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Major Article

Comparison of estimated norovirus infection risk reductions for a single fomite contact scenario with residual and nonresidual hand sanitizers

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Key Words:

Norovirus
Hand sanitizer
Risk reduction
Risk target**Background:** The purpose of this study was to relate experimentally measured log₁₀ human norovirus reductions for a nonresidual (60% ethanol) and a residual (quaternary ammonium-based) hand sanitizer to infection risk reductions.**Methods:** Human norovirus log₁₀ reductions on hands for both sanitizers were experimentally measured using the ASTM International Standard E1838-10 method, with modification. Scenarios included product application to: (1) inoculated fingerpads with 30- and 60-second contact times, and (2) hands followed by inoculation with human norovirus immediately and 4 hours later. Hand sanitizer efficacies were used in a mathematical model estimating norovirus infection risk from a single hand-to-fomite contact under low and high environmental contamination conditions.**Results:** The largest log₁₀ reductions for the residual and nonresidual hand sanitizers were for a 60-second contact time, reducing infection risk by approximately 99% and 85%, respectively. Four hours after application, the residual hand sanitizer reduced infection risks by 78.5% under high contamination conditions, whereas the nonresidual hand sanitizer offered no reduction.**Discussion:** Log₁₀ virus and infection risk reductions were consistently greater for the residual hand sanitizer under all scenarios. Further data describing residual hand sanitizer efficacy with additional contamination or tactile events are needed.**Conclusions:** Residual antinoroviral hand sanitizers may reduce infection risks for up to 4 hours.

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It is widely acknowledged that fomites are an important reservoir of viral pathogens^{1,2} and that some, especially enteric viruses, can survive on surfaces for weeks or months.¹ A single fomite contact contaminated at very low concentrations of virus (ie, a single infectious unit per 100 cm²) has been predicted to have a human norovirus infection risk of 2.7×10^{-3} ,³ and fomites have been implicated as either the source of, or having a large role in, norovirus outbreaks.^{4–6} In addition to surface cleaning and disinfection, increasing hand hygiene compliance and efficacy are important measures for preventing norovirus outbreaks.^{7–9}

Although ethanol-based handrubs have been shown to be effective against a number of viruses,¹⁰ the Centers for Disease Control and Prevention states in the “Guideline for the Prevention and Control of Norovirus Gastroenteritis Outbreaks in Healthcare Settings” that information regarding alcohol-based hand sanitizer efficacy for human strains of noroviruses is an “unresolved issue” and that more research is needed.¹¹ In comparison to other hand hygiene options, such as handwashing, handrubs have been shown to generally be more effective against bacteria than nonenveloped viruses.^{12,13} Within the context of viruses, there is some concern over ethanol-based handrubs replacing handwashing, as they may not be effective against all types of viruses.^{10,14} However, compliance with handrubs may be greater than for handwashing.¹⁵

Quaternary ammonium products have been a commonly used disinfectant since 1935.¹⁶ They have variable action against nonenveloped viruses such as norovirus, and efficacy has been almost exclusively determined using cultivable surrogate viruses, which

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may not be an accurate indicator of human norovirus. Efficacy is formulation-specific¹⁷ and some quaternary ammonium products have been shown to have residual effects.¹⁸ The infection risk reductions owed to products with lower initial degrees of virus inactivation but longer effect duration in comparison to products with larger initial reduction but fleeting effects is unknown.

The purpose of this study was to use pilot experimental data to inform a single fomite contact exposure model scenario to evaluate the potential of residual hand sanitizers to reduce infection risks. Specifically, we compared the potential human norovirus infection risk reductions for a 60% ethanol (nonresidual) and a quaternary ammonium-based (residual) hand sanitizer by informing exposure equations with experimentally measured viral log₁₀ reductions under multiple product use scenarios. These scenarios included (1) inoculation of human fingerpads with norovirus and applying the product for a 30- or 60-second contact time (immediate kill); and (2) treating the hands with the product and then exposing them to norovirus immediately thereafter or 4 hours after hand sanitizer application (residual kill). Understanding how residual reductions may affect infection risk over time will inform infection control and public health strategies.

METHODS

Measuring hand sanitizer efficacy

Six volunteers consented to participate in each of the in vivo efficacy trials. The test product was a liquid quaternary ammonium-based hand sanitizer with a claimed residual action, ULTRA GermFree 24 (Zoono, Shrewbury, NJ); this was benchmarked against a 60% ethanol solution. The liquid formulation of the ULTRA GermFree24 product includes 70% ethyl alcohol, benzalkonium chloride, silica complex, 3 (trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride, and water. The North Carolina State University institutional review board approved all experimental protocols,¹⁹ which were conducted consistent with the ASTM International Standard E1838-10²⁰ fingerpad method, with modifications, particularly with respect to assessing residual hand sanitizer efficacy. Consistencies in the methods across studies are described here. Prior to inoculation with human norovirus or application of test sanitizers, the hands of volunteers were decontaminated by soap and water wash followed by 60% ethanol spray. A 10 μ L volume of human norovirus GII.4 Sydney, obtained as a deidentified stool specimen suspended 20% in deionized water, was used as inoculum on each fingerpad. In some instances, the inoculum was eluted from the fingerpads immediately after deposition (wet control); in other cases, the inoculum was eluted after drying but without (dry control) or with (treatment) exposure to the hand sanitizer. Elution of virus from fingerpads was done using a cryovial (Sigma-Aldrich, St Louis, MO) containing 1 mL of Earle's Balanced Salt Solution (Gibco, Gaithersburg, MD) supplemented with 0.1% Tween, by 20 inversions. Eluates were processed for virus detection as described later. After completion of virus exposure and/or sanitizer treatments, fingerpads were decontaminated by soaking in 10% bleach (5,000 ppm hypochlorite) for 3 minutes, followed by soap and water wash for 1 minute and a final 60% ethanol spray.

Phase I, immediate kill efficacy studies

These studies are most consistent with the ASTM E1838-10 method, in which human fingerpads were inoculated with norovirus and product efficacy was evaluated after 30- and 60-second contact times using the traditional fingerpad method. In this case, the thumbs were inoculated with human norovirus and the virus immediately eluted (wet inoculum control). Thereafter, the other 8 fingertips were each inoculated with 10 μ L of the virus suspension that was allowed

to dry (10–20 minutes). After drying, virus on the index fingers was eluted as described earlier (dry inoculum control). The middle 2 fingers were exposed to 1 mL of hand sanitizer contained in a cryovial for contact times of 30 or 60 seconds followed by elution of residual virus (treatments). The pinkies were exposed to water in a cryovial followed by elution (water rinse control).

Phase II, residual kill efficacy studies

In these experiments, human hands were first treated with the product and then fingerpads were inoculated with human norovirus immediately after or 4 hours postproduct exposure. To account for untreated fingerpads, 2 fingers of each hand (the thumb and the index fingers) were covered with finger cots prior to application of the sanitizer. Hand sanitizer (approximately 1 mL) was applied to clean hands and spread evenly until dried (<1 minute), followed by removal of the finger cots. Immediately or 4 hours after drying (in the latter case, the subjects worked in their normal job functions until the 4 hour time point was reached), the thumbpads were inoculated with 10 μ L of human norovirus and the virus immediately eluted (wet inoculum control). Thereafter, the 3 middle fingers of each hand were inoculated with virus suspension that was allowed to dry. Virus from these fingertips was then eluted as described earlier and served as dry inoculum control (index fingers) or treatment samples (other 4 middle fingers). The uninoculated pinkies served as negative controls, receiving sanitizer but no virus inoculum.

Quantification of virus

Virus eluates were pretreated with RNase and the RNA extracted using the automated NucliSENS easyMag system (bioMerieux, Durham, NC). Detection of residual norovirus was done using quantitative reverse transcription polymerase chain reaction targeting the ORF1-ORF2 GII junction, as previously reported.^{21,22} Virus quantification was calculated by comparison to standard curve, and log₁₀ reductions by comparison to dry virus controls.²¹

Models for predicting momentary norovirus exposure, dose, and infection risk

Models were used to estimate the infection risk for a single hand-to-nonporous fomite contact followed directly by a single hand-to-mouth contact. Uniform distributions, informed by the minimum and maximum log₁₀ reductions measured experimentally, were used to represent log₁₀ reductions in the simulation. An infection risk for a baseline scenario in which no hand sanitizer was applied was compared with scenarios in which either a nonresidual (60% ethanol) or a residual (quaternary ammonium-based) hand sanitizer was applied. Infection risks were estimated for immediate kill (treatment time of 30 and 60 seconds) and residual kill (efficacy immediately postapplication and 4 hours thereafter). The concentration on hands was reduced by a randomly selected log₁₀ reduction from uniform distributions informed by experimental data, described earlier. A low virus contamination and a high virus contamination scenario were modeled for each of the hand sanitizer application scenarios to evaluate the effect of environmental contamination magnitude on estimated infection risk. In the low contamination scenario, it was assumed that surface concentrations were equal to 0.01 viral particles/cm², as this has been assumed in other quantitative microbial risk assessment (QMRA) studies to represent the limit of detection for norovirus on a fomite surface.³ In the high contamination scenario, it was assumed that surface concentrations were equal to 537 viral particles/cm², which corresponds to the largest concentration of norovirus (expressed as genome copies/cm²) quantified on surfaces in a houseboat norovirus

outbreak.⁶ Conservatively, it was assumed that genome copies as determined by quantitative reverse transcription polymerase chain reaction had a direct 1:1 correlation with infectious particles, as this has been recommended for norovirus QMRA.²³ The concentration on hands was first calculated:

$$C_{hand} = \frac{TE_{sh}(A_{contact})(C_{surface})}{10^{\log_{10}reduction}} \quad (1)$$

where C_{hand} = concentration on hand (viral particles)

TE_{sh} = transfer efficiency of virus from surface to hand (fraction)

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

$C_{surface}$ = viral concentration on surface (viral particles/ cm^2)

$\log_{10}reduction$ = $\log_{10}$ reduction corresponding to mean log reduction measured experimentally for that particular hand sanitizer application scenario.

To represent transfer efficiency of virus from the surface to the hand, a uniform distribution informed by the minimum and maximum transfer efficiencies quantified for MS2 for nonporous fomites under low relative humidity (15% to 32%) conditions was randomly sampled.²⁴ For the baseline scenario, $\log_{10}$ reduction was set equal to 0. For all scenarios, the dose due to the single hand-to-mouth contact was then calculated:

$$Dose = TE_{hm}(C_{hand}) \quad (2)$$

where $Dose$ = momentary dose from hand-to-mouth contact (viral particles)

TE_{hm} = transfer efficiency of virus from hand-to-mouth (fraction)

C_{hand} = concentration on hand owing to the previous hand-to-surface contact (viral particles)

This equation assumes that the same surface area of the hand used for the hand-to-surface contact is then used for the hand-to-mouth contact. This removes the potential dilution effect that could occur if the number of particles transferred to the hand during the hand-to-surface contact was divided by the total hand surface area. Therefore, this is a worst-case scenario in which all of the virus transferred to the hand during the hand-to-surface contact is available for transfer to the mouth during the hand-to-mouth contact. To represent the fraction of transfer of virus from hand-to-mouth, a normal distribution with a mean informed by a virus hand-to-mouth transfer efficiency (0.339) and a standard deviation of 0.25, was randomly sampled and left- and right-truncated at 0 and 1, respectively.^{25–27}

The infection risk resulting from this single dose was estimated using the fractional Poisson dose-response curve.^{23,28} There is no single suggested dose-response curve for human norovirus²³ and 1 curve, rather than multiple, was used in this study so that any

difference in infection risk was a function of the intervention efficacy and not of differences between curves. Infection risk was calculated using the following equation:

$$P(\text{infection}) = P\left(1 - e^{-\frac{Dose}{\mu_a}}\right) \quad (3)$$

where $P(\text{infection})$ = probability of infection

P = fraction of susceptible individuals

$Dose$ = momentary dose from hand-to-mouth contact (viral particles) calculated with Equation 2

μ_a = mean aggregate size

This dose-response curve assumes aggregation of viral particles. Parameters for all equations are displayed in Table 1. Estimated infection risks were then compared to a risk target of 1×10^{-6} (1/1,000,000), as this risk target has been used in other QMRA studies in comparisons to estimated risks for single fomite contacts.³ The model was run with 10,000 iterations per scenario.

Sensitivity analysis

To evaluate the influence of $\log_{10}$ reduction variability and other model parameters on estimated dose, a sensitivity analysis was conducted. Spearman correlation coefficients were calculated to relate randomly selected $\log_{10}$ reductions, surface-to-hand transfer efficiencies, and hand-to-mouth transfer efficiencies to estimated infection risk. To evaluate the influence of contact surface area, the assumed contact surface area was independently decreased and increased by 25% holding surface-to-hand transfer efficiency and hand-to-mouth transfer efficiency constant at 0.217 and 0.339, respectively. The estimated doses were then compared.

RESULTS

Hand sanitizer efficacies

The data from the fingerpad studies were reported as $\log_{10}$ reductions adjusted for dry controls for a 60% ethanol (nonresidual) and a quaternary ammonium-based (residual) hand sanitizer. In the case of direct application of the product to contaminated hands (immediate kill) as evaluated by the ASTM E1838-10 fingerpad method, 1.06 ± 0.54 and 1.22 ± 0.56 $\log_{10}$ reductions in genomic copy number were observed after 30- and 60-second contact times, respectively, for the 60% ethanol (nonresidual hand sanitizer) (Table 2). The quaternary ammonium-containing product produced higher antinoroviral efficacy, 2.13 ± 0.50 and 2.09 ± 0.35 $\log_{10}$ reductions after 30 and 60 seconds, respectively (Table 2). Statistically significant differences ($P < .05$) were

Table 1
Model parameters

	Parameter	Variable	Unit	Point value/distribution	Source
Transfer efficiency	Surface-to-hand	TE_{sh}	Fraction	Uniform (min = 0.01, max = 0.406)	24
	Hand-to-mouth	TE_{hm}	Fraction	Normal* (mean = 0.339, SD = 0.25)	25–27
Surface concentration	Low contamination scenario	$C_{surface}$	Viral particles/ cm^2	0.01	3
	High contamination scenario		Viral particles/ cm^2	537.25	6
Contact surface area		$A_{contact}$	cm^2	2	29
$\log_{10}$ reduction		$\log_{10}reduction$		30-second, Nonresidual Uniform: (min = 0.15, max = 1.89)	This study
				30-second, residual Uniform: (min = 1.32, max = 2.94)	
				60-second, nonresidual Uniform: (min = 0.19, max = 2.07)	
				60-second, residual Uniform: (min = 1.56, max = 2.72)	
				Dry, nonresidual Uniform: (min = -0.12, 0.28)	
				Dry, residual Uniform: (min = 0.20, max = 1.76)	
Dose-response curve		P	Fraction	0.722	23,28
		μ_a	Mean aggregate size	1106	

*Left-truncated at 0 and right-truncated at 1.

observed when comparing the 2 hand sanitizer types, but not when comparing contact times for each sanitizer ($P > .05$).

When fingerpads were inoculated with norovirus immediately after sanitizer application, some residual effect was observed for the quaternary ammonium-containing product. Specifically, there was a $0.80 \pm 0.46 \log_{10}$ reduction in genomic copy number for the residual hand sanitizer, and a $0.02 \pm 0.13 \log_{10}$ reduction for the 60% ethanol ($P < .05$) (Table 2). When fingerpads were challenged with norovirus inoculum 4 hours postsanitizer application, the 60% ethanol and quaternary ammonium-containing product reduced norovirus concentrations by -0.08 ± 0.11 (essentially no reduction) and $0.51 \pm 0.26 \log_{10}$ genomic copies, respectively (Table 2). This demonstrates that the quaternary ammonium compound produced some antinoroviral residual activity postapplication relative to 60% ethanol.

Infection risk reductions

Under all scenarios, the residual hand sanitizer reduced baseline (no hand sanitizer) infection risks by $>78.5\%$ on average (Table 2). With a 30- and 60-second contact time, the nonresidual hand sanitizer reduced infection risks, but under dry and 4-hour scenarios, there was no effective reduction (Table 2). The infection risks estimated for the residual hand sanitizer were also less variable than those for the nonresidual hand sanitizer (Fig 1). The residual hand sanitizer reduced infection risk on average by up to 99.1%, which was estimated for the 60-second contact time scenario under low contamination conditions (Table 2). Under high contamination conditions, the baseline infection risk (5.19×10^{-2}) and all nonresidual and residual hand sanitizer scenario mean infection risks still exceeded a 1×10^{-6} risk target (Fig 1, Table 3). Under low contamination conditions, all mean infection risks, with the exception of those for the nonresidual hand sanitizer 4 hours after application and the baseline scenario, were below a 1×10^{-6} risk target. However, the distributions of predicted infection risks suggest that variability of product efficacy may influence whether a risk target is consistently met or not, along with variability in transfer efficiency for hand-to-surface and hand-to-mouth contacts (Fig 1). For example, under low contamination conditions, the average estimated infection risk associated with virus challenge immediately after application of 60% ethanol (nonresidual) was below a 1×10^{-6} risk target, although there were instances in which some estimated infection risks were larger than this number (Fig 1). Under the same low contamination conditions, the 60% ethanol treatment with 4-hour postapplication virus exposure produced a mean infection risk above the 1×10^{-6} risk target, but individual infection risks were below this number on occasion (Fig 1).

Dose estimates

The smallest estimated doses for both the residual and nonresidual hand sanitizer were for scenarios in which there was low environmental contamination and 60 seconds of contact time with the hand sanitizer. Estimated doses and the associated average infection risk for all low contamination scenarios, regardless of hand sanitizer type, were below the 1×10^{-6} risk target, with the exception of the 4-hour scenario for the nonresidual hand sanitizer and the baseline scenario (Table 3). The largest estimated doses were for scenarios in which there was high environmental contamination and residual hand sanitizer had been present for 4 hours. Estimated doses for all high contamination scenarios regardless of hand sanitizer type, resulted in average infection risks above a 1×10^{-6} risk target (Table 3).

Sensitivity analysis

For intervention scenarios, virus $\log_{10}$ reductions were positively correlated with reductions in infection risk (Spearman correlation coefficient -0.434). For all scenarios, surface-to-hand and hand-to-mouth transfer efficiencies were positively correlated with infection risk (0.156 and 0.161, respectively). Reducing or increasing contact area by 25% while holding transfer efficiencies constant had nominal impact on estimated dose. For example, decreasing and increasing contact area by 25% resulted in a change from 1.47×10^{-3} to 1.10×10^{-3} and from 1.47×10^{-3} to 1.84×10^{-3} for estimated dose under low contamination conditions, respectively. For high contamination conditions, decreasing or increasing contact area by 25% resulted in a change from 7.90×10^1 to 5.93×10^1 and from 7.90×10^1 to 9.88×10^1 for estimated dose, respectively.

DISCUSSION

Key findings

In all scenarios, the quaternary ammonium-containing hand sanitizer having residual activity out-performed the nonresidual hand sanitizer in reducing norovirus concentrations on the hand, and therefore reducing dose and infection risk (Tables 2, 3, Fig 1). Using these experimental data in a QMRA modeling framework demonstrated a single application of a residual hand sanitizer with a 30- to 60-second contact time may reduce infection risk from a single fomite contact by approximately 98%–99%, even under high contamination conditions representative of concentrations seen during

Table 2

Experimentally quantified mean $\log_{10}$ reductions adjusted for dry controls for 60% ethanol (nonresidual) and a quaternary ammonium-based (residual) hand sanitizer and estimated mean percentage infection risk reductions compared with baseline (no hand sanitizer) for low and high virus contamination scenarios

Hand sanitizer type	Log ₁₀ reductions							
	30 second		60 second		Dry*		4 hour	
	Mean $\pm$ SD	Min, Max	Mean $\pm$ SD	Min, Max	Mean $\pm$ SD	Min, Max	Mean $\pm$ SD	Min, Max
Nonresidual	1.06 ± 0.54 (n = 10)	0.15, 1.89	1.22 ± 0.56 (n = 10)	0.19, 2.07	0.02 ± 0.13 (n = 5)	−0.12, 0.28	$−0.08 \pm 0.11$ (n = 5)	−0.23, 0.07
Residual	2.13 ± 0.50 (n = 6)	1.32, 2.94	2.09 ± 0.35 (n = 6)	1.56, 2.72	0.80 ± 0.46 (n = 5)	0.20, 1.76	0.51 ± 0.26 (n = 5)	0.33, 1.17
Hand sanitizer type	Infection risk reductions (%)							
	30 second		60 second		Dry*		4 hour	
	Low	High	Low	High	Low	High	Low	High
Nonresidual	82.7 ± 18.0	82.2 ± 18.3	85.0 ± 16.5	85.0 ± 16.5	13.8 ± 22.8	13.8 ± 22.0	$−22.6 \pm 24.1$	$−21.9 \pm 23.1$
Residual	98.7 ± 1.2	98.7 ± 1.3	99.1 ± 0.7	99.0 ± 0.7	82.8 ± 16.1	82.1 ± 16.8	79.3 ± 11.2	78.5 ± 11.6

*Virus was applied after the hand sanitizers had dried.

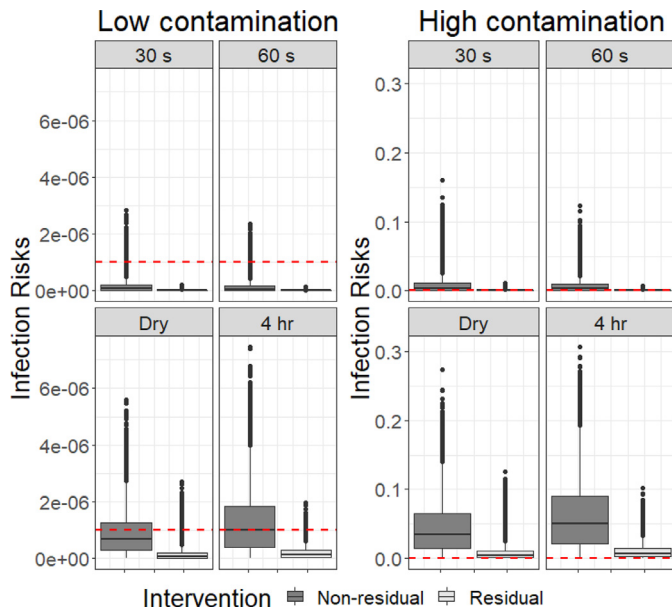


Fig 1. Comparison of estimated infection risk distributions for a 60% ethanol (nonresidual) and a quaternary ammonium-based (residual) hand sanitizer under 4 conditions: 30- and 60-second product contact time, 4-hour postdrying, and immediately after drying with low and high environmental contamination conditions where the red dotted line indicates a 1/1,000,000 infection risk target.

outbreaks (Table 2). Highest infection risk reductions were observed for both hand sanitizers under a 60-second contact time (Table 2). Four hours after application, the residual hand sanitizer may have a protective effect providing 78.5% reduction in infection risk on average from single fomite contacts under high contamination conditions (Table 2). This study demonstrates the potential of residual hand sanitizers to reduce norovirus infection risks in single fomite contact scenarios, supporting future research in modeling the infection risk reduction benefits of residual hand sanitizers over the course of sequential contacts with surfaces.

Table 3
Comparisons of mean estimated virus concentration on hands, dose, and infection risk*

	Concentration on hands									
	30-second scenario		60-second scenario		Dry scenario		4-hour scenario			
	Baseline	Nonresidual	Residual	Nonresidual	Residual	Nonresidual	Residual	Nonresidual	Residual	
Low contamination	4.15×10^{-3}	7.16×10^{-4}	5.32×10^{-5}	6.22×10^{-4}	3.97×10^{-5}	3.59×10^{-3}	7.13×10^{-4}	5.09×10^{-3}	8.64×10^{-4}	
High contamination	2.23×10^2	3.88×10^1	2.81×10^0	3.23×10^1	2.14×10^0	1.91×10^2	3.90×10^1	2.74×10^2	4.67×10^1	
	Dose									
	30-second scenario		60-second scenario		Dry scenario		4-hour scenario			
	Baseline	Nonresidual	Residual	Nonresidual	Residual	Nonresidual	Residual	Nonresidual	Residual	
Low contamination	1.56×10^{-3}	2.72×10^{-4}	2.01×10^{-5}	2.34×10^{-4}	1.49×10^{-5}	1.35×10^{-3}	2.68×10^{-4}	1.92×10^{-3}	3.27×10^{-4}	
High contamination	8.47×10^1	1.47×10^1	1.08×10^0	1.22×10^1	8.12×10^{-1}	7.29×10^1	1.48×10^1	1.04×10^2	1.79×10^1	
	Norovirus infection risk									
	30-second scenario		60-second scenario		Dry scenario		4-hour scenario			
	Baseline	Nonresidual	Residual	Nonresidual	Residual	Nonresidual	Residual	Nonresidual	Residual	
Low contamination	1.02×10^{-6}	1.77×10^{-7}	1.31×10^{-8}	1.53×10^{-7}	9.72×10^{-9}	8.79×10^{-7}	1.75×10^{-7}	1.25×10^{-6}	2.13×10^{-7}	
High contamination	5.19×10^{-2}	9.37×10^{-3}	7.03×10^{-4}	7.80×10^{-3}	5.30×10^{-4}	4.53×10^{-2}	9.45×10^{-3}	6.28×10^{-2}	1.14×10^{-2}	

*Bold values indicate a 1×10^{-6} (1/1,000,000) risk target is not met. There were 10,000 iterations for each scenario.

Interpretation

Because the fractional Poisson dose-response curve used in this study is nonlinear, estimated risk reductions may be notably affected by the baseline infection risk. In this study, we addressed this issue by including 2 modeled scenarios: low and high contamination. Although most of the mean infection risks for low contamination scenarios were below a 1×10^{-6} risk target, all of the mean infection risks for high contamination scenarios were above the 1×10^{-6} risk target (Table 3). This issue highlights the importance of the degree of environmental contamination to overall risk.

Generalizability

Single fomite contacts have been used in other QMRA models to evaluate intervention efficacy.^{3,30} Ryan et al³ calculated infection risks from a single contact with a surface for a number of organisms, including norovirus. The norovirus infection risk estimated by Ryan et al³ for a single fomite contact, 2.7×10^{-3} , was much higher than the baseline infection risk estimated in this study, 1.02×10^{-6} , using the same norovirus concentration on surfaces (0.01 viral particles/cm²). However, the transfer efficiency used by Ryan et al³ was 0.68, a maximum transfer efficiency for viruses among those reported in several studies used to inform a range of transfer efficiencies. In this study, we used a uniform distribution with a maximum of 0.406, the largest transfer efficiency measured for MS2, an enteric virus surrogate, on nonporous surfaces under low relative humidity (15% to 32%) conditions.²⁴ Additionally, a different dose-response model was used to relate estimated doses to infection risk when comparing the 2 studies.

The effect of low versus high contamination conditions are compared in this study. Because this assumption can have an effect on estimated infection risks and whether or not a risk target has been met, varying levels of contamination should be explored to estimate reductions needed in different conditions to meet risk targets. In another QMRA study, the assumed proportion of “clean” (uncontaminated) surfaces had a large effect on estimated doses and therefore infection risks, and a range of proportions of clean surfaces were explored.³¹ This study demonstrates the importance

of addressing this effect either by including multiple scenarios describing different levels of contamination on surfaces, or through a sensitivity analysis demonstrating its effect in a specific model.

Limitations

Some variables in this model were provided as point estimates, such as contact area and the 2 concentrations explored for low and high contamination conditions, and only 1 dose-response curve was considered. Although this was done to simplify the comparisons in infection risk reduction in which differences would be due to differences in $\log_{10}$ hand sanitizer reductions, this model structure did not extensively explore variability and uncertainty, especially for the effects of larger ranges of norovirus surface concentrations on estimated dose, and therefore infection risk. Further, whereas this study does elucidate potential differences in infection risk for a residual and nonresidual hand sanitizer in environments with low and high levels of contamination, there is a lack of information as to how these momentary risk reductions contribute to cumulative risk mitigation over many contacts with surfaces. In reality, a single hand-to-fomite contact followed by a single hand-to-mouth contact is rarely the case, rather multiple hand-to-fomite contacts may be made before a single hand-to-mouth contact. Although the frequency of microactivities, or second-by-second behaviors, for hand-to-fomite and hand-to-mouth contacts have been described,^{29,32,33} little is known about the variability in the sequences of these contacts and the effects of subsequent contacts on microbial transfer. Little is also known about whether differences in contact sequences make a notable difference in estimated infection risk. More empirical microactivity data and their quantified relationships with infection risks are needed to inform QMRA models.

In this study, the efficacy of the hand sanitizers was measured experimentally using the fingerpad method, with modifications. This method is well standardized and widely used, however, it does not necessarily mimic product use exactly as performed by the consumer. Nonetheless, it was the only experimental design possible given the limited supply of human norovirus and the need to use a protocol in which thorough hand decontamination could be assured. In addition, product efficacy was measured during only the first exposure to norovirus after hand sanitizer application and for a small sample size ($n \leq 10$) of participants. Future studies should explore product efficacy over multiple exposures and times, and for a larger group of people. Information such as this will likely show greater variability associated with human behavior, perhaps impacting the degree of residual effects. It could also provide useful information to inform recommended reapplication times. To take this approach, further data would be required quantitatively describing the removal of hand sanitizer residue per contact with a surface, how surface type affects the removal of hand sanitizer residue, and the cumulative $\log_{10}$ reduction over time from the moment of hand sanitizer application. With these types of data, a more complex model accounting for multiple contacts could be used to estimate beyond a momentary infection risk scenario.

CONCLUSIONS

This study demonstrates the potential benefit of residual hand sanitizers in reducing norovirus infection risks from single fomite contacts in low and highly contaminated environments for up to 4 hours. Further studies are needed to quantify the $\log_{10}$ reductions in norovirus due to residual hand sanitizers during repetitive contacts with contaminated surfaces in addition to effects over variable times to inform future QMRAs.

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