Validation of a Stochastic Discrete Event Model Predicting Virus Concentration on Nurse Hands

1. ABSTRACT

Understanding healthcare viral disease transmission and the effect of infection control interventions will inform current and future infection control protocols. Modeling is a cost-effective tool to characterize intervention efficacy. In this study, a model was developed to predict virus concentration on nurses' hands using data from a bacteriophage tracer study conducted in Tucson, Arizona in an urgent care facility. Surfaces were swabbed 2 hours, 3.5 hours, and 6 hours post-seeding to measure virus spread over time. To estimate the full viral load that would have been present on hands without sampling, virus concentrations were summed across time points for 3.5 and 6 hour measurements. A stochastic discrete event model was developed to predict virus concentrations on nurses' hands, given a distribution of virus concentrations on surfaces and expected frequencies of hand-to-surface and -orifice contacts. Box plots and statistical hypothesis testing were used to compare the model-predicted and experimentally-measured virus concentrations on nurses' hands. The model was validated with the experimental bacteriophage tracer data, because the distribution for model-predicted virus concentrations on hands captured all observed value ranges, and interquartile ranges for model and experimental values overlapped for all comparison time points. Wilcoxon rank sum tests showed no significant differences in distributions of model-predicted and experimentally measured virus concentrations on hands. Next steps in model development include addressing viral concentration distributions that would be found naturally in healthcare environments, as opposed to concentrations used in bacteriophage tracer studies, and measuring the risk reductions predicted for various infection control interventions.

Key words: healthcare, exposure simulation, bacteriophage

2. INTRODUCTION

Although virus survival on fomites is variable, many viruses survive on surfaces for days, and some, such as rotavirus and other enteric viruses, may remain viable on surfaces for months (Boone & Gerba, 2007). This is especially of concern in indoor environments, where viruses contribute greatly to infectious disease burden (Barker, Stevens, & Bloom, 2001). Although surface disinfection and hand hygiene compliance are supported infection control interventions to lower microbial load on surfaces, quantifying and understanding the mechanisms through which microbial exposures occur in healthcare settings would further inform infection control intervention (i.e., surface cleaning and hand hygiene) needs. Using environmental data to evaluate intervention efficacy may be more informative than efficiencies measured in laboratory settings. Using real world intervention efficacies can form target microbial reduction goals, which are currently not quantified or defined for healthcare environments.

Due to the financial cost and the time required to regularly survey viral populations in healthcare environments, modeling is a useful tool in characterizing microbial spread and estimating the effect of an intervention in disrupting spread. Mathematical modeling has been used to predict the efficacy of various interventions and to identify the most important influences on intervention efficacy. Many of these models are variations of SIR (susceptible-infectious-recovered) models that account for transition between states (World Health Organization, 2009b). These transition rates are typically defined by differential equations and do not include mechanistic equations that account for momentary exposures or behavioral micro-activities. Other models have addressed human behavior through use of agent-based models. An agent-based model developed by Barnes et al. (2014) addressed multi-drug resistant organisms and the influence of behaviors, such as patient and healthcare worker interactions, on acquisition rates.

However, this model does not address stochasticity in parameters or account for varying transfer efficiencies for different fomite types (Barnes, Morgan, Harris, Carling, & Thom, 2014). Additionally, this model does not track behaviors on the level of hand-to-object or hand-to-orifice contacts, meaning that moments of high exposure are not captured at high time resolution (Barnes et al., 2014). A model developed by King et al. (2015) accounts for stochasticity of behavioral events, using Markov chains informed by observational data to predict MRSA exposures. King et al. (2015) account for individual surface contacts and transfer efficiencies, and incorporate fluid dynamics to address deposition of aerosolized MRSA. The model was validated by means of a Kendall-tau parametric test used to compare the model's predicted colony forming units (CFU) on hands with empirical literature values (King, Noakes, & Sleigh, 2015). Although there is a growing trend in using models to answer questions about transmission and pathogen spread in healthcare, few models address viral pathogens (Kleef, Robotham, Jit, Deeny, & Edmunds, 2013). Additionally, few HAI models compare model predictions to empirical data. In one review of healthcare-acquired infection (HAI) models, only 5% of 96 papers compared model outputs to empirical data (Kleef et al., 2013).

The purpose of this study was to develop and validate a stochastic discrete event model for predicting virus concentration on nurse hands using data from a bacteriophage tracer study performed in an urgent care facility. The framework of the model was based on a stochastic discrete event model for rotavirus exposures through hand-to-fomite and hand-to-mouth contacts (Julian, Canales, Leckie, & Boehm, 2009). The model developed in this study was an expanded version intended to be specific to a healthcare environment, with additional types of contacts, and with the incorporation of handwashing events.

3. METHODS

3.1. Urgent Care Tracer Study

In an urgent care facility in Tucson, Arizona, a registration pen and door handle were seeded with *Escherichia coli* bacteriophage MS2 (ATCC® 15597-B1™), a harmless viral pathogen surrogate. Two, 3.5, and 6 hours after seeding, various surfaces (bathroom handles and faucets, computer mouse, waiting room counter, arm rest, patient room bed, patient room inner door handle, nurse hands, and patient hands) were swabbed with letheen broth Sponge-Sticks (3M, Maplewood, MN). Swabs were transported to the laboratory on ice and processed within 24 hours for MS2 virus using a double agar overlay method For 3.5 hour concentrations, measurements from 2 hours and 3.5 hours were added together to account for viral loss from the first sampling and to estimate the amount of virus that would have accumulated over the 3.5 hours. For 6 hour concentrations, measurements at 2, 3.5, and 6 hours were summed to represent viral concentrations expected on nurse hands without losses that may have occurred due to sampling. MS2 concentrations (PFU/cm^2) for the sampled surfaces assumed to be touched by nurses (bathroom handles, bathroom faucets, waiting room nurse computer mouse, nurse's station computer mouse, nurse's station arm chair, patient room canisters, patient room bed, patient room inner door handles) were fit to a log normal distribution using the fitdistRplus package for RStudio (Delignette-Muller & Dutang, 2015; R Core Team, 2016). A log normal distribution was assumed, because this distribution has been assumed for virus concentrations in multiple quantitative microbial risk assessments (U.S. Environmental Protection Agency, 2010).

3.2. Model Development

A discrete-event model was developed in which the following events had varying probabilities of being chosen per second of simulated activity sequences: contact with a

nonporous surface; contact with a porous surface; contact with mouth, eyes, or nose; compliant hand washing; and no contact with surfaces. For hand-to-nonporous, hand-to-porous, and hand-to-orifice contacts, the probability of an event occurring in the behavior sequence was weighted by contacts/min observed in behavioral studies (Beamer, Luik, Canales, & Leckie, 2012; Nicas & Best, 2008). The probability of a no contact event was the complement of the sum of probabilities for all other event types. For hand washing events, the probability of a compliant hand washing event occurring was weighted by rate of compliant hand washes per minute. To arrive at this rate, the number of hand washing opportunities per a 12-hour shift per healthcare worker, used by Chavali et al. (2014) to measure hand hygiene compliance, was converted to a number of hand washing opportunities per minute per healthcare worker. This rate was then multiplied by a compliance rate to represent the number of compliant hand washing events per minute. A compliance rate of 36% was used, as this was observed in a U.S. healthcare non-intensive care unit (McGuckin, Ascp, Waterman, & Govednik, 2009). Using these values, compliant hand washing was estimated to occur once every ~13 minutes, while 1 hand washing opportunity was estimated to occur once every ~5 minutes. This compliant hand washing rate, in units of hand washing per hour per healthcare worker (4.5) is within the range (1.7 – 15.2) of the average numbers of hand hygiene actions per hour per healthcare worker reported in the *WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge Clean Care Is Safer Care* (2009) (World Health Organization, 2009a).

The duration of hand-to-porous and hand-to-nonporous contacts was 3 seconds, based on a median duration for these contact types observed in behavioral studies (Beamer et al., 2012). The duration of hand washing events was 30 seconds, based on recommended hand washing times (Centers for Disease Control and Prevention, 2002). The duration of hand-to-orifice

contacts was assumed to be 1 second long. Moments without contacts were given a duration of 1 second. The probability of using either the right or left hand for contact events was 0.5, based on the finding of Beamer et al. (2012) that the patterns of right versus left hand contacts were not significantly different (Beamer et al., 2012).

One-thousand iterations were run with R, version 1.0.136 (R Core Team, 2016). Per model iteration, a different sequence of activities for 6 hours (21600 seconds) was generated. This was the length of time between seeding and the last sampling time in the bacteriophage tracer study. During contacts with porous or nonporous surfaces, a concentration was sampled from the log normal distribution of virus concentrations on surfaces. Change in concentration on combined hands was calculated using an equation from a study conducted by Julian et al. (2009). However, the inactivation term was removed, because enteric viruses have been shown to be persistent on fomite surfaces (Abad, Pinto, & Bosch, 1994). Assuming no viral loss due to inactivation allowed for a conservative risk estimate.

$$C_{hand,t} = C_{hand,t-1} - \left(TE\ S\ \left(C_{hand,t-1} - C_f\right)\right)$$

where $C_{hand,t}$ = concentration on hands at time t (PFU/cm^2)

TE = transfer efficiency (fraction)

S = fraction of hand surface area in contact (fraction)

C_f = virus concentration on surface (PFU/cm^2)

This equation accounts for viral gains and losses to the hands, assuming that the direction of transfer is from the surface with a higher concentration to a surface with a lower concentration. All variables used to calculate$C_{hand,t}$ were assumed to be positive, as all distributions for transfer efficiencies were truncated as to not include negative numbers. This model also assumes uniform surface density. Transfer efficiencies specific to porous vs. nonporous surfaces were used in

calculating the current viral concentration on hands for hand-to-porous and hand-to-nonporous surface contacts, respectively. The distribution for fractions of the hand surface area in contact with a surface was not specific to hand-to-porous or -nonporous contacts.

For contacts with orifices, the following equation was used, but inactivation was removed from the original equation by Julian et al. (2009).

$$C_{hand,t} = C_{hand,t-1}\,(1 - TE\ S\,)$$

where $C_{hand,t}$ = current time step concentration on hands (PFU/cm^2)

$C_{hand,t-1}$ = previous time step concentration on hands (PFU/cm^2)

Transfer efficiency distributions used in other viral exposure models were used in this study (Julian et al., 2009; Lopez et al., 2013; Reynolds et al., 2015; Rusin, Maxwell, & Gerba, 2002).). Fractions of hand in contact with orifices during orifice contacts were constructed using distributions of surface area of hand in contact with orifices divided by a value sampled from a distribution of total hand surface area. For nose and eyes, these distributions were from an observational study of 7-12 year olds, where there were no significant differences in contact rates between age categories, indicating that contact rates may become increasingly constant as people age (Beamer et al., 2012).. For this reason, these rates have been used to represent adult activities in other models capturing adult contact behaviors (Beamer et al., 2015). For hand-to-mouth contacts, surface area of the hand in contact with the mouth was informed by studies conducted on adults (Sahmel, Hsu, Avens, Beckett, & Devlin, 2015).

During compliant hand washing events, concentration on hands was decreased by a $\log_{10}$ reduction randomly sampled from a uniform distribution (min=1.55, max=2.19) informed by a reported range of MS2 log reductions (1.55-2.19 $\log_{10}$) for a single hand washing “episode” with nonantimicrobial soap (Sickbert-Bennett et al., 2005). During non-compliant hand washing

events, the concentration on hands was unchanged. Cleaning events were not addressed in this model. It was assumed that the overall influence of any cleaning events was captured in surface concentration measurements from the bacteriophage tracer study used to inform the surface concentration distribution in this study.

3.3. Model Validation

To validate the model, the distribution of model-predicted virus concentrations (PFU/cm^2) on nurse hands at 2, 3.5, and 6 hours were compared to experimental virus concentrations (PFU/cm^2) at these same time points post-bacteriophage seeding. Wilcoxon rank sum tests were also conducted to test for statistically significant differences in distributions between model-predicted virus concentrations on hands and experimental values. This has been used as a means to validate other exposure models with nonparametric outputs that have compared outputs to bacteriophage tracer data (Beamer et al., 2015).

3.4. Sensitivity Analysis

Spearman correlation coefficients were used to compare the effect of stochastic variables on estimated cumulative dose, as this is a recognized method of sensitivity analysis (Marino, Hogue, Ray, & Kirschner, 2009) (Marino et al., 2008) and has been used in other QMRA studies (Hamilton, Ahmed, Toze, & Haas, 2017). Stochastic variables were then ranked based on absolute value of the spearman correlation coefficient, where a lower rank number indicated a greater correlation coefficient and a higher rank number indicated a smaller correlation coefficient.

4. RESULTS

4.1. Model Validation

The model was validated with experimental data. Interquartile ranges for model-predicted and experimental virus concentrations on nurse hands overlapped for all time points (Figure 1). All Wilcoxon rank sum tests used to test for significant differences between model-estimated and experimentally-measured virus concentrations on nurse hands were statistically insignificant, indicating that the model was validated with experimental data for all three compared time points (Table 2). The model and bacteriophage data indicate that virus concentrations on hands may remain constant after two hours of exposure, supporting other exposure models that have assumed steady-state virus concentrations on hands for similar time periods of exposure (Figure 1) (Beamer et al., 2015). However, the model demonstrates that virus concentration over second-by-second scenarios can fluctuate over time, allowing for moments of high exposure (Figure 2). In the case of the simulated nurse with virus concentration on hands shown in Figure 2, a large change in viral concentration on hands occurred at 15,824 seconds (4.4 hours) where the concentration changed from 1.70 PFU/cm^2 to 30.1 PFU/cm^2 on the right hand. This was due to a nonporous contact with a highly contaminated surface with a concentration of 1.01 x 10^3 PFU/cm^2. This concentration on the nurse's hand fluctuated as a result of other contacts with surfaces. At 21,024 seconds (5.8 hours), a hand-washing event decreased concentration on hands from 3.7 PFU/cm^2 (right) and 9.7 PFU/cm^2 (left) to 0.04 PFU/cm^2 (right) and 0.1 PFU/cm^2 (left). This example of events supports the hypothesis that high moments of exposure are possible, even though the central tendency of virus concentrations on hands may remain relatively constant over longer periods of exposure (Figure 2). Figure 3 illustrates the distribution of viral concentration on nurses' hands at the end of the simulation (6 hours). This distribution of concentrations on

nurse hands after the simulated exposure time demonstrates that nurses are more likely to have lower concentrations on hands, but that high concentrations are possible and do not occur as frequently as lower concentrations (Figure 3).

4.2. Estimated Dose

The estimated cumulative doses ranged from 171.5 to 16,720.0 viral particles, with a mean of 1097.0 (SD=1084.289). High variability in cumulative dose is in part due to variable concentrations per hand-to-surface contact and variability in behaviors that would result in viral loading on the hands and transfer from the virus to the mouth upon hand-to-mouth contacts. For context, the infectious dose of rotavirus, an enteric virus, is as low as 6.17 viral particles, according to optimized dose-response curves informed by human feeding studies (cite here!). In the case of this tracer study, the registration pen and door knob were seeded with virus concentrations as great as _____. These concentrations may not be an accurate reflection of the concentrations expected for enteric viruses in healthcare settings. For example, in a study conducted by Ganime et al. (2012), rotavirus was only detected on 14% (73/504), and of detected samples, concentrations ranged from 3.4 to 2.9 x 10^3 genomic copies/mL.

4.3. Sensitivity Analysis

The top five most influential parameters, in order of most to least influential, were the number of hand washes, the number of hand-to-mouth contacts, hand-to-mouth transfer efficiency, surface concentration, and hand-to-nonporous surface transfer efficiency. As the number of hand washes increased, estimated cumulative dose tended to decrease. As the number of hand-to-mouth contacts increased, estimated cumulative dose tended to increase.

5. DISCUSSION

The validation of a microbial exposure model with bacteriophage tracer data represents a new application of tracer studies in healthcare microbial risk assessment. This approach offers an extension of bacteriophage tracer studies as it allows for not only the evaluation of an intervention's effect on microbial concentrations but also of exposure potentials. A discrete event model, as opposed to a steady-state model, can estimate momentary exposures and can be used to evaluate the effect of behavior and intervention timing and frequency. The model developed in this study shows that virus concentrations on hands appears to generally approach a steady state concentration. However, the large range of modeled virus concentrations on hands at each time point demonstrate variability around a general steady state concentration (Figure 2). This variability could affect estimated momentary doses, making models that assume a constant concentration on hands unreliable in estimating high or low cumulative doses in comparison to the central tendency of estimated cumulative dose. A discrete event model that tracks change in virus concentration on hands over time captures momentary exposures that may be higher than the steady-state value. Therefore, models that assume a single approached viral concentration on hands, although consistent with this model's portrayal of the central tendency of concentration on hands over time, may be oversimplifying hand contamination scenarios, resulting in unreliable hand concentration and cumulative dose estimations.

An additional challenge in using models that assume a single steady-state virus concentration on hands includes an inability to address time- or event-dependent interventions, such as compliant hand washing events and the time and frequency of surface cleaning events. Using this model as a framework to explore time-dependent interventions in future studies will inform infection control professionals on intervention effects and optimization strategies.

However, before this model can accurately portray infection risks, an evaluation of pathogen concentrations on surfaces that more closely represents concentrations expected in healthcare environments is recommended. Concentrations of pathogens on surfaces in healthcare settings often have less than10 organisms per cm^2 under contaminated circumstances (Weber, Anderson, & Rutala, 2013). Although this concentration is not specific to viruses or bacteria, it has been primarily compared to bacterial concentrations measured in healthcare environments. For viruses, this concentration is often much lower, and large proportions of samples are often below the limit of detection, even with molecular methods (Ganime et al., 2012). Using distributions of virus concentrations on surfaces from the bacteriophage study would overestimate infection risk, as most of these concentrations are higher in comparison to surface concentrations of viral pathogens found in healthcare environments. For example, Ganime et al. (2012) reported 14% (73/504) surface samples being positive for rotavirus with a limit of detection of 3.4 genome copies/mL. Some infectious doses for viruses, which may be as low as less than 1 tissue culture infective dose ($TCID_{50}$) (Yezli & Otter, 2011). In this study, the average estimated cumulative dose was 1097.0 viral particles. Despite, challenges with using tracer study data to relate exposure to infection risk, the development of exposure models that can account for momentary pathogen concentrations on hands, as demonstrated in Figure 3, is an improvement in risk assessment that can offer infection risk estimations for pathogen concentrations in environments that may otherwise be below a limit of detection.

In addition to incorporating surface concentration data reflective of healthcare environments, this model could be improved by further exploring whether the large range in estimated viral concentrations on hands across time is due to uncertainty in current modeling parameters or due to true variability in parameters. With only four experimental data points per

time point, it is possible that variability in influential parameters, such as micro-activities, are not captured in the range of experimental data points. Aside from sensitivity analyses, more experimental data are needed to better address variability vs. uncertainty in current modeling parameters.

One current limitation in more accurately modeling microbial spread in healthcare settings includes a lack of micro-activity data for healthcare workers. In this model, the two most influential variables were micro-activity parameters (Table 3). Although some activity data does exist for healthcare workers, the data is very contact surface-specific (King et al., 2015). Frequency of orifice contacts and non-porous and porous contacts per minute for various healthcare worker roles would inform the current model, allowing for other interventions to be explored more confidently and to be applied to more specific healthcare scenarios. For example, one intervention in a surgical ward may not be as promising as its implementation in an urgent care, based on differences in behavior and contacts with surfaces. Additionally, because there is wide variety in hand hygiene compliance among healthcare workers, and because this parameter was the most influential on estimated dose in this study (Table 3), pairing an observational behavior study with future tracer studies would allow for more confidence in later modeling applications of resulting data and more available information regarding adult micro-activities that could be applied in a variety of models.

In addition to lacking behavior data, there are opportunities to further improve the current model by informing it with experimentally-informed mechanistic equations. The effect of the duration of a contact on the amount of microbial transfer has been explored in a transfer efficiency study, this was within the context of skin-liquid interfaces (Pitol, Bischel, Kohn, & Julian, 2017). Such transfer efficiency studies could be informative in accounting for droplets

that may settle or land on surfaces, later resulting in exposure through hand-to-surface contacts. However, wetness of surfaces and of hands was not measured in this tracer study. Future tracer studies could benefit from incorporating these parameters so that more current transfer efficiency data related to skin-liquid interfaces could be included. Aside from hand-to-liquid interfaces, the effect of contact duration on microbial transfer efficiency has not been thoroughly explored for hand to surface contacts. Understanding how a one second contact with surface may differ from a 10 second contact would diminish uncertainties in the current model framework.

The validation of an exposure model specific to viruses in healthcare addresses a current gap in healthcare modeling (Kleef et al., 2013). Incorporating environment-specific distributions for contact frequencies and durations along with distributions for viable and quantified virus concentrations in healthcare environments will enhance this model's applicability to infection control questions and can be developed to address time-dependent interventions. Using bacteriophage studies to inform mechanistic models can prove to be a useful validation method. However, to appropriately investigate infection risks, distributions of realistic microbial concentrations in the environment of interest are necessary. Development of this model is an important step toward predicting infection risks in healthcare settings and accounting for the influence of human behavior and of intervention timing on intervention efficacies. This study also demonstrates the promising extension of bacteriophage tracer studies to estimate the influence of behavior and interventions on estimated infection risks.

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Tables and Figures:

Table 1. Discrete Event Model Parameters

Variable Description	Symbol	Units	Distribution (Parameters)*	Source/Reference
Event Frequency				
Non porous contact	NP_C	Contacts/min (Probability per second)	4.1 (4.1 / 60)	(Beamer et al., 2012)
Porous contact	P_C	Contacts/min (Probability per second)	5.5 (5.5 / 60)	(Beamer et al., 2012)
Hand wash Opportunity	HW_O	Opportunities/ min * compliance rate (Probability per second)	0.075 (0.2083 * 0.36 / 60)	(Chavali, Menon, & Shukla, 2014)
Mouth	M_C	Contacts/min (Probability per second)	0.18 (0.18 / 60)	(Beamer et al., 2012)
Eyes	E_C	Contacts/min (Probability per second)	0.06 (0.06 / 60)	(Nicas & Best, 2008)
Nose	N_C	Contacts/min (Probability per second)	0.01 (0.01 / 60)	(Nicas & Best, 2008)
No hand contact	NH	Probability per second	1 - (9.92/60)	Assumed
Event Duration				
Non porous contact		s	3	(Beamer et al., 2012)
Porous contact		s	3	(Beamer et al., 2012)
Hand wash		s	30	(Centers for Disease Control and Prevention, 2002)
Mouth		s	1	Assumed
Eyes		s	1	Assumed
Nose		s	1	Assumed

No contact		s	1	Assumed
Contamination Concentration				
Surface virus concentration	C_f	PFU/cm^2	Lognormal (-1.008, 2.628)	This study
Area of Hand**				
Area of Hand	A_{hand}	cm^2	Uniform (890, 1070)	(Beamer et al., 2015)
Percentage of Object Contacted				
Fraction of object contacted (Porous and Non porous fomite)	S_H	fraction	Uniform (0.13, 0.24)	(Julian et al., 2009)
Fraction of object contacted (Mouth)	S_M	fraction	Uniform ($10.9/A_{hand}$,$13.4/A_{hand}$)	(Sahmel et al., 2015)
Fraction of objected contacted (Eyes)	S_E	fraction	Uniform ($0.10/A_{hand}$, $2/A_{hand}$)	(Beamer et al., 2015)
Fraction of objected contacted (Nose)	S_N	fraction	Uniform ($0.06/A_{hand}$, $0.33/A_{hand}$)	(Beamer et al., 2015)
Fraction of Viral Transfer				
Fraction transferred (Nonporous)	TE_{FHP}	fraction	Uniform (0.05, 0.22)	(Beamer et al., 2015; Lopez et al., 2013)
Fraction transferred (Porous)	TE_{FHNP}	fraction	Uniform (0.0003, 0.0042)	(Beamer et al., 2015; Lopez et al., 2013)
Fraction transferred (mouth)***	TE_{HM}	fraction	Normal (0.41, 0.25)	(Julian et al., 2009)
Fraction transferred (Eyes)	TE_{HE}	fraction	Point Estimate 0.339	(Beamer et al., 2015; Rusin et al., 2002)
Fraction transferred (Nose)	TE_{HN}	fraction	Point Estimate 0.339	(Beamer et al., 2015; Rusin et al., 2002)
Pre-Intervention Parameters				
Pre-Intervention Nurse Hand washing Compliance Rate		%	Point Estimate 36%	(McGuckin et al., 2009)
Pre- Intervention Soap log reduction	R		Uniform ($10^{1.55}$, $10^{2.19}$)	(Sickbert-Bennett et al., 2005)

* Log-normal (meanlog, sdlog); Uniform (minimum, maximum); Normal (mean, sd)
**Values were divided by two to represent % SA of single hand contacts as opposed to combined hands
***The left tail of the distribution for this variable is truncated at zero.

Figure 1. Comparison of Model Estimated Virus Concentrations on Nurse Hands to Experimentally Measured Virus Concentrations on Nurse Hands with 36% Hand Washing Compliance

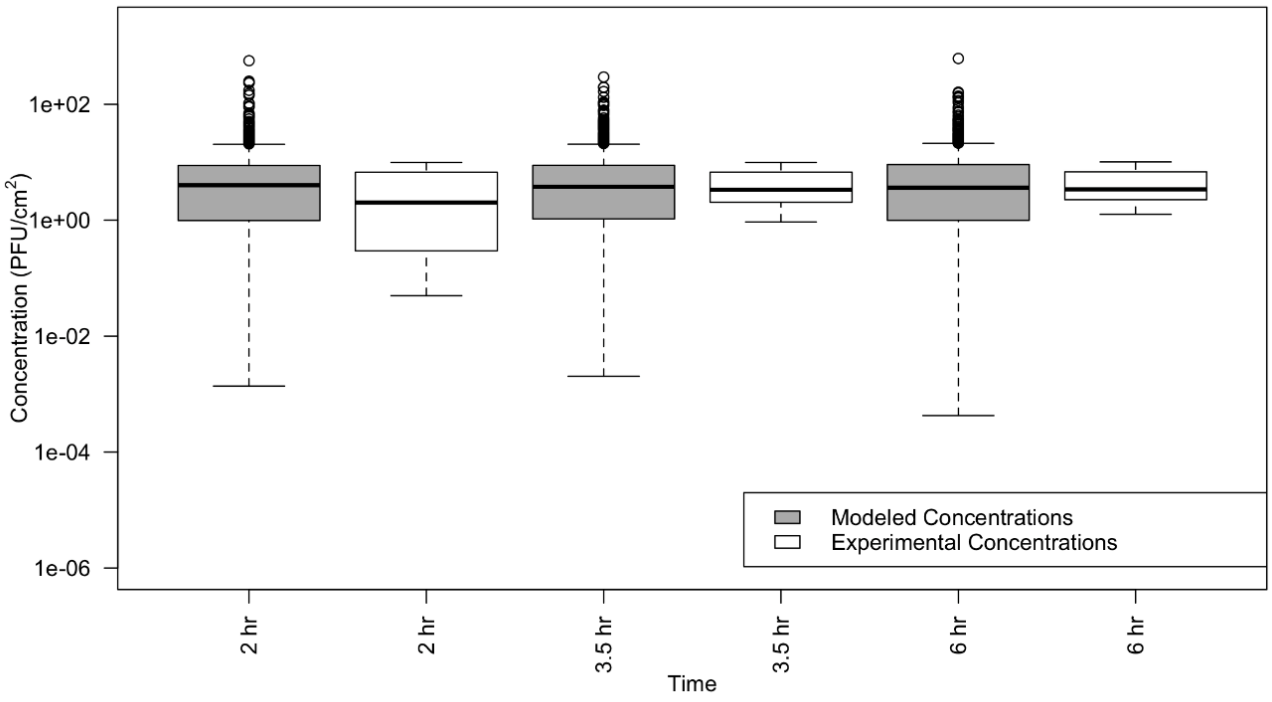

Figure 2. Virus Concentration on Hands over Time for One Simulated Nurse

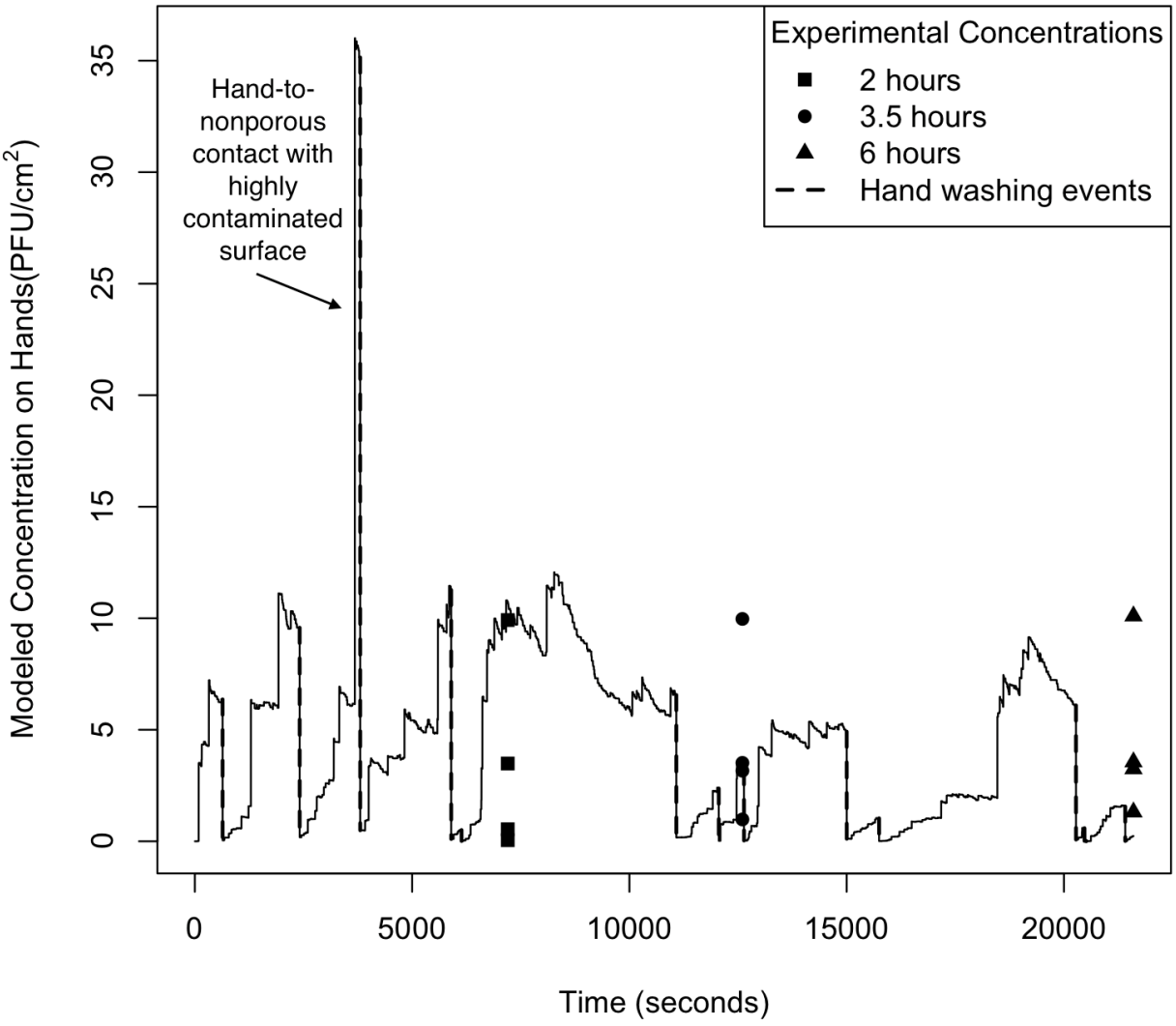

Figure 3. Model-Predicted Distribution of Virus Concentrations on Nurse Hands at 6 Hours

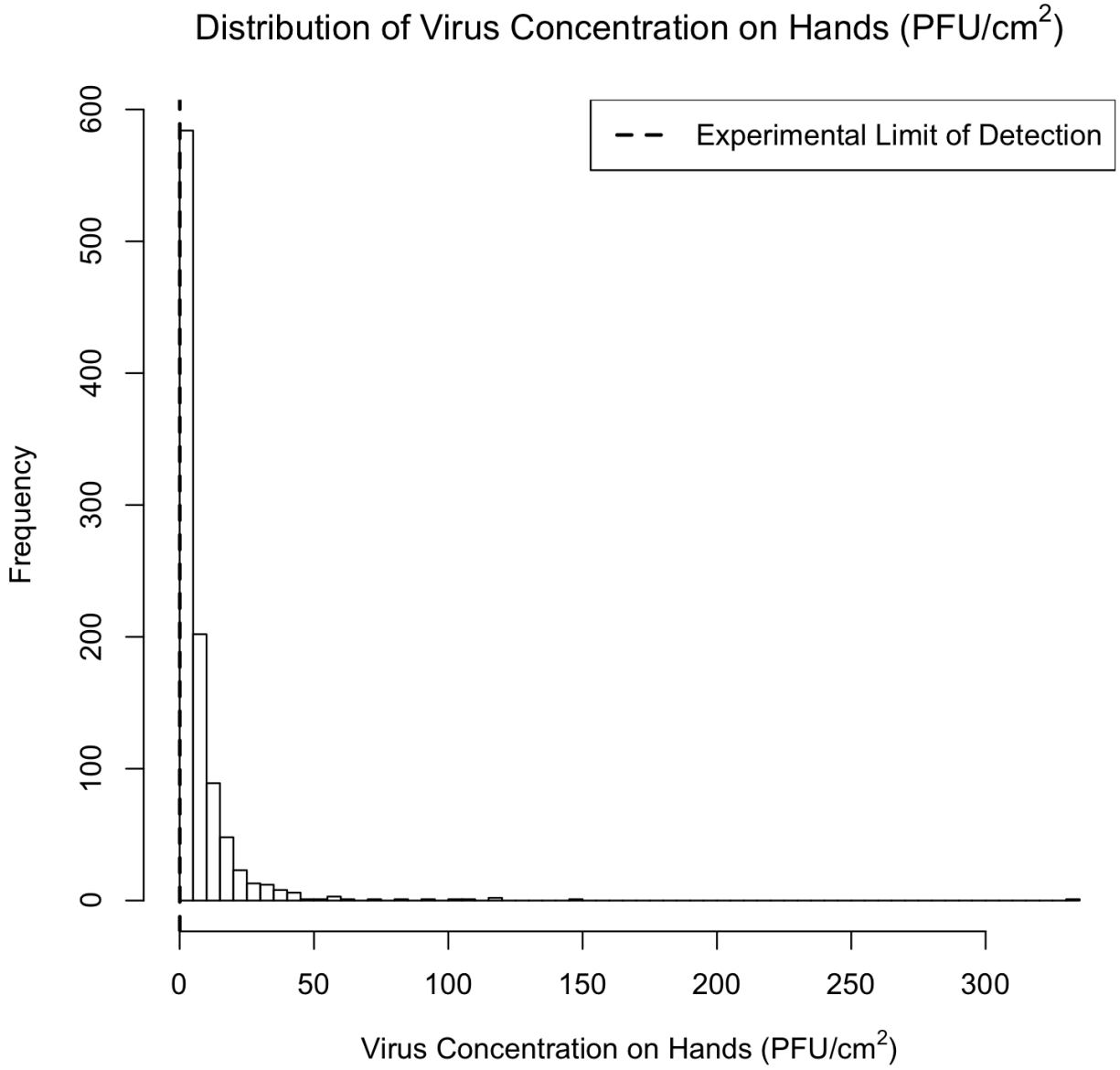

Table 2. Summary Statistics for Model-Predicted and Experimental Virus Concentrations on Hands and P-Values Testing Statistically Significant Differences between Model-Predicted and Experimental Values for 36% Hand Washing Compliance

	Virus Concentration on Hands (PFU/cm^2)					
	2 Hours		3.5 Hours		6 Hours	
	Model (n=1000)	Experimental (n=4)	Model (n=1000)	Experimental (n=4)	Model (n=1000)	Experimental (n=4)
Range (min, max)	(0.0001, 594.67)	(0.05, 9.92)	(0.00, 512.4)	(0.98, 9.97)	(0.0003, 334.3)	(1.31, 10.1)
Median	3.76	2.01	3.69	3.34	3.47	3.40
P-Value, Wilcoxon Rank-Sum	0.37		0.98		0.92	

Table 3. Spearman Correlation Coefficients for Sensitivity Analysis of Stochastic Parameters Where a Lower Rank Indicates a Stronger Relationship with Dose

Variable Description	Symbol	Spearman Correlation Coefficient	Rank
Number of hand washes	HW_C	-0.31	1
Number of hand-to-mouth contacts	M_C	0.29	2
Hand-to-mouth transfer efficiency	TE_{HM}	0.14	3
Surface concentration	C_f	0.10	4
Hand-to-nonporous surface transfer efficiency	TE_{FHNP}	-0.071	5
Number of hand-to-porous surface contacts	TE_{FHP}	0.066	6
Number of hand-to-nonporous surface contacts	NP_C	0.059	7
Number of hand-to-eye contacts	E_C	0.035	8
Number of hand-to-nose contacts	N_C	0.034	9
Hand washing efficacy	R	0.026	10
Fraction of hand used in hand-to-mouth contacts	S_M	0.013	11
Hand-to-porous surface transfer efficiency	TE_{FHP}	-0.012	12
Total hand surface area	A_{hand}	0.0059	13
Fraction of hand used in hand-to-surface contacts	S_H	-0.0040	14
Fraction of hand used in hand-to-eye contacts	TE_{HE}	0.0011	15

7. APPENDIX A: EQUATIONS

7.1. Probability Vector for Event Selection

$$P(NP_C, P_C, M_C, E_C, N_C, HW_C, NC) = \left(\frac{4.1}{60}, \frac{5.5}{60}, \frac{0.18}{60}, \frac{0.06}{60}, \frac{0.01}{60}, \frac{0.075}{60}, \frac{50.1}{60}\right)$$

$$P(NP_C, P_C, M_C, E_C, N_C, HW_O, NC) = (0.0683, 0.0917, 0.003, 0.001, 0.0002, 0.0012, 0.8346)$$

where NP_C = hand-to-nonporous surface contact

P_C = hand-to-porous surface contact

M_C = hand-to-mouth contact

E_C = hand-to-eye contact

N_C = hand-to-nose contact

HW_O = compliant hand washing opportunity

NC = no contact

All following equations provide equations for incremental changes on hands due to a particular contact.

7.2. Hand-to-Nonporous Surface Contact

$$C_{hand,t} = C_{hand,t-1} - \left(TE_{FHNP}\ S_H\ \left(C_{hand,t-1} - C_f\right)\right)$$

7.3. Hand-to-Porous Surface Contact

$$C_{hand,t} = C_{hand,t-1} - \left(TE_{FHP}\ S_H\ \left(C_{hand,t-1} - C_f\right)\right)$$

7.4. Hand-to-Mouth Contact

$$C_{hand,t} = C_{hand,t-1}\ \left(1 - TE_{HM}\ S_M\right)$$

7.5. Hand-to-Eyes Contact

$$C_{hand,t} = C_{hand,t-1}\ \left(1 - TE_{HE}\ S_E\right)$$

7.6. Hand-to-Nose Contact

$$C_{hand,t} = C_{hand,t-1}\ \left(1 - TE_{HN}\ S_N\right)$$

7.7. Reduction on Hands Due to Compliant Hand Washing Opportunity

$$C_{hand,t} = C_{hand,t-1}/R$$

7.8. Moment of No Contact

$$C_{hand,t} = C_{hand,t-1}$$