

Annual Burden of Occupationally-Acquired Influenza Infections in Hospitals and Emergency
Departments in the United States

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ABSTRACT

Infections among healthcare personnel (HCP) occur as a result of providing care to patients with infectious diseases, but surveillance is limited to a few diseases. The objective of this study is to determine the annual number of influenza infections acquired by HCP as a result of occupational exposures to influenza patients in hospitals and emergency departments (EDs) in the United States (US). A risk analysis approach was taken. A compartmental model was used to estimate the influenza dose received in a single exposure, and a dose-response function applied to calculate the probability of infection. A three-step algorithm tabulated the total number of influenza infections, based on: the total number of occupational exposures (tabulated in previous work), the total number of HCP with occupational exposures, and the probability of infection in an occupational exposure. Estimated influenza infections were highly dependent upon the dose-response function. Given current compliance with infection control precautions we estimated 151,300 and 34,150 influenza infections annually with two dose-response functions (annual incidence proportions of 9.3% and 2.1%, respectively). Greater reductions in infectious were

achieved by full compliance with vaccination and IC precautions than with patient isolation. The burden of occupationally-acquired influenza among HCP in hospitals and EDs in the US is not trivial, and can be reduced through improved compliance with vaccination and preventive measures, including engineering and administrative controls.

KEYWORDS

Microbial risk assessment, infection prevention, healthcare workers, influenza

1. INTRODUCTION

The fact that healthcare personnel (HCP) can acquire infectious diseases as a result of their work has been well established for tuberculosis, and recognized through epidemics of emerging diseases, such as Middle East respiratory syndrome⁽¹⁾ and Ebola Virus Disease.⁽²⁾ Emerging infectious diseases among HCP are more easily recognized as occupationally-acquired than endemic diseases since community exposures are rare. HCP, however, are more likely to acquire endemic than emerging infectious diseases as a result of providing care to patients.

The objective of this study was to estimate the mean annual burden of occupationally-acquired (OA) influenza among HCP who provide direct care (clinical activities) and support care (non-

clinical activities required to sustain a patient) to influenza patients in hospitals and emergency departments (EDs) in the United States (US). Infection control (IC) precautions, specifically standard and droplet transmission-based precautions and vaccination, are the current mechanisms for prevention of OA influenza.⁽³⁾ In this study we consider the impact of varied levels of compliance on the burden of OA influenza. We employed a risk-based approach in conjunction with mathematical models of influenza exposure during healthcare activities, an approach we have also applied to characterize the burden of OA pulmonary tuberculosis.⁽⁴⁾ We explored use of surveillance data, such as sick leave, to attain the study objective, but found this approach infeasible as the data are decentralized, the link between sick leave and influenza is indirect,⁽⁵⁾ the difficulty of separating OA influenza from community-acquired influenza, and failure to capture asymptomatic infections. To our knowledge, this is the first effort to characterize this occupational health burden, which can result in influenza transmission to patients and among HCP, and impact care delivery as a result of lost work time.

2. METHODS

2.1 Number of HCP with Potential Exposure

The number of HCP in hospitals and EDs was determined from an industry analysis of 2014 data from the Bureau of Labor Statistics by Eastern Research Group, Inc. (ERG, unpublished data), which tabulated the number of workers in each healthcare setting who had high, low or no probability of contacting patients. It was judged plausible that 75% and 30% of HCWs in hospitals and EDs with high and with low probability of contacting patients, respectively, have potential for occupational exposure to influenza: This is equal to 1.62 million HCP. Some HCP may not interact with influenza patients due to clinical specialty, for example.

2.2 Number of Occupational Exposures

We have reported the mean annual number of occupational exposures to elsewhere ⁽⁶⁾. In this analysis, we focus on the expected epidemic size, which was estimated to result an average of 1.4 million (central 50% range 0.85-1.43 million) and 7.69 million (central 50% range 5.15-10.2 million) occupational exposures in EDs and hospitals on average.⁽⁶⁾ Identification of patients for droplet precautions was not considered to reduce the number of occupational exposures in this analysis. While Morgan et al. ⁽⁷⁾ observed patients identified for contact precautions to receive 36% fewer visits from HCP than patients not identified for contact precautions, the contact rates observed in both groups are within the range of other studies (see Supplementary Materials); and the relevance to droplet precautions is unclear.

2.3 Probability of OA Infection

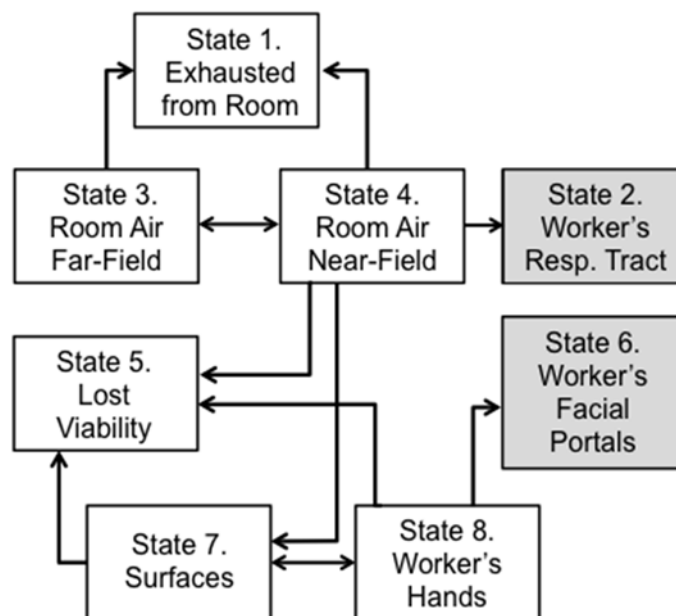
2.3.1 Transmission Routes

The CDC recognizes the primary route of influenza transmission to involve large-particle respiratory droplets (virus laden droplets project onto the facial mucous membranes), but notes that airborne transmission (virus laden droplets are inhaled) may occur in the vicinity of infectious individuals, termed proximal airborne transmission herein. ⁽³⁾ Contact transmission is also relevant (virus transferred to the facial mucous membranes by way of contaminated objects) for influenza.⁽⁸⁾ In this analysis, occupational exposure to influenza virus through the contact, droplet and proximal airborne transmission routes were considered.

Exposure through contact and proximal airborne transmission was modeled using a compartmental Markov model. This model was modified from previous applications to influenza to include two compartments for room air: ^(9,10) HCP were considered to inhale virus only while in proximity to the patient, termed the near-field, which was defined as the half of the room that included the patient's head (Figure 1). Surface contamination occurred in the near-field, and influenza viruses on these surfaces were capable of being transferred to the HCP's hands upon contact (Figure 1), and could then be transferred to the facial portals to the respiratory tract (eyes, nares, lips, mouth, etc.) at any time. A conical dispersion model was used to estimate the number of viruses in projected particles that reach the HCP's facial portals. ⁽¹⁰⁾

Figure 1.

States in the Markov compartmental model of influenza exposure through contact and droplet transmission routes. Arrows indicate direction of virus movement. Healthcare workers are exposed to viruses that deposit in the respiratory tract or are transferred to the facial portals of the respiratory tract (shaded boxes).



2.3.2 The Exposure Model

The compartmental model was implemented using a Markov chain, and mathematical details have been published elsewhere.^(10,11) Virus emitted in coughs entered the near-field air (state 4) and onto surfaces (state 7).⁽¹⁰⁾ Initial virus loads in these compartments were equated with steady state values.⁽¹⁰⁾ The exposure model was implemented with 10,000 replications to characterize the distribution of possible occupational exposures. Distributions were defined for each model input parameter to reflect conditions in all possible occupational exposures. Details are described in the Supplementary Materials.

2.3.3 Dose-Response Functions and Infection Probability

Two dose-response functions were used to estimate the probability of infection from the dose of virus received by HCP in a single occupational exposure. The first function (Function 1) was based on infections in humans who inhaled aerosols of influenza A2/Bethesda/10/63 (H2N2), and was an exponential function with parameter $\kappa = 0.18$ where the unit of dose, d , is TCID₅₀ viruses inhaled⁽¹⁰⁾. The second function (Function 2) was a three-parameter beta-Poisson model based on infectivity studies of wild-type and reassortant influenza viruses (H3N2), with parameters $\alpha = 0.295$, $N_{50} = 4.42 \times 10^5$, and $\gamma = 1.07 \times 10^3$ and the dose is the TCID₅₀ of wild-type virus instilled intranasally.⁽¹²⁾ Of the functions reported by Watanabe et al.,⁽¹²⁾ this one was chosen because it had data in adults from five studies, and the 10% infectious dose for H3N2 fell within the range of that seen for H1N1 virus types in adults.

These dose-response functions are quite different from one another – Function 1 suggests infection is more likely to occur for most doses than Function 2. Unfortunately, at this time there is no established guidance for ranking the plausibility of influenza dose-response functions for microbial risk assessment. Function 1 would be preferred owing to the use of aerosol exposures, but the virus had been passaged extensively in the laboratory. Function 2 has the advantage of integrating wild-type virus and virus types in frequent circulation today. Overall, differences between the dose-response functions are expected owing to the use of different virus types and exposure routes. These two dose-response functions were chosen because they were considered to represent the range of plausible infectivity values.

For each dose-response function, the probability of infection was calculated for the dose received through each route (contact, droplet and proximal airborne), and an inclusion-exclusion formula applied to calculate the overall probability of infection.⁽¹⁰⁾

2.4 Annual Burden of OA Infection

In the first step of a three-step algorithm, the mean annual number of occupational exposures, E , was distributed among the total number of HCP, W , with potential for occupational exposure to influenza. If the w th HCP, $w = \{1, 2, \dots, W\}$ experienced $n_w = \{0, 1, 2, \dots, n_{\max}\}$ occupational exposures per year, then $E = \sum_{w=1}^W n_w$. Let \mathbf{N} be a random variable with multinomial distribution that reflects the probability distribution of the number of occupational exposures experienced by workers. Then n_w is a random sample from \mathbf{N} . The multinomial distribution was developed from a lognormal distribution because it was considered plausible that many HCWs would have few, and some HCWs would have many, occupational exposures to influenza

annually. Let \mathbf{X} be a random variable with a lognormal probability distribution characterized by geometric mean, GM_X , and geometric standard deviation, GSD_X . The probability that \mathbf{N} takes on value n , $0 \leq n \leq n_{\max}$, is denoted $P(N = n)$. The value $P(N = n)$ is calculated from \mathbf{X} as: $P(N = n) = P(X \leq n + 0.5) - P(X > n - 0.5)$. The probability a worker has no occupational exposures to influenza in a year is $P(N = 0) = P(X \leq 0.5)$; and the probability that the w th worker has the maximum number of occupational exposures in a year is $P(N = n_{\max}) = P(X > n_{\max} - 0.5)$. We set $n_{\max} = 400$. The allocation of occupational exposures among the total number of HCWs was implemented in a Monte Carlo simulation. In each replication, a value was randomly selected from the distribution of mean annual occupational exposures and a value of GSD_X was randomly selected from a uniform distribution over the range of 2-8. The mean number of occupational exposures per worker was then calculated, $\bar{x} = E/W$, and \bar{x} and GSD_X used to calculate GM_X .

Second, the probability of infection was calculated for the w th HCP who has n_w occupational exposures over the course of a year. The probability of infection in the i th exposure, p_i where $i = \{1, 2, \dots, n_w\}$, is a random sample from the distribution of values for the probability of infection in a single occupational exposure. The probability of influenza infection as a result of n_w exposures is the complement of the probability of not being infected during any occupational exposures:

$$P_w = 1 - \prod_{i=1}^{n_w} (1 - p_i)$$

The annual probability of infection, P_w , was calculated for a sample of 10,000 HCP; and the proportion infected applied to the total population of HCP. By choosing the p_i values randomly, all HCP had the same overall experience. We determined that at this time there was insufficient

data about the frequency and type of work activities performed, and associated exposure determinants, to permit an analysis that separated the infection risks by job titles or work tasks.

Third, the mean annual number of OA infections among all HCP, I , was calculated by multiplying the mean probability of an OA infection for each of the 10,000 HCP for which this probability was calculated, $\bar{P} = \frac{1}{10000} \sum_{w=1}^{10000} P_w$, with the total number of HCP with potential occupational exposure to influenza, W . That is, $I = \bar{P}W$. The Monte Carlo simulation yielded 10,000 estimates for the mean annual number of OA infections, $\{I_1, I_2, \dots, I_{10000}\}$.

2.5 Infection Control Precautions

The effectiveness and HCP compliance infection control (IC) precautions recommended for influenza and considered in the exposure model are identified in Table I: The rationale for these values is provided in the Supplementary Materials. For routine care, the CDC recommends standard and droplet and precautions (e.g., hand hygiene, gloves, gowns, and facemasks), but N95 filtering facepiece or equivalent respirators are recommended for use during aerosol generating procedures.⁽³⁾ As a result, HCP were considered to wear N95 respirators in 10% of occupational exposures in which they would otherwise wear a facemask. Each IC precaution was used in a proportion of occupational exposures equal to the compliance proportion (Table I), but compliance with each IC precaution was considered independent. Independence may be an unrealistic assumption, as a HCP who complies with one precaution may be more likely to comply with additional precautions and to comply in all occupational exposures, but these data were not available.

Table I. Infection control and prevention precautions considered, with their effectiveness and current rates of compliance.

Precaution	Effectiveness			Compliance	
	Mechanism	Value	Reference	Rate	Reference
Gloves	Fraction of virus transfer to hands upon removal	Uniform: Range 0.0001-0.01	(13,14)	85%	(15-17)
	Percent reduction in frequency of contact with the facial portals	50% ^E	(18,19)		
Hand Hygiene	Fraction of virus remaining on hands after hand hygiene	0.05	(18,19)	40%	(16,20-22)
Eye Protection	Fraction of virus that bypasses the goggles or face shield	0.04	(23)	50%	
Facemask	Fraction of sprayed and contact-transferred virus that penetrates or bypasses facemask	0.10 ^D	(24,25)	50% ^A	(16,17,25-27)
	Percent reduction in frequency of contact with the facial portals	90%	(28)		
N95 Filtering Facepiece Respirator	Fraction of sprayed and contact-transferred virus that penetrates through respirator	0.05 ^D		20% ^A	(16,17,25-27)
	Protection factor ^B	Uniform: Range 5-10	(29,30)		
	Percent reduction in frequency of contact with the facial portals	90%	(28)		
Isolation	Fraction reduction in the duration of occupational exposure	0.18	(7)	80%	(31-34)
	Percent increase in compliance with hand hygiene, eye protection, facemasks or respirators, and full compliance with gloves	25%	(7,32,35,36)		
Surface Decontamination	Fraction of virus remaining on surfaces	0.05	(37,38)	50% ^C	(39-41)

^A Total compliance with facemasks or respirators is 50%, and 20% of people who wear a facemask or respirator wear a respirator.

^B The protection factor is a ratio of the concentration of particles outside the respirator to that inside. The Assigned Protection Factor of these respirators is 10⁽³⁰⁾, but lower performance was considered due to issues with long-term fit and use practices⁽²⁹⁾.

^C Surface decontamination does not occur in each occupational exposure, but when it occurs there is 50% compliance with the selection and application of the agent

^D Equated with filtration effectiveness

Identification of patients for droplet precautions was considered to reduce the duration of occupational exposure by 18%, consistent with the observation of Morgan et al.⁽⁷⁾ for patients identified for contact precautions. In addition, because some studies have observed increased compliance with IC precautions when patients were identified for isolation,^(7,32,35,42) the probability of compliance with IC precautions during care of patients identified for droplet precautions was increased by 25% relative to values shown in Table I. Hospital-based studies have found 80% of patients to be correctly identified for contact precautions,⁽³¹⁻³³⁾ but lower a lower (60%) and higher (100%) value were also considered. In addition, we considered the event of full compliance with IC precautions.

Regular surface cleaning and decontamination is recommended in healthcare settings, but there are no specific guidelines about frequency.⁽⁴³⁾ We considered that cleaning occurred once per day of hospitalization, and every few visits in ambulatory care and emergency departments (once per 90 and 12 occupational exposures, respectively). We considered that correct choice and application of the cleaning agent occurred in 50% of cleaning activities (Table I), consistent with observed low cleaning effectiveness.^(40,41) But, when applied, cleaning removed 95% of viruses, consistent with performance requirements for decontamination products.⁽⁴⁴⁾

Vaccination reduces the number of workers susceptible to influenza infection. We considered that 40.3% of HCP were immune to influenza due to effective vaccination, based on a survey that found 79% of HCP in hospital and non-hospital settings reported receiving the 2010/2011 seasonal influenza vaccine,⁽⁴⁵⁾ and vaccine effectiveness of 51% among adults.⁽⁴⁶⁾ We also

considered 100% of HCP to have been vaccinated, as many healthcare organizations make vaccination a condition of employment; equal to 51% immunity among HCP.

3. RESULTS

The probability of influenza infection in HCP during a single occupational exposure is, on average, on the order of 10^{-2} for dose-response Function 1, and on the order of 10^{-3} for dose-response Function 2 (Table II). The only difference in IC precaution compliance between EDs and hospitals was the frequency of surface decontamination, and small differences (on the order of 10^{-4} and 10^{-5}) were found between the two settings. This small difference suggests that surface decontamination, which interrupts the contact transmission route, is not particularly effective against influenza transmission from patients to HCP. This is consistent with the relatively low contribution of the contact transmission route (3.5-12%) to the probability of influenza infection (Table II). Sensitivity analyses for this model are presented in the Supplementary Materials.

Table II. Probability of an occupationally-acquired influenza infection among HCP resulting from a single occupational exposure for by IC precaution compliance and patient isolation

Dose-Response Function	<i>Emergency Departments</i>				<i>Hospitals</i>			
	Probability of Infection		% Risk by Transmission Route		Probability of Infection		% Risk by Transmission Route	
	Mean	25 th -75 th %tile	Contact	Proximal Airborne	Mean	25 th -75 th %tile	Contact	Proximal Airborne
<i>Current IC Compliance^A</i>								
<i>60% Patients Isolated</i>								
1	4.77×10^{-2}	1.56×10^{-5} - 2.74×10^{-2}	12	1.9	4.78×10^{-2}	1.56×10^{-5} - 2.77×10^{-2}	12	2.0
2	6.30×10^{-3}	6.91×10^{-7} - 1.18×10^{-3}	9.7	1.7	6.52×10^{-3}	6.69×10^{-7} - 1.15×10^{-3}	10	1.9
<i>80% Patients Isolated</i>								
1	4.38×10^{-2}	1.09×10^{-5} - 2.27×10^{-2}	11	2.0	4.35×10^{-2}	1.06×10^{-5} - 2.35×10^{-2}	12	1.9
2	5.74×10^{-3}	4.82×10^{-7} - 9.74×10^{-4}	9.6	1.7	5.80×10^{-3}	4.80×10^{-7} - 9.97×10^{-4}	9.6	1.8
<i>100% Patients Isolated</i>								
1	4.19×10^{-2}	8.59×10^{-6} - 2.15×10^{-2}	11	2.0	4.15×10^{-2}	8.34×10^{-6} - 2.20×10^{-2}	12	2.0
2	5.43×10^{-3}	3.81×10^{-7} - 8.77×10^{-4}	9.2	1.9	5.52×10^{-3}	3.68×10^{-7} - 9.00×10^{-4}	9.7	2.0
<i>Full IC Compliance^B</i>								
<i>60% Patients Isolated</i>								
1	3.78×10^{-2}	1.42×10^{-5} - 2.58×10^{-2}	3.9	3.9	3.72×10^{-2}	1.04×10^{-5} - 2.53×10^{-2}	4.2	3.1
2	5.49×10^{-3}	6.33×10^{-7} - 1.11×10^{-3}	3.5	2.9	5.55×10^{-3}	5.91×10^{-7} - 1.07×10^{-3}	3.7	3.0
<i>80% Patients Isolated</i>								
1	3.46×10^{-2}	9.27×10^{-6} - 2.23×10^{-2}	4.3	3.1	3.45×10^{-2}	9.39×10^{-6} - 2.18×10^{-2}	4.4	2.8
2	4.98×10^{-3}	4.24×10^{-7} - 9.15×10^{-4}	3.9	3.0	4.97×10^{-3}	4.34×10^{-7} - 9.26×10^{-4}	3.9	2.7
<i>100% Patients Isolated</i>								
1	3.33×10^{-2}	7.33×10^{-6} - 2.01×10^{-2}	4.2	3.0	3.30×10^{-2}	7.31×10^{-6} - 2.06×10^{-2}	4.6	3.0
2	4.73×10^{-3}	3.412×10^{-7} - 8.29×10^{-4}	3.8	2.9	4.78×10^{-3}	3.31×10^{-7} - 8.48×10^{-4}	4.1	2.9

^A Patient isolation decreases the duration of exposure and increases compliance with basic IC precautions compliance (Table I)

^B Patient isolation decreases the duration of exposure only as compliance with IC precautions is complete, regardless of isolation status.

Droplet transmission was the dominant transmission route in an occupational exposure, on average, as the contact transmission route contributed 3.5-12% and the proximal airborne route contributed 1.7-3.9%, on average (Table II). The contribution of the contact transmission route was higher for dose-response Function 1 than for Function 2, and decreased with increased IC compliance; and the inverse was observed for the proximal airborne route.

The mean number of influenza infections among HCP is tabulated in Table III, where the variability reflects uncertainty in the mean number of occupational exposures per healthcare visit, and uncertainty and variability in the probability of infection during an occupational exposure (Table II and III). The numbers of influenza infections among HCP in EDs and hospitals are pooled because the number of HCP in these settings was tabulated jointly (1.62 million). Given current compliance with IC precautions and vaccination, and 80% of influenza patients isolated, we estimated 151,300 and 34,150 OA infections annually, on average, based dose-response Functions 1 and 2, respectively. Among 1.62 million HCP in EDs and hospitals with potential for occupational influenza exposure, these annual number of OA infections correspond to incidence proportions of 9.3% and 2.1%, respectively; additional workers in EDs and hospitals were considered not to have potential for exposure to influenza patients. Influenza OA infections estimated in this study may be asymptomatic or symptomatic, as infection in the dose-response functions was measured by immune response, not symptoms^(12,47).

Table III. Mean annual number of occupationally-acquired influenza infections in hospitals and emergency departments by infection control (IC) precaution compliance, patient isolation and vaccination levels.

Dose-Response Function	IC Precaution Compliance	Percentage HCP Vaccinated	Mean (Central 50% Range) Annual Number of Infections		
			Patient Isolation Percentage		
			60%	80%	100%
1	Basic	79%	193,400 (123,600, 193,400)	151,300 (115,100, 181,500)	147,100 (112,200, 176,400)
		100%	132,600 (101,400, 158,700)	124,200 (94,480, 149,000)	120,700 (92,070, 144,800)
	Full	79%	135,000 (103,000, 161,600)	127,800 (97,490, 153,300)	124,000 (94,820, 148,500)
		100%	107,900 (84,560, 132,600)	104,900 (80,000, 125,800)	101,700 (77,810, 121,900)
2	Basic	79%	37,560 (29,470, 45,090)	34,150 (26,950, 40,940)	40,380 (26,650, 40,380)
		100%	33,320 (26,340, 40,000)	30,190 (23,940, 36,190)	30,080 (23,950, 35,900)
	Full	79%	33,320 (26,340, 40,000)	30,190 (23,940, 36,190)	30,080 (23,950, 35,900)
		100%	27,340 (21,620, 32,830)	24,770 (19,640, 29,700)	24,680 (19,650, 29,460)

The percentage change in OA infections due to changes in IC precaution compliance by HCP, patient isolation and HCP vaccination were tabulated for each of the 10,000 simulation iterations, and then averaged. Vaccination compliance of 79% to 100% was equivalent to immunity among 40.3% and 51% of HCP, respectively; and increased vaccine compliance was found to eliminate 6.4% of OA infections, on average. The impact of increased HCP compliance with IC precautions varied slightly with vaccination compliance, patient isolation and between the two dose-response functions (Table IV), but was in the range of 2.5-5.8%. Increasing the percentage of patients isolated from 60% to 80% had a larger impact on the reduction of OA infections, a 1.3-3.3% reduction, than isolating 80% to 100% of patients, which reduced the number of OA infections by < 1% (Table V).

Table IV. Percent reduction in occupationally-acquired (OA) influenza infections resulting from increased healthcare personnel (HCP) compliance with infection control (IC) precautions.

Dose-Response Function	Percentage HCP Vaccinated	Mean Percent Reduction in OA Infections		
		Patient Isolation Percentage		
		60%	80%	100%
1	79%	5.8%	5.5%	5.5%
	100%	3.9%	3.7%	3.7%
2	79%	3.9%	4.0%	3.7%
	100%	2.6%	2.7%	2.5%

Table V. Percent reduction in occupationally-acquired (OA) influenza infections resulting from increased patient isolation, by compliance with infection control (IC) precautions and healthcare personnel (HCP) vaccination.

Dose-Response Function	IC Precaution Compliance	Percentage HCP Vaccinated	Mean Reduction in OA Infections	
			Change in Patient Isolation Percentage	
			60% to 80%	80% to 100%
1	Basic	79%	2.3%	1.0%
		100%	1.5%	0.7%
	Full	79%	1.9%	1.0%
		100%	1.3%	0.7%
2	Basic	79%	3.1%	0.4%
		100%	2.1%	0.2%
	Full	79%	3.3%	<0.1%
		100%	2.2%	<0.1%

4. DISCUSSION

Many people are appropriately skeptical of results from models and risk analysis, such as used in this study. For influenza, the absence of surveillance data limits model evaluation. However, surveillance for pulmonary tuberculosis disease is robust, and previous application of this analysis framework has been found to provide reasonable estimates.⁽⁴⁾ Specifically, the most likely estimate of annual occupationally-acquired pulmonary tuberculosis infections annually 3,288 cases, which, considering chemoprophylaxis and the progression of infection to disease, was estimated to yield 82 cases of pulmonary TB disease. Surveillance data from the CDC, in contrast, identified about 320 incident cases of pulmonary tuberculosis disease among HCP in 2013⁽⁴⁸⁾. It was anticipated that the analysis would underestimate the observed incidence because not all occupational exposures were included in the analysis, and many incident cases among HCP could be community, not occupationally, acquired.

This analysis has shown that the annual burden of occupationally-acquired influenza infections is not trivial among HCP in hospitals and EDs in the U.S., with mean annual incidence of 9.3% and 2.1% for dose-response Functions 1 and 2, respectively. Not all of these infections will result in the development of symptoms. Despite the absence of surveillance programs for influenza, influenza infections among HCP have been measured in other countries in the context of IC precaution effectiveness interventions. In China, MacIntyre et al.⁽⁴⁹⁾ observed a laboratory-confirmed symptomatic influenza incidence proportion of 1.3% among HCP at control facilities. In contrast, Loeb et al.⁽⁵⁰⁾ observed laboratory-confirmed influenza in 22% of nurses in Canada enrolled in a study of facemask and N95 effectiveness. The symptomatic trigger for laboratory-based diagnosis was lower in the Loeb et al.⁽⁵⁰⁾ study than in MacIntyre et al.⁽⁴⁹⁾, which may explain the difference in observed incidence. Infections among HCP in these studies are not exclusively the result of occupational exposures, and likely underestimate the total burden since symptoms precede laboratory-based diagnosis. However, they indicate that results of this analysis are reasonable.

Occupationally-acquired influenza infections may result in adverse consequences for HCP and their employers. Symptomatic infection and more severe outcomes may result in absenteeism, healthcare utilization and death. In the community, approximately 40% of influenza infections are symptomatic;^(51,52) and of symptomatic influenza cases, approximately 22.5% seek care in ambulatory care settings, 1% seek care in emergency departments,⁽⁵³⁻⁵⁶⁾ and 0.15% are hospitalized.⁽⁵³⁻⁵⁷⁾ The mortality rate varies among epidemics.^(54,57,58) Considering 151,300 OA influenza infections from dose-response Function 1 and current levels of IC precaution and vaccination compliance, and isolation of 80% of patients, we estimate 60,520 symptomatic OA

infections in HCP, resulting in 13,617 cases seeking ambulatory care, 605 cases seeking emergency department care, and 91 hospitalizations. A healthy worker effect is commonly identified in studies of occupational epidemiology, which, through a variety of mechanisms, yields lower cancer incidence and mortality among workers than among the general public. ^(59,60) A healthy worker effect has not been established for infectious diseases to date, but, if present, would suggest that community-based rates of adverse outcomes to infection would over-estimate adverse outcomes among HCP.

The size of influenza epidemics varies from year-to-year. Increasing the incidence proportion of symptomatic influenza in the community from 1.5% to 10.5% (small to large epidemic) increases the mean number of OA infections in acute care settings 3.5- to 4-fold (Table V). We only considered symptomatic influenza in the community to result in occupational exposures in acute care settings. By neglecting occupational exposures to patients with asymptomatic influenza and to HCP infected with influenza, ⁽⁵⁾ we likely underestimated the number of occupational exposures and influenza OA infections. By considering the annual burden, we were able to neglect the seasonality of influenza.

The difference in the mean number of OA influenza infections associated with the two dose-response functions is similar to the difference associated with epidemic size (Table V), indicating the large contribution of the dose-response function to overall uncertainty. Dose-response Functions 1 and 2 have different functional forms, and were developed from different data sets, involving different routes of exposure. The relevance of virus inhalation and intranasal instillation of exposure to droplet and contact transmission of influenza in healthcare settings is

unclear: The routes lead to different deposition patterns of influenza virus in the respiratory tract, but the virus deposition patterns resulting from naturally-occurring droplet or contact transmission in natural settings are unknown.⁽⁶¹⁾ This is an area in need of research.

The probability of infection during a single occupational exposure estimated in this analysis (Table II) is similar to previous work, but the contribution of contact transmission to infection risk is lower.^(10,62) The difference may have arisen due to the use of a near-field and far-field in this study. In previous work, surfaces were not separated in two zones, and contact with the virus-contaminated surfaces could occur at any location, which would lead to more frequent contact between the worker's hands and virus-contaminated surfaces. In addition, in this analysis we considered that facemasks, gloves and respirators reduced the frequency of contact between the HCP hands and facial portals, interrupting the contact transmission route. We updated the literature review to define parameters in the occupational exposure model since previous applications,^(10,62) but few changes were made (see Supplementary Materials).

To perform this analysis, as in related previous work, many simplifying assumptions were made.^(6,10,62) Some simplifying assumptions likely tended to over-estimate, and others to under-estimate real values, but impacts are difficult to evaluate due to data scarcity. Data scarcity led to the assumptions that IC precaution compliance, including patient isolation (Table III), and features of occupational exposures (HCP activities and patient characteristics) are the same in different healthcare settings: Most studies have been performed in hospitals, but conditions are likely different in ambulatory care settings. Operationally, an occupational exposure was defined as the event of a HCP being in a room with an infectious patient, and this simplification of HCP-

patient interactions was made to allow the occupational exposure model to be tractable.

Evaluation of healthcare delivery activities and IC precaution compliance in ambulatory care settings and by HCP job title is a key area for future research that will enable more refined assessment of risk and targeting of IC precautions.

5. CONCLUSIONS

Ultimately, the mean annual burden of OA influenza infections is not trivial in hospital and ED settings, and reflects avoidable illness and costs, including lost work. We recommend that healthcare organizations consider occupational surveillance for influenza; and move to increase compliance with vaccination and IC precautions, which were found to have a greater impact on OA infections than increased patient isolation (Tables IV and V). Vaccination and IC precautions are incomplete barriers (Table I), and cannot eliminate the risk of seasonal OA influenza infections. To achieve further reductions in OA influenza infections among HCP, adoption of engineering and administrative controls that change the frequency and magnitude of occupational exposures should be prioritized. Though surface cleaning and decontamination were found to have little impact on the probability of OA influenza infections in this study (Table II), this precaution may prevent the transmission of other infectious diseases and have other benefits. There are significant data gaps about the nature of occupational exposures to influenza that should be prioritized for research so that improved interventions can be designed.

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COMPETING INTERESTS

The authors have no competing interests relevant to this article.

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