Draft 2

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Risk of infection from touching surfaces contaminated with SARS-CoV-2

Abstract

Objective. Use a stochastic mechanistic model to quantify the effect of surface and hand disinfection on SARS-CoV-2 infection risks. The results from this model can inform cleaning practices.

Introduction

SARS-CoV-2, the virus responsible for the COVID-19 pandemic, is transmitted via both direct (person-to-person) and indirect (via a contaminated environment) routes (WHO 2020; CDC 2020). Direct transmission appears to be the leading route and occurs via prolonged exposures to respiratory droplets produced while talking, coughing, and sneezing. Infection control recommendations, based on the assumption that direct contact transmission is the leading route, include maintaining social/physical distances, wearing masks, case isolation, contact tracing, and quarantine (Ferretti et al. 2020).

Despite knowledge that SARS-CoV-2 transmission is primarily through direct transmission, indirect transmission - or transmission occurring due to interaction with a contaminated environment – remains possible. People infected with SARS-CoV-2 shed the virus into the environment, as evidenced by extensive environmental contamination detected on surfaces in cruise ships, hospitals, and XXX (Ong et al. 2020; Ye et al. 2020). Infective coronavirus, including SARS-CoV-2, persists in the environment, with experimental evidence of persistence on surfaces for prolonged periods up to 9 days (Kampf et al. 2020). Viruses readily transfer from contaminated surfaces to the skin upon contact (Julian, Leckie, and Boehm 2010; Lopez et al. 2013; Bidawid et al. 2004; Rusin, Maxwell, and Gerba 2002; Ansari et al. 1991) and from the skin to the mouth and saliva of individuals (Pitol et al. 2017; Rusin, Maxwell, and Gerba 2002). Taken together, this evidence suggests surface contamination poses a risk for indirect SARS-CoV-2 transmission, similar to other respiratory viruses (Boone and Gerba 2007).

Indirect transmission events of SARS-CoV-2, even if not the dominant transmission route, complicate infection control efforts using contact tracing. Contact tracing efforts focus on identifying people sharing spaces coincidentally with cases (Ferretti et al. 2020). Indirect transmission could occur in the absence of shared spaces. As an example, transmission of SARS-CoV-1 in a Taiwanese hospital led to nosocomial infection of 31 patients. In 6 (20%) of the patients, contact tracing failed to detect direct contacts with other SARS patients, although RNA of SARS-CoV-1 was detected throughout the hospital on drinking water buttons, beds, and chairs (Chen et al. 2004). Based on these findings, the authors suggest indirect transmission as the cause of transmission amongst a subset of those infected. (Chen et al. 2004). If indirect transmission is an important route for SARS-CoV-2, control strategies will necessarily have to integrate hand hygiene interventions and surface disinfection alongside contact tracing (Gottlieb et al. 2020).

Despite the potential importance of indirect transmission, it is difficult to estimate its importance relative to direct transmission (Bar-on et al. 2020). Quantitative Microbial Risk Analysis (QMRA) provides a framework for understanding health risks from indirect transmission and provides insights into potential impacts of infection control recommendations. Mechanistic models of fomite-mediated transmission events within the context of QMRA frameworks have been used to inform risks for children interacting with contaminated toys (Julian et al. 2009), sanitation workers collecting and processing urine for nutrient recovery (Bischel et al. 2019), transmission of norovirus within a houseboat (Canales et al. 2019), and impact of surface disinfection (Ryan et al. 2014). QMRA has also been adapted to evaluate risks for hospital transmission of

MERS-CoV through droplets and aerosolized particles. The analysis highlighted reductions in risk to hospital staff through mask use (>90% estimated risk reduction) and increased air exchange (up to 58% estimated risk reduction) (Adhikari et al. 2019).

In this study, a mechanistic model of indirect transmission within the QMRA framework is developed to estimate likelihood of transmission in community settings and inform guidance on surface disinfection strategies. Specifically, the risks of infection with SARS-CoV-2 are estimated for interactions with shared spaces (i.e., use of ATMs, buttons on cross walks and trains). Risk reductions are further estimated under various feasible surface disinfection strategies.

Materials and Methods

Hazard Identification

Whenever an infected individual coughs, sneezes or speaks, droplets containing pathogens make their way to the proximal surfaces (Bourouiba, Dehandschoewercker, and Bush 2014). It has been shown that SARS-CoV-2 can persist on surfaces like plastic, metal, or glass at room temperature for hours to days (Doremalen et al. 2020). Additionally, viruses are known to transfer from surfaces to the hands upon contact (Julian, Leckie, and Boehm 2010; Lopez et al. 2013; Bidawid et al. 2004; Rusin, Maxwell, and Gerba 2002; Ansari et al. 1991), as well as from hands to the lips and saliva of individuals (Rusin, Maxwell, and Gerba 2002; Pitol et al. 2017). Given the fact that people frequently touch their faces and the mucous membranes within the face (nose, eyes and mouth) (Kwok, Gralton, and McLaws 2015; Nicas and Best 2008), we have identified the indirect (surface-mediated) transfer of SARS-CoV-2 as a relevant transmission pathway. Therefore, this risk assessment is designed to explore the risks of infection associated with the surface-mediated transmission of SARS-CoV-2.

Exposure Assessment

Scenario definition

Only one potential exposure pathway was analysed: the indirect transmission of viruses through contaminated surfaces. Two different scenarios where modelled: single touch (frequently touched buttons) and multiple touches (ATM or cash machine). The stochastic and mechanistic model used to model the risk of surface-mediated transmission of SARS-CoV-2 infection is based on models described elsewhere (Julian et al. 2018, 2009).

Scenario 1. Single touch buttons. Frequently touched buttons such as traffic light buttons, train buttons, and elevator buttons are of risk concern due to their frequent use by multiple people. In this scenario, we modelled the risk of touching a contaminated button followed by touching mucous membranes on the face. The material of the button was assumed to be either plastic or steel. The sequence of events leading to the viral inoculation of the susceptible individual was considered to be the following: 1) contamination event (infected person coughing directly on the surface), 2) virus decay on the surface, 3) virus transfer from the surface to the finger, 4) virus transfer from the finger to the mucous membranes of the nose, mouth and eyes.

Scenario 2. Multiple touches. ATM/cash machines are another example of surfaces that are frequently visited by individuals and are not frequently cleaned, as they are located in public spaces. For this risk assessment model, the ATM was assumed to be made of steel. The sequence of events leading to virus inoculation was considered to be the following: 1) contamination event (infected person coughing directly on the surface), 2) virus decay on the surface, 3) virus transfer from the surface to the finger and from finger to surface through multiple contacts, 4) virus transfer from the finger to the mucous membranes in the face (eyes, mouth, nose).

Virus concentration and transfer

Viral loads in the saliva or sputum of symptomatic COVID-19 patients within the first 14 days of symptom onset were used as model input. The virus titers used in the risk assessment were measured using quantitative reverse-transcription polymerase chain reaction (RT-qPCR) (Wölfel et al. 2020; Pan et al. 2020; Kim et al. 2020; To et al. 2020). The RT-qPCR method estimates the number of copies of viral RNA present in the

samples. Nevertheless, the presence of coronavirus RNA does not imply the presence of infectious viruses. In risk assessments whenever data on the concentration of infectious viruses is not available, it is commonly accepted to use a gene copies to infectivity ratio to convert the concentration measured in gene copies to the concentration of infective viruses (Chigor, Sibanda, and Okoh 2014). The gene copy number to infectivity ratio is, to our knowledge, not available for SARS-CoV-2. In the absence of SARS-CoV-2 data, we used the relationship reported for seasonal A(H1N1), influenza A(H3N2), and influenza B Ip et al. (2015) (Table 1). Both, influenza viruses and coronaviruses, are enveloped, RNA viruses with similar sizes.

The concentration of viruses in the surface after inoculation (through cough) was estimated using the following equation:

$$C(0) = \frac{C_{sp} V_s}{\frac{4\pi x_i^2}{a}} \tag{1}$$

where $C(0)$ [virus/cm^2] is the concentration of virus in the surface, V_s [mL/cough] is the volume of saliva expelled per cough, C_{sp} [virus/mL] is the concentration of infective viruses in the saliva or sputum, x_i [cm] is the inoculation distance or the distance between the surface and the infected individual at the time of the cough for activity i, and a is the XXX. This equation assumes that the droplets are expelled in a conical shape and a proportion of the spheric part of the cone is in contact with the surface. After surface inoculation, the concentration of the virus on the surface at time = t was estimated using the following equation:

$$C(t) = C(0)e^{-nt} \tag{2}$$

where $C(t)$ [virus/cm^2] is the concentration of infective viruses at time t, $C(0)$ [virus/cm^2] is the initial concentration of virus in the surface, t[min] is the time lapsed after surface inoculation, and n [m^{-1}] is the decay rate of the virus in the selected surface (metal or plastic). The concentration of virus on the hand after a single touch was estimated to be a function of the transfer efficiency of viruses between the hands and the surfaces. The concentration of viruses in the hand after multiple touches was estimated as reported elsewhere (Julian et al. 2009, 2018), where the transfer of virus is a function of the gradient in the concentration of viruses bwteen the hand and the surface.

$$C_{f_f} = C(t)TE_{sh} \tag{3}$$

or

$$C_{f_f} = (C(t) - C_{f_i})TE_{sh} + C_{f_i} \tag{4}$$

where C_{f_i} and C_{f_f} [virus/cm^2] are the initial and final concentration of virus in the finger, $C(t)$ [virus/cm^2] is the concentration of virus in the surface at time = t, TE_{sh}[%] is the transfer efficiency of viruses between surfaces and hands. The dose of viruses that entered the susceptible individual through facial membranes, D [virus], was estimated as follows:

$$D = C_{f_f} S_{fm} TE_{hm} \tag{5}$$

where C_{finger_f} [virus/cm^2] is the final concentration of virus in the finger, S_f [cm] is the surface area of the finger in contact with the mucous membranes, and TE_{hm} [%] is the transfer efficiency of the virus from the hand to the mucous membranes.

Dose-response

In the case of highly virulent pathogens, where no prophylaxis is available, it is common practice to use data of animal trials to generate dose-response models. The dose-response relationship used in this model was obtained from the QMRA wiki http://qmrawiki.org/experiments/sars and is based on two studies (De Albuquerque et al. 2006; DeDiego et al. 2008) of SARS-CoV and Murine hepatitis virus (MHV-1) infection in mice. MHV is a commonly used surrogate for human coronaviruses. The risk of infection was estimated with the following equation:

$$P_{inf} = 1 - e^{-kD} \tag{6}$$

where P_{inf} [%] is the probability of infection, k [-] is the infectivity parameter of the exponential model and D [virus] is the dose of virus that entered the individual through mucous membranes.

Model parameters used in the risk assessment

Parameter	Units	Description	Input values / Equation	Distribution	Reference and comments
C_{spGC}	gene copies/mL	Concentration of SARS-CoV-2 in sputum or saliva	Log_{10} gene copies/mL (data set)	ReSample	(Wölfel et al. 2020; Pan et al. 2020; Kim et al. 2020; To et al. 2020) RT-qPCR data from 9, 2, 2, and 23 patients with COVID-19
$GC : TCID_{50}$	-	Genome copies to infectious virus conversion factor	10^2-10^3	Uniform	(Ip et al. 2015) Mean RT-qPCR to TCID_{50} ratio of 708, 547, and 185 gene copies per TCID_{50} for seasonal A(H1N1), A(H3N2), and influenza B, respectively
C_{sp}	TCID_{50}/mL	Concentration of infective SARS-CoV-2 in sample	$C_{sp} = \frac{C_{spGC}}{GC:TCID_{50}}$	-	calculated
V_s	mL	Volume of saliva expelled per cough	0.0484-0.0396	uniform	(Nicas and Jones 2009) volume = 0.044mL, (Adhikari et al. 2019) uniform ± 10%

Parameter	Units	Description	Input values / Equation	Distribution	Reference and comments
$N_{cgh/min}$	min^{-1}	Number of coughs per minute	0.57(1)	Normal	(Leung et al. 2020), based on data of 17 individuals with seasonal CoV
t_{ATM}	min	Time spent on the ATM	0.75(0.38)	Normal	This study. Otained from 20 hours of observational data
$t_{btw-ATM}$	min	Time between visits	0.13, 0.80	Weibull	This study. Otained from 20 hours of observational data
$t_{btw-btn}$	min	Time between pressing button	1-20	Uniform	Assumed
x_{ATM}	cm	ATM inoculation distance	40	Point value	This study. Assumed from the observational data
x_{btn}	cm	Button inoculation distance	50	Point value	Assumed
$t_{\frac{1}{2}stl}$	min	Half life of CoV-2 in steel	338(35)	Normal	Doremalen et al. (2020), SARS-CoV-2 infectivity assays, 40% RH and 21-23°C
$t_{\frac{1}{2}pl}$	min	Half life of CoV-2 in plastic	409(39)	Normal	Doremalen et al. (2020), SARS-CoV-2 infectivity assays, 40% RH and 21-23°C
n_x	min^{-1}	Decay rate in surface x (steel or plastic)	$n_x = \frac{ln(2)}{t_{\frac{1}{2}}}$	-	calculated

Parameter	Units	Description	Input values / Equation	Distribution	Reference and comments
TE_{sh-stl}	%	Transfer efficiency of virus between steel to hand	37.4(16)	Normal	Lopez et al. (2013), transfer efficiency of viruses (MS2) between surface and skin at 40-65% humidity
TE_{sh-pl}	%	Transfer efficiency of virus between plastic to hand	79.5(21.2)	Normal	Lopez et al. (2013), transfer efficiency of viruses (MS2) between surface and skin at 40-65% humidity
TE_{hm}	%	Transfer efficiency from hand to mucouse membranes	20(6.3)	Normal	(Pitol et al. 2017), transfer efficiency of viruses (MS2) from hand to saliva
A_f	cm^2	Finger surface area	3.9-5.9	Uniform	Fractional surface area of partial finger (AuYeung, Canales, and Leckie 2008) times average hand surface area (US Environmental Protection Agency 2011)
k	PFU^{-1}	Parameter of the exponential dose-response	0.00107, 0.00135, 0.00680	Triangular	Data obtained from QMRAwiki, based on 2 studies De Albuquerque et al. (2006), DeDiego et al. (2008), using the from 0.5th, 50th, and 99.5th percentiles as min, mode, and max
:–	:–	:–	:–	:–	:–

The input parameters of the distributions are: Normal: mean (SD); Uniform: lower-bound - upper-bound; Triangular: min, mode, max; Weibull: scale, shape.

Risk Characterization

Monte Carlo simulation: method is used to incorporate uncertainty and variability of the input parameters in the risk characterization.

Sensitivity analysis

A sensitivity analysis was performed to investigate hot the variabilty and uncertainty of the parameters in the model onfluenced the estimated risks. The sensitivity was estimated using Spearman correlation coefficients between the inputs and outputs of the model.

Results and Discussion

"Persons that are sneezing and/or coughing are advised by governments to stay at home."

SARS-CoV-2 QMRA model design to investigate the relative contribution of different transmission routes (contact, droplet, inhalation) for healthcare workers suggested that, although fomite-mediated transmission is not the main route of expossure, it accounts for 8% of the probability of infection without the use of PPE (Jones 2020).

"The guidance also includes considerations based on the current level of community transmission,"

Supporting Information

Author Information

Aknowledgements

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