

# Draft 2

Ana Karina

4/7/2020

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

### Abstract

### Introduction

### Materials and Methods

### Hazard Identification

Whenever an infected individual coughs, sneezes or speaks, droplets containing pathogens make their way to the proximal surfaces (Bourouiba, Dehandschoewerker, 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 were 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; ???).

*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:

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

where  $C(0)$  [virus/cm<sup>2</sup>] 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:

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

where  $C(t)$  [virus/cm<sup>2</sup>] is the concentration of infective viruses at time  $t$ ,  $C(0)$  [virus/cm<sup>2</sup>] is the initial concentration of virus in the surface,  $t$  [min] is the time lapsed after surface inoculation, and  $n$  [m<sup>-1</sup>] 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 between the hand and the surface.

$$C_{ff} = C(t)TE_{sh} \quad (3)$$

or

$$C_{ff} = (C(t) - C_{fi})TE_{sh} + C_{fi} \quad (4)$$

where  $C_{fi}$  and  $C_{ff}$  [virus/cm<sup>2</sup>] are the initial and final concentration of virus in the finger,  $C(t)$  [virus/cm<sup>2</sup>] 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:

$$D = C_{ff}S_{fm}TE_{hm} \quad (5)$$

where  $C_{finger_f}$  [virus/cm<sup>2</sup>] 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:

$$P_{inf} = 1 - e^{-kD} \quad (6)$$

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 <sub>10</sub> 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 calculated
$C_{sp}$	$TCID_{50}$ /mL	Concentration of infective SARS-CoV-2 in sample	$C_{sp} = \frac{C_{spGC}}{GC:TCID_{50}}$	-	
$V_s$	mL	Volume of saliva expelled per cough	0.0484-0.0396	uniform	(Nicas and Jones 2009) volume = 0.044mL, (Adhikari et al. 2019) uniform $\pm 10\%$

Parameter	Units	Description	Input values / Equation	Distribution	Reference and comments
$N_{cgh/min}$	$\text{min}^{-1}$	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. Obtained from 20 hours of observational data
$t_{btw-ATM}$	min	Time between visits	8.4(7.1)	Normal	This study. Obtained from 20 hours of observational data
$t_{btw-btn}$	min	Time between pressing button	0.5-20	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
$n_x$	$\text{min}^{-1}$	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 <sup>2</sup>	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 <sup>-1</sup>	Parameter of the exponential dose-response	0.00107, 0.00135, 0.00680	Triangular	Data obtained from QMRWiki, 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 the variability and uncertainty of the parameters in the model influenced the estimated risks. The sensitivity was estimated using Spearman correlation coefficients between the inputs and outputs of the model.

## **Results and Discussion**

## **Supporting Information**

## **Author Information**

## **Aknowledgements**

## **References**

- Adhikari, Umesh, Alexandre Chabrelie, Mark Weir, Kevin Boehnke, Erica McKenzie, Luisa Ikner, Meng Wang, et al. 2019. "A Case Study Evaluating the Risk of Infection from Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) in a Hospital Setting Through Bioaerosols." *Risk Analysis* 39 (12): 2608–24. <https://doi.org/10.1111/risa.13389>.
- Ansari, S, V Springthorpe, S Sattar, S Rivard, and M Rahman. 1991. "Potential role of hands in the spread of respiratory viral infections: studies with human parainfluenza virus 3 and rhinovirus." *Journal of Clinical Microbiology* 29 (10): 2115–9. <http://jcm.asm.org/content/29/10/2115.full.pdf>.
- AuYeung, Willa, Robert A Canales, and James O Leckie. 2008. "The fraction of total hand surface area involved in young children's outdoor hand-to-object contacts." *Environmental Research* 108 (3): 294–99. <https://doi.org/10.1016/j.envres.2008.07.010>.
- Bidawid, S, N Malik, O Adegkunrin, S A Sattar, and J M Farber. 2004. "Norovirus cross-contamination during food handling and interruption of virus transfer by hand antisepsis: experiments with feline calicivirus as a surrogate." *J Food Prot* 67 (1): 103–9. <https://doi.org/10.4315/0362-028X-67.1.103>.
- Bourouiba, Lydia, Eline Dehandschoewercker, and John W. M. Bush. 2014. "Violent expiratory events: On coughing and sneezing." *Journal of Fluid Mechanics* 745: 537–63. <https://doi.org/10.1017/jfm.2014.88>.
- Chigor, Vincent N., Timothy Sibanda, and Anthony I. Okoh. 2014. "Assessment of the Risks for Human Health of Adenoviruses, Hepatitis A Virus, Rotaviruses and Enteroviruses in the Buffalo River and Three Source Water Dams in the Eastern Cape." *Food and Environmental Virology* 6 (2): 87–98. <https://doi.org/10.1007/s12560-014-9138-4>.
- De Albuquerque, Nadine, Ehtesham Baig, Xuezhong Ma, Jianhua Zhang, William He, Andrea Rowe, Marlena Habal, et al. 2006. "Murine Hepatitis Virus Strain 1 Produces a Clinically Relevant Model of Severe Acute Respiratory Syndrome in A/J Mice." *Journal of Virology*. <https://doi.org/10.1128/jvi.00747-06>.
- DeDiego, Marta L., Lecia Pewe, Enrique Alvarez, Maria Teresa Rejas, Stanley Perlman, and Luis Enjuanes. 2008. "Pathogenicity of severe acute respiratory coronavirus deletion mutants in hACE-2 transgenic mice." *Virology*. <https://doi.org/10.1016/j.virol.2008.03.005>.
- Doremalen, Neeltje van, Trenton Bushmaker, Dylan H. Morris, Myndi G. Holbrook, Amandine Gamble, Brandi N. Williamson, Azaibi Tamin, et al. 2020. "Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1." *The New England Journal of Medicine*, 1–3. <https://doi.org/10.1056/NEJMc2004973>.

- Ip, Dennis K. M., Lincoln L. H. Lau, Kwok Hung Chan, Vicky J. Fang, Gabriel M. Leung, Malik J. S. Peiris, and Benjamin J. Cowling. 2015. "The Dynamic Relationship between Clinical Symptomatology and Viral Shedding in Naturally Acquired Seasonal and Pandemic Influenza Virus Infections." *Clinical Infectious Diseases* 62 (4): 431–37. <https://doi.org/10.1093/cid/civ909>.
- Julian, Timothy R., Robert a. Canales, James O. Leckie, and Alexandria B. Boehm. 2009. "A model of exposure to rotavirus from nondietary ingestion iterated by simulated intermittent contacts." *Risk Analysis* 29: 617–32. <https://doi.org/10.1111/j.1539-6924.2008.01193.x>.
- Julian, Timothy R., Hasitha S. K. Vithanage, Min Li Chua, Matasaka Kuroda, Ana K. Pitol, Pham Hong Lien Nguyen, Robert A. Canales, Shigeo Fujii, and Hidenori Harada. 2018. "High time-resolution simulation of *E. coli* on hands reveals large variation in microbial exposures amongst Vietnamese farmers using human excreta for agriculture." *Science of the Total Environment* 635: 120–31. <https://doi.org/10.1016/j.scitotenv.2018.04.100>.
- Julian, T. R., J. O. Leckie, and A. B. Boehm. 2010. "Virus transfer between fingerpads and fomites." *Journal of Applied Microbiology* 109: 1868–74. <https://doi.org/10.1111/j.1365-2672.2010.04814.x>.
- Kim, Jin Yong, Jae Hoon Ko, Yeonjae Kim, Yae Jean Kim, Jeong Min Kim, Yoon Seok Chung, Heui Man Kim, Myung Guk Han, So Yeon Kim, and Bum Sik Chin. 2020. "Viral load kinetics of SARS-CoV-2 infection in first two patients in Korea." *Journal of Korean Medical Science* 35 (7): 1–7. <https://doi.org/10.3346/jkms.2020.35.e86>.
- Kwok, Yen Lee Angela, Jan Gralton, and Mary Louise McLaws. 2015. "Face touching: A frequent habit that has implications for hand hygiene." *American Journal of Infection Control* 43 (2): 112–14. <https://doi.org/10.1016/j.ajic.2014.10.015>.
- Leung, N H L, D K W Chu, E Y C Shiu, K H Chan, and... 2020. "Respiratory Virus Shedding in Exhaled Breath and Efficacy of Face Masks." *Nature Medicine*. <https://doi.org/10.1038/s41591-020-0843-2>.
- Lopez, Gerardo U., Charles P. Gerba, Akrum H. Tamimi, Masaaki Kitajima, Sheri L. Maxwell, and Joan B. Rose. 2013. "Transfer efficiency of bacteria and viruses from porous and nonporous fomites to fingers under different relative humidity conditions." *Applied and Environmental Microbiology* 79: 5728–34. <https://doi.org/10.1128/AEM.01030-13>.
- Nicas, Mark, and Daniel Best. 2008. "A study quantifying the hand-to-face contact rate and its potential application to predicting respiratory tract infection." *Journal of Occupational and Environmental Hygiene* 5 (6): 347–52. <https://doi.org/10.1080/15459620802003896>.
- Nicas, Mark, and Rachael M. Jones. 2009. "Relative contributions of four exposure pathways to influenza infection risk." *Risk Analysis* 29 (9): 1292–1303. <https://doi.org/10.1111/j.1539-6924.2009.01253.x>.
- Pan, Yang, Daitao Zhang, Peng Yang, Leo L M Poon, and Quanyi Wang. 2020. "Viral load of SARS-CoV-2 in clinical samples." *The Lancet Infectious Diseases* 20 (4): 411–12. [https://doi.org/10.1016/s1473-3099\(20\)30113-4](https://doi.org/10.1016/s1473-3099(20)30113-4).
- Pitol, A K, H N Bischel, T Kohn, and T R Julian. 2017. "Virus Transfer at the Skin-Liquid Interface." *Environmental Science and Technology*. <https://doi.org/10.1021/acs.est.7b04949>.
- Rusin, P, S Maxwell, and C Gerba. 2002. "Comparative surface-to-hand and fingertip-to-mouth transfer efficiency of gram-positive bacteria, gram-negative bacteria, and phage." *Journal of Applied Microbiology* 93: 585–92. <https://doi.org/10.1046/j.1365-2672.2002.01734.x>.
- To, Kelvin Kai Wang, Owen Tak Yin Tsang, Wai Shing Leung, Anthony Raymond Tam, Tak Chiu Wu, David Christopher Lung, Cyril Chik Yan Yip, et al. 2020. "Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study." *The Lancet Infectious Diseases* 20 (5): 565–74. [https://doi.org/10.1016/S1473-3099\(20\)30196-1](https://doi.org/10.1016/S1473-3099(20)30196-1).
- US Environmental Protection Agency. 2011. "Exposure Factors Handbook: 2011 Edition." *U.S. Environmental Protection Agency* 1: 1–1466. <https://doi.org/EPA/600/R-090/052F>.

Wölfel, Roman, Victor M. Corman, Wolfgang Guggemos, Michael Seilmaier, Sabine Zange, Marcel A. Müller, Daniela Niemeyer, et al. 2020. "Virological assessment of hospitalized patients with COVID-2019." *Nature*, 1–14. <https://doi.org/10.1038/s41586-020-2196-x>.