#### RESEARCH ARTICLE



## **REVISED** Hand Hygiene Practices and the Risk of Human

# Coronavirus Infections in a UK Community Cohort [version 2;

## peer review: 2 approved]

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V2 First published: 20 May 2020, 5:98 https://doi.org/10.12688/wellcomeopenres.15796.1 Latest published: 22 Jun 2021, 5:98 https://doi.org/10.12688/wellcomeopenres.15796.2

#### Abstract

**Background:** Hand hygiene may mitigate the spread of COVID-19 in community settings; however, empirical evidence is limited. Given reports of similar transmission mechanisms for COVID-19 and seasonal coronaviruses, we investigated whether hand hygiene impacted the risk of acquiring seasonal coronavirus infections. Methods: Data were drawn from three successive winter cohorts (2006-2009) of the England-wide Flu Watch study. Participants (n =1633) provided baseline estimates of hand hygiene behaviour. Coronavirus infections were identified from nasal swabs using RT-PCR. Poisson mixed models estimated the effect of hand hygiene on personal risk of coronavirus illness, both unadjusted and adjusted for confounding by age and healthcare worker status. **Results:** Moderate-frequency handwashing (6-10 times per day) predicted a lower personal risk of coronavirus infection (adjusted incidence rate ratio (aIRR) =0.64, p=0.04). There was no evidence for a dose-response effect of handwashing, with results for higher levels of hand hygiene (>10 times per day) not significant (aIRR =0.83, p=0.42). **Conclusions:** This is the first empirical evidence that regular handwashing can reduce personal risk of acquiring seasonal coronavirus infection. These findings support clear public health messaging around the protective effects of hand washing in the context of the current COVID-19 pandemic.

#### **Keywords**

coronavirus, hand washing, respiratory hygiene, pandemic, COVID-19, respiratory infection

# Reviewer Status Invited Reviewers 1 2 version 2 (revision) 22 Jun 2021 version 1 20 May 2020 report report

**Open Peer Review** 

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Any reports and responses or comments on the article can be found at the end of the article.



This article is included in the Coronavirus

(COVID-19) collection.

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Author roles: Beale S: Conceptualization, Formal Analysis, Investigation, Writing – Original Draft Preparation; Johnson AM: Investigation, Methodology, Writing – Review & Editing; Zambon M: Investigation, Methodology, Writing – Review & Editing; Hayward AC: Conceptualization, Funding Acquisition, Investigation, Methodology, Writing – Review & Editing; Fragaszy EB: Conceptualization, Formal Analysis, Investigation, Supervision, Writing – Review & Editing

**Competing interests:** AH and MZ serve on UK New and Emerging Respiratory Virus Threats Advisory Group. AMJ was a Governor of Wellcome Trust from 2011-18 and is Chair of the Committee for Strategic Coordination for Health of the Public Research. The other authors declare no competing interests.

**Grant information:** The Flu Watch study received funding from the Medical Research Council (MRC) and the Wellcome Trust (G0600511, G0800767 and MC\_U122785833). S.B. is supported by an MRC doctoral studentship (MR/N013867/1). The funders were not actively involved in the design, delivery, or analysis of this research. The views expressed in this publication are those of the authors and not necessarily of the MRC or the Wellcome Trust. AH is an NIHR Senior Investigator. The views expressed in this Article are those of the authors and not necessarily those of the NIHR, or the Department of Health and Social Care.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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How to cite this article: Beale S, Johnson AM, Zambon M *et al*. Hand Hygiene Practices and the Risk of Human Coronavirus Infections in a UK Community Cohort [version 2; peer review: 2 approved] Wellcome Open Research 2021, 5:98 https://doi.org/10.12688/wellcomeopenres.15796.2

First published: 20 May 2020, 5:98 https://doi.org/10.12688/wellcomeopenres.15796.1

#### **REVISED** Amendments from Version 1

This updated version of the article contains an additional descriptive table reporting hand hygiene frequency by age group and healthcare worker status, and amendments to the discussion to provide clarification around study interpretation and limitations based on reviewers' comments.

Any further responses from the reviewers can be found at the end of the article

#### Introduction

The expanding global outbreak of Coronavirus Disease 2019 (COVID-19) demands an evidence-based public health response. Seasonal human coronavirus strains and COVID-19 appear to be transmitted via droplets, direct and indirect contact with infected secretions and, to an unknown extent by aerosol<sup>1-4</sup>. Hand hygiene measures are recommended by health authorities and public health experts worldwide to interrupt these transmission mechanisms by preventing viral transfer via contact with infected people and surfaces<sup>5-9</sup>. While hand hygiene recommendations are acceptable in a variety of community settings worldwide<sup>10,11</sup> and are widely recommended by health authorities<sup>5-9</sup>, evaluation of their effects on the risk of illness in the general population is limited.

Clinical trials of hand hygiene interventions for acute respiratory viral infections in community settings have focused on influenza and yielded mixed results. The balance of evidence suggests small but significant reductions in rates of influenza and influenza-like-illness, likely impacted by the specific community context<sup>12-14</sup>. Trial outcomes reflect both the effectiveness of the intervention at altering behaviour as well as the relationship between the behaviour and risk of subsequent illness. As such, observational studies assessing the effect of handwashing on risk of illness are warranted. Limited observational evidence of varying quality has linked increased handwashing with lower risk of influenza and influenza-like illness<sup>15-19</sup>, while others have found no relationship<sup>20-22</sup>. Larger, population-representative studies are warranted for non-influenza respiratory viruses, particularly coronaviruses, in the current context of the ongoing COVID-19 pandemic.

We aimed to address this gap in the literature using data from a population-based English community cohort study examining transmission of influenza and other respiratory viruses, including seasonal coronaviruses<sup>23,24</sup>. As COVID-19 appears to demonstrate similar transmission mechanisms to circulating seasonal coronavirus strains<sup>1–4</sup>, understanding the effects of widely-recommended hand hygiene practices may beneficially inform public health campaigns. Understanding the impact of hand hygiene behaviour in community settings is particularly relevant in the absence of an effective vaccine. Consequently, our objective was to investigate whether participants' frequency of handwashing predicted their overall risk of laboratory-confirmed coronavirus infection.

#### Methods

#### Study design and procedure

All data were collected as part of Flu Watch, a national household-level prospective cohort study investigating transmission, burden and risk factors associated with influenza and other acute respiratory infections across England. The study methodology has been described in detail elsewhere<sup>23,24</sup>. Cohorts were followed up across three winter seasons (2006–2007, 2007–2008, 2008–2009) and the three waves of the 2009 H1N1 pandemic (spring/summer 2009 and winter 2009–2010 and 2010–2011). Data for the present study were drawn from the first three cohort seasons (2006–2009) when coronavirus was regularly monitored in the study.

Demographic data and self-reported hand hygiene were collected at baseline of each season. Participants were followed up weekly by telephone or online to report any acute respiratory illness, and were asked to take a posterior nasal swab in each nostril on the second day of any illness. These samples were requested for all respiratory illnesses during follow up, although in the first winter (2006/7) swabbing was restricted to periods when influenza was known to be circulating. Swabs were placed in a vial of viral transport medium and posted to the Health Protection Agency (HPA) in the same manner as national surveillance samples<sup>25,26</sup>. Samples were screened by real-time PCR for a panel of viruses, including seasonal coronaviruses<sup>27–30</sup>.

#### Participants

Participants were 1633 individuals who participated in the Flu Watch study in any of the three seasons from 2006–2009 and completed a baseline hygiene survey. Participants were randomly selected from patient lists at general practices, and letters were sent inviting their entire household to participate in the study. Households were recruited annually ahead of the influenza season and those who had previously participated were re-invited to the next season in winter 2008–2009. Eligibility criteria were that the full household agreed to follow-up across the whole season and that adults ( $\geq 16$  years) agreed to have blood samples drawn for other Flu Watch research<sup>23</sup>. Exclusion criteria were living in a >6-person household, terminal or severe illness or incapacity, and substantial involvement in other ongoing research.

#### Measures

*Exposure definitions.* To assess overall handwashing frequency, the exposure of interest, participants were asked at baseline of each season to "Estimate how many times you washed your hands yesterday". Frequency of daily handwashing was subsequently categorised as low ( $\leq$ 5 times daily), moderate (6–10 times daily), or high (>10 times daily) guided by literature around influenza-like illness in Western community settings<sup>20</sup>.

The outcome of interest was whether participants contracted any PCR-confirmed coronavirus infection in a season. Detected coronavirus strains (NL63, OC43, and 229E) were combined into a binary outcome (yes/no coronavirus) as the effect of hand hygiene is believed to be consistent across these strains. **Covariates.** Age and healthcare worker status were considered important a-priori potential confounders to be adjusted in analyses due to their relationship both with hygiene practices and with risk of contracting coronavirus infections. Children tend to demonstrate poorer hygiene practices and are more likely to be exposed and to contract acute viral respiratory infections<sup>12</sup>. Conversely, healthcare workers may be more likely to engage in high-frequency handwashing but also experience more frequent and intense exposure to respiratory viruses, including coronaviruses. Binary indicators (age: child <16 years vs adult  $\geq$  16 years; healthcare worker status: yes vs no) were created collapsing age and profession categories from the baseline survey.

#### Statistical methods

Robust Poisson mixed models were used to estimate the association between hand hygiene and risk of coronavirus infection. Participants' daily frequency of handwashing was tested as an exposure variable for personal risk of developing PCR-confirmed coronavirus in a season. Hand washing frequency was imputed from the most recent past season for individuals who participated across multiple seasons but did not re-complete the hand hygiene baseline rating.

All models included random effects to account for clustering at the household and individual level (across seasons). Models accounted for person-follow-up-time and were weighted using the inverse of household size to account for the sampling design. Follow-up time was expressed in person-seasons – the proportion of weeks that each participant was active in the study in a given season. Seasons corresponded to the period when coronavirus was estimated to be circulating – defined as the period (in weeks) between the first and last PCR-confirmed case. We excluded participants who participated for a single week. Subsequently, the model was adjusted for confounding by age and healthcare worker status. Results were expressed as incidence rate ratios.

#### Ethics statement

The protocol was approved by the Oxford Multi-Centre Research Ethics Committee (06/Q1604/103).

#### Results

#### **Descriptive statistics**

**Participants.** Table 1 reports demographic characteristics and hand hygiene behaviour for the cohort participants included in this study. The majority of included participants (79.85%) were adults over 16 years of age. Each category of handwashing frequency was followed by a considerable subset of the sample (25.88%–39.47%). Participants' median follow-up time across all seasons was 1.00 person-seasons (IQR 0.94 – 1.00). Further analyses related to clinical details of coronavirus cases and household transmission events are currently in preparation by the Flu Watch group.

Table 2 reports hand hygiene frequency by age group and healthcare worker status, the a-priori potential confounders included in the statistical analyses. The majority of children between 0-4 (71.58%) and 5-15 (52.99%) reported low-frequency

handwashing, which was reported by a lower proportion of participants across adult age groups (14.11-21.69%). Low frequency handwashing was reported by 26.62% of non-healthcare workers versus 8.99% of healthcare workers.

#### Hygiene behaviours and risk of coronavirus infection

Table 3 reports the results of models estimating the relationship between frequency of handwashing and participants' risk of coronavirus infection. Moderate-frequency handwashing was associated with significantly reduced risk of contracting coronavirus compared to low handwashing, (adjusted IRR= 0.64, 95% CI: 0.42, 0.99, p=0.046). For higher intensity handwashing there was no significant effect (adjusted IRR = 0.83, 95% CI (0.53, 1.30) p=0.42.

#### Discussion

This study aimed to assess the relationship between hand hygiene and the risk of contracting seasonal coronavirus infection in an English community cohort. Moderate-frequency handwashing was associated with reduced overall risk of coronavirus infection. These results provide support for public health messages endorsing regular handwashing for personal protection. Given that COVID-19 appears to demonstrate similar transmission mechanisms to seasonal coronaviruses<sup>1-4</sup>, these findings indicate that public health campaigns to increase uptake of regular hand hygiene in community settings are warranted during the current pandemic.

We show a valuable reduction in the risk of acquiring coronavirus infection in moderate-frequency handwashers. This is consistent with the limited observational literature on influenza and influenza-like-illness in community settings<sup>15-19</sup>. The study did not demonstrate a clear dose-response relationship for the protective effect of hand hygiene frequency, with the strongest personal protective effect seen in the moderate-level hand hygiene group and a non-significant protective effect in the highest-frequency hand hygiene group. However, numbers in the highest-frequency handwashing group were lower, limiting power. It is also possible that there is residual confounding. For example, while we adjusted for healthcare worker status, those working in other public-facing professions may be more likely to be high-frequency handwashers and may have increased exposure to coronavirus, which would have mitigated against seeing a protective effect of high-frequency handwashing. The context of handwashing and compliance with recommended handwashing procedures are likely also important. Both longer duration of handwashing and the context of handwashing (e.g. after shaking hands or before eating) have been associated with lower overall risk of influenza or influenza-like-illness in previous studies<sup>15,18</sup>. Only handwashing frequency, and not duration and context of handwashing, were assessed in the behavioural questionnaire used in the current study. Further research into the relationship between hand hygiene practices and risk of coronavirus infections should include all these elements of hand hygiene behaviour.

Despite Flu Watch being the one of the largest cohort studies of respiratory infection, the relatively small number of

Variable		n (%)	
Age (years)	0–4	95 (5.82%)	
	5–15	234 (14.33%)	
	16–44	461 (28.23%)	
	45–64	574 (35.15%)	
	65+	269 (16.47%)	
Sex	Female	854 (52.30%)	
	Male	779 (47.70%)	
Ethnicity	White	1573 (96.33%)	
	Non-white	46 (2.82%)	
	Unknown	14 (0.86%)	
IMD quintile	1 – most deprived	83 (5.08%)	
	2	233 (14.27%)	
	3	473 (28.97%)	
	4	485 (29.70%)	
	5 - least deprived	359 (21.98%)	
Urban/rural status	Urban	1042 (63.81%)	
	Town and fringe	178 (10.90%)	
	Village, hamlet and isolated dwellings	409 (25.05%)	
	Unknown	4 (0.24%)	
Area of England	North	213 (13.04%)	
	West Midlands	152 (9.31%)	
	East and East Midlands	289 (17.70%)	
	London	103 (6.31%)	
	South East	259 (15.86%)	
	South West	617 (37.78%)	
Household Size ( <i>n</i> people)	1	91 (5.57%)	
	2	632 (38.70%)	
	3	302 (18.49%)	
	4	392 (24.00%)	
	5+	216 (13.23%)	
Healthcare Worker	Yes	89 (5.45%)	
	No	1544 (94.55%)	
How many times did you wash your hands yesterday?*	0–5	499 (25.88%)	
	6–10	761 (39.47%)	
	>10	668 (34.65%)	

Table 1. Participant demographic characteristics and hand hygiene behaviour.

\*Note: handwashing frequencies include all seasons of participant follow-up

coronavirus diagnoses limited power and ability to control for confounding. Examining asymptomatic cases was not feasible as samples were only taken from symptomatic cases. Data were also limited to the winter, though included coronavirus strains demonstrate winter seasonality in temperate climates<sup>31,32</sup>. Hand hygiene was self-reported and therefore may have been affected

		Wash hands – previous day: n (row %)			
		0–5 times	6–10 times	11+ times	
Age (years)	0-4	68 (71.58)	25 (26.32)	2 (2.11)	
	5–15	124 (52.99)	96 (41.03)	14 (5.98)	
	16-44	100 (21.69)	194 (42.08)	167 (36.23)	
	45-64	81 (14.11)	243 (42.33)	250 (43.55)	
	65+	46 (17.10)	103 (38.29)	120 (44.61)	
Healthcare Worker	Yes	8 (8.99)	26 (29.21)	55 (61.80)	
	No	411 (26.62)	635 (41.13)	498 (32.25)	

# Table 2. Hand Hygiene Frequency by Age Group and Healthcare Worker Status.

Table 3. Handwashing frequency and participant risk of coronavirus infection.

				Risk - Overall				
				IRR (95% CI)				
		n - No Infection	n -Confirmed Infection	Baseline	р	Adjusted	р	
Wash hands – previous day	0–5 times	443	56					
	6–10 times	706	55	0.65 (0.43, 0.99)	0.04	0.64 (0.42, 0.99)	0.046	
	11+ times	606	62	0.83 (0.55, 1.25)	0.37	0.83 (0.53, 1.30)	0.42	

by social desirability and recall biases. The handwashing frequency item was only measured at baseline and was estimated from the previous 24-hour period so may not reflect usual behaviour for all participants, or behaviour at time of exposure.

This study was the first to examine the personal protective effect of hand hygiene on respiratory coronavirus infections in a community setting. The findings are likely to be generalisable to similar high-income countries. The generalisability of the findings to other coronavirus infections, notably COVID-19, also depends on similarity of epidemiological features. Given the indication of similar transmission mechanisms for COVID-19, corresponding protective effects of handwashing are highly plausible. Strength of effects, however, may depend on the transmissibility of the pathogen and levels of population immunity. Nevertheless, our findings represent important empirical evidence of the value of hand washing, supporting public communication about the importance of this behaviour. Hand washing is minimally disruptive and socially acceptable in a variety of community settings and has an important role in raising awareness and slowing transmission alongside measures such as physical and social distancing<sup>10,11</sup>.

#### Data availability

#### Source data

Open Science Framework: Hand Hygiene Practices and the Risk of Human Coronavirus Infections in a UK Community Cohort. https://doi.org/10.17605/OSF.IO/UGRMY<sup>33</sup>.

This project contains the following underlying data:

- FluWatch\_HandHygiene\_C0V\_HygRisk.dta (hand hygiene data; DTA format).
- HygRisk.csv dta (hand hygiene data; CSV format).

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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# **Open Peer Review**

### Current Peer Review Status: 💙

Version 2

Reviewer Report 29 June 2021

https://doi.org/10.21956/wellcomeopenres.18769.r44599

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#### Peggy Or 匝

The Education University of Hong Kong, Hong Kong, Hong Kong

I have no further comment. Approved for indexing.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infection control.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 06 July 2020

https://doi.org/10.21956/wellcomeopenres.17322.r38956

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#### ? 🛛 Peggy Or 匝

The Education University of Hong Kong, Hong Kong, Hong Kong

• If applicable, is the statistical analysis and its interpretation appropriate: **Partly.** 

There was no statistical analysis on demographic data and in Table 1. no interpretation on demographic characteristics and hand hygiene behaviour. There was no further elaboration on hand washing frequency and participants' demographic data and confirmed cases.

The result section was thin and it was difficult to draw solid conclusion. The arguments in the discussion were not drawn from the study findings such as "both longer duration of handwashing and the context of handwashing have been associated with lower overall risk of influenza or influenza-like-illness". However, there were no such information on duration and context of handwashing in the study.

• Are the conclusions drawn adequately supported by the results? **Partly.** 

The conclusion drawn from handwashing can reduce personal risk of acquiring seasonal coronavirus infection, it was general. It did not further explain why only moderate-frequency handwashing was associated with significantly reduced risk of contracting coronavirus compared to low or high frequency handwashing.

Is the work clearly and accurately presented and does it cite the current literature?  $\ensuremath{\mathsf{Yes}}$ 

Is the study design appropriate and is the work technically sound? Yes

Are sufficient details of methods and analysis provided to allow replication by others?  $\ensuremath{\mathsf{Yes}}$ 

If applicable, is the statistical analysis and its interpretation appropriate? Partly

Are all the source data underlying the results available to ensure full reproducibility?  $\ensuremath{\mathsf{Yes}}$ 

#### Are the conclusions drawn adequately supported by the results?

Partly

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* Infection control.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 17 Jun 2021 Sarah Beale, UCL, London, UK

Many thanks for your helpful comments on the manuscript. We have carefully considered your feedback and present a point-by-point response to each comment below.

"There was no statistical analysis on demographic data and in Table 1. no interpretation on demographic characteristics and hand hygiene behaviour. There was no further elaboration on hand washing frequency and participants' demographic data and confirmed cases."

Thank you for raising this point. We have now added a new table (Table 2) which presents hand hygiene frequency by age group and healthcare worker status, the demographic covariates included in statistical analyses; corresponding text is in Paragraph 2 of the Results. Table 1 was intended to describe the demographic composition of the sample, and the full table was not stratified by hand hygiene frequency as not all demographic variables were included in the main analyses due to limited power (as highlighted in Paragraph 2 of the discussion) and not being selected as most relevant potential confounders a-priori. The main analyses (Table 3) were adjusted for a-priori selected demographic variables (age and healthcare worker status) and regression coefficients of the demographic covariates were not reported separately to avoid the Table 2 fallacy (https://doi.org/10.1093/aje/kws412). Investigation into demographic features of confirmed cases is planned for separate analyses (please see Descriptive Statistics paragraph 1).

"The result section was thin and it was difficult to draw solid conclusion. The arguments in the discussion were not drawn from the study findings such as "both longer duration of handwashing and the context of handwashing have been associated with lower overall risk of influenza or influenza-like-illness". However, there were no such information on duration and context of handwashing in the study."

Thank you for highlighting this issue. We included discussion about duration and context to indicate that these were other important hand hygiene-related factors that have been associated with risk of influenza or influenza-like-illness in the literature but could not be assess in the present study as they were not measured. We have now clarified this point in Paragraph 2 of the discussion, as follows: "Both longer duration of handwashing and the context of handwashing e.g. after shaking hands or before eating – have been associated with lower overall risk of influenza or influenza-like-illness in previous studies (15,18). Only handwashing frequency, and not duration and context of handwashing, were assessed in the behavioural questionnaire used in the current study. Further research into the relationship between hand hygiene practices and risk of coronavirus infections should include all these elements of hand hygiene behaviour."

"The conclusion drawn from handwashing can reduce personal risk of acquiring seasonal coronavirus infection, it was general. It did not further explain why only moderate-frequency handwashing was associated with significantly reduced risk of contracting coronavirus compared to low or high frequency handwashing."

We discuss this finding and potential explanations, including low power and residual confounding, in Paragraph 2 of the discussion. To clarify that this is the topic of discussion in this paragraph, we have rephrased the following sentence leading into this discussion (Discussion paragraph 2, sentence 3): "The study did not demonstrate a clear dose-response relationship for the protective effect of hand hygiene frequency, with the strongest personal protective effect was seen in the moderate-level hand hygiene group and a non-significant protective effect in the highest-frequency hand hygiene group."

*Competing Interests:* No competing interests were disclosed.

Reviewer Report 27 May 2020

https://doi.org/10.21956/wellcomeopenres.17322.r38788

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#### Colum P. Dunne

University of Limerick, Limerick, Ireland

This report is timely and relevant in developing insight into hand hygiene practices, and benefits, in community settings with relevance to the SARS-CoV2 (COVID-19) pandemic. Not prospective, the study utilises existing data generated with respect to seasonal influenza in 2006-2009. Specifically, the authors focus on self-declared hand hygiene (general hand-washing) by community-based participants, and subsequent incidence of flu, with supporting confirmation of infection via nasal swabs.

Overall, the conclusions from this study are measured, and the biases involved are identified. In particular, the challenges associated with self-declaration of practices and memory-based estimation. The authors also discuss the issue of lack of appropriate hand hygiene training or education. This is especially topical as, in the current pandemic, there has been considerable promotion of good practices and an adoption, to some degree, of effective hand-washing procedures and the WHO 5 moments...adapted for community settings and routine living outside of hospitals. The shortage of alcohol gel sanitisers and wipes speaks to this change.

One statement by the Authors is slightly challenging; the conclusion that this study is generalisable "probably also in low- and middle-income countries". This is an assumption that does not consider clean water or soap/surfactant/alcohol gel availability in countries where supply chains, economics, nutrition and basic living conditions do not mirror developed countries.

Otherwise, this is a timely and useful paper.

# Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

#### Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?  $\ensuremath{\mathsf{Yes}}$ 

If applicable, is the statistical analysis and its interpretation appropriate? Not applicable

#### Are all the source data underlying the results available to ensure full reproducibility?

No source data required

#### Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

*Reviewer Expertise:* Translational research, microbiology, infectious disease, outbreaks, management, characterisation.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 17 Jun 2021 Sarah Beale, UCL, London, UK

Many thanks for your positive feedback about the manuscript. Following on from your comments, we have now revised the statement about generalisability in the discussion to read: "The findings are likely to be generalisable to similar high-income countries."

*Competing Interests:* No competing interests were disclosed.