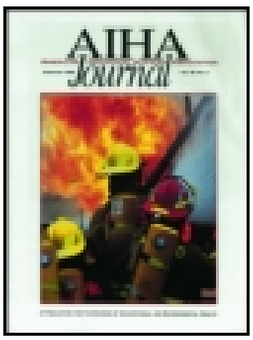

AIHAJ - American Industrial Hygiene Association

ISSN: 1529-8663 (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/uaah20

Regulating the Risk of Tuberculosis Transmission Among Health Care Workers

Mark Nicas

To cite this article: Mark Nicas (2000) Regulating the Risk of Tuberculosis Transmission Among Health Care Workers, AIHAJ - American Industrial Hygiene Association, 61:3, 334-339, DOI: 10.1080/15298660008984541

To link to this article: https://doi.org/10.1080/15298660008984541

Published online: 04 Jun 2010.

Regulating the Risk of Tuberculosis Transmission Among Health Care Workers

AUTHOR
Mark Nicas

Center for Occupational and Environmental Health, School of Public Health, University of California, Berkeley, CA 94720

The 1994 Centers for Disease Control and Prevention guidelines on preventing tuberculosis (TB) transmission among health care workers (HCWs), and the 1997 Occupational Safety and Health Administration (OSHA) proposed TB standard, do not address the issue of acceptable risk. Further, many infection control personnel oppose OSHA's promulgating a standard because they believe most TB infections among HCWs are nonoccupational in origin. This article examines the relationship between TB infection and disease rates, and introduces a probability framework to apportion infection risk between occupational and nonoccupational exposure. It is argued that most TB infections among HCWs are work-related. A 0.2% overall annual risk of TB infection (accounting for both workplace and community exposure) is proposed as acceptable, because in the context of an infection surveillance program it limits an HCW's cumulative disease risk close to the value for the general United States population. Based on the probability framework, an estimate of the background community infection rate, and the traditional Wells-Riley risk model, it is shown that a target workplace infection risk value can be derived and expressed in terms of an expected pulmonary dose. The latter target dose informs risk management decision-making.

An increased incidence of active pulmonary tuberculosis (TB) in the U.S. population in the early 1990s, combined with nosocomial outbreaks of multidrug-resistant TB, has led to renewed concern for TB transmission among health care workers (HCWs).[1–3] Infection usually occurs via inhalation of respirable particles carrying viable *Mycobacterium tuberculosis* (*M. tb*) bacilli that are emitted in respiratory aerosols by persons with pulmonary TB. It is estimated that 10% of infected persons eventually develop clinical disease absent receiving prophylactic antibiotic therapy, and that half of these cases occur in the first year following infection.[4]

Prior to the advent of antibiotic therapy in the 1950s, HCWs experienced high rates of *M. tb* infection, and substantial numbers developed active TB.[3] Rates of *M. tb* infection currently reported for HCWs are much lower. In a mail questionnaire survey of hospital epidemiologists, employee infection rates in 1992 as reported for 109 hospitals had a median value of 0.5% (range: 0–7.7%).[5] In an ongoing prospective cohort study involving 29,000 HCWs, the cohort annual infection rate is reported to be approximately 1%.[6] Note that infection rates for particular groups of HCWs can be considerably higher.[7]

In 1992 the National Institute for Occupational Safety and Health (NIOSH) issued recommendations on respiratory protection against *M. tb* aerosol.[8] In 1994 the Centers for Disease Control and Prevention (CDC) issued final guidelines for preventing TB transmission in health care facilities.[9] In 1997 the Occupational Safety and Heath Administration (OSHA) proposed a comprehensive standard on preventing TB transmission among HCWs.[10] Although these guidelines/standards have been valuable in promoting integrated *M. tb* infection control plans, none have directly addressed the issue of acceptable risk. Further, many infection control professionals oppose OSHA's promulgation of a TB standard, in part because they believe that most *M. tb* infections among HCWs are not work-related.[6]

This research was funded by a grant from the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Award K01-OH001555–03. The ideas expressed are solely the author's responsibility and do not necessarily represent the official views of the funding agency.

This article has two overall purposes—to argue that most HCW *M. tb* infections are occupational in origin, and to propose an acceptable occupational *M. tb* infection risk in the context of cumulative disease risk. To this end, a probability framework is presented to apportion *M. tb* infection risk between occupational and nonoccupational exposure, and to inform risk management decisions.

APPORTIONING INFECTION RISK

It is the author's experience that hospital infection control staff attribute most employee *M. tb* infections to nonoccupational exposures, particularly where infected employees have not had documented contact with TB patients and/or where infection rates in different job categories have no clear association with the expected frequency of TB patient contact. As a case in point, the CDC's classification of a hospital area or staff group as "low risk" involves the criterion that the observed *M. tb* infection rate (based on tuberculin skin test conversions) is no greater than for other hospital areas or staff groups in which occupational exposure to *M. tb* was unlikely.[9] Absent such differences, the CDC assumes that most observed infections are not work-related. Note that the 1994 CDC guidelines described some scenarios as low risk even though the annual rates of infection (ARIs) across all hospital employees were 1.2 to 1.8%.

Apportioning *M. tb* infections between occupational and nonoccupational exposure is complicated by the lack of direct assessment of background infection rates in the general U.S. population and in specific metropolitan areas. The ARI for the general U.S. population in the 1970s was estimated to be .008%.[11] Based on 1994 data, OSHA estimated the general U.S. population ARI to be 0.15%, with a range across the 50 states of .02 to 0.35%.[10]

The Relationship Between Infection and Disease Rates

Absent direct knowledge of the background ARI, is it reasonable to attribute most of an ARI among HCWs of say, 1%, to nonoccupational exposure? One approach is to consider the annual TB disease rate that would correspond to a nonoccupational ARI of 1%. The annual number of TB disease cases per 10^5 population members, denoted I, is related to the ARI and to the population prevalence of latent *M. tb* infection (PREV, a fraction between 0 and 1) by the following approximation (derived in Appendix 1):

$$I \approx [ARI(1 - PREV)(0.05) + (PREV)(0.00097)] \times 10^5 \quad (1)$$

In the preamble to the proposed TB standard, OSHA estimated that 6.6% of general U.S. population members carry latent *M. tb* infections.[10] If ARI = .01 (1%) and PREV = .066 (6.6%), then $I \approx 53$ TB disease cases per 10^5 population members per year. In contrast, in 1997 the reported TB disease incidence rate for the general U.S. population was 7.4 per 10^5.[12] In other words, a background ARI of 1% would correspond to an annual TB disease rate seven times greater than the reported U.S. population rate. Moreover, a background ARI of 1.8% (termed "low risk" as previously noted) would correspond to $I \approx 91$ TB disease cases per 10^5 per year, which is 12 times the reported population rate. Therefore, absent additional information concerning nonoccupational contacts among infected HCWs, it is unreasonable to assume that a 1% ARI (much less a 1.8% ARI) is predominantly nonoccupational in origin.

Note that Equation 1 can be used to obtain an estimate of the current general U.S. population ARI by setting I = 7.4 and PREV = .066; the corresponding ARI is 2×10^{-4} (.02%). For the U.S. population disease rate of 9.4 per 10^5 in 1994 (the year for which OSHA estimated the ARI to be 0.15%), Equation 1 yields ARI = 6.4×10^{-4} (.064%), which is 60% lower than OSHA's estimate.

A Probability Framework

Infection risk can be apportioned between occupational and nonoccupational exposure in the following manner. Let λ_W denote the per-hour probability of infection while in the workplace, and let λ_C denote the per-hour probability of infection while in the general community outside the workplace (which includes the home environment). For simplicity, assume that (1) both λ_W and λ_C are constant over time; (2) infection in the workplace and in the community are mutually exclusive events; and (3) an HCW spends 5 hours at work and 19 hours in the community each day. The latter statistics correspond to spending 1825 hours at work per year, or 228 shifts of 8 working hours per shift.

For a susceptible HCW subject to this process for n days, the cumulative risk (probability) of being infected on the job, Pr[HCW Workplace Infection | *n* days], and being infected in the community, Pr[HCW Community Infection | *n* days], are given by the following expressions (derived in Appendix II):

$$\Pr[\text{HCW Workplace Infection} \mid n \text{ days}] = \frac{5 \cdot \lambda_W}{5 \cdot \lambda_W + 19 \cdot \lambda_C} \cdot [1 - e^{-n(5 \cdot \lambda_W + 19 \cdot \lambda_C)}] \quad (2)$$

$$\Pr[\text{HCW Community Infection} \mid n \text{ days}] = \frac{19 \cdot \lambda_C}{5 \cdot \lambda_W + 19 \cdot \lambda_C} \cdot [1 - e^{-n(5 \cdot \lambda_W + 19 \cdot \lambda_C)}] \quad (3)$$

Because workplace versus community infection are mutually exclusive events, an HCW's total n-day cumulative infection risk, Pr[HCW Infection | *n* days], is the sum of Equations 2 and 3, or:

$$\Pr[\text{HCW Infection} \mid n \text{ days}] = 1 - e^{-n(5 \cdot \lambda_W + 19 \cdot \lambda_C)} \quad (4)$$

For a non-HCW, it is assumed that λ_C applies 24 hr/day, in which case the background general population (non-HCW) *n*-day cumulative infection risk is

$$\Pr[\text{Background Infection} \mid n \text{ days}] = 1 - e^{-n(24 \cdot \lambda_C)} \quad (5)$$

Note that the framework permits a health care workplace to exert a protective effect if $\lambda_W < \lambda_C$. The latter circumstance would pertain if a facility does not admit or treat TB patients. To illustrate, if $\lambda_C = 1.7 \times 10^{-7}$/hour and n = 365 days, Equation 5 indicates the general population annual infection risk is 0.15%, which corresponds to OSHA's estimate for the general U.S. population. If $\lambda_W = 0$ for a HCW in a particular facility, Equations 2–4 indicate that the HCW's annual infection risk is 0.12%, all due to community exposure.

Clearly, one needs values for λ_W and λ_C to compute an absolute risk. An estimate for λ_C can be obtained by equating Pr[Background Infection | n days] with an estimated general population ARI, although an estimate for λ_W may not be available. However, the framework still proves useful for apportioning infection risk given relative values for the λ parameters.

In this regard, consider the prevalence of persons with TB disease in a hospital versus the community. In one study of three urban hospitals the numbers of TB patients admitted in 1995 were 28, 56, and 57, respectively; in all three hospitals, TB patients comprised approximately 0.4% of inpatients.[13] The latter prevalence corresponds to 400 TB cases per 10^5 inpatients. In the two counties in which these hospitals were located, the TB disease rates for 1995 were, respectively, 19 per 10^5 and 36 per 10^5.[13] Because

TB disease cases must be reported, it is thought that TB disease prevalence and incidence rates are close in value.

If one assumes random mixing or contacts between HCWs and non-HCWs in both the hospital and community, the ratio λ_W/λ_C is equal to the ratio of the TB case prevalence among hospital inpatients to the TB case prevalence among community members. Based on the preceding prevalence values, $\lambda_W = 11 \times \lambda_C$ to $21 \times \lambda_C$. Note that random mixing corresponds to the standard mass action assumption used in population modeling of infectious disease transmission.[14] Further, the random mixing assumption likely understates the difference between λ_W and λ_C, because HCWs as a group are unlikely to share several important characteristics associated with community members having TB disease (e.g., homelessness, HIV infection, recent jobless status).

Next, consider an observed ARI of 1% among a large HCW cohort; this value is within the range of ARIs observed in the three-hospital study.[15] In Equation 4, by setting Pr[HCW Infection | n = 365] = .01 and $\lambda_W = 11 \times \lambda_C$, one finds that $\lambda_W = 4.1 \times 10^{-6}$/hour and $\lambda_C = 3.7 \times 10^{-7}$/hour. By using these λ values in Equations 2 and 3, one finds that Pr[HCW Workplace Infection | n = 365] = 2.7 × Pr[HCW Community Infection | n = 365]. In the alternative, if $\lambda_W = 21 \times \lambda_C$, Pr[HCW Workplace Infection | n = 365] = 5.7 × Pr[HCW Community Infection | n = 365]. In brief, these results suggest that HCWs subject to an ARI of 1% in the urban hospital study had a three- to sixfold greater chance of acquiring *M. tb* infection on the job than in the community.

ACCEPTABLE INFECTION RISK

Cumulative Risk

The idea of acceptable infection risk should properly be considered in the context of cumulative risk. The reason is that an annual risk that seems acceptably low can produce an alarming cumulative risk over a working lifetime or portion thereof. For discussion purposes, the annual rate of infection also can be viewed as an annual risk of infection. If the ARI (as a fraction between 0 and 1) is constant over m years, the cumulative risk of infection, denoted CRI, is

$$CRI = 1 - (1 - ARI)^m \quad (6)$$

For example, if ARI = .01 (1%), and if m = 45 yr (a working lifetime), then CRI = 0.36 (36%), or a one-in-three chance of infection. In this context, the 1994 CDC guidelines' description of an ARI = .018 (1.8%) as low risk is a misnomer, because it produces a 45-yr CRI of 0.56 (56%).

To integrate risk over time, many infection controllers use the related concept of the expected time to infection, defined as 1/ARI (in years), rather than the CRI. For example, if ARI = .01, the expected time to infection is 100 yr, which is greater than an expected lifetime, say, 75 yr. However, the expected time to infection understates the degree of risk on the individual and cohort level, while the CRI has a clear meaning on both levels.

First, if ARI = .01 for an individual, the CRI after 10 years is 0.1 (a 1-in-10 chance). Most individuals would likely appreciate this nontrivial degree of infection risk when posed in cumulative risk terms, but dismiss the risk when posed in terms of taking 100 years on average to become infected. Second, if ARI = .01 for all individuals in a cohort of size N, the expected number of infections after 10 years is 0.1 N, which is the product of the CRI and the cohort size. In contrast, the expected time to infection has an ambiguous meaning at the cohort level, because there is a different expected time for the first infection, for the second infection, and so forth. In fact, if the ARI value is the same for all N individuals, the expected time to the first infection is equal to the quantity 1/(ARI × N). Therefore, if N = 1000 and ARI = .01, the expected time to observe the first infection is only 0.1 yr (37 days), not 100 yr.

A Proposal for Acceptable Risk

Specifying an acceptable risk of infection or disease is a complex issue, involving value judgments and economic analyses that are beyond the scope of this article. The tack taken here is to propose an overall ARI value that, in the context of an *M. tb* infection surveillance program, limits an HCW's risk of developing TB disease close to the general population risk value.[16] In this regard, the 1997 general U.S. population TB disease rate of 7.4 per 10^5 can be interpreted as an annual TB disease risk. Over a 12-year period, this annual risk produces a cumulative TB disease risk of approximately 1 per 1000, or: $1 - (1 - .000074)^{12} = .00089$. The latter computation is analogous to finding a CRI via Equation 6.

In a previous analysis, it was shown that in the absence of a surveillance program that detects and prophylactically treats new *M. tb* infections, an ARI of 0.2% produces a cumulative 12-year disease risk of .0013 (or 1.3 per 1000); in the presence of a perfect surveillance program (i.e., all new *M. tb* infections are detected and successfully treated) using a 12-month tuberculin skin test interval, an ARI of 0.2% produces a 12-year cumulative disease risk of .0006 (or 0.6 per 1000).[16] CDC guidelines recommend, and the proposed OSHA standard requires, that all susceptible HCWs with potential exposure to infectious TB patients be skin tested at least annually. If the surveillance program is only 50% effective (due to the combination of negative test error, noncompliance with testing, and failure of antibiotic prophylaxis),[16] an ARI of 0.2% produces a 12-year cumulative disease risk of .00095, or approximately 1 per 1000, which is similar to the general population 12-year disease risk. Therefore, an overall ARI of 0.2% is proposed as acceptable.

In the context of the framework previously described, this ARI corresponds to Pr[HCW Infection | n = 365] = .002, which has workplace and community components. If a value for λ_C is specified, the permissible value of λ_W can be determined from Equation 4, and the corresponding value of Pr[HCW Workplace Infection | n = 365] can be determined from Equation 2. The latter quantity provides a target risk value for designing infection control measures. For example, OSHA's estimated ARI = 0.15% for the general U.S. population corresponds to $\lambda_C = 1.7 \times 10^{-7}$/hour. Given this λ_C and Pr[HCW Infection | n = 365] = .002, it follows that $\lambda_W = 4.5 \times 10^{-7}$/hour and Pr[HCW Workplace Infection | n = 365] = .0008 (.08%). The manner in which the latter target risk value can be used is now described.

A Proposal for Risk Assessment/Management

The Wells-Riley risk model for *M. tb* infection relates the expected pulmonary dose d (which depends on the airborne *M. tb* concentration) to an infection risk r over a specified exposure period,[17,18] and can be written as

$$r = 1 - e^{-d} \quad (7)$$

Pertinent details of the model, including the relationship between d and the airborne *M. tb* concentration, are provided elsewhere.[19] If the occupational exposure period is taken as 5 hr/day over n days, r can be equated with Pr[HCW Workplace Infection | n

days], in which case a specified workplace infection risk corresponds to a specified pulmonary dose, or

$$d = \ln(1 - \Pr[\text{HCW Workplace Infection} \mid n \text{ days}]) \quad \textbf{(8)}$$

Given an estimate for an HCW's pulmonary dose, one can use the traditional industrial hygiene framework of applying controls at the source (most often a TB patient), pathway (air), and receptor (the HCW) to select one or more measures to attain the target dose value. Because there is still no practical method for measuring the airborne concentration of viable *M. tb*, an HCW's pulmonary dose in the absence of new controls must be estimated. One method is using the past ARI in the same work group or an analogous work group. The second method is using published estimates of *M. tb* emission rates in combination with measurements of workspace ventilation characteristics.[19] The following scenario illustrates the first method.

Consider personnel who perform bronchoscopies, and assume that their past ARI is .06 (6%). The latter value is similar to the ARI observed in a 2-year study of pulmonary physicians who performed bronchoscopies.[20] If $\lambda_C = 1.7 \times 10^{-7}$/hour (corresponding to a general population background ARI = 0.15%), then Pr[HCW Workplace Infection | n = 365] = .0588 and Pr[HCW Community Infection | n = 365] = .0012 by Equations 2 and 3, respectively. In turn, the current expected occupational dose is d = .0606 by Equation 8. Given that the target occupational risk is Pr[HCW Workplace Infection | n = 365] = .0008, in which case the overall ARI would equal .002, the target dose is d = .0008 by Equation 8. Therefore, the current expected occupational dose must be reduced by 99% (from .0606 to .0008) to arrive at an acceptable infection risk. If the sole source of occupational *M. tb* exposure is the bronchoscopy suite, a combination of increased ventilation, in-room air filtration, and high-level respiratory protection (e.g., wearing a hooded powered air-purifying respirator during bronchoscopies on known and suspect TB patients) should be sufficient to limit d ≤ .0008.

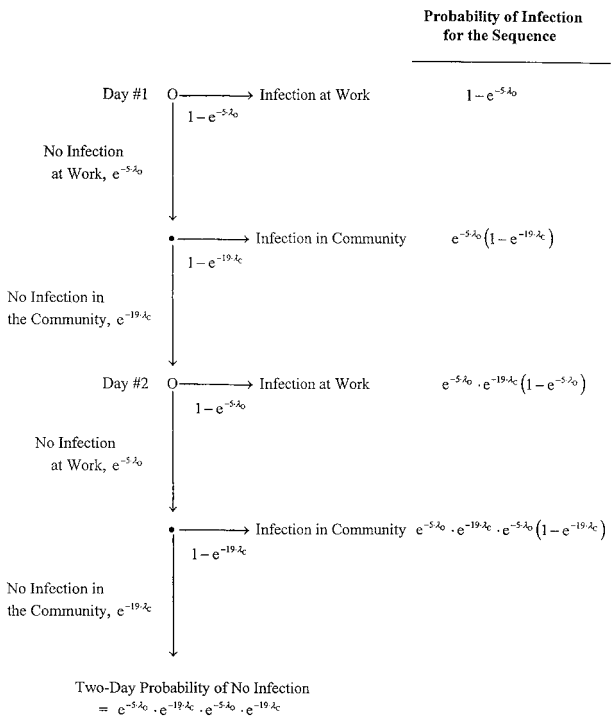

FIGURE 1. Flow diagram of the pathways by which a susceptible HCW can acquire *M. tb* infection over the course of 2 days. Each day the HCW spends 5 hr at work and then spends 19 hr in the community. Given that the HCW is not infected when entering either environment, a horizontal arrow shows probability of infection in the indicated environment during the exposure period, and a vertical arrow shows probability of not being infected in the indicated environment during the exposure period.

DISCUSSION

The preceding probability framework is a reasonable approach to apportioning infection risk between workplace and community exposure. Further, in combination with the Wells-Riley risk model and a specified acceptable overall ARI of 0.2%, the probability framework permits a quantitative method for occupational risk assessment and management. At the same time, the proposed risk assessment method is subject to uncertainty, primarily due to uncertainty in the estimates for λ_C and λ_W.

As previously noted, there are no recent surveys that have directly assessed the background population ARI by state or metropolitan area. In the preamble to its proposed TB standard, OSHA did estimate the background population ARI for all 50 states based on 1994 data.[10] Therefore, a state-specific λ_C can be derived by equating Pr[Background Infection | n = 365] in Equation 5 with the OSHA ARI estimate, and solving for λ_C. It is certainly preferable to use a more recent estimate for the state-specific ARI, but even then the corresponding λ_C value can overstate or understate the true λ_C value for a particular group of HCWs. Overestimating versus underestimating the HCW λ_C value would have the effect of, respectively, overly restricting versus inadequately restricting the target occupational risk value.

Given that OSHA's population ARI estimates are based in part on TB disease rates, the author judges that the corresponding λ_C value from Equation 5 would more likely overestimate the true HCW λ_C, because HCWs as a group do not share important characteristics associated with many community members with TB disease. Although a biased estimate for λ_C is not desirable, an overestimate is health-conservative by overly constraining the target occupational risk value. It is also noted that OSHA's estimated 1994 ARI values for 3 of 50 states (Alaska, Hawaii, New York), and for the District of Columbia are sufficiently high such that a HCW's overall ARI would exceed 0.2% even if $\lambda_W = 0$. If this circumstance remains after using more recent ARI estimates, the recommended approach is to select infection control measures that bring the future expected occupational dose to a value as low as reasonably achievable.

Estimating a λ_W value, which corresponds to a future expected occupational dose, is subject to perhaps greater uncertainty. If one uses a past ARI value for a group of HCWs, as previously illustrated, one inherently assumes that the future occupational risk (in the absence of new controls) will be the same as the past. However, infection risk depends in part on the number of TB patients seen and their degree of infectivity. Therefore, changes in the future number of TB cases treated and in patient infectivity can increase or decrease the λ_W value relative to the current estimate.

Even if the risk construct and estimates for λ_C and λ_W were perfect, it must be recognized that infection and disease incidence are stochastic processes, in which case there is inherent uncertainty in the incidence outcomes.[16] For example, if there are 2 infections expected among 1000 susceptible persons after 1 year, it would not be unreasonable to see 0 infections (probability ≈ 14%) or 5

infections (probability ≈ 4%). The latter probabilities are based on a Poisson distribution with an expected value of two for the future number of infections.

Although the risk assessment method proposed in this article is subject to uncertainty, as are all risk assessment methods, it offers the benefits of being proactive and promoting a reasoned selection of infection control measures. Without an estimate of current occupational infection risk (i.e., the expected pulmonary dose in the absence of new controls), "risk assessment" becomes an after-the-fact count of infection and disease incidence. Moreover, without an infection risk estimate and a target risk value, there is no objective way to design infection controls. For example, the 1994 CDC guidelines recommend that newly constructed TB patient isolation rooms be provided with at least 12 nominal air changes per hour (ACH), a rate for which there can be a high operational cost. However, no justification was offered for a minimum of 12 ACH versus, say, 8 ACH or 20 ACH. Further, no effort was made to assess the magnitude of infection risk remaining with 12 ACH, nor to decide whether the residual risk was acceptable. In essence, there was no quantitative basis for making this ventilation recommendation.

In conclusion, the author recommends that OSHA adopt a 0.2% overall ARI as the measure of acceptable infection risk, and that the probability framework and risk assessment method described here be incorporated into an HCW tuberculosis standard. In offering this recommendation, it is not intended that a health care employer be cited for noncompliance if the observed ARI among a group of HCWs exceeds 0.2%. Rather, the 0.2% overall ARI is to be used to estimate a target occupational dose and select appropriate control measures. At a minimum, this analysis can contribute to future deliberations by public health agencies regarding occupational tuberculosis transmission.

REFERENCES

1. **Bloom, B.R., and C.J.L. Murray:** Tuberculosis: Commentary on a reemergent killer. *Science 257*:1055–1064 (1992).
2. **Menzies, D., A. Fanning, L. Yuan, and M. Fitzgerald:** Tuberculosis among health care workers. *New Engl. J Med. 332*:92–98 (1995).
3. **Sepkowitz, K.A.:** Tuberculosis and the health care worker: A historical perspective. *Ann. Int. Med. 120*:71–79 (1994).
4. **American Thoracic Society/Centers for Disease Control:** Diagnostic standards and classification of tuberculosis. *Am. Rev. Respir. Dis. 142*:725–735 (1990).
5. **Fridkin, S.K., L. Manangan, E. Bolyard, and W.R. Jarvis:** SHEA-CDC TB survey, part 1: Status of TB infection control programs at member hospitals, 1989–1992. *Infect. Control Hosp. Epidemiol. 16*: 129–134 (1995).
6. **Nardell, E.:** Is a tuberculosis exposure a tuberculosis exposure if no one is infected? [editorial] *Infect. Control Hosp. Epidemiol. 19*:484–486 (1998).
7. **Zaza, S., H.M. Blumberg, C. Beck-Sague, W.H. Haas, et al.:** Nosocomial transmission of *Mycobacterium tuberculosis*: Role of health care workers in outbreak propagation. *J. Infect. Dis. 172*:1542–1549 (1995).
8. **National Institute for Occupational Safety and Health (NIOSH):** *NIOSH Recommended Guidelines for Personal Respiratory Protection of Workers in Health-Care Facilities Potentially Exposed to Tuberculosis.* Atlanta: NIOSH, 1992.
9. **Centers for Disease Control and Prevention:** Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. *Morb. Mort. Wkly. Rep. 43(RR-13)*:1–132 (1994).
10. "Occupational Exposure to Tuberculosis; Proposed Rule." *Federal Register* 62:54159–54308 (17 October 1997).
11. **Reider, H.L., G.M. Cauthen, G.W. Comstock, and D.E. Snider:** Epidemiology of tuberculosis in the United States. *Epidemiol. Rev. 11*:79–98 (1989).
12. **Centers for Disease Control and Prevention (CDC):** *Reported Tuberculosis in the United States, 1997*. Atlanta: CDC, 1998.
13. **Sutton, P.M., M. Nicas, F. Reinisch, and R.J. Harrison:** Evaluating the control of tuberculosis among healthcare workers: adherence to CDC guidelines of three urban hospitals in California. *Infect. Control Hosp. Epidemiol. 19*:487–493 (1998).
14. **Anderson, R.M., and R.M. May:** *Infectious Diseases of humans. Dynamics and Control.* Oxford, UK: Oxford University Press, 1992. p. 7.
15. **Sutton, P.:** "Annual Skin Test Conversion Rates in the Three-Hospital Study." January 1999. [Personal communication] California Department of Health Services, 1515 Clay Street, Oakland, CA 94612.
16. **Nicas, M.:** A risk/cost analysis of alternative screening intervals for occupational tuberculosis infection. *Am. Ind Hyg. Assoc. J 59*:104–112 (1998).
17. **Wells, W.F.:** *Airborne Contagion and Air Hygiene*. Cambridge, MA: Harvard University Press, 1955. pp. 105–141.
18. **Riley, R.L., and F. O'Grady:** *Airborne Infection: Transmission and Control.* New York: MacMillan, 1961. pp. 95–125.
19. **Nicas, M.:** Respiratory protection and the risk of *Mycobacterium tuberculosis* infection. *Am. J. Ind. Med.* 27:317–333 (1995).
20. **Malasky, C., T. Jordan, F. Potluski, and L.B. Reichman:** Occupational tuberculosis infection among pulmonary physicians in training. *Am. Rev. Respir. Dis. 142*:505–507 (1990).

APPENDIX I: The Relationship Between Infection and Disease Rates

TB disease incidence has two components—cases that arise among newly infected individuals, and cases that arise among those latently infected. For newly infected persons, there is an estimated 5% probability of developing disease in the first year following infection, and a 10% lifetime probability.[4] Given values for the ARI and the PREV, these probabilities can be used to estimate disease incidence as follows.

In a given year, the expected number of TB disease cases that occur due to new infections, I_{New}, is the product of the ARI, the number of uninfected individuals, S, and the probability .05 of developing disease in the first year of infection. The number S equals the population size, N, times the complement of the prevalence of latent infections, or: S = (N)(1−PREV). Therefore:

$$I_{New} = (ARI)(N)(1-PREV)(.05) \qquad \textbf{(A1)}$$

Next, consider that an estimated 5% of newly infected persons develop disease over their remaining lifetimes subsequent to the first year of infection, although the length of a "remaining lifetime" was not defined.[4] However, if 75 yr is the expected lifetime in the United States, and if 18 yr is taken as the age of infection, the remaining lifetime after the first year of infection is 56 yr. To produce a 10% lifetime disease risk, the remaining lifetime disease risk subsequent to the first year of infection must be 5.3%. To explain, if 1000 individuals are newly infected, and 50 (5%) develop disease in the first year, then 50 of 950 (5.3%) must develop disease in the remaining 56 years to produce a 10% lifetime risk.

To compute the annual disease risk among latently infected persons, a constant hazard rate is assumed such that each year subsequent to the first year of infection, a fraction .00097 of latently infected persons develop TB disease. Note that: $1 - (1 - .00097)^{56} = .053$. In a given year, the expected number of TB disease cases that occur due to latent infections, I_{Latent}, is the product of .00097 and the number who are latently infected (N)(PREV), or:

$$I_{Latent} = (N)(PREV)(.00097) \quad \textbf{(A2)}$$

If $N = 10^5$, the sum of Equations A1 and A2 is the expected annual incidence of TB disease per 10^5 population members, I, which is the typical reporting unit:

$$I = [(ARI)(1 - PREV)(0.05) + (PREV)(0.00097)] \times 10^5 \quad \textbf{(A3)}$$

Equation (A3) also assumes the following conditions: (1) the ARI is stable over several years; (2) there is a negligible influx into the community of individuals with TB disease; (3) there is a negligible population fraction of immunocompromised individuals infected with *M. tb;* and (4) the population size is stable. Note that a large influx of individuals with TB disease and/or a large population fraction of immunocompromised persons infected with *M. tb* would increase the observed disease incidence rate. A large influx of persons with TB disease would increase the count of newly diagnosed cases. Immunocompromised persons infected with *M. tb* are estimated to have an 8% annual risk of developing TB disease,[1] which is 80-fold greater than the annual risk for nonimmunocompromised persons infected with *M. tb* (i.e., .08/.00097).

APPENDIX II: Apportioning the Risk of Infection

λ_W and λ_C denote the per-hour probability of infection in, respectvely, the workplace and the community. It is assumed that: (1) λ_W and λ_C are constant over time; (2) infection in the workplace and in the community are mutually exclusive; and (3) an HCW spends 5 hours at work and 19 hours in the community each day. Consider how a susceptible HCW might become infected over 2 consecutive days (see Figure 1).

The HCW begins Day 1 by spending 5 hours on the job. The probability of not being infected in this 5-hour period is $e^{-5\cdot\lambda_W}$, and the probability of being infected is the complement $1 - e^{-5\cdot\lambda_W}$. Next, the HCW spends 19 hours in the community. Given that the HCW was not previously infected, the probability of not being infected in this 19-hour period is $e^{-19\cdot\lambda_C}$, and the probability of being infected is $1 - e^{-19\cdot\lambda_C}$. At the end of Day 1, the probability of having been infected at work is $1 - e^{-5\cdot\lambda_W}$, and the probability of having been infected in the community is $e^{-5\cdot\lambda_W}(1 - e^{-19\cdot\lambda_C})$. The latter quantity is the product of the sequential probabilities of not being infected at work and subsequently being infected in the community.

Given no infection on Day 1, the individual's probability of not being infected at work on Day 2 is again $e^{-5\cdot\lambda_W}$, and the probability of being infected at work is $1 - e^{-5\cdot\lambda_W}$. Given no infection on the job on Day 2, the probability of not being infected in the community during the rest of the day is again $e^{-19\cdot\lambda_C}$, and the probability of being infected in the community is $1 - e^{-19\cdot\lambda_C}$. At the end of Day 2, the 2-day cumulative probability of having been infected at work is: $1 - e^{-5\cdot\lambda_W} + e^{-5\cdot\lambda_W}.e^{-19\cdot\lambda_C}(1 - e^{-5\cdot\lambda_W})$. The first term in the sum is the probability of being infected at work on Day 1. The second term is the product of the sequential probabilities of not being infected at work or in the community on Day 1 and subsequently being infected at work on Day 2.

Similarly, the 2-day cumulative probability of being infected in the community is: $e^{-5\cdot\lambda_W}(1 - e^{-19\cdot\lambda_C}) + e^{-5\cdot\lambda_W}.e^{-19\cdot\lambda_C}.e^{-5\cdot\lambda_W}(1 - e^{-19\cdot\lambda_C})$. The first term in the sum is the probability of being infected in the community on Day 1. The second term is the product of the sequential probabilities of not being infected at work or in the community on Day 1, not being infected at work on Day 2, and subsequently being infected in the community on day 2.

If the process continues for n days, an HCW's n-day cumulative probability of being infected on the job is

$$\Pr[\text{HCW Workplace Infection} \mid n \text{ days}] = (1 - e^{-5\cdot\lambda_W})\left[1 + \sum_{i=1}^{n-1} (e^{-(5\cdot\lambda_W + 19\cdot\lambda_C)})^i\right] \quad \textbf{(B1)}$$

This expression in the brackets can be simplified by using the series relationship:

$$1 + x + x^2 + \ldots + x^{n-1} = \frac{1 - x^n}{1 - x}, \quad \text{for } |x| < 1$$

If $x = e^{-(5\cdot\lambda_W + 19\cdot\lambda_C)}$, Equation (B1) becomes

$$\Pr[\text{HCW Workplace Infection} \mid n \text{ days}] = (1 - e^{-5\cdot\lambda_W})\frac{1 - e^{-n(5\cdot\lambda_W + 19\cdot\lambda_C)}}{1 - e^{-(5\cdot\lambda_W + 19\cdot\lambda_C)}} \quad \textbf{(B2)}$$

Next, consider the quotient $(1 - e^{-5\cdot\lambda_W})/(1 - e^{-(5\cdot\lambda_W + 19\cdot\lambda_C)})$. In general, $\lambda_W \ll 1$ and $\lambda_C \ll 1$, in which case the quotient can be written as: $5 \times \lambda_W/(5 \times \lambda_W + 19 \times \lambda_C)$. The latter step uses the approximation $e^{-a} \approx 1 - a$, as $a \to 0$. Therefore, Equation B2 may be written as

$$\Pr[\text{HCW Workplace Infection} \mid n \text{ days}] = \frac{5\cdot\lambda_W}{5\cdot\lambda_W + 19\cdot\lambda_C}\cdot[1 - e^{-n(5\cdot\lambda_W + 19\cdot\lambda_C)}] \quad \textbf{(B3)}$$

The above expression corresponds to Equation 2 of the main text. In an analogous fashion, an HCW's n-day cumulative probability of being infected in the community is given by

$$\Pr[\text{HCW Community Infection} \mid n \text{ days}] = e^{-5\cdot\lambda_W}(1 - e^{-19\cdot\lambda_C})\left[1 + \sum_{i=1}^{n-1} (e^{-(5\cdot\lambda_W + 19\cdot\lambda_C)})^i\right]$$

$$= e^{-5\cdot\lambda_W}(1 - e^{-19\cdot\lambda_C})\frac{1 - e^{-n(5\cdot\lambda_W + 19\cdot\lambda_C)}}{1 - e^{-(5\cdot\lambda_W + 19\cdot\lambda_C)}} \quad \textbf{(B4)}$$

Using the approximation $e^{-a} \approx 1 - a$, as $a \to 0$, the above expression becomes:

$$\Pr[\text{HCW Community Infection} \mid n \text{ days}] = e^{-5\cdot\lambda_W}.\frac{19\cdot\lambda_C}{5\cdot\lambda_W + 19\cdot\lambda_C}\cdot[1 - e^{-n(5\cdot\lambda_W + 19\cdot\lambda_C)}] \quad \textbf{(B5)}$$

In general, $\lambda_W \ll 1$, in which case $e^{-5\cdot\lambda_W} \approx 1$. Therefore, Equation B5 is equivalent to Equation 3 of the main text.