Modeling the role of fomites in a norovirus outbreak

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ABSTRACT

Norovirus accounts for a large portion of the gastroenteritis disease burden, and outbreaks have occurred in a wide variety of environments. Understanding the role of fomites in norovirus transmission will inform behavioral interventions, such as hand washing and surface disinfection. The purpose of this study was to estimate the contribution of fomite-mediated exposures to infection and illness risks in outbreaks. A simulation model in discrete time that accounted for hand-to-porous surfaces, hand-to-nonporous surfaces, hand-to-mouth, -eyes, -nose, and hand washing events was used to predict 17 hrs of simulated human behavior. Norovirus concentrations originated from monitoring contamination levels on surfaces during an outbreak on houseboats. To predict infection risk, two dose-response models (fractional Poisson and ${}_2F_1$ hypergeometric) were used to capture a range of infection risks. A triangular distribution describing the conditional probability of illness given an infection was multiplied by modeled infection risks to estimate illness risks. Infection risks ranged from 70.22% to 72.20% and illness risks ranged from 21.29% to 70.36%. A sensitivity analysis revealed that the number of hand-to-mouth contacts and the number of hand washing events had strong relationships with model-predicted doses. Predicted infection risks ranged from 21.29% to 70.36%, overlapping with leisure setting and environmental attack rates reported in the literature. In the outbreak associated with the viral concentrations used in this study, attack rates ranged from 50% to 86%. This model suggests that fomites may have accounted for 25% to 82% of illnesses in this outbreak. Fomite-mediated exposures may contribute to a large portion of total attack rates in outbreaks

involving multiple transmission modes. The findings of this study reinforce the importance of frequent fomite cleaning and hand washing, especially when ill persons are present.

INTRODUCTION

Transmitted via the fecal-oral and vomitus-oral routes, norovirus is a well-described cause of epidemic gastroenteritis in both adult and pediatric populations across a wide range of geographic regions.[1] It is estimated that norovirus accounts for 19-21 million cases in the United States each year.[2] Noroviruses are members of the *Norovirus* genus in the *Caliciviridae* family. They are non-enveloped, positive sense, icosahedral, single-stranded RNA viruses. Outbreaks of norovirus gastroenteritis occur in multiple settings such as schools, daycare centers, nursing homes, hospitals, and cruise ships.[3,4]

There are multiple sources of norovirus exposures, including environmental (often implying contaminated surfaces), waterborne, person-to-person, and foodborne routes.[5] In a study by Bitler et al.[5] in which 432 published outbreaks were included, no significant relationships between transmission route and attack rates were found. However, it was acknowledged that the setting of the outbreak could be a confounder for this relationship.[5] Understanding how a particular level of environmental contamination contributed to the outbreak could shed light upon the influence of human behaviors within that environment upon observed health outcomes.

It is possible that multiple transmission routes may be involved in a single outbreak. This makes it challenging to understand how each transmission route may contribute to individual exposures. Regardless of the main transmission route within an outbreak, contamination of an infected individual's environment is of concern, as this can lead to indirect exposures and subsequent infections. The role of environmental surfaces, referred to as "fomites," in the transmission of enteric viruses in indoor environments has been widely discussed.[6-9]

Understanding the contribution of contaminated fomites to attack rates in norovirus outbreaks can inform cleaning protocols aimed at preventing or diminishing the impact of norovirus infections.

Extending beyond hypothesis testing or statistical models, quantitative microbial risk assessment (QMRA) can be utilized to predict the contribution of a particular transmission route to an individual's exposure by using mechanistic, mathematical modeling. QMRA is a methodological framework that incorporates exposure modeling to estimate the probability that an infection will occur given exposure of an individual. This methodology can be utilized to investigate the relationships between human behaviors, environmental contamination, exposures, and predicted health outcomes.

Mathematical modeling has been used to explore how inhalation exposures and contacts with surfaces result in microbial exposures in a variety of contexts.[9-12] Some model frameworks use compartment modeling and Markov chains to account for transitions of microbes between hands, surfaces, air, and inactivation states[10,11], while others use independent behavior events in discrete time that account for the independent probability of a particular event occurring per time period.[12] Although the Markov chain approach allows for more control over the rates of particular events occurring in the simulation, some models that utilize Markov chains inform transition rate calculations with assumptions as opposed to empirical data.[11] One reason for this is that some scenario-relevant human activity data are not always available as a sequence that can be easily implemented with a Markov chain approach.[13]

In addition to predicting overall exposure and health risk, models have been used to estimate individual contributions of various exposure routes to health risk within a norovirus context, specifically.[9] Originally, it was hypothesized that the airborne transmission route was

the main contributor to observed attack rates in this outbreak. However, Xiao et al.[9] predicted with multi-agent modeling that a fomite transmission route could have accounted for the observed attack rates. Although this study offered a novel approach for investigating the contribution of transmission routes to observed attack rates, models predicting surface contamination were used as opposed to sampled surface concentrations. The purpose of this study was to use experimentally measured surface concentrations to inform a discrete-event viral exposure model to investigate the role of fomites in an outbreak of gastrointestinal illness among participants in a houseboat trip. Our specific aim was to quantify the contribution of fomite-mediated exposures to overall attack rates observed in this outbreak.

METHODS

Norovirus Concentrations on Surfaces Informed by Outbreak Data

Details of the houseboat outbreak were described by Jones et al.[6] Briefly, a norovirus outbreak among senior citizens at a recreational lake in northern Arizona occurred over the course of multiple houseboat trips. Of the 20 participants who were interviewed, illness attack rates ranged from 50% to 86% for these trips.[6] Norovirus concentrations on surfaces were quantified with an MPN (most probable number) method using dilution series and the U.S. EPA Most Probable Number Calculator (2.0, U.S. Environmental Protection Agency, Washington D.C.). The MPN general-purpose program was adapted from the method of Hurley and Roscoe.[14] Tenfold dilutions of nucleic acid extracts (10^1 to 10^5) were amplified in triplicate for each dilution. Sampled surfaces included a kitchen sink, kitchen tap handles, door handles, toilet lids, refrigerator door handles, and a restroom lavatory door. Non-detects were treated as true zero value concentrations. Although this assumption does not account for swab recovery efficiency, it was unknown whether all surfaces would be contaminated. The inclusion of zero

values allowed for the acknowledgement that not all portions of surfaces contacted would be contaminated. The norovirus involved in this outbreak was identified as genogroup II. In modeling exposure, surface concentrations were randomly sampled from the measured surface values. These concentrations can be viewed in Table 1. This model assumed that the distribution of norovirus concentrations on surfaces was not changed by hand-to-surface contacts, as new portions of the same surfaces may be contacted per hand-to-surface contact, contact surface areas may be small in comparison to total surface areas of objects, and high volumes of shedding of those infected may re-contaminate surfaces that have previously lost norovirus due to hand-to-surface contacts.

Exposure Scenario

The houseboat outbreak occurred among senior citizens [6] and thus behaviors were simulated for assumed waking hrs of individuals 60 years or older. Because the median sleep time for those 60 years or older has been shown to be 7 hrs [15], it was assumed that exposure to contaminated surfaces for full waking hrs would occur over 17 hrs. Dietary exposures and inhalation exposures to norovirus were not considered in this scenario, because the objective was to quantify the specific role of fomite-mediated exposures during a norovirus outbreak. As recommended by Van Abel et al.[16] and implemented in other norovirus QMRA studies [17], it was assumed that all viral particles on these surfaces were viable.

Exposure Model

A stochastic simulation model in discrete time was used for exposure simulations, where activities and changes in virus concentration on hands and dose were tracked per sec. Hand-to-porous surface; hand-to-nonporous surface; hand-to-eyes, -nose, -mouth; hand washing events; and no contact moments were accounted for in the model. The probabilities of hand-to-surface or

hand-to-orifice contacts occurring per sec were weighted by contact frequencies informed by behavior study data.[18-20] These data have been used to model the behavior of adults in other quantitative microbial risk assessments.[19] The probability of hand washing was weighted by the expected rate of hand washing events per min, where the rate of hand washes per day was informed by The Soap and Detergent Association 2009 National Clean Hands Report Card Survey in which 50% of participants reported washing their hands more than 10 times per day.[20] A point estimate of 10 hand washes per 17 waking hrs was used in this model. The probability of a moment of no contact occurring in the simulation was set equal to the complement of the sum of probabilities for other events. Parameters used to weight the event probabilities can be seen in Table 2. The probability of either using the right or left hand was 0.5, as non-significant differences between right and left hand activity patterns have been observed.[13]

The duration of hand-to-porous and hand-to-nonporous contacts was set for 3 secs long, because this was a median duration time that has been observed for hand-to-surface contacts and has been implemented in other microbial exposure models.[13, 19] The duration of hand-to-orifice contacts was assumed to be 1 sec, a median time reported for hand-to-mouth contacts.[13] Durations where hands did not touch any surface were also given a duration of 1 sec. Hand washing events were given durations ranging from 1 to 25 secs long, where the probability of a particular hand wash duration being selected was informed by proportions of participants in the 2009 National Clean Hands Report Card Survey.[20]

The total surface area of a single hand was equal to half of a randomly sampled surface area from a uniform distribution (min=890 cm^2, max=1070 cm^2) that represented the surface area of both hands combined.[19, 21] The fraction of the hand touching the orifice during hand-to-orifice contacts was calculated by dividing a surface area of contact by the total surface area of a

single hand.[19, 22] For hand to surface contacts, a distribution for the fraction of total hand surface area used during hand-to-surface contacts was used.[12] Transfer efficiencies for hand-to-surface and hand-to-orifice contacts were informed by distributions of viral transfer efficiencies utilized in other microbial risk assessments based on laboratory data.[12, 19, 23-24]

Equations used to track changes in norovirus concentration on hands and dose were based on equations used by Julian et al.[12] Because it has been noted that enteric viruses survive on fomites for days [25], greater than the simulated exposure time, portions of equations used by Julian et al.[12] to account for viral inactivation were excluded from this study. This model assumed that inactivation of virus on hands and surface over the exposure time would be negligible. Therefore, this model may overestimate viral concentrations on hands and surfaces. During a hand-to-surface contact, the following equation was used, in which transfer efficiency was specific to porous or nonporous surfaces:

$$C_{hand,t} = C_{hand,t-1} - \left(TE \cdot S_H \cdot \left(C_{hand,t-1} - C_{fomite}\right)\right) \quad (1)$$

where $C_{hand,t}$ = viral particles/cm^2 at simulation time t

TE = transfer efficiency specific to nonporous or porous fomite (fraction of transfer)

S_H = fraction of hand used in hand-to-surface contact

C_{fomite} = concentration of norovirus (viral particles/cm^2) on fomite surface

This equation accounts for attachment and detachment of virus, where the direction of transfer is from the more contaminated surface to the less contaminated surface. After a contact event, this model assumes that virus is distributed evenly across the hand that contacted the surface. During hand-to-orifice contacts, the following equations were used, in which transfer efficiency and area of hand in contact with the orifice are orifice-specific:

$$C_{hand,t} = C_{hand,t-1} \cdot \left(1 - TE \cdot \frac{A_{orifice\ contact}}{A_{hand}}\right) \quad (2)$$

where TE = transfer efficiency specific to orifice (fraction of transfer)

$A_{orifice\ contact}$ = surface area of orifice contact (cm^2)

A_{hand} = surface area of a single hand (cm^2)

Here, the concentration on the hand is calculated per sec of simulated time.

A momentary dose during hand-to-mouth contacts was calculated as a function of transfer efficiency for hand-to-mouth contacts, the fraction of the hand in contact, the surface area of the hand, and the norovirus concentration on the hand at the moment of hand-to-orifice contact.

$$Dose = TE \cdot \frac{A_{orifice\ contact}}{A_{hand}} \cdot A_{hand} \cdot C_{hand,t} \quad (3)$$

During hand-to-nose and –eyes contacts, a dose was not calculated. However, the viral loss expected from the hand due to hand-to-eyes or -nose was accounted for.

During hand washing events, viral reductions were estimated by sampling from a uniform distribution with minimum and maximum log reductions that were observed for Norwalk virus on hands following hand washing with water rinse and with antimicrobial liquid soap.[26] Parameters relevant to the exposure model can be seen in Table 2.

Dose-Response Models

As recommended by Van Abel et al.[16], multiple dose-response models were chosen with consideration given to represented genogroups and assumptions regarding viral aggregation on surfaces because there is currently no single recommended norovirus dose-response model. Dose-response models that accounted for norovirus genogroup II in addition to norovirus genogroup I were preferred. It was assumed that viruses present on fomites were aggregated, as it has been shown that a parameter affecting viral aggregation is interaction with a solid surface.[27] The two models that met these assumptions, a fractional Poisson and a ${}_2F_1$

hypergeometric, were used with parameters listed by Van Abel et al.[16] and Messner et al.[28] Parameters specific to these dose-response models can be seen in Table 2. The fractional Poisson model is described by:

$$P_{infection} = P \cdot \left(1 - e^{-\frac{dose}{\mu}}\right) \quad (4)$$

where $P_{infection}$ = probability of infection

P = fraction of people who are immune to norovirus

$dose$ = cumulative dose over the exposure time (number of viral particles)

μ = mean aggregate size

The ${}_2F_1$ hypergeometric model, transformed with the Pfaff transformation [16], is described by:

$$P_{infection} = 1 - \left[\left(2F1\left(\beta, \frac{dose(1-a)}{a}; \alpha + \beta, a\right)\right)\left(\frac{1}{1-a}\right)^{\left(-\frac{dose(1-a)}{a}\right)}\right] \quad (5)$$

where β = shape parameter

α = shape parameter

a = aggregation factor greater than or equal to 0 and less than 1, signifying the level of aggregation, where 0 would signify no aggregation

The R package "gsl," developed by Hankin, was used to implement this dose-response model (1.9-10.3, Hankin, R.K.S.).

To predict illness risk from the probability of infection, a method implemented by Van Abel et al.[17] was used in which a sampled value from a triangular distribution, informed by norovirus infection and illness rates in human feeding participants [17, 29] describing the probability of becoming ill given being infected ($P_{illness|infection}$), was multiplied by the probability of infection. This process is described by:

$$P_{illness} = P_{illness|infection} \cdot P_{infection} \quad (6)$$

Sensitivity Analysis

Because correlation coefficients have been acknowledged as one method for exploring relationships between model parameters, Spearman correlation coefficients were calculated for 17 input model variables and dose.[30] The input variables included: the number of contacts with contaminated surfaces (surfaces with a norovirus concentration > 0 genome copies/cm^2), the mean of randomly sampled transfer efficiencies (hand-to-nonporous surfaces, hand-to-porous surfaces, hand-to-mouth) per simulated person; the mean of randomly sampled hand surface areas per simulated person; the mean of randomly sampled fractions of the hand in contact with mouth, surfaces, nose, and eyes per simulated person; the mean duration of hand washing events; the number of hand washing events; the efficacy of the hand washing event, and the numbers of hand-to-mouth, -eyes, -nose, -nonporous-surface, and -porous-surface contacts. Variables were then ranked from 1 to 17 with 1 corresponding to the greatest absolute correlation coefficient (indicating greater influence on estimated dose) and 17 corresponding to the smallest absolute correlation coefficient.

RESULTS

Predicted Infection and Illness Risks

The full range of model-predicted infection risks was 70.22% to 72.20%. Because the range of predicted cumulative doses was on the portion of the curve that approached a horizontal asymptote (Figure 1), all summary statistics for infection risk estimated by the dose-response curves were similar if not equal in value (Table 3). All cumulative doses were larger than the greatest concentration of norovirus measured on sampled surfaces (53,725 MPN/100cm^2) due to multiple contacts overtime resulting in accumulation of virus on the hand. The full range of model-predicted illness risks was 21.29% to 70.36%. The ${}_2F_1$ hypergeometric dose-response

model estimated a mean illness risk of 40.98%, while the fractional Poisson dose-response model estimated a mean illness risk of 42.25%. (Table 3)

Insights from Simulated Behaviors

The mean concentration of viruses on combined hands at any given sec in the simulation was 153.7 particles/cm^2 (sd=51.6 particles/cm^2). Half of simulated people reached a viral concentration on combined hands greater than or equal to this mean value within approximately 44 mins (2669 secs), demonstrating that viral loading can occur quickly over a short exposure time.

Although steady state models that assume a constant viral concentration on hands have been used in other studies to evaluate viral exposures, this discrete event model demonstrates that moments of high exposures may result in large doses that would not be captured by assuming a constant viral concentration on hands.[18-19] In Figure 2, a large dose from a hand-to-mouth contact occurs that is soon followed by a hand washing event.

Sensitivity Analysis Results

The input variable with the greatest effect on dose was the number of hand-to-mouth contacts, followed by the number of hand washes, the transfer efficiency of hand-to-mouth contacts, the fraction of total hand surface area used in hand-to-nose contacts, and the fraction of total hand surface area used in hand-to-surface contacts (Table 4). As the number of hand-to-mouth contacts increased, the estimated total dose increased linearly. As the number of hand washes increased, the estimated total dose decreased linearly (Figure 3). Of the five variables with the largest absolute Spearman correlation coefficient, variables other than number of hand-to-mouth contacts and number of hand washes did not have strong linear relationships with estimated total dose.

DISCUSSION

Generalizability of Attack Rate Predictions

The mean illness risks predicted in this study were 40.89% and 42.25% using the ${}_2F_1$ hypergeometric and the fractional Poisson dose-response models, respectively. These risks are slightly higher than median attack rates reported for environmental (surface contamination) and leisure setting (such as cruise ships) norovirus outbreaks but are within reported ranges. In a review of norovirus outbreaks, Matthews et al.[31] found that occurrences with environmental transmission routes had primary median attack rates of 26% (IQR: 9% to 41%). Leisure setting outbreaks had primary median attack rates of 29% (IQR: 11 to 48%). Wikswo et al. (2015) reported a median guest/resident attack rate of 28% for person-to-person/environmental outbreaks and an attack rate of 32% for norovirus, specifically.[32] Although the full range of illness risks predicted in this study (21.29% to 70.36%) includes higher rates than these interquartile ranges, the mean illness risks are within these reported interquartile ranges. This model assumes a full waking hr day of possible exposure to contaminated surfaces, which may account for attack rates that are greater than the third quartiles in these ranges reported by Matthews et al.[31]

The measured attack rates for the outbreak associated with the surface concentrations used in this study ranged from 50% to 85%. Dietary and inhalation norovirus exposures were not included in this model in order to quantify the proportion of attack rates attributable to fomite-mediated exposures alone. This study demonstrates that fomite-mediated exposures may have accounted for anywhere between 25% (minimum estimated illness probability: 21.29 / maximum recorded attack rate for this outbreak: 86) to 82% (maximum estimated illness probability: 70.36 / maximum recorded attack rate for this outbreak: 86) of observed attack rates in this houseboat

outbreak. Understanding the role of fomites in other norovirus outbreaks should be further evaluated so that the efficacy of surface cleaning interventions can be estimated.

Limitations

Although the predicted attack rates are reasonable in comparison to epidemiological norovirus attack rates and those observed for the houseboat outbreak, uncertainty in some parameters could have influenced the model results. For example, one sec contacts were assumed for hand-to-eye and hand-to-nose contacts, based on the contact duration of hand-to-mouth contacts. The transfer efficiency was assumed to not be a function of duration. Mathematically describing how contact duration affects viral transfer efficiencies could allow for more accurate representations of viral attachment and detachment to and from the hand over time. This issue has been addressed within the context of pesticide exposures. Rohrer et al.[33] found that increased contact duration between floor surfaces contaminated with pesticides and foods resulted in greater transfer, with one min durations having mean transfer efficiencies ranging from 0% to 1% and 60 min durations having mean transfer efficiencies ranging from 55% to 82%. To the authors' knowledge, the only data describing viral transfer efficiency as a function of duration is within the context of skin and liquid contacts.[34] Although information regarding the relationship between contact duration and transfer efficiency may change implementation in future exposure models, transfer efficiencies for hand-to-surface contacts did not have strong linear relationships with dose in this model (Table 4).

Another limitation in this study was the lack of available behavioral data for the specific/relevant population. Using behavior data for a different population of interest could have under- or over-estimated viral exposures. However, the behavioral data used to inform this model has been used in other models to represent adult human behaviors.[19] In the case of this

study, a behavior-related parameter (number of hand-to-mouth contacts) was the most influential stochastic variable on infection risk (Table 4). This reiterates the importance of understanding how sequences of behaviors influence risk. Although the frequency of events may influence the number of opportunities for exposures, the sequence of events is important in assessing the efficacy of interventions, such as hand washing, to disrupt behavioral sequences resulting in exposures.

The equation utilized in this model to estimate the attachment or detachment of virus from the hand assumed the direction of transfer was from the more contaminated surface to the less contaminated surface.[12] However, this has not necessarily been observed with microbial data. Microbial transfer studies have traditionally involved measuring the transfer between one contaminated surface and another uncontaminated surface.[23-24, 34-35] The direction of transfer has been shown to affect transfer efficiency within a hand-to-food context and in some hand-to-surface contexts.[36-37] The effect of using the same transfer efficiency distributions used for hand-to-surface versus surface-to-hand transfers in this study is unknown. The influence of relative contamination levels of two surfaces in contact on microbial transfer efficacy is also unknown. More environmental and laboratory studies are needed to evaluate assumptions regarding transfer between two contaminated surfaces and how the direction of transfer effects transfer efficiencies for a variety of surface types and organisms.

In addition to limitations regarding specific parameters, this model did not account for dietary or inhalation exposures. Because only fomite-mediated exposures were accounted for, it is possible that the role of fomites may have been overestimated, as simulated persons were not given opportunities to become infection by other means. Future studies should include all types

of exposures that may occur during outbreaks and address how these exposure routes contribute to estimated infections and illnesses.

CONCLUSIONS

The attack rates predicted by the exposure model in this study are comparable to the upper end of attack rate ranges for those measured in environmental and leisure norovirus outbreaks. This study demonstrated that fomite-mediated exposures may account for a large portion of attack rates in outbreaks that involve multiple transmission modes. The sensitivity analysis revealed that the number of hand-to-mouth contacts and the number of hand washing events had linear relationships with the predicted total dose. More data characterizing the distribution of hand-to-mouth contact frequency for adults will further inform current exposure models to predict norovirus doses for adults with more confidence. Exposure models such as the one in this study can be used to mathematically describe and explore the relationship between hand washing events and estimated health outcomes. Further development of exposure models will allow for intervention optimization to mitigate pathogen exposures.

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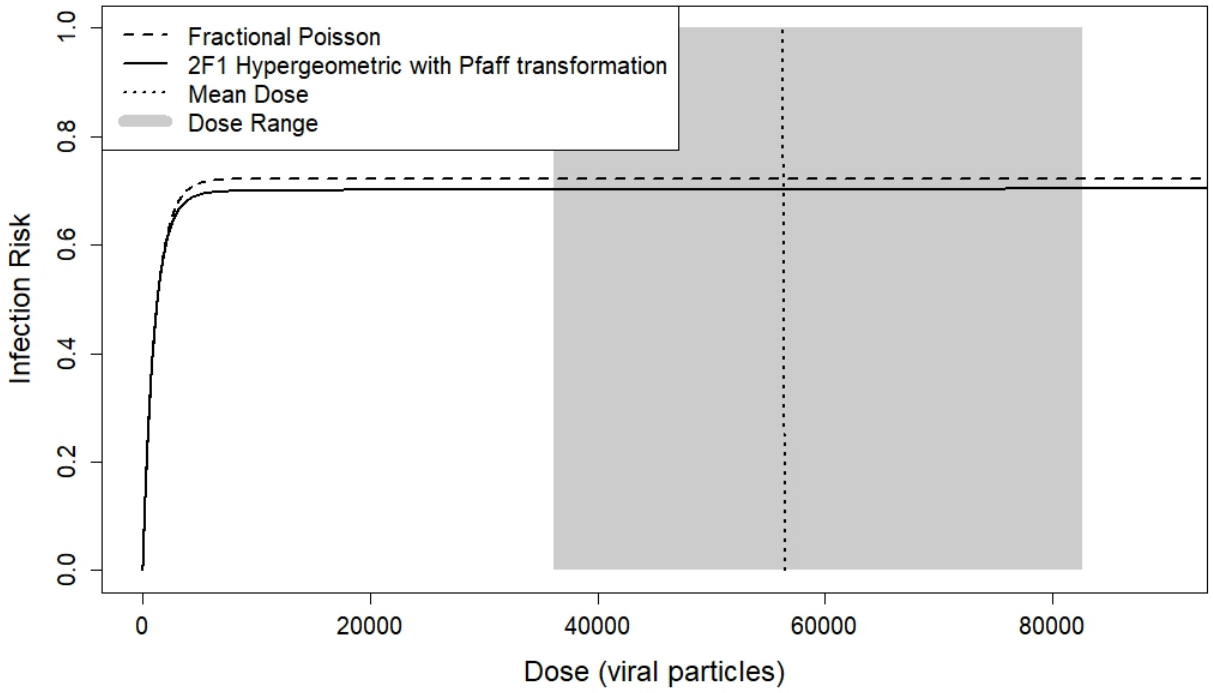
Figure 1. Comparing infection risk predictions based on estimated cumulative doses for 1,000 persons over the simulated exposure period with utilized dose-response models shown ($_2F_1$ hypergeometric and fractional Poisson)*



*cumulative dose range shaded in gray with a vertical line corresponding to the mean estimated dose

Figure 2. An example of estimated viral concentration on hands and momentary doses for one simulated person over a fraction of simulated time: A demonstration of the importance of event sequences and how they relate to momentary exposures

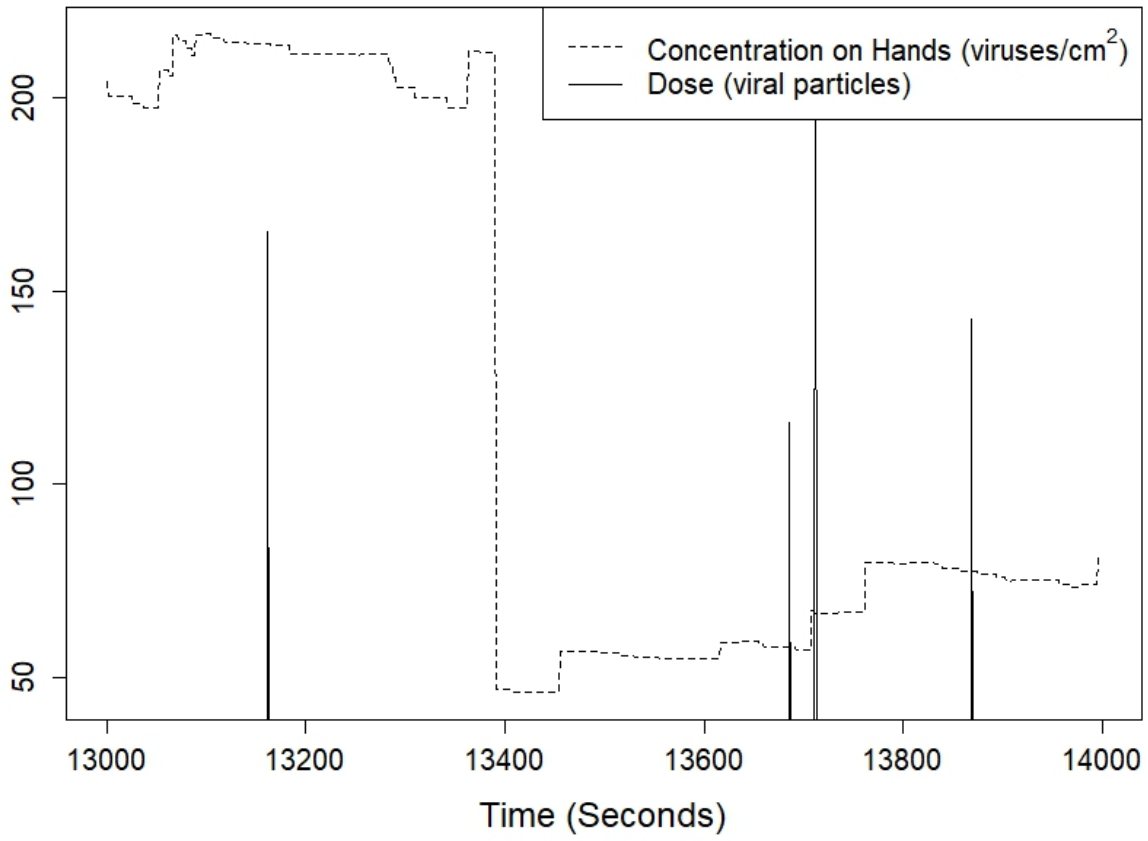


Figure 3. Scatterplots of the five most influential parameters plotted against total estimated doses for 1,000 simulated individuals (A.) Hand-to-mouth contacts, B.) Number of hand washes, C.) Hand-to-mouth transfer efficiency, D.) FSA of hand-to-nose contacts, and E.) Fractional surface area (FSA) of hand-to-surface contacts)

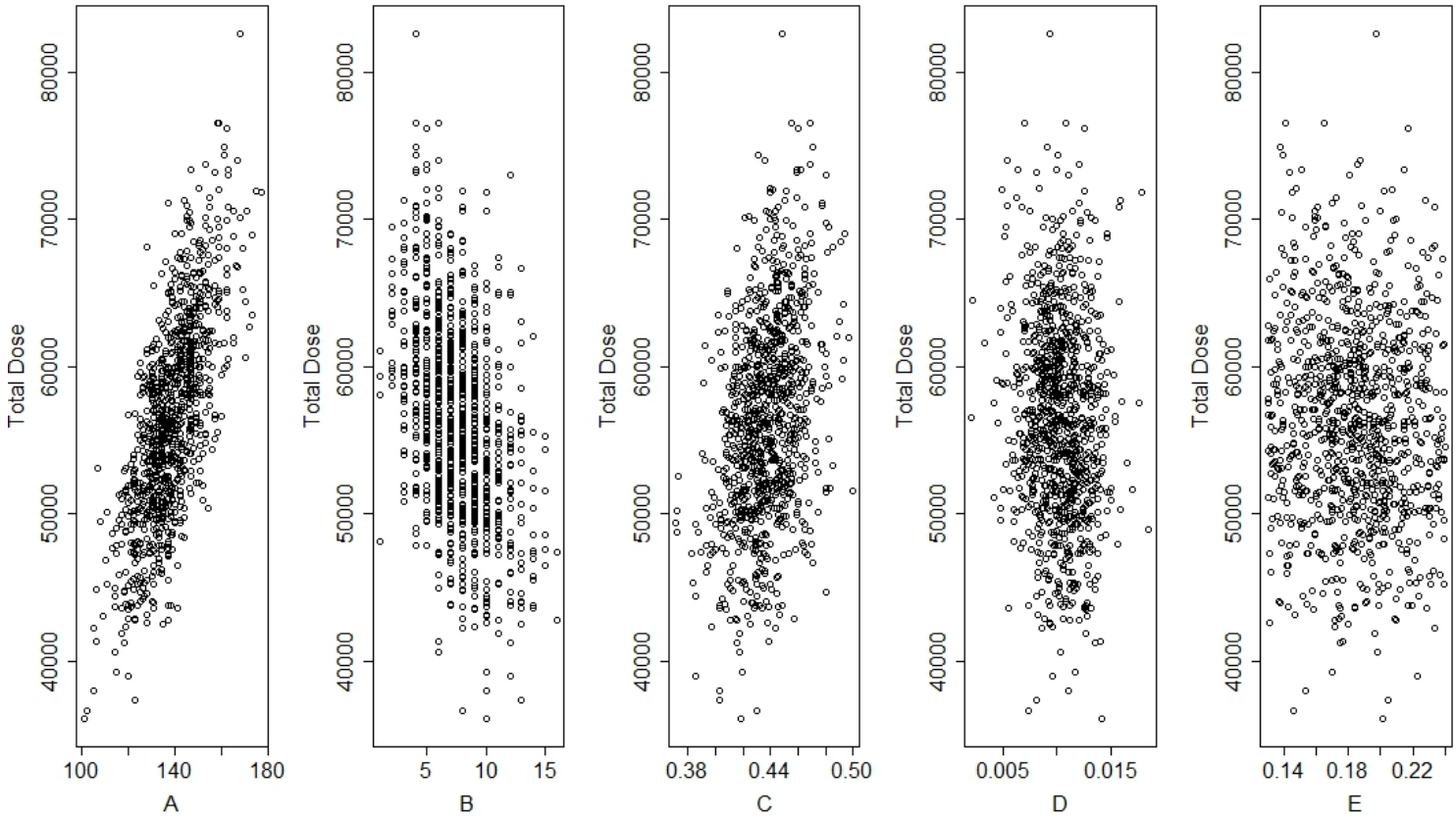


Table 1. Norovirus concentrations (most probable number/100cm^2) on sampled fomite surfaces in three different houseboats during a houseboat outbreak

Houseboat Number	Sampled Surface	Number of Genomes (MPN)*/100 cm^2
2	Kitchen Sink	53,725
	Door handles	24,314
	Toilet lid	0
10	Door handles	24,314
	Toilet lid	1,029
	Kitchen sink & tap handle	0
	Refrigerator door	0
13	Bathroom toilet lid	0
	Refrigerator door handle	5,392
	Kitchen sink & tap handle	0
	Door handles	2,451
	Restroom lavatory door	2,451

* MPN (most probable number) for samples that were norovirus positive.

Table 2. Exposure and dose-response model parameters with units, distribution parameters, and specified sources

Variable	Units	Distribution*	Source
Event Frequency			
Nonporous contact	contacts/min probability per sec	4.1 4.1/60	(13)
Porous contact	contacts/min probability per sec	5.5 5.5/60	(13)
Hand washing	hand washes/min probability per sec	0.0098 0.0098/60	(20)
Hand-to-mouth contact	contacts/min probability per sec	0.18 0.18/60	(13)
Hand-to-eyes contact	contacts/min probability per sec	0.06 0.06/60	(18, 19)
Hand-to-nose contact	contacts/min probability per sec	0.01 0.01/60	(18, 19)
No hand contact	probability per sec	0.836	Assumed
Event Duration			
Nonporous contact	s	3	(13)
Porous contact	s	3	(13)
Hand washing	s	Uniform (21, 25): 26.3% Uniform (20, 15): 27.3% Uniform (15,10): 31.3% Uniform (10, 1): 15.2%	(20)
Hand-to-mouth contact	s	1	(13)
Hand-to-eyes contact	s	1	Assumed
Hand-to-nose contact	s	1	Assumed

No hand contact	s	1	Assumed
Viral Concentration on Surfaces			
Viral concentration on surfaces	viral particles/cm^2	Discrete distribution (0, 0, 0, 0, 0, 10.29, 24.51, 24.51, 53.92, 243.14, 243.14, 537.25)	This study
Surface Area Parameters			
Area of Hand	cm^2	Uniform (445, 535)	(19, 21)
Fraction of hand used in hand to surface contact	fraction	Uniform (0.13, 0.24)	(12)
Hand-to-mouth contact	cm^2	Uniform (10.9,13.4)	(22)
Hand-to-eyes contact	cm^2	Uniform (0.10, 2)	(19)
Hand-to-nose contact	cm^2	Uniform (0.06, 0.33)	(19)
Transfer Efficiency			
Hand-to-porous	fraction of transfer	Uniform (0.003, 0.0042)	(19, 24)
Hand-to-nonporous	fraction of transfer	Uniform (0.05, 0.22)	(19, 24)
Hand-to-mouth	fraction of transfer	Normal (0.41, 0.25)**	(12,23)
Hand-to-eyes	fraction of transfer	Point estimate 0.339	(19, 23)
Hand-to-nose	fraction of transfer	Point estimate 0.339	(19, 23)
Hand Washing Efficiency			
Viral Loss during Hand Wash	$\log_{10}$ removal	Uniform (0.58, 1.58)	(26)
Dose-response Models			

Fractional Poisson		P=0.722 μ=1106	(16, 28)
${}_2F_1$ hypergeometric		α=0.0044 β=0.0020 a=0.99989323	(16, 28)
Probability of Illness Given Infection			
$P_{illness\|infection}$		Triangular (0.3, 1, 0.6)	(17, 29)

*Uniform (minimum, maximum); Normal (mean, standard deviation); Lognormal (geometric mean, geometric standard deviation); Triangular (min, max, mode)
**Truncated normal distribution with minimum allowed value of zero

Table 3. Summary statistics for model-estimated infection risks and illness risks stratified by the dose-response models utilized ($_2F_1$ hypergeometric and fractional Poisson)

	Infection Risks		Illness Risks	
Dose-Response Model	Range (Min, Max)	Mean (SD)	Range (Min, Max)	Mean (SD)
$_2F_1$ Hypergeometric	(70.22%, 70.34%)	70.28% (1.7×10^{-2})	(21.29%, 68.39%)	40.98% (9.67%)
Fractional Poisson	(72.20%, 72.20%)	72.20% (1.9×10^{-14})	(21.99%, 70.36%)	42.25% (10.19%)

Table 4. Spearman correlation coefficient rankings for stochastic variables and total dose

Variable	Spearman Correlation Coefficient	Rank
Number of hand-to-mouth contacts	0.69	1
Number of hand washes	-0.43	2
Hand-to-mouth transfer efficiency	0.36	3
Fraction of hand in hand-to-nose contacts	-0.096	4
Fraction of hand in hand-to-surface contacts	-0.07	5
Nonporous fomite transfer efficiency	0.066	6
Hand washing efficacy	-0.065	7
Fraction of hand in hand-to-mouth contacts	0.051	8
Number of contacts with contaminated surfaces	0.051	9
Mean duration of hand washing event	0.039	10
Fraction of hand in hand-to-eye contact	0.035	11
Number of hand-to-nose contacts	-0.01	12
Number of hand-to-eye contacts	0.0083	13
Number of hand-to-nonporous surface contacts	0.0065	14
Number of hand-to-porous surface contacts	0.0060	15
Porous fomite transfer efficiency	0.0058	16
Total hand surface area	-0.0032	17

* a smaller rank signifies a greater influence on total dose