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Modeling of Human Viruses on Hands and Risk of Infection in an Office Workplace Using Micro-Activity Data

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Abstract

Although the number of illnesses resulting from indirect viral pathogen transmission could be substantial, it is difficult to estimate the relative risks because of the wide variation and uncertainty in human behavior, variable viral concentrations on fomites, and other exposure factors. The purpose of this study was to evaluate the micro-activity approach for assessment of microbial risk by adapting a mathematical model to estimate probability of viral infection from indirect transmission. To evaluate the model, measurements of phage loading on fomites and hands collected before and after implementation of a Healthy Workplace Project™ intervention were used. Parameter distributions were developed from this data, as well as for micro-activity rates, contact surface areas, phage transfer efficiencies, and inactivation rates. Following the Monte Carlo simulations (n=1,000), the estimated phage loading on hands was not significantly different from the loading of phage on hands measured in the experimental trials. The model was then used to demonstrate that the Healthy Workplace Project™ intervention significantly reduced risk of infection by 77% for rotavirus and rhinovirus. This is the first published study to successfully evaluate a model focused on the indirect transmission of viruses via hand contact with measured data and provide an assessment of the micro-activity approach to microbial risk evaluation.

Keywords

indirect pathogen transmission; micro-activity; workplace intervention; office workers; infection risk; viral infection

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INTRODUCTION

Common respiratory and enteric viruses are readily spread among populations living and working together through direct transmission (i.e., inhalation of droplets from coughing and sneezing or ingestion of contaminated foods and beverages), as well as through indirect transmission via contact with contaminated surfaces and hand-to-mucus membrane contact.[1] Although the incidence of illnesses resulting from indirect routes could be significant, it is difficult to estimate the relative risk of indirect transmission because of the variability and uncertainty in human behavior, varying viral concentrations on fomites, and other exposure factors such as transfer between surfaces and virus survival rates on different surface types.

Few models exist that facilitate quantitative correlation of viral concentration on fomites with infection risk, while considering variable individual behaviors that influence the indirect viral transmission.[2–5] The limited number of models results, in part, from the difficulty in obtaining the detailed activity data needed to generate quantified estimates of contact rates between hands and fomites, hands and mucus membranes, and fomites and mucus membranes. Measurements of contact rates are difficult because of the high frequency and relatively short duration of these activities. For example, children have been shown to contact an average of more than 500 objects per hour with their hands with a median duration of 3 seconds.[6] Techniques have been developed using videography and specialized software to transcribe micro-activities (e.g., hand-to-mouth frequency).[7] These micro-activities have then been successfully used to evaluate exposure models for contaminants such as lead and pesticides.[8–10]

Nicas and Best[3] recently developed a model to estimate the dose of pathogens transferred to facial mucus membranes, while considering the rate of pathogen transfer to hands via contact with fomites, pathogen die-off rates on the hands, and pathogen transfer from hands to source. Although they presented a hypothetical evaluation of their model by estimating the infection risk of influenza A in the workplace, they did not evaluate their model with empirical data. Similarly, Julian et al.[2] presented a hypothetical evaluation of the micro-activity approach to assessing risk of rotavirus infection in daycare settings, but they also did not evaluate their model with experimental data. No previous studies were found in the literature reporting estimated pathogen loading on hands from contact with fomites evaluated with real-time environmental sampling.

The purpose of this study was to adapt and evaluate the model developed by Nicas and Best[3] to estimate probability of infection from enteric and respiratory viruses in a workplace setting. As part of a study to assess the effectiveness of a Healthy Workplace Project™ (HWP) intervention, phage tracers were utilized to monitor the transmission of viruses throughout the workplace and on the hands of office workers.[11] This experiment provided a unique opportunity to simultaneously evaluate the micro-activity approach for estimating pathogen loading on hands and subsequent infection risk. The model was used to estimate expected phage levels on the hands that were then compared with the actual measured phage levels on the hands of the participating office workers. The estimated phage levels on hands were then used to estimate risks of rotavirus and rhinovirus infection. The

model was adapted so that stochastic inputs and Monte Carlo simulations could be used to provide a distribution of probability of infection for each virus in the office worker population. Input distributions were developed for phage concentrations on fomites, micro-activity patterns, and other exposure factors. The model was also used to evaluate the effectiveness of the HWP as a method of risk management by comparing the probability of infection from pre- and post-intervention simulations. This is the first study to validate a model focused on the indirect transmission of viruses via hand contacts and provide an evaluation of the micro-activity approach for microbial risk assessment.

MATERIALS AND METHODS

Model adaptation

A model framework, originally proposed by Nicas and Best,[3] was adapted and modified to estimate pathogen loading on hands, dose to target membranes (i.e., eyes, nose, and mouth), and infection risk. The original model applied the mass balance approach to estimate pathogen loading on the hands in which the concentration of pathogen on the hands is equal to the rate of transfer from surfaces to hands minus the rate of pathogen transfer from the hands back to surfaces, the rate of pathogen transfer to target membranes and the rate of pathogen die-off on the hands. Dose is then calculated as a function of the pathogen loading on hands and the frequency of contact between hands and target membranes. Finally, risk is calculated as a function of the target membrane dose and the probability of infection by a single pathogen. In the adaptation of this model, based on the authors' previous research of pathogen-surface interactions and human activity patterns, some key modifications to the model assumptions and to the derivation of the equations were made.

The first key difference in this adaptation of the model relates to contact surface area. For simplicity, Nicas and Best[3] assumed that the same hand surface area contacted all surfaces including the target membranes. While this simplified model development and equations, dermal contact surface areas differ by surface type and contaminant loading on hands is not typically uniform.[12,13] Unique parameters for contact surface area between hands and environmental surfaces, hands and target membranes, and for the entire hand surface area were incorporated into the model. For example, a typical hand-to-eye contact will have a much smaller surface area than a hand-to-door knob contact. Thus, there is a high likelihood that the number of microbes transferred will differ.

The efficiency of microbial transfer between surfaces and hands differs substantially for non-porous and porous surface types.[14] Because of this difference, in this adaptation of the model the rate of transfer was calculated separately for non-porous and porous surface types. Therefore, the modified equation for rate of microbial transfer to the hands (R_{hands}) expressed asnumber of pathogens per minute is:

$$R_{hand} = \sum_{j=1}^{j=m} (f_{12,j} \times H_{surface,j}) \times C_{surface} \times A_{surface} \quad (1)$$

where $f_{12,j}$ is the fraction of pathogen transferred between the j^{th} surface type and hands, $H_{surface,j}$ is the contact frequency (contacts/min) between the j^{th} surface type and hands,

$C_{surface}$ is the concentration of pathogens on the surface (pathogens/cm^2), and $A_{surface}$ is the area of contact between the hands and the surface (cm^2). For the current simulation, there are two surface types, porous and non-porous, selected based on their unique transfer efficiency characteristics.

Previous work has demonstrated that the microbial transfer efficiency from hands to surfaces, regardless of the surface type, is similar to that for non-porous hard surfaces to hands.[14] Therefore, it was assumed that rate of transfer from the hands back to the surface ($R_{surface}$) expressed as number of pathogens per minute is:

$$R_{surface}=f_{21}\times\sum_{j=1}^{j=m}H_{surface,j}\times C_{hands}\times A_{surface} \quad (2)$$

where f_{21} is the fraction of pathogen transferred from hands to surfaces and C_{hands} is the concentration of pathogen on the hands (pathogens/cm^2). The contact frequencies for both types of surfaces are summed to obtain a total surface contact frequency.

Given that some target membranes may be more prone to infection by various pathogens, the equation for the rate of transfer from hands to target membranes was modified to account for multiple target orifices unique to different pathogens. For example, rotavirus is an enteric pathogen and the target port-of-entry is the mouth, whereas rhinovirus is a respiratory virus and the target membranes are the eyes and nose. The modified equation for rate of transfer to target membranes ($R_{orifice}$) expressed as number of pathogens per minute is:

$$R_{orifice}=f_{23}\times C_{hands}\times\sum_{n=1}^{n=k}\left(H_{orifice,n}\times A_{orifice,n}\right) \quad (3)$$

where f_{23} is the fraction of pathogen transferred from the hand to the targeted orifice, $H_{orifice,n}$ is the contact frequency between the hands and the n^{th} orifice (contacts/min) and $A_{orifice,n}$ is the contact surface area between the hands and the n^{th} orifice (cm^2). The specific orifices and the total number of orifices, k, will depend on the specific pathogen being modeled. The equation from Nicas and Best[3] to account for rate of pathogen die-off on hands, which is simply the product of C_{hands}, the surface area of the hands (A_{hands}), and the rate of viable pathogen die-off on hands (α_{dieoff}) in terms of number of pathogens per minute, was not modified.

If the overall exposure duration is much longer than the rate of pathogen loss from the hands, then steady state can be assumed. The overall rate of pathogen loss from the hands ($1/\lambda$) in minutes is equal to:

$$\frac{1}{\lambda}=\alpha_{dieoff}+f_{21}\times FSA\times\sum_{j=1}^{j=m}H_{surface,j}+f_{23}\times\sum_{n=1}^{n=k}H_{orifice,n}\times\left(\frac{A_{orifice,n}}{H_{hands}}\right) \quad (4)$$

where FSA is the fractional surface area and is the ratio of the hand-to-surface contact area to the total hand surface area ($A_{surface}/A_{hand}$). At steady state, the predicted mean hand

concentration loading ($\overline{C_{hand,T}}$) in terms of number of viable pathogens per cm^2 is calculated as:

$$\overline{C_{hand,T}} = \frac{\sum_{j=1}^{j=m} (H_{surface,j} \times f_{12,j}) \times C_{surface} \times FSA}{\alpha_{die-off} + \left(\sum_{j=1}^{j=m} H_{surface}\right) \times f_{21} \times FSA \times f_{23} \times \sum_{n=1}^{n=k} (H_{orifice,n} \times A_{orifice,n}) / A_{hand}} \quad (5)$$

Table I summarizes the different parameters used to calculate $\overline{C_{hand,T}}$. The dose of viable phage delivered to the targeted orifice was calculated as described by Nicas and Best.[3]

Another key modification that was made to the Nicas and Best[3] model was in the calculation of infection risk from an estimated dose delivered to the target orifice. Nicas and Best[3] assumed an exponential dose-response curve, while in this adaptation a beta-Poisson model that better fits the dose response for the selected viruses was selected.[15] Therefore the probability of infection was calculated as:

$$P(infection) = 1 - \left[1 + D_T \frac{\left(2^{1/\alpha} - 1\right)}{N_{50}}\right]^{-\alpha} \quad (6)$$

where D_T is the dose delivered to the target membranes, N_{50} is the median infectious dose, and α is a parameter of the beta distribution and the slope of the dose-response curve. Model inputs for the simulations were obtained from the HWP study, the scientific literature, and government guidance documents.

The Healthy Workplace Project™ intervention study

As part of the HWP intervention study, phage tracers were measured on fomites and hands in an office setting.[11] This data on microbial loadings from both fomites and hands—sampled simultaneously after a known exposure duration—provides a unique opportunity to evaluate and validate the proposed model. The HWP and key findings from this study are described in another publication, therefore only a brief description of that work is included.[11] The HWP intervention was implemented in an office setting with approximately 80 employees. Two baseline and two post-intervention experiments were conducted. For the baseline experiments, the subjects conducted their normal office hygiene practices. They were subsequently instructed in HWP intervention practices focused on proper hand washing, the use of disinfectant wipes in communal areas and personal workspace, and the use of hand sanitizer and tissues when blowing/wiping the nose. During one baseline and one post-intervention study the push plate of the entrance door was inoculated once with MS-2 virus to seed the office. During another baseline and post-intervention study, one randomly selected, blinded participant had their hand inoculated with MS-2 virus while the other participants were inoculated with a phosphate buffered saline solution placebo. MS-2 was measured on 22 participants' hands, 36 communal fomites, and

16 personal fomites using the method previously described by Hewitt et al.[16] Because of the large number of samples below the detection limit, it was not possible to fit a theoretical distribution to the phage concentration measured on fomites, thus the empirical distribution from the measurements was used for the model simulations.

Activity pattern parameters

The rate of hand-to-fomite contacts, $H_{surface}$, and the rate of hand-to-mouth contacts, H_{mouth}, were derived from micro-activity data reported by Beamer et al.[6] Given the lack of micro-activity data collected in adults, it was assumed that the contact frequency for adults in this modeling scenario would be similar to those of these 7–12 year-old children. The children's behaviors were analyzed for micro-level dermal contact and mouthing activity. As children develop and age, the frequency of their dermal and mouthing activities decreases over time, but this study found that there was no difference in the frequency of mouthing activities after age 7. It was assumed that the children's mouthing activities had matured and that their activities were therefore equivalent to those of adults, however this may be a conservative estimate. $H_{surface}$ was differentiated into two groups, $H_{surface,non\text{-}porous}$ and $H_{surface,porous}$. The body, floor, clothes, fabric, food, and paper towels were considered porous surfaces. Metal, plastic, rock/brick, toys, vegetables, and wood were regarded as non-porous surfaces. Log-normal distributions were fit to the empirical distributions for H_{mouth}, $H_{surface,non\text{-}porous}$, and $H_{surface,porous}$ reported by Beamer et al.,[6] and the fit of the distributions were confirmed using the Shapiro-Wilk test for normality (Table II).

The H_{eyes} and H_{nose} were extrapolated from an observational study of 10 adults conducted by Nicas and Best.[3] H_{nose} and H_{eyes} were calculated as contacts per hour by dividing the subjects' total number of observed contacts with the orifices by the duration of the experiment in minutes. Log-normal distributions were fit to this data to generate the distributions described in Table II.

Surface area parameters

Distributions were developed for the surface area of the entire hand (A_{hand}), as well as the contact surface area between hands and fomites or orifices (Table II). The US EPA Exposure Factors Handbook[17] reports that adult females ≥21 years old have a mean A_{hand} of 890 cm^2 and adult men have a mean A_{hand} of 1070 cm^2. The 95% confidence interval for the measured surface area was 760–1060 cm^2 and 900–1310 cm^2 for women and men, respectively. It was assumed that A_{hand} for this study's participants (i.e., workplace employees) was uniformly distributed from 890–1070 cm^2 (i.e., the mean hand surface area values for women and men).

The area of the mouth that is touched during each contact event (A_{mouth}) was previously reported by Leckie et al.[18] It was assumed A_{mouth} to have a uniform distribution between the minimum area of 1 cm^2 and the maximum area of 41 cm^2 measured from adults simulating mouthing events (Table II). The distribution for FSA was derived by AuYeung et al.[12] AuYeung and colleagues determined the FSA for 11 children and 20 adults using painted objects and analyzing gripping behaviors from digital scans of the paint coverage on their hands. They found no correlation between age and FSA. Table II describes the fit of

the log-normal distribution to the empirical distribution for FSA of "all objects" as reported by AuYeung et al.[12] The fit of the distribution was confirmed using the Shaprio-Wilk test for normality.

Phage parameters

The values used in the model for MS-2 transfer between surfaces, hands, and target membranes were reported by Lopez et al.[14] The transfer efficiencies were selected from the low relative humidity (19–30% humidity) category—comparable to office environment conditions in Arizona—and were divided into two surface-type categories. It was assumed that the transfer efficiency from porous surfaces ($f_{12,porous}$) could be represented by measurements of MS-2 transfer to hands from money, polyester, and cotton. Cotton was found to have the lowest average transfer efficiency of 0.03% and money was found to have the highest transfer efficiency of 0.42%. Given the low number of data points and the variety of fomites contacted in the office environment, it was assumed that the transfer efficiency of MS-2 from hands to porous fomites was uniformly distributed between 0.03% and 0.42% (Table III). It was further assumed that the transfer efficiency for non-porous surfaces ($f_{12,non\text{-}porous}$) could be characterized by experimental data from acrylic, glass, stainless steel, ceramic tile, and plastic laminate surfaces. For MS-2, plastic laminate had the lowest average transfer efficiency of 5% while acrylic had the highest average transfer efficiency of 22%. The transfer efficiency of MS-2 phage to the hands from non-porous objects was assumed to be uniformly distributed between 5% and 22% (Table III). Fingertips, as well as the palm of the hand, are assumed to behave similarly to other non-porous surfaces.[19] The transfer efficiency of phage from hands to the fomites, f_{21}, was assumed to be approximately equal to $f_{12,non\text{-}porous}$.

Rusin et al.[20] measured the transfer efficiency of P-22 between the hands and the mouth of 20 individuals under laboratory conditions. Given that this is the only published data that examines the transfer efficiency of any phage from hands to mouth, it was assumed that the transfer efficiencies would be the same for all orifices and that the transfer efficiency of MS-2 would be equal to that of P-22. A point value of 33.9% was used (Table III).

The inactivation rates of MS-2 ($\alpha_{die\text{-}off}$) are 0.0133 and 0.0264 log reductions per hour on stainless steel and laminate surfaces, respectively.[21] Because there are only two data points available, the decay constant was assumed to be uniformly distributed between the stainless steel and laminate values (Table III).

Pathogen-specific parameters

Using a beta-Poisson model, the risk of infection for different pathogens (i.e., rotavirus and rhinovirus) in the office environment was calculated from the estimated dose of phage introduced to each of the targeted orifices. The recommended best-fit parameters, provided in Table IV, from the Center for Advancing Microbial Risk Assessment Quantitative Microbial Risk Assessment (QMRA) Wiki[15] were used. Rhinovirus is the causative agent of the common cold and rotavirus is the causative agent of gastroenteritis in both children and adults. The reported dose response for rotavirus was used to represent viral

gastroenteritis because it has the most highly developed dose-response information from human feeding experiments.[15]

Model simulations and data analysis

The model was used to estimate the loading of MS-2 phage on the hands for both the baseline and post-HWP intervention trials. Monte Carlo simulations were conducted using probability distributions for the input parameters in order to address environmental variability and experimental uncertainty. For each simulation, a single value was randomly selected from each of the distributions presented in Tables II and III and from the empirical distribution for phage loading measured on the surfaces. These inputs were then used to estimate hand-loading, dose to orifices, and subsequent risk utilizing the steady state equations. Microsoft Excel® 2007 (Microsoft Corporation, Seattle, WA) was used to conduct the simulations and generate the distribution of phage concentration on hands at steady state for each trial. To achieve stability in the results, 1000 simulations were conducted. The modeled estimates and the measured phage concentrations on the hands were compared using the Wilcoxon rank-sum test. Statistical analysis was performed using STATA® 10 (StataCorp LP, College Station, TX). An alpha level of 0.05 was used for statistical significance.

A sensitivity analysis was performed using Crystal Ball™ software (Oracle Corporation, Redwood Shores, CA) by running separate Monte Carlo distributions to determine what percent of the uncertainty was caused by each parameter in the modeled results for the concentration of MS-2 on the hands. The methods outlined by Nayak and Kundu[22] were followed to complete the sensitivity analysis. The Bayesian analysis was performed at the 5^{th} and 95^{th} percentile of each parameter's distribution. Because none of the measured $C_{surface}$ values fit any of the distributions examined, the 5^{th} and 95^{th} percentiles were selected from the measured data. The median of C_{hand} was used as the central value for comparison. In separate analyses, each parameter's 5^{th} and 95^{th} percentile values were substituted into the original model.

The distributions of simulated phage loading on the hands were then used to develop distributions for the total dose to each orifice. Then the risk of infection was computed for each of the pathogenic viruses (Table IV) for each of the experimental trials. It was assumed that the target orifices for rhinovirus are the eyes and nose and that the target orifice for rotavirus is the mouth. The efficacy of the intervention in reducing the risk of infection for each virus was also tested using the Wilcoxon rank-sum test.

RESULTS

When the exposure time is much greater than $1/\lambda$, the phage concentration on the hands can be assumed to be at steady state.[3] After four hours or 240 minutes, λ_{MS2} has a mean of 0.23. Therefore the assumption of steady state is appropriate in this scenario and the loading of pathogens on hands can be modeled using equation 5.

The distribution of the simulated and measured phage loading on hands during each trial is provided in Table V. For the four individual studies and the two combined studies

(combined baseline and combined post-intervention), the median concentration of phage measured on the hand was not found to be statistically different than the concentration of phage modeled using the concentrations of MS-2 measured on the fomites.

A summary of the sensitivity analysis is provided in Table VI. The loading of pathogens on the hand was most affected by the concentration of pathogens on the fomites, which can vary by several orders of magnitude in the environment. The second most sensitive parameter was the hand contact rate with non-porous objects, closely followed by the transfer efficiency for non-porous objects, although each accounted for less than 2% of the model's variance.

The modeled pathogen loading on hands estimated using the concentration of MS-2 measured on fomites was then used to model the dose of MS-2 delivered to the mouth, nose, and eyes, and subsequently the risk of viral infection. The combined baseline and combined post-intervention concentrations were analyzed. A summary of the infection risk for each virus at baseline and after the intervention is provided in Table VII. After implementation of the HWP intervention, the mean risk of infection was reduced by 77% for both rotavirus and rhinovirus. The intervention produced a statistically significant risk reduction where $p<0.0001$ for all viruses modeled.

DISCUSSION

In this study, the micro-activity approach to microbial risk assessment was evaluated by adapting a previously developed mathematical model to assess the risk from indirect pathogen transmission.[3] Simultaneous measurements of phage loading on fomites and hands in the same environment provided a unique opportunity to assess this modeling framework. After modifying some key assumptions and developing the necessary input parameter distributions, the simulated median levels of phage on hands were not significantly different from those measured empirically. Furthermore, the model was utilized to assess the efficacy of the HWP intervention in reducing infection risk for several viruses of concern in the workplace. To the authors knowledge, this is the first study to successfully validate a model focused on the indirect transmission of viruses via hand contact.

Nicas and Best[3] describe their model as a "relatively crude first-pass estimate" of pathogen dose to target membranes, in part because of lack of quantitative data for the model. The necessary quantitative data includes: 1) pathogen concentration on environmental surfaces; 2) rate of contact with surfaces; 3) transfer efficiencies upon contact; and 4) pathogen die-off rates on hands. Quantitative data for most of these parameters was obtained from the authors' own measurements or from the peer-reviewed literature. As a result, most of the quantitative data (i.e., pathogen loading on hands) necessary to validate the model calculations was secured.

Based on the quantitative data previously collected, several key assumptions were made in this adaptation of the model. First, it was not assumed that the same hand surface area contacted all objects, including the target membranes. The fraction of the hand that comes into contact with surfaces can vary widely.[12] Assuming the same contact surface area of 2

cm^2, as described by Nicas and Best,[3] likely underestimates the transfer of microbes to the hands and to the target membranes when compared to the distributions that were used in these simulations (Table II). Transfers from contact with non-porous and porous surfaces were differentiated in this adaptation of the model. Thus, the substantially lower transfer efficiencies from porous surfaces were accounted for.[14] Although measured contact rates are higher with non-porous surfaces,[12] assuming the same transfer efficiency for non-porous and porous surfaces would overestimate the rate of transfer to the hands. Similarly, the model was adapted to account for the dose delivered to each of the target membranes. Although data is limited, the contact rate between hands and the eyes and nose are lower than the contact rate between the hands and mouth.[3] In addition, not all of these mucus membranes are appropriate targets for the viruses assessed in this study. For example, if the hand-to-mouth contact rate were used to estimate the dose of rhinovirus, the estimated risk of infection would increase substantially even though this result is not likely to be as relevant. Finally, the dose-response relationship was modeled using a beta-Poisson model instead of an exponential model. This modification results in lower estimated risk, but this model better fits the available dose-response data for the selected viruses of concern and likely provides a more realistic estimate of the infection risk.[21]

Although the quantitative data necessary to validate this model was obtained, there are several limitations in the values used that highlight key data gaps. Although the risk of viral infection in an office setting was modeled, there is no available micro-activity data collected from adults. Therefore, it was necessary to use micro-activity data collected in the oldest age group available—children aged 7–12 years. Although the use of activity data collected in children is likely to provide conservative estimates because adults probably have fewer contacts with both fomites and their mouths, there is no quantitative data to support that assumption. There is a substantial need for contact activity data in adults to provide a basis for both microbial and chemical risk assessments. Furthermore, there is almost no data on hand-to-eye and hand-to-nose contact rates in any population, even though these could be some of the most important indirect transmission pathways for a variety of microbial pathogens. The data reported by Nicas and Best[3] was used. This was collected by videotaping a small group (n=10) of students working on computers, however it is not clear how representative this data would be of typical workers in an office setting.

Although our modeled results were not significantly different from measured concentrations of phage on the hands, we did underestimate the higher percentiles of the distribution. This is most likely because we modeled an office worker population with distributions of activity patterns, rather than model individual workers who would engage in different activities or spend more time in certain parts of the office that may have greater phage concentrations like the seeded door handle. We have previously demonstrated, using individual micro-level activity time series, that dermal exposure has greater between-individual variability that within-individual variability in part due to individual's unique activity patterns.[8,9] It is like that certain people would be at increased risk for viral loading, as demonstrated by the high measured values, because of their own personal activity patterns and their proximity to contaminated fomites. In the future this model could be adapted into a simulation model whereby individual workers could be simulated and spatial and temporal components could be incorporated.

Because of the lack of empirical data, it was also assumed that the amount of pathogen transferred from hands to any fomite would approximate that of pathogen transferred from non-porous fomites to hands. Additional studies are needed to understand the effect of different surface types and microorganisms on transfer rates. Future studies should also focus on establishing distributions for the assumed parameters of contact area and transfer efficiency between the hands and the eyes and nose, which have not been examined experimentally. Although in the sensitivity analysis the concentration of pathogens on fomites was the single most sensitive parameter, contact rates and transfer efficiencies also contributed to the observed variance; thus, future studies are warranted to better understand these parameters.

Previous viral inactivation studies suggest that MS-2 is a conservative tracer for respiratory viruses, so the actual results would be expected to indicate a lower risk of infection by a number greater than, or equal to, the number calculated.[23] Thus, the reduction in infection risk observed after implementation of the HWP may actually be greater than the modeled estimate of 77%. Additionally, inactivation rates of the viruses modeled in this study may actually be lower than the inactivation rate for MS-2. To more accurately model potential hand loading and subsequent dosing for each virus, unique inactivation rates should be determined experimentally in future studies.

Another limitation of the current modeling scenario is that is does not incorporate hand hygiene behaviors as part of the mass balance on the hands. Part of the intervention was to increase hand washing and hand sanitizer utilization. However, given that the model performs as well for the baseline as it does for the intervention scenarios, this would not likely have affected our overall results. Based upon our results, it appears that steady state of phage loading on the hands is achieved relatively quickly. These results also demonstrate importance of the spread of virus in the office and on fomites and that interventions should incorporate surface decontamination as well as hand hygiene components that have a disinfecting residual. In the future the model could be adapted to incorporate time series simulations where the affect of hand hygiene, as well as temporal changes in the concentrations on surfaces could be better assessed than in the current steady state scenario.

The model developed here allows for analysis of environmental virus transmission and infection risks below the detection limits of traditional field methods. For example, some pathogens—like rotavirus—may have an infective dose of as little as one virus particle, which may be below the limit of detection or quantification of viral plaque assays.[24] To assess the effectiveness of hygiene interventions, a seeded study is typically performed using phage concentrations that are several orders of magnitude greater than those of viruses normally present in the environment. However, if all of the parameters associated with the phage and the human viruses are known, the model can be used to assess the efficacy of an intervention at realistic levels of viruses present in the environment based on the observed field measurements of the phage. In addition, this model may be adapted to estimate exposures and infection risks for multiple viral pathogens with similar physical properties.

CONCLUSIONS

In conclusion, using empirical data, the first successful validation of a mathematical model for indirect transmission of pathogens using microactivity data was achieved. The model was used to simulate the potential for significant reduction (77%) of rhinovirus and rotavirus infection risk in an office setting after implementation of an HWP intervention. Introduction of HWP intervention measures could result in substantial cost-savings for employers because common illnesses such as colds or gastroenteritis can have a significant impact on healthcare costs, absenteeism, and productivity.[25,26] This work also highlights the need for additional studies to collect more data on micro-activity in adults, contact surface areas with fomites and mucus membranes, and pathogen transfer parameters. In combination with empirical studies, this model can provide improved risk assessments for evaluation of proposed interventions.

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Table I

Parameters for predicting pathogen loading on hands

Parameter	Definition
Contact Frequencies	
$H_{surface,j}$	Rate of hand-to-fomite contacts for the j^{th} surface type
$H_{orifice,n}$	Rate of hand-to-mouth contacts for the n^{th} orifice
Surface Areas	
$A_{surface}$	Area of the hand in contact with a fomite
A_{hand}	Area of the hand
$A_{orifice,n}$	Area of the hand in contact with the n^{th} orifice
FSA	Fraction of surface area per area of the hand per contact
Pathogen Transfer Efficiencies	
$f_{12,j}$	Fomite-to-hand transfer efficiency for the j^{th} surface type
f_{21}	Hand-to-fomite transfer efficiency
f_{23}	Hand-to-orifice transfer efficiency
Pathogen Inactivation	
$\alpha_{die\text{-}off}$	Expected fraction of pathogen inactivated per hour
Pathogen Loading	
$C_{surface}$	Concentration of pathogens on the surface (pathogens/cm^2)
C_{hands}	Concentration of pathogens on the hands (pathogens/cm^2)

Table II

Contact activity and surface area parameter distributions (see Table I for parameter definitions)

Parameter	Distribution	GM*	GSD*	Min*	Max*	Unit	Source
$H_{surface,non\text{-}porous}$	log-normal	4.1	1.6			contacts/min	(6)
$H_{surface,porous}$	log-normal	5.5	1.5			contacts/min	(6)
H_{mouth}	log-normal	0.18	3.3			contacts/min	(6)
H_{eyes}	log-normal	0.06	3.3			contacts/min	(3)
H_{nose}	log-normal	0.01	66.7			contacts/min	(3)
A_{hand}	uniform			890	1070	cm^2	(17)
A_{eye}	uniform			0.10	2	cm^2	Assumed
A_{nose}	uniform			0.10	10	cm^2	Assumed
A_{mouth}	uniform			1	41	cm^2	(18)
FSA	log-normal	0.15	1.2			unitless	(12)

* log-normal distribution defined by geometric mean (GM) and geometric standard deviation (GSD); uniform distribution defined by minimum (Min) and maximum (Max).

Table III

Model MS-2 phage transfer and survival distribution parameters (see Table I for parameter definitions)

Parameter	Distribution	Min*	Max*	Unit	Source
$f_{12,non\text{-}porous}$**	uniform	0.05	0.22	contacts/min	(14)
$f_{12,porous}$	uniform	0.0003	0.0042	contacts/min	(14)
f_{21}	uniform	0.05	0.22	contacts/min	(14)
f_{23}**	point value	0.339		contacts/min	(20)
$\alpha_{die\text{-}off}$	uniform	5.1×10^{-5}	1.0×10^{-4}	fraction/min	(21)

* uniform distribution defined by minimum (Min) and maximum (max)

** A point value was used for f_{23}

Table IV

Beta-Poisson infection parameters for select human respiratory and enteric viruses.[15]

Virus	α	N_{50}
Rotavirus	0.253	6.17
Rhinovirus	0.221	1.81

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Table V

Distribution of measured and modeled loadings of phage on hands (C_{hands}) in PFUs/cm^2 during the baseline and post HWP intervention trials.

Trial	n	%[c]	Min	5th	25th	Median	75th	95th	Max	p[d]
Baseline 1[a]										
Measured	51	39	ND[e]	ND	ND	ND	4	58	320	0.79
Modeled	1000	56	0	0	0	0	1	16	287	
Baseline 2[b]										
Measured	50	38	ND	ND	ND	ND	2	280	2360	0.44
Modeled	1000	45	0	0	0	0	0	2	162	
Baseline 1+2										
Measured	101	39	ND	ND	ND	ND	4	90	2360	0.72
Modeled	1000	50	0	0	0	0	1	11	257	
Intervention 1[a]										
Measured	42	7	ND	ND	ND	ND	ND	12	5700	0.69
Modeled	1000	9	0	0	0	0	0	0	1217	
Intervention 2[b]										
Measured	44	14	ND	ND	ND	ND	ND	9	68	0.95
Modeled	1000	15	0	0	0	0	0	1	12	
Intervention 1+2										
Measured	86	11	ND	ND	ND	ND	ND	12	5700	0.84
Modeled	1000	12	0	0	0	0	0	0	1217	

[a] During baseline 1 and intervention 1 a hand was seeded with phage.

[b] During baseline 2 and intervention 2 a door was seeded with phage.

[c] Percent that were detected or estimated to be >0

[d] P-values obtained from Wilcoxon Rank Sum Test

[e] None Detected

Table VI

Sensitivity Analysis for Modeled C_{hand} (PFU/cm^2). This table includes the parameter values used for the sensitivity analysis, including the base values and the lower and upper bounds. The table also includes the computed values of C_{hand}, from those values and how much each parameter contributed to the overall variance.

	5–95% Parameter Range			5–95% C_{hand} Range			% Contribution to Variance
Parameter	***Base***	***Lower***	***Upper***	***Lower***	***Upper***	***Range***	
$C_{surface}$	0.38	0.00	29.10	0.00	2.04	2.04	95.8
$H_{surface,non\text{-}porous}$	3.94	1.84	8.43	0.01	0.05	0.04	1.8
$f_{12,non\text{-}porous}$	0.13	0.06	0.21	0.01	0.04	0.03	1.4
FSA	0.15	0.12	0.20	0.02	0.03	0.01	0.5
f_{21}	0.14	0.06	0.21	0.03	0.02	0.00	0.2
$H_{surface,porous}$	5.42	2.60	11.29	0.03	0.02	0.00	0.1
$f_{12,text}$	0.0022	0.0005	0.0040	0.03	0.03	0.00	0.0
H_{mouth}	0.20	0.03	1.39	0.03	0.03	0.00	0.0
H_{eyes}	0.01	0.00	11.76	0.03	0.03	0.00	0.0
A_{mouth}	20.99	2.98	39.00	0.03	0.03	0.00	0.0
H_{nose}	0.06	0.01	0.40	0.03	0.03	0.00	0.0
$\alpha_{die\text{-}off}$	0.00075	0.00051	0.001	0.03	0.03	0.00	0.0
A_{hand}	980	899	1061	0.03	0.03	0.00	0.0
A_{nose}	5.04	0.59	9.49	0.03	0.03	0.00	0.0
A_{eyes}	1.05	0.20	1.91	0.03	0.03	0.00	0.0

Table VII

Summary of risk of virus infection (%) and effect of the HWP intervention (n=1000)

Virus	Mean	SD	Min	Max	*Mean % Reduction*	*P*
Rotavirus						
Baseline	30.9	34.4	0	96.8	77	<0.0001
Intervention	7.04	21.1	0	97.9		
Rhinovirus						
Baseline	33.2	35.5	0	97.6	77	<0.0001
Intervention	7.56	21.9	0	97.2		