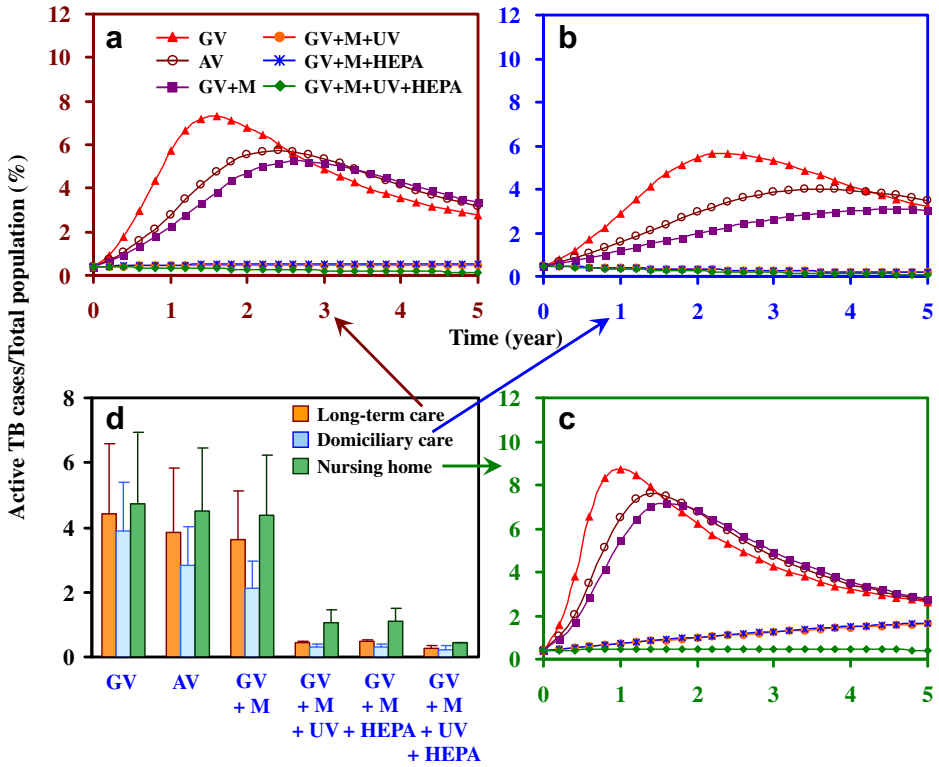

Fig. 4. Modeling the progress of 5-year time-course proportions of active TB cases and intervention by multiple engineering control measures for (a) long-term care facility, (b) domiciliary care facility, and (c) nursing home. (d) Overall effectiveness of average proportion of active TB cases. The error bar represents the standard deviation.

[34] and Ko et al. [39] used TST conversions to characterize the relationship among the TB infection, dose, and risk, and estimated the efficacy of different control strategies in hospital based on a predictable mathematical modeling. Gammaitoni and Nucci [34] revealed that UVGI had the best protection efficacy than other control strategies. Ko et al. [39] also indicated that UVGI is the best additional environmental control measure for effectively preventing TB transmission by using cost-effectiveness analysis. Therefore, we suggested that UVGI is the best additional engineering control measure for effectively preventing TB transmission in this study.

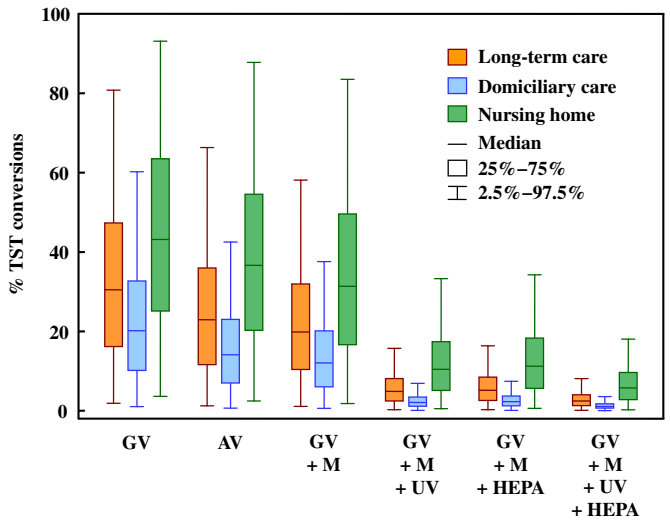

Fig. 5. The box and whisker plots illustrated the percentage of tuberculosis skin test (TST) conversion for long-term care facility, domiciliary care facility, and nursing home with multiple engineering control measures.

However, the potential health risk tradeoffs introduced by the use of UVGI should also be considered. Brief overexposure to high-intensity UV-C irradiation may cause erythema or photokeratoconjunctivitis and has been as a potential carcinogen for human [66].

TB may present any clinical signs in the senior people, and, thus, this disease should be suspected even with no typical clinical signs and radiology. Besides, decreased body weight, weakness and cough may result from aging [19]. Therefore, we also implicated that sound TB infection control measures, including not only environmental controls and respiratory-protection but also early diagnosis and prompt treatment of infectious cases should be prioritized [13,19]. Moreover, the emergence of multi-drug resistant strain of *M. tuberculosis* emphasizes the urgency for implementing such measures, which would also benefit reduction of person-to-person transmission in senior care facilities [2,21]. We hope that our study could enhance our understanding of the complex interactions between the TB pathogen and its human host in indoor environments.

5. Conclusion

This study developed an integrated-level mathematical model, incorporating the TB transmission dynamics, the Wells–Riley mathematical equation, and the competing-risks model to assess the impacts of potential control strategies for reducing the risk for TB infection among elderly in senior care facilities. We also provided the suggestions for sound TB infection control measures in all senior care facilities with aged people suspected of having infectious TB. The results of our study revealed that the risk for TB among elderly in senior care facilities is consistently higher than the risk among the general population. We demonstrated that individuals living in hospital-based nursing homes had much

Please cite this article in press as: Liao C-M, et al., Modeling the impact of control measures on tuberculosis infection in senior care facilities, Building and Environment (2012), http://dx.doi.org/10.1016/j.buildenv.2012.08.008

higher exposure to TB than those in long-term care and domiciliary care facilities. Our results also indicated that UVGI was the best additional engineering control measure for effectively preventing TB transmission. The introduction of appropriate TB transmission control measures may decrease TB annual incidence in senior care facilities by as much as 76–90% of TST conversion. This study concluded that the present integrated-level mathematical model is a necessary tool for helping optimal determination of the intervention strategies for TB infections.

References

[1] WHO (World Health Organization). Global tuberculosis control. Available from: http://www.who.int/tb/publications/global_report/en/index.html; 2011.
[2] Koul A, Arnoult E, Lounis N, Guillemont J, Andries K. The challenge of new drug discovery for tuberculosis. Nature 2011;469:483–90.
[3] Nardell EA, Keegan J, Cheney SA, Etkind SC. Airborne infection: theoretical limits of protection achievable by building ventilation. Am Rev Respir Dis 1991;144:302–6.
[4] Kaufmann SHE. Tuberculosis: deadly combination. Nature 2008;453:295–6.
[5] Malasky C, Jordan T, Potulski F, Reichman LB. Occupational tuberculosis infections among pulmonary physicians in training. Am Rev Respir Dis 1990;142:505–7.
[6] Catanzaro A. Nosocomial tuberculosis. Am Rev Respir Dis 1982;125:559–62.
[7] Haley CE, McDonald RC, Rossi L, Jones Jr WD, Haley RW, Luby JP. Tuberculosis epidemic among hospital personnel. Infect Control Hosp Epidemiol 1989;10:204–10.
[8] Hutton MD, Stead WW, Cauthen GM, Bloch AB, Ewing WM. Nosocomial transmission of tuberculosis associated with a draining abscess. J Infect Dis 1990;161:286–95.
[9] Kanto HS, Poblete R, Pusateri SL. Nosocomial transmission of tuberculosis from unsuspected disease. Am J Med 1988;84:833–8.
[10] Luciani F, Sisson SA, Jiang H, Francis AR, Tanaka MM. The epidemiological fitness cost of drug resistance in *Mycobacterium tuberculosis*. Proc Natl Acad Sci USA 2009;106:14711–5.
[11] Abu-Raddad LJ, Sabatelli L, Achterberg JT, Sugimoto JD, Longini Jr IM, Dye C, et al. Epidemiological benefits of more-effective tuberculosis vaccines, drugs, and diagnostics. Proc Natl Acad Sci USA 2009;106:13980–5.
[12] Russell DG, Barry 3rd CE, Flynn JL. Tuberculosis: what we don't know can, and does, hurt us. Science 2010;328:852–6.
[13] Nazaroff WW, Nicas M, Miller SL. Framework for evaluating measures to control nosocomial tuberculosis transmission. Indoor Air 1998;8:205–18.
[14] CDC (Centers for Disease Control and Prevention). Guidelines for environmental infection control in health-care facilities: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). MMWR; 2003. 52(RR-10). p. 1–42.
[15] Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. PLoS Med 2006;3:e494.
[16] Menzies D, Joshi R, Pai M. Risk of tuberculosis infection and disease associated with work in health care settings. Int J Tuberc Lung Dis 2007;11:593–605.
[17] Baussano L, Nunn P, Williams B, Pivetta E, Bugiani M, Scano F. Tuberculosis among health care workers. Emerg Infect Dis 2011;17:488–94.
[18] Centers for Disease Control, Department of Health, ROC. Taiwan tuberculosis incidence and mortality rate, 2002 – 2008. Available from: http://www2.cdc.gov.tw/public/Data/9123117163971.pdf. Chinese. [accessed 06.08.10].
[19] Tsai YC, Pan TC, Yen MY, Jiang DDS. The incidence of tuberculosis in senior centers in Taipei City, 2004 – 2006. Epidemiol Bull (Taipei Taiwan) 2008;24:663–75.
[20] Blower SM, McLean AR, Porco TC, Small PM, Hopewell PC, Sanchez MA, et al. The intrinsic transmission dynamics of tuberculosis epidemics. Nat Med 1995;1:815–21.
[21] Dye C, Williams BG. The population dynamics and control of tuberculosis. Science 2010;328:856–61.
[22] Rudnick SN, Milton DK. Risk of indoor airborne infection transmission estimated from carbon dioxide concentration. Indoor Air 2003;13:237–45.
[23] Liao CM, Chang CF, Liang HM. A probabilistic transmission dynamic model to assess indoor airborne infection risks. Risk Anal 2005;25:1097–107.
[24] Chen SC, Chang CF, Liao CM. Predictive models of control strategies involved in containing indoor airborne infections. Indoor Air 2006;16:469–81.
[25] Brookmeyer R, Johnson E, Bollinger R. Modeling the optimum duration prophylaxis in an anthrax outbreak. Proc Natl Acad Sci USA 2003;100:10129–32.
[26] Brookmeyer R, Johnson E, Bollinger R. Public health vaccination policies of containing an anthrax outbreak. Nature 2004;432:901–4.
[27] Brookmeyer R, Johnson E, Barry S. Modeling the incubation period of anthrax. Stat Med 2005;24:531–42.
[28] Barnhart S, Sheppard L, Beaudet N, Stover B, Balmes J. Tuberculosis in health care settings and the estimated benefits of engineering controls and respiratory protection. J Occup Environ Med 1997;39:849–54.
[29] Yau YH, Chandrasegaran D, Badarudin A. The ventilation of multiple-bed hospital wards in the tropics: a review. Building Environ 2011;46:1125–32.
[30] Sung M, Kato S. Estimating the germicidal effect of upper-room UVGI system on exhaled air of patients based on ventilation efficiency. Building Environ 2011;46:2326–32.
[31] Fennelly KP, Martyny JW, Fulton KE, Orme IM, Cave DM, Heifets LB. Cough-generated aerosols of *Mycobacterium tuberculosis*: a new method to study infectiousness. Am J Respir Crit Care Med 2004;169:604–9.
[32] Riley RL, Mills CC, O'grady F, Sultan LU, Wittstadt F, Shivpuri DN. Infectiousness of air from a tuberculosis ward: ultraviolet irradiation of infected air: comparative infectiousness of different patient. Am Rev Respir Dis 1962;85:511–25.
[33] Liao CM, Chen SC, Chang CF. Modeling respiratory infection control measures effects. Epidemiol Infect 2008;136:299–308.
[34] Gammaitoni L, Nucci MC. Using a mathematical model to evaluate the efficacy of TB control measures. Emerg Infect Dis 1997;3:335–42.
[35] Porco TC, Blower SM. Quantifying the intrinsic transmission dynamics of tuberculosis. Theor Popul Biol 1998;54:117–32.
[36] Department of Social Affairs, Ministry of the Interior, ROC (Taiwan). Available from: http://www.moi.gov.tw/dsa/ [accessed 14.01.10].
[37] Wang LF, Tzeng SY. A study on daily life behavior and territory activity for the elderly in nursing home – Southern Taiwan's two hospital-based nursing homes for example. J Archit 2006;57:25–53 [Chinese].
[38] Bureau of Health Promotion, Department of Health, ROC (Taiwan). Available from: http://www.bhp.doh.gov.tw/BHPnet/Portal/ [accessed 14.01.10].
[39] Ko G, Burge HA, Nardell EA, Thompson KM. Estimation of tuberculosis risk and incidence under upper room ultraviolet germicidal irradiation in a waiting room in a hypothetical scenario. Risk Anal 2001;21:657–73.
[40] Xu P, Kujundzic E, Peccia J, Schafer MP, Moss G, Hernandez M, et al. Impact of environmental factors on efficacy of upper-room air ultraviolet germicidal irradiation for inactivating airborne mycobacteria. Environ Sci Technol 2005;39:9656–64.
[41] Centers for Disease Control, Department of Health, ROC. (Taiwan). Taiwan tuberculosis control report 2007, 2008, 2009, and 2010. Available at: http://www.cdc.gov.tw [accessed 13.08.10].
[42] Department of Statistics, Ministry of the Interior, ROC (Taiwan). Available from: http://www.moi.gov.tw/stat/index.aspx [accessed 28.01.10].
[43] Vynnycky E, Fine PEM. The natural history of tuberculosis: the implications of age-dependent risks of disease and the role of reinfection. Epidemiol Infect 1997;119:183–201.
[44] Dye C, Garnett GP, Sleeman K, Williams BG. Prospects for worldwide tuberculosis control under the WHO DOTS strategy. Lancet 1998;12:1886–91.
[45] Wang CS, Chen HC, Yang CJ, Wang WY, Chong IW, Hwang JJ, et al. The impact of age on the demographic, clinical, radiographic characteristics and treatment outcomes of pulmonary tuberculosis patients in Taiwan. Infection 2008;36:335–40.
[46] Jones RM, Masago Y, Bartrand T, Haas CN, Nicas M, Rose JB. Characterizing the risk of infection from *Mycobacterium tuberculosis* in commercial passenger aircraft using quantitative microbial risk assessment. Risk Anal 2009;29:355–65.
[47] Rubin LG. Bacterial colonization and infection resulting from multiplication of a single organism. Rev Infect Dis 1987;9:488–93.
[48] Beggs CB, Noakes CJ, Sleigh PA, Fletcher LA, Siddiqi K. The transmission of tuberculosis in confined spaces: an analytical review of alternative epidemiological models. Int J Tuberc Lung Dis 2003;7:1015–26.
[49] Volk WA, Benjamin DC, Kadner RJ, Parseus JT. Essentials of medical microbiology. 4th ed. Philadelphia: J.B. Lippincott; 1991.
[50] Loudon RG, Bumgarner LR, Lacy J, Coffman GK. Aerial transmission of mycobacteria. Am Rev Respir Dis 1969;100:165–71.
[51] Ice GH. Daily life in a nursing home: has it changed in 25 years? J Aging Stud 2002;16:345–59.
[52] Pruchno RA, Rose MS. Time use by frail older people in different care settings. J Appl Gerontol 2002;21:5–23.
[53] Riley RL. Airborne infection. Am J Med 1974;57:466–75.
[54] Riley EC, Murphy G, Riley RL. Airborne spread of measles in a suburban elementary. Am J Epidemiol 1978;107:421–32.
[55] Escombe AR, Oeser CC, Gilman RH, Navincopa M, Ticona E, Pan W, et al. Natural ventilation for the prevention of airborne contagion. PLoS Med 2007;4:e68.
[56] Chen SC, Liao CM, Li SS, You SH. A probabilistic transmission model to assess infection risk from *Mycobacterium tuberculosis* in commercial passenger trains. Risk Anal 2010;31:930–9.
[57] Brooks-Pollock E, Cohen T, Murray M. The impact of realistic age structure in simple models of tuberculosis transmission. PLoS One 2010;5:e8479.
[58] Basu S, Andrews JR, Poolman EM, Gandhi NR, Shah NS, Moll A, et al. Prevention of nosocomial transmission of extensively drug-resistant tuberculosis in rural South African district hospitals: an epidemiological modelling study. Lancet 2007;370:1500–7.
[59] Lin HH, Murray M, Cohen T, Colijn C, Ezzati M. Effects of smoking and solid-fuel use on COPD, lung cancer, and tuberculosis in China: a time-based, multiple risk factor, modelling study. Lancet 2008;372:1473–83.
[60] Legrand J, Sanchez A, Le Pont F, Camacho L, Larouze B. Modeling the impact of tuberculosis control strategies in highly endemic overcrowded prisons. PLoS One 2008;7:e2100.

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[61] Wu P, Lau EH, Cowling BJ, Leung CC, Tam CM, Leung GM. The transmission dynamics of tuberculosis in a recently developed Chinese city. PLoS One 2010; 5:e10468.
[62] Keeler E, Perkins MD, Small P, Hanson C, Reed S, Cunningham J, et al. Reducing the global burden of tuberculosis: the contribution of improved diagnostics. Nature 2006;444:49–57.
[63] Chang CM, Lee NY, Lee HC, Wu CJ, Chen PL, Lee CC, et al. Positive tuberculin skin tests in nursing home residents in Southern Taiwan. Arch Gerontol Geriatr 2010;51:e129–32.
[64] Chan-Yeung M, Cheung AH, Dai DL, Chan FH, Kam KM, Tam CM, et al. Prevalence and determinants of positive tuberculin reactions of residents in old age homes in Hong Kong. Int J Tuberc Lung Dis 2006;10: 892–8.
[65] Mikami M, Kawasaki Y. Two step tuberculin testing among elderly Japanese admitted to residential homes. Kekkaku 2000;75:643–8.
[66] IARC. IARC monographs on the evaluation of carcinogenic risks to humans: solar and ultraviolet radiation, vol. 55. Lyon: International Agency for Research on Cancer, World Health Organization; 1992.

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