Technical Report for Time-Based N95 Reuse Risk Management

Much of the available literature on decontamination of N95 FFRs is a result of recent efforts to relieve the shortage of N95 FFRs during the SARS-CoV-2 outbreak. Because of this, some of the research cited in this document is not yet peer reviewed. **For clarity, wherever non-peer-reviewed results are cited in this report, the citation is preceded by a "*".**

Executive Summary

Time—simply waiting for a minimum period before re-using an N95 FFR that is stored in a clean, breathable environment at moderately humid, room temperature conditions—is potentially the simplest and lowest cost viral inactivation method. In addressing the global shortage of N95 Filtering Facepiece Respirators (N95 FFRs), time between uses is a first recommendation for decontaminating N95 FFRs between re-use in a healthcare setting (CDC, 2020b). However, published data on the lifetime of SARS-CoV-2 on surfaces are sparse, making it difficult to draw conclusions about decontamination on N95 FFRs.

In this report, we analyze recent literature, comparing results on a common quantitative basis. **This is an area where new experimentation is urgently needed to provide more clear, actionable advice.**

For an N95 FFR that is stored individually in a clean and breathable container at room temperature, a 7 day waiting period before reuse is expected to significantly decrease risk of exposure to SARS-CoV-2 via the N95 FFR. With additional precautions, such as individual storage in a clean, breathable container, user seal checks, hand hygiene, and proper donning and doffing, this waiting time can significantly reduce SARS-CoV-2 infection risk with re-use of N95 FFRs. This method will not protect against bacterial or fungal infection.

Viral inactivation is sensitive to temperature and humidity. **Storage at temperatures below 22°C or at very low or very high humidities is expected to significantly increase the acceptable waiting period. More data are needed to quantify these effects.**

1. Overview

The novel coronavirus (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) has led to a global shortage of N95 Filtering Facepiece Respirators (N95 FFRs, also referred to as "N95 masks"). In this document, we review the use of a waiting time between uses as a method to decontaminate N95 FFRs with the goal of increasing the useful lifetime of N95 FFRs worn by healthcare providers during the COVID-19 pandemic. Effective decontamination requires inactivation of the SARS-CoV-2 virus and maintenance of both the fit and filtration efficiency of the N95 FFR while minimizing the risk of cross-contamination.

Time—simply waiting for a minimum period before re-using an N95 FFR that is stored in a clean, breathable environment at room temperature conditions—is potentially the simplest and lowest cost viral inactivation method. Enveloped RNA viruses, such as the coronavirus SARS-CoV-2, eventually lose their infectious capacity at room temperature. The precise timing and variability of this process are addressed experimentally in a number of studies that we review in this document.

Here, we evaluate studies based on the time required to reach a 3-log level of viral inactivation. This is the time for the viral load to be reduced by a factor of 1000, which is the target level of reduction identified in FDA guidance documents for decontamination (FDA, 2020). The reduction in viral load may not be identical to the reduction in probability of infection. With a probabilistic dose-response model, e.g. (Watanabe et al., 2010), the viral infection risk decreases more slowly than the viral load decreases. For example, if the viral load decreases by 90%, the viral infection risk decreases by <90%.

In this report, we survey the existing literature, highlighting assumptions that are required to interpret the data and clear qualitative conclusions that can be drawn from multiple studies. A waiting period of 7 days (168 hr) encompasses the available experimental data on decontamination (as defined by 3-log decay on the sample mean) of a single N95 FFR and of a surgical mask. **This is an area where new experimentation is urgently needed to provide more clear, actionable advice.**

Reusing the same mask within a day (i.e. at next shift) is not expected to, in general, allow sufficient time for viral inactivation and is not recommended if the N95 is not also decontaminated via another effective method. Given the sensitivity of the virus to material and local environment, we do not have enough data to make a precise recommendation that encompasses all N95 FFR models in reasonable room temperature conditions. **For an N95 FFR that is stored individually in a clean and breathable container at room temperature, a 7 day waiting period before reuse is expected to significantly decrease risk of exposure to SARS-CoV-2 via the N95 FFR.**

The time needed to reduce infection risk of an enveloped RNA virus to an acceptable level depends on the amount that is originally deposited, the threshold for infectiousness, and the environmental conditions including temperature, humidity, surface type, and the presence of other agents including proteins and salt. **Critically, cooler temperatures will extend the life of SARS-CoV-2. For example, storage at temperatures colder than tested (e.g. in an unheated cabinet, basement or vehicle where temperature falls below 22°C) could substantially extend the life of the virus beyond what is described.**

2. Status of Federal Guidance

In this unprecedented COVID-19 pandemic, due to a limited supply of N95 FFRs, the Centers for Disease Control and Prevention (CDC) have provided guidance that healthcare workers can practice extended use or limited reuse of N95 FFRs (CDC, 2020a). In addition, the CDC has provided guidance to hospitals on methods for decontaminating N95 FFRs during a crisis (CDC, 2020b).

The Occupational Safety and Health Administration (OSHA) states that cosmetics or other barriers should not be present during respirator use (OSHA, n.d.). Emergency use authorizations (EUAs) that the FDA has granted for N95 FFR decontamination during the COVID-19 pandemic also stipulate that cosmetics not be present on respirators sent for decontamination (*Instructions for Healthcare Personnel: Preparation of Compatible N95 Respirators for Decontamination by the Battelle Memorial Institute Using the Battelle Decontamination System*, 2020).

After decontamination, the CDC recommends that a 'user seal check' is performed when the respirator is donned to ensure adequate seal (CDC, 2020b). A user seal check after every decontamination cycle is especially important because there is evidence that the fit factor of N95 respirators decreases with numerous don/doffs (Bergman et al., 2012).

Per FDA guidelines for N95 FFR decontamination EUAs, virucidal decontamination requires ≥ 3-log reduction (corresponding to a 99.9% reduction) in viral activity (FDA, 2020). Based on this guideline, we describe a process as sufficiently "decontaminating" or "inactivating" only when it leads to a ≥ 3-log reduction in viral activity. **Note that our definition of decontamination in this report, unless otherwise specified, only considers virucidal activity and does *not* consider mycobactericidal or sporicidal activity**, for which the FDA has other guidelines (FDA, 2020). **N95 FFR decontamination processes for SARS-CoV-2 do not necessarily result in sterilization (killing of all microorganisms) of the N95 FFR**.

A first recommendation from the CDC's recent guidance on reuse (CDC, 2020b) is for each healthcare worker to be issued at least five N95 FFRs, to wear one per day, and to store each in a breathable paper bag between uses. The healthcare worker is to rotate through the five N95 FFRs so that there is a waiting period of at least 5 days before reuse.

Any new methods for decontamination should be verified through organizations' internal processes, which may include FDA clearance prior to implementation. Please refer to current CDC guidelines that are updated regularly, as well as N95DECON's Full Legal Disclaimer.

3. Mechanism

For N95 FFRs that are stored at room temperature, environmental conditions can eventually lead to disruption of the virus envelope, proteins, or RNA. Viral inactivation can additionally be affected by the surface material, protein content, pH, chemicals, and the medium in which the virus is prepared (e.g. Coulliette et al., 2013; Firquet et al., 2015). Details of how this inactivation happens are beyond the scope of this report.

Virus inactivation with time is often assumed to follow first-order kinetics (e.g. Seo et al., 2012), which means that the number of active organisms decreases at a rate proportional to the number that exist at that moment in time. The assumption of first-order kinetics implies 1) an exponential decrease with time in the number of infectious organisms, characterized by a time constant (also called a rate constant), and 2) that the fold-decay in a given time-interval does not depend on the size of the initial viral inoculum, i.e. the time to get from 1000 active particles to 1 active particle is the same as the time to get from 5000 to 5.

On a real mask, different virus particles may experience dramatically different local environments, leading to a broad distribution of decay rates and a deviation from the idealized exponential decay at the population level. Many experiments observe non-exponential decay, a characteristic feature of which is that the decay rate becomes slower over time. One should thus be cautious in extrapolating measured decays beyond the measurement interval.

Thus, 3-log decay time is influenced by a number of environmental factors and ideally should be assessed via direct experiment.

4. Potential for SARS-CoV-2 Inactivation

Experiments that test persistence and inactivation of a virus on a surface all share the same high-level steps:

(1) Re-suspend virus in a medium
(2) Inoculate this suspension onto the material being tested
(3) Wait a specific amount of time
(4) Recover the virus from the material
(5) Quantify amount of infectious virus recovered
(6) Repeat in parallel steps (2)–(5) for different wait times
(7) Fit data to a model
(8) From the model fit, report a number that characterizes how the virus is inactivated over time.

Different choices in each of these steps can lead to different reported results for how virus inactivation changes with time.

In this section, we summarize the recent papers that study SARS-CoV-2 and two earlier papers that study other coronaviruses applied to materials relevant to a hospital setting. In a more extensive review of earlier literature without any experiments on SARS-CoV-2, (Kampf et al., 2020) focus on the survival of coronaviruses on surfaces and coronavirus inactivation with biocidal agents. Across experiments reviewed there, there are large variations in the reported "persistence" time for viruses even on nominally the same material in similar conditions. For example, across the cited experiments, the reported times for the un-defined "persistence" span more than an order of magnitude from 8 *hours* to 9 *days*. Part of this variation is likely due to what "persistence" time means; it is undefined in (Kampf et al., 2020) and the papers that are cited in that review report varying metrics.

In contrast, here we attempt to compare all papers using the same metric of inactivation: the 3-log decay time. We focus on medical materials and SARS-CoV-2 experiments. Even when making the comparison of the 3-log time across different studies, varying experimental and mathematical choices in the published literature lead to substantial variations in, for example, the reported 3-log decay time on stainless steel.

Studies are summarized in this section and the resulting 3-log decay times are quantified in the data tables below. Methods are highlighted in this section to show the variations in experimental choices.

In a non-peer-reviewed preprint, **(*Fischer et al., 2020)** evaluate the stability of SARS-CoV-2 on samples of stainless steel and N95 filter material from AOSafety N9504C respirators. The virus is recovered from the material by adding 1 mL of medium. The data are fit using Bayesian regression assuming exponential decay. The 3-log decay time from this study is the reported median "time to one thousandth" from Bayesian regression. For the N95 FFR, that time is 13 hr, with a 95% confidence interval spanning 11–15 hr.

In the table below, the maximum measured time is where the estimated mean titre across replicates is shown in plotted data to reach the measurement threshold (Morris,

personal communication, April 22, 2020). The data at https://github.com/dylanhmorris/n95-decontamination show the time intervals used.

(van Doremalen et al., 2020) test both SARS-CoV-1 and SARS-CoV-2, choosing an inoculum at a level relevant to samples from the human respiratory tract. For the test on cardboard, the virus is recovered by swabbing the surface and adding 1 mL DMEM. For other surfaces, the virus is recovered by adding 1 mL DMEM. Data show that the viruses persist longer on plastic and stainless steel than on cardboard or copper. Virus persistence as an aerosol is also significantly less than on stainless steel or plastic.

It is noted in this paper that data for copper and cardboard do not show exponential (or even monotonic) decreases in viral load with time and thus fits are to be interpreted with caution.

For the data tables below, the maximum time at which data were measured is the time at which the estimated titre from all three replicates first reaches the threshold for detectability. In almost all cases this time is shown on the plots and the raw data are on Github at https://github.com/dylanhmorris/sars-cov-2-stability.

Though the raw data in (van Doremalen et al., 2020) for stainless steel are the same as in (*Fischer et al., 2020), the two papers use different titre inference methods (Morris, personal communication, 4/19/20). To estimate the 3-log decay time, we multiply the median reported half-life by 9.966.

(Chin et al., 2020) tests SARS-CoV-2 on various surfaces, including the inner and outer layer of a surgical mask. While N95 FFRs differ from surgical masks, the N95 FFRs commonly used in medical settings, sometimes referred to as “surgical N95 FFRs,” are FDA-certified for functionality as surgical masks. Without further information about the material used by (Chin et al., 2020), we cannot judge the relevance of this experiment to N95 FFRs. **The decay time reported by (Chin et al., 2020) is substantially longer than what is reported in the other measurements reviewed here. In the interest of being conservative, we have included this result in our overall assessment.**

The stability of the virus in the viral transport medium at varying temperature is also tested in (Chin et al., 2020). Using a simple linear fit to the reported log data yields 3-log decay times of 2070 hr at 4℃ (the temperature of a household refrigerator), 167 hr at 22℃ (‘room temperature’), and 20 hr at 37℃. This implies that for a temperature change of 10℃, the 3-log decay time could change by a factor of 4 or 5. Though these data were taken for virus in solution, not on a surface, they show that virus stability is highly sensitive to temperature.

In this study, the virus was recovered from each material by soaking in 200 uL of viral transport medium for 30 min. SARS-CoV-2 was found to remain infectious longer on non-porous materials (glass, stainless steel, plastic) than on porous materials (paper, tissue paper, wood, cloth).

Data were fit to a bi-phasic model, instead of to the simple exponential model. Data were fit assuming that the kinetics follow exponential decay with one time constant at the beginning and a longer time constant for much longer times. Thus, the reported model fits

cannot be directly compared with model fits from other papers that assume exponential decay with one time constant.

Instead, the 3-log decay time given in the tables below has been deduced directly from the reported raw data instead of from the model fit. Raw data are reported at 0 min, 30 min, 3 hr, 6 hr, 1 day, 2 days, 4 days, 7 days. In the table below, the 3-log decay time is the time at which the mean measurement shows a 3-log reduction from the mean measurement at 0 min. If the detection threshold is reached before the 3-log reduction, the 3-log decay time is reported here as greater than the time at which the threshold was reached. The maximum measured time in the table below is the time at which the reported data are first at the measurement threshold (undetectable) or the last time at which data were reported (even if still above threshold).

For the surgical mask on the outer layer, it is notable that there is a relatively large standard deviation (0.46) on the final measurement (mean of 2.79), which is both the measurement that defines the 3-log decay time and the longest measurement made.

(Lai et al., 2005) tested the earlier SARS-CoV-1 virus, measuring its lifetime in stool and respiratory specimens as well as on paper (from a laboratory request form), a disposable gown made of impervious material, and a cotton gown. To recover the virus, material was inoculated into cell culture tubes and incubated.

In the stool samples, the virus persisted longer at higher pH. In respiratory specimens, the virus persisted above the 3-log level for about a week at room temperature and 3 weeks at 4℃.

The raw data were not shown; instead the times to inactivation (at the measurement threshold) for three different starting titres were reported for each material. In the table below, the maximum measured time is the reported “time taken to inactivate” for the largest titre of 10^6 $TCID_{50}$/mL (where $TCID_{50}$ is the median tissue culture infectious dose).

Estimating the 3-log decay time from such minimal data requires many assumptions. Two possible approaches, both assuming that the system follows first-order kinetics, are:

1) If the system follows first-order kinetics, the time to inactivation should be a linear function of the log of the titre. With the three data points given, this fit is good only for the case of the disposable gown. For all three materials, this method yields a 3-log decay time that is on the order of twice the longest measurement time.
2) Alternatively, if it is assumed that the threshold measurement for inactivation is 1 PFU (plaque-forming unit), a first-order kinetics model would yield a 3.5-log-decay from the inoculation using the titre 10^6 $TCID_{50}$/mL to the threshold. This method of estimation yields a number that is less than the total measurement time.

Both methods were applied to the data from this publication. These two methods yield different results for each material case and the reported one in the table below is the larger of the two (to be conservative). These numbers should be considered to be very rough estimates; the difference in the estimates produced by these methods further illustrates the need for more data and evaluation of models used for fitting.

(Sizun et al., 2000) evaluates the lifetime of human coronaviruses HCoV-229E and HCoV-OC43 when dried on surfaces and in various aqueous solutions. The difference in survival times in the different aqueous suspensions points to a challenge in doing experiments on surfaces: if there are persistent droplets, the liquid in which the virus is suspended can impact the survival time.

To recover the virus from the materials, the material was incubated in a sonicating water bath and eluate is analyzed. The 3-log decay time cannot be extracted from the data in this paper because the data are only presented as a plot on a linear (not logarithmic) scale and thus this paper is not summarized in the data tables below. For both viruses, the infectivity in the first 3 hr drops the slowest for aluminum, compared to latex gloves and sterile sponges.

5. Data Summary Tables

The table below summarizes the above-mentioned tests of virus lifetime on surfaces. Many of these papers include other experiments (such as lifetime in stool and respiratory specimens or responsiveness to disinfectants); those additional results are not summarized here. Cited numbers below are mean (for frequentist analysis) or median (for Bayesian analysis) unless otherwise specified. All log values are assumed to be base 10.

Material	***Virus (medium*)***	***Starting Titre/ Inoculum***	***Environmental Conditions***	***Maximum measured time (hr)****	***Estimated 3-log decay time (hr)*****	***Ref***
Personal Protective Equipment Materials						
N95 FFR material	SARS-CoV-2	10^5 $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	24	13	(*Fischer et al., 2020)
Surgical mask, inner layer	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	168	96	(Chin et al., 2020)
Surgical mask, outer layer	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	168	168	(Chin et al., 2020)
Disposable gown	SARS-CoV-1 (PBS)	10^4–10^6 $TCID_{50}$/mL; apply 5 µL	*Not Reported*	48	70.5	(Lai et al., 2005)
Cotton gown	SARS-CoV-1 (PBS)	10^4–10^6 $TCID_{50}$/mL; apply 5 µL	*Not Reported*	24	46.1	(Lai et al., 2005)
Metals						
Stainless steel	SARS-CoV-2	10^5 $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	48	48.2	(*Fischer et al., 2020)

	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	168	168	(Chin et al., 2020)
	SARS-CoV-2	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	96	56.1	(van Doremalen et al., 2020)
	SARS-CoV-1	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	72	41.5	(van Doremalen et al., 2020)
Copper	SARS-CoV-2	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	8	7.7	(van Doremalen et al., 2020)
	SARS-CoV-1	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	24	14.9	(van Doremalen et al., 2020)
Organic Materials						
Wood	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	48	6	(Chin et al., 2020)
Cloth	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	48	>24	(Chin et al., 2020)
Other						
Glass	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	96	48	(Chin et al., 2020)
Banknote	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	96	48	(Chin et al., 2020)
Paper-based Materials						
Cardboard	SARS-CoV-2	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	48	34.5	(van Doremalen et al., 2020)
	SARS-CoV-1	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23°C, 40% RH	24	5.9	(van Doremalen et al., 2020)
Tissue paper	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	3	0.5	(Chin et al., 2020)
Paper	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22°C, ~65% RH	3	>0.5	(Chin et al., 2020)
	SARS-CoV-1 (PBS)	10^{4}–10^{6} $TCID_{50}$/mL; apply 5 µL	*Not Reported*	24	42.7	(Lai et al., 2005)
Plastic						

Plastic (type not specified)	SARS-CoV-2 (VTM)	$10^{7.8}$ $TCID_{50}$/mL; apply 5 µL	22℃, ~65% RH	168	48	(Chin et al., 2020)
	SARS-CoV-2	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23℃, 40% RH	96	67.9	(van Doremalen et al., 2020)
	SARS-CoV-1	10^{5} $TCID_{50}$/mL; apply 50 µL	21–23℃, 40% RH	96	75.2	(van Doremalen et al., 2020)

*VTM=viral transport medium. PBS=phosphate buffered serum. If not named, the medium is not specified in the given study.
**The maximum measured time is estimated differently for each reference. See details in the text above.
***The method by which the 3-log decay time is estimated from the published data varies by reference. See details in the text above.

6. Integrity of N95 Filtering Facepiece Respirators

If N95 FFRs are stored in a clean, vented container at *room temperature* between uses, a primary risk to integrity is the degradation in fit over multiple donnings and doffings. For some N95 FFR models, fit was found to be unacceptable after 5 don/doff cycles, while others maintained fit for >15 don/doff cycles (Bergman et al., 2012). Storage conditions should not deform or crush the N95 FFR.

Furthermore, risk with reuse can be reduced by discarding N95 FFRs with visible blood, hair, soiling with facial cosmetics, or damage (CDC, 2020a; OSHA, n.d.).

7. Strategies

NIOSH and the CDC give recommendations for N95 FFR reuse, including storage in a clean, breathable container (e.g., paper bag) or hanging N95 FFRs between reuse (CDC, 2020a). N95 FFRs contaminated with blood, respiratory or nasal secretions, or other bodily fluids should be discarded (CDC, 2020a). N95 FFRs should be re-used only by the original user.

Using time as a method for virus inactivation is viewed as risk mitigation for extraordinary circumstances rather than complete decontamination or sterilization. Risk is further mitigated if a re-used N95 FFR is treated, in terms of hand hygiene for example (CDC, 2020a), as if the N95 FFR might still be contaminated.

Given the unknowns in using time for decontamination, proper donning, doffing, and hand hygiene are critical for reducing risk. (Brady et al., 2017) shows that improper doffing of an N95 FFR can lead to higher contamination from N95 FFR to hands than proper doffing and reuse (without decontamination). Hand hygiene is another part of the recent NIOSH / CDC recommendations (CDC, 2020a).

As summarized above, virus persistence is expected to be much greater at lower temperatures. The presented studies all use moderate humidity; higher or lower humidity may increase virus inactivation time (Lin & Marr, 2020; Coulliette et al. 2013).

After the waiting period and before re-use, physical inspection and a 'user seal check', as recommended by the CDC, should be performed to ensure N95 FFR integrity and adequate seal (CDC, 2020b).

8. Primary Risks and Unknowns

Enveloped RNA viruses such as SARS-CoV-2 tend to be more rapidly inactivated by time than other clinically relevant pathogens that could co-inoculate an N95 such as mycobacterium, antibiotic resistant bacteria, bacterial spores, or other pathogens. An adequate wait time that inactivates SARS-CoV-2 may not inactivate other common pathogens. Analysis of an appropriate waiting time for inactivation of other common pathogens is currently beyond the scope of this report.

The existing literature leaves several gaps that necessitate judgment in choosing a time period for decontamination of SARS-CoV-2. The range of values across papers for stainless steel illustrates this: (Chin et al., 2020) shows 168 hr, (van Doremalen et al., 2020) shows 56 hr and *from the same data* (*Fischer et al., 2020) reports 48.2 hr. The discrepancy between (Chin et al., 2020) and (van Doremalen et al., 2020) cannot be reconciled from the available data and it presents a large uncertainty on enumerating an appropriate waiting period for decontamination.

Here, we enumerate some of the experimental and modeling choices and assumptions that leave uncertainty.

(1) The assumption of first-order kinetics is a mathematically-convenient assumption that has proven to be effective (Peleg & Cole, 1998). However, it is not always the best model for fitting the data. Indeed, in (Chin et al., 2020), the data for survival of CoV-2 on different surfaces are fit to a model where the time constant in the first-order kinetics is different in the first hour than over the rest of a day. None of the studied papers give assessments of the quality of one model vs another. As an example of a different model for virus kinetics, in (Seo et al., 2012), a Weibull model is found to fit the data better for murine norovirus.

(2) If the first-order kinetics model is not the right model, then the time for each additional log of decay might be longer than for the previous log of decay.

(3) Model fits may not be appropriate for 3-log decay time if the assessed time is much longer than the time of the experiment. In (Chin et al., 2020), 7 days is the longest measurement time used. In (van Doremalen et al., 2020), the experiments are less than 100 hr at maximum and extrapolation to the 3-log decay time may be longer than what was measured.

(4) It is expected that the time constant, even in a first-order model, will depend on environmental conditions. In (Vejerano & Marr, 2018), for example, it is shown that the relative humidity determines the evaporation rate of a droplet and it is argued that virus survival is impacted by the micro-environment of this evaporating droplet. Other viruses has been shown to persist longer at extreme values of humidity than at moderate values (Lin & Marr, 2020). Temperature has a dramatic impact on virus survival times as shown, for example, in (Seo et al., 2012) for the norovirus and in (Chin et al., 2020) for SARS-CoV-2. User conditions may be highly variable and different from the controlled

environment of a lab. **For example, storage at temperatures colder than tested (e.g. in an unheated cabinet, basement or vehicle where temperature falls below 22°C) could substantially extend the life of the virus beyond what is described.**

(5) Even with the same model, *how* the data are analyzed can matter. (Peleg & Cole, 1998) give one example for how choices in fitting data to a model can matter. Incidentally, the data for stainless steel in (van Doremalen et al., 2020) and in (*Fischer et al., 2020) are reported to be the same data, with a difference in titer inference methods (Morris, personal communication, 4/19/20). That yields a difference of almost 10 hr in the 3-log decay time.

(6) Experiments in the literature use different viruses, different media, and different methods for recovering the virus from the surface and all of these can impact the results. (Chin et al., 2020) uses viral medium and the other two SARS-CoV-2 studies do not report what medium is used. This may mean that the studies presented here underestimate the inactivation time for a virus protected by mucus, for example.

(7) Virus inactivation times vary widely across different materials, as shown in the reviewed papers. These data are presented without a fundamental understanding of why a certain material might promote longer or shorter virus survival times. This creates a challenge in extrapolating from data on one material to inactivation times for another material. For example, the material of the N95 FFR in (*Fischer et al., 2020) may be different, from the point of view of virus inactivation, from the material used in the N95 FFRs that are marketed for use in medical settings. The surgical mask used in (Chin et al., 2020) is not specified and it is unknown how this material compares to a given N95 FFR. In general, N95 FFRs are fabricated from layers of differently-textured polypropylene, and layers sometimes include other materials like polyester. They have hydrophobic and hydrophilic layers varying by model. Surgical N95 FFRs (which are FDA-certified for additional functionality as surgical masks, and which are typical in healthcare settings) commonly have an additional hydrophobic outer layer, while non-surgical N95 FFRs may have a hydrophilic outer layer (Viscusi et al., 2009). Common models including the 3M 1860 additionally feature an external aluminum noseclip (*3M Technical Data Sheet: Disposable respirator, 1860, 1860S, N95*, 2018). These material differences are another source of uncertainty in the data.

In comparing the two peer-reviewed studies on SARS-CoV-2 (Chin et al., 2020; van Doremalen et al., 2020), the environmental conditions (in terms of temperature and humidity) are similar. There are two surfaces tested in both of these papers: stainless steel and plastic, without further details on the materials. When the results from these two references are compared *using the same gauge of persistence*—a 3-log decay in virus level—then the results are closer to each other than the large ranges given in (Kampf et al., 2020). From (Chin et al., 2020), the 3-log decay time of the mean SARS-CoV-2 on stainless steel is between 4 and 7 days. From (van Doremalen et al., 2020), it is ~2.3 days. (Chin et al., 2020) shows a 3-log decay time on plastic of 2 days and (van Doremalen et al., 2020) shows 68 hr (almost 3 days). **With the limited number of studies on SARS-CoV-2 and coarse data, the variation between different studies can be as much as 3–5 days.**

(van Doremalen et al., 2020) compares SARS-CoV-1 and SARS-CoV-2, which gives a sense of the uncertainty that may be incurred from extrapolating from the results of one virus to another virus. Across the 5 tested cases, these differences (median, extrapolated to 3-log decay) range from ~1 hr (for the short life of aerosols) to ~1 day (for cardboard).

(van Doremalen et al., 2020) gives 95% confidence intervals for each result. **These confidence intervals for the SARS-CoV-2, again extrapolating to the 3-log decay time, are approximately 1 day in all cases.**

Together, these results point to the high uncertainty in the published data and the need for more experiments.

In this report, we have used 3-log decay time as a standard way of comparing across different experiments. This choice is in the absence of a clear specification on the amount of viral load on an N95 FFR that constitutes “decontamination”. All N95 FFRs used in a clinical setting should be considered contaminated. The initial infectious viral load will greatly impact what the infection risk is after waiting a given period of time. N95 FFRs directly exposed to droplet or aerosol-generating procedures with infected patients would be more likely to require a longer duration of treatment.

9. Conclusions

SARS-CoV-2 and other enveloped viruses survive for a limited time on surfaces at room temperature; the precise time period needed for satisfactory inactivation depends on a number of environmental variables.

Though there are many modeling assumptions that go into the experiments as well as variability in the tested environments, across the literature surveyed here, there are clear qualitative conclusions that can be drawn:

- Coronaviruses survive longer at colder temperatures than at warmer temperatures, which makes storage temperatures a critical consideration in using time as a method of decontamination.
- Coronaviruses, including SARS-CoV-2, generally live longer on surfaces that are qualitatively described as smooth or non-porous, than on surfaces described as rough or porous. A notable exception from experiments is copper, which yields a very short lifetime for SARS-CoV-2 (van Doremalen et al., 2020). There is a need for a better understanding of which material properties determine virus lifetime on a surface.
- There is not a fundamental understanding of why SARS-CoV-2 might live longer one one surface than another and without that it is a challenge to extrapolate experimental results from one material to another.
- Proper donning, doffing, and hand hygiene are critical, irrespective of decontamination procedures.
- The risk of exposure to SARS-CoV-2 virus from an N95 FFR stored individually in a clean, breathable, room-temperature environment goes down the longer one waits before re-using the N95 FFR.

From the reviewed literature, a 5-day waiting period encompasses the 3-log decay time for tested coronaviruses on a variety of surfaces at room temperature conditions for most of the published results, including the most recent non-peer-reviewed experiment on an N95 FFR. The exceptions are: 4–7 days for stainless steel and 7 days for the outer layer of a surgical mask tested with SARS-CoV-2 (Chin et al., 2020). As explained above, the experimental results on the surgical mask are conservatively judged to be relevant for this discussion of N95 FFR decontamination.

An N95 FFR stored in a moderately-humid room-temperature environment (22°C, 40–65% relative humidity) will eventually achieve 99.9% reduction in viral load after some waiting period, thereby meeting the threshold for viral reduction from the FDA (FDA, 2020). The two most relevant studies show significant variation and yield **estimates between less than 1 day and about 1 week required for this decontamination time for SARS-CoV-2 on materials that could be relevant for an N95 FFR. This is an area where new experimentation is urgently needed to provide more clear, actionable advice.**

Because many factors regulate viral decay, users should understand that small changes in temperature, humidity, or initial high viral loads on a N95 FFR could reduce the margin of safety. More studies are needed to have higher confidence in recommendations, especially considering the range of room temperature conditions that exist in health care situations and the range of materials used for different models of N95 FFRs. It would be especially useful to have further studies that encompass measurement times well beyond the 3-log decay time and prepare the virus in a suspension of a medium that is similar to human mucus.

Irrespective of the waiting time that is chosen, proper donning and doffing of the N95 FFR and hand hygiene are critical. Moreover, this waiting time is only an estimate and it is not expected to decontaminate the N95 FFR against other pathogens or infectious agents.

References

3M Technical Data Sheet: Disposable respirator, 1860, 1860S, N95. (2018). 3M.

Bergman, M. S., Viscusi, D. J., Zhuang, Z., Palmiero, A. J., Powell, J. B., & Shaffer, R. E. (2012). Impact of multiple consecutive donnings on filtering facepiece respirator fit. *American Journal of Infection Control*, *40*(4), 375–380. https://doi.org/10.1016/j.ajic.2011.05.003

Brady, T. M., Strauch, A. L., Almaguer, C. M., Niezgoda, G., Shaffer, R. E., Yorio, P. L., & Fisher, E. M. (2017). Transfer of bacteriophage MS2 and fluorescein from N95 filtering facepiece respirators to hands: Measuring fomite potential. *Journal of Occupational and Environmental Hygiene*, *14*(11), 898–906. https://doi.org/10.1080/15459624.2017.1346799

CDC. (2020a, March 27). *Recommended Guidance for Extended Use and Limited Reuse of N95 Filtering Facepiece Respirators in Healthcare Settings*. https://www.cdc.gov/niosh/topics/hcwcontrols/RecommendedGuidanceExtUse.html

CDC. (2020b, April 9). *Decontamination and Reuse of Filtering Facepiece Respirators*. https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/decontamination-reuse-respirators.html

Chin, A., Chu, J., Perera, M., Hui, K., Yen, H.-L., Chan, M., Peiris, M., & Poon, L. (2020). Stability of SARS-CoV-2 in different environmental conditions. *The Lancet Microbe*, *medrxiv;2020.03.15.20036673v2*, 2020.03.15.20036673. https://doi.org/10.1101/2020.03.15.20036673

Coulliette, A. D., Perry, K. A., Edwards, J. R., & Noble-Wang, J. A. (2013). Persistence of the 2009 pandemic influenza A (H1N1) virus on N95 respirators. *Applied and Environmental Microbiology*, *79*(7), 2148–2155. https://doi.org/10.1128/AEM.03850-12

FDA. (2020, April). *Enforcement Policy for Face Masks and Respirators During the Coronavirus Disease (COVID-19) Public Health Emergency (Revised)*. https://www.fda.gov/media/136449/download

Firquet, S., Beaujard, S., Lobert, P.-E., Sané, F., Caloone, D., Izard, D., & Hober, D. (2015). Survival of Enveloped and Non-Enveloped Viruses on Inanimate Surfaces. *Microbes and Environments / JSME*, *30*(2), 140–144. https://doi.org/10.1264/jsme2.ME14145

Fischer, R., Morris, D. H., van Doremalen, N., Sarchette, S., Matson, J., Bushmaker, T., Yinda, C. K., Seifert, S., Gamble, A., Williamson, B., Judson, S., de Wit, E., Lloyd-Smith, J., & Munster, V. (2020). Assessment of N95 respirator decontamination and re-use for SARS-CoV-2. *medRxiv*. https://doi.org/10.1101/2020.04.11.20062018

Instructions for Healthcare Personnel: Preparation of Compatible N95 Respirators for Decontamination by the Battelle Memorial Institute Using the Battelle Decontamination System. (2020). https://www.fda.gov/media/136532/download

Kampf, G., Todt, D., Pfaender, S., & Steinmann, E. (2020). Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *The Journal of Hospital Infection*, *104*(3), 246–251. https://doi.org/10.1016/j.jhin.2020.01.022

Lai, M. Y. Y., Cheng, P. K. C., & Lim, W. W. L. (2005). Survival of severe acute respiratory syndrome coronavirus. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, *41*(7), e67–e71. https://doi.org/10.1086/433186

Lin, K., & Marr, L. C. (2020). Humidity-Dependent Decay of Viruses, but Not Bacteria, in Aerosols and Droplets Follows Disinfection Kinetics. *Environmental Science & Technology*, *54*(2), 1024–1032. https://doi.org/10.1021/acs.est.9b04959

OSHA. (n.d.). *OSHA Technical Manual, Section VIII - Use of Respirators*. Retrieved April 22, 2020, from https://www.osha.gov/dts/osta/otm/otm_viii/otm_viii_2.html#8

Peleg, M., & Cole, M. B. (1998). Reinterpretation of microbial survival curves. *Critical Reviews in Food Science and Nutrition*, *38*(5), 353–380. https://doi.org/10.1080/10408699891274246

Seo, K., Lee, J. E., Lim, M. Y., & Ko, G. (2012). Effect of temperature, pH, and NaCl on the inactivation kinetics of murine norovirus. *Journal of Food Protection*, *75*(3), 533–540. https://doi.org/10.4315/0362-028X.JFP-11-199

Sizun, J., Yu, M. W., & Talbot, P. J. (2000). Survival of human coronaviruses 229E and OC43 in

suspension and after drying on surfaces: a possible source of hospital-acquired infections. *The Journal of Hospital Infection*, *46*(1), 55–60. https://doi.org/10.1053/jhin.2000.0795

van Doremalen, N., Bushmaker, T., Morris, D. H., Holbrook, M. G., Gamble, A., Williamson, B. N., Tamin, A., Harcourt, J. L., Thornburg, N. J., Gerber, S. I., Lloyd-Smith, J. O., Wit, E. de, & Munster, V. J. (2020). *Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1*. https://doi.org/10.1056/NEJMc2004973

Vejerano, E. P., & Marr, L. C. (2018). Physico-chemical characteristics of evaporating respiratory fluid droplets. *Journal of the Royal Society, Interface / the Royal Society*, *15*(139). https://doi.org/10.1098/rsif.2017.0939

Viscusi, D. J., Bergman, M. S., Eimer, B. C., & Shaffer, R. E. (2009). Evaluation of Five Decontamination Methods for Filtering Facepiece Respirators. *The Annals of Occupational Hygiene*, *53*(8), 815–827. https://doi.org/10.1093/annhyg/mep070

Watanabe, T., Bartrand, T. A., Weir, M. H., Omura, T., & Haas, C. N. (2010). Development of a dose-response model for SARS coronavirus. *Risk Analysis: An Official Publication of the Society for Risk Analysis*, *30*(7), 1129–1138. https://doi.org/10.1111/j.1539-6924.2010.01427.x