Estimation of Environmental Control Measures for Tuberculosis Transmission in Care Facilities for the Elderly

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Objectives: Exogenous reinfections in tuberculosis (TB) have been reported among elderly patients in long-term care facilities. This study estimated the impact of upper room ultraviolet germicidal irradiation (UVGI) and negative air ionization on the reduction in TB infection assuming that current TB control failed.
Methods: Estimated probability distributions R_A, R_M, R_{UV+M}, and R_{IO+M}, denoting the reproduction numbers of cases with no intervention, wearing surgical mask of infector, upper room UVGI, and negative ionization with wearing mask, respectively were determined.
Results: It was assumed that 1 TB patient and 29 susceptibles stayed for 10 hours per day when ACH was 3; all subjects stayed for 60 consecutive days. The median R_A increased from 7.38 (15th day) to 11.72 (two month). The percent reductions of R_M, R_{UV+M}, and R_{IO+M} ranged from 52.4% (15th day) to 41.6% (two month), from 76.6% to 68.3%, and from 74.9% to 63.0%, respectively. The percent reductions of slopes; the change of median R_M, R_{UV+M}, and R_{IO+M} for a change in length of stay, were estimated to be 50.8%, 87.3% and 73.7% when ACH was 1.
Conclusions: In addition to case detection and source control measures, environmental control measures may be effective in preventing exogenous reinfection of TB in elderly care facilities.

Key words: tuberculosis, care facilities, ultraviolet germicidal irradiation, negative air ionization, Wells-Riley model

INTRODUCTION

Patients older than 70 years represent 50.1% of newly registered tuberculosis (TB) patients [1]. As the elderly population has grown, the number of nursing homes has increased [1], and these nursing homes have been identified as high-risk environments for TB infection. In a survey of nosocomial infection of TB in elderly patients in nursing homes in Osaka city from 2002 to 2004, TB was diagnosed in 22% of 197 care facilities [2]. Okumura [3] and Kondo [4] reported exogenous reinfections at nursing home for the elderly, and insisted the cause of exogenous reinfections is that the elderly tend to be immunosuppressed by having other complications and malnutrition. Ito [5] reviewed the literatures on exogenous reinfection of TB in HIV-negative persons, and concluded that risk of exogenous reinfection was not rare, and its risk will increase as the growing elderly population who has dementia and other complications, and the increasing number of nursing homes.

It was also reported that automated ventilation systems were installed in 59% of these facilities, and the mean number of air changes per hour (ACH) was 3 in 14% of these facilities [2]. Evidence shows that ventilation rates lower than 2 ACH are associated with higher tuberculin skin test conversion rates among staff in non-isolation rooms [6]. As natural ventilation is reduced in winter or during the night, ventilation rates lower than 2 ACH likely occur in some facilities.

Health examination at acceptance and annual health examination in two kinds of care facilities for the elderly like moderate fee home and health care facility were not regulated by law. Routine tuberculosis examination was not done in fee-based home and health care facility. A delay in tuberculosis case finding in care facilities for the elderly has been pointed out. Shishido [7, 8] analyzed 15 elderly TB patients who had been diagnosed in 23 nursing homes during 5 years and reported that 5 of 15 TB patients required more than 2 months before consulting a doctor, and 2 patients needed more than 6 months.

Thus, care facilities for the elderly where tuberculosis examination was insufficient under the condition of ventilation rates lower than 3 ACH, have had higher exogenous reinfection risk. Further environmental control measures might reduce its risk, but its magnitude of reduction was not known.

Riley *et al.* [9] demonstrated the germicidal efficacy of unshielded ultraviolet (UV) lights inside air ducts in the 1950s, and Riley and Nardell [10, 11] defined the airborne nature of TB transmission using a guinea pig air-sampling model. However, upper room or shielded ultraviolet germicidal irradiation (UVGI) was used infrequently in the following decades. Recently UVGI has received renewed interest, and evidence of its efficacy and proper use has been proposed [12]. Now, UVGI is an established means of disinfection and has been shown to prevent the spread of airborne infection [10]. On the other hand, some reports indicate that negative air ionizers have bactericidal effects and reduce airborne *Salmonella* transmission in poultry

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hatching [13]. Escombe *et al.* [14] showed that upper-room UV lights and negative air ionization prevented most airborne transmission of TB using a guinea pig air-sampling model.

This study used a mathematical model to estimate the impact of upper-room UV light and negative air ionization on the prevention of exogenous reinfection of TB in elderly care facilities with a delay in finding tuberculosis cases.

MATERIALS AND METHODS

Scenario

In this study, a "model" healthcare facility with 300 m^2 of floor space and a ceiling height of 3 m was used. It was assumed that 30 residents and care workers were present in the facility; of these, 29 who were exposed to each other for 10 hours per day were considered susceptible, and 1 was considered a pulmonary TB resident wearing surgical mask. Health examination at acceptance and annual health examination assumed not to be done in this healthcare facility. A delay of up to 60 days in finding tuberculosis cases in the care facility before consulting a doctor was hypothesized. To reduce TB infection, either upper-room UV lights installed at 2.1 m or negative air ionization units were considered as environmental control measures.

Models

The Wells-Riley equation is a well known transmission model used to quantify the risk associated with inhalation of indoor airborne microbes [10]. This model was used to estimate the reproduction number for an airborne infectious disease in an enclosed environment (R_A).

The reproduction number R_A for susceptible people (S) in an enclosed space was assumed to be a function of the number of infectious people (I), their infectivity (q), the exposure time (t) per day, susceptible respiration rate (p), room ventilation rate (Q), and total number of exposed days (n) as follows:

$$R_A = S \times (1 - \{\exp(- Ipqt/Q)\}^n) \quad (1)$$

Quantum generation rate q was back-calculated using the Wells-Riley equation with the mean risks of TB infection in a commercial airline as reported by Ko *et al.* [15] using epidemiologic transmission data of multidrug resistant TB during an 8.75-h airplane flight. Details of the method of estimating distribution for the quantum generation rate of TB were based on a previous article [16].

Log normal distributions with a geometric mean 0.0127 and a geometric standard deviation of 2.2992 (LN(0.0127, 2.2992)) were used, for which a median 17.58 was estimated for quantum generation rate q that closely represented active TB patients without chemotherapy.

Efficacy of a surgical face mask used by an infector

Dharmadhikari *et al.* [17] represented 56% risk reduction in TB transmission when patients used masks. If η is the efficiency of a respiratory protection device used by a infector, the reproduction number R_M within susceptible people S with reducing transmission at the source calculated by modifying Equation (1) as follows:

$$R_M = S \times (1 - \{\exp(- Ipqt(1 - \eta)/Q)\}^n) \quad (2)$$

Efficacy of upper room air UVGI

The efficacy of environmental control can be expressed as an equivalent ventilation rate in the lower room that is able to reduce TB incidence by the same amount as would occur by increasing the mechanical ventilation rate [10]. The efficacy of upper room air UVGI depends on the disinfection rate per hour (/h) due to UVGI in the upper room (ΔK_{UW}) and can be expressed as follows:

$$\Delta K_{UW} = 3600 \cdot Z \cdot IR \quad (3)$$

where Z is UV susceptibility ($\mu W \times s/cm^2)^{-1}$ and IR is UV irradiance ($\mu W/cm^2$) [18].

The lower room air exchange rate (/h) due to upper room UVGI (ΔK_{LW}) is expressed as follows:

$$\frac{1}{\Delta K_{LW}} = \frac{1}{\dot{V}/V_T}\left(\frac{V_L}{V_T}\right) + \frac{1}{\Delta K_{UW}}\left(\frac{V_T}{V_U}\right) \quad (4)$$

where $\dot{V}/V_T$ is air mixing inside the room, $\dot{V}$ is the volume of air coming from the upper part of the room per hour (m^3/hr), V_L is the volume of the nonirradiated lower room (m^3), V_U is the volume of the irradiated upper room (m^3), and V_T ($V_T = V_U + V_L$) is the total volume of the room (m^3) [19]. The reproduction number R_{UV} within susceptible people S in an enclosed space with upper room air UVGI is calculated by modifying Equation (1) as follows:

$$R_{UV} = S \times (1 - \{\exp(- Ipqt/(Q + \Delta K_{LW} \cdot V_L)\}^n) \quad (5)$$

Efficacy of negative air ionization

Escombe *et al.* [14] found that negative air ionization brought 51% of TB disease compared with no intervention. The reduced quantum generation rate was applied by multiplying 0.51 times q to represent the negative ionization effect; this was inserted into Equation (1) to get the reproduction number R_{IO} within susceptible people (S) in an enclosed space with negative air ionization.

Values for model inputs

Basic values for variables used to estimate R_A, R_M, R_{UV}, and R_{IO} for TB infection are shown in Table 1. Values related to the efficacy of upper room UVGI are shown in Table 2 [20–22].

Based on the estimated quantum generation rate and using Equations (1), (2), (3), (4) , and (5) with values in Table 1 and 2, R_A, R_M, R_{UV}, and R_{IO} for TB infection were quantified by Monte Carlo simulation with Oracle Crystal Ball software (Oracle Corporation, Redwood Shores, CA, USA). The goodness of fit of distributions was tested using Anderson-Darling statistics.

RESULTS

The estimated probability distribution R_A, R_M , R_{UV+M}, and R_{IO+M}, which denoted the reproduction numbers of cases with only room ventilation (no

Table 1 Base values for variables used to estimate R_A, R_{UV}, and R_I for TB infection

Parameters	Base value
Number of people in enclosed airspace (N)	30
Volume of shared airspace (V m^3)	900
Total exposure time per day (t hours)	10
Breathing rate (p m^3/h)	0.3
Number of infectious people (I)	1
Air exchange rate per hour (A /h)	1, 3, 6
Number of exposed days (n days)	1–60
Efficiency of a mask used by a infector (η)	0.56

Table 2 Values related to the efficacy of upper room UVGI

Parameters	Base value
V_T (V_U + V_L): Volume of the room (m^3)	300 × 3
V_U: Volume of irradiated upper room (m^3)	300 × 0.9
V_L: Volume of nonirradiated lower room (m^3)	300 × 2.1
ν: Vertical air velocity of air [15, 16] (m/h)	Lognormal (0.5, 0.5)*
V/V_T: Air mixing rate inside room	(ν × 300 × 3600)/2/V_T
Z: UV sensitivity [12] (μW × s/cm^2)$^{-1}$	Lognormal (0.0024, 0.0023)*
IR: UV irradiance [17] (μW/cm^2)	3
ΔK_{UW}: Ventilation rate equivalent to efficacy of upper room air UVGI	Lognormal (26.11, 25.19)*
ΔK_{LW}: Ventilation rate equivalent to efficacy of lower room air UVGI	Lognormal (7.47, 6.83)*

*The lognormal distribution is defined by the geometric mean and standard deviation, respectively.
ΔK_{UW} is calculated by the equation (3), and ΔK_{LW} is calculated by equation (4).

intervention), surgical mask used by infector, upper room UVGI with surgical mask used by infector, and negative ionization with surgical mask used by infector, respectively, was then observed. When the room ventilation rate was 3 ACH, the distribution of R_A for 1 day of exposure was fitted to a log-normal distribution that had a median of 0.56, with a geometric mean of 0.50528 and a geometric standard deviation of 1.73696 (LN (0.50528, 1.73696)). The distribution of R_M was fitted to a log-normal distribution LN (0.24640, 1.76979) with median 0.25, the distribution of R_{UV+M} was fitted to a log-normal distribution LN (0.12473, 1.87586) that had a median of 0.12, and the distribution of R_{IO+M} was fitted to a log-normal distribution LN (0.12862, 1.74109) that had a median of 0.13 for 1 day of exposure. Relationships between the medians of estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M}, and days of exposure up to 6 days are shown in Fig. 1. The median of estimated probability distributions of R_A increased from 0.56 (first day) to 3.21 (sixth day) as baseline risk. The mean percent reductions with R_M, R_{UV+M}, and R_{IO+M} were 55.2, 78.4% and 76.9%, respectively, from day 1 through day 6.

To investigate the effect of monthly exposure with the same room ventilation rate, the distribution of R_A was fitted to a beta distribution B (α, β) with α = 2.29850, β = 4.23926, and a median of 12.89; the distribution of R_M was fitted to a gamma distribution with a median of 6.61, a location parameter of 0.62000, a scale parameter of 1.92000, and a shape parameter of 3.44356; the distribution of R_{UV+M} was fitted to a log-normal distribution LN (3.66403, 1.74034) with median 3.37; and the distribution of R_{IO+M} was fitted to a log-normal distribution LN (3.81323, 1.64799) with median 3.59 for 30 days of exposure. Relationships between the medians of estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M}, and months of exposure up to 2 months are shown in Fig. 2. The median of estimated probability distributions of R_A increased from 7.38 (15th day) to 11.72 (two month). The values of percent reduction of R_M, R_{UV+M}, and R_{IO+M} ranged from 52.4% (15th day) to 41.6% (two month), from 76.6% (15th day) to 68.3% (two month), and from 74.9% (15th day) to 63.0% (two month), respectively.

If ACH was 1, the distribution of R_A for 1 day of exposure was fitted to a log-normal distribution LN (1.68343, 1.71981) with a median of 1.65. The distribution of R_M was fitted to a log-normal distribution LN (0.74299, 1.75384) that had a median of 0.74, the distribution of R_{UV+M} was fitted to a log-normal distribution LN (0.18094, 2.09491) that had a median of 0.18, and the distribution of R_{IO+M} was fitted to a log-normal distribution LN (0.38208, 1.77192) that had a median of 0.38 for 1 day of exposure. Relationships between the medians of estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M}, and days of exposure in the room where ventilation rate was 1 ACH are shown in Fig. 3. The median of estimated probability distributions of R_A increased from 1.65 (first day) to 8.64 (sixth day) as baseline risk. The mean percent reductions of R_M, R_{UV} and R_{IO} were 53.4%, 88.4% and 75.7%, respectively, from day 1 through day 6. Results showed

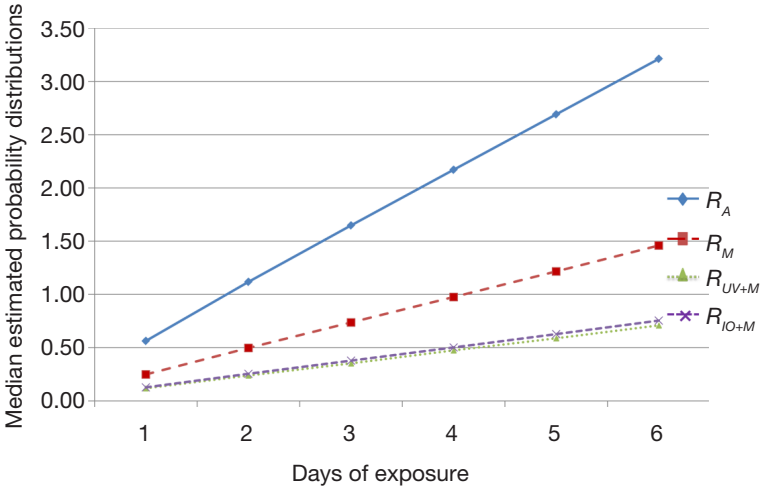

Fig. 1 Relationship between days of exposure and median estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M} with an air-exchange rate per hour (ACH) of 3. *Filled diamonds* denote the absence of intervention, *filled squares* denote the wearing surgical mask of an infector, *filled triangles* denote the use of upper-room UV light, and *crosses* denote the use of negative ionization.

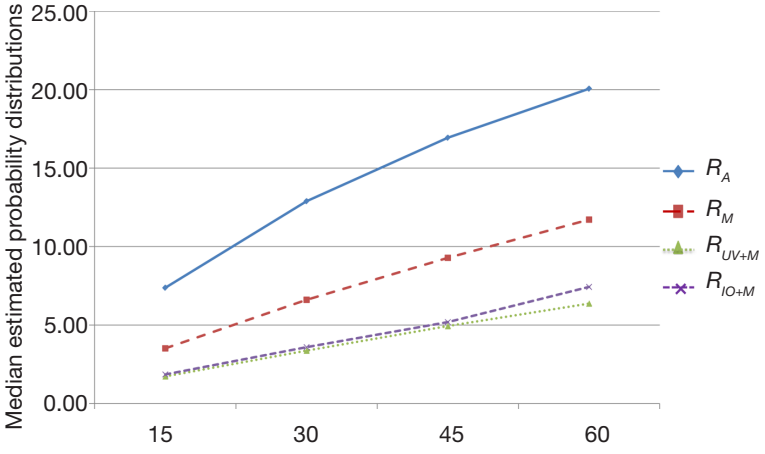

Fig. 2 Relationship between days of exposure and median estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M} with an air-exchange rate per hour (ACH) of 3. *Filled diamonds* denote the absence of intervention, *filled squares* denote the wearing surgical mask of an infector, *filled triangles* denote the use of upper-room UV light, and *crosses* denote the use of negative ionization.

that the median R_{UV+M} was lower than the median R_{IO+M} during 6 days, and the difference between the median R_{UV+M} and R_{IO+M} increased with exposure days.

If room ventilation rate was 6 ACH, the distribution of R_A for 1 day of exposure was fitted to a log-normal distribution LN (0.27841, 1.79159) with a median of 0.28. The distribution of R_M was fitted to a log-normal distribution LN (0.12862, 1.74109) that had a median of 0.12, the distribution of R_{UV+M} was fitted to a log-normal distribution LN (0.08079, 1.83459) that had a median of 0.08, and the distribution of R_{IO+M} was fitted to a log-normal distribution LN (0.06784, 1.77578) that had a median of 0.06 for 1 day of exposure. The relationships between the medians of estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M}, and days of exposure where ventilation rate was 6 ACH are shown in Fig. 4. The median of estimated probability distributions of R_A increased from 0.28 (first day) to 1.66 (sixth day) as baseline risk.

The mean percent reductions of R_M, R_{UV+M} and R_{IO+M} were 55.6% and 71.6%, and 77.2%, respectively from day 1 through day 6. The median R_{IO+M} was lower than the median of R_{UV+M} during 6 days, and the difference between median R_{UV+M} and R_{IO+M} increased as exposure days passed.

The slopes of the change in median R_A, R_M, R_{UV+M}, and R_{IO+M} for a change in number of days of stay (Δ median R_A, R_M, R_{UV+M}, and R_{IO+M} / Δ days of exposure) were calculated for each ACH, and the relationships between the slopes and ACHs were investigated (Fig. 5). The slopes Δmedian R_A, R_M, R_{UV+M}, and R_{IO+M} / Δ days of exposure increased exponentially as the air-exchange rate per hour decreased, and the slope Δ median R_{UV+M}/ Δdays of exposure was the lowest. The percent reductions of Δmedian R_M, R_{UV+M} and R_{IO+M} / Δ days of exposure were 50.8%, 87.3%, and 73.7% when the ventilation rate was 1 ACH, and 55.1%, 71.5% and 76.9% when the ventilation rate was 6 ACH, respectively.

DISCUSSION

In this study, we showed the additional percent reductions of R_{UV+M} and R_{IO+M} to the percent reduction of R_M, and the additional percent reductions of Δ median R_{UV+M} and R_{IO+M} / Δdays of exposure to the percent reduction of R_M. And the effect of R_{UV+M} seemed to be same as R_{IO+M} when the ventilation rate was 3 ACH for 2 months. If the room ventilation rate was 1 ACH, the upper-room UV light was estimated to be most effective as exposure days increased. If the ventilation rate was 6 ACH, negative ionization was estimated to be most effective as exposure days increased.

The rationale for using a simple surgical face mask on infectious patients is based on the theory of droplet nuclei, but the lack of data on this potentially useful, commonly recommended, and low-risk method of TB

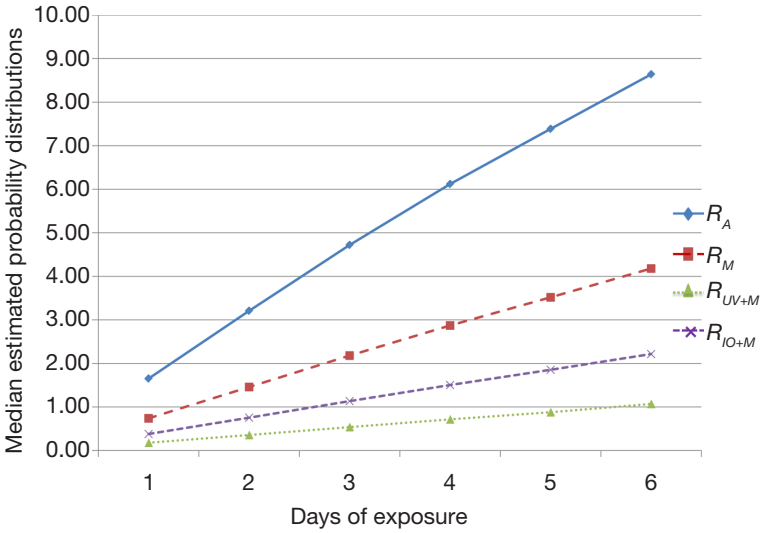

Fig. 3 Relationship between days of exposure and median estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M} with an air-exchange rate per hour (ACH) of 1. *Filled diamonds* denote the absence of intervention, *filled squares* denote the wearing surgical mask of an infector, *filled triangles* denote the use of upper-room UV light, and *crosses* denote the use of negative ionization.

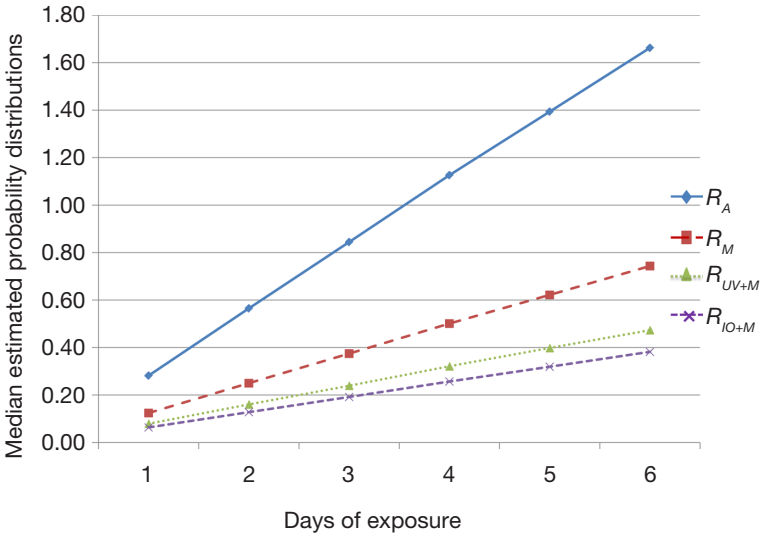

Fig. 4 Relationship between days of exposure and median estimated probability distributions of R_A, R_M, R_{UV+M}, and R_{IO+M} with air-exchange rate per hour (ACH) of 6. *Filled diamonds* denote the absence of intervention, *filled squares* denote the wearing surgical mask of an infector, *filled triangles* denote the use of upper-room UV light, and *crosses* denote the use of negative ionization.

infectious source control. Dharmadhikari *et al.* [17] conducted a prospective study to evaluate the efficacy of surgical face masks worn by patients with MDR-TB in reducing transmission, and they showed 56% decreased risk of TB transmission from infectious patients. Even if surgical face mask was assumed to be worn by a coughing patient, TB infection risk remained with delay in TB case-finding from this result, and further control measures for TB transmission is required.

Reed [23] summarized the history of UVGI for air disinfection and reported that UVGI has recently received renewed interest, and safe and effective commercial products have been introduced. Ko *et al.* [15] showed that upper room UVGI reduced the mean annual new infection rate in a hypothetical hospital waiting room and that upper room UVGI was the most effective among additional ventilation and a high-efficiency particulate air filters using a cost-effectiveness analysis and a simulation model. Escombe *et al.* [14] showed that upper-room UV lights and negative air ionization prevented most airborne TB transmission using guinea pig air sampling. Fletcher *et al.* [24] exposed bacterial species to positive and negative ions to distinguish among effects arising from: (1) the action of the air ions; (2) the action of the electric field, and (3) the action of ozone, and indicated that the bactericidal action attributed to negative air ions was overestimated in previous reports. Escombe *et al.* [14] considered that the reduction of TB infection was mainly brought by the effect of negative air ions; however, this reduction may have been due to an overall effect that included other factors.

Sze-To and Chao [25] reviewed the methods of risk assessment of infectious respiratory diseases by comparing the Wells-Riley model and dose-response approaches and insisted the infectivity of the pathogen described in the quanta generation rate always refers to the infectivity of the pathogens in humans, as the quanta generation rate is back-calculated from the number of outbreak cases of the disease by the Wells-Riley model. Therefore, airborne TB infection risk for humans in an enclosed space can be extrapolated by using the quanta generation rate calculated backward from the guinea pig TB infection experiment.

In terms of the model for analysis of upper room UVGI systems, Riley, Permutt, and Kaufman [19, 26] built a two-zone transient model based on the experi-

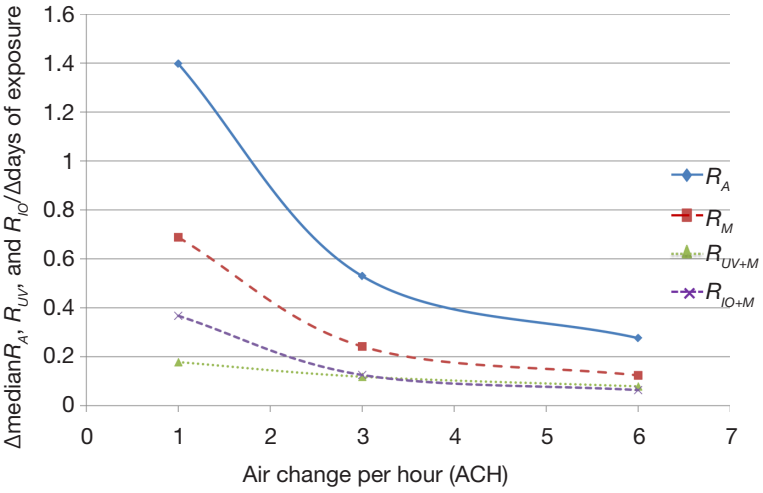

Fig. 5 Relationship between Δmedian R_A, R_M, R_{UV+M}, and R_{IO+M} / Δdays of exposure and air-exchange rate per hour. *Filled diamonds* denote the absence of intervention, *filled squares* denote the wearing surgical mask of an infector, *filled triangles* denote the use of upper-room UV light, and *crosses* denote the use of negative ionization.

mental data of artificial dissemination rates of a test organism (*Serratia marcescens*). Begss and Sleigh [27] extended this model to be suitable for assessing UVGI systems for a wide range of ventilation conditions. Noakes *et al.* [28] compared the analytical mixing models with computational fluid dynamic (CFD) models to evaluate the effect of upper room UVGI systems. They reported that analytical mixing models reasonably gave good average zone concentrations. The original Riley and Permutt model [19] is suitable for estimating the effect of upper room UVGI systems under the assumption that the air-mixing rate in the room is only dependent on the vertical air velocity in this scenario.

Suzuki and Sone [1] reported that 90% of 40 facilities for elders undertook annual routine TB examinations, but most fee-based homes did not implement sufficient preventive measures against TB in a Tokyo metropolitan district. They observed that TB cases occurred in these fee-based homes, as a result of poor use of TB examinations. Shimouchi *et al.* [2] observed occasional TB patients, though residents had annual chest X-ray screening in 94% of 197 nursing homes in Osaka City. Patient delay was defined as the duration in days from the reported onset of symptoms to the first physician consultation [29]. Doctor delay was defined as the length of time between the first medical examination (including chest radiography, sputum smear, or sputum culture) to the diagnosis of pulmonary TB [29]. As TB diagnosis is difficult for the elderly due to non-specific appearances of signs/symptoms, X-ray shadows or negative tuberculin reaction tests, patient delay and doctor delay could easily have occurred [29]. They insisted that the strength of TB infection control measures in care facilities for the elderly was adequate. Okumura [3] and Kondo [4] reported exogenous reinfections at nursing home for the elderly, and insisted the cause of exogenous reinfections is that the elderly tend to be immunosuppressed by having dementia, other complications and malnutrition. Ito [5] reviewed the literatures on exogenous reinfection of TB in HIV-negative persons and Chiang and Riley [30] also reviewed exogenous reinfection, and both reviews showed the evidence supporting exogenous reinfection of TB.

The limitation of this study is that estimation of R_A did not consider the protection rate of already-infected persons, because data showing absolute risk and frequency of exogenous reinfection of TB have remained unavailable. Estimated R_A was based on the assumption that the protection rate of already-infected person was similar with that of BCG vaccination. Therefore, the estimation of R_A overestimated infection risk.

Additional control measure to case-finding and source-control is required in care facilities for the elderly having complications and malnutrition. Based on the results of this study, delay in TB case-finding produced TB infection risk, even if surgical face mask was assumed to be worn by a coughing patient, and negative air ionization may have the same effect at reducing the risk for TB as upper-room UV lights when the room ventilation rate is 3 ACH. The effect of upper-room UV lights seems to be predominant if the room ventilation rate is 1 ACH, and the effect of negative air ionization seems to be predominant if room ventilation rate is 6 ACH. Thus, environmental control measures such as UVGI and air ions seem to be effective under conditions in which adequate ventilation is not maintained.

In terms of upper room UVGI, sufficient laboratory information to develop guidelines is available [10]; however, less evidence is available regarding the reduction of TB infection by negative air ions. Further studies are needed to establish effective environmental control measures for TB transmission in elderly care facilities.

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CONFLICT OF INTEREST

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There are no other conflicts of interest to declare.

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