Assessing the Relative Importance of the Components of an Occupational Tuberculosis Control Program

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Hospital-based occupational tuberculosis (TB) control programs have four basic components: rapid detection of TB disease in presenting patients; use of environmental controls, including personal respiratory protection; periodic tuberculin skin testing; and administration of prophylactic antibiotic therapy to newly infected employees. This article assesses which component is the most important in reducing TB disease risk among health care workers. A quantitative framework for estimating disease risk is developed, and two important results are described. First, the rapid identification of TB disease in presenting patients is the most important element in the overall program. Second, once TB disease has been identified, the use of highly efficient environmental controls (which include respiratory protection) becomes the most important element; these controls are especially important for procedures such as bronchoscopy and autopsy, which can aerosolize large numbers of viable Mycobacterium tuberculosis *bacilli.*

Occupational tuberculosis (TB) disease control programs in most hospital settings have the following four components: (1) rapid detection of TB disease in presenting patients; (2) the use of environmental controls, including respiratory isolation of known/suspected TB cases and personal respiratory protection when attending infectious patients; (3) periodic tuberculin skin testing of staff for new infections; and (4) administration of prophylactic antibiotic therapy to newly infected employees. These components are interventions in a series of events whereby hospital staff can be infected by TB patients and subsequently develop disease. The following question arises: Which intervention is the most important in reducing the risk of TB disease among health care workers? The answer is of practical importance because, given limited resources, efforts should be directed primarily toward those components that effect the greatest decrease in disease risk.

The purpose of this article is to quantitatively estimate the relative impact of the different interventions that comprise an occupational TB disease control program. Two important results will be described. First, the rapid identification of TB disease is the most important element in the overall prevention program. Second, once TB disease has been identified, the use of highly efficient environmental controls (which include respiratory protection) becomes the most important element; high-efficiency

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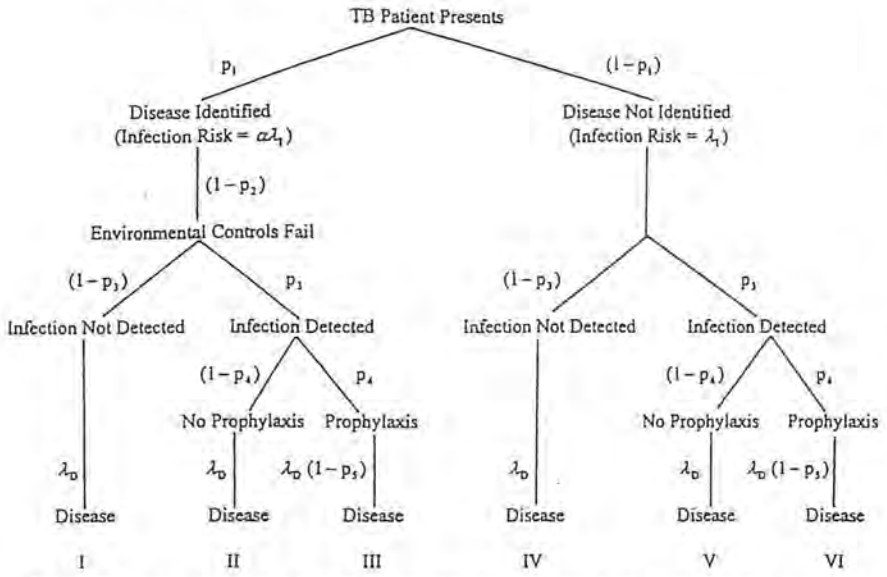

Fig. 1. Six event series that can lead to occupational tuberculosis disease among susceptible health care workers in the presence of an infection/disease control program. The notation is summarized in Table 1.

controls are especially needed for procedures such as bronchoscopy, autopsy, and laboratory work, which can aerosolize large numbers of viable *Mycobacterium tuberculosis (M. tb)* bacilli.

A Framework for Quantifying TB Disease Risk

In the absence of a control program, the average risk of TB disease among health care staff is equal to $\lambda_I \cdot \lambda_D$, where λ_I denotes the average infection risk to staff posed by TB patients who are all unrecognized, and λ_D denotes the subsequent risk of developing TB disease if the infection is not detected and prophylactically treated. Given that a control program is in place, however, Figure 1 depicts six event series that can still result in TB disease among health care staff. The notation for the parameters utilized is described here and summarized in Table 1.

To begin, a TB patient (hereafter presumed to be an infectious patient with untreated pulmonary TB) who presents to the facility may or may not be identified as having the disease. Let p_1 denote the probability that TB disease is rapidly detected, in which case $1 - p_1$ is the probability that disease is not rapidly detected. Because λ_I is the infection risk posed by unrecognized TB patients, let $\alpha \cdot \lambda_I$ (where $0 \leq \alpha \leq 1$) denote the infection risk posed by recognized TB patients. In general, $\alpha < 1$ because patients with recognized TB receive antibiotic therapy that decreases the *M. tb* concentration in respiratory aerosols and decreases cough frequency[1]; in turn, both of these outcomes decrease infectivity. The left-hand side of Figure 1 depicts three alternate event series that may occur when disease is detected in TB patients, while the right-hand side depicts three alternate series when TB disease goes unrecognized.

First, consider the three left-hand side event series (labeled I, II, and III). Because the disease is recognized, it is assumed that environmental controls (which for this discussion include personal respiratory protection) are implemented. The usual controls are placing the patient in a negative-pressure isolation room (for protection of staff outside the room) and use of disposable particulate filter respirators while directly attending the patient. Let p_2 denote the overall efficiency of the combination of control measures in reducing exposure intensity; in the alternative, p_2 may be defined as the probability that the control measures eliminate exposure and risk. Therefore, the quantity $1 - p_2$ is the probability that infection risk is not reduced.

Because of treatment of known TB patients, the facility is assumed to have a tuberculin skin-testing program in place. However, an infection screening program is usually imperfect in that not all employees scheduled for testing actually undergo testing, and some newly infected employees who undergo testing have false negative test results.[2] Therefore, let p_3 denote the probability that newly infected employees successfully undergo skin testing such that their infections are identified, in which case $1 - p_3$ is the probability that newly infected employees are not identified. Note that the left-hand series in Figure 1 bifurcates at the screening step in a corresponding manner.

Next, consider the circumstance that skin testing successfully identifies new infections. Let p_4 denote the probability that infected employees undergo and complete antibiotic prophylaxis, in which case $1 - p_4$ is the probability that they do not. In cor-

TABLE 1
Summary of Notation Used in Figure 1 and Equation 1

λ_I = average infection risk to employees due to patients with undetected TB disease
α = fraction of average infection risk to employees due to early treatment of patients with identified TB disease
λ_D = risk of developing TB disease subsequent to infection without antibiotic prophylaxis
p_1 = probability that TB disease in a presenting patient is rapidly detected
p_2 = probability that environmental controls eliminate exposure to infectious aerosol
p_3 = probability that a new infection in an employee is detected
p_4 = probability that a newly infected employee undergoes antibiotic prophylaxis
p_5 = probability that antibiotic prophylaxis eliminates the risk of developing TB disease

respondence, the series involving successful screening branches at the prophylaxis step. Now let p_5 denote the probability that completing prophylaxis eliminates disease risk, in which case $1 - p_5$ is the probability that completing prophylaxis does not eliminate disease risk. For the event series involving successful skin testing followed by prophylaxis (Series III, Figure 1), the risk of TB disease is the product $\alpha \cdot \lambda_I \cdot p_1(1 - p_2)p_3 \cdot p_4 (1 - p_5)\lambda_D$. For the event series involving successful skin testing not followed by prophylaxis (Series II, Figure 1), the risk of TB disease is the product $\alpha \cdot \lambda_I \cdot p_1(1 - p_2)p_3(1 - p_4)\lambda_D$. For the event series not involving successful skin testing or prophylaxis (Series I, Figure 1), the risk of TB disease is the product $\alpha \cdot \lambda_I \cdot p_1(1 - p_2)(1 - p_3)\lambda_D$.

The three right-hand side event series (labeled IV, V, and VI) in Figure 1 are the same as the respective series I, II, and III, with the exceptions that the environmental controls step is absent because the TB cases are not detected and that the infection risk posed by untreated TB patients is λ_I. For event series IV, V, and VI, the TB disease risks are the respective products $\lambda_I \cdot (1 - p_1)(1 - p_3)\lambda_D$, $\lambda_I \cdot (1 - p_1)p_3(1 - p_4)\lambda_D$, and $\lambda_I \cdot (1 - p_1)p_3 \cdot p_4(1 - p_5)\lambda_D$.

In the presence of an infection control program, the total risk of TB disease, denoted R_D, is the sum of the disease risks for the six event series in Figure 1 and is given by the expression:

$$R_D = \lambda_I \cdot \lambda_D(1 - p_1)(1 - p_3 \cdot p_4 \cdot p_5) + \alpha \cdot \lambda_I \cdot \lambda_D \cdot p_1(1 - p_2)(1 - p_3 \cdot p_4 \cdot p_5) \quad (1)$$

The exact value of R_D depends on knowing the values of all of the input parameters, which may be difficult to specify. At the same time, Equation 1 is useful in assessing the relative importance of the different interventions over a reasonable range of parameter values, as will now be described.

The Relative Impact of Different Interventions

A simple way to compare impacts is to pose a set of values for the intervention parameters and graph the reduction in R_D while increasing the value of each parameter one at a time. For example, consider the following hypothetical scenario, which might be considered "worst-case" because of the low values for the first four parameters: $p_1 = 0.5$, $p_2 = 0.5$, $p_3 = 0.2$, $p_4 = 0.2$, $p_5 = 0.93$, and $\alpha = 0.1$. Worst-case values of p_5 and α are not considered because these parameter values are assumed to be clinically demonstrated outcomes and/or independent of the TB control program. The chosen value of p_5 is based on the observed five-year reduction in TB disease incidence among individuals completing 52 weeks of treatment with isoniazid (INH).[3] As explained below, the posited value of α is based on: (1) the efficacy of antibiotic therapy in reducing the sputum *M. tb* concentration; (2) the efficacy of antibiotic therapy in reducing cough frequency; and (3) an assumed small fraction of cases that are difficult to treat.

A mixed antibiotic regimen is reported to reduce the sputum *M. tb* concentration to 1% of the initial value in 2 days and to 0.1% of the initial value over the next 12 days.[1] If antibiotic therapy is not started until the second day of a 15-day hospital admission, and if a two-phase exponential decrease in the sputum *M. tb* concentration is assumed, these statistics correspond to a 15-day average sputum *M. tb* concentration that is about 10% of the initial concentration. Antibiotic therapy is reported to reduce cough frequency by 40% after one week and by 65% after two weeks[1]; in this case, the total volume of respiratory aerosol emitted during a 15-day admission by a treated TB patient is about one-half that emitted by an untreated TB patient. This reduced volume, combined with the decreased sputum *M. tb* concentration, signifies that a treated TB patient emits about 5% as many *M. tb* as does an untreated TB patient. On the other hand, it is posited that a small percentage of cases, say 5%, do not respond rapidly to antibiotic therapy; such cases would include multiple-drug–resistant strains of *M. tb*. If 5% of admitted TB patients do not experience a rapid decrease in *M. tb* emission, and if the average *M. tb* emission

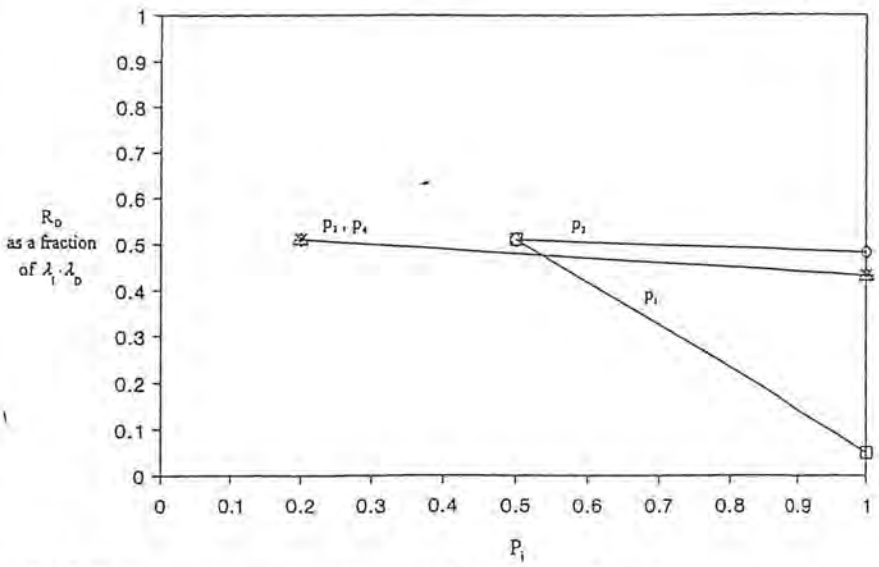

Fig. 2. The decrease in occupational tuberculosis disease risk, R_D, with one-at-a-time increases in the respective intervention parameters p_1, p_2, p_3, and p_4. Initial parameter values are $p_1 = 0.5$, $p_2 = 0.5$, $p_3 = 0.2$, $p_4 = 0.2$, $p_5 = 0.93$, and $\alpha = 0.1$. The low values of p_1 through p_4 constitute a "worst-case" scenario. The p_1 line is indicated by squares, the p_2 line by diamonds, the p_3 line by asterisks, and the p_4 line by triangles.

rate of the remaining cases is 5% that of untreated cases, then $\alpha = 0.1$.

For the above scenario, Figure 2 shows how the value of R_D decreases with increases in p_1 through p_4 made one at a time. For example, the line labeled "p_1" (where p_1 is the probability of detecting a TB patient) graphs R_D as p_1 increases from 0.5 to 1.0, while holding p_2, p_3, and p_4 fixed at their posited values. For the "p_1" line, R_D equals 0.51 $\lambda_I \cdot \lambda_D$ at $p_1 = 0.5$ (the worst-case value) and decreases to 0.048 $\lambda_I \cdot \lambda_D$ at $p_1 = 1.0$. In contrast, one-at-a-time increases in the values of parameters p_2, p_3, and p_4 effect limited reductions in disease risk. For example, increasing p_2 to 1 (where p_2 is the efficiency of environmental controls) decreases R_D to only 0.48 $\lambda_I \cdot \lambda_D$.

The overall meaning of Figure 2 is the following: In a worst-case scenario, where p_1 through p_4 all have low values, the greatest reduction in disease risk will be achieved by increasing the probability of rapidly detecting TB disease. Perfect efficiency in environmental controls ($p_2 = 1.0$) has little impact in this scenario because 50% of all TB patients are not identified, in which case these perfect controls are not applied half of the time.

A summary measure of the relative impact of the intervention parameters p_1 through p_4 is the value of the first partial derivative of R_D with respect to each parameter, or $\partial R_D/\partial p_i$, for $i = 1, 2, 3, 4$. Expressions for these partial derivatives are given in Appendix 1. For the hypothetical worst-case scenario posed above: $\partial R_D/\partial p_1 = -0.91 \lambda_I \cdot \lambda_D$; $\partial R_D/\partial p_2 = -0.048 \lambda_I \cdot \lambda_D$; $\partial R_D/\partial p_3 = -0.10 \lambda_I \cdot \lambda_D$; and $\partial R_D/\partial p_4 = -0.10 \lambda_I \cdot \lambda_D$. The value of $\partial R_D/\partial p_1$ is nine to nineteen times more negative than the other derivatives, which indicates that increases in p_1 cause the greatest decrease in disease risk. These four derivatives also have a simple algebraic meaning; namely, they are the slopes of the corresponding lines depicted in Figure 2. Therefore, the "p_1" line has slope equal to $-0.91 \lambda_I \cdot \lambda_D$, the "$p_2$" line has slope equal to $-0.048 \lambda_I \cdot \lambda_D$, and so forth.

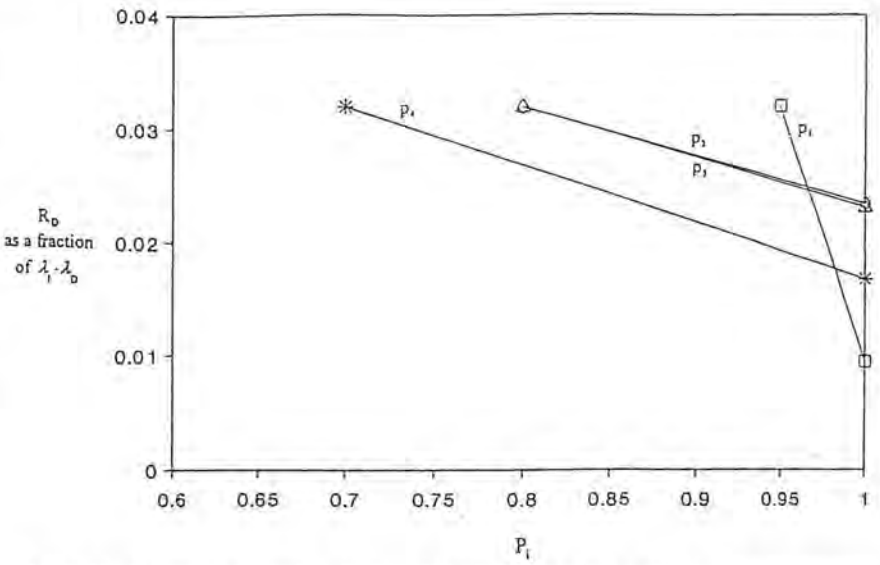

Fig. 3. The decrease in occupational tuberculosis disease risk, R_D, with one-at-a-time increases in the respective intervention parameters p_1, p_2, p_3, and p_4. Initial parameter values are $p_1 = 0.95$, $p_2 = 0.8$, $p_3 = 0.7$, $p_4 = 0.8$, $p_5 = 0.93$, and $\alpha = 0.1$. The values of p_1 through p_4 constitute a "typical" scenario. The p_1 line is indicated by squares, the p_2 line by diamonds, the p_3 line by asterisks, and the p_4 line by triangles.

Although $\partial R_D/\partial p_i$ is a useful metric of relative impact, it does not indicate the final value of R_D per se. For example, consider a more "typical" scenario for which $p_1 = 0.95$, $p_2 = 0.8$, $p_3 = 0.7$, $p_4 = 0.8$, $p_5 = 0.93$, and $\alpha = 0.1$. In this case, the initial value of R_D is 0.032 $\lambda_I \cdot \lambda_D$. Figure 3 depicts the decrease in R_D with increases in p_1 through p_4 made one at a time. The partial derivatives are as follows: $\partial R_D/\partial p_1 = -0.46 \lambda_I \cdot \lambda_D$; $\partial R_D/\partial p_2 = -0.044 \lambda_I \cdot \lambda_D$; $\partial R_D/\partial p_3 = -0.052 \lambda_I \cdot \lambda_D$; and $\partial R_D/\partial p_4 = -0.046 \lambda_I \cdot \lambda_D$. The value of $\partial R_D/\partial p_1$ is nine to ten times more negative than the other derivatives, yet the final values of R_D differ by less than a factor of 2.5, as indicated in Figure 3 for $p_i = 1$. The overall meaning of Figure 3 is the following: In a more "typical" scenario, the greatest reduction in disease risk will still be achieved by increasing the probability of rapid detection of TB disease, but improving the reliability of other interventions may achieve a comparable decrease overall.

In Figures 2 and 3, the values of p_1 through p_4 have been allowed to increase to one. However, there are likely upper limits less than one for these intervention parameters. In the absence of relevant, published survey data from a large sample of hospitals, the following values are offered as possible upper bounds: $p_1 \approx 0.99$, $p_2 \approx 0.99$, $p_3 \approx 0.9$, and $p_4 \approx 0.8$. The p_1 value recognizes that some patients will present with symptoms that are not consistent with pulmonary TB, in which case the necessary diagnostic tests will not be quickly ordered. The p_2 value assumes simultaneous use of two or more high-level controls, such as a large amount of dilution ventilation (eg, 12 air changes per hour) and high-efficiency respiratory protection. The p_3 value accounts for the lack of compliance on the part of some staff in undergoing testing and for the false-negative error inherent in tuberculin skin testing. The p_4 value recognizes that some individuals will decline undergoing antibiotic prophylaxis and that other individuals will initiate prophylaxis but discontinue it because of adverse side effects such as hepatitis.

A Conditional Scenario: TB Disease Identified

To this point, the relative impact of different interventions has been considered across all of the steps

shown in Figure 1. However, because the probability of rapidly detecting TB disease is already high in many hospitals, line staff most frequently encounter the scenario in which TB disease has already been identified. Given that $p_1 = 1.0$, the conditional risk of disease, denoted $R_{D|P_i=1}$, is obtained by simplifying Equation 1 to yield:

$$R_{D|P_i=1} = \alpha \cdot \lambda_I \cdot \lambda_D(1 - p_2)(1 - p_3 \cdot p_4 \cdot p_5) \quad (2)$$

Expressions for the first partial derivatives of $R_{D|P_i=1}$ with respect to p_2 through p_4 are given in Appendix 1.

Now consider the worst-case scenario analogous to that depicted in Figure 2 for which $p_2 = 0.5$, $p_3 = 0.2$, $p_4 = 0.2$, $p_5 = 0.93$, and $\alpha = 0.1$. The partial derivatives are as follows: $\partial R_{D|P_i=1}/\partial p_2 = -0.096\ \lambda_I \cdot \lambda_D$, $\partial R_{D|P_i=1}/\partial p_3 = -0.0095\ \lambda_I \cdot \lambda_D$, and $\partial R_{D|P_i=1}/\partial p_4 = -0.0095\ \lambda_I \cdot \lambda_D$. The fact that $\partial R_{D|P_i=1}/\partial p_2$ is ten times more negative than the other two derivatives indicates that increasing the efficiency of environmental controls (p_2) will effect the greatest decrease in disease risk. To illustrate, Figure 4 shows that the initial value of $R_{D|P_i=1}$ in this scenario is $0.048\ \lambda_I \cdot \lambda_D$. Increasing p_2 to one reduces $R_{D|P_i=1}$ to zero, while increasing either p_3 or p_4 to one, decreases $R_{D|P_i=1}$ to $0.041\ \lambda_I \cdot \lambda_D$.

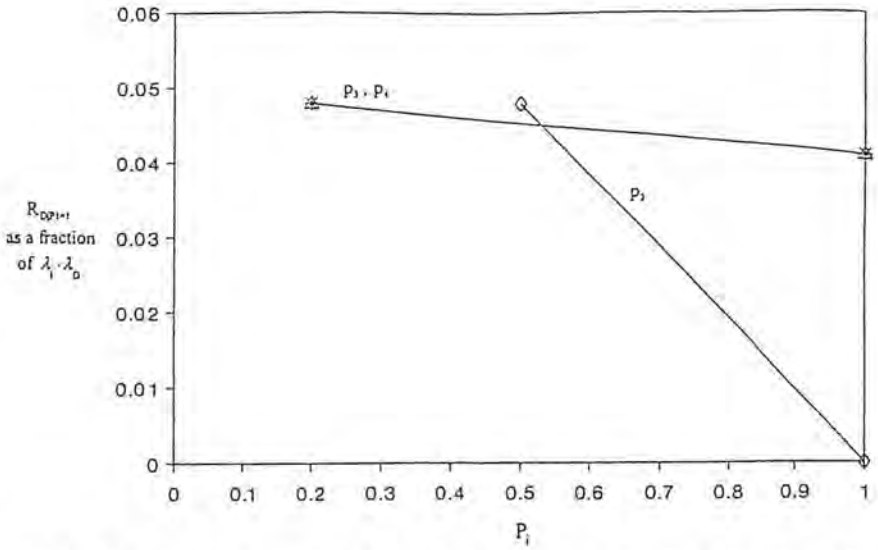

Fig. 4. The decrease in occupational tuberculosis disease risk given that patient disease has been identified, $R_{D|P_i=1}$, with one-at-a-time increases in the respective intervention parameters p_2, p_3, and p_4. Initial parameter values are $p_2 = 0.5$, $p_3 = 0.2$, $p_4 = 0.2$, $p_5 = 0.93$, and $\alpha = 0.1$. The low values of p_2 through p_4 constitute a "worst-case" scenario. The p_2 line is indicated by diamonds, the p_3 line by asterisks, and the p_4 line by triangles.

Discussion

Specifying the Values of λ_I and λ_D to Estimate R_D

To this point, values for infection risk λ_I and disease risk λ_D have not been specified because specification depends on the length of the time period involved. To explain, the usual statement concerning λ_D is that an individual infected with *M. tb* who does not undergo antibiotic prophylaxis has a 10% lifetime risk of developing disease and a 5% risk of developing disease in the first year subsequent to infection.[4] Therefore, the λ_D value differs if one examines performance of the TB disease control program over a one-year versus a 20-year interval, because a person infected early in the interval has a higher risk of developing disease as more time elapses. Similarly, the λ_I value may be a moderate annual infection risk if a one-year period is considered, versus a large cumulative infection risk if a 20-year interval is considered.

Computing cumulative TB disease risk given a constant rate of infection operating over a defined time interval involves a piece-wise method that accounts for the point in the interval that infection might occur and the change in the hazard rate of developing active disease in the remaining time subsequent to infection.[5] For this discussion, it is simpler to consider a five-year time period, in which case λ_I is the five-year cumulative infection risk due to TB patients all of whom are unrecognized and $\lambda_D \approx 0.05$. Equation 1 can now be used to estimate TB disease risk over a five-year period.

To illustrate, assume that the five-year cumulative value of λ_I is 0.2, which corresponds to a 4.4% annual infection risk. In the absence of a TB control program, the five-year cumulative value of R_D is 0.01 (equal to the product $\lambda_I \cdot \lambda_D$), which signifies 10 disease cases per 1000 initially susceptible workers. For comparison, the current US population background TB disease risk for a five-year period is 0.43 cases per 1000, which is lower by a factor of 23. The background risk value follows from interpreting the general population TB disease incidence rate of 8.7 per 100,000 as an annual disease risk,[6] in which case the five-year disease risk is: $1 - (1 - 0.000087)^5 = 0.00043$. Now consider a TB control program with the Figure 2 "worst-case" parameter values. According to Equation 1, $R_D = 0.51\ \lambda_I \cdot \lambda_D$ for the posited parameter values, in which case the TB control program reduces R_D to 0.0051, or 5.1 disease cases per 1000 initially susceptible workers. Therefore, implementing a poor TB control program halves the disease risk, but the remaining risk is still 12-fold greater than the population background value.

High-Risk Scenarios Involving Identified TB Disease

Although rapidly detecting TB disease is the most effective inter-

vention in protecting hospital staff as a whole, some employee groups may still be at high risk of infection when disease has been identified. These groups include personnel who perform bronchoscopies on TB patients, who conduct autopsies on individuals who had active TB, and who handle laboratory specimens containing viable *M. tb*. The high risk results because the work tasks generate the release of infectious aerosol. In the context of the parameter λ_I, which is the average infection risk across all hospital staff due to unrecognized TB patients, these employee groups likely have an infection risk $\lambda_{I|HRG}$ (where the subscript HRG signifies high-risk group) that is greater than both λ_I and $\alpha \cdot \lambda_I$.

In these high-risk situations, $R_{D|P_I=1}$, as defined by Equation 2, measures TB disease risk, but with the infection risk parameter $\lambda_{I|HRG}$ substituting for $\alpha \cdot \lambda_I$. As previously noted, increasing the efficiency of environmental controls in these scenarios effects the greatest decrease in disease risk. In the laboratory, working with *M. tb* specimens while contained within a Class II biological safety cabinet is the usual control. For bronchoscopy and autopsy procedures, which require close proximity to the patient or corpse, respectively, effective local exhaust ventilation devices are not presently available, and general dilution ventilation does not prevent release of infectious aerosol into the breathing zone of the staff. Therefore, use of high-level respiratory protection such as a hooded powered air-purifying respirator (PAPR) is likely the most feasible control.

To justify the PAPR recommendation, consider the bronchoscopy scenario: According to a recent SHEA-CDC survey, the *M. tb* infection rate for bronchoscopists ranged from 0% to 33% among 210 hospitals reporting data for 1992.[7] In an earlier study, the annual *M. tb* infection rate was approximately 5.7% among 62 pulmonary physicians who performed or assisted at bronchoscopies and 1.2% among 42 infectious disease physicians who did not.[8] Finally, one case study found that 10 of 13 staff (77%) became infected while present during an intubation and bronchoscopy procedure on a TB patient.[9] Therefore, it is reasonable to posit that in some hospitals, the five-year cumulative infection risk for bronchoscopy personnel is, say, $\lambda_{I|HRG} = 0.41$ (corresponding to an annual infection risk of 10%). If $\lambda_D = 0.05$, and if maximum values are $p_3 = 0.9$, $p_4 = 0.8$, and $p_5 = 0.93$, then, according to Equation 2:

$$R_{D|P_I=1} = 0.0069(1 - p_2)$$

which signifies that the five-year disease risk absent environmental controls is 6.9 cases per 1000. This value is 16-fold greater than the corresponding population background TB disease risk of 0.43 cases per 1000. The assumed p_2 value for both disposable Type N95 and Type N100 (similar to a high-efficiency particulate air filter) particulate respirators is 0.9,[10] while the assumed p_2 value for a hooded PAPR is 0.96.[11] Therefore, the disposable respirators would reduce $R_{D|P_I=1}$ to 0.7 cases per 1000, which is still above the background risk level. In contrast, the PAPR would reduce $R_{D|P_I=1}$ to 0.3 cases per 1000, which is below the background risk level. Note that the most recent occupational TB control guidelines from the Centers for Disease Control and Prevention also recommend considering use of respirators more protective than the disposable Type N95 in high-infection–risk situations such as bronchoscopy.[12]

The Target Risk Value

When considering measures to reduce TB disease risk, it is useful to identify a target risk level. In the examples posed in this article, the five-year disease risk for the general US population has been used for comparison. In fact, this value may be too high. First, part of the population disease rate involves individuals whose latent *M. tb* infections progress to active disease, whereas no initially susceptible health care workers are latently infected by definition. Second, part of the population disease rate involves individuals who are HIV-infected, or homeless, or in prison. It is likely that few health care workers share the latter two characteristics, and it is reasonable to speculate that the prevalence of HIV infection is lower among health care workers than among the general population.

Determining the target risk value for a specific cohort of health care workers is quite difficult, however, because it involves uncertainty in the true background disease risk that applies to the cohort (which might vary, based on socioeconomic status, geography, race, sex, and age) and involves agreement among managers and line workers about acceptable risk. Perhaps the most feasible policy is to use the general population TB disease risk as the target value in designing occupational TB control programs. Note that specifying the acceptable occupational risk of TB disease is within the purview of public health agencies such as the Occupational Safety and Health Administration, the National Institute for Occupational Safety and Health, and the Centers for Disease Control and Prevention, although none of these agencies has made explicit efforts to define this quantity.

Conclusions

Equation 1, for the outcome parameter R_D, provides a reasonable framework for considering TB disease risk and the intervention efforts that would likely be most effective across hospital staff as a whole. Equation 2, for the outcome parameter $R_{D|P_I=1}$, provides a similar framework where TB disease has already been identified. The first result of the analysis is that the rapid identification of TB disease is the most important element in the overall prevention program. The second result is that once TB disease has

been identified, the use of highly efficient environmental controls, including respiratory protection, is the most important intervention measure, particularly for personnel performing high-infection–risk procedures such as bronchoscopy, autopsy, and laboratory work, which can aerosolize large numbers of viable *M. tb.* In designing interventions based on Equation 1 or 2, it is useful to identify a target risk value. Perhaps the most feasible target value is a five-year cumulative disease risk of 0.4 cases per 1000 initially susceptible workers, which corresponds to the current five-year disease risk for the general US population.

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Appendix 1

The First Partial Derivatives of R_D

For convenience, Equation 1 in the main text is restated here as:

$$R_D = \lambda_I \cdot \lambda_D(1 - p_1)(1 - p_3 \cdot p_4 \cdot p_5) + \alpha \cdot \lambda_I \cdot \lambda_D \cdot p_1(1 - p_2)(1 - p_3 \cdot p_4 \cdot p_5) \quad (A1)$$

If parameters p_1 through p_4 are variables, and parameters p_5 and α are constants, the first partial derivatives are as follows:

$$\partial R_D/\partial p_1 = \lambda_I \cdot \lambda_D(1 - p_3 \cdot p_4 \cdot p_5)[\alpha(1 - p_2) - 1] \quad (A2)$$

$$\partial R_D/\partial p_2 = -\alpha \cdot \lambda_I \cdot \lambda_D \cdot p_1(1 - p_3 \cdot p_4 \cdot p_5) \quad (A3)$$

$$\partial R_D/\partial p_3 = -\lambda_I \cdot \lambda_D \cdot p_4 \cdot p_5[1 - p_1 + \alpha \cdot p_1(1 - p_2)] \quad (A4)$$

$$\partial R_D/\partial p_4 = -\lambda_I \cdot \lambda_D \cdot p_3 \cdot p_5[1 - p_1 + \alpha \cdot p_1(1 - p_2)] \quad (A5)$$

The First Partial Derivatives of $R_{D|P_1=1}$

For convenience, Equation 2 in the main text is restated here as:

$$R_{D|P_1=1} = \alpha \cdot \lambda_I \cdot \lambda_D(1 - p_2)(1 - p_3 \cdot p_4 \cdot p_5) \quad (A6)$$

If parameters p_2 through p_4 are variables, and parameters p_5 and α are constants, the first partial derivatives are as follows:

$$\partial R_{D|P_1=1}/\partial p_2 = -\alpha \cdot \lambda_I \cdot \lambda_D(1 - p_3 \cdot p_4 \cdot p_5) \quad (A7)$$

$$\partial R_{D|P_1=1}/\partial p_3 = -\alpha \cdot \lambda_I \cdot \lambda_D(1 - p_2)p_4 \cdot p_5 \quad (A8)$$

$$\partial R_{D|P_1=1}/\partial p_4 = -\alpha \cdot \lambda_I \cdot \lambda_D(1 - p_2)p_3 \cdot p_5 \quad (A9)$$

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