

# Annual Burden of Occupationally-Acquired Influenza Infections

in Hospitals and Emergency Departments in the United States

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## Supplementary Materials:

### Parameters in the Occupational Exposure Model and Sensitivity Analysis

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## **1. EMISSION OF INFLUENZA**

### **1.1 Cough Particle Size Distribution**

Previous applications of the occupational exposure model used the particle size distribution measured by Loudon and Roberts [1], based on a review by Nicas et al. [2]. Since this review, two new studies were published: Chao et al. [3] enumerated more small particles than other investigators, while Xie et al. [4] enumerated more large particles than other investigators. The new studies were judged to be no more compelling based on experimental design and measurement techniques than Loudon and Roberts [1]. Thus, the Loudon and Roberts size distribution was used in the exposure model (Table S-I).

Influenza virus has been measured in cough particles in the respirable size range [5-9], but studies have not sought to identify influenza in larger particles, or did not consider particle size [10,11]. Thus, we considered that influenza virus was present in cough particles of all sizes.

### **1.2 Cough and Sneeze Volume**

The volume of expiratory fluid emitted in cough particles has been estimated from particle size and count distribution data, and found to range 0.044-4.0 mL for particles of all sizes [1,3], and  $2.4 \times 10^{-9}$ - $1.4 \times 10^{-7}$  mL [2,12] for particles in the respirable size range. Most studies of cough particle emission have used healthy human volunteers, but Lindsley et al. [12] did not find statistically significant differences in the number of respirable particles or total fluid volume emitted by volunteers with influenza and after recovery. Thus, cough emission data measured among healthy persons was considered relevant to influenza patients. Inter-individual variability in the number of expired particles, expiratory volume and size distribution is high [12,13], consistent with the wide range observed in other studies [1-3,12]. Thus, the volume of fluid emitted in a cough was modeled by a triangular distribution over the range of 0.004 mL to 4.0 mL and mode 0.044 mL, which spans the range of observed values (Table S-III).

### **1.3 Virus Concentration in Cough and Sneeze Particles**

The concentration of virus in cough and sneeze particles was equated with the concentration of virus in respiratory secretions. Influenza virus in respiratory secretions has been measured by swabbing the back of the nasopharynx and/or throat, aspirating the nasopharynx, or washing the nasal passages; and quantifying the number of plaques formed in tissue culture or genome copies by quantitative polymerase chain reaction (qPCR). The source of the volume unit is uncertain in all methods. For example, for swab samples, the volume is likely the 2-3 mL of viral transport medium into which the swab is placed after sample collection. Comparison of the aspiration and swab methods have found no statistically significant difference in the copies of influenza A (H1N1) virus [14], though aspiration may be more sensitive [15]; but studies directly comparing other methods were not identified.

Concentrations of influenza virus in respiratory secretions measured in selected studies of participants 0-4 days after symptom onset and prior to antiviral medication are shown in Table S-II. In this analysis, the  $\log_{10}$  RNA copy number was converted to the  $\log_{10}$  TCID<sub>50</sub> by subtracting

three [16] to obtain the correct units (TCID<sub>50</sub>) for the dose-response functions. Two studies of pandemic 2009 H1N1 influenza [17,18] reported virus concentrations two-orders of magnitude greater than other studies (Table S-II). Reasons for this discrepancy were not identified, but the difference was not observed for all studies pandemic 2009 H1N1 influenza. Based on the data in Table S-II, the concentration of influenza viruses in respiratory secretions and cough particles was modeled by a uniform distribution over the range of 1.5 to 6.5 log<sub>10</sub> TCID<sub>50</sub> mL<sup>-1</sup> (Table S-III). This range encompasses the values observed with seasonal influenza viruses, and the mean values observed for pandemic 2009 H1N1 influenza viruses.

## 1.4 Cough and Sneeze Frequency

No studies were identified which quantified the frequency of cough and sneezes in patients with influenza. As a result, studies of cough among patients with acute respiratory illness and upper respiratory tract infection (but not pneumonia or TB disease) were considered [19-24]. Only two studies [20,23] were judged appropriate to describe the frequency of influenza expiratory events because they measured cough in patients with acute upper respiratory tract infection over  $\geq 24$  hours, capturing temporal variation in cough:

- Kuhn et al. [20] measured coughs in ten consecutive six-hour periods among 21 young adults who had acute respiratory infection but were otherwise healthy. Data from the first 24 h were used. Data from the treatment group (patients were given an experimental anti-cough medication) and control group were combined because the treatment was shown to have no effect. The cough frequency was described by a lognormal distribution with GM = 31.7 coughs h<sup>-1</sup> and GSD = 1.96.
- Sunger et al. [23] measured cough over 24 h among 54 young adults who had acute cough but were otherwise healthy, and reported GM = 12.1 coughs h<sup>-1</sup>. The cough frequencies ranged from 3-100 coughs h<sup>-1</sup>. GSD = 2.5 was selected because it gave 2.5<sup>th</sup> and 97.5<sup>th</sup> percentiles equal to 2.0 and 88 coughs h<sup>-1</sup>, which are similar to the observed range of cough frequencies.

A single distribution was generated by drawing random samples from the lognormal distribution for each study. The integrated distribution had 5<sup>th</sup>, 50<sup>th</sup> and 95<sup>th</sup> percentiles equal to 3.77, 19.6 and 84.1 coughs h<sup>-1</sup>.

## 2. CONTACT RATE AND DURATION

### 2.1 Rates of Self-Contact

Few published studies have reported rates of self-contact between the hand and facial mucous membranes. Hendley et al. [25] observed workers in an auditorium to pick noses 3.1 times per hour and rub eyes 2.7 times per hour. Nicas and Best [26] observed adults doing office-type work using a video system, and counted the number of times participants touched their eyes, nostrils or lips. The total contact rate was 15.7 times per hour ( $\sigma = 11.5$  h<sup>-1</sup>). Lip touching occurred, on average 8.0 times per hour ( $\sigma = 7.9$  h<sup>-1</sup>); followed by nose touching ( $\mu = 5.2$  h<sup>-1</sup>,  $\sigma = 3.7$  h<sup>-1</sup>) and eye touching ( $\mu = 2.5$  h<sup>-1</sup>,  $\sigma = 1.9$  h<sup>-1</sup>). The rates observed by Nicas and Best [26] are likely higher than those observed by Hendley et al. [25] due to the private setting, and more general definition of touching.

The study conditions of Hendley et al. [25] and Nicas and Best [26], because they involved observation of private or semi-private activities, were judged to not be directly relevant to occupationally-acquired infections in the healthcare sector, where workers are in a public setting and have received infection control training. Other modeling studies of influenza transmission assumed the rate of hand to facial mucous membrane contacts was in the range of 1.2-18 touches  $\text{h}^{-1}$  [27,28], which falls within the observed rates [25,26].

For this analysis, the rate of contact between the hand and facial mucous membranes was modeled as a uniform distribution over the range of 1.2 to 18 touches  $\text{h}^{-1}$  (Table S-VII).

## **2.2 Rate of Hand-to-Surface Contact**

Workers touch surfaces and objects that may be contaminated with influenza. Hayden et al. [29] observed nurses and physicians to make 47 contacts with environmental surfaces or the patient during a patient care episode in a medical intensive care unit: 44% of workers touched only the environment, averaging 5.1 contacts per patient care episode, while 56% of workers touched the patient and the environment, averaging 8.5 contacts per patient care episode. Smith et al. [30] observed approximately half of workers to touch patients directly, half handled patient notes and 25% touched the bed. Huslage et al. [31] observed bed rails to be the most frequently touched substrate, touched an average of 7.76 and 3.12 times per worker-patient interaction in an intensive care unit and on a medical surgical floor, respectively. Accounting for other objects, the number of touches could be as high as 40 per worker-patient interaction [31]. Other studies were not considered because the data were insufficient to estimate the rate of contacts [30,32].

Studies that measured the rate of hand to substrate contacts per worker-patient interaction [29,31] suggest the rate of contact varies from one to 40 contacts per patient care episode. It was judged plausible that more hand to substrate contacts occur during longer worker-patient interactions. If worker-patient interactions last 0.5-20 minutes, the rate of contact could range from 0.5-20 contacts per minute. In the exposure model, substrates potentially contaminated with infectious agents were located near the patient. Given a worker spends half of the worker-patient interaction near the infectious person, and a steady contact rate over time, then half of the contacts would involve contaminated substrates near the patient and contribute to exposure: 0.25-10 contacts per minute (15 to 1,200 contacts per hour) contribute to exposure. As a result, the rate of contact between the worker's hand and substrates containing infectious agents was modeled by a uniform distribution over the range of 15 to 12,00 contacts per hour (Table S-VII), but only half of these contacts involved the near-field.

## **2.3 Duration of Contact with an Influenza Patient**

The duration of occupational exposure was equated with the time spent by a worker attending an infectious person, or being present in a room with an infectious person. The duration was developed from a review of time-activity studies, with a focus on time-and-motion studies that provide data on task duration and frequency.

Table S-IV summarizes data about the duration of worker-patient interactions, emphasizing studies conducted in the United States. Data were from studies of direct care workers. Similar

data were not identified for workers providing support care. Overall, these data suggest that the duration of worker-patient interactions is frequently short (< 10 min) and infrequently very long (> 60 min). This pattern is consistent with a lognormal distribution. The diversity in study designs and data presentation made statistical integration of the data in Table S-IV difficult. As a result, a lognormal distribution with GM = 6 min and GSD = 2.5 was judged appropriate to represent the duration of worker-patient interactions. This distribution has 10<sup>th</sup>, 25<sup>th</sup> and 95<sup>th</sup> percentiles equal to 1.8, 3.23 and 27.1 minutes, respectively, and is consistent with the data in Table S-IV. Only values sampled from this distribution in the range of 0.25 to 90 minutes were used in the exposure model (Table S-VII).

During worker-patient interactions, the worker is not continuously in close proximity to the patient. During primary care, physicians were observed to spend approximately 30% of direct patient care time performing the examination, and 65% of direct patient care time talking with the patient [33]. Additional time in the patient's room may involve preparation or clean-up for specific medical tasks [34]. In the exposure model of occupational exposures, when proximity to the infectious agent was considered by a two-zone model, it was assumed that workers spend 50% of the time in the patient's room in close proximity to the infectious patient (e.g., in the near-field).

## **4. VIRUS INACTIVATION**

### **4.1 Inactivation in Air**

Jones [35] reviewed studies of the inactivation of influenza viruses in air: Results are presented in Table S-V. In each study, the inactivation rate of influenza changes between 40-50% relative humidity. In healthcare settings, indoor air quality guidelines recommend relative humidity in the range of 30-60% [36]. Since this range spans the transition in inactivation rates, the probability distributions in Table S-V were combined by Monte Carlo simulation. Equal weight was given to each study (row of the table). The median values of the resulting distribution were used – e.g., the solid line in Figure S.

### **4.2 Inactivation on Substrates**

Traditionally, porous substrates have been separated from non-porous substrates because the voids in porous matrices facilitate fluid dispersion and evaporation; and drying of the fluid in which influenza viruses are suspended may increase the rate of virus inactivation. Jones [35] reviewed the inactivation of influenza viruses, but additional studies have been published [37-39]. Calculated inactivation rates are presented in Table S-VI. Owing to lack of experimental replication and a lack of diversity in the influenza A and B virus subtypes and strains tested, the variability in inactivation rates by substrate, virus subtype or strain could not be tested statistically.

Studies on non-porous substrates included virus in droplets that rapidly dried upon deposition, and virus in droplets that were so large as to remain moist for the duration of the experiments. Expiratory droplets contain small volumes of water relative to those used in experimental

studies, and dry rapidly upon emission [2,40-42]. Thus, only results from dried droplets were considered in the analysis.

Among porous substrates, a lognormal distribution with  $GM = 0.434 \text{ h}^{-1}$  and  $GSD = 2.15$  described the inactivation rate. Among non-porous substrates (dried droplet), a lognormal distribution with  $GM = 0.556 \text{ h}^{-1}$  and  $GSD = 3.83$  described the inactivation rate. The Wilcoxon test did not reject the null hypothesis of equal medians in the distributions for inactivation rate on porous and non-porous substrates ( $p = 0.227$ ). As a result, the data for porous and non-porous (dried droplet) substrates were pooled: The inactivation rate was modeled by a lognormal distribution with  $GM = 0.496 \text{ h}^{-1}$  and  $GSD = 3.01$  (Table S-VII).

### **4.3 Inactivation on Skin**

The only study of influenza inactivation on the skin identified was by Bean et al., [43] who inoculated stainless steel or tissue with influenza A virus, and asked participants to handle the inoculated object. Nicas and Jones [44] estimated that the inactivation rates in two experimental trials were  $88.4 \text{ h}^{-1}$  and  $55.3 \text{ h}^{-1}$ . Given the limited sample size and the fact that the data were from experimental trials, these two values were judged drawn from a normally distributed population. The inactivation of influenza virus on the skin was modeled by a normal distribution with  $\mu = 71.9 \text{ h}^{-1}$  and  $\sigma = 23.5 \text{ h}^{-1}$  (Table S-VII).

## **5. VIRUS TRANSFER UPON CONTACT**

### **5.1 Transfer between Substrates and Skin**

The efficiency of influenza virus transfer from substrates to skin was equated with the efficiency of transfer from skin to substrates. Evidence for this reciprocity includes studies of enteric viruses [45,46] and the bacteriophage MS2 [47]. Among studies of respiratory viruses, statistically significant differences were observed between the efficiency of transfer from substrates to skin and from skin to substrates, but the magnitudes of the differences were small [48,49].

The only study of influenza A virus transfer efficiency identified was conducted by Bean et al. [43]: Immediately after inoculation of steel with a high dose or a low dose ( $10^{4.5}$  and  $10^{3.0}$  TCID<sub>50</sub>) of virus, handling the steel for three seconds transferred 7.9% and 0.25% inoculated virus, respectively. Transfer efficiencies in this range have also been observed with rhinovirus and bacteriophages during the handling of inoculated doorknobs, faucets and other household objects [50], but other investigators have observed higher rates [49,51]. Reasons for the discrepancies are unclear.

The study by Julian et al. [49] was used to define the transfer efficiency of influenza virus between substrates and skin owing to the inclusion experimental replication, though the experiment only considered transfer between finger pads and glass. Graphical display of the pooled data suggests that the Weibull distribution is more appropriate than other models fitted by the authors [49]. The fitted Weibull (shape = 0.94, scale = 0.23) distribution has a median of 0.155 (15.5%) and a central 90% range of 0.0097 (0.97%) to 0.739 (73.9%). These transfer

efficiencies are consistent with those used by Zhao et al. [28] in a modeling study of fomite mediation of influenza transmission. The distribution was truncated at 0 and 1 (0 and 100%), based on physical plausibility.

## **5.2 Transfer between Skin and Skin**

No studies of influenza virus transfer from skin to skin were identified. Pancic et al. [50] found 1.1% to 10.4% of rhinovirus in normal mucus transferred between fingertips. Rusin et al. [51] observed 33.9% of PRD-1 bacteriophage transferred from the fingertip to lip, on average. These data are consistent with observations of hepatitis A virus, but higher than the 0.02% efficiency observed for the transfer of  $\phi$ X174 bacteriophage and *E. coli* between fingertips [52,53]. Overall, these data span a wide range of transfer efficiencies, and the range overlaps with the efficiency of transfer between substrates and skin. As a result, the Weibull (shape = 0.94, scale = 0.23) distribution developed for influenza virus transfer between substrates and skin was applied to influenza virus transfer between skin and skin (Table S-VII).

## **6. ENVIRONMENTAL CONDITIONS**

### **6.1 Room Volume**

An occupational exposure was considered to involve a worker entering a patient care room. The room volume,  $V$  ( $\text{m}^3$ ) was modeled by a uniform distribution over the range of  $20 \text{ m}^3$  to  $50 \text{ m}^3$  (Table S-VIII), which includes the size of clinical examination and patient room volumes described in the peer-reviewed literature. [54]

### **6.2 Near-field and Far-field Air Compartments**

A two-zone model was used to capture the effect of proximity to the patient for infectious agents transmitted through the droplet route [55]. The near-field zone included the half of the room containing the patient, measured from the patient's head, while the remainder of the room was the far-field zone. Air, including airborne infectious agents, was assumed to exchange between the two zones with air speed  $3.7 \text{ m min}^{-1}$ ,  $S = 3.7 \text{ m min}^{-1}$  [56]. The room height was assumed 3 m,  $H = 3 \text{ m}$ . The room was assumed square, such that the width and length,  $W$  and  $L$ , equaled the square root of the room floor area. The surface area across which air could flow between the two zones was  $H \times W$ . The volumetric rate of air exchange between the two zones is one-half the surface area times the air speed,  $\beta = \frac{1}{2} \times H \times W \times S$ .

### **6.3 Mechanical Ventilation**

The American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) recommends air exchange rates of six to fifteen per hour for patient care environments, where the level of air exchange in a room depends upon the activities designated for that room, and the building age [57,58]. The ASHRAE guidelines represent building design and performance specifications, which may not be met in all circumstances [59], but are recommended by the CDC and HICPAC [60]. Air exchange rates were modeled as a uniform distribution over the

range of 6-15 h<sup>-1</sup>, and applied to both the near-field and far-field air compartments (Table S-VIII).

The specific features of airborne infection isolation rooms (AIIRs) or protective environment rooms were not considered in the model. The primary objective of AIIRs is to prevent the dispersion of infectious agents from the patient rooms into common areas by maintaining negative pressure relative to adjacent areas. The primary objective of protective environment rooms is to prevent the introduction of infectious agents into the patient rooms from common areas by maintaining positive pressure relative to adjacent areas. In both cases, the pressure differential between the patient room and adjacent areas falls beyond the scope of the occupational exposure, which considered only emission from the patient and occupational exposures occurring inside a patient room. In addition, the patterns of airflow vary among AIIRs owing to the configuration of mechanical ventilation [61-63]. It is unknown if the within-room dispersion of infectious agents and occupational exposures differ systematically between AIIRs and regular patient rooms.

## **6.4 Environmental Surfaces**

The area of surfaces touched by workers was equated with 1 m<sup>2</sup>, consistent with previous applications of the Markov model [44,64]. Half of the surface was considered in the near-field, where it was touched by workers.

# **7. INFECTION CONTROL INTERVENTIONS**

## **7.1 Respirators and Facemasks**

The use of respirators and facemasks in healthcare settings has been studied in the context of the 2009 H1N1 influenza pandemic. Recommendations for the use of facemasks or respirators, however, varied geographically. In this study healthcare workers were considered to comply with use of a facemask or respirator in 50% of occupational exposures, with workers equally likely to use a facemask or N95 filtering facepiece respirator. Studies of facemask and respirator use in the context of influenza have found compliance to vary from 22% to 72%, depending upon study site, worker job title and the healthcare activity being performed [65-69].

Facemasks were not considered to prevent the inhalation of influenza virus because they are not certified by NIOSH to offer respiratory protection. Facemasks have been found to offer some protection against the inhalation of particles, and by neglecting this potential effect, the model will over-estimate occupational exposure to influenza when a facemask is worn in the presence of airborne viruses.

The maximum effectiveness of N95 filtering facepiece respirators was equated with the Assigned Protection Factor, APF = 10, [70] which means that the concentration of influenza inside the respirator is 1/10<sup>th</sup> of the concentration outside the respirator. Lower effectiveness was also considered owing to concerns that healthcare workers may not achieve optimal respirator fit in each donning owing to: changes in fit over time, [71] repeated donning of the same respirator [72], or incorrect doffing [73-76]. The minimum effectiveness of N95 filtering facepiece



respirators was equated with  $APF = 5$ , which is consistent with experimental observations by Lee et al. [71].

The barrier protection offered by facemasks and respirators against projected particles has not been tested. The penetration of projected virus-laden particles through facemasks and respirators was equated with their filtration performance. Studies of facemasks have observed penetration of 5-16% [67,77]: Penetration of 10% was assumed. By definition,  $\leq 5\%$  of particles penetrate N95 filtering facepiece respirators: Penetration of 5% was assumed.

Facemasks and respirators were also considered to reduce the frequency of contact between the worker's hand and facial portals to the mucous membranes and respiratory tract. No studies have specifically observed this effect in healthcare settings, but Ng et al. [78] observed in other settings that the hand-to-mouth contact frequency decreased by approximately one order of magnitude. Many of the workers observed by Ng et al. [78] also wore gloves, which may have contributed to the reduction in contact frequency. Based on the observations of Ng et al., [78] we considered that workers wearing a facemask or respirator had 90% fewer contacts between their hands and facial portals.

## **7.2 Gloves**

Gloves provide a physical barrier that prevents infectious agents from reaching the hands. Studies have found, however, that some material on gloves are transferred to the hands during use or doffing [79,80]: Based on these studies, the fraction of influenza that transfers to the hands upon the doffing of gloves was modeled by a uniform distribution over the range 0.0001-0.01. Observations of healthcare workers have found compliance with glove use to 80-90%, but may be lower among some job titles [65,66,81,82].

## **7.3 Hand Hygiene**

Hand hygiene may be performed with soap and water or hand sanitizers, such as alcohol-based rubs. For influenza, all hand hygiene methods have been found to remove  $\geq 95\%$  of culture-detectable viruses [83,84]: Based on these data, hand hygiene was considered to remove 95% of influenza viruses from the hands.

The CDC recommends hand hygiene be performed upon entry to a patient room, prior to touching a patient, after touching a patient and/or upon room exit [85]. Compliance with hand hygiene as been observed to vary with, with higher levels of compliance (approximately 60%) in medical-surgical units and during the 2009 H1N1 influenza pandemic [86,87], and lower levels (approximately 30%) in other contexts [65,87,88]. For this analysis, hand hygiene compliance was equated with 40%.

## **7.4 Eye Protection**

Eye protection shields the facial mucous membranes from projected particles, but the quantitative reduction in exposure to projected particles has not been measured for goggles or face shields. Lindsley et al. [89] found face shields prevented the inhalation of 96% of influenza

viruses in large-particle ( $\leq 100 \mu\text{m}$ ) aerosols within five minutes of a simulated cough. Lacking other data, 4% of projected virus-laden particles to penetrate the face shields and goggles. No data were identified with respect to the use of eye protection or face shields: 50% compliance was assumed.

## **8. SENSITIVITY ANALYSIS**

A simple sensitivity analysis was performed to identify the influence of exposure variables in the estimation of occupational exposure and calculation of the probability of infection during an occupational exposure. The analysis was performed for the case of current compliance with infection control precautions in hospitals, with 80% of patients in isolation. The influence of continuous variables on the outcomes (dose via each route of transmission and probability of infection with each dose-response function) was indicated by the magnitude and direction of Spearman's correlation coefficient (Table S-IX). The ratio of the maximum to the minimum value for each variable is reported in Table S-IX because variables with more variation provide greater opportunity of association with changes in the outcome. The influence of dichotomous variables on the outcomes was indicated by the difference in the median values between the two values (Yes or No): The p-value of the Wilcoxon test is reported in Table S-X, median values are not shown since most were much less than one.

Overall, the results of the sensitivity analysis are consistent with the model assumptions, and the most important variables identified are as expected. For example, pathogen emission variables, particularly the concentration of influenza viruses in cough particles, are strongly positively correlated with dose and infection risk (Table S-IX). With respect to dichotomous variables, use of interventions are statistically significantly associated with differences in dose through the route of transmission interrupted by the intervention (Table S-X).

**Table S-I. Particle size and count distributions measured by Loudon and Roberts [1]**

Equilibrium Particle Diameter Range ( $\mu\text{m}$ )	Initial Particle Diameter Range ( $\mu\text{m}$ )	Initial Particle Mean Volume (mL)	Diameter of Particle with Mean Volume ( $\mu\text{m}$ )	Per Cough		Per Counting 1-100	
				Observed Particle Number	Total Particle Volume (mL)	Observed Particle Number	Total Particle Volume (mL)
1-2.9	2-5.8	$3.8 \times 10^{-11}$	4.2	120.9	$4.6 \times 10^{-9}$	76.7	$2.9 \times 10^{-9}$
>2.9-5.8	>5.8-11.6	$3.8 \times 10^{-10}$	9.0	100.3	$3.8 \times 10^{-8}$	35.3	$1.4 \times 10^{-8}$
>5.8-8.7	>11.6-17.4	$1.7 \times 10^{-9}$	14.7	6.2	$1.0 \times 10^{-8}$	0	0
>8.7-11.2	>17.4-22.4	$4.2 \times 10^{-9}$	20.0	3.3	$1.4 \times 10^{-8}$	32.7	$1.4 \times 10^{-7}$
>11.2-26.0	>22.4-52.0	$3.2 \times 10^{-8}$	39.1	18.3	$5.7 \times 10^{-7}$	100.0	$3.1 \times 10^{-6}$
>26.0-55.5	>52.0-111	$3.2 \times 10^{-7}$	84.9	64.0	$2.1 \times 10^{-5}$	257.5	$8.3 \times 10^{-5}$
>55.5-85.0	>111-170	$1.5 \times 10^{-6}$	142	57.8	$8.8 \times 10^{-5}$	417.5	$6.3 \times 10^{-4}$
>85.0-114	>170-200	$4.2 \times 10^{-6}$	200	30.8	$1.3 \times 10^{-4}$	310	$1.3 \times 10^{-3}$
>114-144	>200-228	$9.1 \times 10^{-6}$	259	19.8	$1.8 \times 10^{-4}$	187.5	$1.7 \times 10^{-3}$
>144-173	>228-288	$1.7 \times 10^{-5}$	318	11.7	$2.0 \times 10^{-4}$	87.5	$1.5 \times 10^{-3}$
>173-203	>288-346	$2.8 \times 10^{-5}$	377	5.3	$1.5 \times 10^{-4}$	50.0	$1.4 \times 10^{-3}$
>203-232	>346-406	$4.3 \times 10^{-5}$	436	4.3	$1.9 \times 10^{-4}$	50.0	$2.2 \times 10^{-3}$
>232-262	>406-464	$6.4 \times 10^{-5}$	495	3.5	$2.2 \times 10^{-4}$	22.5	$1.4 \times 10^{-3}$
>262-291	>464-524	$8.9 \times 10^{-5}$	554	2.7	$2.4 \times 10^{-4}$	20.0	$1.8 \times 10^{-3}$
>291-350	>524-582	$1.4 \times 10^{-4}$	643	5.0	$7.0 \times 10^{-4}$	52.5	$7.3 \times 10^{-3}$
>350-439	>582-700	$2.6 \times 10^{-4}$	792	0.5	$1.3 \times 10^{-4}$	30.0	$7.8 \times 10^{-3}$
>439-586	>700-878	$5.8 \times 10^{-4}$	1032	5.0	$2.9 \times 10^{-3}$	15.0	$8.6 \times 10^{-3}$
>586-734	>878-1172	$1.2 \times 10^{-3}$	1326	1.8	$2.2 \times 10^{-3}$	10.0	$1.2 \times 10^{-2}$
>734-881	>1172-1762	$2.2 \times 10^{-3}$	1619	1.3	$3.0 \times 10^{-3}$	0.0	0
>881-1029	>176-2058	$3.7 \times 10^{-3}$	1914	0.3	$1.2 \times 10^{-3}$	0.0	0
>1029-1176	>2058-2352	$5.6 \times 10^{-3}$	2208	0.7	$3.8 \times 10^{-3}$	0.0	0
>1176-1471	>2352-2942	$9.8 \times 10^{-3}$	2657	1.7	$1.6 \times 10^{-2}$	2.5	$2.5 \times 10^{-2}$
>1471-1776	>2942-3532	$1.8 \times 10^{-2}$	3246	0.7	$1.2 \times 10^{-2}$	5.0	$9.0 \times 10^{-2}$
<b>TOTAL:</b>				466	0.044	1762	0.162

**Table S-II. Influenza virus concentration measured in the nasopharynx or throat 0-4 days after symptom onset, before antiviral therapy. <sup>A</sup>**

Method <sup>B</sup>	Days since Symptom Onset	Number of Participants	Original Results		Adjusted to log <sub>10</sub> TCID <sub>50</sub> mL <sup>-1</sup> <sup>D</sup>	Ref.
			Concentration <sup>C</sup>	Unit		
Seasonal Influenza A and B						
NPTS	0-2	71	3.5 (0.5 - 6.5)	log <sub>10</sub> TCID <sub>50</sub> mL <sup>-1</sup>	3.5 (0.5 - 6.5)	[90]
	1-3	71	2.3 (0.0 - 5.5)	log <sub>10</sub> TCID <sub>50</sub> mL <sup>-1</sup>	2.3 (0.0 - 5.5)	[90]
NPS	1	10	6.0 (4.3 - 7.5)	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.0 (1.3 - 4.5)	[11]
	2	15	5.0 (4.2 - 6.5)	log <sub>10</sub> RNA copies mL <sup>-1</sup>	2.0 (1.2 - 3.5)	[11]
	3	7	6.2 (4.4 - 7.0)	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.2 (1.4 - 4.0)	[11]
Seasonal Influenza A						
NPTS	1	88	6.3 ± 1.4	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.3 ± 1.4	[91]
	2	88	5.8 ± 1.1	log <sub>10</sub> RNA copies mL <sup>-1</sup>	2.8 ± 1.1	[91]
	3	88	4.5 ± 1.9	log <sub>10</sub> RNA copies mL <sup>-1</sup>	1.5 ± 1.9	[91]
	4	88	4.5 ± 2.1	log <sub>10</sub> RNA copies mL <sup>-1</sup>	1.5 ± 2.1	[91]
NPA, NPTS	1	6	7.7 ± 1.7	log <sub>10</sub> RNA copies mL <sup>-1</sup>	4.7 ± 1.7	[92]
	2	20	7.3 ± 1.0	log <sub>10</sub> RNA copies mL <sup>-1</sup>	4.3 ± 1.0	[92]
	3	6	6.7 ± 1.3	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.7 ± 1.3	[92]
	4	6	6.9 ± 1.5	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.9 ± 1.5	[92]
Pandemic 2009 H1N1 Influenza A						
NPS	2	76 <sup>D</sup>	5.7 ± 1.2	log <sub>10</sub> RNA copies mL <sup>-1</sup>	2.7 ± 1.2	[93]
	1	27	6.4 ± 1.0	log <sub>10</sub> RNA copies μL <sup>-1</sup>	6.4 ± 1.0	[17]
	2	9	6.5 ± 1.2	log <sub>10</sub> RNA copies μL <sup>-1</sup>	6.5 ± 1.2	[17]
NPA	0-4	48	6.5 ± 1.2	log <sub>10</sub> RNA copies μL <sup>-1</sup>	6.5 ± 1.2	[18]
	0-1	7	8.0 ± 1.3	log <sub>10</sub> RNA copies mL <sup>-1</sup>	5.0 ± 1.3	[94]
	2-3	10	7.2 ± 0.94	log <sub>10</sub> RNA copies mL <sup>-1</sup>	4.2 ± 0.94	[94]
NPA, NPTS	1	8	6.8 ± 1.7	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.8 ± 1.7	[92]
	2	6	6.2 ± 1.7	log <sub>10</sub> RNA copies mL <sup>-1</sup>	3.2 ± 1.7	[92]
	3	5	5.1 ± 1.3	log <sub>10</sub> RNA copies mL <sup>-1</sup>	2.1 ± 1.3	[92]

<sup>A</sup> The table presents selected studies that included ≥ five participants and presented measures of variability in the viral load.

<sup>B</sup>NPS: nasopharyngeal swab; NPA: nasopharyngeal aspirate; NPTS: nasopharyngeal-throat swab.

<sup>C</sup>Median (range) or mean ± standard deviation.

<sup>D</sup> Concentrations reported in log<sub>10</sub> RNA copies mL<sup>-1</sup> was adjusted to log<sub>10</sub> TCID<sub>50</sub> mL<sup>-1</sup> by subtracting 3, since 10<sup>3</sup> RNA copies were associated with a single infectious virus when measured in a tissue culture system [16].

<sup>E</sup>Number estimated from eFigure 1 in Meschi et al. [93]

**Table S-III. Parameter values for the influenza virus emission in the occupational exposure model.**

<b>Model Parameter Description</b>	<b>Distribution</b>		<b>Reference</b>
	<b>Shape</b>	<b>Parameter</b>	
Cough frequency among persons with influenza, coughs h <sup>-1</sup>	Non-Parametric	Median = 19.6 Central 90% Range 3.77- 84.1	[20,23]
Cough particle size and count distribution	Non-parametric	Table S1	[1]
Volume of fluid in a cough	Triangular	Mode = 0.044 Range 0.004-4.0	[2,63,95]
Concentration of influenza viruses in cough particles, log <sub>10</sub> TCID <sub>50</sub> mL <sup>-1</sup>	Uniform	Range 1.5-6.5	[17,18,90-94]

**Table S-IV. Duration of worker-patient interactions in healthcare settings.**

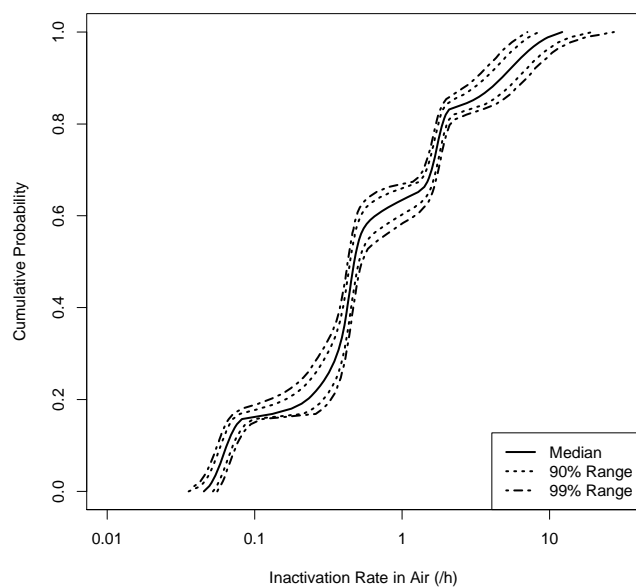
<b>Job Title</b>	<b>Country</b>	<b>Context</b>	<b>Activity</b>	<b>Duration (min)<sup>A</sup></b>	<b>Reference</b>
Oncologists	US	Medical Procedure	Brachytherapy	6.7 ± 2.2	[96]
Nurses	US	Residential facility	Patient care	3.5 ± 5.8	[97]
Nurses	US	Residential facility	Clinical activities	6.9 ± 11.1	[97]
Nurses	US	Residential facility	Medication administration	17.8 ± 26.3	[97]
Nurses	US	Hospital	Patient rounds	several	[98]
Nurses	US	Hospital	All tasks	Median 0.33	[98]
Healthcare	US	Hospital ICU	Patient care	Median 2, [ $< 1$ , 51]	[99]
Primary Care Providers	US	Ambulatory care	Patient Care	about 30	[100]
Nurses	Netherlands	Hospital Burn Ward	Wound care	[60, 480]	[101]
Physicians	US	Ambulatory care	Patient care	17.5 ± 7.4	[102]
Healthcare	US	Hospital	Patient transport	7	[103]
Medical Residents	US	Ambulatory Care	Patient Care	17.7 ± 7.7	[104]
Nurse Practitioners	US	Nursing Home	Patient Care	20.8 ± 14.1	[105]
Physician	Australia	Emergency Department	In cubicle with patient	2.7	[106]
Nurses	US	Home care (spirometry)	Patient care	Median 7.50, [1, 39]	[107]
Physician	US	Ambulatory care	Patient care	12.6	[108]
Physician	US	Ambulatory care	Attending physician	5	[108]
Physician	US	Ambulatory care	Patient care	16	[109]
Medical Assistant or Registered Nurse	US	Ambulatory care	Patient care	3.4	[110]
Healthcare workers	Australia	Nursing Homes	Patient care	Median 0.58	[111]
Physicians	US	Ambulatory Care	Patient care	26	[33]
Physicians	Australia	Hospital	All tasks	Median 0.63, [0.02, 90.6]	[112]

<sup>A</sup>Mean or mean ± standard deviation, range denoted with square brackets, and median values are identified as such.

**Table S-V. Inactivation rate of influenza A (H1N1) virus strain PR8 in room temperature (20-24°C) air.**

Relative Humidity (%)	Inactivation Rate (h <sup>-1</sup> )				Reference
	Mean	GM	GSD	SD	
50 – 90	5.46	5.49	1.6		[113]
50 – 81	0.445	0.443	1.11		[114]
43 – 73	1.71			0.192	[115]
15 – 40	0.438	0.555	2.06		[113]
20 – 36	0.062	0.061	1.2		[114]
8 – 30	0.361			0.115	[115]

**Figure S-VI. Inactivation rate of influenza A virus in air estimated by Monte Carlo simulation [35].**



**Table S-VII. Inactivation rates of influenza A and B viruses on substrates at room temperatures.**

Substrate	Mean (Standard Deviation) Inactivation Rate (h <sup>-1</sup> )		Wet Droplet	Reference
	Influenza A	Influenza B		
<i>Porous Substrates</i>				
Banknotes	0.313	1.15		[35,116]
Handkerchief	>1.06	0.373		[35,43]
J-Cloth	1.38			[38]
Magazines	0.451	0.522		[35,43]
Oak Wood	0.806			[38]
Pajamas	0.117	0.332		[35,43]
Particulate Respirator	0.258			[37]
Pine Wood	0.345			[38]
Silver-containing Cloth	0.173			[38]
Soft Toy	0.518			[38]
Surgical Mask	0.281			[37]
Tissue	1.02	0.334		[35,43]
<i>Non-Porous Substrates</i>				
Aluminum	0.806			[38]
Coated Wood	0.286		Yes	[37]
Coated Wood	1.27			[38]
Glass <sup>A</sup>	0.020 (0.106)			[39]
Glass <sup>B</sup>	0.649 (0.003)		Yes	[39]
Glass (20% RH) <sup>C</sup>	1.43 (0.200)			[117]
Glass (84% RH) <sup>C</sup>	2.81 (0.580)			[117]
Glass (Window)	1.50			[38]
Plastic	0.102	0.178		[35,43]
Plastic (Computer Keyboard)	0.461			[38]
Plastic (Kitchen Counter)	0.633			[38]
Plastic (Light Switch)	0.806			[38]
Plastic (Polystyrene)	0.898			[38]
Plastic (Telephone)	1.67			[38]
Rubber Glove	0.053		Yes	[37]
Stainless Steel	0.112	0.265		[35,43]
Stainless Steel	0.553			[38]
Stainless Steel	0.253		Yes	[37]
Tyvek®	0.292		Yes	[37]

<sup>A</sup> Inactivation rates calculated for four experiments (two replicates with two strains of influenza A (H1N1) virus) after drying of droplets, on days d<sub>0</sub> to d<sub>8</sub>. Data presented are mean values (standard deviation).

<sup>B</sup> Inactivation rates calculated for four experiments (two replicates with two strains of influenza A (H1N1) virus) while droplet is wet, based on the theoretical concentration (d<sub>theoretical</sub>), concentration while wet (d<sub>wet</sub>) at d<sub>0</sub>.

<sup>C</sup> Data for inactivation rates for the WS and swine strains of influenza A H1N1 virus are combined.



**Table S-VIII. Influenza virus transport and exposure parameter values in the occupational exposure model.**

<b>Model Parameter Description</b>	<b>Distribution</b>		<b>Reference</b>
	<b>Shape</b>	<b>Parameter</b>	
Rate of influenza A virus inactivation in room temperature air, h <sup>-1</sup>	Non-Parametric	eFigure 1	[113-115]
Rate of influenza A virus inactivation on substrates at room temperature, h <sup>-1</sup>	Lognormal	GM = 0.496, GSD = 3.01	[35,37-39,43,116,117]
Rate of influenza A virus inactivation on skin, h <sup>-1</sup>	Normal	$\mu = 71.9$ $\sigma = 23.5$	[43,44]
Fraction of influenza viruses transferred upon contact between substrates and skin and between skin and skin	Weibull	Shape = 0.94, Scale = 0.23 Range 0-1	[49]
Fraction of influenza at the facial portals to the respiratory tract that reach cellular receptors	Uniform	Range 0.001- 0.01	[44]
Fraction of time during the exposure that a worker is in proximity to the infectious patient	Fixed	0.50	[34,118]
Fraction of coughs emitted by an infectious patient that spray onto a worker's facial portals to the respiratory tract.	Fixed	0.05	[64]
Rate of self-contact (hand to face, portals to the respiratory and gastrointestinal tract), touches h <sup>-1</sup>	Uniform	Range 1.2-18	[25-28]
Rate of hand-to-surface contact with contaminated surfaces, touches h <sup>-1</sup>	Uniform	15-1,200	[29,31]
Proportion of time worker is in close contact with an infectious patient during a worker-patient interaction	Fixed	0.5	[33,34]

**Table S-IX. Environment parameter values in the occupational exposure model.**

Parameter Description	Parameter Distribution		Reference
	Shape	Value	
Room volume, V, m <sup>3</sup>	Uniform	Range 20-50	[64]
Room height, H, m	Fixed	3	
Room width and length, m	Calculated	$\sqrt{V \div H}$	
Volume of room near-field and far-field, m <sup>3</sup>	Calculated	$\frac{1}{2} \times V$	
Random air speed between the near-field and far-field, m s <sup>-1</sup>	Fixed	3.7	[56]
Ventilation air exchange rate, h <sup>-1</sup>	Uniform	Range 6-15	[57]
Area of surfaces contacted by workers, m <sup>2</sup>	Fixed	1	[44,64]

**Table S-X. Sensitivity analysis for continuous variables in the calculation of the probability of infection during an occupational exposure. Results shown for the case of current compliance with infection control precautions in hospital, with 80% of patients isolated.**

Variable		Spearman's Correlation Coefficient				
		Dose via			Infection Risk	
Name	Range Ratio <sup>1</sup>	Contact	Inhalation	Spray	Function 1	Function 2
Room Volume	2.5	0.01	-0.03	0.01	0.01	0.01
Ventilation air exchange rate	2.5	-0.02	-0.03	-0.01	-0.02	-0.02
Cough frequency among persons with influenza,	96	0.36	0.38	-0.02	0.39	0.38
Volume of fluid in a cough	528	0.13	0.18	0.21	0.16	0.16
Concentration of influenza viruses in cough particles	99,700	0.47	0.63	0.75	0.59	0.60
Number of Coughs	250 <sup>2</sup>	0.53	0.57	-0.02	0.56	0.55
Rate of influenza A virus inactivation in room temperature air	270	-0.01	-0.01	0.01	0.00	0.00
Rate of influenza A virus inactivation on skin at room temperature	1,150	-0.01	0.01	0.01	0.02	0.02
Fraction of influenza viruses transferred upon contact between substrates and skin and between skin and skin	267,000	0.28	-0.02	-0.01	0.00	0.00
Rate of hand-to-surface contact with contaminated surfaces,	40	0.08	0.01	0.00	0.01	0.00
Rate of self-contact	380	0.23	0.02	0.13	0.12	0.12
Probability of Intercepting Spray	10	0.08	0.00	0.00	0.10	0.10
Duration of Occupational Exposure	330	0.37	0.42	-0.02	0.38	0.37

<sup>1</sup> Ratio of maximum value to minimum value<sup>2</sup> Minimum value for the number of coughs is zero, 250 is the maximum number of coughs

**Table S-XI. Sensitivity analysis for dichotomous variables in the calculation of the probability of infection during an occupational exposure. Results shown for the case of current compliance with infection control precautions in hospital, with 80% of patients isolated.**

Variable	Wilcoxon Test <i>p-value</i>				
	Dose Via			Infection Risk	
	Contact	Inhalation	Spray	Function 1	Function 2
Hand Hygiene Compliance	0.14	0.88	0.07	0.31	0.53
Surface Cleaning and Decontamination	0.01	0.60	0.41	0.30	0.57
Patient Isolation	<0.01	<0.001	<0.01	<0.001	<0.01
Glove Compliance	<0.01	0.28	0.36	0.02	0.01
Respirator Worn (versus Facemask or Nothing)	<0.01	<0.01	<0.01	0.02	0.01
Facemask Worn	<0.01	0.14	<0.01	<0.01	<0.01
Eye Protection Worn	<0.01	0.79	<0.01	<0.01	<0.01

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