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The potential impact of intensified community hand hygiene interventions on respiratory tract infections: a modelling study

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Abstract

Hand hygiene is amongst the most fundamental and widely-used behavioural measures to reduce the person-to-person spread of human pathogens and its effectiveness as a community intervention is supported by evidence from randomised trials. However, a theoretical understanding of the relationship between hand hygiene frequency and change in risk of infection is lacking. Using a simple model-based framework for understanding the determinants of hand hygiene effectiveness in preventing viral respiratory tract infections we show that a crucial, but overlooked, determinant of the relationship between hand hygiene frequency and risk of infection via indirect transmission is persistence of viable virus on hands. If persistence is short, as has been reported for influenza, hand-washing needs to be performed very frequently or immediately after hand contamination to substantially reduce the probability of infection. When viable virus survival is longer (e.g., in the presence of mucus or for some enveloped viruses) less frequent hand washing can substantially reduce the infection probability. Immediate hand washing after contamination is consistently more effective than at fixed-time intervals. Our study highlights that recommendations on hand hygiene should be tailored to persistence of viable virus on hands and that more detailed empirical investigations are needed to help optimise this key intervention.

1. Introduction

Promotion of hand hygiene is a key public health intervention in preventing the spread of infectious diseases. Since the mid-1800s, when Ignaz Philip Semmelweis demonstrated that hand washing could dramatically reduce maternal mortality due to puerperal fever [1], hand hygiene has been the cornerstone of infection prevention and control policies. In hospital settings, hand hygiene has played a major role in successfully controlling hospital-acquired infections, especially those caused by methicillin-resistant *Staphylococcus aureus* [2]. In the community, there is evidence from randomised controlled trials that hand hygiene interventions can be effective in reducing both the risk of diarrhoeal disease [3] and respiratory tract infections [4–6].

Hand hygiene is simple, low-cost, minimally disruptive and, when widely adopted, may lead to substantial population-level effects [5, 7]. While randomized controlled trials of hand hygiene interventions in the community provide evidence that such interventions are effective in reducing the incidence of respiratory tract infections, reported effect sizes are highly variable [4, 6]. It is unclear to what extent this variability is explained by success in achieving substantial changes in hand hygiene behaviour in these trials. Understanding how the effectiveness of hand hygiene in reducing transmission scales with hand hygiene frequency is important for assessing the extent to which interventions that aim at achieving a large and sustained increase in community hand hygiene can contribute to infection suppression.

Fomite-mediated transmission has been modelled for various respiratory viruses such as SARS-CoV-2 [8, 9] and influenza [10–14]. These studies usually involve a Quantitative Microbial Risk Assessment (QMRA) approach that explicitly models the level of contamination on hands and surfaces assuming a dose-response relationship. This approach leads to realistically detailed models that are particularly useful if detailed environmental data and respective parameters are available. Several studies have also evaluated the effect of hand hygiene on the transmission risk and compared hand hygiene interventions to surface disinfection (e.g., [9, 12]). While hand hygiene compliance was taken into account, none of these previous studies compared different timings and hand hygiene strategies.

In this study, we took a theory-based approach and developed a simple mechanistic mathematical model to understand the relationships between the various components of respiratory tract infection transmission pathways involving hand contamination. We aimed to quantify the expected impact of different hand hygiene behaviours on risks of respiratory tract infection. Our work is motivated by published data on the survival of influenza A on human fingers. We therefore focus on viral respiratory tract infections but our model also applies to pathogens for which similar assumptions apply. Finally, we consider the implications of the outcomes of these analyses for the potential contribution of intensifying community hand hygiene to the suppression of respiratory tract infections.

2. Methods

(a) Overview

We consider human pathogens where transmission is mediated by contaminated hands. We neglect direct droplet and aerosol transmission. Hands are assumed to become contaminated with infectious material via contact with contaminated surfaces or an infected person. In the absence of hand washing, hands do not remain contaminated indefinitely; instead, as has been shown experimentally, the probability of remaining contaminated and capable of transmitting infection declines over time (Figure 1, top panel) [15, 16]. If contaminated hands of a susceptible host make contact with the host's mucous membranes in the eyes, nose or mouth there is some probability of the host becoming infected. Effective hand washing interrupts this process by removing viable virus from the hands. An immediate consequence of this conceptualisation is that the time interval

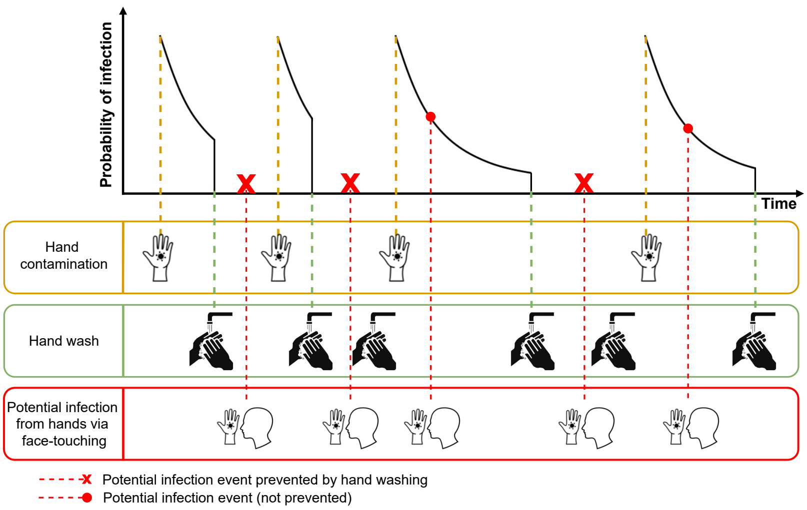

Figure 1: **Hand hygiene model.** Illustration of potential infection events from hands via face-touching, hand contamination events, and hand washing events. Hand contamination events cause a stepwise increase in the probability of infection resulting from face-touching events, which then decreases exponentially with time. Effective hand washing reduces the probability of infection to zero during subsequent face-touching if no further hand contamination events occur. An infection may occur between a hand contamination event and hand washing, depending on the probability of infection at the moment of face-touching.

between the hands becoming contaminated and the potential transmission to the host can have a critical impact on how effective a given frequency of hand washing will be at interrupting transmission (Figure 2). Given a certain probability of infection, the time interval between hand contamination and transmission to the host's mucosa tends to be longer if pathogen persistence on hands is long and vice versa. If this time interval is relatively long, i.e., the virus survives on hands for a long time, regular effective hand hygiene will have a high chance of blocking potential transmission events (red crosses in Figure 2 panel A) in the absence of hand hygiene. In contrast, if this time interval is short, i.e. the pathogen persists for only a short amount of time, much more frequent hand hygiene will be needed to block an appreciable proportion of transmission events (Figure 2 panel B).

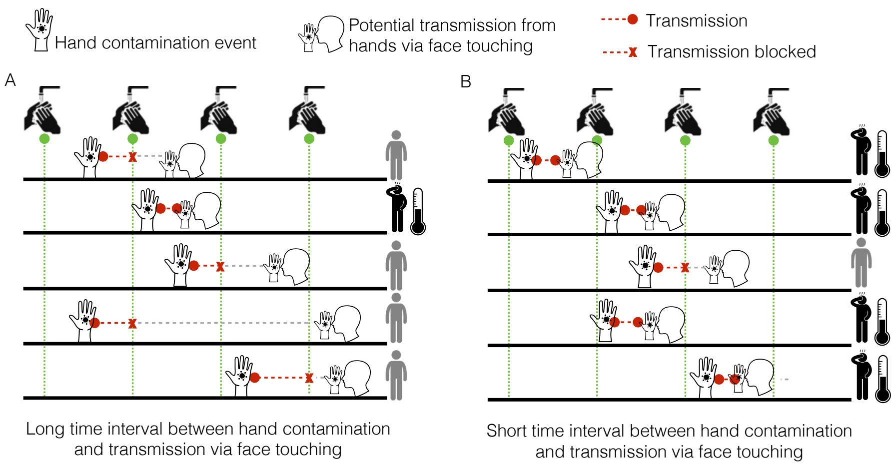

Figure 2: Long versus short time interval between hand contamination and infection with regular hand washing. A) When there are long time intervals between hand contamination and potential infection from hands via face-touching, hand washing can block many infection events and substantially reduce the risk of infection. B) When there are short time intervals between hand contamination and face-touching, it is likely that hand washing can disrupt only a few infections.

(b) Hand hygiene scenarios

We explored the effect of hand hygiene on the probability of infection and considered two hand washing schemes that are distinguished by different timings of hand washing:

(i) fixed-time hand washing (uniformly at fixed time intervals)
(ii) event-prompted hand washing (with a delay after hand contamination events).

(c) Mathematical model

We assumed that hands of susceptible individuals become contaminated at random. These contamination events are assumed to occur independently of each other, and to follow a Poisson distribution with a mean of λ_c events per hour. Once contaminated, we assumed that in the absence of hand washing there is a constant rate at which hands get decontaminated. Thus, the probability of the virus persisting on hands at time t after contamination, $P(t)$, is assumed to decay exponentially with a half-life of $T_{1/2}$. This is consistent with experimental data for influenza A [16]. We further assumed that, in a given time interval $[0, T]$, individuals touch their face at random times $t_1, \ldots, t_F$ leading to potential self-infection events that are assumed to occur independently of each other, and follow a Poisson distribution with a mean of λ_f events per hour. The probability that a single face-touching contact with contaminated hands actually leads to transmission is denoted by ϵ. This parameter represents the transfer efficiency from fomites to hands and combines several factors such as the level of contamination on hands, the infectivity of the virus, and the susceptibility of the host. We do not explicitly model a dose-response relationship, thus ϵ represents the average probability of infection per hand-mucosa contact. In case of a sequence of hand contamination events, we assumed that the probability $P(t)$ is reset to its baseline value of one and that the transmission probability ϵ is kept the same. The probability $P(t)$ is assumed to always have the same functional shape even after sequential hand contamination events. We, therefore, do not account for accumulation of infection risks neither for heterogeneity of hand contamination events. The force of infection that a susceptible individual at time t becomes infected is, therefore, $\lambda_{\text{inf}}(t) = \epsilon P(t)$. The cumulative probability of infection over a given time period T is then given by: $1 - e^{-\sum_{i=1}^{F} \epsilon P(t_i)}$. We assumed that when hand washing is performed after the last hand contamination event and before a face-touching event at time t_i, the respective probability of pathogen persistence $P(t_i)$ is reduced to zero. Thus, hand washing is assumed to remove all virus on contaminated hands completely after one wash, regardless of the number of hand contamination events that took place between hand washing events. A more detailed mathematical description of the model is included in the supplementary material (pp. 15).

(d) Parameters

When available, parameter estimates were obtained from the literature. Otherwise, we performed sensitivity analyses where parameters were varied within plausible ranges (see Table 1).

The probability of transmission per face-touching event, ϵ, was constrained to meet a fixed probability of infection to reflect the fact that we are interested in how our beliefs about the potential impact of enhanced hand hygiene for a pathogen of known transmissibility will vary according to what we know or believe about its survival on hands. In our main analysis, we assumed a cumulative probability of infection of 10% over a time period of 12 hours. This is roughly based on secondary attack rates for influenza, influenza-like-illnesses and acute respiratory illness in household studies [17–20] accounting for the relative contribution of fomite-mediated transmission [10, 14, 21]. Note that high uncertainty lies around these parameters as the quantification of routes of transmission remains difficult [13, 22, 23]. In sensitivity analyses, we examine the results for cumulative probabilities of infection of 0.1%, 1%, 5%, 30% and 50%. By covering such a broad range, we ensure that our conclusions are robust to this parameter that highly depends on the setting and the pathogen.

In the fixed-time hand washing scheme, we varied time intervals between hand washing to be 5 minutes to 6 hours. For event-prompted hand washing, the delay of hand washing after hand contamination events was varied from 1 minute to 6 hours.

There is little published data on the rate of hand contamination events susceptible individuals are exposed to when in contact with infected individuals who are shedding respiratory viruses. In a direct observation study conducted by Zhang et al [24], surface touching behaviour in a graduate student office was recorded. Approximately 112 surface touches per hour were registered. Another study by Boone et al [25] found that the influenza virus was detected on 53% of commonly touched surfaces in homes with infected children (using reverse transcriptase-polymerase chain reaction (RT-PCR)). Informed by these values, we used 60 events per hour as the upper bound for the rate of hand contamination events λ_c. Note that $\lambda_c = 60$ hour^{-1} is based on a RNA to viable virus ratio of 1:1 and should be seen as a theoretical upper bound as in practice, this ratio is likely much smaller. We chose one hand contamination event per hour as the lower bound. In our main analyses, we used a rate of 4 hand contamination events per hour.

In [16], the survival of influenza A on human fingers was experimentally investigated. We fitted exponential decay curves to these results in order to determine the half-life of the probability of persistence of H3N2 for two viral volumes, 2 μL and 30 μL (Table 1 and supplementary material). We use these values as examples for the half-life of the probability of pathogen persistence. In addition, we vary the half-life of the probability of persistence from 1 to 60 min in our analysis.

(e) Model analyses and outcomes

The model output is the cumulative probability of a susceptible person becoming infected in twelve hours and we will refer to it subsequently as simply the probability of infection. We investigated the impact of hand washing on the probability of infection for different hand

Table 1: **Parameter values**

		Value	Source
Time period		12 hours	Assumed
Rate of infection events through face-touching (per hour)	λ_f	10 (5, 20, 50)	[26–29]*
Cumulative probability of infection (in 12 hours)		10 % (0.1%, 1%, 5%, 30 %, 50 %)†	Assumed
Probability of transmission per face-touching event	ϵ	Computed from cumulative probability of infection	
Rate of hand contamination events (per hour)	λ_c	4 hour^{-1} (1, 20, 60 hour^{-1})†	[24, 25]
Time between hand washing events (fixed-time)	t_F	5, 15, 30 min, 1 hour, 2, 6 hours	Assumed
Delay of hand washing after hand contamination events	t_D	1, 5, 15, 45 min, 1 hour, 2, 6 hours	Assumed
Half-life of virus persistence	$T_{1/2}$	1–60 min	Varied
Half-life of H3N2 persistence for 2 μL of viral inoculum		5.4 min	[16]
Half-life of H3N2 persistene for 30 μL of viral inoculum		36.1 min	[16]

* Mean face-touching frequency involving mucous membranes (eyes, mouth, nose)
† Sensitivity analyses

contamination rates. In addition, we compared the two hand washing schemes (fixed-time vs. event-prompted) to find the optimal hand washing strategy that will lead to the greatest reduction of the probability of infection. The model was implemented in R version 3.6.3 [30]. The code reproducing the results of this study is available at `https://github.com/tm-pham/handhygiene_modelling` [31].

3. Results

(a) Impact of half-life of pathogen persistence on probability of infection

Viral persistence on hands plays a key role on the effect of increasing hand hygiene frequency. The longer the virus survives on the hands, the larger the impact of increasing hand washing uptake on the probability of infection. For example, when the half-life of viral persistence is 1 minute, hand washing every 15 minutes reduces the probability of infection from 10 % to 9.2 % (Figure **??**A). When the half-lives increase to 5.4 minutes and 36.1 minutes (equivalent to the half-lives of H3N2 persistence of 2 μL and 30 μL viral inoculum, respectively), the same hand washing frequency decreases the probability of infection to 6.9 % and to 4.6 %, respectively. Consequently, fewer hand washes are necessary to reduce the probability of infection by 50 % for long compared to short durations of viral persistence (see Figure **??**). This observation can be explained by the fact that the shorter the virus persists on hands, the shorter the intervals between hand contamination and transmission events tend to be (with a higher transmission probability per contact needed for the same cumulative probability of infection, see Figure **??**) and, therefore, the less likely hand washing is able to interrupt infection events. Figure **??** shows that the delay between hand contamination and hand washing needed to prevent 50% of transmissions is shorter when the half-life of viral persistence on the hands is shorter, confirming the hypothesis that timely hand washing is especially crucial if the virus survives only a short time on hands. Furthermore, the effect of hand washing on reducing the probability of infection plateaus with increasing duration of virus persistence (Figure **??**). This can be attributed to the hand contamination rate, i.e. new events occur before the virus decays.

(b) Comparison of hand washing schemes

The second notable finding from the model is that event-prompted hand washing is more effective than fixed-time hand washing in reducing the probability of infection. We illustrate this in Figure 4 by comparing both schemes using four different hand washing frequencies/delays, each with approximately the same average number of hand washing events performed per hour. For

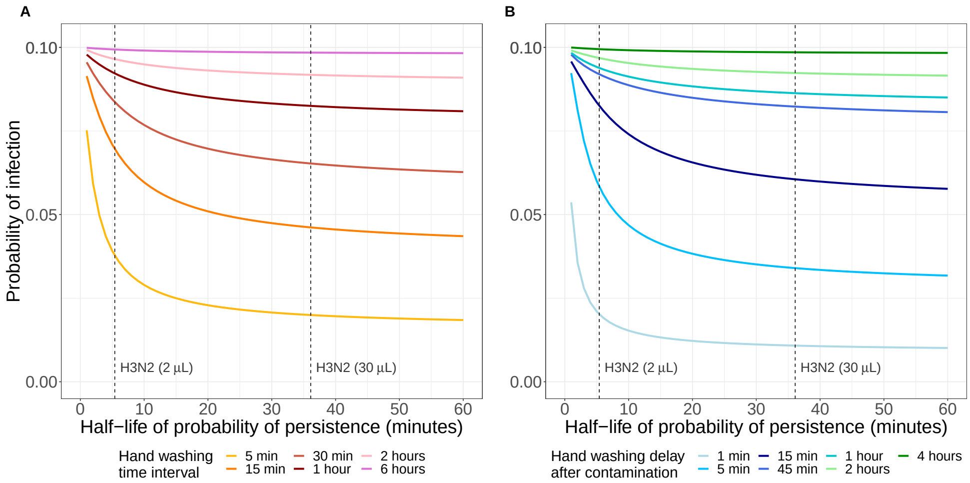

Figure 3: Impact of half-life of viral persistence on probability of infection for different hand washing schemes and frequencies. (A) Fixed-time hand washing (B) Event-prompted hand washing. In this graph, we assumed that a susceptible individual is exposed to a baseline probability of infection of 10% if no hand washing is performed within the time period of twelve hours. The dashed lines represent the half-life of viral persistence for H3N2 inoculum volumes of 2 μL and 30 μL (calculated from [16]). For each half-life value, the probability of transmission per face-touching event ϵ was determined for a probability of infection of 10% in the case of no hand washing. The probability of infection for the different hand washing frequencies/delays was then computed using this ϵ value. Hand contamination events are assumed to occur on average 4 times per hour. Sensitivity analyses with different values for baseline probabilities of infection as well as the half-life calculations are presented in the supplementary material.

example, hand washing regularly every fifteen minutes is compared to event-prompted hand washing one minute after each hand contamination event (set at four per hour). If the half-life of viral persistence is similar to 2 μL of H3N2 inoculum ($T_{1/2} = 5.4$ minutes), the baseline probability of infection of 10% (no hand washing) is reduced to about 6% and 2% when hand washing is performed every 15 minutes and one minute after hand contamination events, respectively. The differences between the two hand washing schemes are less pronounced if hand washing is performed less frequently or with a longer delay after hand contamination events since the two hand washing schemes become more similar. It follows that delays between hand contamination and hand washing decrease the effect of hand washing on reducing the probability of infection.

(c) Hand contamination rate

Another important parameter that affects the effect of hand hygiene is the hand contamination rate. Figure 5 shows the increase in hand hygiene frequency required to halve the probability of infection from 10% (no hand washing) to 5%. When the hand contamination rate is relatively low (i.e., less than 10 contamination events per hour), fewer hand washes are needed to reduce the probability of infection if hand washing is event-prompted. In addition, the longer the virus persists on hands, the smaller the number of hand washing events necessary to achieve a given reduction in the probability of infection. This effect is less pronounced for event-prompted than for time-fixed hand washing, re-emphasizing the finding that when hand contamination events occur very frequently, hand washing would need to be very frequent to have a substantial impact on reducing the probability of infection (e.g., at least five times per hour to prevent 50% of transmission in the case of a half-life of 36.1 min). In this case, susceptible individuals are exposed to a continuous risk of hand contamination and hand washing has only a limited impact on

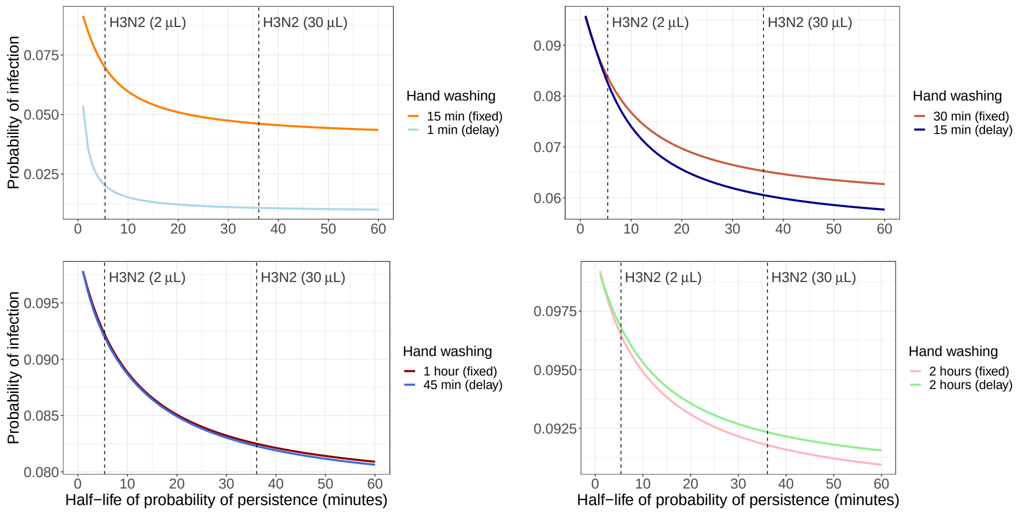

Figure 4: Comparison of the impact of the two hand washing schemes on the cumulative probability of infection. Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 4$ hour^{-1}. A baseline probability of infection of 10% is assumed when there is no hand washing. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

reducing the risk of infection.

Our qualitative conclusions do not change with respect to different baseline probabilities of infection and hand contamination rates (see supplementary material for sensitivity analyses with respect to these parameters).

Discussion

Our study provides new insights into factors that affect the effectiveness of hand hygiene behaviour in reducing the probability of infection. Firstly, we found that the shorter the virus survives on hands, the less effective increasing hand washing frequency is in reducing infection. The logic behind this is that when the virus dies off quickly before hand washing is performed, the time intervals between hand contamination and transmission tend to be shorter and the respective transmission probability per contact needs to be higher for the same cumulative probability of infection. Secondly, the contact frequency with contaminated surfaces is crucial for the effect of hand washing. The more often hands become contaminated, the more frequently hands need to be washed to reduce infection risk. Lastly, when hands are not constantly contaminated, event-prompted hand washing is more efficient than fixed-time hand washing given the same hand washing frequency. This is because delays in hand washing after contamination of hands in fixed-time compared to event-prompted hand washing tend to be longer, and, during this delay, susceptible hosts may become infected through face-touching.

These findings provide additional insights into the modest and heterogeneous effects of hand hygiene reported by hand hygiene trials aimed at reducing respiratory tract infections in the community [4, 6, 32], and also provide pointers to potentially more effective hand hygiene interventions. These trials are challenging to conduct due to the difficulties in implementing behaviour change, including poor adherence to hand washing recommendations [33], and loss to follow-up [34, 35]. However, given the low-cost and minimally-disruptive nature of the

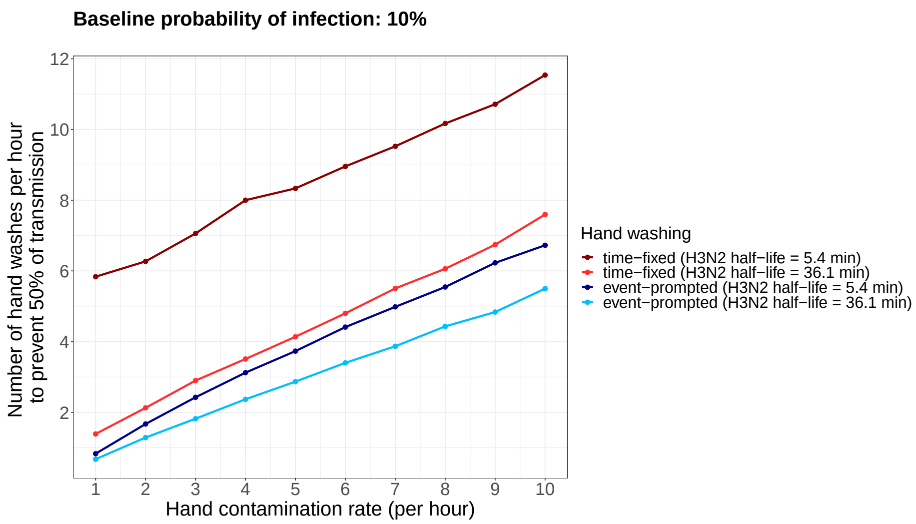

Figure 5: **Number of hand washes necessary to prevent 50% of transmissions.** For a baseline probability of infection of 10%, the number of hand washing events necessary to reduce the probability of infection to 5% was computed for time-fixed and event-prompted hand washing and a range of hand contamination rates. We used the half-life of H3N2 persistence for viral inoculum volumes of 2 μL and 30 μL (calculated from [16]).

intervention we believe there would be considerable value in building on this experimental work and the theory outlined above to develop improved hand-hygiene interventions. This could offer considerable public health benefit both in interpandemic and pandemic periods.

Since the hand contamination rate directly impacts the effect of hand hygiene, specific hand hygiene advice should cater for different situations where surface contamination differs markedly. For example, contacts in the community and in a household with an infectious person would likely result in very different hand contamination rates. In the first case, where hand contamination events occur at a moderate rate, hand washing needs to be performed frequently or immediately after hand contamination events in order to substantially reduce the probability of infection. While individuals may not always be aware of all hand contamination events, event-prompted hand washing can be facilitated by installing or providing hand sanitisers in public areas with high-touch surface areas, such as public transportation and supermarkets, to reduce the delay in hand cleansing. Furthermore, in the second case, where hands become contaminated very frequently, a substantial reduction in the probability of infection is unlikely to be attained unless hand washing frequency is increased drastically, i.e., every one to five minutes. Because hand washing at such a high rate is not practical (neither for fixed-time nor event-prompted hand washing), the recommendations in this scenario are to regularly clean the environment (such as surfaces), reduce the rate of surface touching (if possible), and/or isolate infected individuals to reduce hand contamination events.

We performed sensitivity analyses with varying parameter values and distributions to ensure our conclusions are qualitatively robust. Nevertheless, our results have several limitations which reflect our decision to use a simple model that subsumes much of the biological complexity into a few basic parameters.

We specifically modelled indirect transmission routes via hands and did not consider direct droplet and aerosol transmission. To date, there is little known about the relative importance of the various transmission routes of respiratory pathogens [10, 22, 36, 37]. In particular, the relative contribution of each route may depend on the pathogen itself, the setting, and environmental conditions [23]. For example, in a two-route transmission model, the fomite route was estimated to contribute 6% to the infections caused by influenza in a nosocomial outbreak in Hong Kong [38]. For SARS-CoV-2, Azimi and colleagues developed a mechanistic transmission modeling framework with multiple transmission routes and used detailed information available from the Diamond Princess cruise ship outbreak [39]. The fomite-mediated mode was estimated to contribute to 21% (median) of infected cases aboard the ship. In a healthcare setting, the contribution of contact transmission was estimated to contribute 8.2% (0.0, 0.37%) to the overall infection risk for SARS-CoV-2 [40]. In a comparative analysis of outbreaks of influenza H1N1, SARS-CoV, and norovirus in aircabins, the fomite route was estimated to play the dominant role for SARS-CoV (50%, 95% CI: 48%-53%) while its contribution was minor for H1N1 (less than 1%) [41]. When other routes are considered, the baseline probability of infection needs to be adapted with lower values leading to a lower absolute effect of hand hygiene.

We assumed no accumulation of the probability of infection for a sequence of hand contamination events and did not account for heterogeneity of hand contamination events. Instead, the probability of viral persistence is reset to its baseline value of one and the transmission probability ϵ is kept equal for consecutive hand contamination events. Our model, therefore, might underestimate the reduction in the probability of infection induced by hand washing. However, since we do not expect this to affect the hand washing schemes differently, we do not expect this to change our qualitative conclusions.

We did not account for variation and likely auto-correlation in the probability of infection per hand-mucosa contact or for non-homogeneity in the rate of hand contamination. While incorporating such factors would have some effect on precise quantitative results reported, they would not affect the broad qualitative conclusions. Further analyses included in our supplementary material show that the relationship between the hand contamination rate and viral survival on hands is an important determinant for evaluating the effect of hand washing on the risk of fomite-mediated infection. This relationship remains underexplored and further investigations are needed for each pathogen in question to reliably estimate the potential impact of hand washing.

We assumed that hand washing reduced the probability of persistence on hands to zero and hence that hand washing is maximally efficacious in removing the virus from hands. Although a high efficacy of hand hygiene with soap and water and alcohol-based hand rubs has been demonstrated [42, 43], its real world effectiveness depends on how well it is practised by the individual. Our model, therefore, demonstrates the maximal effect of the two different hand washing schemes in this regard, but since we made this assumption for both, we do not expect it to impact our overall qualitative conclusions.

We have evaluated the effectiveness of hand washing on an individual's risk of infection mediated by the fomite-hand contamination route and did not take onward transmission into account.

There is limited literature on many parameters used in the model, which prevents us from making more precise quantitative conclusions. These include the probability of infection with contaminated hands, the survival of pathogens on contaminated hands and on surfaces and the infective dose. Furthermore, we modelled all infection events with the same rate of decay, i.e., the same probability of pathogen persistence on the hands. In reality, hand contamination events are likely to be heterogeneous with small droplets persisting only a short amount of time and heavy contamination with mucus decaying at a slower rate. In addition, we specifically focus on viral respiratory infections and assumed an exponential decay for the probability of viral persistence. While our model can be applied to all pathogens where hand hygiene is relevant for reducing respiratory tract infections, our results are only applicable for pathogens with a similar persistence behaviour. However, our model can be easily adapted if information on the persistence behaviour of specific pathogens is available.

4. Conclusion

To conclude, in this study we highlight the important considerations in hand hygiene behaviour to improve its effect in stopping the community spread of respiratory tract infections.

Recommendations on hand hygiene should be tailored to the expected hand contamination rate and the half-life of virus persistence on hands.

Ethics. Not applicable.

Data Accessibility. Data and code used in the analysis are publicly available: https://github.com/tm-pham/handhygiene_modelling

Authors' Contributions. TMP, BC, and MY conceptualised and developed the model. TMP wrote the model code and performed the model analysis. TMP, MY, and BC interpreted the results. MY, TMP, and BC performed the literature search. TMP and MY drafted the manuscript. All authors read, reviewed, and approved the final manuscript, and all authors have read and agreed to the published version of the manuscript.

Competing Interests. The authors declare no competing interests.

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Supplementary material

(a) Model

We assumed that hands of susceptible individuals get contaminated at random. These contamination events are assumed to occur independently of each other, and follow a Poisson distribution with a mean of λ_c events per hour. The probability of the virus to persist on hands at time t after contamination, $P(t)$, is assumed to decay exponentially with a half-life of $T_{1/2}$. This is consistent with experimental data for influenza A [16]. We further assumed that, in a given time interval $[0, T]$ individuals touch their face at random times $t_1, \ldots, t_F$ leading to potential infection events that are assumed to occur independently of each other, and follow a Poisson distribution with a mean of λ_f events per hour. The probability that a single face-touching contact with contaminated hands actually leads to transmission is denoted by ϵ. Thus, the probability that a single face-touching contact leads to transmission accounting for the probability of virus persistence is $\epsilon P(t_i)$. The cumulative probability of infection over the time period T is given by:

$$1 - \prod_{i=1}^{F} 1 - \epsilon P(t_i)$$

and can be approximated by

$$1 - e^{-\sum_{i=1}^{F} \epsilon P(t_i)}.$$

This represents the complement of the probability that the transmission events $1, \ldots, F$ do not lead to infection. We assume that when hand washing is performed after the last hand contamination event and before a face-touching event at time t_i, the respective probability of virus persistence $P(t_i)$ is reduced to zero.

Probability of viral persistence on contaminated hands

The decay of the probability of viral persistence on contaminated hands is modeled as an exponential decay with probability distribution:

$$f_{\text{decay}}(t) = \lambda_d e^{-\lambda_d t} \tag{4.1}$$

where λ_d is the decay constant. The probability that virus will die off within time t is given by the integral of the decay distribution function from 0 to t:

$$\int_0^t f_{\text{decay}}(t) = \int_0^t \lambda_d e^{-\lambda_d t}$$

The probability that the virus will persist at time t is one minus the probability that it will die off within the same period:

$$P(t) = 1 - \int_0^t f_{\text{decay}}(t) = 1 - \int_0^t \lambda_d e^{-\lambda_d t} = e^{-\lambda_d t}$$

The average survival time (or mean lifetime) is given by:

$$\tau = \frac{1}{\lambda_d} = \frac{T_{1/2}}{\ln 2} \tag{4.2}$$

(b) Estimation of virus half-life

We estimated the half-life of viral survival on contaminated hands using experiments conducted by Thomas et al,[16] where $2\,\mu$L and $30\,\mu$L of influenza A (H3N2) viral suspension mixed with respiratory secretions were deposited on finger tips. The half-lives were calculated using data from both the $2\,\mu$L ([16] Figure 2) and $30\,\mu$L ([16] Figure 3) H3N2 viral inoculum experiments with an exponential decay model:

$$n(t) = n_0 \cdot e^{-\lambda_d t}$$

where λ_d is the decay rate. The decaying quantity, $n(t)$, represents the number of fingers with recoverable infectious viral particles and is assumed to have an initial value of n_0 at time zero.

In the experiment with 2 μL inoculum, 18 contaminated fingers from six individuals were tested for the presence of infectious virus at 1, 3, 5, 15 and 30 min after initial contamination. Figure **S1** depicts the data and the fitted curve for the 2 μL inoculum. The decay rate was estimated to be $\lambda_d^{(1)} \approx 0.1279$. The half-life is therefore given by $T_{1/2}^{(1)} = \frac{\ln(2)}{\lambda_d^{(1)}} = 5.4$ min.

For 30 μL of viral inoculum, a total of 12 fingers were contaminated and the presence of H3N2 was tested after 15 min. We estimated the half-life by using these two data points (see Figure 3 in [16]). Thus, $\lambda_d^{(2)} = -\frac{\ln(9/12)}{15} \approx 0.0192$. Therefore, $T_{1/2}^{(2)} = \frac{\ln(2)}{\lambda_d^{(2)}} = 36.1$ min.

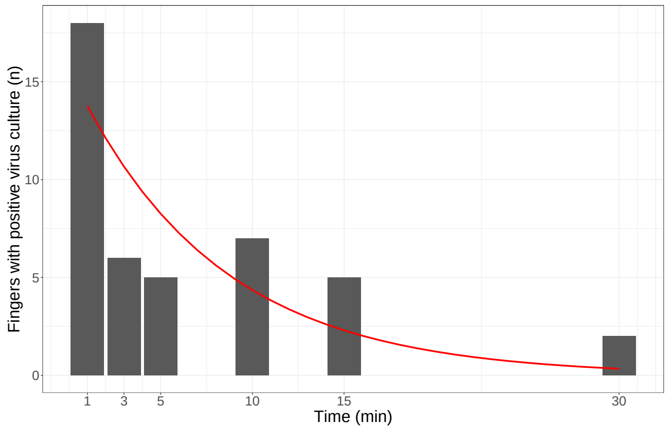

Figure S1: **Influenza A(H3N2) virus survival on fingers over time.** Data was retrieved from [16]. A 2 μL drop of influenza A (H3N2) viral suspension mixed with respiratory secretions was deposited on fingertips. Bars represent the absolute number of fingers from which infectious virus was recovered. The red line represents the exponential decay curve $n(t) = 15.65e^{-0.1279t}$ fitted to this data .

(c) Hand washing and half-life of virus persistence

The shorter the half-life of virus persistence, the higher the frequency of hand washing necessary in order to prevent 50% of infections (see Figure **S2** left). In addition, the time intervals between hand contamination and hand washes have to be shorter in order to prevent 50% of the infections (see Figure **S2** right).

(d) Transmission probability per contact and half-life of virus persistence

Figure **??** shows that the shorter the virus persists on hands, the higher the probability of transmission per face-touching contact has to be if the cumulative probability of infection is assumed to be fixed.

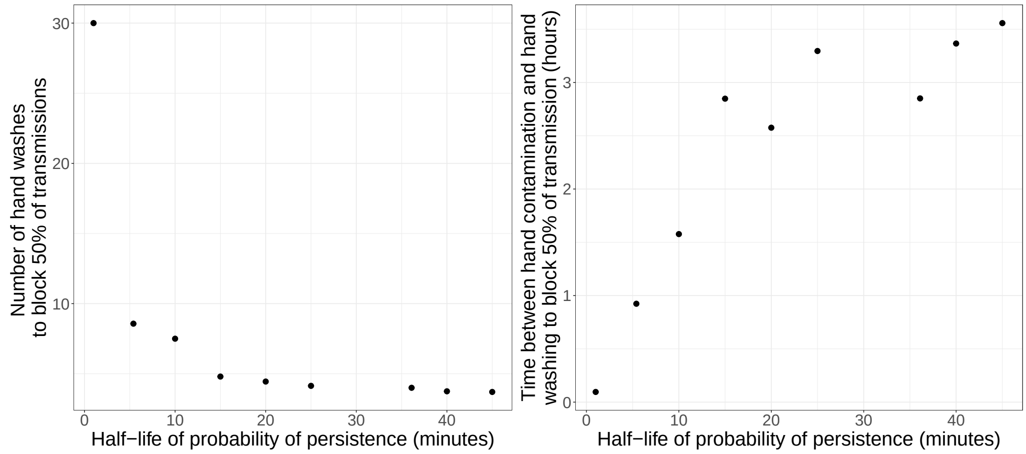

Figure S2: **Number of fixed-time hand washes and cumulative time between hand contamination events and fixed-time hand washes necessary to prevent 50% of transmissions.** For each half-life value of virus persistence, the number of hand washes necessary to prevent 50% of transmission was computed for a baseline probability of infection of 10%. Hand contamination events are assumed to occur on average 4 times per hour.

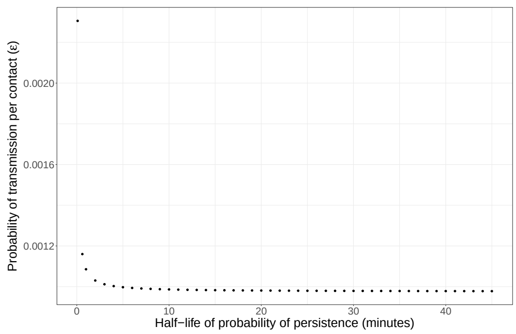

Figure S3: **Probability of transmission per face-touching contact for different half-lives of virus persistence.** For a baseline cumulative probability of infection of 10% and each half-life value of virus persistence, the probability of transmission per single face-touching contact was computed. Hand contamination events are assumed to occur on average 4 times per hour.

(e) Sensitivity analyses

Our model relies on various parameters for which we obtained values from the literature when available. However, high uncertainty remains and we thus performed sensitivity analyses with respect to various parameters and investigated their effect on the results and conclusions. In particular, we varied

- Cumulative probability of infection
- Rate of infection events through face-touching
- Rate of hand contamination events

We briefly discuss the results for each of the sensitivity analyses below.

(i) Cumulative probability of infection

The cumulative probability of infection may vary across pathogens and settings. We performed sensitivity analyses for probability of infections of 0.1%, 1%, 5%, 30%, and 50%. As such, we cover a broad spectrum of values. We only report the results for 0.1% (Figures **S4**-**S5**), 5% (Figures **??**-**S7**) and 30% (Figures **S8**-**S9**) here. The remaining figures can be found online [31]. Similar to our main results, event-prompted hand washing is more effective than fixed-time hand washing when both schemes are compared according to similar average numbers of hand washing events performed per hour. Note that when hand washing is performed every two hours (fixed-time and with delay), the average number of hand washing events per hour is slightly higher for fixed-time than for event-prompted hand washing and therefore, the reduction in the probability of infection is higher for fixed-time hand washing. However, even then, the difference between the two schemes is small.

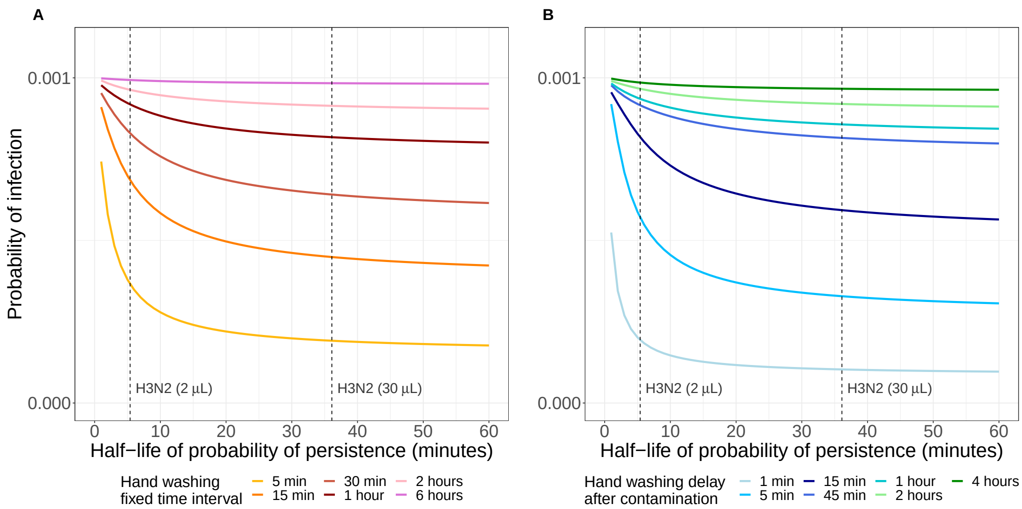

Figure S4: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies (baseline = 0.1%).** (A) Fixed-time hand washing (B) Event-prompted hand washing. The dashed lines represent the half-life of probability of persistence for H3N2 for viral inoculum volumes of 2 μL and 30 μL (calculated from [16]). Hand contamination events are assumed to occur on average 4 times per hour.

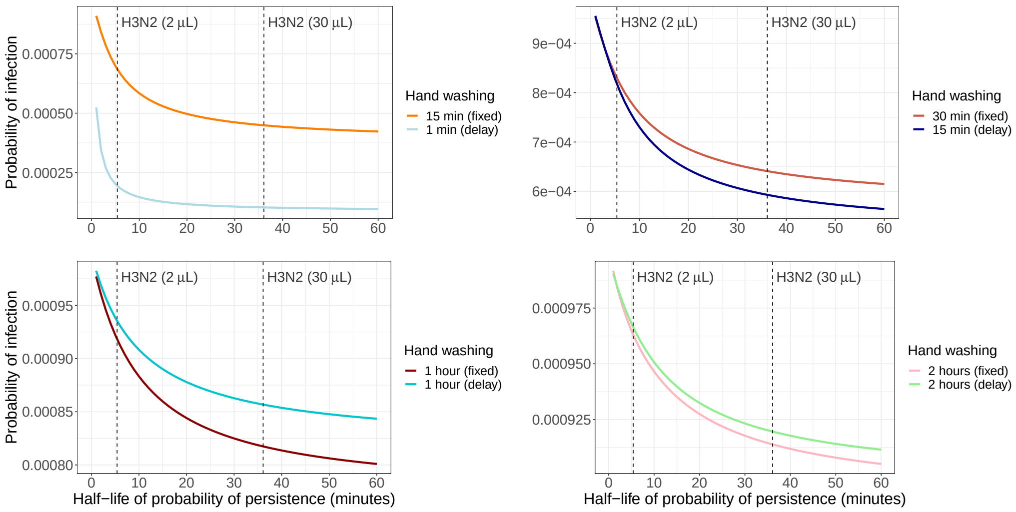

Figure S5: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection (baseline = 0.1%).** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 4$ hour^{-1}.The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

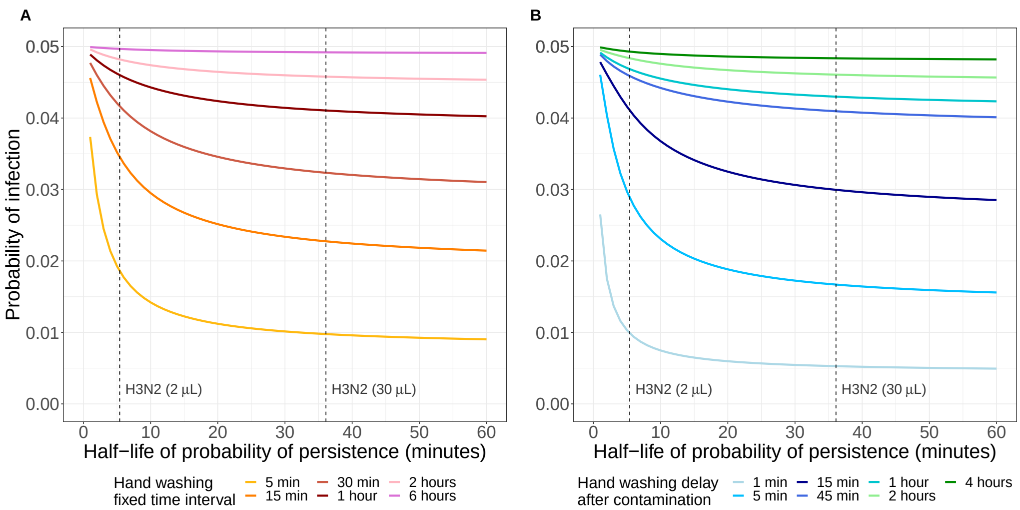

Figure S6: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies (baseline = 5%).** (A) Fixed-time hand washing (B) Event-prompted hand washing. The dashed lines represent the half-life of probability of persistence for H3N2 for viral inoculum volumes of 2 μL and 30 μL (calculated from [16]). Hand contamination events are assumed to occur on average 4 times per hour.

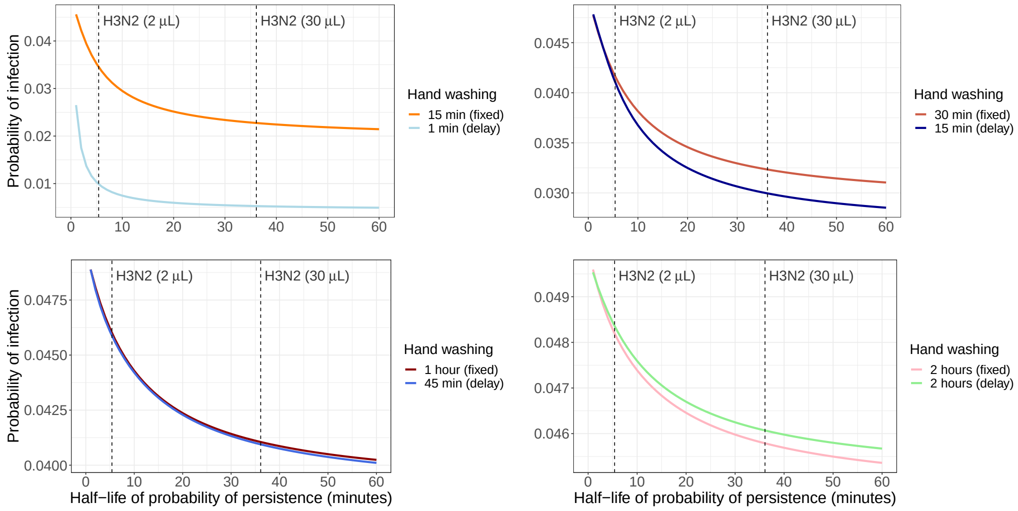

Figure S7: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection (baseline = 5%).** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 4$ hour^{-1}. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

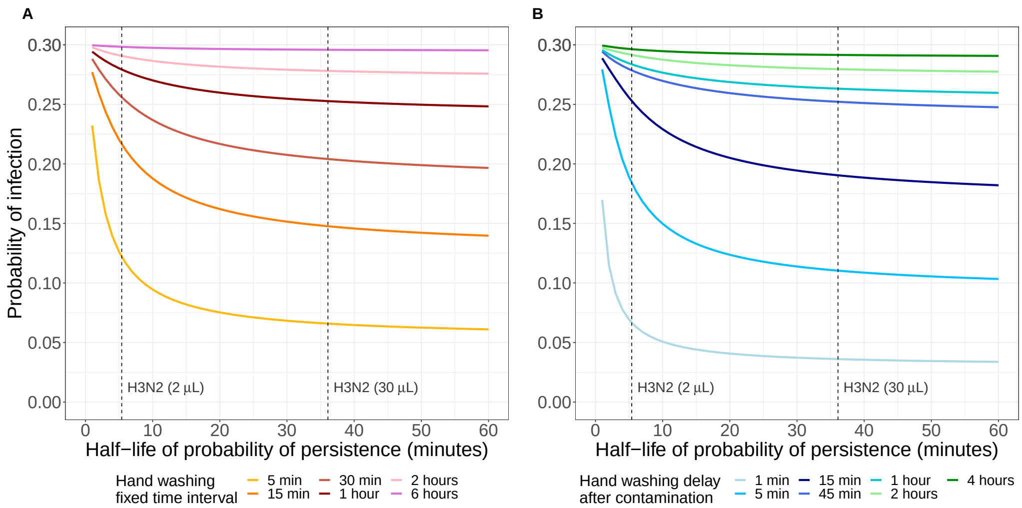

Figure S8: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies (baseline = 30%).** (A) Fixed-time hand washing (B) Event-prompted hand washing. The dashed lines represent the half-life of probability of persistence for H3N2 for viral inoculum volumes of 2 μL and 30 μL (calculated from [16]). Hand contamination events are assumed to occur on average 4 times per hour.

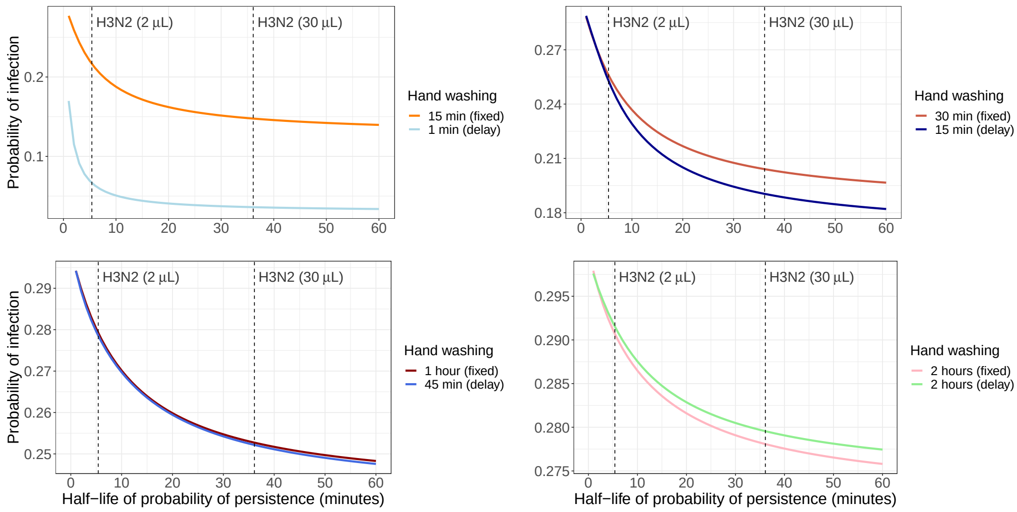

Figure S9: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection (baseline = 30%).** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 4$ hour^{-1}. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

(ii) Rate of infection events through face-touching

The rate of infection events mediated by face-touching λ_f may vary across individuals (e.g. may depend on age), activities (e.g. eating vs. non-eating), settings (e.g., public vs private settings, use of face masks, etc.), and also the area of the face that is considered. Frequencies for hand-face contacts vary considerably between studies (e.g., 15.7 reported in Nicas et al (2008 [27]), 27.7 reported in Lewis et al (2020) [28]). Wilson et al (2020) [29] showed that this rate depends also on the activity, with generally higher contact rates for eating vs non-eating activities, as well as the area of the face (lower contact frequencies for mouth, eyes, and nose vs all other face areas). To account for this variability, we performed the analyses for $\lambda_f = 5$ (Figures **S10**-**S11**), $\lambda_f = 20$ (Figures **S12**-**S13**), and $\lambda_f = 50$ (omitted here but can be found online [31]). Our overall conclusions do not change with respect to λ_f. Note that for $\lambda_f = 5$, event-prompted hand washing is superior to fixed-time hand washing throughout even when intervals between hand washing events are large (Figure **S11**). However, as in the main analysis, the differences are small.

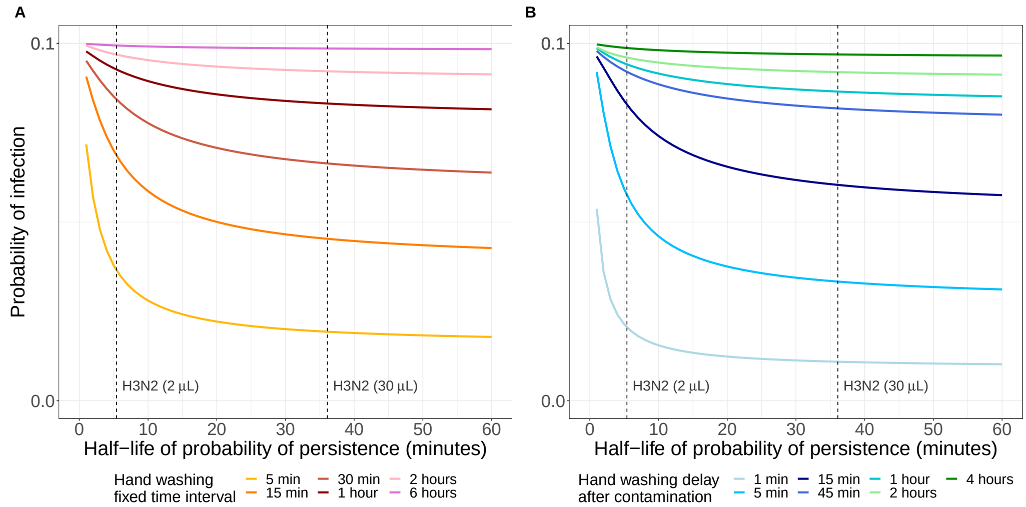

Figure S10: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies (baseline = 10%).** (A) Fixed-time hand washing (B) Event-prompted hand washing. Hand contamination events are assumed to occur on average 4 times per hour. Infection events through face-touching are assumed to occur 5 times per hour. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

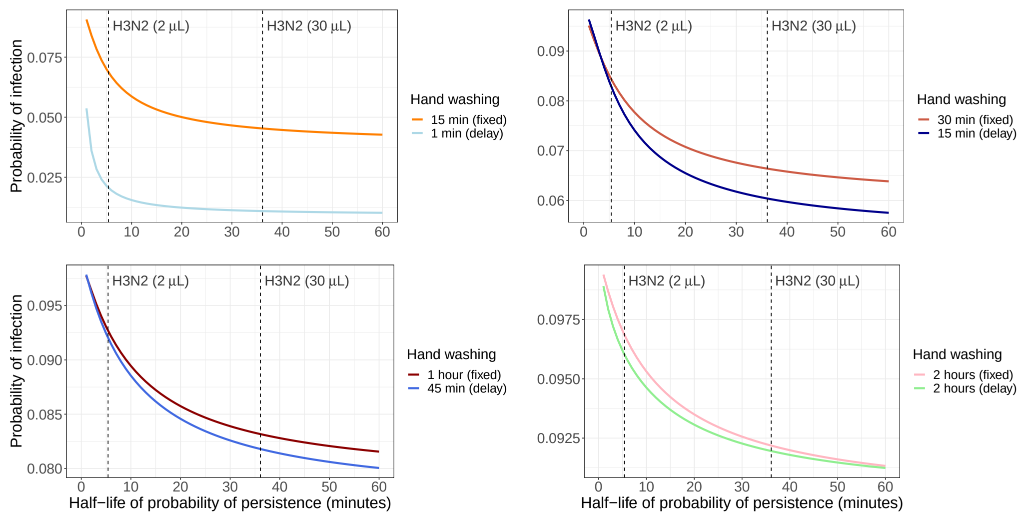

Figure S11: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection (baseline = 10%).** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 4$ hour^{-1}. Infection events through face-touching are assumed to occur 5 times per hour. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

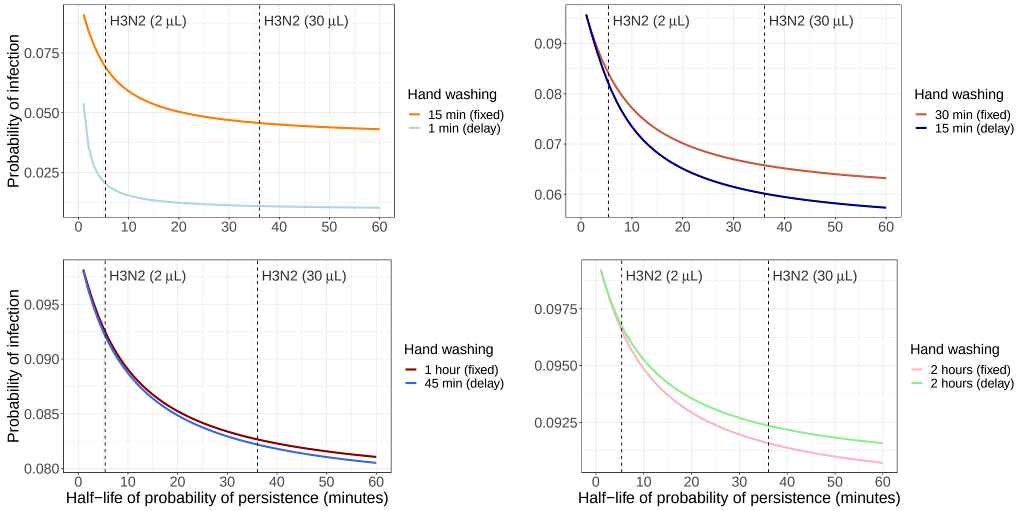

Figure S12: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies (baseline = 10%).** (A) Fixed-time hand washing (B) Event-prompted hand washing. Hand contamination events are assumed to occur on average 4 times per hour. Infection events through face-touching are assumed to occur 20 times per hour. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

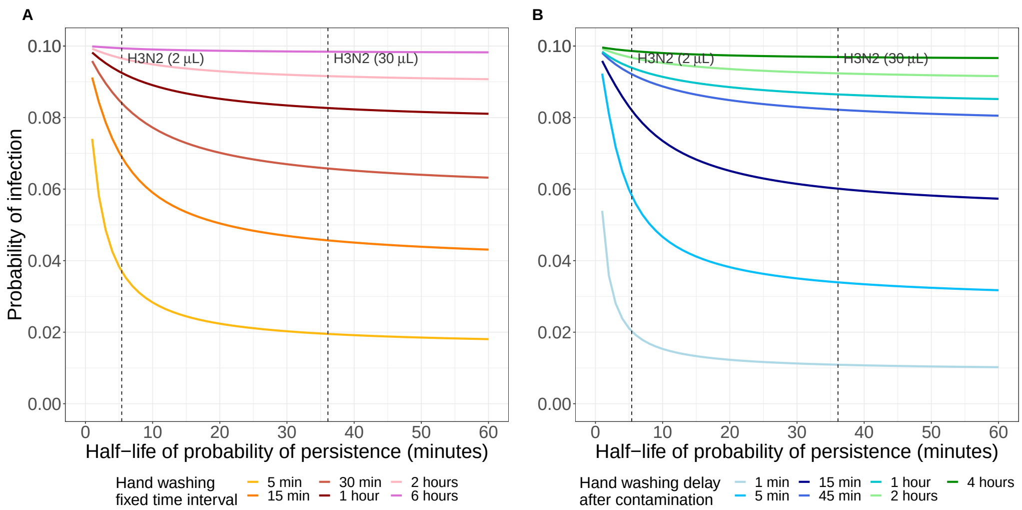

Figure S13: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection (baseline = 10%).** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 4$ hour^{-1}. Infection events through face-touching are assumed to occur 20 times per hour. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

(iii) Hand contamination event rate

We performed sensitivity analyses for different rates of hand contamination events and present the results for hand contamination rates of 1, 20, and 60 times per hour. The less frequently hands get contaminated, the larger the impact of increasing hand washing frequencies or reducing the delay of hand washing after hand contamination events and the larger the impact of the half-life of the probability of persistence of the virus on the actual probability of infection reduction

Hand contamination rate once per hour. For a low hand contamination rate of $\lambda_c = 1$, the average number of hand washing events per hour is also low (≥ 1) for event-prompted hand washing but is unaffected for fixed-time hand washing. Fewer comparisons are possible for such a low rate of hand contamination while maintaining the average number of hand washing events per hour since only few event-prompted hand washing events will be performed (Figure **S14**). Thus, all vent-prompted hand washing scenarios can only be compared to fixed-time hand washing scenarios with a very low frequency. Generally, event-prompted hand washing is still more efficient than fixed-time hand washing (Figure **S16**).

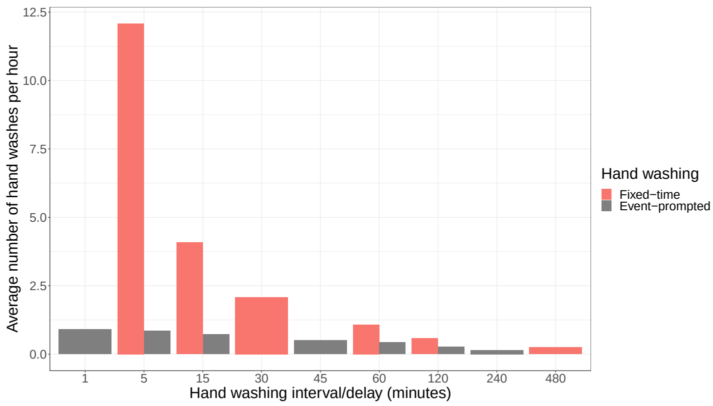

Figure S14: **Average number of hand washing events per hour for fixed-time hand washing and event-prompted hand washing**. Hand contamination events are assumed to occur on average once per hour. We considered the following time intervals for fixed-time hand washing: 5 min, 15 min, 30 min, 60 min, 120 min, 480 min. For event-prompted hand washing we simulated the following delay between hand contamination and hand washing event: 1 min, 5 min, 15 min, 45 min, 60 min, 120 min, 240 min. These values were motivated by our main analysis for an adequate comparison of the two hand washing schemes.

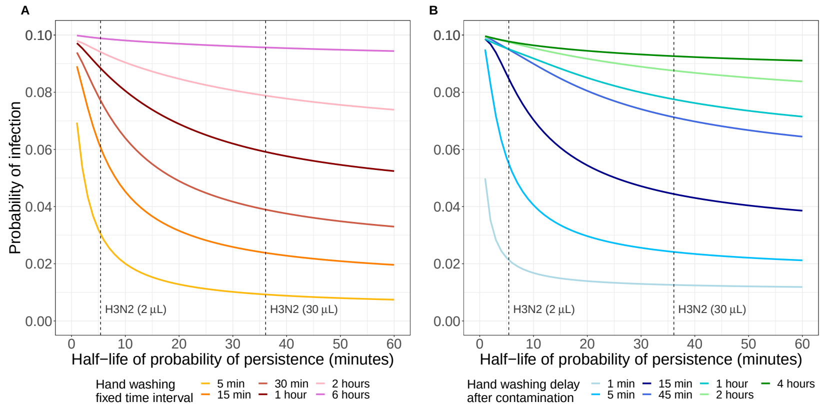

Figure S15: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies for a hand contamination rate of once per hour.** (A) Fixed-time hand washing (B) Event-prompted hand washing. Infection events through face-touching are assumed to occur 10 times per hour. A baseline probability of infection of 10% is assumed when there is no hand washing. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

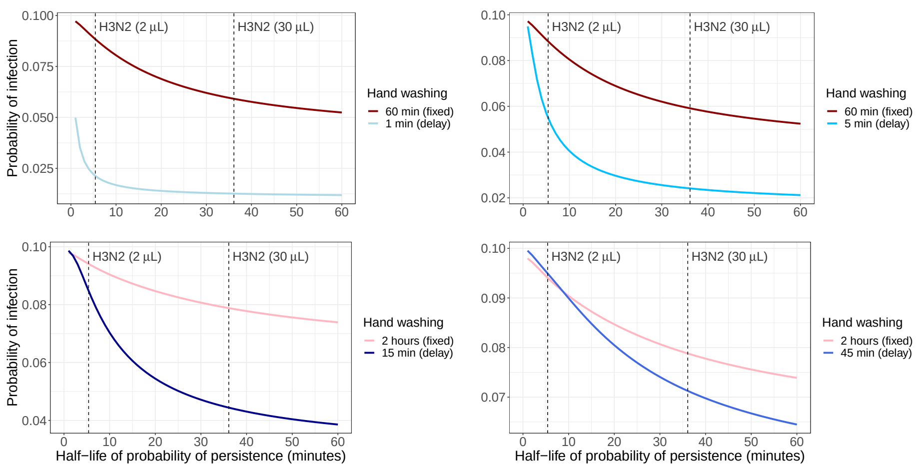

Figure S16: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection.** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 1$ hour^{-1}. Infection events through face-touching are assumed to occur 10 times per hour. A baseline probability of infection of 10% is assumed when there is no hand washing. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

Hand contamination rate 20 times per hour. The effect of both hand washing schemes becomes smaller for higher hand contamination rates. In addition, the average number of hand washing events per hour increases for high hand contamination events (Figure **S17**). In this scenario, fixed-time hand washing can be more efficient than event-prompted hand washing when accounting for the average number of hand washes per hour (Figure **S19**). In addition, event-prompted hand washing with a short delay is unlikely to be feasible in practice for very high hand contamination rates, and this would also be the case for fixed-time hand washing with comparable frequency. Note that the differences are small as the reduction in the probability of infection is small for both hand washing schemes for such a high hand contamination rate. The most effective intervention is event-prompted hand washing with only 1 min delay. This is, however, not feasible due to the high frequency of contamination events.

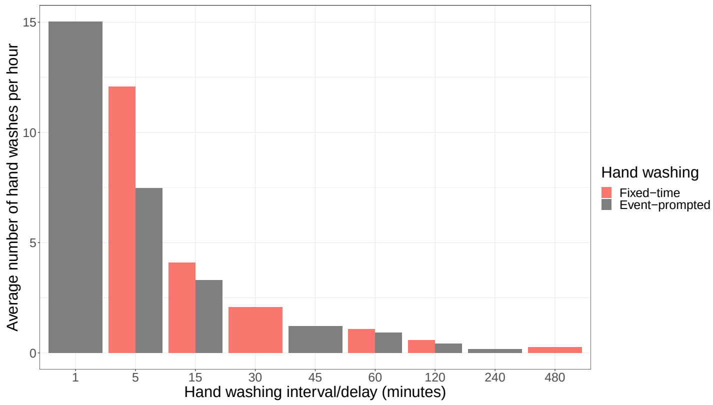

Figure S17: **Average number of hand washing events per hour for fixed-time hand washing and event-prompted hand washing**. Hand contamination events are assumed to occur on average 20 times per hour. We considered the following time intervals for fixed-time hand washing: 5 min, 15 min, 30 min, 60 min, 120 min, 480 min. For event-prompted hand washing we simulated the following delay between hand contamination and hand washing event: 1 min, 5 min, 15 min, 45 min, 60 min, 120 min, 240 min. These values were motivated by our main analysis for an adequate comparison of the two hand washing schemes.

Hand contamination rate of 60 times per hour. The results are similar to the previous section. Figures are omitted here but can be found online [31].

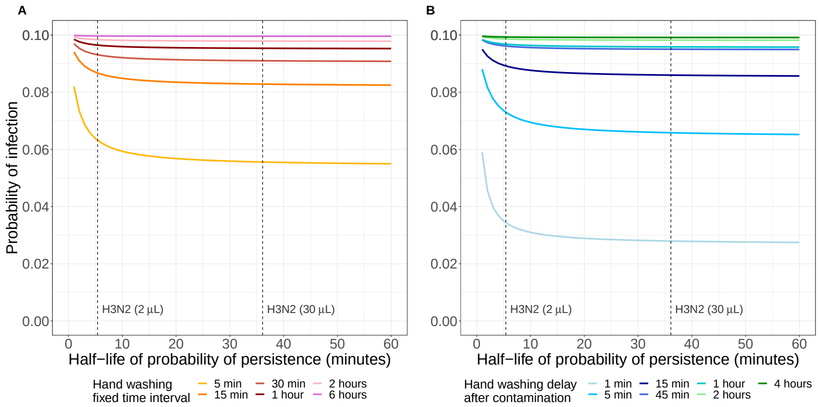

Figure S18: **Impact of half-life of probability of virus persistence on probability of infection for different hand washing schemes and frequencies for a hand contamination rate of 20 times per hour.** (A) Fixed-time hand washing (B) Event-prompted hand washing. Infection events through face-touching are assumed to occur 10 times per hour. A baseline probability of infection of 10% is assumed when there is no hand washing. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

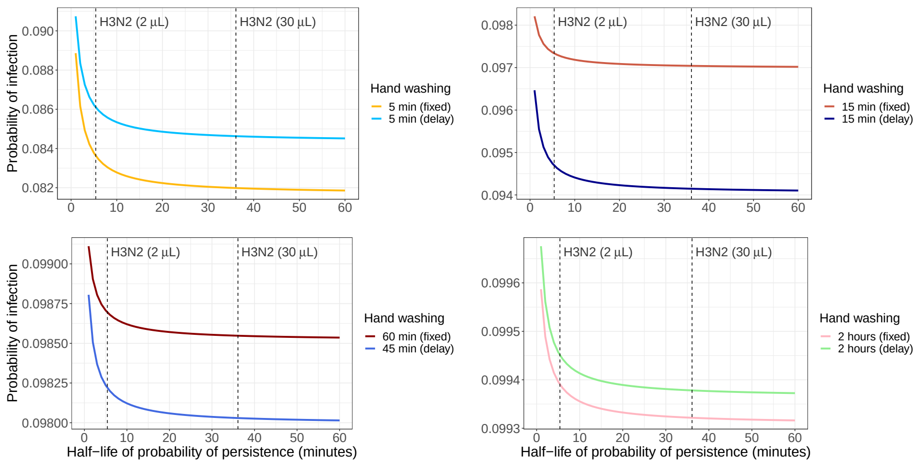

Figure S19: **Comparison of the impact of the two hand washing schemes on the cumulative probability of infection.** Hand washing at fixed time intervals and event-prompted hand washing (with a time delay) with similar average number of hand washing events per hour are compared for a hand contamination rate of $\lambda_c = 20$ hour^{-1}. Infection events through face-touching are assumed to occur 10 times per hour. A baseline probability of infection of 10% is assumed when there is no hand washing. The dashed lines represent the half-life values of H3N2 persistence for 2 μL and 30 μL inoculum volumes [16].

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(f) Correlation between half-life of viral persistence on hands and hand contamination rate

In our main analysis, we investigated the effect of hand washing on the cumulative probability of infection varying the half-life of the probability of viral persistence on hands (1-60 minutes) and keeping the remaining parameters fixed at values informed from literature (see Table 1). In particular, we assumed a fixed baseline probability of infection in the absence of hand washing and a fixed hand contamination rate. We highlighted that for a new pathogen with observed secondary attack rates, the effect of hand washing on the cumulative probability of infection is highly dependent on the half-life. In an alternative scenario, the hand contamination rate might not be known (and therefore not fixed) and might be correlated with the half-life of the probability of viral persistence on hands. For example, longer virus survival on hands could be associated with longer survival on surfaces. This would lead to a higher probability of hand contamination per surface touch and, consequently, a higher hand contamination rate. This may vary across pathogens and depend on the surface type and environmental conditions. We have explored this scenario by not only varying the half-life (between 1 and 60 minutes) but also the hand contamination rate (between 1 and 60 minutes). We have chosen wide ranges for these parameters to reflect the high uncertainty about their values for common pathogens.

Fixed-time hand washing

Figure **S20** shows that the lower the hand washing frequency (i.e., the higher the time interval between hand washing events), the smaller the effect of hand washing on the cumulative probability of infection (lighter colours represent smaller effect of hand washing on reducing the infection risk). Notably, hand washing achieves a substantial reduction in the probability of infection only for low hand contamination rates (approximately less than about 10 contamination events per hour). How varying the half-life of the probability of viral persistence would impact the effect of hand washing on the infection risk strongly depends on the hand contamination rate. For example, if the half-life of the probability of persistence and the hand contamination rate were linearly related, the effect of hand washing (i.e., reduction in probability of infection) is first small (for low hand contamination rates and half-lives), then increases, subsequently decreases, and finally reaches a plateau (best seen in Figure **S20** top left panel). The quantitative impact of hand washing highly depends on the quantitative relationship between these two parameters (half-life and hand contamination rate). Our analysis shows that this relationship is an important determinant for the effect of hand washing on reducing the risk of infection.

Event-prompted hand washing

Similar to the fixed-time hand washing scenario, the longer the delay between hand contamination and hand washing, the smaller the reduction in the probability of infection (Figure **S21**). Again, for long hand washing delays, hand washing becomes only effective for low hand contamination rates. The qualitative conclusions drawn in the fixed-time hand washing scenario are similarly applicable here.

Conclusions

The results of this analysis show that:

- the effect of hand washing depends on the relationship between the half-life of the probability of infection and the hand contamination rate;
- for long time intervals between hand washing events, or long delays of hand washing after hand contamination events, hand washing is only strongly effective for low hand contamination events. This emphasizes that another effective intervention for reducing fomite-mediated infection risk is reducing the hand contamination rate.

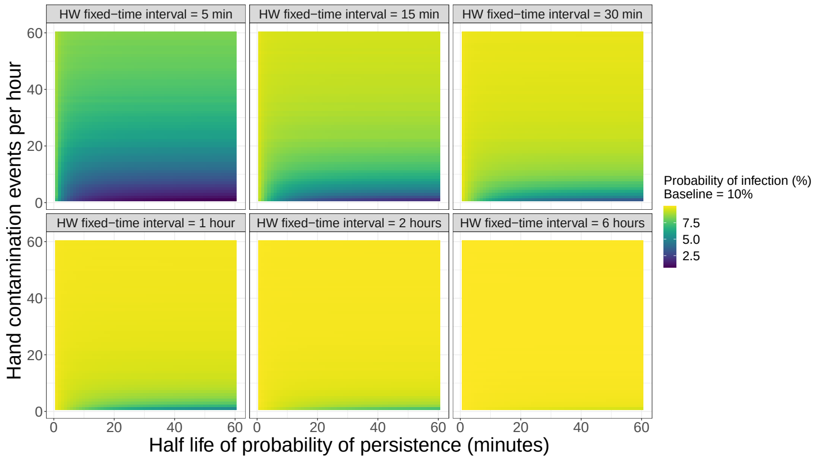

Figure S20: **Impact of fixed-time hand washing on probability of infection when varying both the hand contamination rate and half-life of probability of viral persistence on hands.** A baseline probability of infection of 10% (in the absence of hand washing) was used for the simulations. Different panels denote the time intervals between hand washing events. HW = Hand washing.

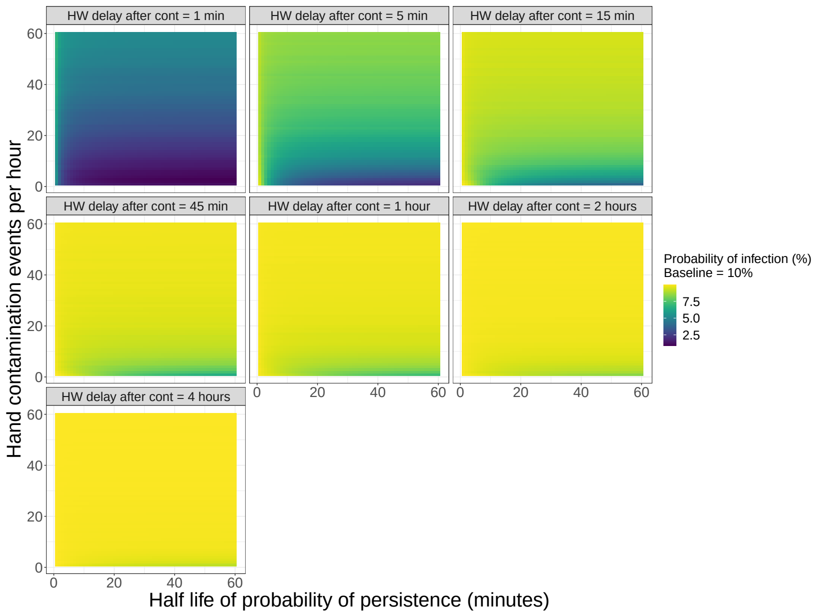

Figure S21: **Impact of event-prompted hand washing on probability of infection when varying both the hand contamination rate and half-life of probability of viral persistence on hands.** A baseline probability of infection of 10% (in the absence of hand washing) was used for the simulations. Different panels denote the delay between hand washing and hand contamination event. HW = Hand washing.