PHILIPPINE COVID-19
LIVING CLINICAL PRACTICE GUIDELINES

As of January 2022

NON-PHARMACOLOGIC INTERVENTIONS for COVID-19

EVIDENCE and RECOMMENDATIONS

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Institute of Clinical Epidemiology, National Institutes of Health
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Cooperating Agency:
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Disclaimer

As a living guideline, the recommendations will be updated, and new recommendations will be added as the evidence evolves. The living recommendations are based on the best evidence available in scientific literature at the time of its formulation. However, this living CPG is not a comprehensive guide to all practice questions and management options on COVID-19. This is not meant to restrict the practitioner in using sound clinical judgement and sharing the decision with the patient, and from considering other management options according to the patient's particular needs and preferences. This CPG can serve to inform policy, but it is not meant to serve as a basis for approving or denying financial coverage or insurance claims merely because of nonconformance with recommendations. Neither are the recommendations supposed to be considered as legal rules for dictating certain modes of action to the exclusion of others.

Contact Us

Send us an email at covidcpg.ph@gmail.com for any questions or clarifications on the outputs and process of this Living CPG. You may also suggest a clinical question for the consideration of the Living Clinical Practice Guidelines COVID-19 Taskforce.

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Quick Guide on How to Interpret the Evidence

Evidence on Therapy

Table 1. Ways of expressing effectiveness

Outcome	Summary of result within each group	Comparison of results between two groups
Dichotomous (e.g. lived or died, BP controlled or not)	Proportion (e.g. deaths per 100 patients)	Relative risk reduction, absolute risk reduction, relative risk (see Table 2)
	Rate = e.g. deaths per 100 patients	Hazard ratio = rate in treatment/rate in control group
Continuous (e.g. blood pressure in mmHg, quality of life on a scale of 0 to 1)	Mean (e.g. mean blood pressure)	Mean difference = mean in control – mean in treatment group

When researchers express the effect of treatment using the relative risk reduction, absolute risk reduction, or relative risk, they often give us a range of possibilities rather than a single estimate. This range of possibilities is called a ‘95% Confidence Interval (95% CI)’ to mean ‘we are 95% sure that the true effect of a drug lies in this range’. Go through Table 2, to discover how helpful 95% CIs are.

Table 2. Interpreting 95% Confidence Intervals (CIs)

Measure of effectiveness and interpretation of estimates	Interpretation of 95% Confidence Intervals (CIs)			
	Superior (treatment surely better than control)	Inferior (treatment surely worse than control)	Inconclusive (we need more studies)	Equivalent (the treatments are equal)[a]
Relative Risk (RR) = R_t/ R_c	Both ends of 95% CI <1.0	Both ends of 95% CI > 1.0	95% CI wide; straddles 1.0	95% CI narrow; straddles 1.0
<1.0 Treatment beneficial =1.0 Treatment no effect >1.0 Treatment harmful	Example: RR = 0.7 [95% CI: 0.6, 0.8]	Example: RR = 2.4 [95% CI: 1.8, 3.2]	Example: RR = 1 [95% CI: 0.2, 5.3]	Example: RR = 1 [95% CI: 0.9, 1.1]
Absolute Risk Reduction (ARR) = R_c - R_t (usually in percent)	Both ends of 95% CI >0%	Both ends of 95% CI <0%	95% CI straddles 0%; either end is far from 0%	95% CI straddles 0%; either end is close to 0%
>0% Treatment beneficial =0% Treatment no effect <0% Treatment harmful	Example: ARR = 2% [95% CI: 1%, 3%]	Example: ARR = -3% [95% CI: -7%, -1%]	Example: ARR = 1% [95% CI: -20%, 32%]	Example: ARR =0.2% [95% CI: -0.1%, 0.5%]

[a] In both inconclusive and equivalent results, the 95% CI interval straddles the point of no effect (ARR = 0% or RR = 1.0). One end reflects the worst possible harm, while the other end reflects the best possible benefit. The only difference is that, in equivalence, either end is close to “no effect” (i.e. any benefit is ignorable and any harm is ignorable too). Consider the ends of the 95% CI to make sure you agree that the benefits and harms are ignorable.

R_c is the rate of the outcomes in the Control group
R_t is the rate of the outcome in the Treatment group

Note: The interpretations in this table only hold if the dichotomous events are expressed as adverse rather than desirable events, e.g. death rather than survival, treatment failure rather that cure, or disease rather than disease-free. When dichotomous outcomes are expressed as desirable events, the interpretation of benefit and harm is reversed.

The balloons below (Figure 1) label the most important parts of the forest plot. Go through these labels and familiarize yourself with the anatomy of the graph. Once you feel sufficiently familiar with the anatomy, go through the notes below on what the forest plot can signify.

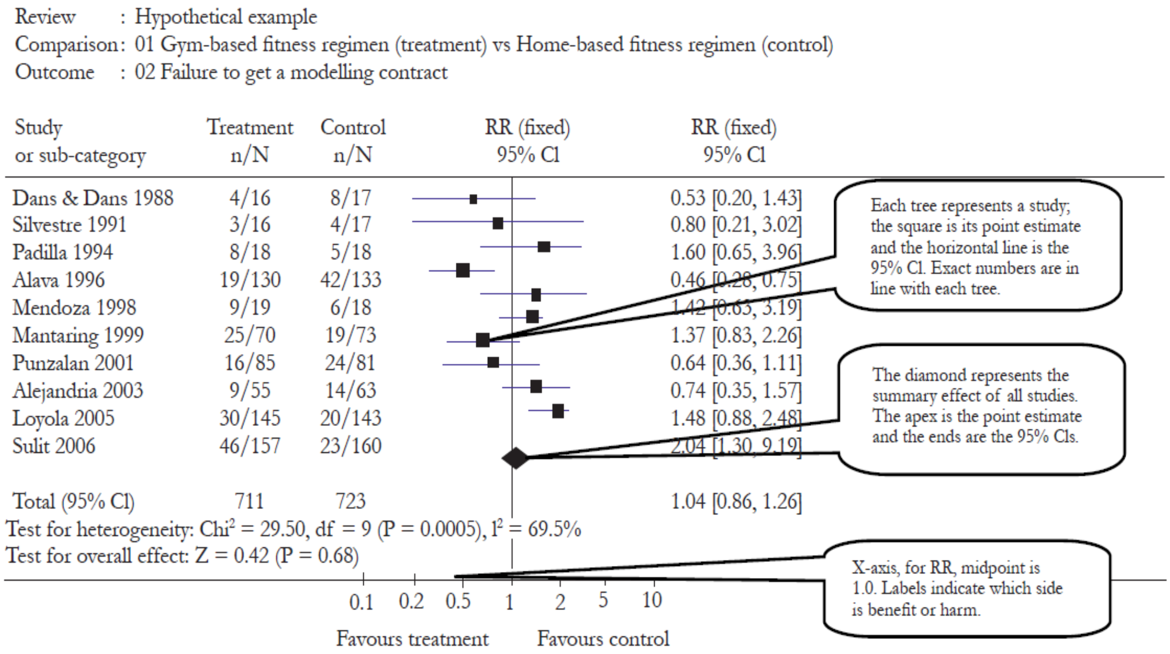

Figure 1. How to interpret forest plots

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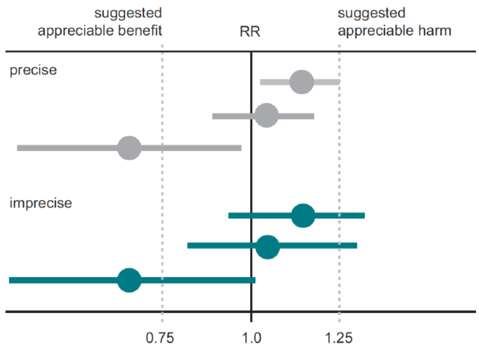
Dans, AL, et al. (2017). Painless Evidence-Based Medicine, 2nd Ed. UK: John Wiley & Sons Ltd.

GRADE Approach in Assessing the Quality of Evidence

(GRADE: Grading of Recommendations Assessment, Development and Evaluation)

These quality ratings apply to the body of evidence assessed for the research question, not to individual studies. Evidence based on randomized controlled trials is initially given a high-quality rating and evidence from observational studies is given a low-quality rating. The level is then adjusted according to the following criteria.

Table 3. Standard criteria for grading of evidence

Domain	Grade	Characteristic
Study Design	0	All randomized controlled trials
	-1	All observational studies
Study Design Limitations	0	Most of the pooled effect provided by studies, with low risk of bias ("A")
	-1	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs <40%
	-2	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs ≥40%
	Note: *Low risk of bias (no limitations or minor limitations) – "A"* *Moderate risk of bias (serious limitations or potentially very serious limitations including unclear concealment of allocation or serious limitations, excluding limitations on randomization or concealment of allocation) – "B"* *High risk of bias (limitations for randomization, concealment of allocation, including small blocked randomization (<10) or other very serious, crucial methodological limitations) – "C"*	
Imprecision	0	The confidence interval is precise according to the figure below. The total cumulative study population is not very small (i.e. sample size is more than 300 participants) and the total number of events is more than 30. 
	-1	One of the above-mentioned conditions is not fulfilled.
	-2	The two above-mentioned are not fulfilled.
	Note: *If the total number of events is less than 30 and the total cumulative sample size is appropriately large (e.g. above 3000 patients, consider not downgrading the evidence). If there are no events in both intervention and control groups, the quality of evidence in the specific outcome should be regarded as very low.*	
Inconsistency	0	No severe heterogeneity (I^2< 60% or X^2<0.05)
	-1	Severe, non-explained, heterogeneity (I^2 ≥60% or X^2<0.05)

Domain	Grade	Characteristic
		If heterogeneity could be caused by publication bias or imprecision due to small studies, downgrade only for publication bias or imprecision (i.e. the same weakness should not be downgraded twice)
Indirectness	0	No indirectness
	-1	Presence of indirect comparison, population, intervention, comparator, or outcome
Publication Bias	0	No evident asymmetry in the funnel plot or less than five studies to be plotted.
	-1	Evident asymmetry in funnel plot with at least five studies

Table 4. Quality of evidence in GRADE

Quality Level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of effect.
Very Low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

REFERENCE

Schünemann H, Brozek J, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. The GRADE Working Group. Available at: https://gdt.gradepro.org/app/handbook/handbook.html.

Evidence Base

List of Questions

This section presents the evidence base for the recommendations on the non-pharmacologic interventions for COVID-19. The following key questions were addressed:

Q1. Should cloth masks be used to prevent COVID-19 infection caused by Variants of Concern (VoC)?

Q2. Is a facemask with face shield more effective than facemask alone in reducing SARS COV2 transmission?

Q3. Should copper-containing masks be used to decrease SARS-CoV-2 transmission?

Q4. Should ionizing air filter be used in the prevention and control of COVID-19 infection in public spaces with sustained community transmission?

Q5. Should foot baths be used in the prevention and control of COVID-19 infection?

Q6. Should misting tents or disinfection chambers be used in preventing and controlling COVID-19 transmission?

Q7. Should ultraviolet (UV) lamps be used in the prevention and control of COVID-19 infection in public spaces in locations with sustained community transmission?

Q8. Should high efficiency particulate air (HEPA) filters be used in the prevention and control of COVID-19 infection in public spaces and locations with sustained community transmission?

Q9. Should carbon dioxide (CO2) monitors be used to reduce transmission of COVID-19?

Q10. What are effective decontamination techniques for N95 reuse?

Q11. What is the appropriate PPE to be used use during surgeries to reduce the risk of virus transmission?

Q12. What is the appropriate PPE for healthcare workers in the outpatient setting to reduce the risk of virus transmission?

Q13. What is the appropriate PPE for health care workers in the wards, ICU and emergency room to reduce the risk of virus transmission?

Q14. Should protective physical barriers be used to prevent COVID-19?

Q15. Should surfaces be disinfected to prevent COVID-19 infection?

Q1. Should cloth masks be used to prevent COVID-19 infection caused by Variants of Concern (VoC)?

As of 03 December 2021

RECOMMENDATION

We recommend the proper use of either a well-fitted cloth mask or a medical mask in the community setting. If a cloth mask will be used, we suggest that it should be made of at least two layers of cotton (e.g., t-shirt fabric) or non-woven nylon with aluminum nose bridge. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues

The panel unanimously recommended the proper use of either a well-fitted cloth or a medical mask in the community setting. Whether to add qualifiers or not (regarding, for instance, the type of fabric and the particular setting) to this updated recommendation, as was done in the previous one, weighed heavily on the consensus panel and was discussed extensively. Eventually, it was highlighted that regardless of the community area or situation (e.g., crowded places, close-contact settings, confined and enclosed spaces, indoors or outdoors), proper wearing of a well-fitted mask must be emphasized and is still strongly recommended.

KEY FINDINGS

At the time of writing, there were no published nor preprint studies that directly investigated the efficacy or effectiveness of cloth masks in preventing COVID-19 infection caused by specific SARS-CoV-2 variants of concern (VoC). There was indirect evidence from two studies that investigated cloth masks for the prevention of COVID-19 in general: one was a case-control study that showed no significant difference between cloth mask and medical mask, and the other was a cluster-randomized trial which showed that both cloth and surgical mask reduced the proportion of people with COVID-19-like symptoms in the community. The indirect evidence from these two studies suggested that cloth masks can reduce symptomatic COVID-19 cases at the community level, albeit at a lesser degree compared to medical masks. It also suggested that the community use of both surgical and cloth masks can reduce symptomatic COVID-19 cases at the community level.

INTRODUCTION

SARS-CoV-2 can be transmitted via direct, indirect, or close contact with an infected person through infected respiratory droplets (>5-10 μm), respiratory secretions, saliva, or through aerosols especially in poorly-ventilated and/or crowded indoor settings.[1] The World Health Organization uses the “3Cs” concept ((1) crowded places; (2) close contact settings, especially when people have conversations very near each other; (3) confined and enclosed spaces with poor ventilation) to illustrate settings where COVID-19 is more readily transmitted.[1]

The use of face masks was one of the consistently recommended non-pharmacologic interventions to prevent COVID-19 transmission when COVID-19 vaccines were not yet available, and remains to be so. Israel stopped the mandatory use of face masks when it was able to vaccinate 80% of its adult population, which corresponded to 50% of its total population.[2] However, the resurgence of COVID-19 cases despite the high vaccination rate prompted the country to reimpose its nationwide mask mandate.[3] The rise in COVID-19 cases was attributed to the presence of the Delta variant in the said country.[4] In other countries, the use of face masks has been reemphasized in the presence of the more transmissible SARS-CoV-2 variants.

Just like other viruses, SARS-CoV-2 evolves over time. Persistent circulation of a virus in the community increases its likelihood to mutate.[5] The first SARS-CoV-2 VoC was identified in the United Kingdom in September 2020 and was designated as a VoC later in December 2020.[6]

This review was undertaken to determine the efficacy or effectiveness of cloth mask in preventing COVID-19 infection due to Variants of Concern.

Table 5. SARS-CoV-2 Variants of Concern as of 05 October 2021 [6–9]

WHO Label	Pango lineage	Location of first known outbreak	Date earliest samples were documented	Designation date	Description
Alpha	B.1.1.7	United Kingdom	September 2020	18 December 2020	Easier to transmit, associated with more severe COVID-19, and possibly more transmissible than the original strain.
Beta	B.1.351	South Africa	May 2020	18 December 2020	Known to have some resistance to certain SARS-CoV-2 vaccines.
Gamma	P.1	Brazil	November 2020	11 January 2021	May reduce the protective effect of antibodies.
Delta	B.1617.2	India	October 2020	11 May 2021	Has increased transmissibility and makes vaccines less efficacious.

REVIEW METHODS

The team conducted a systematic search of published articles in PubMed for MEDLINE, the Cochrane Library, SCOPUS, Google Scholar, Clinical Key (Elsevier), and HERDIN Plus. Preprints in MedRxiv and BioRxiv were also searched for any study related to the research question. The team also looked at *Clinicaltrials.gov* and Epistemonikos for any ongoing studies related to cloth mask use against any VoC. The team used the keywords and mesh terms “cloth mask”, “nonmedical mask”, “disposable mask”, “nonwoven mask”, “face mask”, “medical mask”, and “surgical mask” to search for both cloth mask and other masks. To search for COVID-19, the team used some COVID-related search strings.[10] The team searched for systematic reviews, randomized controlled trials, and observational studies until October 5, 2021.

We included articles with the following PICO:

Table 6. PICO table for Q1.

Population	People with no COVID-19 or suspected to be at risk from COVID-19 Healthcare Workers Essential frontliners Household and occupational contacts General public People who are vaccinated (partially or fully)
Intervention	Cloth mask
Comparator	Basic surgical mask
Outcome	Proportion of people with confirmed COVID-19 infection caused by any VoC

RESULTS

We found no articles that directly compared cloth masks to basic surgical masks in preventing COVID-19 transmission caused by any VoC. The two studies included in this review (one cluster-randomized trial and one case-control study) investigated cloth masks for the prevention of COVID-19 transmission in general, without considering any VoC.

The case-control study done in Thailand evaluated the effectiveness of various personal protective measures against COVID-19 in 211 asymptomatic cases and 839 asymptomatic controls.[11] Using their data, we analyzed the subset of participants who used either a cloth mask (n=102) or a medical mask (n=281). Among those who wore a cloth mask, 25 developed COVID-19; in the medical mask group, 72 had COVID-19. There was no significant difference between the two groups (OR 0.94, 95% CI 0.56 – 1.59).

The cluster-randomized trial was done in a rural area in Bangladesh to ascertain strategies to increase mask-wearing (subclassified into cloth mask and surgical mask users) and to learn the impact of increasing mask use on symptomatic COVID-19. Two outcomes were used to determine the impact of mask-wearing on community COVID-19 cases. The first outcome involved getting the symptomatic seroprevalence of all participants from the intervention group and the control group, the latter of which used surgical masks, while the other outcome used the WHO-defined COVID-19 symptomatic status.

The study showed that general mask use can reduce symptomatic seroprevalence of COVID-19 in the community by 9.3% (p = 0.043), given a 29-percentage point increase in mask wearing over 8 weeks. When segregated by type of face mask, the use of surgical masks led to a relative seroprevalence reduction of 11.2% (p = 0.043), while the use of cloth masks resulted in a relative seroprevalence reduction of 5.0% (p = 0.540).[12] The study also demonstrated that mask use can reduce the proportion of individuals in the community with COVID-19-like symptoms by 11.9% (p = 0.000). Both surgical and cloth mask use can reduce the proportion of people with COVID-19-like symptoms in the community by 13.6% (p = 0.000) and 8.5% (p = 0.048), respectively

[12]. This also supports the finding of one study that cloth masks can be used as an alternative to medical masks especially when there is a low supply of the latter.[13]

EVIDENCE TO DECISION

Economic Impact of a Mask Mandate in a Community

Cloth masks are available in online stores in the Philippines for P15.00 per piece [14] and used by a person for up to 4 times per day [15]. One study done in Luzon, Philippines suggested that face mask use, together with other interventions like healthy lifestyle, social distancing, face mask, proper hygiene, and lockdown seemed to enhance the perceived effectiveness of COVID-19 preventive measures [16].

- No cost-effectiveness study found on use of cloth mask vs. medical mask.
- Costing
    - Cloth mask - P15.00/ piece, to be used by a person for up to 4 times per day [15]
    - Disposable surgical mask, 3 ply: Php 35-140/ 50pcs (Shopee – shipping fee not included)
- In a study conducted in Metro Manila, regarding the attitude towards mask use in general, majority of the respondents believe that mask use is an effective preventive measure against COVID-19 transmission, are comfortable when other people wear masks, and believe that mask wearing does not lead to non-compliance to social distancing [22]

RECOMMENDATIONS FROM OTHER GROUPS

The World Health Organization still recommends the use of non-medical, fabric masks by the general public below 60 years of age who do not have comorbidities even in settings where VoC are present in the community.[17,18]

The United Kingdom's Scientific Advisory Group for Emergencies – Environmental and Modelling group (SAGE-EMG) recommends more consistent and effective use of fabric face coverings and physical distancing, alongside other interventions to mitigate transmission of the B117 (Alpha) variant. Despite the uncertainties as to the increased transmissibility of the Alpha variant, the behavior of the respiratory particle is likely unchanged.[19] Fabric masks in conjunction with physical distancing are important mitigation strategies against the Alpha variant, albeit in a more consistent and effective manner.

On July 27, 2021, a guidance specific to the Delta variant was released by the United States Centers for Disease Control and Prevention (CDC). It reiterated the use of masks in public indoor spaces, including those who are fully vaccinated.[20] Cloth masks are recommended to be used in this setting, provided it has (1) proper fit over the wearer's nose and mouth to prevent leaks, (2) has multiple layers of tightly woven, breathable fabric, (3) with a nose wire, and (4) made up of fabric that blocks light when held up to a bright light source.[21]

RESEARCH GAPS

Currently, there are no ongoing or completed studies looking into the efficacy or effectiveness of cloth masks in reducing infections caused specifically by SARS-CoV-2 variants. There is a need to investigate what fabrics of cloth mask, or how many layers of cloth, are required to effectively prevent infection with the more transmissible variants. Evidence would be needed for the efficacy of cloth masks against transmission of new variants, as they are identified and named to be of variants of concern. There is also necessity to guide public health measures among fully vaccinated individuals compared to non- or partially vaccinated ones, with regard to cloth mask use.

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Appendix 1. Evidence to Decision

Table 7. Summary of initial judgments prior to the actual panel meeting (n = 9).

FACTORS	JUDGMENT					RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
Problem	No	Yes (9)				• In other countries, the use of face masks has been reemphasized in the presence of the more transmissible SARS-CoV-2 variants

Benefits	Large (2)	Moderate (4)	Small (1)	Uncertain (2)		• Outcome 1: Proportion of people with confirmed
						  ○ There was an inconclusive result with regard to COVID-19 infection caused by any VoC
						• Outcome 2: Seropositivity from COVID-19
						  ○ Results were inconclusive.
						• Outcome 3: Presence of COVID-19-like symptoms
						  ○ Results showed a 5% reduction in the presence of COVID-19-like symptoms.
						Benefits depend also on proper wearing of masks, quality of masks and other hygienic practices

Harm	Large (2)	Small (3)	Uncertain (4)	Varies		• None reported.
Certainty of Evidence	High	Moderate	Low (4)	Very low (5)		• The overall certainty of evidence is very low due to risk of bias, indirectness and imprecision.

Balance of effects	Favors cloth mask (3)	Does not favor cloth mask (2)	Uncertain (4)	Varies		• Outcome 1: Proportion of people with confirmed
						  ○ There was an inconclusive result with regard to COVID-19 infection caused by any VoC
						• Outcome 2: Seropositivity from COVID-19
						  ○ Results were inconclusive.
						• Outcome 3: Presence of COVID-19-like symptoms
						  ○ Results showed a 5% reduction in the presence of COVID-19-like symptoms.
						• No harms were reported.

Values	Important uncertainty or variability (2)	Possibly important uncertainty or variability (2)	Possibly NO important uncertainty or variability (4)	No important uncertainty or variability (1)		

Resources Required	Uncertain	Large cost (1)	Moderate Cost (2)	Negligible cost or savings (4)	Moderate savings (2)	Large savings	• Cloth mask - P15.00/ piece, to be used by a person for up to 4 times per day Disposable surgical mask, 3 ply: Php 35-140/ 50pcs (Shopee – shipping fee not included) • *Cloth masks are cheaper.*
Certainty of evidence of required resources	No included studies (5)	Very low	Low (2)	Moderate (1)	High (1)		• No cost-effectiveness study found on use of cloth mask vs. medical mask. • Cloth mask - P15.00/ piece, to be used by a person for up to 4 times per day [15]. Disposable surgical mask, 3 ply: Php 35-140/ 50pcs (Shopee – shipping fee not included)
Cost effectiveness	No included studies (7)	Favors the comparison	Does not favor either the intervention or the comparison (1)	Favors the intervention (1)			• No cost-effectiveness study found on use of cloth mask vs. medical mask.
Equity	Uncertain (6)	Reduced (1)	Probably no impact (1)	Increased (1)			• No research evidence found.
Acceptability	Uncertain (2)	No	Yes (7)	Varies			• In a study conducted in Metro Manila, as regards the attitude towards mask use in general, majority of the respondents believe that mask use is an effective preventive measure against COVID-19 transmission, are comfortable when other people wear masks, and mask wearing does not lead to non-compliance to social distancing • *Cloth masks are cheaper and cause less environmental pollution because of reuse. Poor disposal of medical mask is a problem.*
Feasibility	Uncertain	No (1)	Yes (8)	Varies			• In a study conducted in Metro Manila, sociodemographic profile of the respondents does not correspond to their knowledge and attitudes towards the proper use of PPEs amidst the pandemic. Economic status and sex do not show any significant association with the practice of Filipinos towards the COVID-19 pandemic. Age and educational attainment has association with their practices.

Appendix 2. Search Yield and Results

Search date: 11 September 2021

Search	Query	Results
#1	"COVID-19" AND (("cloth mask" OR "non-medical mask") AND ("medical mask" OR "surgical mask"))	17

Other databases searched:

- Published: *Scopus, Google Scholar, Clinical Key (Elsevier), and HERDIN Plus.*
- Preprints: *MedRxiv and BioRxiv*
- Ongoing studies: *Clinicaltrials.gov and Epistemonikos*

Appendix 3. Characteristics of Included Studies

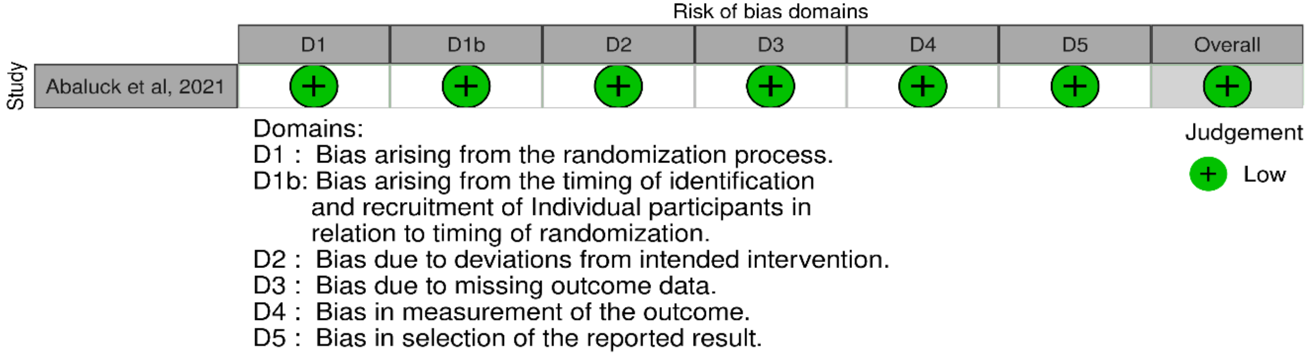
Author	Population	Intervention	Comparator	Outcome	n
Doung-Ngern et al, 2020	Asymptomatic Thai individuals who reported mask use	Cloth mask	Medical mask	Proportion of persons who turned out to be asymptomatic positive for COVID-19	Case = 211 Control = 839 n = 1050
Abaluck et al, 2021	Residents of selected rural villages in Bangladesh	Cloth mask	Medical mask	(1) Prevalence ratio of symptomatic seropositive individuals from COVID-19 (2) Prevalence ratio of persons with COVID-19_like symptoms as defined by the WHO	(1) Cloth mask = 400; Medical mask = 7115 n = 146783 (2) Cloth mask = 4487; Medical mask = 8364 n = 155268

Appendix 4. Study Appraisal

A. Observational studies (Newcastle Ottawa Scale)

Study	Selection	Comparability	Exposure
Doung-ngern et al, 2020	***	**	*

B. Cluster-Randomized Trial (Cochrane ROB 2 for Cluser-Randomized Trials)



Appendix 5. GRADE Evidence Profile

Question: Cloth mask compared to Medical mask against COVID-19 for COVID-19 Variants of Concern

Bibliography:

Doung-Ngern P, Suphanchaimat R, Panjangampatthana A, et al. Case-Control Study of Use of Personal Protective Measures and Risk for SARS-CoV 2 Infection, Thailand. Emerg Infect Dis 2020; 26: 2607–2616.

Abaluck J, Kwnong L, Styczynski A, et al. The Impact of Community Masking on COVID-19: A Cluster-Randomized Trial in Bangladesh, https://www.poverty-action.org/sites/default/files/publications/Mask_RCT____Symptomatic_Seropositivity_083121.pdf (2021, accessed 17 September 2021).

CERTAINTY ASSESSMENT							NO. OF PATIENTS		EFFECT		CERTAINTY	IMPORTANCE
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cloth mask	Medical mask	Relative (95% CI)	Absolute (95% CI)		
Proportion of people with confirmed COVID-19 infection												
1	Observational studies	Serious	Not serious	Serious[a]	Serious[b]	None	25/102	72/281	OR 0.94 (0.56 to 1.59)	5 fewer per 1,000 (from 38 fewer to 47 more)	⊕◯◯◯ Very low	
Seropositivity from COVID-19 (assessed with: Prevalence Ratio)												
1	Randomised trials	Not serious	Not serious	Serious[a]	Serious[c]	None	401/54112 (0.7%)	712/106201 (0.7%)	RR 0.91 (0.80 to 1.02)	1 fewer per 1,000 (from 1 fewer to 0 fewer)	⊕⊕◯◯ Low	
Presence of COVID-19-like symptoms (assessed with: Prevalence Ratio)												
1	Randomised trials	Not serious	Not serious	Serious[a]	Serious[c]	None	4488/56803 (7.9%)	8365/111525 (7.5%)	RR 0.95 (0.92 to 0.98)	4 fewer per 1,000 (from 6 fewer to 2 fewer)	⊕⊕◯◯ Low	

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

[a] Study does not take into account the presence of SARS-CoV-2 variants of concern.
[b] The confidence interval is wide
[c] Some values, like the number of people with COVID-19 on each study arm, were not given in the paper.

Q2. Is a facemask with face shield more effective than facemask alone in reducing SARS COV2 transmission?

As of 05 November 2021

RECOMMENDATIONS

We suggest against requiring the use of face shields in addition to face masks among the general public in non-healthcare settings. *(Very low certainty of evidence; Weak recommendation)*

We recommend the addition of face shields to face masks among the general public in areas with sustained community transmission of SARS-CoV-2. *(Very low certainty of evidence; Strong recommendation)*

We recommend the use of face shield plus medical face mask and standard personal protective equipment among health care workers not directly involved in the care of COVID-19 patients in areas with sustained community transmission of SARS-COV2. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues

For the first statement, which suggests against obligatory public use of face shields, the panel's primary consideration was the insufficient evidence from existing literature that was assessed to be of very low certainty. This assessment stemmed from the indirectness of the studies in which they enrolled healthcare workers – rather than the general public – in the community, and included laboratory experiments not directly involving humans, as well as studies that investigated different viral infections with varied routes of transmission. Other factors affecting the panel's decision were public preference and observed poor compliance, environmental pollution, safety issues particularly in workplaces, additional costs, increasing vaccination rates, declining COVID-19 incidence, and the individuals' capacity to assess their own risk in the community. Despite this suggestion to rescind the mandatory use of face shields, continued proper use of well-fitted face masks is still recommended.

Due to the perceived benefit of providing an additional mechanical barrier against viral infections, the panel maintained a strong recommendation for wearing both face masks and face shields in high-risk environments such as crowded public transit, poorly ventilated spaces, and areas with high incidence of COVID-19 cases. In support of this, the panel considered the indirect evidence taken from a high-quality meta-analysis that showed a 78% reduction of risk in contracting respiratory infections from SARS-CoV-2, SARS, or MERS when an eye protector such as face shield or goggles was used compared with none.

There was a unanimous decision on adopting the previous recommendation on the use of face shield plus medical face mask for the healthcare workers and no concerns were mentioned.

PREVIOUS RECOMMENDATIONS
We suggest the use of face shield plus face mask among the general public in areas with sustained community transmission of SARS-COV2. *(Very low quality of evidence; Conditional recommendation)* We recommend the use of face shield plus medical face mask and standard personal protective equipment among health care workers not directly involved in the care of COVID-19 patients in areas with sustained community transmission of SARS-COV2. *(Very low quality of evidence; Strong recommendation)* We suggest using a cloth mask that fits snugly on the face and made of at least two layers of cotton (e.g., t-shirt fabric) or non-woven nylon with aluminum nose bridge by the general public with low risk of exposure to COVID-19 in outdoor or indoor areas to prevent COVID-19 infections. *(Low quality of evidence; Conditional recommendation)* *Previous Consensus Issues* The very low quality of evidence was due to biases and imprecision seen in the observational studies included in the review. It was noted that none of the studies considered ventilation or testing in an enclosed space. Since the World Health Organization declared COVID-19 as airborne, there can be transmission if there is no eye covering or face shield

WHAT'S NEW IN THIS VERSION?

This updated review includes two new case-control studies that were not included in the original evidence. Analysis of the effect estimates was performed according to setting (hospital and community), and then according to study design (case-control, and pre- and post-surveillance studies).

KEY FINDINGS

There was no available direct evidence for face shield plus face mask versus face mask alone in the general public. In the initial review done in May 2021, there were three studies that were included; for this updated review (until September 2021) we found two additional case-control studies. All these five studies were conducted among health care workers: four were done in the health care setting and one in the community. Three case-control studies showed a trend toward benefit with the use of face shields but this was inconclusive (OR 0.85, 95% CI 0.68-1.08). Two pre- and post- face shield use surveillance studies showed significant benefit (OR 0.28, 95% CI 0.22-0.37 and OR 0.04, 95% CI 0.00-0.69), respectively. The overall certainty of evidence was very low as the studies were non-randomized, unadjusted for confounders and with high risk of bias as well as indirectness.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is mainly transmitted through respiratory droplets and close contact, with a particular concern for airborne transmission especially during aerosol-generating procedures. In SARS-CoV-2, SARS or MERS, reduced risk of infection was observed with the use of surgical or 12-16 layer cotton masks (OR 0.15, 95% CI 0.07-0·34); the use of eye protectors showed significant protection (OR 0.22, 95% CI 0.12-0.39), translating to 78% relative risk reduction.[1] The use of face shields was found to reduce the potential for autoinoculation by preventing one from touching the front and side of the face, and to protect viral entry into the eyes, nose and mouth.[2]

REVIEW METHODS

We comprehensively searched various electronic databases that included PUBMED, MEDLINE, Cochrane CENTRAL, ChinaXiv, MedRXIV, BioRXIV, as well as the following registries for ongoing and completed trials: USA - https://clinicaltrials.gov/; China - http://www.chictr.org.cn/searchprojen.aspx; and the WHO - https://www.who.int/clinical-trials-registry-platform. We also searched for published/ongoing studies on the COVID-19 Open Living Evidence Synthesis: https://covid-nma.com/ and the Living Evidence on COVID-19: https://zika.ispm.unibe.ch/assets/data/pub/search_beta/. The last search date was September 30, 2021 using a combination of subject headings and keywords for the following PICO: P – general public; I – face shield with face mask, face shield; C – no face shield; and O – prevalence of SARS-CoV-2 transmission. We included any type of study that investigated the effects of face shield or face mask on the incidence of SARS-COV-2 infection. We checked the reference lists of included papers and relevant systematic reviews. We also did a free search of online sources, preprint articles, and various coronavirus resource centers. We screened abstracts, reviewed full texts and extracted relevant information on study design, settings, population and outcomes. There was no language restriction. We screened studies, extracted data, assessed risk of bias and certainty of evidence using the GRADE approach.

RESULTS

Similar to the previous evidence synthesis [3], there is no available direct evidence for face shield plus face mask versus face mask alone in the general public. For this update, we only found two additional case-control studies that dwelt on healthcare workers in the hospital and community settings. A summary of our five included studies is shown in Appendix 3.

The three case-control studies[4-6] included in this review enrolled a total of 1164 healthcare workers in a hospital/healthcare setting. Of these, 608 used or always used face shield or goggles while 556 did not use or did not always use face shield or goggles. In the former group, 295 tested positive for COVID-19; in the latter, 291 had positive results. The pooled estimate for the outcome of COVID-19 infection showed a trend toward benefit with the use of face shield or goggles, but this was inconclusive (OR 0.85, 95% CI 0.68-1.08).

The critical appraisal of these three studies is shown in Appendix 4. There were issues related to representativeness, selection of controls, and ascertainment of exposure. The overall certainty of evidence was judged to be very low (see Appendix 5A).

The pre- and post-surveillance study of Mohajer et al. [7] done in a healthcare setting reported that before the use of face shields was instituted in their hospital, 166 individuals out of the 2486 tested had positive RT-PCR results. After the hospital-wide directive on face shield use, only 80 of the 4041 persons tested were positive on RT-PCR. This study showed significant benefit with the use of face shields (OR 0.28, 95% CI 0.22-0.37); however, the certainty of evidence was very low because of serious risk of bias and indirectness (see Appendix 5B).

The pre-and post-surveillance study done in the community by Bhaskar and Arun [8] involved 62 healthcare workers serving in the community. Before the use of face shields, 12 of the healthcare workers contracted COVID-19. After the initiation of face shield use, none of the remaining 50 contracted the infection. There was significant protection with the use of face shields (OR 0.04, 95% CI 0.00-0.69). The certainty of evidence was assessed to be very low because of very serious risk of bias, imprecision and indirectness.

RECOMMENDATIONS FROM OTHER GROUPS

The Center for Disease Control [9], as of 19 April 2021, recommends the use of masks in addition to staying at least 6 feet apart in the following situations: (1) when indoors around people who don't live in the same household; (2) traveling on a plane, bus, train, or other form of public transportation traveling into, within, or out of the United States and in U.S. transportation hubs such as airports and stations; (3) in public settings and when around people who don't live in the same household; and (4) inside the house if a household member is sick with symptoms of COVID-19 or has tested positive for COVID-19. Goggles or other eye protection may be used in addition to a mask.

The World Health Organization [10], as of 01 December 2020, recommends the use of mask in areas where the virus is circulating, when at least 1 meter distance from others is not possible, poor or unknown ventilation which depends on the rate of air change, recirculation and outdoor fresh air. There was no recommendation made on the use of face shield

The Interagency Task Force For the Management of Emerging Infectious Disease, as of 14 December 2020 [11], recommends that all persons are mandated to wear full-coverage face shields together with face masks, ear-loop masks, indigenous, reusable, or do-it-yourself masks, or other facial protective equipment which can effectively lessen the transmission of COVID-19, whenever they go out of their residences. In 23 September 2021, this was amended to limit
the use of face shields, on top of face mask, in high-risk activities in closed, crowded areas and if with close contact.

RESEARCH GAPS

We do not have data on the use of face shield in addition to face mask as protection against COVID 19 infection for the general public in the community during the pandemic.

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Appendix 1. Evidence to Decision

Summary of initial judgements prior to the actual panel meeting (N = 8)

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
Problem	No	Yes (8)					
Benefits	Large (3)	Moderate (3)	Small (1)	Uncertain (1)			• NO EVIDENCE for the reduction of risk in the general public • BENEFIT among healthcare workers in both hospital (OR 0.28, 95% CI 0.23-0.37) and community settings; INCONCLUSIVE BENEFIT from 3 cohort studies among HCW in hospital • These PPE can prevent transmission of other respiratory infectious organisms
Harm	Large (2)	Small (6)	Uncertain	Varies			• OR 0.85, 95% CI 0.68 – 1.08: Tendency to have minimal risk of COVID-19 infection among HCW in the hospital setting
Certainty of Evidence	High	Moderate (2)	Low (4)	Very low (2)			• The overall certainty of evidence: VERY LOW
Balance of effects	Favors drug (4)	Does not favor drug	Uncertain (4)	Varies			
Values	Important uncertainty or variability (3)	Possibly important uncertainty or variability (3)	Possibly NO important uncertainty or variability (2)	No important uncertainty or variability			
Resources Required	Uncertain	Large cost (1)	Moderate Cost (6)	Negligible cost (1)	Moderate savings	Large savings	• No cost-effectiveness studies available. • Costing(1): ○ Facemask + Face shield: Php 50 - 250 ○ Facemask: Php 25-200
Certainty of evidence of required resources	No included studies (5)	Very low (2)	Low (1)	Moderate	High		• No cost-effectiveness studies available.

Cost effectiveness	No included studies (6)	Favors the comparison (1)	Does not favor either the intervention or the comparison (1)	Favors the intervention		• No cost-effectiveness studies available.
Equity	Uncertain (3)	Reduced (2)	Probably no impact (1)	Increased (2)		• No local studies available.
Acceptability	Uncertain (1)	No (5)	Yes (2)	Varies		• In the survey of 400 adults, 90.75% perceived that face mask is the most effective PPE. 35/400 among adults in Metro Manila believed that face shield is most effective personal protective equipment(2) • Ease of use • Vaccination status should be considered
Feasibility	Uncertain	No (1)	Yes (7)	Varies		• No local studies available.

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Appendix 2. Search Yield and Results

14	#6 AND #1:	Most Recent	("covid 19"	68
13	#8 AND #1:	Most Recent	("covid 19"	30
12	#10 AND #:	Most Recent	("covid 19"	22
11	transmissic	Most Recent	"transmiss;	587,541
10	#1 AND #9	Most Recent	("covid 19"	30
9	N95 mask	Most Recent	"n95 respir	1,133
8	#1 AND #2	Most Recent	("covid 19"	46
7	eye goggle	Most Recent	("eye"[MeS	2,805
6	#1 AND #2	Most Recent	("covid 19"	114
5	face shield	Most Recent	("face"[Me	1,415
4	#1 AND #2	Most Recent	("covid 19"	2,939
3	surgical ma	Most Recent	("surgical p	8,303
2	Mask	Most Recent	"masks"[M	45,852
1	(COVID 19)	Most Recent	("covid 19"	111,590

Appendix 3. Characteristics of Included Studies

	Setting	Population	COVID (+)	COVID (-)	Intervention	Comparator	Outcome
Khalil SN	Dhaka Bangladesh	190 Medical staff in 19 health facilities	98	92	Face shield	No Face Shield	Number of HCW with face shield infected with COVID 19
Mojajer A	Houston Texas	6527 Health Care Personnel (HCP) of a quartemary health hospital	246	6281	Face shield[1] with standard PPE	Standard PPE	Number of HCP infected before and after implementation of use of face shield with standard PPE Number of HCP with HAI before and after implementation of use of face shield with standard PPE
Bhaskar	India	112 HCW	12	100	Face shield and PPE	PPE alone	Number of HCW with COVID 19 before and after implementation of use of face shield with PPE
Chatterjee	India	751 HCW	378	373	Use of Face shield or goggles (either or both)	No face shield/goggles	Number of HCW with face shield infected with COVID 19
Rodriguez Lopez	Cali Colombia	223 HCW	120	103	Use of Face shield/goggles always	Use of Face shield/goggles not always	Number of HCW with face shield infected with COVID 19

[1] Face shield used was a Lazarus 3D (Corvallis, OR, USA)
[2] Personal protective equipment included alcohol hand rub, 3-layered surgical masks, gloves, and shoe covers and physical distancing.
Abbreviation: HCW – health care workers; HAI – hospital acquired infection; PPE – personal protective equipment

Appendix 4. Appraisal of Included Studies

Case control studies	**Khalil 2020**	**Chatterjee 2020**	**Rodriguez-Lopez 2021**
Selection			
Is case definition adequate	Yes (RT PCR +)	Yes (RT PCR+)	Yes (RT PCR+)
Representatives of the cases	Not stated how they were selected from the list	Not stated how they were selected from the data portal	Selected by random sample from those identified as HCW with or without symptoms
Selection of control	Not stated how they were selected from the list	Not stated how they were selected from the data portal	Selected by random sample from those identified as HCW with or without symptoms
Definition of control **Comparability of cases and controls on the basis of the design and analysis**	Yes (RT PCR -) Yes (Cases and controls were selected on the basis of their RT PCR tests). No difference in the baseline characteristics of cases and controls	Yes (RT PCR -) Yes (Cases and controls were selected on the basis of their RT PCR tests). In those who were positive, there were more males and with duration of work in the workplace >1 year)	Yes (RT PCR -) Yes (Cases and controls were selected on the basis of their RT PCR tests); There were more COVID positive who were males, worked in high risk areas and night shift
Exposure Ascertainment of Exposure	Information was obtained online thru a Google form using a predesigned structured questionnaire	No statement that the telephone interviewer was blinded to COVID status of the interviewee (no interviewer variability was reported)	Data collected by two trained researchers by telephone interview using structured questionnaire who were blinded to the COVID status of the

Appendix 5. GRADE Evidence Profile

A. Case control studies

Face Shield compared to No Face Shield for Health Care Workers

CERTAINTY ASSESSMENT							SUMMARY OF FINDINGS				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates		Relative effect (95% CI)	Anticipated absolute effects	
							With no face shield	With face shield		Risk with no face shield	Risk difference with face shield
COVID-19 Infection (assessed with RT-PCR)											
										High	
586 COVID positive; 578 COVID negative 295/556 without face shield (3 observational studies)	Very Serious[a]	Serious[b]	Serious[c]	Not serious	Strong association All plausible residual confounding would reduce the demonstrated effect	⊕◯◯◯ Very low	586 COVID positive; 578 COVID negative 295/556 without face shield (3 observational studies)		OR 0.85 (0.68 to 1.08)	0 per 1,000	0 fewer per 1,000 (from 0 fewer to 0 fewer)

CI: confidence interval; **OR:** odds ratio

Explanations

[a] Compliance with face shield use and other health protocols was not assessed; some studies were based on interview or structured questionnaire and may have caused recall bias

[b] Considerable heterogeneity (I2=92%) with overlap on the confidence intervals of the studies

[c] Research question should answer 'use of face shield and face mask vs face mask alone'

B. Pre- and post-surveillance study among health care workers

Author(s): Germana Emerita Gregorio, MD; Myzelle Anne Infantado, PTRP, MSc (cand.) Maria Teresa Sanchez-Tolosa, MD, D Clin Epi, FPDS

Question: Is Facemask with Face Shield more effective than Facemask alone in reducing SARS COV2 transmission?

Setting: Community setting

Bibliography: Mojajer M, Panthagani KM, Lasco T, Lembcke B, Hemmige V. Association between universal face shield in a quaternary care center and reduction of SARS-COV-2 infections among healthcare personnel and hospitalized patients. International JJournal of Infectious Diseases. 2021 Apr;105:252–5.
Bhaskar ME, Arun S. SARS-CoV-2 Infection Among Community Health Workers in India Before and After Use of Face Shields. JAMA. 2020 Oct 6;324(13):1348.

CERTAINTY ASSESSMENT							NO. OF PATIENTS		EFFECT		CERTAINTY	IMPORTANCE
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	With face shield	With no face shield	Relative (95% CI)	Absolute (95% CI)		
In the Hospital: COVID-19 Infection (assessed with COVID-19 RT-PCR)												
1 6527 participants	Observational studies	Serious[a]	Not serious	Very serious[b]	Not serious	Strong association	80/4041 (2.0%)	166/2486 (6.7%)	**OR 0.28** (0.22 to 0.37)	**48 fewer per 1,000** (from 52 fewer to 42 fewer)	⊕◯◯◯ Very low	
In the Community Setting: COVID-19 Infection (assessed with COVID-19 RT-PCR)												
1 112 participants	Observational studies	Very serious[a]	Not serious	Very serious[b]	Very serious[c]	None	0/50 (0.0%)	12/62 (19.4%)	**OR 0.04** (0.00 to 0.69)	**186 fewer per 1,000** (from 60 fewer to --)	⊕◯◯◯ Very low	

CI: confidence interval; **RR:** risk ratio

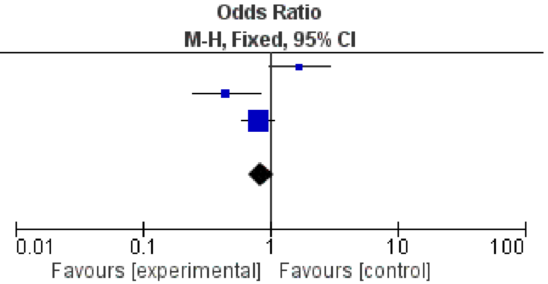
Explanations
[a] Compliance with face shield use and other health protocols was not assessed
[b] Study was not done in the general population but among healthcare workers. Research question should answer Use of Face shield and face mask vs Face mask alone
[c] Very wide confidence interval

Appendix 6. Forest plots

A. Case control studies

Study or Subgroup	Face Shield Events	Face Shield Total	No Face Shield Events	No Face Shield Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Rodriguez Lopez 2021	77	142	33	81	12.6%	1.72 [0.99, 2.99]
Khalil 2020	55	123	43	67	20.1%	0.45 [0.24, 0.83]
Chatterjee 2020	163	343	215	408	67.3%	0.81 [0.61, 1.08]
Total (95% CI)		**608**		**556**	**100.0%**	**0.85 [0.68, 1.08]**
Total events	295		291			

Heterogeneity: Chi² = 10.47, df = 2 (P = 0.005); I² = 81%
Test for overall effect: Z = 1.32 (P = 0.19)

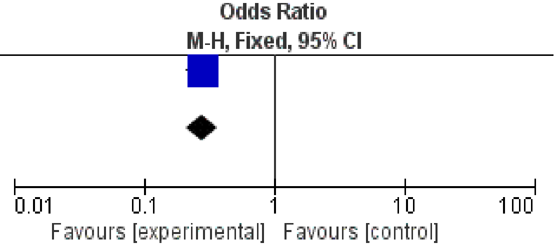


B. Pre- and post-surveillance study among health care workers

1. In the hospital/health setting

Study or Subgroup	Face Shield Events	Face Shield Total	No Face Shield Events	No Face Shield Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Mojajer 2021	80	4041	166	2486	100.0%	0.28 [0.22, 0.37]
Total (95% CI)		**4041**		**2486**	**100.0%**	**0.28 [0.22, 0.37]**
Total events	80		166			

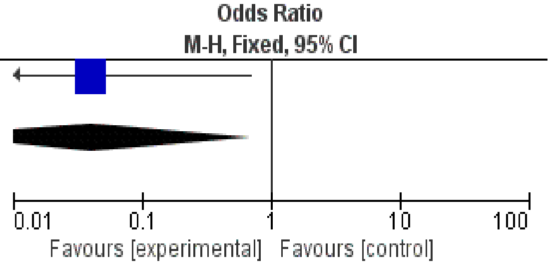
Heterogeneity: Not applicable
Test for overall effect: Z = 9.13 (P < 0.00001)



2. In the community

Study or Subgroup	Face Shield Events	Face Shield Total	No Face Shield Events	No Face Shield Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bhaskar 2020	0	50	12	62	100.0%	0.04 [0.00, 0.69]
Total (95% CI)		**50**		**62**	**100.0%**	**0.04 [0.00, 0.69]**
Total events	0		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.21 (P = 0.03)



Q3. Should copper-containing masks be used to decrease SARS-CoV-2 transmission?

As of 03 December 2021

RECOMMENDATION

There is no evidence to recommend the use of copper-containing over non-copper-containing masks to decrease SARS-CoV-2 transmission.

Consensus Issues

Due to the absence of clinical trials on the efficacy of copper-containing masks in reducing COVID-19 transmission, the panel members opted to have no recommendation. One panelist voted against the use of copper masks because of the higher costs compared with using surgical or cloth masks and the potential harm of metal leaching from copper-containing textiles.

KEY FINDINGS

Currently, there are no clinical trials directly comparing copper-containing masks with non-copper-containing masks in terms of SARS-CoV-2 transmission. There are no clinical trials directly comparing copper-containing masks with non-copper-containing masks in terms of SARS-CoV-2 transmission, except for two in-vitro studies. One study demonstrated that the metal leaching potential of copper-containing textiles could potentially lead to adverse events attributed to inhalation or ingestion of copper. In terms of cost, copper-containing masks are more expensive than regular masks.

INTRODUCTION

SARS-CoV-2, the causative agent of COVID-19, is an enveloped single-stranded RNA virus of the Coronaviridae family.[1] It is mainly transmitted through respiratory droplets which can be spread by infected persons as they breathe, talk, cough, or sneeze. The wearing of face masks reduces this transmission by blocking exhaled droplets of infected persons as well as preventing inhalation of droplets by those who are not infected. To put it simply, it provides a physical barrier between the virus and uninfected individuals.[2] To further improve the efficacy of these face masks, manufacturers sought to apply a chemical barrier which would inactivate the virus as it passes through the material. Copper, an anti-microbial chemical used in clinical settings, was the most popular choice.[1] Though its mechanism of action against viruses is not yet fully understood, it is theorized that it inactivates proteases necessary for viral replication.[3] In earlier studies on SARS-CoV, MERS-CoV, HCoV, and different strains of influenza, various forms of copper were shown to inhibit, inactivate, and destroy the viruses within minutes. It was hypothesized that copper-containing masks would be as effective against SARS-CoV-2.[1 This review aims to determine the efficacy and safety of copper masks in decreasing SARS-CoV transmission.

REVIEW METHODS

We searched the Cochrane Library, PubMed, MEDLINE, Google Scholar, JSTOR, HERDIN, WHO ICTRP and ClinicalTrials.gov using a combined MeSH and free text search with the terms “SARS-CoV-2”, “COVID-19”, “virus”, “viral”, “viral load”, “copper”, “Cu”, “mask”, “face mask”, “infused”, “coated”, “containing”, “filter”, “transmission”, “transmissibility”, and “inactivation”. The study characteristics that were searched for were: Population – people without COVID-19/suspected to be at risk for COVID-19; Intervention – copper-containing masks; Comparator – non-copper-containing masks; Outcomes – viral load, adverse events. Randomized controlled trials were prioritized in the search. When none were found, non-randomized and observational studies were screened as well. When systematic reviews or meta-analyses were found, the individual studies were assessed for possible inclusion.

RESULTS

As of this date, there are no randomized controlled trials on the use of copper-containing masks against SARS-CoV-2 transmission. There were two in-vitro studies which tested for the anti-viral capabilities of copper-containing masks.

One study used real-time polymerase chain reaction (RT-PCR) and immunochemical staining to detect SARS-CoV-2 in exposed Vero cells protected with either regular KF94 masks or copper-coated [75% cuprous oxide (Cu_2O), 25% cupric oxide (CuO)] KF94 masks. A SARS-CoV-2-containing medium was applied to the copper-coated and non-coated materials for one hour. Viruses extracted from the different materials were then transferred to Vero cells. A separate group of Vero cells were directly infected with the viral medium to serve as the control. Fluorescent images were acquired using an automated microscope, and image analysis using proprietary software was done to quantify the nucleocapsid expression. After 36 hours, there was a 75% decrease in fluorescence in the copper-coated group; after 48 hours, RT-PCR did not detect SARS-CoV-2 genes in the same group. Meanwhile, the non-coated group showed similar results with the control group.[4]

Another study used microscopy, immunofluorescence assay, and RT-PCR on exposed Vero cells to compare the efficacy of mixed-fiber (nylon, polyester, spandex) masks and three-layer copper sulfide (CuS)-impregnated masks. Discs of the copper-containing cloth and the non-copper-containing cloth were transferred to plates which were then exposed to a SARS-CoV-2 suspension. The different plate groups were incubated for 30 minutes, 1 hour, and 2 hours. Afterwards, the discs were washed with a clean medium. The collected fluids were then used to infect Vero cell plates which were incubated for 1 hour. Cell plates directly inoculated with SARS-CoV-2 were used as a control group. Fluorescence was completely absent in the copper-containing cloth group for all incubation periods while the non-copper-containing cloth group showed similar results with the control group. Similarly, RT-PCR showed a remarkable decrease in viral copy numbers in the copper-containing cloth group for all incubation periods. The same study tested different concentrations of CuS (5%, 10%, 15%, 20%) directly inoculated in a SARS-CoV-2 medium. The resulting suspensions were incubated for 30 minutes, 1 hour, and 2 hours, after which the extracted supernatants were used to infect Vero cells for 1 hour. The observed fluorescence and viral copy numbers were found to be inversely proportional to the concentration of the CuS solution used.[5]

One safety issue found was the potential for metal leaching from copper-containing textiles. The study of Pollard et al. on different antimicrobial fabrics showed that copper was more susceptible to leaching at higher concentrations. This increased the possibility of inhalation or ingestion of copper which can lead to headache, vertigo, respiratory irritation, hepatomegaly, and other gastrointestinal issues.[6] For dermatologic effects, however, copper-containing cloths were found to have low risk of causing adverse skin reactions.[7]

EVIDENCE TO DECISION

There were no cost-effectiveness studies on copper-containing masks found during the literature search. In the Philippines, surgical masks usually cost about ₱120 for a box of 50 pieces (~₱2.4/mask) and regular cloth masks cost approximately ₱50-₱300 per mask depending on the material. Copper-containing masks, whether branded or not, are generally more expensive at around ₱140-₱980 per mask.[8]

Mask Type	Cost per piece
Copper Mask	₱140-₱980
Cloth Mask	₱50-₱300
Surgical Mask (Polypropylene)	₱2.4

RECOMMENDATIONS FROM OTHER GROUPS

Currently, there are no recommendations from medical organizations regarding the use of copper-containing masks against SARS-CoV-2 transmission. The Department of Health stated that copper-containing masks provide a physical barrier from droplets, which is similar to how regular masks offer protection. However, it also warns against using advertised copper masks with holes or slits as they allow unfiltered air flow.[9]

RESEARCH GAPS

From the article search, there are currently no ongoing trials on copper-containing masks registered on HERDIN, on the WHO International Clinical Trials Registry Platform, or on *ClinicalTrials.gov*. Studies have yet to be conducted which address the benefits and harms of copper-containing masks on human participants.

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Appendix 1. Evidence to Decision

Summary of initial judgments prior to the actual panel meeting (n = 11)

FACTORS	JUDGMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
Problem	No (3)	Yes (8)					
Benefits	Large (2)	Moderate (3)	Small (4)	Uncertain (2)			• Reduced detected SARS-CoV-2 in Vero cells by 75%
Harm	Large (6)	Small (2)	Uncertain (3)	Varies			• Copper have the potential to leach and can be inhaled, ingested or absorbed by wearer • *Consider the adverse effect of copper mask related to prolonged use; alcohol-based hand rub cannot be used for hand hygiene after touching the copper part; needs soap and water.*
Certainty of Evidence	High	Moderate	Low	Very low (11)			• None
Balance of effects	Favors copper mask	Does not favor copper mask (2)	Uncertain (9)	Varies			• In vitro studies showed that copper masks can reduce the detected and inhibit replication of SARS-CoV-2 but they have the potential to leach. Copper can be inhaled, ingested or absorbed by wearer.
Values	Important uncertainty or variability	Possibly important uncertainty or variability (3)	Possibly NO important uncertainty or variability (5)	No important uncertainty or variability (3)			• No clinical trial on effectiveness of copper mask in reducing SARS-CoV-2 transmission.
Resources Required	Uncertain	Large cost (9)	Moderate Cost (2)	Negligible cost	Moderate savings	Large savings	• Copper mask: Php 140 – Php 980 • Surgical masks: Php 120 per box of 50 pcs (Php 2.4/pc) or cloth mask: Php50—300 depending on material
Certainty of evidence of required resources	No included studies (7)	Very low (2)	Low (1)	Moderate	High (1)		• No research evidence found.

FACTORS	JUDGMENT					RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
Cost effectiveness	No included studies (9)	Favors the comparison (1)	Does not favor either the intervention or the comparison (1)	Favors the intervention		• No research evidence found.
Equity	Uncertain (8)	Reduced (2)	Probably no impact	Increased (1)		• No research evidence found.
Acceptability	Uncertain (7)	No (3)	Yes (1)	Varies		• No research evidence found.
Feasibility	Uncertai (8)	No (2)	Yes (1)	Varies		

Appendix 2. Search Yield and Results

1. Summary

#	Query	Results
1	“copper” OR “Cu”	6,064,719
2	“infused” OR “coated” OR “containing” OR “filter”	9,208,873
3	“mask” OR “face mask”	3,967,523
4	“SARS-CoV-2” OR “COVID-19”	170,721
5	“virus” OR “viral”	5,397,143
6	“transmission” OR “transmissibility”	6,252,741
7	“inactivation”	2,655,892
8	“viral load”	1,224,058
9	#1 AND #2	4,015,788
10	#3 AND #9	403,351
11	#4 AND #5	79,774
12	#5 AND #7	1,297,515
13	#6 AND #11	32,657
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	**2,504**

2. Cochrane Library

#	Query	Results
1	“copper” OR “Cu”	4296
2	“infused” OR “coated” OR “containing” OR “filter”	71383
3	“mask” OR “face mask”	11260
4	“SARS-CoV-2” OR “COVID-19”	2
5	“virus” OR “viral”	46151
6	“transmission” OR “transmissibility”	11479
7	“inactivation”	3072
8	“viral load”	6703
9	#1 AND #2	531
10	#3 AND #9	28
11	#4 AND #5	2
12	#5 AND #7	249
13	#6 AND #11	0
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	**0**

3. PubMed

#	Query	Results
1	“copper” OR “Cu”	19,587
2	“infused” OR “coated” OR “containing” OR “filter”	115,235
3	“mask” OR “face mask”	5,795
4	“SARS-CoV-2” OR “COVID-19”	137,106
5	“virus” OR “viral”	174,454
6	“transmission” OR “transmissibility”	80,954
7	“inactivation”	13,102
8	“viral load”	9,249
9	#1 AND #2	2,150
10	#3 AND #9	8
11	#4 AND #5	58,489
12	#5 AND #7	1,284
13	#6 AND #11	10,275
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	**1**

4. MEDLINE

#	Query	Results
1	“copper” OR “Cu”	8,120
2	“infused” OR “coated” OR “containing” OR “filter”	19,222
3	“mask” OR “face mask”	3,985
4	“SARS-CoV-2” OR “COVID-19”	3,303
5	“virus” OR “viral”	14,642
6	“transmission” OR “transmissibility”	10,926
7	“inactivation”	476
8	“viral load”	257
9	#1 AND #2	5,173
10	#3 AND #9	1,452
11	#4 AND #5	469
12	#5 AND #7	111
13	#6 AND #11	932
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	1

5. Google Scholar

#	Query	Results
1	“copper” OR “Cu”	5,490,000
2	“infused” OR “coated” OR “containing” OR “filter”	7,460,000
3	“mask” OR “face mask”	3,780,000
4	“SARS-CoV-2” OR “COVID-19”	17,800
5	“virus” OR “viral”	4,900,000
6	“transmission” OR “transmissibility”	5,690,000
7	“inactivation”	2,590,000
8	“viral load”	1,200,000
9	#1 AND #2	3,830,000
10	#3 AND #9	395,000
11	#4 AND #5	17,900
12	#5 AND #7	1,280,000
13	#6 AND #11	20,100
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	2,500

6. JSTOR

#	Query	Results
1	“copper” OR “Cu”	541,781
2	“infused” OR “coated” OR “containing” OR “filter”	1,524,422
3	“mask” OR “face mask”	164,268
4	“SARS-CoV-2” OR “COVID-19”	2,268
5	“virus” OR “viral”	251,567
6	“transmission” OR “transmissibility”	457,879
7	“inactivation”	49,169
8	“viral load”	7,274
9	#1 AND #2	177,665
10	#3 AND #9	6,834
11	#4 AND #5	717
12	#5 AND #7	14,667
13	#6 AND #11	1,350
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	2

7. HERDIN

#	Query	Results
1	"copper" OR "Cu"	93
2	"infused" OR "coated" OR "containing" OR "filter"	216
3	"mask" OR "face mask"	47
4	"SARS-CoV-2" OR "COVID-19"	81
5	"virus" OR "viral"	1178
6	"transmission" OR "transmissibility"	579
7	"inactivation"	15
8	"viral load"	209
9	#1 AND #2	216
10	#3 AND #9	28
11	#4 AND #5	1178
12	#5 AND #7	1191
13	#6 AND #11	0
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	0

8. WHO ICTRP

#	Query	Results
1	"copper" OR "Cu"	842
2	"infused" OR "coated" OR "containing" OR "filter"	18,395
3	"mask" OR "face mask"	2,168
4	"SARS-CoV-2" OR "COVID-19"	10,161
5	"virus" OR "viral"	9,151
6	"transmission" OR "transmissibility"	924
7	"inactivation"	58
8	"viral load"	366
9	#1 AND #2	53
10	#3 AND #9	1
11	#4 AND #5	1,019
12	#5 AND #7	13
13	#6 AND #11	0
14	#8 AND #9 AND #10 AND #11 AND #12 AND #13	0

Appendix 3. Characteristics of Included Studies

Study ID	Patients (n)	Interventions	Outcomes	Method
Jung 2021	None	75% cuprous oxide (Cu_2O) and 25% cupric oxide (CuO) coated KF94 face masks	SARS-CoV-2 infection of Vero cells	In Vitro Study
Hewawaduge 2021	None	Three-layer copper sulfide (CuS) impregnated face masks	SARS-CoV-2 infection of Vero cells SARS-CoV-2 replication	In Vitro Study

Q4. Should ionizing air filter be used in the prevention and control of COVID-19 infection in public spaces with sustained community transmission?

As of 30 June 2021

RECOMMENDATION

We recommend against the use of ionizing air purifier to reduce COVID-19 transmission in the community. *(Low certainty of evidence; Strong recommendation)*

Consensus Issues

One of the studies noted that when an area is inhabited, reducing the particulate matter becomes insignificant once people move within the household, which consequently makes the ionizing air purifier ineffective. The panel also recognized that the harm caused by this intervention outweighs its benefit because one of the apparent disadvantages of ionizers is the emission of ozone, a powerful oxidant that may inflict health hazards through long-term or high-dose exposure.

KEY FINDINGS

No direct evidence was found assessing the effectiveness of ionizing air filters in reducing SARS-CoV-2 infections. Five experimental studies reported using an ionizing air purifier in reducing airborne particles, mostly in uninhabited laboratory settings. Ionizing air purifiers can efficiently remove the fine and ultrafine particles. However, its effectiveness in eliminating airborne organisms for infection control is lacking. Ozone, a dangerous respiratory irritant produced by some ionizing air purifiers, is a health risk to users. Overall quality: Most of the studies were at high risk of bias, with common issues on selecting tested ionizing air purifiers and the assessor's blinding.

INTRODUCTION

Ion air generators are among the variety of portable air cleaners used to improve indoor air quality [1]. Their operating principle is ion emission through corona discharge. Aerosol particles are repelled and become heavier as they attract negatively charged ions emitted by the air purifier, causing them to precipitate onto surfaces [2].

REVIEW METHODS

After a thorough search on PUBMED, the Cochrane CENTRAL, ChinaXiv, MedRxiv, National COVID-19 Clinical Evidence Task Force, COAPLiving Evidence on COVID-19, NIH. US National Library of Medicine. ClinicalTrials.gov, and Chinese Clinical Trial Registry, there was a systematic review and five experimental studies. No randomized controlled trials reporting the effects of ionizing air filters on quarantined individuals were found after a comprehensive literature search of various electronic databases last January 31, 2021. We also excluded studies that used other air filters (e.g., high-efficiency particulate air (HEPA) filter), articles not written in English, and other types of articles (e.g., abstracts, posters, review articles, book chapters, letters, guidelines, points of view).

RESULTS

No clinical studies were found assessing the effectiveness of ionizing air filters in preventing or reducing COVID-19 infections. Five experimental studies reported using ionizing air purifiers in reducing airborne particles, mostly in uninhabited laboratory settings. Although ionizing air purifiers were efficient in removing fine and ultrafine particles, none of these studies reported its effects on reducing SARS-CoV-2 viral load, either in laboratory or actual clinical settings [2–6]. Appendix 2 summarizes the ionizing air purifier's benefit (i.e., particle removal efficiency) and harm (i.e., ozone development).

One of the 5 experimental studies reported that commercial ionizing air purifiers in a residential apartment did not significantly reduce the particulate matter (PM) size, with an average indoor/outdoor mass concentration ratio from 1.03 to 0.73 for most PM size fractions [2]. In experimental chambers, however, ionizing air purifiers alone or with heating, ventilation, and air conditioning (HVAC) effectively reduced PM concentrations [2–5]. Ion emission increased the filter collection efficiency for bacteriophage MS2 virus [4], bacteria (*B. subtilis, E. coli*) by as much as 3 to 4 times and for viable fungal spores (*A. versicolor, A niger*) by a factor of 2 [6]. Units with higher ion emission rates provided higher particle removal efficiency [3–5]. Due to its high ion emission rates, bipolar ions are better by 1.7x than unipolar ions in removing PM [4].

One disadvantage of ionizers is ozone emission, a powerful oxidant that may harm health by long-term or high-dose exposure. Factors found to be associated with higher ozone levels include longer duration of exposure, higher ion emission, and use of bipolar ions. Compared with unipolar ions, bipolar ions can emit up to 30 ppb compared to unipolar ion's 2-10 ppb ozone concentration [4]. Ozone exposure was found to be negligible within 2 hours, but significantly increased to > 77 ppb after 8 hours of exposure [2]. Ozone levels also varied across different commercially available ionizer models despite similar exposure times [5].

RECOMMENDATIONS FROM OTHER GROUPS

No guideline or agency has explicitly recommended the use of ionizing air purifiers. The US-CDC acknowledged bipolar ionizers as emerging technologies used in HVAC systems or portable air cleaners, but mentioned limited research supporting its effectiveness outside laboratory conditions [7].

RESEARCH GAPS

No study reports the effects of ionizing air purifiers in reducing or eliminating SARS-CoV-2 in the community. No on-going studies are addressing this research gap.

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Appendix 1. Characteristics of Included Studies

Author, year	Particle/Bioaerosols	Ionizer air purifier	Comparator	Outcomes
Hyun et al. (2017)(4)	Aerosolized bacteriophage MS2	Carbon-fiber ionizer of a medium air filter	NA	Overall filtration efficiency Pressure drop Antiviral efficiency Ozone concentration
Shi et al. (2016)(5)	Particles	4 wearable ionizers	NA	Ozone concentration $PM_{2.5}$ concentration Particle size distribution Mass removal rates
Huang et al. (2008)(6)	B-subtilis, E. coli, A. versicolor, A. niger	Ionizer and HVAC	NA	Aerosol concentration Removal efficiency
Berry et al. (2007)(2)	Particles	Commercially available ionic air cleaner	NA	Indoor/outdoor airborne particle number Mass concentration ratios Indoor ozone levels Ion concentration levels
Grinshpun et al. (2005)(3)	NaCl, PSL, Pseudomonas fluorescens bacteria	five ionic air purifiers (two wearable and three stationary	NA	Concentration decay of respirable particles Particle removal efficiency

Appendix 2. Ionizing air purifier's benefit and harm

Outcomes	Study	Basis	Effect Estimate	Level of evidence
Particle removal efficiency (household)	4 Experimental	Grinshpun et al, 2005 (3)	Model 1: 15% in 15 min, 30–40% in 1 h, 50% after 1.5 h, 80% after 3 h	Low[1]
			Model 2: 50% in 15 min, 100% in 1.5 h	
			Model 3: almost 90% within 5-6 min, 100% within 10-12 min	
Particle removal efficiency (commercially available wearable air purifier)		Shi et al., 2016 (5)	$PM_{2.5}$ mass removal rates:	
			AC1: 1.85 h^{-1}	
			AC2: 0.48 h^{-1}	
			AC3: 1.52 h^{-1}	
			AC4: 5.37 h^{-1}	
Particle removal efficiency: (with low efficiency HVAC)		Huang et al. 2008 (6)	B-subtilis: 16.4±5.3 to 80.4±14.3%	
			E. coli: 17.6±4.2 to 73.3±11.1%	
			A. versicolor: 83.1±12.3%	
			A. niger: 96.5±10.1%	
			Filter only: 9.09±4.84%	
Particle removal efficiency (unipolar vs. bipolar)		Hyun et al, 2017(4)	Unipolar ions: 46.1% at 15 min, 78.8% at 30 min, and 83.7%, at 45 min	
			Bipolar ions: 64.3% at 15 min, 89.1% at 30 min, 97.4% at 45 min	
Ozone levels (unipolar vs. bipolar)	3 Experimental	Hyun, 2017 (4)	Unipolar air ions emit 2-10 ppb ozone, whereas bipolar air ions emit 30 ppb ozone.	Low[1]
		Shi, 2016 (5)	The 10-h average ozone emission rates: AC1: 0.67 mg.h^{-1} AC2: 3.40x 10^{-2} mg.h^{-1} AC3/AC4: negligible.	
		Berry, 2007 (2)	Negligible ozone emissions in 2 hours	
			1st hour: 13-19 ppb in the 1st hour	
			≥8 hours: 77 ppb	

[1]The studies offered indirect evidence and inconsistent findings on the effects of ionizers in laboratory and real-environment settings. The tested ionizers were not systematically selected. Assessors were not blinded to ionizers used; however, the included studies used objective outcome measures.

Legends: HVAC, heating, ventilation aircon; ppb, part per billion; h^{-1}, the number removal rates of total particles measures in size range from 18.1 to 289 nm

Q5. Should foot baths be used in the prevention and control of COVID-19 infection?

As of 30 June 2021

RECOMMENDATION

We recommend against the use of foot baths for prevention and control of COVID-19 transmission. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues
No issues were raised during the consensus panel meeting.

KEY FINDINGS

No evidence was found evaluating the effectiveness of footbaths in preventing or controlling COVID-19 infections.

INTRODUCTION

The SARS-CoV-2 virus has been found to remain viable and infectious in aerosols for hours and on different kinds of surfaces within controlled laboratory settings [1]. Because of this finding, foot baths and other environmental strategies have been proposed to potentially mitigate the spread of the virus in households and establishments.

Footbaths involve placing a container soaked with diluted sodium hypochlorite or other acceptable disinfectant at the entrance of an establishment. Although foot baths have already been used in agricultural facilities to prevent potential spread of microorganisms that survive in the dirt for several days or weeks [2], its effectiveness for preventing or controlling COVID-19 infections remains to be determined.

REVIEW METHODS

We searched for evidence on January 25, 2021 in the following search engines and databases using free text and keywords related to "COVID-19" and "foot bath": PubMed, Google Scholar, Cochrane CENTRAL, pre-print databases such as Chinaxiv.org, Medrxiv and biorxiv.org, trial registries of EU, Canada, IISRCTN, China, ANZ, Brazil, Germany, Japan, Korea, India, the Netherlands and Pan Africa. We also checked for recommendations and evidence summaries from the USPSTF, NICE, WHO, EU, Canadian Preventive Task Force, Australia and Covid-19 Open Living Evidence Synthesis site.

RESULTS

We found no study that directly assessed the effectiveness of foot baths for COVID-19 prevention or control. The only study that could possibly explain the concomitant use of foot baths was the presence of SARS-CoV-2 particles found on the front of shoes of a health professional in Singapore [3]. However, the risk of transmission through this route was low since the viral particle was isolated only in that one PPE swab and was not replicated in any of the other samples taken within the facility. Furthermore, viral culture was not done to demonstrate the viability of that viral particle found on the shoe [3].

RECOMMENDATIONS FROM OTHER GROUPS

The WHO recommendation (15 May 2020) for disinfecting and cleaning environmental surfaces did not include footbaths but emphasized that floors and very low-touch surfaces should be disinfected last [4]. Direct application of properly and freshly prepared disinfectant solutions, usually sodium hypochlorite, in appropriate concentration, remains to be the ideal and more effective method. Similarly, other agencies such as the Canadian Preventive Task Force, CDC, USPSTF, and NICE did not have any recommendations on the use of footbaths.

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Q6. Should misting tents or disinfection chambers be used in preventing and controlling COVID-19 transmission?

As of 30 June 2021

RECOMMENDATION

We recommend against the use of misting tents or disinfection chambers for preventing and controlling COVID-19 transmission. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues

The strong recommendation was based on the intrinsic irritant properties of the chemicals used in disinfection. Although some health facilities have implemented misting tents, evidence was not established to show their effectiveness to prevent and control COVID-19 transmission. Likewise, it was noted that aerosols are not actually recommended because the contact time is not enough to kill the microorganism.

KEY FINDINGS

There are no existing or ongoing studies investigating the effectiveness and safety of sanitation tents for preventing and/or controlling COVID-19 infections. Indirect evidence from a rapid systematic review of 6 laboratory studies and 1 in-vitro case control study showed effective viral inactivation after application of various cleaning products. However, disinfecting substances pose significant health risks, especially when used outside their manufacturer's recommendation or with repeated, prolonged exposure.

INTRODUCTION

Disinfection chambers or misting tents became widely popular in the Philippines and other countries during the second quarter of 2020. Disinfectant chambers commonly use chloroxylenol, benzalkonium chloride and chlorine-based chemicals [3]. Mists are sprayed on a person for 20-30 seconds using the recommended disinfectant, usually diluted household bleach [2].

Although these are currently used as methods to minimize the spread of the virus and avoid cross-infection inside workplaces, a rapid review (April 2020) found no evidence regarding the efficacy of these strategies for COVID-19 prevention and control [1]. At the time there were no completed studies on the topic and most commonly used agents were household bleach, alcohol and povidone iodine, all of which were potential irritants to skin and mucous membranes. This review aims to determine current evidence regarding the benefits and harms of these environmental interventions.

REVIEW METHODS

A comprehensive literature search of various electronic databases as of 09 Feb 2021 in the following search engines and databases for clinical trials: PubMed, Google Scholar, Cochrane CENTRAL, pre-print databases such as Chinaxiv.org, medrxiv and biorxiv.org, trial registries of EU, Canada, IISRCTN, China, ANZ, Brazil, Germany, Japan, Korea, India, the Netherlands and Pan Africa. We also checked for recommendations and evidence summaries from the USPSTF, NICE, WHO, EU, Canadian Preventive Task Force, Australia and Covid-19 Open Living Evidence Synthesis site. Search terms included misting tents, sanitation booths, disinfecting tunnels or chambers, fog chambers, or disinfectant sprays.

RESULTS

No direct evidence was found assessing the effectiveness of misting tents for COVID-19 prevention or control after. Indirect evidence from a rapid systematic review [6] of 6 laboratory studies and 1 in-vitro case control study, showed effective viral inactivation after application of various cleaning products such as chlorine-based disinfectants, alcohol, detergents, glutaraldehyde, iodine-containing detergents, hydrogen peroxide compounds and household bleaches, with alcohol showing immediate activity [6].

This review only assessed the efficacy of these cleaning products when applied on surfaces and not as misting agents or sprays. There was no evidence that spraying can prevent an infected person's ability to infect another person. The mists can also irritate the nasal passage and causing an infected person to sneeze and potentially spread the virus [2,3].

When used outside its manufacturer's recommendation, adverse reactions may be encountered. The aerosolized particles may find its way into the mucosal lining of the respiratory tract, exposed skin, and the cornea. Chlorinated compounds, alcohol and hydrogen peroxide can cause immediate danger to health or life at 10ppm, 2000 ppm and 75 ppm, respectively. The most common symptoms include irritation of the eyes, nose, throat, respiratory tract and skin hypersensitivity (Appendix 1, Table 1). Repeated and increased duration of exposure further magnify the potential hazards [3,4,5]. One news article reported the death of one doctor following an accidental inhalation of disinfectant [14].

No ongoing studies or clinical trials were found in the different trial registries searched.

RECOMMENDATIONS FROM OTHER GROUPS

Local and international health agencies currently do not support the use of misting tents or disinfecting chambers. WHO recommends against the use of these interventions under any circumstances, citing physical and psychological harm such as skin and eye irritation, bronchospasm due to inhalation, and gastro-intestinal effects like nausea and vomiting [8].

The Department of Health (DOH) guidelines echoes the WHO recommendation to avoid using misting tents and spraying for lack of evidence of its efficacy. This recommendation has remained unchanged since it was published last 10 April 2020 [1].

The CDC has maintained its position on using disinfectants only based on the manufacturer's recommendation of its preparation and use on surfaces. It has provided a list of approved disinfectants with the proper dilution and use [9].

The USPSTF, NICE and Canadian Preventive Task Force do not have any recommendations for the use of sanitation or disinfection tents/chambers.

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Appendix 1. Summary of Findings

Comparison of commonly used chemicals in disinfecting chambers (Philippines)

Comparison of commonly used chemical in disinfecting chambers.(*a-e*)

CHEMICAL	FLASH POINT (°C)	Immediately Dangerous To Health or Life (ppm)	Permissible Exposure limit (ppm)*	OSHA Short term exposure limit (ppm)**	Reactivities	HEALTH CONCERNS - symptoms	TARGET ORGANS
Isopropyl alcohol	10°C	2000 ppm (10% (LEL	400 ppm (980 mg/m3)	400 ppm	Strong oxidizer	Irritation of eyes, nose, throat, upper respiratory tract, Drowsiness, dizziness, headache, Dry skin	
Chlorine (includes Na hypochlorite)	Non-flammable	10 ppm	1ppm (3 mg/m3)	1 ppm	Strong oxidizer, Explosive with turpentine, fuel, ammonia	Burning of eyes, nose, mouth. Lacrimation and rhinorrhea, Cough and choking, Nausea, vomiting, headache, dizziness, Pulmonary edema, pneumonia	Eyes, Skin, Respiratory system
Hydrogen peroxide	Non-combustible	75 ppm	1 ppm (1.4 mg/m3)	Not available	powerful Oxidizer with selective metals	Irritation of eye, nose, throat,, Corneal ulcers,, Skin damage and bleaching of hair	
Chloroxylenol	Potentially flammable	no limit	no limit	no limit	Stable under normal conditions	Irritation and corrosion of skin and eyes, Skin hypersensitivity	Eyes, Skin, Respiratory system
Benzalkonium chloride	Flammable	no limit	no limit	no limit	Corrosive	Irritation of eyes, skin, mucosa, Skin Hypersensitivity, Respiratory irritation, Acute toxicity	Eyes, Skin, Respiratory system
Povidone Iodine	Potentially flammable	no limit	no limit	no limit	Explosive with hydrogen peroxide	Irritation of eye, nose, Contact dermatoses; Acute renal failure	Eyes, Skin, Renal system
Acetic Acid	39°C	50 ppm	10 ppm (25 mg/m3)	15 ppm	Strong oxidizer	Irritation of eyes, skin, nose, throat. Damage to skin and eyes. Discoloration of skin, Skin hypersensitivity, Dental erosion, Pharyngeal edema, chronic bronchitis	Eyes, Skin, Respiratory system

Table adapted from:
OSHA, Occupational Safety and Health Administration
A ACGIH TLVs and BEIs for Chemical Substances and Physical Agents.
NIOSH Pocket Guide to Chemical Hazards, Department of Health and Human Services (CDC and NIOSH)

Q7. Should ultraviolet (UV) lamps be used in the prevention and control of COVID-19 infection in public spaces in locations with sustained community transmission?

As of 30 June 2021

RECOMMENDATION

We recommend against the use of UV lamps or other UV devices in any place outside of a controlled clinic or hospital setting to prevent and control COVID-19 transmission. *(Low certainty of evidence; Strong recommendation)*

Consensus Issues

A strong recommendation was made based on the potential adverse reactions and the risks associated with UV lamps. Although the panel recognizes the germicidal effect of UV light in clinical settings, emphasis was made to limiting its use only in controlled environments (i.e., without the presence of human beings) with trained staff to minimize its potential health hazards. Since the use of personal UV lamps and devices in households has also become widespread following advertisements, the public must be appropriately informed that misuse of these devices may cause harmful, long-term effects on health.

KEY FINDINGS

No direct evidence was found evaluating the effectiveness of ultraviolet lamps in the prevention and control of COVID-19 infections in public spaces in locations with sustained community transmission. Indirect evidence of low quality showed some benefit in reducing the incidence of viral infection in a hospital ward. However, the evidence for its potential harm such as skin erythema, ocular itching, blurring and conjunctival injections, was more significant.

INTRODUCTION

Ultraviolet light C (UVC), as a germicidal, is widely used in health care facilities for sterilization of instruments and rooms. Its wavelength of 250-280 nm can inactivate microorganisms by breaking the DNA or RNA causing defects in cell replication and eventually cell death [1]. There are various UVC devices used in hospital units, namely: UV-C surface-disinfecting devices, UV-C germicidal irradiation technologies, UV-C irradiation lamps and mercury-based, light emitting diodes (LED), and pulsed xenon (PX) lamps [2].

The generally acceptable dose of UVC to kill at least 99.9% of any pathogenic microorganism is 40mJ/cm2 of 254 nm light. But the current guidelines for exposure to UVC radiation for eyes and skin should not exceed 3 mJ/cm^2 at 270 nm. At 254 nm, the maximum exposure limit is set at 6mJ/cm^2 [6]. The more common health risks associated with UV-C exposure are skin and eye irritation [3]. In addition, the UVC photons are only effective if they make direct contact with the surface, limiting its effectiveness on creases or on areas that cannot be reached by light [8].

REVIEW METHODS

We searched for relevant studies on 12 February 2021 in various electronic databases (PubMed, Google Scholar, Cochrane CENTRAL, pre-print databases such as Chinaxiv.org, Medrxiv and biorxiv.org, trial registries of EU, Canada, IISRCTN, China, ANZ, Brazil, Germany, Japan, Korea, India, the Netherlands and Pan Africa) and recommendations from health agencies (USPSTF, NICE, WHO, EU, Canadian Preventive Task Force, Australia and Covid-19 Open Living Evidence Synthesis). Search terms include both free text and MeSH terms for "ultraviolet light," "UVC," "ultraviolet rays," "black light," or "far UVC," and "disinfection," or "sterilization."

RESULTS

We did not find any direct evidence that studied the effects of UV germicidal irradiation in preventing or reducing infection rates in community settings. Indirect evidence from 2 systematic reviews [7,12] of non-clinical studies on SARS-CoV-2 virus and 2 in-vitro studies [5,9] assessed the efficacy of various types of UV lamps in deactivating or reducing viral load in laboratory and hospital settings [7].

The rapid review summarized existing literature on the viability (7 studies; Table 1) of the SARS-CoV-2 virus, and the efficacy of UVGI in reducing viral load under laboratory conditions (20 studies). UVGI showed partial to complete viral elimination ($\geq$ 4.0 $\log_{10}$ reduction) on N95 masks and filtering facepiece respirators (Appendix 1, Table 2). Results varied depending on factors such as viral titers, inoculum size, viral medium and the shape, contour and type of material or surface, and thus also explains the relatively inconsistent findings in literature [7].

Another systematic review was done on the efficacy and safety of UV-C in sterilizing hospital units such as operating rooms, hallways, wards and patient rooms [6]. Twelve (12) eligible studies including 1 cluster RCT, 7 quasi-experimental and 4 uncontrolled before and after) used various UV-C lamps and Pulsed Xenon UVC (PX-UV) lamps (Table 3). The overall certainty of evidence from these 12 studies was rated low because study design limitations, imprecision, and high risk of bias. Only one study reported a 44% reduction in incidence of viral infections (influenza, rhinovirus, enterovirus, pneumovirus) among pediatric patients in that facility (Incidence risk ratio = 0.56, 95%CI: 0.37, 0.84, p=0.003)) [12]. Ten of the 12 studies concluded that UV-C is an efficacious complement to existing cleaning protocols, adding that the latter remained far more superior in removing microorganisms [6].

Two in vitro studies utilized 222nm UVC (far UVC) to deactivate cells incubated with coronaviruses and concluded that far UVC can be used in public places because it has very limited penetration in biological materials such as the stratum corneum [5,9]. However, they found that the applied dose was not the same as the actual dose received by the target virus, citing the influence of surface irregularities, shadowing, and type of surrounding medium and structures [7].
Although only 5% of UVC penetrates the stratum corneum, UVC from artificial light sources are readily absorbed by the eyes and skin and with increased exposure time, intensity and distance from the source. Thus, it can potentially cause adverse reactions such as skin erythema, ocular itching, blurring and conjunctival injections, among others. The magnitude of adverse reactions is dependent on the exposure duration, intensity, and number of cycles. One laboratory study showed the effective

protection provided by clear face shields, UV goggles and sunscreen to protect against side effects of UVC exposure [8].

RECOMMENDATIONS FROM OTHER GROUPS

WHO recommends not to use UV lamps to disinfect hands or other skin surfaces It can cause irritation and damage to the eyes [10]. Similarly, the Philippine DOH warns against the use of devices emitting ultraviolet (UV) light to disinfect objects or surfaces [11] because of adverse effects such as damage to one's sight, skin irritation, burns, and increased the risk of skin cancer. Their use should only be limited to hospitals, clinics, and other health-care centers [11].

The Philippine Society for Microbiology and Infectious Diseases (PSMID) did not mention the use of UV lamps in its Unified COVID-19 Algorithms. Other international groups (NICE, USPSTF and the Australian National Covid-19 Clinical Evidence Task Force) did not have any recommendation on UV-C use.

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Appendix 1. Summary of Findings

A. Studies reporting the efficacy of UV germicidal irradiation (UVGI) against SARS-CoV-2 (Derriak, 2020)

Author, Year	Inoculum	UV Exposure	Key Findings
Fischer, 2020	Stainless steel and N95	UVC 260-285nm	Stainless steel - ≥4Log10 reduction N95 – LOD not reached with 1980 mJ/cm^2
Heilingloh 2020	Well plates	UVC 254	>6.7 log10 reduction at 1048 mJ/cm^2
Inagaki 2020	Petri dish	Deep UV-LED 280 nm	Below LOD (~3.2 log10 reduction at 75 mJ/cm^2
Smith 2002	N95 models with direct infiltration of high viral titers	UVC 254	UVC did not inactivate the virus from N95 at 630 mJ/cm^2
Ozog 2020	Viral droplets on N95 parts (nosepiece, apex, chin piece, strap)	UVC 254	Most facepiece samples (n=32) had viral loads <LOD but 4 samples from 2 models did not at 1500 mJ/cm^2

LOD, Limit of detection

B. UVC devices and their known effects on viral load reduction and duration to effect

Author, Year	UV device	Effectivity/ viral load reduction
Simmons 2020 Aug	Pulsed Xenon UV	>4.54 log10 (99.992% reduction) at 2 min
Storm 2020 Dec	UVC 254nm	>99.9 reduction at 9 sec wet virus >99.9% reduction at 5 sec for dry virus (droplets)
Fischer 2020	UVC 254nm	>4 log10 reduction with 330mJ/cm2 on stainless steel
Heilingloh 2020	UVC 254nm	>6.7 log10 reduction at 1048 mJ/cm2 on well plates
Inagaki 2020	DUV-LED 280 nm	~3.2 log10 reduction at 75 mJ/cm2
Bianco 2020	Low pressure Hg-lamp	ca5.7 log10 reduction at 15 mJ/cm2
Buonanno 2020	far UVC 217-222	99.9% reduction at 1.2 to 1.7 mJ/cm2 for 25 minutes

C. Results of efficacy studies on UV-C (Ramos, 2020)

Author, Year	Study Design	Hospital type	UV device	Findings
Anderson, 2017	Cluster RCT	9 hospitals	UVC Tru-D	Incidence of target organisms (C difficile, MRSA, VRE) reduced RR 0.70 (95%CI 0.5 to 0.98, p=0.036
Cooper 2016	Quasi-experimental	Community hospital	UVC Sanuvox	Treated bathroom had 35.2% (aerobic) and 47.7% (anaerobic) reduction in bacterial bioaerosol concentration
Dippenaar 2018	Quasi-experimental	Acute care	PX-UV Xenex	90% reduction in total surface bioburden; risk trend/wk = 0.19 (95%CI (0.056 to 0.67) p=0.01
El Haddad 2017	Quasi-experimental	Cancer center	PX-UV Xenex	Significant reduction of 72.5% (p=0.0328) at 2min and 73.1% (p=0.0075) at 8 min in high touch surfaces
Ethington 2018	Quasi-experimental	Acute care	UVC, Am Green tech	Reduced bacterial viable air particles by 42% (p=0.035)
Jinadatha 2014	Quasi-experimental	Acute care	PX-UV Xenex	IRR adjusted = 7 (95%CI 1-41)
Morikane 2020	Before & After	Tertiary Care	PX-UV Xenex	Incidence of MRSA reduced IRR 0.71 (p=0.002) from 13.8 to 9.9/10000 px days
Nerandzic 2012	Before & After	Acute care	Sterilray, Healthy Env Innov	Signif reduction in frequency of C difficile and MRSA cultures (p=0.007)
Pavia 2018	Quasi-experimental	Pediatric center	UVC Chlorox Healthcare	44% reduction in VIRAL infection incidence among pedia pxs (IRR 0.56; 95% CI (0.37-0.84)
Penno 2017	Before & After	Tertiary care	UVC Steritrak	Reduced risk of overall contamination by 0.48X with 1.04 log10 reduction ([p<0.001)
Sampathkumar 2016	Quasi-experimental	Tertiary Care	PX-UV Xenex	C difficile infection reduced from 28.7/10000 pxdays to 11.2 (p=0.03)
Villacis 2019	Before & After	Secondary Care	PX-UV Xenex	Signif reduction in CFU counts in ORs 87% (p<0.001) and patient rooms 76% (p<0.001)

Q8. Should high efficiency particulate air (HEPA) filters be used in the prevention and control of COVID-19 infection in public spaces and locations with sustained community transmission?

As of 30 June 2021

RECOMMENDATION

We suggest the use of HEPA filter as an option to improve air quality for COVID-19 prevention and control in indoor spaces with inadequate ventilation. *(Low certainty of evidence; Weak recommendation)*

Consensus Issues

A weak recommendation was made because of indirect evidence showing the benefit of HEPA filter in improving air quality. HEPA filters may be useless in public spaces with uncontrolled airflow and should be used only in areas where air exchange is compromised. To ensure that HEPA filters serve their purpose, the amount of air that can be filtered per hour by the machine must be matched with the size of the room. Proper installation and regular maintenance are likewise important to avoid contaminated air from recirculating back to the room and to maximize the machine's lifespan. In spite of the use of HEPA filters, minimum health standards should still be observed.

KEY FINDINGS

No direct evidence was found assessing the effectiveness of HEPA filters in preventing and controlling COVID-19 infection in public spaces and locations with sustained community transmission. Low quality evidence from 3 laboratory experiments and 1 case series demonstrated that HEPA filters appear to significantly improve air quality.

INTRODUCTION

Airborne transmission of the COVID-19 virus is possible under circumstances and settings where aerosol generating procedures are performed [1]. Ventilation, filtration and air cleaners such as the high efficiency particulate air (HEPA) filter are believed to assist in reducing the risk of transmission of infectious diseases by removing the particles or large droplets to which pathogens may be attached [2,3,4].

REVIEW METHODS

We searched for published studies on February 21, 2021 on MEDLINE, Cochrane CENTRAL, pre-print databases, primary trial registries, and guideline sites such as the NICE, WHO, USPSTF and Canadian Task Force on Preventive Health. We used keywords "HEPA," "HEPA filtration," "HEPA filter," or "air purifier" together with specific search words for COVID-19. We included both clinical trials or non-clinical experiments that measured the efficiency of HEPA filters.

RESULTS

We found no direct evidence assessing the effectiveness of HEPA filters in preventing and controlling COVID-19 infections in public spaces and locations with sustained community transmission. There were, however, indirect evidence from 3 laboratory experiments [3,5,7] and 1 case series [6] showing its potential benefit. Majority of the studies were about specific devices that incorporated HEPA filters as a component of the entire mechanism, or as a co-intervention. Outcomes measured included particle concentrations or capture/filtration efficiency. The quality of this body of evidence was rated low primarily due to indirectness and imprecision.

A case series from India [5] reported using HEPA filters in a hospital setting for 6 COVID-19 patients with tension pneumothorax who warranted chest tube thoracostomy. Two closed underwater drainage systems (CUDS) were joined together, then a HEPA filter was added to the port of the second CUDS to reduce high concentrations of SARS-CoV-2 from intrapleural air that passes through the CUDS. Although the study reported that no hospital staff were infected with COVID-19 during the 15-day study period, sufficient information was not available in the article to allow appraisal.

One non-clinical, repeated measures experimental study done in Hong Kong following earlier outbreaks of SARS and avian flu demonstrated significant reductions in particle concentration levels with the use of a portable HEPA filter in a 6.7m x 6.0m x 2.7m (LxWxH) room [3]. Another laboratory experiment assessed the efficacy two HEPA filter configurations, together with 4 other modifications to personal protective equipment (PPE) consisting a standard helmet, hood and gown “spacesuit” draped on a mannequin. Particulate testing (range of particles were 0.3-1.0 micrometer) was the outcome measure. Results showed that the configurations with modified HEPA filters had lowered the mean percentage particulate penetrations compared to its counterparts by 20% [6] .

A technical memorandum by the US - National Aeronautics Space Administration reported on the filtration efficiency of HEPA-rated media filters through its ability to capture particles of various sizes across its multi-layered media [7]. Larger particles are captured by the filter’s mechanism of inertial impaction and interception, while smaller particles are captured in the inner layers via particle diffusion. Moreover, filtration efficiency of HEPA filters were significantly enhanced when airborne particles were smaller, to diameters below the most penetrating particle size (MPPS), which was typically 120 nm. HEPA filters were concluded to have efficient filtration across the spectrum of different-sized particles, down to the very smallest airborne particles or MPPS [7].

RECOMMENDATIONS FROM OTHER GROUPS

The American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) maintains that HEPA filters are more than 99.97% efficient at capturing airborne viral particles associated with SARS-CoV-2 [2].

The Centers for Disease Control (CDC) (9 Feb 2021) has enlisted the use of portable HEPA fan/filtration systems to help enhance air cleaning, particularly in higher risk settings such as health clinics, medical testing locations, workout rooms, or public waiting areas, where there is an increased likelihood of COVID-19 and/or increased risk of getting COVID-19 [8].

WHO (28 Mar 2020) considers the use of single-space air cleaners with HEPA filters for health care facilities without adequate natural or mechanical ventilation, provided that they are appropriately selected, deployed and maintained [1]. No specific recommendation related to community use was made.

Guidelines from PSMID, PHICS, and PCP (17 May 2020) state that HEPA filters provide additional benefit in improving air quality especially in settings where adequate ventilation cannot be achieved. The guideline maintained that HEPA filter use must follow the manufacturer's operating protocols, including configuration, maintenance and replacement of the HEPA filters [4].

RESEARCH GAPS

Clinical studies that directly investigate the effectiveness of HEPA filters in preventing COVID-19 infections are still lacking.

ONGOING STUDIES

In Australia, there is an ongoing review by the National COVID-19 Clinical Evidence Taskforce on evidence of the levels of ventilation and portable air cleaning devices. No additional information has been indicated in the website concerning details of the said review [9].

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Appendix 1. Characteristics of Included Studies

Study	Population	Intervention	Control	Outcome	n
Qian et al., (2010)	Laboratory study	HEPA filter	HEPA filter and HVAC (heating, ventilation and air-conditioning) system	Particle concentration Air change rate	6 beds
Gedic & Alar (2020)	Patients diagnosed with COVID-19 (+) tension pneumothorax For chest tube thoracostomy (CTT)	closed underwater drainage systems (CUDS) with HEPA filter	None	Clinical outcomes Healthcare workers who developed COVID-19	6 patients
Gibbons et al., (2021)	PPE configurations	PPE configuration with HEPA filter material	PPE configuration without HEPA filter material	Mean percentage particulate penetration	6 configurations
[NASA] Perry et al. (2016)	Not mentioned	HEPA filter	Not mentioned	Filtration efficiency	Not mentioned

Q9. Should carbon dioxide (CO_2) monitors be used to reduce transmission of COVID-19?

As of 05 November 2021

RECOMMENDATION

We recommend the use of carbon dioxide (CO2) monitors in enclosed spaces to guide actions to improve ventilation and reduce transmission of SARS-CoV-2. *(Moderate certainty of evidence; Strong recommendation)*

Consensus Issues

The panel made a strong recommendation for the use of carbon dioxide (CO2) monitors because of the moderate certainty of evidence based on an indirect study that showed much higher risk of contracting tuberculosis when exposed to a room whose air reached 1000 parts per million (ppm) of carbon dioxide. The panel believed CO2 monitors could serve as a real-time guide to initiate activities that improve air ventilation (such as promoting distancing, opening windows, or turning on electric fans). However, two panelists still voted for a weak recommendation due to (1) unknown accuracy of various commercial monitors in detecting CO2 levels and (2) concerns regarding the actual use of industrial-grade monitors (training of personnel, number of monitors needed, calibration, preventive maintenance) in different institutions. Even with the use of CO2 monitors, the public must continue to observe the precautionary measures of handwashing, wearing face masks, and observing physical distancing to avoid infection with COVID-19.

KEY FINDINGS

We found no studies that directly answered the question on whether carbon dioxide level determination can be used to prevent SARS-CoV-2 infection. There were observational studies that reported no infection when there was increased air ventilation and the CO2 levels were low. In these studies, many factors affecting CO2 levels were considered simultaneously and in real-time, such as use of personal protective equipment (PPEs), activity of persons in the room, duration of stay in the room, and size of the room, among others. The CO2 levels, as detected by carbon dioxide sensors, were correlated with air ventilation and in most studies, the CO2 level was designated to be a surrogate or proxy to COVID-19 risk of transmission. Indirect evidence showed that people exposed to a room with more than or equal to 1000 parts per million (ppm) of carbon dioxide in the air, as measured by a CO2 monitor, had as high as 16x higher risk of contracting tuberculosis, compared to those in a room with lower CO2 levels.

The other studies investigated the presence of the virus in air (aerosol and droplets), and as fomites. Although disagreement existed among the studies, as two studies were able to isolate the virus in the air, while the other was only able to isolate the virus as fomites, it may be possible that the negative growth of the virus may not mean that it is absent.

INTRODUCTION

The transmission of SARS-CoV-2 via aerosols has been reported to be one of the mechanisms of the spread of the virus.[1] Several studies have shown that indoor air quality is associated with carbon dioxide levels, and CO2 levels have been considered to be a surrogate measure of transmission risk of respiratory infections that are spread through droplet and aerosol mechanisms.[2-5] SARS-CoV-2 virus has been detected in particles with diameters of <100um that can float in the air for hours, and in exhaled air of COVID-19 patients as well as in hospital air [6,7]. Carbon dioxide is postulated to contain infected viral pathogens as it is exhaled from COVID-19 patients.[6] In addition, CO2 levels may indicate an increase in the number of occupants in an enclosed area and their activity level.[8] Through mathematical modelling and indoor scenarios, the CO2 levels can proxy the COVID-19 infection risk by applying the Wells-Riley model and its modifications.[4] Following this logic, increasing levels of CO2 may indicate poor indoor air quality and thus increased infection risk.[9-13] This was the focus of a recent review on indoor CO2 sensors for COVID-19 risk mitigation, which concluded that although CO2 monitoring can help address ventilation inadequacy, indoor CO2 levels should not be interpreted as a proxy for COVID-19 risk since SARS-CoV-2 transmission depends on many factors, of which ventilation is only one [13]. There was one simulation study that measured the relationship of aerosol concentration and CO2 concentration in a simulated enclosed area such as a concert hall. The study showed a linear positive correlation between aerosol concentration (p/cm3) and CO2 level (ppm).[14]

VIRAL PRESENCE

We found three studies that directly measured the virus in exhaled breaths or air samples within the vicinity of the COVID-19 patient. In the study by Ma et al. (2020) [6], they measured the presence of the virus in the exhaled breath, air and surface of patients with COVID-19. Their results showed that the highest virus content was in EBC (exhaled breath condensate) 14/52 (26.9%), then in surface swabs (13/242; 5.4%) and lastly, in air 1/26 (3.8%).

In a case-control study by Lednicky et al. (2020) [7] with six cases (five positive controls, including one as case and control), air samples were collected in the rooms of two COVID-19 patients, one with active RT-PCR and virus culture. Viable virus was isolated from air samples collected 2 to 4.8 m away from the patients. The genome sequence of the SARS-CoV-2 strain isolated from the material collected by the air samplers was identical to that isolated from the NP swab from the patient with an active infection.

In the last paper, Cheng et al. (2020) [15], did a diagnostic study with six COVID-19 patients (symptomatic and asymptomatic). They collected air samples in single rooms of patients with airborne infected isolation rooms (AIIR) with 12 air changes per hour (ACH). All air samples were negative for SARS-CoV-2 RNA in the six patients singly isolated inside the AIIR. A second group of samples yielded 19/377 (5%) of environmental samples (bedrails, lockers, bed tables – area of 9 cm^2) near 21 patients. The cell phone had the highest concentration of the virus: 7.8% (7/77) followed by bed rail 4/74 (5.4%). There was significant correlation between viral loads in clinical samples and positivity of environmental samples ($p<0.001$).

In a closed space with an infected individual, it is possible that viral presence through exhaled particles may be present both in air samples and as fomites that can settle in environmental areas near the infected individual such as bed rails, chairs and tables within the closed room.

REVIEW METHODS

We searched Pubmed, TRIP database, clinicaltrials.gov, Epistemonikos, medrxiv, Google Scholar, and Google to identify articles related to indoor CO2 monitoring and COVID-19 risk of infection. Public health guidance documents that used CO2 monitoring as a surrogate for infection risk were also sourced. Our search included the following PICO elements: P – individuals without COVID-19, at risk for COVID-19, healthcare workers, essential frontliners, household and occupational contacts, vaccinated individuals, general public; I – use of CO2 monitors/levels; C – non-use of CO2 monitors/levels; O – risk of COVID-19 infection, risk for respiratory diseases, indoor air quality. Our search also utilized Boolean operator combinations and synonyms like “rooms,” “enclosed spaces,” “indoor,” “CO2,” “carbon dioxide,” “air quality,” “COVID-19,” and “SARS CoV-2.”

We included cross sectional studies, retrospective cohort and experimental studies (before and after an intervention) to determine CO2 levels in real-time with the different types of ventilation. We included preprints and examined study protocols as well.

RESULTS

We found no studies that directly answered the research question, and the studies subsequently presented constitute indirect evidence

The studies included in this review evaluated (1) effects of CO2 level in risk of tuberculosis or nosocomial infection, (2) relationship of air ventilation on CO2 concentration, (3) CO2 and aerosol concentration, (4) effects of CO2 level in sick building syndrome (SBS), and (5) possible harm/misinterpretation in the use of CO2 monitors.

Effect of Ventilation and CO2 concentration on TB transmission

The similarity in the mode of transmission for SARS-CoV-2 and Tuberculosis may show indirect evidence for SARS-CoV-2 transmission in a group where the CO2 level is more than 1000ppm in an enclosed area. In a retrospective cohort study on the effect of ventilation and level of CO2 concentration on TB infection, Du et al. [16] evaluated 1665 contacts and investigated how ventilation rate was improved with CO2 monitoring and, as a corollary to this, how improvement of ventilation rate decreased the number of tuberculosis cases.

The study noted the differences between those who acquired and did not acquire TB in terms of the CO2 levels, with a threshold set at 1000 parts per million in the room where their exposure or contact occurred. Comparing the exposed group (room with CO2 levels ≥1000ppm) and the non-exposed group (room with CO2 levels < 1000ppm) in accordance with the number of TB cases, the exposed group was 16 times more likely to have TB infection (RR 16.1, 95% CI 2.17-119.5).

The results of the study are summarized in the table below:

Table 8. Acquired TB infection and Room CO2 level (ppm)

Contact under CO2 level ≥1000ppm	Acquired TB (n=22)	Did not acquire TB (n=1643)	P value
NO	1 (4.5%)	722 (43.9%)	< 0.0001
YES	21 (95.5%)	921 (6.1%)	

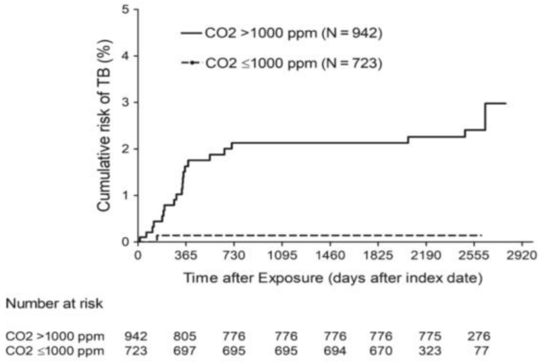

Figure 2. Kaplan-Meier estimates for the risk of contacts by ventilation status

Air Ventilation Protocol on CO2 Concentration

The studies by Di Gilio et al. [2], Vassella et al. [12], and Lu et al. [17] showed the relationship between CO2 concentration and ventilation rate: the higher the ventilation rate, the lower the CO2 levels. The study by Lu et al. [17] investigated, over a one-month period (February 2020), places where COVID-19 patients were present. They placed CO2 monitors in two major areas of the hospital and monitored the CO2 levels, air ventilation rates and the occurrence of nosocomial COVID-19 infections during this period. According to their data, approximately 90 patients were registered at the hospital each day so for the whole month of February in 2020, approximately 2520 patients were included. During the study period, five COVID-19 patients were present. However, no one contracted the COVID-19 infection during the study period.

CO2 level and Aerosol Concentration

In a simulated study [14] using a concert hall as a setting of an enclosed area, aerosol generation was made with a dummy infector with and without mask. Their study showed a direct linear positive correlation between aerosol concentration and CO2 concentration with an r = 0.77 (Figure 3).

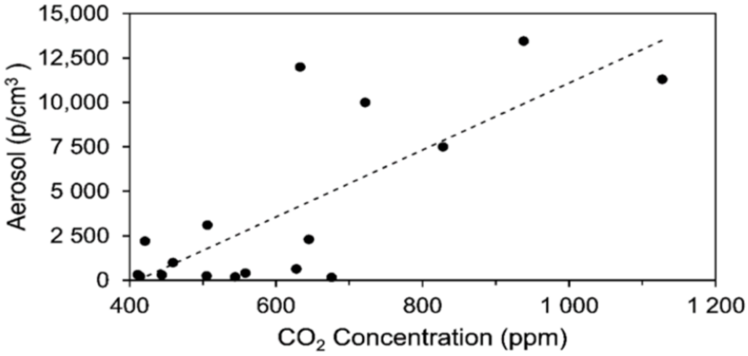

Figure 3. Relationship between aerosol and CO2 concentration.

CO2 level and Sick Building Syndrome

Studies by Tsai et al. [18] and Hou et al. [19] found a correlation between CO2 levels and sick building syndrome (SBS), which was defined as having symptoms that cannot be associated with a well-defined cause but that appear to be linked with time spent in a building. Symptoms of SBS include eye irritation, headache, feeling of stuffiness, URTI, or GI complaints. The study by Tsai et al. [19] was a cross sectional study with 111 office workers in an office floor. The OR was measured for each symptom and correlated with CO2 concentration of <500ppm vs. >800 ppm. Results showed that eye irritation had an OR = 1.7 (95% CI 1.1-2.7; p = 0.01) and URTI had an OR = 1.7 (95% CI 1.0-2.7; p=0.03).

The second study by Hou et al. [19] was conducted over an 11-month period (March 2018-February 2019). A questionnaire was given every month to the sample population (n=1285). The AOR (adjusted odds ratio) of relative humidity for general (fatigue, heavy head, headache, dizziness, difficulty concentrating) and skin SBS (dry facial skin, dry ears, dry hands) was higher in areas with high CO2 concentrations than in those with low CO2 concentrations (OR= 1.02, 95% CI 0.97-1.08 for general SBS; OR = 1.03, 95% CI 0.99-1.08 for skin SBS).

Possible Harm on the Use of CO2 monitors

The review by Eykelbosh [13] on the use of indoor CO2 sensors for COVID-19 risk mitigation identified two risks of using CO2 sensors: technological dependency and misinterpretation. The article argued that although CO2 has been proposed as a proxy for COVID-19 risk, many factors may come into play such as the size of the room, occupants' activity, use of masks, etc.

They explained that the use of CO2 monitors may be 1) threshold-based, where one sets an appropriate action limit, or 2) trend-based, where a data logging feature is used to display the CO2 curve and an action is taken when the curve is going upward. For both approaches, the actions to reduce CO2 levels may include the following: open windows and doors, take periodic breaks where occupants can leave the room, reduce occupancy and avoidance of high intensity activities, increase fresh air supply, keep ventilation fans running during occupied periods, and install local exhaust systems. Placement of CO2 monitors should be 0.5-2.0 meters above floor and should be avoided in the following: near windows, near 2m of any human contact and within 2m of open flame.

In theory, technological dependence and misinterpretation may occur. Technological dependence occurs when the focus becomes the readout on the sensor rather than on promoting awareness: eg. masks, distancing, etc. Misinterpretation may include a sense of complacency when CO2 level is low or below threshold.

EVIDENCE TO DECISION

The price of a CO2 sensor/monitor ranges in online shops from Php865 – Php4,501.[20] While these are readily accessible and available to individual users in metropolitan areas with internet connection, the same cannot be said for all rural or geographically isolated and disadvantaged areas (GIDAs) unless funded and sourced by third parties.

APPRAISAL OF INCLUDED STUDIES

We appraised the study by Du et al [17] using the Newcastle Ottawa Scale (NOS) for cohort studies. The over-all certainty of evidence was moderate using GRADEPRO, since we downgraded for indirectness but increased by 2 steps because of large magnitude of association.

RECOMMENDATIONS FROM OTHER GROUPS IN PANDEMIC ERA

From Eykelbosh [13]

Source	Document Type	Description	CO2 Action Limit
German Umweltbundesamt [21]	Guidance document	Recommends fixed or portable CO2 “traffic lights” in schools to remind teachers and students to periodically open windows to facilitate classroom ventilation.	Lower green-yellow threshold set at 1000 ppm; yellow- red threshold set at 2000 ppm.
Minnesota Department of Health [22]	Guidance document	Recommends CO2 monitoring to assess ventilation adequacy in classrooms with high occupancy.	Keep rooms below 800 ppm.
UK Scientific Advisory Group for Emergency [23]	Public health guidance document	Supports the notion of using CO2 monitors to identify poorly ventilated spaces and prioritize them for remediation. Notes that low CO2 levels do not necessarily indicate sufficient ventilation in low-occupancy or high-volume spaces. Rejects the notion that CO2 can be used as a direct proxy of COVID-19 risk.	Spaces with CO2 levels >1500 ppm should be prioritized for remediation. Spaces with aerosol-generating activities should aim for 800 ppm CO2.
US Centers for Disease Control and Prevention [24]	Public health guidance document	Supports using portable CO2 sensors with a logging function to monitor indoor spaces.	A portable air cleaner should be considered for spaces that cannot be maintained below 800 ppm.
Washington State [25]	Public health guidance document	CO2 monitoring required to ensure that “open air” eating places (i.e., patios or restaurants with large open windows) are truly open to the outdoors.	If seated occupants are exposed to >450 ppm for 15 min, they must be moved to a better ventilated table.
Department of Labor and Employment (Philippines) [26]	Public Guidelines for workplaces and public transport to prevent and control the spread of Covid-19	CO2 monitoring (Section 6.B.2. Quantitative Assessment). CO2 level inside an enclosed space may be determined by using a calibrated CO2 monitoring device	CO2 shall not exceed 1,000ppm.

RESEARCH GAPS

Although CO2 monitoring may indicate indoor air quality, there is still paucity of evidence regarding the relationship of CO2 levels and COVID-19 transmission risk. There are no studies that compare CO2 levels with a control group. Direct studies looking into the role or benefit of using CO2 monitors to decrease COVID-19 cases are needed.

There is one ongoing study [27] that aims to determine the efficacy and feasibility of CO2 monitors to maintain indoor CO2 concentrations below 800-1000 ppm.

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Appendix 1. Evidence to Decision

Summary of initial judgements prior to the actual panel meeting (N = 6)

FACTORS	JUDGEMENT					RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
Problem	No (2)	Yes (4)				• CO_2 levels have been considered to be a surrogate measure of transmission risk of respiratory infections that are spread through droplet and aerosol mechanisms • CO_2 levels may indicate an increase in the number of occupants in an enclosed area and their activity level [8]. • Through mathematical modelling and indoor scenarios, the CO_2 levels can proxy the COVID-19 infection risk by applying the Wells-Riley model and its modifications [4]. • Increasing levels of CO_2 may indicate poor indoor air quality and thus increased infection risk. [9-12]
Benefits	Large (2)	Moderate (1)	Small (2)	Uncertain (1)		• Detects CO_2 levels: Indirect evidence showed increased likelihood of TB infection in individuals who had been in the room with CO_2 levels ≥1000ppm when compared to those in room with CO_2 level < 1000 ppm (RR = 16.1, 95% CI: 2.17-119.5) • In most studies that investigated CO_2 levels and air ventilation, increased air ventilation has been associated with a decrease in CO_2 levels. Some studies found also found a correlation between CO_2 levels and sick building syndrome (SBS). • Beneficial in construction planning to know no. of occupants in enclosed spaces (even in not COVID)
Harm	Large	Small (3)	Uncertain (3)	Varies		None reported aside from technological dependency and misinterpretation
Certainty of Evidence	High	Moderate (4)	Low (1)	Very low (1)		The overall certainty of evidence is moderate.
Balance of effects	Favors intervention (2)	Does not favor intervention (1)	Uncertain (3)	Varies		• Indirect evidence showed increased likelihood of TB infection in individuals who had been in the room with CO_2 levels ≥1000ppm when compared to those in room with CO_2 level < 1000 ppm (RR = 16.1, 95% CI: 2.17-119.5) • In most studies that investigated CO_2 levels and air ventilation, increased air ventilation has been associated with a decrease in CO_2 levels. Some studies found also found a correlation between CO_2 levels and sick building syndrome (SBS). • None reported aside from technological dependency and misinterpretation

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS FROM PANEL MEMBERS
Values	Important uncertainty or variability	Possibly important uncertainty or variability (3)	Possibly NO important uncertainty or variability (1)	No important uncertainty or variability (2)			• No research evidence found
Resources Required	Uncertain	Large cost (6)	Moderate Cost	Negligible cost	Moderate savings	Large savings	• No research evidence found
Certainty of evidence of required resources	No included studies (3)	Very low (2)	Low	Moderate	High (1)		• No research evidence found
Cost effectiveness	No included studies (4)	Favors the comparison	Does not favor either the intervention or the comparison (2)	Favors the intervention			• No cost-effectiveness studies available.
Equity	Uncertain (5)	Reduced (1)	Probably no impact	Increased			• No published studies available on use of CO2 monitors in the Philippines.
Acceptability	Uncertain (6)	No	Yes	Varies			• No published studies available on use of CO2 monitors in the Philippines. DOLE has recommended air change per minute within occupied workspaces maintains CO2 levels below 1000 ppm at all times.
Feasibility	Uncertain (4)	No	Yes (2)	Varies			• No published studies available on use of CO2 monitors in the Philippines. DOLE has recommended air change per minute within occupied workspaces maintains CO2 levels below 1000 ppm at all times.

Appendix 2. Search Yield and Results

PubMedSearchHistory-7

Search number	Query	Sort By	Filters	Search Details	Results	Time
18	Exhaled CO2 as COVID-19 infection risk proxy for different indoor environments and activities			("exhalate"[All Fields] OR "exhalation"[MeSH Terms] OR "exhalation"[All Fields] OR "exhalations"[All Fields] OR "exhaled"[All Fields] OR "exhaling"[All Fields] OR "exhale"[All Fields] OR "exhales"[All Fields]) AND "CO2"[All Fiel	0	12:09:13
17	Exhaled CO2 as COVID-19 infection risk proxy for different indoor environments and activities - Schema: all			"Exhaled"[All Fields] AND "CO2"[All Fields] AND "COVID-19"[All Fields] AND "infection"[All Fields] AND "risk"[All Fields] AND "proxy"[All Fields] AND "different"[All Fields] AND "indoor"[All Fields] AND "environments"[All Field	0	12:09:13
16	(#1) AND (#12)			("sars cov 2"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[All Fields]) AND ("crowd s"[All Fields] OR "crowding"[MeSH Terms] OR "crowding"[All Fields] OR "crowd"[All Fields] OR "crowded"[All Fields] OR "crowd	1	11:56:42
15	crowding			"crowd s"[All Fields] OR "crowding"[MeSH Terms] OR "crowding"[All Fields] OR "crowd"[All Fields] OR "crowded"[All Fields] OR "crowds"[All Fields]	21,874	11:56:11
12	((#6) AND (#9)) AND (#11)			("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "cov	13	11:55:17
14	(#9) AND (#6)			(("C02"[All Fields] AND ("level"[All Fields] OR "levels"[All Fields])) OR (("carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[All Fields]) OR "carbon dioxide"[All Fields]) AND ("level"[All Fields] OR "levels"[All Fi	262	11:37:38
13	Similar articles for PMID: 32837691			32837691,34177075,33085569,33615383,34051507,33797051,32834937,34456454,33778137,33967376,21431823,34181766,32288019,16297217,23074468,19812072,32874703,34414068,27611368,33746487,31172603,3	62	11:01:48
11	((indoor space) OR (closed space)) OR (closed ventilation)			(("indoor"[All Fields] OR "indoors"[All Fields]) AND ("space"[All Fields] OR "space s"[All Fields] OR "spaces"[All Fields])) OR (("close"[All Fields] OR "closed"[All Fields] OR "closely"[All Fields] OR "closeness"[All Fields] OR "clo	34,158	10:49:09
10	Indoor space			("indoor"[All Fields] OR "indoors"[All Fields]) AND ("space"[All Fields] OR "space s"[All Fields] OR "spaces"[All Fields])	1,879	10:48:37
9	(#8) OR (#7)			("C02"[All Fields] AND ("level"[All Fields] OR "levels"[All Fields])) OR (("carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[All Fields]) OR "carbon dioxide"[All Fields]) AND ("level"[All Fields] OR "levels"[All Fie	129,905	10:47:48
8	(C02 level) OR (Carbon Dioxide Level)			("C02"[All Fields] AND ("level"[All Fields] OR "levels"[All Fields])) OR (("carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[All Fields]) OR "carbon dioxide"[All Fields]) AND ("level"[All Fields] OR "levels"[All Fie	21,754	10:47:21
7	(C02) OR (Carbon Dioxide)			"C02"[All Fields] OR ("carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[All Fields]) OR "carbon dioxide"[All Fields])	129,905	10:46:38
6	(((COVID-19) OR (SARS-CoV-2)) OR (COVID infection)) OR (COVID)			"covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covi	177,529	10:45:03
5	(#3) AND (#2)			("indoor air"[Journal] OR "indoor air int conf indoor air qual clim"[Journal] OR ("indoor"[All Fields] AND "air"[All Fields]) OR "indoor air"[All Fields]) AND ("carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[Al	874	10:43:49
4	(#2) OR (#3)			"carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[All Fields]) OR "carbon dioxide"[All Fields] OR ("indoor air"[Journal] OR "indoor air int conf indoor air qual clim"[Journal] OR ("indoor"[All Fields] AND "air"	149,474	10:02:43
3	indoor air			"indoor air"[Journal] OR "indoor air int conf indoor air qual clim"[Journal] OR ("indoor"[All Fields] AND "air"[All Fields]) OR "indoor air"[All Fields]	21,309	10:02:17
2	Carbon dioxide			"carbon dioxide"[MeSH Terms] OR ("carbon"[All Fields] AND "dioxide"[All Fields]) OR "carbon dioxide"[All Fields]	129,039	10:01:47
1	(SARS-CoV-2) AND (crowding)			("sars cov 2"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[All Fields]) AND ("crowd s"[All Fields] OR "crowding"[MeSH Terms] OR "crowding"[All Fields] OR "crowd"[All Fields] OR "crowded"[All Fields] OR "crowd	344	09:56:31

Appendix 3. Table of Included Studies

<table>
<tr><th>Title/Author</th><th>Study design</th><th>Country</th><th>No of patients</th><th>Population</th><th>Intervention Group(s)</th><th>Control</th><th>Outcomes</th></tr>
<tr><td colspan="8">Effect of Ventilation and CO2 concentration on TB transmission</td></tr>
<tr><td>Du et al. (2020)

Effect of ventilation improvement during a tuberculosis outbreak in under ventilated university buildings. Indoor Air.</td><td>Retrospective Cohort study design (for all contacts in outbreak)</td><td></td><td></td><td>Evaluated 1665 contacts

Acquired TB = 22
Did not have TB = 1643

Contact under CO2 >1000ppm<table><tr><th></th><th>(+) TB</th><th>(-) TB</th></tr><tr><td>No</td><td>1 (4.6%)</td><td>722 (44%)</td></tr><tr><td>Yes</td><td>21 (95.5%)</td><td>921 (56%)</td></tr></table>p-value < 0.0001</td><td>Room <1000ppm CO2

Improving ventilation rate to 23.6-25.1 L/s/p (14-15 ACH) helped end the TB outbreak.

Ventilation improvement to lessen CO2 to <1000ppm was associated</td><td>Room >1000ppm CO2</td><td>1/21 had TB infection in the INTERVENTION group while 21/22 had TB infection in the CONTROL group

97% decrease in infectious TB cases among contacts (95% CI: 50-99.9%) for those CO2 <1000ppm</td></tr>
<tr><td colspan="8">Air Ventilation Protocol on CO2 concentration</td></tr>
<tr><td>Di Gilio et al. (2021)

CO2 concentration monitoring inside educational buildings as a strategic tool to reduce the risk of Sars-CoV-2 airborne transmission. Environmental Research.</td><td>Experimental, pilot study.

*The premise is that indoor CO2 monitoring was suggested as a practical proxy of transmission risk of respiratory infectious disease. In indoor environments an excess of CO2 levels over outdoor levels could be related to the increased probability to inhaled breath exhaled by other people – thus to infection risk.</td><td>Italy</td><td>9 classrooms

147-152 students</td><td>Students
Pre-school</td><td>1st stage: realtime CO2 monitoring

2nd stage: if CO2 levels approach 700 ppm, the following were done: Leave door open, open windows for 10min during breaks, open windows if the above don't work to lower CO2 levels.</td><td>No protocols</td><td>Lowering of CO2 levels after instituting the protocol.</td></tr>
<tr><td>Vassella et al. (2021)

From spontaneous to strategic natural window ventilation: Improving indoor air quality in Swiss</td><td>Cross sectional</td><td></td><td>100 classrooms

Range/classroom 3-26</td><td>CO2 levels decrease with increased ventilation and reminders for people to be aware of the benefits of ventilation compared to standard [no reminders/flyers on ventilations during breaks].</td><td>CO2 level
Median: 1600pmm</td><td colspan="2">CO2 level.Median: 1097 ppm
Natural ventilation + mechanical + flyers, lessons on ventilation, + ventilation during breaks or open</td></tr>
</table>

Schools. Int J Hyg Environ Health.						
Lu et al. (2021) Affordable measures to monitor and alarm nosocomial SARS-CoV-2 infection due to poor ventilation. Indoor Air.	Experimental Used CO2 levels as surrogate assessment method of noscomial infection risk. Prospective cohort: Case Study	Infrared CO2 sensors: Moderate [characterize exhaled breath]. +/- 50ppm. Measurement interval of 5 minutes [0.8-1.2m above ground]. Placed in the fever clinic [natural ventilation]; emergency department [mechanical ventilation] **CO2 level was used to estimate ventilation rates and can be diluted when ventilation rates are increased.	No infections were observed. No comparator. Infection among HCWs were just monitored and the airflow rate was noted at the time of the encounters with patients in different areas of the hospital based on number of infectors [Covid-19 patients]. Under the protection of level 2 PPE, an outdoor airflow rate of 21 L/(s·person) was sufficient to prevent SARS-CoV-2 hospital-acquired infection in Changgung Hospital. *Indoor CO_2 concentration represents the comprehensive effects of occupancy and the outdoor airflow rate. The ventilation can be sufficient to maintain a relatively low CO_2 concentration in an overrowded room, which is dangerous for diseases that can be transmit- ted through close contact, such as COVID-19.	In this study, aided with personal protection and disinfection measures, outdoor airflow rate per person of 15–18 L/(s·person) was sufficient to prevent nosocomial infection when there was only one COVID-19 patient, and 21 L/(s·person) was sufficient during throat swab sampling.	Theoretical determination of upper limit of CO2	Practical implications: The study showed that with personal protection and disinfection, the outdoor airflow rate per person of 15–18 L/(s·person) was sufficient to prevent nosocomial infection when there was only one COVID-19 patient, and 21 L/(s·person) was sufficient during throat swab sampling.
CO2 level and Sick Building Syndrome						
Dai-Hua et al. (2012) Office Workers' Sick Building Syndrome and Indoor Carbon Dioxide Concentrations, Journal of Occupational and Environmental Hygiene	Cross-sectional study that used an SBS questionnaire and compared it to CO2 levels.	Correlate SBS [sick building syndrome] and CO2 concentrations -SBS, symptoms that cannot be associated with a well-defined cost but appear to be linked with time spent in a building.	CO2 concentrations are used as surrogate for indoor ventilation. SBS included eye irritation, headache, tiredness, fatique, tension, URTI, or GI complaints, skin irritations.	Used two time periods for questionnaire. Participants should be able to answer both.	CONCLUSION Indoor CO2 ≥800ppm were associated with an increase in workers' SBS, especially eye irritation and URTI.	+association between SBS and indoor CO2 levels: specifically [tired/strained eyes, dry/irriitated eyes, difficulty in remembering
Hou et al. (2021) Associations of indoor CO2 concentrations, air temperature, and humidity with perceived air quality and sick building syndrome symptoms in Chinese homes. Indoor Air.	Cross-sectional study Correlate CO2 levels with perception of dry air and skin SBS symptoms.	*CO2 was positively associated with the percentage of perceived stuffy odor. Low CO2 levels were less likely to have skin SBS symptom (dry facial skin, dry ears, dry hands)				

Appendix 4. Detailed Study Appraisal

Author(s): Emmanuel P. Estrella, MD, MSc, Maria Teresa S. Tolosa, MD, D Clin Epi, FPDS Myzelle Anne Infantado, PTRP, MSc (cand.)
Question: CO_2 levels below 1000ppm versus =/> 1000ppm
Setting: Community or healthcare setting
Bibliography: Du CR, Wang SC, YU MC, Chiu TF Wang JY, Chuang PC, Jou R, Chan PC, Fang CT. Effect of ventilation improvement during a tuberculosis outbreak in under ventilated university buildings. Indoor Air.2020; 30:422-432.

Assessment of quality of a cohort study – Newcastle Ottawa Scale	
Selection (tick one box in each section):	
1. Representativeness of the intervention cohort	
a) Truly representative ★	□
b) **Somewhat representative ★**	√
c) Selected group of patients	□
d) No description of the derivation of the cohort	□
2. Selection of the non intervention cohort	
a) **Drawn from the same community as the intervention cohort ★**	√
b) Drawn from a different source	□
c) No description of the derivation of the non intervention cohort	□
3. Ascertainment of intervention	
a) Secure record ★	√
b) Structured interview ★	□
c) Written self report	□
d) Other / no description	□
4. Demonstration that outcome of interest was not present at start of study	
a) Yes ★	√
b) No	□
Comparability (tick one or both boxes, as appropriate): 2 vs 1	
1. Comparability of cohorts on the basis of the design or analysis	
a) Study controls for age, sex, marital status ★	□
b) **Study controls for any additional factors (e.g. socio-economic status, education) ★**	√
Outcome (tick one box in each section): 3 vs 3	
1. Assessment of outcome	
a) Independent blind assessment ★	□
b) **Record linkage ★**	√
c) Self-report	□
d) Other / no description	□
2. Was follow up long enough for outcomes to occur	
a) **Yes, if median duration of follow-up ≥ 6 month ★**	√
b) No, if median duration of follow-up < 6 months	□
3. Adequacy of follow up of cohorts	
a) **Complete follow up: all subjects accounted for ★**	√
b) Subjects lost to follow up unlikely to introduce bias: number lost <= 20%, or description of those lost suggesting no different from those followed ★	□
c) Follow up rate < 80% (select an adequate %) and no description of those lost	□
d) No statement	□

The assessment for this study using the Newcastle Ottawa Scale is that the study had 4 STARS in the Selection Domain, 1 STAR in the Comparability Domain, 3 STARS in the OUTCOME Domain.

Converting NOS scales to AHRQ (Agency for Health Research and Quality) standards, 4 Stars in Selection domain, 1 Star in the Comparability Domain, and 3 Stars in the outcome Domain, the study is of GOOD QUALITY.

Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor):
Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Appendix 5. GRADE Evidence Profile

A recent study on the effect of ventilation and CO2 levels on TB infection was published by Du et al. The following figures are grade evidence profile tables for the study. This was a cohort study on university students and employees and the effect of ventilation improvement on TB infection. The intervention here was increasing ventilation to have a CO2 level of < 1000pmm.

Author(s): Chun-Ru Du, Shun-Chic Wang, Ming-Chih Yu, Ting-Fang Chiu, Yann-Yuan Wang, Pei-Chun Chuang, Ruwen Jou, Pei-Chun Chan, Chi-Tai Fang
Question: CO2 ≥ 1000ppm compared to CO2 < 1000 in preventing TB Transmission
Setting: University Setting
Bibliography: Du CR, Wang SC, YU MC, Chiu TF Wang JY, Chuang PC, Jou R, Chan PC, Fang CT. Effect of ventilation improvement during a tuberculosis outbreak in under ventilated university buildings. Indoor Air.2020; 30:422-432.

CERTAINTY ASSESSMENT							NO. OF PATIENTS		EFFECT		CERTAINTY	IMPORTANCE
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 ≥ 1000ppm	CO2 < 1000ppm	Relative (95% CI)	Absolute (95% CI)		
TB Infection (assessed with: CXR, Sputum)												
1	Observational studies	Not serious[a]	Not serious[a]	Serious[b]	Not serious[c]	Very strong association	21/942 (2.2%)	1/723 (0.1%)	**RR 16.12** (2.17 to 119.54)	**21 more per 1,000** (from 2 more to 164 more)	⊕⊕⊕◯ Moderate	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

[a] Wide variation in the type of patients that were included in the study
[b] Different type of infection, but related in the manner of transmission

Q10. What are effective decontamination techniques for N95 reuse?

As of 30 June 2021

RECOMMENDATIONS

In situations where there is shortage of filtering facepiece respirators (FFR), we suggest the use of Hydrogen Peroxide Vapor (HPV), Ultraviolet Germicidal Irradiation (UVGI), moist heat and peracetic acid dry fogging system (PAF) as options for N95 mask decontamination as recommended by the manufacturer based on their ability to reduce SARS-COV-2 load and infectivity while still maintaining N95 mask integrity. *(Low certainty of evidence; Weak recommendation)*

We recommend against the use of autoclave and alcohol as these methods alter filtering facepiece respirator's (N95) integrity and degrade filtration efficacy. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues

Reuse of N95 masks should be considered only in cases of shortages and not during times of normal supply. It is important to specify the maximum number of cycles by which the decontamination techniques can still preserve the functional and physical integrity of the N95 mask: (1) autoclave- up to 2 cycles; and (2) moist heat, HPV and PAF- up to10 cycles.

Regarding local availability, some noted that HPV is usually not affordable in resource-limited settings, making UVGI the preferred option due to its lower cost. In practice, however, HPV is considered more effective in decontamination. Its mist can reach all the spaces once halo fogging is done, which is beneficial to N95 mask since it has many pores. In contrast, UVGI can only disinfect the area reached by the UV light. Although HPV is available in the country, its use will entail the need for a special decontamination room and a machine. Some noted that HPV is usually not affordable in resource-limited settings. The panel also stressed the importance of checking the condition of the N95 mask before decontamination and not just solely rely on the manufacturer's recommendation. Likewise, the proper procedure before decontamination should also be emphasized.

On the recommendation against the use of autoclave, it was clarified that although it can destroy the virus, the physical and functional integrity of the N95 mask are affected.

In terms of the other decontamination techniques, no study was found on the effectiveness of air dry alone, exposure to sunlight, soap and water, 0.5% chlorine solution, and for other disinfecting agents such as benzalkonium chloride.

KEY FINDINGS

Eight quasi-experimental studies reported the effects of six decontamination techniques (i.e., alcohol, autoclave, moist heat, HPV, PAF, UVGI) on SARS-CoV-2 laden N95 masks. There is low evidence on use of Hydrogen Peroxide Vapor (HPV), Ultraviolet Germicidal Irradiation (UVGI), moist heat and peracetic acid dry fogging system (PAF) as options for N95 mask decontamination. These decontamination methods resulted in ≥4.79 log_{10} reductions in SARS-CoV-2. Except for autoclave, they preserved the quality fit of N95 masks after 10 decontamination cycles. There is very low evidence against the use of autoclave and alcohol for N95 mask decontamination as these methods alter N95 integrity and degrade filtration efficacy.

INTRODUCTION

N95 masks are single-use devices that should be discarded after use to avoid self-inoculation & cross-contamination, especially after aerosol-generating procedure.[1,2] The Asia Pacific Center for Evidence-Based Healthcare and PSMID (Apr 3, 2020) has stated that based on available evidence prior to 2020, ultraviolet germicidal irradiation (UVGI), microwave-generated steam, warm moist heat, and HPV all effectively reduced viral or bacterial loads and maintained N95 mask integrity. [2,3] However, the effectiveness of these methods against SARS-CoV-2 remains unclear. [5]

REVIEW METHODS

We comprehensively searched various electronic databases[1] until Feb 5, 2021, for any study type investigating the decontamination effects on N95 masks' sterilization efficiency, filtration efficiency, mask integrity, or incidence of infection. We used these keywords in searching for the relevant literature: 1. N95 masks OR respiratory devices; 2 infection control OR decontamination; 3. reuse OR extended use. We excluded studies that focused on decontamination of other mask types (e.g., gauze, cloth, spun-lace, elastomeric, powered-air-purifying, surgical masks) and other article types (e.g., abstracts, posters, review, articles, book chapters, letters, guidelines, points of view. We included only articles with full-text reports written in English.

RESULTS

Characteristics of included studies

Eight quasi-experimental studies reported on the effects of six decontamination methods on SARS-CoV-2- inoculated N95 masks. Seven laboratory-based studies [4-10] and one hospital-based study [11] were included, all published in the year 2020. The effects of alcohol (n=2 studies) [4,5], autoclave (n=2 studies) [6,11], heat (n=1 study) [7], HPV (n=3 studies) [4,6,8], PAF (n=1 study) [6], UVGI (n=3 studies) [4,9,10] for SARS-COV 2 inactivation and on mask integrity were investigated. One study assessed only the effect on physical integrity of the mask, one study on the ability to decontaminate alone, while six analyzed both. Various commercially available N95 models, both medical and industrial grade were tested. No study investigated effect of decontamination on incidence of COVID- 19 infection. Studies by Smith et al. (2020) [5], Kumar et al. (2020) [6], and Fischer et al. (2020) [4] examined effects of several decontamination procedures.

Methodological quality

SARS-CoV-2 containing liquid media was applied directly to the N-95 masks [6-12]. The masks were not randomly allocated to decontamination groups [4-11]. Although

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[1] MEDLINE through Pubmed, Cochrane CENTRAL Database, ChinaXiv.org, USA clinical trials, China chictr.org, WHO, COVID-19 Open Living Evidence Synthesis, Living Evidence on COVID-19, Australia covid19 evidene.net.au, WHO Therapeutics, and COVID-19 guidelines.

assessors were not blinded to the decontamination method used, objective measures were used to determine virucidal activity and mask integrity [4-11]. Kumar et al. (2020) did not report the effect size on N95 functional integrity, after a series of decontamination cycles [6]. These limited number of studies reported decontamination effects on a few new or unused N95 models artificially contaminated:

a. 2 alcohol studies on 4 masks
b. 2 autoclave on 6 masks
c. 1 moist heat study on 4 masks
d. 3 HPV studies on 6 masks
e. 1 PAF study on 6 masks
f. 3 UVGI studies on masks

Outcomes

Effectiveness outcomes based on the ability to remove infectious potential of SARS-COV2 were established based on real time reverse transcriptase polymerase chain reaction (RT-PCR) viral detection and viability in culture. Mask integrity was determined based on the ability to preserve filtration efficiency using quantitative FIT testing and visual and tactile analysis of facemask structure after one or several cycles of decontamination. No study reported on incidence or transmission of COVID-19 infection.

Alcohol

Seventy percent (70%) ethanol was sprayed on the mask exterior and interior. For overnight application, masks were saturated with 70% ethanol, placed in a sealed plastic bag overnight, removed in the morning and allowed to airdry for ~8 hours before the FIT test.

Ethanol treatment demonstrated sufficient virucidal activity in the studies. A single treatment however led to a drop in functional and physical integrity even when the mask felt dry to touch. The impact on integrity appeared to be time-bound. Some masks dried overnight showed detached nose guards. [5]

Autoclave

One autoclave cycle effectively reduced the SARS-CoV-2 virus on N95 masks and maintained its structural and functional integrity. [12] More than one autoclave cycle resulted in the failed quantitative fit test using Portacount of the rigid and molded an N95 subset (i.e., 3M 1860 and 8210). [6] In a study conducted in a hospital setting, undisclosed number of staff reported no change with ability to breathe while wearing N95 masks that had been autoclaved once, although there were comments on a slight change in respirator odor, less elasticity in the straps, and a ‘softer’ texture to the mask material. [11]

Heat

A single 70°C heat for 5 minutes inactivated the SARS-CoV-2 in all N95 masks. [13] The same effect was noted with a longer duration of heating (60 minutes) at 70°C. Besides, 60 minute-heating decontaminated the N95 masks with virus-laden blood and saliva. [7] The effects of heat on SARS-CoV-2 virus-infected N95 straps have not been investigated. [7] Moist heat (50–85% RH) disinfected SARS-CoV-2 or similar viruses at a shorter exposure time than dry heat. [14]

The polypropylene microfibres of N95 masks degrades above 130°C, suggesting that N95 masks may withstand repetitive exposure to 70°C. [15] Ten thermal cycles of 60 min at 70 ◦C with either 0% or 50% relative humidity did not degrade the mask's structural integrity. Masks maintained fibre diameters similar to untreated masks and continued to meet standards for fit (185.4–203.6; n = 23) ($p < 0.001$), filtration efficiency (95.1–97.5; n = 12) ($p = 0.003$) and breathing resistance (62.9–95.5; n = 12) ($p < 0.001$). [7] In contrast, more than 2 rounds of decontamination resulted in decrease in filtration performance among heat treated masks. [6]

A pilot study utilizing 2 industrial laundry dryers maintained mask integrity even after 3 dry heat cycles at 80 ◦C for 65 min. In this study, the masks were sealed in Ziplocs bags and placed in the cardboard boxes positioned at the rear half of the dryer, The idea is to keep the masks protected from the extreme temperatures on the cylinder itself, and to stabilize the temperature both by using the region in the tumbler with lower temperature gradients and by using the more uniform equilibrium in the cardboard box. Laundry drivers are not designed for medical decontamination purposes. [17]

HPV

HPV and HP plasma led to immediate and rapid inactivation of SARS-CoV-2 on N95 mask upon treatment exposure. [6,10] Complete inactivation of SARS-COV2 was demonstrated with extended HPV cycle time of 5 hours. [8] In contrast, HP did not completely eliminate infectious SARS-CoV-2 RNA in all masks but the two healthcare grade masks did show an approximately five log10 reduction in SARS- CoV-2 RNA relative to the positive control. Such a log10 reduction in infectivity would exceed the ‘99.97%’ germicidal efficacy quoted by some hand sanitizers and exceeds the three log10 reduction estimated to fully decontaminate a mask in an influenza model. [7]

N95 masks showed acceptable filtration performance even after multiple (i.e.,10) HPV cycles.[8]

PAF

A single PAF cycle deactivated the SARS-CoV-2 virus on N95 masks. [6]

UVGI

In a laboratory setting, 5 minutes of PX-UV resulted in a >4.79 log10 rapid reduction in SARS-CoV-2 viral load on N95 masks. [9] A 5-minute PX-UV did not alter the physical or functional integrity of N95 masks (9). N95 masks maintained their filtration performance up to three UV cycles. [4] Appendix 2 reports the effects of the six decontamination methods used in this review.

RECOMMENDATIONS FROM OTHER GROUPS

The CDC (April 2020) has stated that N95 mask decontamination for reuse is only a contingency strategy to conserve supplies during the COVID-19 pandemic. UVGI, HPV, and moist heat has shown most promise in decontaminating N95 masks. Decontamination method should be evaluated for each FFR model.

The European Center for Disease Control and Prevention (June 2020) has listed UVGI, ethylene oxide, HPV, and dry and moist heat as N95 decontamination procedures that have favorable effectiveness and safety profile. However, these are considered only as a last resort if PPE shortages occurs. [18]

ONGOING STUDIES

There were 8 ongoing pre-print studies investigating the decontamination effects of UVGI, HPV, heat, methylene blue and light on SARS-CoV-2-laden N95 masks.

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Appendix 1. Characteristics of Included Studies

Study, year	Virus/Bacteria	Intervention	Outcome
Fischer, 2020	SARS-CoV-2	Alcohol HPV UVGI	Virus titer ($TCID_{50}$ /mLmedia) Mask integrity (fit factor) Kill rate (per virus per min)
Smith, 2020	SARS-CoV-2	Alcohol HPV	FIT score
Kumar, 2020	SARS-CoV-2 Vesicular stomatitis virus Indiana serotype	Autoclave PAF	Sterilization efficacy Quantitative fit test
Czubryt, 2020	SARS-CoV-2	Autoclave	Fit test Pre- and post-sterilization reject
Daeschler, 2020	SARS-CoV-2 Escherichia coli	Heat	SARS-Cov-2 inactivation Bacterial inactivation Microstructural analysis of the N95 filter layer Quantitative N95 respirator fit testing Filtration efficiency and breathing resistance testing
Ibáñez-Cervantes, 2020	SARS-CoV-2 Staphylococcus aureus Acinetobacter baumannii	HPV	Sterilization efficiency
Simmons, 2020	SARS-CoV-2	UVGI	Sterilization efficiency
Ozog, 2020	SARS-CoV-2	UVGI	Sterilization efficiency

Appendix 2. The effects of decontamination methods on N95 masks

Study	Method	Studies; # N95 model	Outcomes			Level of evidence
			SARS-CoV-2 Inactivation	Physical integrity	Functional integrity	
Fischer, 2020 (4)	Alcohol	2:4	Rapid inactivation	Loss after 2nd round	↓ filtration efficiency	Very low[1]
Smith, 2020 (5)			Undetectable	Detached nose guards, affected integrity (time-bound)	Impaired filtration (time-bound)	
Kumar, 2020 (6)	Autoclave	2:6	5.2-6.3 $\log_{10}$ reduction	NR	↓ quality fit after 10 cycles	Very low[1]
Czubryt, 2020 (11)			NR	Less elastic straps, softer mask, with odor	↓ fit test after 2 cycles	
Daeschler, 2020(7)	Moist heat	1:4	Undetectable	Comfortable masks	Passed after 10 cycles	Very low[1]
Ibáñez-Cervantes, 2020 (8)	HPV	3:6	Undetectable	NR	NR	Low[2]
Fischer, 2020 (4)			Extremely rapid		Intact	
Kumar, 2020 (6)			5.2-6.3 $\log_{10}$ reduction		Passed quality fit after 10 cycles	
Kumar, 2020 (6)	PAF	1:6	5.2-6.3 $\log_{10}$ reduction	NR	Passed quality fit after 10 cycles	Very low[1]
Simmons, 2020(9)	UVGI	3:6	>4.79 $\log_{10}$ reductions after 5 minutes	NR	NR	Low[2]
Fischer, 2020 (4)			Slow deactivation		Intact	
Ozog, 2020 (10)			Effective decontamination		NR	

[1] ≤ 2 studies, high risk of bias
[2] 3 studies, high risk of bias

Legends: HPV, Hydrogen plasma vapor; NR, not reported; PAF, Peracetic acid dry fogging system; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; UVGI, ultraviolet germicidal irradiation

Appendix 3. Characteristics of Ongoing Studies

Study	Virus/Bacteria	Intervention	Comparator	Outcome
Campos et al	SARS-CoV-2 Human coronavirus NL63 (HCoV-NL63) Chikungunya virus, Vaccine strain 181/25 (CHIKV-181)	Heat	NA	Filtration efficiency Pressure drop Sterilization efficiency
Derr et al	Phi6 bacteriophage HSV-1 CVB3 SARS-CoV-2	Aerosolized hydrogen peroxide	NA	Filtration efficiency test Sterilization efficiency Fit test
Geldert et al	SARS-CoV-2	UVGI	NA	Sterilization efficiency UV-C dose Dose-response for SARS-CoV-2 viral inactivation by UV-C Validating an optical model of a UV-C decontamination system Intra-N95 variation in UV-C dose and SARS-CoV-2 inactivation
Golovkine et al	SARS-CoV-2	UVGI	NA	Sterilization efficiency UV-C dose measurements
Lendvay et al	SARS-CoV-2 (a Betacoronavirus) Nurine hepatitis virus (MHV) (a Betacoronavirus) Porcine respiratory coronavirus (PRCV) (an Alphacoronavirus)	Methylene Blue and Light	Hydrogen peroxide plus ozone	Sterilization efficiency Respirator and mask integrity
Lensky et al	SARS-CoV-2	Heat using commercial laundry dryer	NA	Sterilization efficiency Mask integrity Filtration efficiency Manikin fit factor Strap integrity
Rathnasinghe et al	SARS-CoV-2	UVGI	NA	Sterilization efficiency Validation of the irradiation protocol Establishment of the germicidal UVC exposure protocol
Smith et al	SARS-CoV-2	HPV UVGI Ethanol	NA	Sterilization efficiency FIT test

Q11. What is the appropriate PPE to be used use during surgeries to reduce the risk of virus transmission?

As of 30 June 2021

RECOMMENDATION

We recommend the use of appropriate PPE to include mask (N95 or higher standard), fluid repellent sealed well-fitting long gown, double gloves, apron, full face shield or goggles or visor, scrub hat, and disposable shoe covers or dedicated closed footwear among surgeons engaged in aerosol generating procedures of suspected or confirmed COVID-19 patients. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues

Although shoe cover was not mentioned in the assessed studies and in the recommendations from other groups, the panel agreed to include this in the minimum PPE required in surgery as it is part of the standard precaution. A strong recommendation was given despite the very low quality of evidence since the enumerated PPE is the existing minimum standard protection recommended for healthcare workers directly caring for COVID-19 patients. The panel also emphasized strict adherence to protocols and the appropriate use of this minimum PPE to prevent COVID-19 infection.

KEY FINDINGS

Five observational studies (2 cohorts, 2 cross-sectional, and 1 case series) investigated the effectiveness of PPE use in reducing SARS-CoV-2 transmission among healthcare workers involved in surgical aerosol-generating procedures (AGP).

Very low evidence suggests the protective effect of an appropriate PPE on surgeons engaged in AGP procedures of suspected or confirmed COVID-19 patients. Consistent N95 mask use reduced the odds of SARS-CoV-2 infections significantly (OR 0.37 [95% CI 0.21, 0.67], 1 study, n= 195 participants) than inconsistent N95 use among healthcare workers involved AGP. Consistent gown use significantly reduced the odds of SARS-CoV-2 infections (OR 0.59 [95% CI 0.46, 0.77] I2= 0%, 2 studies, n= 941 participants) than inconsistent gown use amongst healthcare workers performing AGP. Consistent glove use reduced the odds of SARS-CoV-2 significantly (OR 0.42 [95% CI 0.43, 0.55] I^2=34%, 3 studies, n=978) than inconsistent glove use among healthcare workers performing AGP. Very low evidence suggests the protective effects of N95 mask, gown, gloves, face shield/goggles, apron, and scrub hat in reducing SARS-CoV-2 transmission among healthcare workers performing AGP procedures.

INTRODUCTION

COVID-19 transmission mainly occurs through respiratory droplets generated by coughing or sneezing or through contact with contaminated surfaces. During aerosol-generating procedures, the risk of spreading SARS-CoV-2 via aerosols is significantly increased. Endotracheal intubation, non-invasive ventilation, and administration of nebulized medications increased healthcare workers' odds for contracting SARS-CoV

1 or SARS-CoV-2 infections by 3 to 10 times [1]. Several surgical procedures[2] were classified as AGPs [2]. Since the COVID-19 pandemic affected patients requiring elective and emergency surgical procedures [3] and since PPE supply is limited, guidance on the appropriate PPE to use for surgical procedures is urgently needed.

REVIEW METHODS

A systematic search of electronic databases MEDLINE and Cochrane Central base was performed last March 21, 2021, using a combination of subject headings and keywords for SARS-CoV-2, PPE, and surgery. We included studies that determined the effectiveness of PPE by healthcare workers during surgery of suspected or confirmed COVID-19 patients. We excluded studies that used PPE for non-surgical interventions, articles not written in English, and other types of articles (e.g., abstracts, posters, review articles, book chapters, letters, guidelines, points of view).

RESULTS

Characteristics of included studies

Five observational studies (2 cohorts [4,5], 2 cross-sectional [6,7], and 1 case series [8]) investigated the effectiveness of PPE use in reducing SARS-CoV-2 transmission among healthcare workers involved in AGP procedures. Three systematic reviews [9–11] reported PPE guidelines during AGP and non-AGP procedures.

Overall quality

The overall body of evidence on the effectiveness of PPE for surgery was rated very low. Downgrading occurred due to serious risk of bias (as all included non-randomized studies had biases related to confounding, participant selection, intervention classification, recall bias, intervention deviation, and publication bias), inconsistency, and imprecision (total participants <980).

Appendix 2 reports the GRADE Evidence Profile on N95, gown, glove, and PPE use of healthcare workers during AGP.

Outcomes

Five observational studies provided direct evidence on N95, gown, glove, and PPE effectiveness in reducing SARS-CoV-2 transmission during AGP [4–8]. No studies reported on the use of PPE equipment on non-AGP.

PPE for AGPs

Consistent PPE use vs. inconsistent PPE use

There is very low evidence reported by Khalil et al. (2020) that PPE use did not significantly reduce the odds of SARS-CoV-2 (OR 0.54 [95% CI 0.12, 2.38]) among healthcare workers performing AGP (6). Most physicians had to reuse their PPEs which may have increased their likelihood of getting COVID-19 infection. A cross-sectional study from Wuhan, China, reported contrasting findings, with all 420

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[2] autopsy, surgery/postmortem procedures with high-speed devices, intubation and extubation procedures, bronchoscopy, sputum induction, manual ventilation, airway suctioning, cardiopulmonary resuscitation, tracheostomy and tracheostomy procedures, non-invasive ventilation, high-flow oxygen therapy, breaking closed ventilation systems (intentionally or unintentionally), nebulized or aerosol therapy, nasopharyngoscopy or laryngoscopy, high-frequency oscillatory ventilation, coughing mechanical ventilation, chest physiotherapy, and nasopharyngeal aspirate

healthcare workers who wore a complete PPE (i.e., N95, medical suit, isolation gown, apron, gloves, eye protection, and hair cover) while engaging in AGPs reporting no SARS-CoV-2 infections [7]. In this study, the healthcare workers were trained in donning and doffing PPE and performing AGPs. They suggested that wearing appropriate PPE and adherence to standard recommendations effectively protected the healthcare workers from SARS-CoV-2 transmission during AGPs [7].

Consistent N95 use vs. inconsistent N95 use

Very low quality evidence from 1 cross-sectional study suggested that consistent N95 mask use reduced the odds of SARS-CoV-2 infections significantly (OR 0.37 [95% CI 0.21, 0.67]) compared to inconsistent N95 use among 195 healthcare workers involved in AGP [6]. A case series study reported no COVID-19 infection among 25 healthcare workers who wore N95 masks during AGP [8].

Consistent gown use vs. inconsistent gown use

Based on 2 studies with low quality evidence, consistent gown use significantly reduced the odds of SARS-CoV-2 infections (OR 0.59 [95% CI 0.46, 0.77] I^2= 0%, 2 studies, n= 941 participants) compared to inconsistent gown use amongst healthcare workers performing AGP. Figure 1 shows the Forest plot on gown use by healthcare workers during AGP.

Consistent glove use vs. inconsistent glove use

There is low evidence from 3 observational studies that consistent glove use reduced the odds of SARS-CoV-2 significantly (OR 0.42 [95% CI 0.43, 0.55] I^2=34%, 3 studies, n=978) than inconsistent glove use among healthcare workers performing AGP. In the study of Liu et al. (2020), none of the 420 healthcare workers wearing complete PPE (i.e., N95, medical suit, isolation gown, apron, gloves, eye protection, and hair cover) was infected with SARS-CoV-2 when performing AGPs [7]. Figure 2 shows the Forest plot on glove use by healthcare workers during AGP.

Consistent face shields/goggles use vs. Inconsistent face shields/goggles use

Very low-quality evidence showed that consistent use of face shields/goggles did not significantly reduce the odds of SARS-CoV-2 transmission (OR 0.70 [95% CI 0.31, 1.59]) than inconsistent face shields/goggles use among healthcare workers performing AGP.

RECOMMENDATIONS FROM OTHER GROUPS

Different societies formulated separate PPE guidelines for surgical procedures comprising aerosol-generating or non-aerosol-generating procedures.

Surgical procedures with AGP

The following PPE is recommended for tracheostomy procedures for COVID-19 patients based on a systematic review of 17 international tracheostomy guidelines: full PPE, which includes N95 or N99 (USA) / FFP2 or FFP3 (Europe) mask, double gloves, goggles or eye protection, face shield, and an apron or gown [9]. Three guidelines (USA, UK, Singapore) recommended the use of a powered air-purifying respirator (PAPR) [9].

When working in high-risk units (e.g., ICU, high-dependency unit, accident, and emergency, resuscitation, wards with non-invasive ventilation or continuous positive airway pressure ventilation, operating rooms, endoscopy units) or in operating rooms where AGPs are being undertaken, then a respirator (N99 or FFP3 equivalent, which can be valved or unvalved) is recommended instead of a surgical mask along with a fluid repellent long gown (WHO), and full-face shield or visor (WHO, Public Health England) [10].

Surgical procedures without AGP

Agrawal et al. (2021) reviewed 41 surgery guidelines during COVID-19. The guidelines were written by national associations (27/41), regional societies (9/41), and international societies (5/41). Eight of the 41 guidelines were from LMICs. These guidelines are not evidence-based in terms of evidence level and methodology adopted for guideline development. The level of evidence was uniformly rated "low," as assessed by GRADE guidelines, as they were based on level 3 evidence and grade C recommendations [11]. The common recommendations include gloves, head cap, N95 respirator, gown, and face shield. All staff should wear enhanced EPPE in operating rooms and during AGP. Appendix C reports the PPE recommendations from the 41 guidelines.

RESEARCH GAPS

The PPE recommendation was invariably based on two primary considerations: the patient's COVID-19 status and the procedure's risk of infection (i.e., AGP or non-AGP). Most of the PPE recommendations were not based on preoperative test results, and about 25% of the included studies did not specify the PPE need about AGP. Also, limited data is available for resource-constrained settings. The economic repercussions of PPE wastage and the cost-effectiveness of various PPE or PPE combinations were also not studied. PPE recommendation was guided by fear over science. This was obvious with EPPE recommendation by all staff in the operation room by most studies [11].

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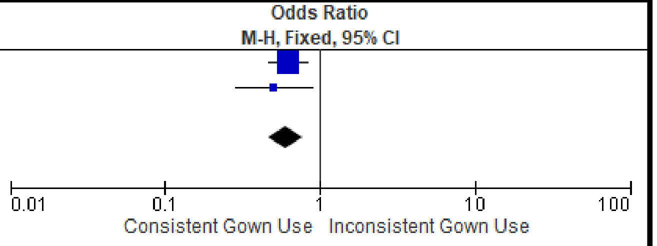
Appendix 1. Characteristics of Included Studies and Summary of findings on use of N95, gown, glove and PPE during AGP.

Author, Year	Study design	Virus	Population	Total (intervention: control)	Intervention: Consistent use	Comparator: Inconsistent use	OR (95% CI)	Risk of Bias
Chatterjee et al. (2020)	Prospect cohort	SARS-CoV-2	Doctors, nurses, housekeeping staff guards, laboratory technicians, and others	378:373	Gown	Gown	0.62 (0.46, 0.83)	Serious
					Glove	Glove	0.38 (0.26, 0.55)	
					Glove	Glove	not estimable	
Heinzerling et al. (2020)	Prospect cohort	SARS-CoV-2	Nurses, respiratory therapists, nursing assistants, physicians, and others	3:34	Glove	Glove	4.40 (0.21, 91.92)	Serious
Liu et al. (2020)	Cross-sectional	SARS-CoV-2	Doctors, nurses	420	PPE use	None		Serious
Periyasamy et al. (2020)	Retro case series	SARS-CoV-2	Healthcare workers	25	N95	N95		Serious
Khalil et al. (2020)	Cross-sectional comparative study	SARS-CoV-2	Physicians	98:92	Faceshield/ goggles	Faceshield/goggles	0.70 (0.31, 1.59)	Serious
					N95	N96	0.37 (0.16, 0.87)	
					Glove	Glove	0.52 (0.28, 0.94)	
					Gown	Gown	0.50 (0.28, 0.90)	
					Water-proof apron	Water-proof apron	0.40 (0.24,1.03)	
					PPE	PPE	0.54 (0.12, 2.38)	

A. Forest plot on effects of gown use on SARS-CoV-2 transmission during AGP

Study or Subgroup	Consistent Gown Use Events	Consistent Gown Use Total	Inconsistent Gown Use Events	Inconsistent Gown Use Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chatterjee (2020)	152	378	194	373	78.3%	0.62 [0.46, 0.83]
Khalil (2020)	43	98	56	92	21.7%	0.50 [0.28, 0.90]
Total (95% CI)		**476**		**465**	**100.0%**	**0.59 [0.46, 0.77]**
Total events	195		250			

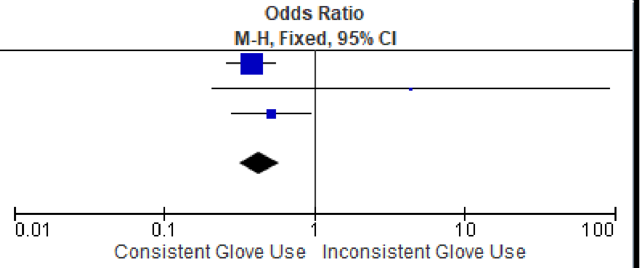
Heterogeneity: Chi² = 0.41, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 3.94 (P < 0.0001)



B. Forest plot on effects of glove use on SARS-CoV-2 transmission during AGP

Study or Subgroup	Consistent Glove Use Events	Consistent Glove Use Total	Inconsistent Glove Use Events	Inconsistent Glove Use Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chatterjee (2020)	267	378	322	373	75.5%	0.38 [0.26, 0.55]
Heinzerling (2020)	3	3	21	34	0.4%	4.40 [0.21, 91.92]
Khalil (2020)	53	98	64	92	24.1%	0.52 [0.28, 0.94]
Total (95% CI)		**479**		**499**	**100.0%**	**0.43 [0.32, 0.59]**
Total events	323		407			

Heterogeneity: Chi² = 3.01, df = 2 (P = 0.22); I² = 34%
Test for overall effect: Z = 5.35 (P < 0.00001)



Appendix 2. GRADE Evidence Profile on use of N95, gown, glove and PPE during AGP.

CERTAINTY ASSESSMENT							NO. OF PATIENTS		EFFECT		CERTAINTY	IMPORTANCE
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Consistent PPE use	Inconsistent PPE use	Relative (95% CI)	Absolute (95% CI)		
PPE use												
2	Observational studies	Serious [a]	Not serious	Not serious	Serious [b]	Publication bias strongly suspected All plausible residual confounding would suggest spurious effect, while no effect was observed [c]	58/518 (11.2%)	64/92 (69.6%)	**OR 0.54** (0.12 to 2.38)	**143 fewer per 1,000** (from 480 fewer to 149 more)	⊕◯◯◯ VERY LOW	Not graded
Consistent N95 use vs. inconsistent N95 use												
2	Observational studies	Serious [d]	Serious [e]	Not serious	Serious [f]	Publication bias strongly suspected Strong association All plausible residual confounding would reduce the demonstrated effect [g]	36/101 (35.6%)	56/92 (60.9%)	**OR 0.37** (0.21 to 0.67)	**243 fewer per 1,000** (from 362 fewer to 98 fewer)	⊕◯◯◯ VERY LOW	Not graded
Consistent gown use vs. inconsistent gown use												
2	Observational studies	Serious [h]	Not serious	Not serious	Not serious	Publication bias strongly suspected Strong association All plausible residual confounding would reduce the demonstrated effect [i]	195/476 (41.0%)	250/465 (53.8%)	**OR 0.59** (0.46 to 0.77)	**131 fewer per 1,000** (from 189 fewer to 65 fewer)	⊕⊕◯◯ LOW	Not graded
Consistent glove use vs. inconsistent glove use												
3	Observational studies	Serious [j]	Not serious	Not serious	Not serious	Publication bias strongly suspected Strong association All plausible residual confounding would reduce the demonstrated effect [k]	323/479 (67.4%)	407/499 (81.6%)	**OR 0.43** (0.32 to 0.59)	**160 fewer per 1,000** (from 230 fewer to 93 fewer)	⊕⊕◯◯ LOW	Not graded
Consistent face shields/goggles use vs. Inconsistent face shields/goggles use												
1	observational studies	Serious [l]	Not serious	Not serious	Serious [m]	Publication bias strongly suspected All plausible residual confounding would suggest spurious effect, while no effect was observed [n]	39/98 (39.8%)	52/92 (56.5%)	**OR 0.70** (0.31 to 1.59)	**89 fewer per 1,000** (from 278 fewer to 109 more)	⊕◯◯◯ VERY LOW	Not graded

CI: Confidence interval; **OR:** Odds ratio

Explanations

[a] Confounding, classification of interventions, selection of participants, recall bias
[b] Contrasting results
[c] Only two studies with a study with non-estimable result
[d] Selection of participants, classification of intervention, confounding, recall bias, unclear deviation from intervention and missing data
[e] Not estimable results in one study
[f] less than 300 participants
[g] Only two studies with a study with non-estimable result
[h] Confounding, classification of intervention, selection of participants, recall bias, unclear deviations from intended interventions
[i] Only two studies were included.
[j] confounding, selection of participants, classification of intervention, unclear deviations from intended interventions
[k] Only three studies were included.
[l] confounding, selection of participants, classification of intervention, unclear deviations from intended interventions, recall bias
[m] Sample size is only 190
[n] Only one study was included.

Appendix 3. PPE recommendations during the COVID-19 (n=41) [19]

PPE	Recommended		Not recommended		Not mentioned	
	n	%	n	%	n	%
Gloves	37	90.24	0	0	4	9.75
Head cap	37	90.24	0	0	4	9.75
N95 respirator	34	82.92	5	12.19	2	4.87
Front doffing gown	37	90.24	0	0	4	9.75
Face shield	36	87.8	1	2.43	4	9.75
EPPE worn by all staff in OR	28	68.29	5	12.19	8	19.51
Use of EPPE in a negative patient in OR	24	58.53	9	21.95	8	19.51
Use of EPPE in a positive patient in OR	38	92.68	0	0	3	7.32
EPPE in HAGP	30	73.17	1	2.43	10	24.39
Donning PPE	9	21.95	26	63.41	6	14.63
Doffing PPE	9	21.95	26	63.41	6	14.63
PPE disposal	3	7.317	0	0	38	92.68

Legend: EPPE, enhanced personal protective equipment; OR, operating room; HAGP, high-risk aerosol-generating procedure; PPE, personal protective equipment

Appendix 4. Electronic databases and Search Strategy

Electronic databases: Pubmed, MEDLINE, Cochrane Database

Search strategy:

1. ((("COVID-19" [Supplementary Concept] OR "COVID-19 diagnostic testing" [Supplementary Concept] OR "COVID-19 drug treatment" [Supplementary Concept] OR "COVID-19 serotherapy" [Supplementary Concept] OR "COVID-19 vaccine" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR "2019-nCoV" OR "2019nCoV" OR "cov 2" OR "Covid-19" OR "sars coronavirus 2" OR "sars cov 2" OR "SARS-CoV-2" OR "severe acute respiratory syndrome coronavirus 2" OR "coronavirus 2" OR "COVID 19" OR "COVID-19" OR "2019 ncov" OR "2019nCoV" OR "corona virus disease 2019" OR "cov2" OR "COVID-19" OR "COVID19" OR "nCov 2019" OR "nCoV" OR "new corona virus" OR "new coronaviruses" OR "novel corona virus" OR "novel coronaviruses" OR "SARS Coronavirus 2" OR "SARS2" OR "SARS-COV-2" OR "Severe Acute Respiratory Syndrome Coronavirus 2") OR ((19[tiab] OR 2019[tiab] OR "2019-nCoV" OR "Beijing" OR "China" OR "Covid-19" OR epidem*[tiab] OR epidemic* OR epidemy OR new[tiab] OR "novel"[tiab] OR "outbreak" OR pandem* OR "SARS-CoV-2" OR "Shanghai" OR "Wuhan") AND ("Coronavirus Infections"[Mesh] OR "coronavirus"[MeSH Terms] OR coronavirus*[all] OR corona-virus*[all] OR cov[tiab] OR pneumonia-virus*[tiab]))) AND 2019/12/1:3000/12/31[PDAT])
2. Personal protective equipment OR PPE
3. Surgeons OR surgery OR operating room or AGP or aerosol generat* procedure*

Q12. What is the appropriate PPE for healthcare workers in the outpatient setting to reduce the risk of virus transmission?

As of 30 June 2021

RECOMMENDATION

We recommend the use of at least surgical face mask and face shield for protection against COVID-19 infection among healthcare workers in the outpatient setting not performing aerosol generating procedures. Additional PPEs such as medical gowns and gloves should be worn as part of standard precautions during the performance of other procedures. *(Very low certainty of evidence; Strong recommendation)*

Consensus Issues

The superiority of N95 over medical face masks cannot be established based on the imprecise effects noted from the evidence. The high likelihood of dermatosis or skin infections while using N95 respirators was also noted. Considering these issues, the panel deemed that medical face masks would be more cost-effective as long as only non-aerosol generating procedures are done in the outpatient setting. The use of additional PPEs may be required depending on the procedure that will be performed, consistent with the recommendation of the US Centers for Disease Control (CDC). Face shields are preferred over goggles as it offers a greater level of protection from droplets.

Despite the very low quality of evidence, a strong recommendation was formulated as the listed PPEs are already considered the minimum standard protection needed by the healthcare workers. Strict adherence to appropriate use of these PPEs is emphasized.

KEY FINDINGS

There are no available direct evidence comparing the effectiveness of N95 versus surgical mask in COVID-19 infection among healthcare workers in the outpatient setting. Meta-analysis comparing the two among healthcare workers in general showed no significant difference in their effectiveness in preventing clinical and laboratory viral infection. One RCT investigated the difference of N95 and surgical mask in protecting healthcare workers in different outpatient setting from viral respiratory infection and noted no significant difference between the two. Indirect evidence also shows more adverse skin reactions for those wearing N95 respirators as compared to surgical masks. The use of face shield on the other hand in addition to face mask provided added protection from acquiring COVID-19 among community healthcare workers in India based on a before and after study. The use of gowns and gloves are standards of care in medicine whenever handling patient's body fluids and this recommendation is still applicable in the current setting.

INTRODUCTION

In communities with moderate to high risk of transmission, a large part of COVID-19 cases would be coming from the people who are asymptomatic or with mild symptoms. As these individuals typically present in outpatient settings, it is important that healthcare workers who interact with them use personal protective equipment (PPE) that confer adequate safety against COVID-19 infections. The effectiveness of various

PPEs in preventing COVID-19 infections among healthcare workers in outpatient settings needs to be determined as supply of PPE is also limited.

Different guidelines have advocated the use of PPE, most especially masks, to prevent droplet transmission [1]. In terms of different masks, N95 respirators and regular surgical face masks were not found to differ significantly in their protection against other respiratory infections [2,3]. Face shields have been proposed as an alternative to face masks in preventing aerosol transmission of respiratory infections [4]. Although face shields offer some advantages over masks in terms of reusability, breathability, and ease of communication, they have been shown to be less effective in blocking smaller aerosols that are able to flow around the edges of the shield [5].

REVIEW METHODS

We searched for articles that investigated on the transmissibility and incidence of COVID-19 infections among healthcare workers in the outpatient setting who used various PPE (e.g., mask, face shield, gown, gloves). We performed a systematic literature search up to 08 April 2021 using online databases such as MEDLINE, Cochrane, and Google Scholar, using combination of free text and subject headings for “COVID-19 or SARS-CoV2”, “healthcare workers,” “personal protective equipment,” “face mask,” “face shield”, “eye protection” and “transmission”. Additional searches in MedRxiv, BioRxiv, clinicaltrials.gov, and WHO ICTRP were also done to look for articles awaiting publication and ongoing clinical trials, respectively. References from systematic reviews and meta-analyses were also manually searched for additional articles. Letters, narrative reviews, and case reports, single-arm studies were excluded. Investigations involving healthcare workers working inside the hospital wards or intensive care units or exposed to aerosol generating procedures were also excluded.

RESULTS

Characteristics of included studies

Two studies were included in this review. Evidence for face masks came from one indirect randomized controlled trial [6], while evidence for face shields came from one before and after study [9]. No direct evidence was found for gloves, gowns, N95 or surgical masks. Appendix 1 shows the summary of included studies.

Face masks

One randomized controlled trial (RCT) [6] deemed to have low risk of bias investigated N95 respirators versus surgical mask in preventing the influenza virus among 4051 healthcare personnel (5180 observations) in outpatient departments of six different medical centers via a clustered randomization method. The study spanned a period of 48 weeks.

Face shields

One before and after study [9] evaluated the effect of wearing face shields among community healthcare workers (CHCWs) in India from 03 May to 30 June 2020. These CHCWs were tasked to interview and counsel family contacts of COVID-19 confirmed patients in a locality with COVID-19 community transmission. The CHCWs were housed in a hostel and were not allowed to go out in public thus limiting their exposure. Before adding face shields, the standard PPE worn by the participants were 3 layered surgical masks, gloves, and a shoe cover. They did frequent alcohol hand rub and maintained a minimum of 6 ft all throughout their interviews with the family members. Weekly RT-PCR testing was done.

Outcomes

Prevention of COVID-19

N95 and surgical masks offered similar levels of protection against viral influenza. No significant difference for positive viral influenza culture (adjusted odds ratio 1.18, 95% CI 0.95-1.45) between the N95 group and surgical mask group. Likewise, there was also no significant difference in acute respiratory illness events (mean difference (MD) -21.9 events, 95% CI -48.2 to 4.4, p=0.10). Compliance in wearing masks were comparable between control and intervention groups. This RCT was assigned a GRADE quality of very low due to issues on indirectness of evidence and imprecision.

The addition of face shields was associated with significantly lower odds of getting COVID-19 (OR 0.05, 95% CI 0.003 to 0.86, *P* = 0.04). Before the addition of face shields, 62 CHCWs interviewed a total of 31,164 persons, of whom 222 (0.71%) eventually tested positive for COVID-19. After 2 weeks, two CHCWs developed symptoms prompting testing and addition of face shields. From the 62 CHCWs, 12 eventually tested positive (19%) with 8 eventually developed symptoms while 4 remained asymptomatic. None of the remaining 50 CHCWs who used face shields while visiting 118,428 people (2682 or 2.3% tested positive for COVID-19) contracted COVID-1. This study had the advantage of isolating the CHCWs, limiting their exposure to only the families they interviewed and thus making the result more likely due to the intervention. The quality of evidence for face shields for this outcome is low. The quality of evidence was downgraded due to risk of bias in terms of study design and small sample size. Risk of bias was deemed significant as the study design utilized was a before-and-after study rather than a randomized trial or a large cohort study. Furthermore, there was some degree of indirectness in the activities and patient encounter as described in the study and in the clinical question. The activities of health care workers in the study did mainly interviews rather than assessing and physically examining COVID-19 patients.

Appendix 2a shows the GRADE Evidence Table for N95 respirator versus medical mask for outpatient healthcare workers in places with sustained community transmission.
Appendix 2b shows the GRADE Evidence Table for no face shield versus use of face shield for outpatient healthcare workers in places with sustained community transmission.

Adverse reactions

In a cross-sectional survey, healthcare workers were reported to have increased events of skin reactions due to wearing of either N95 or surgical masks as part of their PPE during the COVID-19 pandemic [7]. Of the 390 participants, 96% reported experiencing some form of skin irritation while 61.7% of those with previous skin conditions experienced worsening. Similar findings regarding adverse reactions related to PPE use were reported in one observational study done during the SARS-COV-1 outbreak in Singapore [8]. Among the 307 participants who wore N95 masks, 35.5% experienced skin problems while no one wearing face mask reported any skin problems. The most common reported skin problems were acne, itch and rash.

RECOMMENDATIONS FROM OTHER GROUPS

The World Health Organization recommends healthcare workers to do targeted continuous masking whenever they are in their respective clinical areas. In non-aerosol-generating procedures, surgical masks (together with other PPE) are recommended over N95 respirators [11]. Face shields were recommended to be used only with a surgical mask or N95 respirator [11].

The CDC also recommends against the use of face shields alone for source control and should be used as part of other PPE, which include N95 respirators when handling aerosol generating procedures, surgical mask if respirator is not available and no AGPs, gowns, and gloves. These should be recommended among healthcare workers whenever they are handling confirmed and suspected cases in communities with at least moderate transmission risk [12]. Gloves and gowns are included as standard precaution in caring for all patients in all settings depending on the activities that will be performed, especially when there is a possible exposure to blood or body fluids of the patient [10].

RESEARCH GAPS

Only 1 ongoing clinical trial was found related to this topic. This is a cluster-randomized trial (NCT04823351) in Switzerland that aims to compare the protective effects of surgical mask versus FFP2 masks among health care workers in low-risk settings (i.e., nursing homes).

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Appendix 1. Summary of included studies

Study Author	Study Design	Population	Intervention n = 2512	Comparator n = 2668	Outcome
Radonovich 2019	Randomized pragmatic effectiveness trial	Healthcare workers working in outpatient settings of 7 US medical centers from Sept 2011 to May 2015	Wearing of N95 respirators	Wearing of medical mask	Laboratory confirmed influenza infection Acute respiratory illness events Laboratory-detected respiratory infections Laboratory-confirmed respiratory illness
Bhaskar 2020	Before and After Study	Community health workers in India assigned to counsel asymptomatic family contacts of laboratory confirmed COVID-19 patients	Face shield plus baseline PPE (3 layered surgical mask, gloves, shoe cover)	Baseline PPE (3 layered surgical mask, gloves, shoe cover)	RT-PCR test Development of symptoms

Appendix 2A. GRADE Evidence Table for N95 respirator versus medical mask for outpatient healthcare workers in places with sustained community transmission

Author(s): Christopher G. Manalo, MD & Frangelo Conrad P. Tampus, MD
Question: N95 mask compared to medical mask for outpatient healthcare workers in places with sustained community transmission
Setting: Outpatient Setting
Bibliography: Radonovich LJ, Simberkoff MS, Bessesen MT, Brown AC, Cummings DAT, Gaydos CA, et al. N95 respirators vs medical masks for preventing influenza among health care personnel: A randomized clinical trial. JAMA - J Am Med Assoc. 2019;322(9):824–33.

CERTAINTY ASSESSMENT							NO. OF PATIENTS		EFFECT		CERTAINTY	IMPORTANCE
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	N95 mask	Surgical Mask	Relative (95% CI)	Absolute (95% CI)		
Laboratory-confirmed Influenza												
1	Randomised trials	Not serious	Not serious	Serious [a]	Serious [b]	None	207/2512 (8.2%)	193/2668 (7.2%)	**OR 1.18** (0.95 to 1.45)	**12 more per 1,000** (from 3 fewer to 29 more)	⊕◯◯◯ VERY LOW	CRITICAL
Acute Respiratory Illness												
1	Randomised trials	Not serious	Not serious	Serious [a]	Serious [b]	None	1556/2512 (61.9%)	1711/2668 (64.1%)	**OR 0.99** (0.92 to 1.06)	**22 fewer per 1,000** (from 48 fewer to 4 more)	⊕◯◯◯ VERY LOW	
Laboratory-Detected Respiratory Infections												
1	Randomised trials	Not serious	Not serious	Serious [a]	Serious [b]	None	679/2512 (27.0%)	745/2668 (27.9%)	**OR 0.99** (0.89 to 1.09)	**9 fewer per 1,000** (from 33 fewer to 15 more)	⊕◯◯◯ VERY LOW	
Laboratory-confirmed Respiratory Illness												
1	Randomised trials	Not serious	Not serious	Serious [a]	Serious [b]	None	371/2512 (14.8%)	417/2668 (15.6%)	**OR 0.97** (0.85 to 1.09)	**9 fewer per 1,000** (from 28 fewer to 11 more)	⊕◯◯◯ VERY LOW	
Influenza-like Illness												
1	Randomised trials	Not serious	Not serious	Serious [a]	Serious [b]	None	128/2512 (5.1%)	166/2668 (6.2%)	**OR 0.86** (0.68 to 1.10)	**11 fewer per 1,000** (from 24 fewer to 1 more)	⊕◯◯◯ VERY LOW	

CI: Confidence interval; **OR:** Odds ratio

Explanations
[a] The study included coronavirus subtypes HKU1, NL63, OC43, and 229E but not SARS-COV-2
[b] Confidence interval of treatment effect and/or rate ratios crosses the line of no effect

Appendix 2B. GRADE Evidence Table for No face shield versus use of face shield for outpatient healthcare workers in places with sustained community transmission

Author(s): Christopher G. Manalo, MD & Frangelo Conrad P. Tampus, MD
Question: No face shield compared to face shield for outpatient healthcare workers in places with sustained community transmission
Setting: Outpatient Setting
Bibliography: Bhaskar ME, Arun S. SARS-CoV-2 Infection among Community Health Workers in India before and after Use of Face Shields. Vol. 324, JAMA - Journal of the American Medical Association. American Medical Association; 2020. p. 1348–9.

CERTAINTY ASSESSMENT							NO. OF PATIENTS		EFFECT		CERTAINTY	IMPORTANCE
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	N95 mask	Surgical Mask	Relative (95% CI)	Absolute (95% CI)		
RT-PCR confirmed COVID-19 infection												
1	Observational studies	Very serious [a]	Not serious	Not serious	Not serious	None	12/62 (19.4%)	0/50 (0.0%)	**OR 0.040** (0.002 to 0.850)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations
[a] Issues on study design and small sample size

Appendix 3. Registered study protocol

	Clinical Trial ID / Title	Status	Start and estimated primary completion date	Study design	Country	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	Clinical Efficiency of Surgical Masks and Filtering face-piece 2 masks NCT04823351	Not yet recruiting	Study start: April 8, 2021 Estimated primary completion: July 8, 2021	Allocation: Randomized Intervention Model: Crossover Assignment Design:cluster-randomized, parallel, controlled, non-inferiority study Masking: None (Open Label) Primary Purpose: Prevention	Switzerland	Health care workers in nursing homes Subgrouped into vaccinated and unvaccinated	FFP2 mask Surgical Mask	Surgical Mask FFP2 mask	SARS-CoV-2 infection

Q13. What is the appropriate PPE for health care workers in the wards, ICU and emergency room to reduce the risk of virus transmission?

As of 30 June 2021

RECOMMENDATION

We recommend the use of the following PPE: disposable hat, medical protective mask (N95 or higher standard), goggles or face shield (anti-fog), medical protective clothing, disposable gloves and disposable shoe covers or dedicated closed footwear as an effective intervention in the prevention of COVID-19 among health care workers in areas with possible direct patient care of COVID-19 positive patients and aerosol generating procedures. *(Moderate certainty of evidence; Strong recommendation)*

Consensus Issues

Direct patient care[1] is defined as hands on, face-to-face contact with patients for the purpose of diagnosis, treatment and monitoring. This recommendation was made by the panel as it prioritized giving the best available protection to the healthcare workers. Whenever possible, hospital administrators should invest in these PPEs. Strict adherence to the appropriate use of PPEs must be observed even if healthcare workers have already been vaccinated against COVID-19.

[1]National Center for Emerging, Zoonotic and Infectious Diseases- Division of Healthcare Quality Promotion. (2020). *The National Healthcare Safety Network (NHSN) Manual- Healthcare Personnel Safety Component Protocol: Healthcare Personnel Exposure Module.* Atlanta, GA, USA: CDC

KEY FINDINGS

Four studies and a case report were found on the use of PPE among health care workers to prevent COVID infection. Moderate certainty evidence from three of the studies showed that the use of Level 2 PPE (disposable hat, medical protective mask (N95 or higher standard), goggles (anti-fog) or protective mask (anti-fog), medical gown clothing or white coats covered by medical protective clothing, disposable gloves and disposable shoe covers), N95 respirators and face shields protected health care workers in hospital settings from COVID-19 infections. On the other hand, very low certainty evidence showed no significant protective effect from the use of face/surgical masks, gowns, and/or disposable gloves if used individually.

INTRODUCTION

The COVID-19 pandemic has placed the health care workers (HCW) at high risk of infection. The use of personal protective equipment (PPE) has been shown to be effective in preventing infection against related betacoronaviruses that have caused epidemics, such as severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS) [1,2]. PPE use depends on the risk of exposure, availability, and environmental control. The evidence on PPE recommendations, including the use of face mask, face shield, gowns and gloves, to prevent COVID 19 infection among health care workers are limited.

REVIEW METHODS

We searched MEDLINE, Cochrane CENTRAL, ChinaXiv, MedRXIV, BioRXIV and ongoing and completed trials on USA: https://clinicaltrials.gov/; China: http://www.chictr.org.cn/searchprojen.aspx and WHO: https://www.who.int/clinical-trials-registry-platform. We also searched for published/ongoing studies on the COVID-19 Open Living Evidence Synthesis: https://covid-nma.com/ and the Living Evidence on COVID-19: https://zika.ispm.unibe.ch/assets/data/pub/search_beta/. The initial search date was 31 March 2021 (updated 30 April 2021).

The following keywords were used: 'covid', 'COVID-19', 'coronavirus', 'SARS-CoV-2', 'viral', 'infection', 'respiratory' 'respirator', 'surgical mask', 'N95 mask', 'PPE', 'personal protective equipment', 'face shield', 'googles', 'eye protector', 'gown', 'gloves', 'health care worker', 'COVID-19', 'coronavirus', 'SARS-CoV-2'. Subject headings and free text were combined[3]. We included experimental or observational studies, meta-analysis/systematic reviews, completed trials and/or preprints that investigated the efficacy of PPE in preventing COVID 19 infection among health care workers in non-surgical areas (wards, ICU, emergency room). Two reviewers appraised the methodological quality of included studies using the Newcastle Ottawa Scale. We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the certainty of the evidence related to the outcomes.

RESULTS

Characteristics of included studies

Four observational studies (cohort, case control and cross sectional) and a case report were included. Two of these studies were also found in two systematic reviews [1,2] that reported on the association of COVID 19 infection with the use of PPE. Only data relevant to health workers in these studies were considered. Population of the studies were on health care workers mostly employed in health care facilities that attend to patients with COVID 19. Information on the various PPEs that were used by the health care workers while working in the health care facilities was gathered and their association with COVID 19 infection were assessed. Refer to Appendix 1 for detailed characteristics of these included studies.

Methodological quality

Four studies, two cohort [3,4], a case control [5] and a cross sectional [6], were assessed as having low quality and a case report [7] as very low quality The studies were direct evidence and with no inconsistencies, however with high risk of bias. For the three observational studies, two used a structured questionnaire [3] [6]and one reviewed infectious records [5] to gather data and thus subject to recall and information bias. Another study [4] was a surveillance data of COVID positive HCW before and after the implementation of the use of face shield. For the protective effect of the use of face shield in two studies [4] [6], confounders in the assessment could be its use together with the standard PPE, compliance of HCW on properly wearing it and in

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[3] (((((((((COVID 19[MeSH Terms]) AND health care workers (personal protective equipment[MeSH Terms])) OR (face mask[MeSH Terms])) OR (surgical mask[MeSH Terms])) OR (respirators[MeSH Terms])) OR (goggles[MeSH Terms])) OR (face shield[MeSH Terms])) OR (eye protector[MeSH Terms])) OR (gowns, surgical[MeSH Terms])) OR (gloves, surgical[MeSH Terms]))) AND (health care worker[MeSH Terms])

other preventive measures and the type of work done whether or not it is an aerosol generating procedure.

Level 2 Protection

Moderate quality evidence from a retrospective cohort study by Wang et al. [3] showed the protective effect of Level 2 protection among 5442 medical staff of Neurosurgery Departments of 107 hospitals in Hubei China (OR 0.03 [95% CI 0, 0.19]). Of the 120 who were infected, 54 were neurosurgeons and 66 were nurses involved with COVID 19 patients with patient contact time between 5 to 90 minutes (average time: 35 minutes) Level 2 in their center involved the use of the following: disposable hat, medical protective mask (N95 or higher standard), goggles (anti-fog) or protective mask (anti-fog), medical gown clothing or white coats covered by medical protective clothing, disposable gloves and disposable shoe covers.

Additional data from a cross sectional study in Bangladesh involving 190 HCW in 19 health facilities [6], a possible protective effect in using PPE was reported (OR 0.15 [95% CI 0.02, 1.21]). The evidence was downgraded due to imprecision. However, the type of PPE used in this study was not specified; thus, this was not included in the analysis.

N95 respirators

Moderate certainty evidence involving 493 participants demonstrated a protective effect with the use of N95 respirators (OR: 0.035 [95% CI 0.002 to 0.603]). This was a case control study in Wuhan China [5] but was assessed as to have a large effect. Another study [6] from Bangladesh involving 190 health workers also demonstrated the N95 protective effect during aerosol generating procedure (OR 0.37 [95% CI 0.16-0.87]).

Face mask

In the cross-sectional study in Bangladesh [6], very low certainty evidence suggested that the use of medical/surgical masks while attending to COVID 19 patients was not associated with infection among 190 health workers (OR 1.40 [95% CI 0.30, 6.42]) [5]. The evidence was downgraded as very low due to imprecision. The study used a structured questionnaire which was answered by the participants and therefore subject to recall bias. A case report [6], however, showed that among 37 health care workers who were exposed to a COVID-19 patient, 3/34 (8.8%) who did not wear a mask were infected while none of the three who were wearing a mask were infected.

Face shield

Moderate certainty evidence [4] before and after face shield use was implemented demonstrated the protective effect of face shield with standard PPE among 6527 health care personnel (HCP) who were tested for COVID. (RR 0.297 [95% CI 0.228, 0.385]). The type of PPE used was not discussed. The data was from a surveillance study in a quarternary health care system in Texas. Biweekly testing for HCP in high-risk units (emergency department, transplant units and COVID-19 units) and weekly testing for HCP in cluster areas (>= 3 cases of HCP with COVID-19 diagnosis or any case of hospital-acquired infection) were done. Testing was voluntary for HCP and HCP in other areas if they desire or if with exposure history. HCP with previous positive COVID-19 diagnosis were excluded. This was a cohort study and was initially graded as low but was upgraded due to the large effect.

A cross sectional study [6] showed that using face shield/googles when attending to COVID-19 patients was protective for health care workers (OR 0.44 [95% CI 0.23, 0.843]). The evidence was downgraded to very low as the study used a structured questionnaire which may have increased risk of recall bias. In both studies cited, confounders in the assessment of the protective effect of face shield may be present as cited in the methodological quality.

Disposable gowns/gloves

No significant difference in the incidence of COVID infection was observed among 190 health care workers who used disposable gowns (OR 1.08 [95% CI 0.53, 2.20]) and disposable gloves (OR 1.01 [95% CI 0.38, 2.68]) while caring for infected patients [6]. For aerosol-generating procedures, no benefit was also noted for gowns (OR 0.77 [95% 0.31, 1.88)] and gloves (OR 0.62 [95% CI 0.13, 2.90]). This effect was based on very low-quality evidence from one study [5]. The evidence was downgraded due to imprecision and risk of bias with use of a structured questionnaire subject to recall bias.

RECOMMENDATIONS FROM OTHER GROUPS

The table below provides a summary of PPE recommendations from four different health agencies. [8] PPE recommendations across countries differ in terms of setting, type of personnel, and activity.

Table 1. Comparisons of personal protective equipment recommendations from the World Health Organization, the US Centers for Disease Prevention and Control (CDC), the European CDC, and Korea CDC [9, 10, 37, 47]

Settings	KCDC (March 2020)	WHO (April 2020)	CDC (May 2020)	ECDC (May 2020)
Triage: patient examination with direct contact	· KF94 mask or equivalent respirator · Eye protection[a] · Gown[b] or coveralls with foot covers · Gloves	· Medical mask · Eye protection[a] · Gown[b] · Gloves	· N95 respirator (or facemask if a respirator is not available) · Eye protection[a] · Gloves	· Surgical mask or, if available, FFP2 respirator · Eye protection[a] · Gown[b] or apron · Gloves
Usual inpatient care	· KF94 mask or equivalent respirator · Eye protection[a] · Gown[b] or coveralls with foot covers · Gloves	· Medical mask · Eye protection[a] · Gown[b] · Gloves	· N95 respirator (or higher-level respirator) or facemask (if a respirator is not available) · Eye protection[a] · Gown · Gloves	· Surgical mask or, if available, FFP2 respirator · Eye protection[a] · Gown[b] or apron · Gloves
Aerosol-generating procedures[c]	· KF94 mask, equivalent respirator, or PAPR · Eye protection[a] · Gown[b] or coveralls with foot covers · Gloves	· N95, FFP2, or FFP3 respirator · Eye protection · Gown[b] · Gloves · Apron (if gowns are not fluid-resistant)	· N95 or higher-level respirator · Eye protection[a] · Gown[b] · Gloves	· FFP3 respirator · Eye protection[a] · Gown[b] · Gloves
Collecting specimens (not involving aerosol-generating procedures)	· KF94 mask, equivalent respirator, or PAPR · Eye protection[a] · Gown[b] or coveralls with foot covers · Gloves	· Medical mask · Eye protection[a] · Gown[b] · Gloves	· N95 or higher-level respirator (or facemask if a respirator is not available) · Eye protection[a] · Gown[b] · Gloves	Enclosed spaces: · Surgical mask or, if available. FFP respirator · Eye protection[a] · Gown[b], gloves Drive-through or outdoor facilities: · Surgical mask

WHO, World Health Organization; CDC, Centers for Disease Prevention and Control; ECDC, European Centers for Disease Prevention and Control; KCDC, Korea Centers for Disease Prevention and Control; PAPR, powered air-purifying respirator; FFP, filtering facepiece.
[a]Eye protection includes goggles or a face shield.
[b]Gown refers to a long-sleeved, fluid-resistant gown.
[c]Aerosol-generating procedures include endotracheal intubation, non-invasive ventilation, tracheostomy, cardiopulmonary resuscitation, manual ventilation, bronchoscopy, open suctioning, sputum induction, nebulizer therapy, etc.

World Health Organization (19 March 2020) [9] stated that the types of PPE to be used when caring for COVID-19 patients will vary according to the setting and type of personnel and activity. Healthcare workers involved in the direct care of patients should use the following PPE: gowns, gloves, medical masks, and eye protection (goggles or face shield). For aerosol-generating procedures (e.g., tracheal intubation, non-invasive ventilation, tracheostomy, cardiopulmonary resuscitation, manual ventilation before intubation, bronchoscopy) healthcare workers should use respirators, eye protection, gloves, and gowns; aprons should also be used if gowns are not fluid resistant.

The European Center for Disease Control (9 Feb 2021) [10] recommends healthcare workers in contact with a possible or confirmed COVID-19 case to wear a well-fitted respirator, eye protection (i.e., visor or goggles), gloves, and a long-sleeved gown if there is risk for contact with body fluids and in settings where contamination is presumably high, such as where aerosol generating procedures are performed. Aprons can be used in place of gowns, if contact with body fluids is low. Gloves and the gown or apron should be changed between patient contacts.

The Australia Department of Health (09 Nov 2020) [11] included the following in the routine care of patients with suspected or confirmed COVID-19: surgical mask or particulate filter masks (P2 or N95 masks) depending on risk of blood body fluid, long sleeves gown/aprons, eye protection, face shield, wrap-around safety glasses/visor /goggles, and disposable non sterile gloves. Head cover and boots or shoe covers is not recommended unless gross contamination is anticipated or they are required as standard attire in operating theatre or trauma room.

The US Centers for Disease Control (23 Feb 2021) [12] had recommendations similar to the Australian Department of Health which included N95 or higher respirators (If not available, use face mask), face shield/googles, clean non-sterile gloves and isolation gown.

RESEARCH GAPS

Based on clinicaltrials.gov, there is one completed trial on the use of PPE in health care workers (completed January 2021) and one ongoing trial on with or without PPE during neonatal resuscitation.

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Appendix 1. Characteristics of Included studies

Author	Setting	Population	Intervention	Comparator	Outcome
Wang Q	Hubei China	5442 medical staff of 107 Neurosurgery Departments	Adequate Level 2 PPE[1]	Inadequate PPE	Number of HCW infected and not infected with COVID 19
Wang X	Wuhan China	493 Medical staff of Zhongnan Hospital	With N95 respirator	No N95 respirators	Number of HCW infected and not infected with COVID 19
Khalil SN	Dhaka Bangladesh	190 Medical staff in 19 health facilities	Face mask		Number of HCW with face mask infected with COVID 19
			Face shield		Number of HCW with face shield infected with COVID 19
			PPE		Number of HCW with PPE infected with COVID 19
			Gloves		Number of HCW with gloves infected with COVID 19
			N95		Number of HCW with N95 respirator infected with COVID 19
Mojajer A	Houston Texas	6527 Health Care Personnel of a quarternary health hospital	Face shield[2] with standard PPE	Standard PPE	Number of HCP infected before and after implementation of use of face shield with standard PPE Number of HCP with HAI before and after implementation of use of face shield with standard PPE
Heinzerling A	Solano California	37 Medical staff exposed to Index patient	Face mask		Number of HCW with face mask infected with COVID 19
			Gloves		Number of HCW wearing gloves infected with COVID 19

[1] Adequate PPE: disposable hat, medical protective mask (N95 or higher standard), goggles (anti-fog) or protective mask (anti-fog), medical gown clothing or white coats covered by medical protective clothing, disposable gloves and disposable shoe covers.
[2] Face shield used was a Lazarus 3D (Corvallis, OR, USA)
[3] Abbreviations: HCW: health care worker; HCP: health care personnel

Appendix 2. GRADE Evidence Profile

A. PPE Level 2 compared to No PPE Level 2 in prevention of COVID 19 infection in health care workers

CERTAINTY ASSESSMENT							SUMMARY OF FINDINGS				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates		Relative effect (95% CI)	Anticipated absolute effects	
							With no PPE Level 2	With PPE Level 2		Risk with no PPE Level 2	Risk difference with PPE Level 2
COVID-19 Infection (assessed with RT-PCR)											
5442 (1 observational study)	Not serious	Not serious	Not serious	Serious [a]	Strong association All plausible residual confounding would reduce the demonstrated effect	⊕⊕⊕◯ MODERATE	119/4155 (2.9%)	1/1287 (0.1%)	**RR 36.9** (5.2 to 263.6)	29 per 1,000	**1,000 more per 1,000** (from 120 more to 1,000 more)

CI: Confidence interval; **RR:** Risk ratio

Explanations

[a] Wide confidence interval

B. N95 respirators compared to no N95 respirators for prevention of COVID 19 infection in health care workers

CERTAINTY ASSESSMENT							SUMMARY OF FINDINGS				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates		Relative effect (95% CI)	Anticipated absolute effects	
							With no N95 respirator	With N95 respirator		Risk with no N95 respiratory	Risk difference with N95 respirator
N95 respirators vs no N95 respirators in prevention of COVID-19 infection											
										Moderate	
10 cases 483 controls (1 observational study)	Not serious	Not serious	Not serious	Not serious	Strong association	⊕⊕⊕◯ MODERATE	10 cases 483 controls		**OR 0.035** (0.002 to 0.603)	0 per 1,000	**0 fewer per 1,000** (from 0 fewer to 0 fewer)

CI: Confidence interval; **OR**: Odds ratio

C. Face Shield compared to No Face Shield for prevention of COVID 19 infection in health care workers

CERTAINTY ASSESSMENT							SUMMARY OF FINDINGS				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates		Relative effect (95% CI)	Anticipated absolute effects	
							With no face shield	With face shield		Risk with no face shield	Risk difference with face shield
Face shield vs no face shield in the prevention of COVID 19 infection											
6527 (1 observational study)	Serious [a]	Not serious	Not serious	Not serious	Strong association All plausible residual confounding would suggest spurious effect, while no effect was observed	⨁⨁⨁◯ MODERATE	166/2486 (6.7%)	80/4041 (2.0%)	**RR 0.297** (0.228 to 0.385)	67 per 1,000	**47 fewer per 1,000** (from 52 fewer to 41 fewer)

CI: Confidence interval; **RR:** Risk ratio

Explanations

[a] Protective effect of face shield may be compounded by its use with standard PPE, compliance of health care personnel on its use and other preventive measures and the type of work that is done

Appendix Table 3. Characteristics of ongoing clinical trials

No	Clinical Trial ID / Title	Study design, status	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	NCT04712045 (UK) Rational Use of Personal Protective Equipment: a Randomised Trial and Quality Improvement Intervention During COVID-19 Pandemic	Interventional clinical trial, completed (15 Jan 2021)	Health care workers	**New PPE:** Level 2 PPE which involves wearing a short-sleeve gown and a single pair of gloves	**Old PPE** Level 2 PPE which involves wearing a long-sleeve gown and double pairs of gloves	Primary outcome: Proportion of participants and simulated patients with contamination as assessed by ultraviolet light Secondary Outcome: 1. Participants' perception of personal comfort and safety and safety of the patients as assessed through structured questionnaire [Time Frame: immediately before simulations and immediately after simulations] 2. Changes in participants perception of personal comfort and safety and safety of patients as assessed through a semi-structured questionnaire [Time Frame: immediately before training, immediately after training and immediately after simulation] 3. The difference in the area of contamination between New and Standard PPE as analyzed through python script [Time Frame: immediately after simulations]
2	NCT04666233 (Padova, Italy) Personal Protective Equipment for the Prevention of SARS-Cov-2 During Neonatal Resuscitation	Randomized open label trial, not yet recruiting (no date)	Health care workers	**With PPE**	**Without PPE**	Primary Outcome: Initiation of positive pressure ventilation [Time Frame: 5 minutes] Secondary Outcome: 1. Duration of intubation procedure [Time Frame: 5 minutes 2. Correct use of personal protective equipment [Time Frame: 20 minutes] 3. Participant's opinion on discomfort using personal protective equipment [Time Frame: 20 minutes Level of discomfort in performing the procedures: 0 (no discomfort), 1 (low discomfort) ,2 (high discomfort) 4. Time of initiation of chest compressions [Time Frame: 20 minutes]

Q14. Should protective physical barriers be used to prevent COVID-19?

As of 30 June 2021

RECOMMENDATIONS

We suggest against the use of protective physical barrier enclosures (ex. aerosol box) for the prevention of COVID-19 among health care providers who perform aerosol generating medical procedures*. *(Very low certainty of evidence; Weak recommendation)*

**Proper PPEs should be used by health care providers when performing aerosol-generating procedures.*

We suggest the use of protective physical barriers in the prevention of COVID-19 in areas where social distancing cannot be adhered to (e.g., offices, reception desk). *(Very low certainty of evidence; Weak recommendation)*

***Adequate ventilation, physical distancing, use of facemasks and personal hygiene should still be maintained to prevent COVID-19 infections. Regular cleaning and disinfection of physical barriers should be practiced.*

Consensus Issues

Protective physical barrier enclosures refer to passive protective barriers that were used to protect the health care workers during the early stages of the pandemic when PPE supplies were limited. The physical barrier enclosure can be used as an additional layer of protection in situations where the HCP does not have adequate PPE for aerosol generating procedures. However, these barriers should be used with suction or negative pressure devices to reduce the risk of transmission from secondary aerosols that are trapped underneath the plastic barrier. Previous studies showed that aerosols can still escape a physical barrier enclosure. In addition, concerns related to efficiency and usability of such barriers have also been reported, such as: (1) longer intubation time; (2) difficulty in maneuvering the arms because of the rigidity of the box; (3) view of the anesthesiologist or ER doctor is blocked by the plastic or acrylic box). The Philippine Society of Anesthesiologists (PSA) also no longer recommends the use of physical barrier enclosures.

The use of physical barriers is not mandatory, but an option in areas where social distancing cannot be maintained. The proper disinfection of these barriers is emphasized. It was noted that the World Health Organization and Centers for Disease Control and Prevention have specifications and instruction for disinfection of barriers.

KEY FINDINGS

Two case series reported that there were no COVID-19 infections among health care providers who used protective barrier enclosures during aerosol generating procedures on COVID-19 patients. One systematic review reported that barrier devices were effective at either preventing or reducing the number of particles escaping the system only when negative pressure suction was applied. As for physical barriers (i.e., sneeze guards), we did not find any studies on its efficacy in preventing COVID-19 infections. Two computational fluid-particle dynamics (CFPD) simulation studies, however, showed that physical barriers could potentially reduce aerosol transmission within shared spaces such as classrooms or airplane cabins.

INTRODUCTION

The transmission of SARS-CoV-2 from an infected person is mainly through the air in the form of droplets and aerosol particles. A protective physical barrier is a form of engineering control to reduce the transmission of SARS-CoV 2 by blocking droplets and aerosols as they adhere to the barrier. When physical distancing is not possible, the transparent physical barrier allows workers, customers, health care workers to see through these barriers and interact normally. It is a supplement and not a substitute for masks and physical distancing [1].

This review covers two types of barriers:

1. Protective barrier enclosure for aerosolizing procedures: a transparent device consisting of either clear acrylic box or plastic drapes (suspended from a frame or laid over the patient) designed to cover a patient's head and upper body. It incorporates one or more ports (arm sheaths, gloves, or slits) through which the health care provider's hands are passed to perform medical procedures and airway management. It may be used alone or with suction devices to create a negative pressure. This type of barrier is intended to protect the health care provider from airborne pathogens [2] but the question remains: do they adequately protect health care providers against aerosolized SARS-CoV2 viral particles?

2. Physical barriers for public spaces ("sneeze guard"/ "cough guard"): one of the commonly used measures to reduce COVID-19 transmission in transportation, indoor or work spaces is the use of sneeze guards in the form of transparent glass or plastic barriers. A sneeze guard is typically made from either plexiglass, acrylic, or clear plastic sheets. It works by blocking spittle or spray from a person's nose or mouth before it can infect other areas. Since the 1970s, the U.S. Food and Drug Administration (FDA) has required that all unpackaged food on display be protected by clear glass or plastic cases (sneeze guards), especially at buffets [3]. Styles of sneeze guards are: free-standing, cubicle, hanging, or portable. The types of plastic used are either polymethyl methacrylate (acrylic), polycarbonate, or polyethylene terephthalate (PETG). Fire-resistant material (polycarbonate) is recommended for fixed barriers [4].

Physical barriers have increased in use since the onset of the COVID-19 pandemic, however, the evidence on their protective efficacy and safety is not well-established.

REVIEW METHODS

We searched for existing traditional/ living systematic reviews and/or traditional/ living COVID-19 databases and CPGs, published studies (PubMed, Cochrane Library, Herdin), MedRxIV, and BioRxIV (search date up to May 24, 2020). Ongoing trials were searched in Clinicaltrials.gov Registry (search date up to May 24, 2020). We used the following keywords and MeSH terms: "plastic barrier," "glass barrier," "aerosol box," "sneeze guard," and COVID-19 related terms in the search strategy.

The following PICO criteria were used:

Population	People at risk for COVID-19
Intervention	Protective physical barriers (enclosures/sneeze guards), any material (acrylic, plastic, glass)
Comparator	No barrier, other non-pharmacological intervention
Outcomes	Incidence of COVID-19; Adverse events
Study design	Systematic reviews, randomized controlled trials, controlled clinical trials, quasi-experimental, observational studies, case reports/series, simulation trials

RESULTS

Protective barrier enclosure for aerosol generating procedures

Efficacy to prevent COVID-19 infection among health care providers

We found two case series that reported COVID-19 infection rates among health care providers who used the protective barrier enclosures during intubation and other procedures on COVID-19 patients. No SARS-CoV-2 infections were recorded among health care providers after using a plastic sheet barrier on 8 COVID-19 cases [5] and in a private practice of 30 anesthesiologists who used an isolation biohazard hood (the Vacuum Assisted Negative Pressure Isolation Hood) for one month [6].

Efficacy to contain particles/prevent contamination

One systematic review assessed efficacy of barrier enclosure devices during medical aerosolizing procedures. Price et al. conducted a scoping qualitative review (N=123 studies; year 2000 to July 2020) but majority of the studies were letters and observational studies. Three studies were conducted prior to 2020 and did not involve COVID-19 cases (very low quality evidence).

Three general device types identified for use in airway management (intubation, extubation, tracheostomies or respiratory support) or general aerosolizing medical procedures:

1. Acrylic box
2. Plastic sheet with frame
3. Plastic sheet without frame systems

In studies with qualitative visual assessment of droplets/smoke/smell (71%, n = 39/55), the use of a barrier device was effective in either preventing or reducing the number of particles escaping the system. In quantitative studies (77%, n = 17/22), particle counts only increased when negative pressure suction was applied [7].

Physical barriers for public spaces ("sneeze guard"/ "cough guard")

We did not find any clinical studies on the efficacy of physical barriers on the prevention of COVID-19 infection. Two computational fluid-particle dynamics (CFPD) simulation studies assessed the ability of physical barriers to reduce aerosol transmission within shared spaces as a means of COVID-19 mitigation.

The study of Abuhegazy [8] investigated aerosol removal and surface deposition in a realistic classroom environment. A model classroom with nine students and a teacher was constructed. Air conditioning and ventilation standards for acceptable indoor air quality were included. Four different factors were considered:

1. Particle size (1 μm–50 μm),
2. Source location (students 1, 2, 5, 8, and 9),
3. Presence of barriers/sneeze guards, and
4. Opening windows (10%–50% of window width).

On average, the total fraction of aerosols transmitted from a source student to others in the classroom decreased by ~92% in the case with screens. In the presence of screens, very few aerosol particles (<0.01%) are transmitted from student 1 to the others in the room, and self-deposition is significantly reduced from 1.5% to 0.3%. Sneeze guards/glass barriers were found to effectively reduce the transmission of 1 μm aerosol between students by ~92% on average. The effectiveness of screens varied depending on source location within the classroom with respect to the air conditioning system.

Talaat et al investigated different intervention measures to reduce aerosol transmission on a Boeing 737 aircraft cabin. The investigators simulated the flow of air and the movement of aerosol particles emitted from a patient onboard a Boeing 737. They considered three scenarios/models:

1. Full capacity: 60 passengers across 10 rows of seats
2. Reduced capacity of 40 passengers
3. Full capacity of 60 passengers with sneeze guards/shields between passengers

The investigation considered a wide range of particle sizes (1–50 μm) which were released during exhalation, speech, and coughing.

Sneeze guards were more effective at directly stopping smaller particles than larger particles (8.6% of 20 μm particles deposited directly on sneeze guards compared to 9.8% of 1 μm particles). Only 4.3% of 50 μm particles deposited on the shields. The investigators reported that there was a 70% reduction in the inhalable fraction and 42% reduction in the total deposition fraction to passengers because shields were able to reduce lateral particle transfer. [8]

Harms
Time to Intubation (TTI) using the box system was reported by two systematic reviews (Price 4 out of 10 studies [7]; Lim: 12 studies [9]). Lim reported that, over-all, TTI was significantly longer when an aerosol box was used (MD 4.0 seconds; 95% CI: 2.4 to 5.6; P<0.001; I^2.38%).[9]

According to the US FDA, passive protective barrier enclosures may contribute to complications such as: increased intubation times, lower first-pass intubation success rates, increased patient hypoxia time, and damage or tearing to PPE from the enclosures. These complications may be due in part to "the barrier enclosure design characteristics and restricted mobility of the HCP's arms in a restricted space to maneuver the accessories needed to establish a definitive airway" [11].

RECOMMENDATIONS FROM OTHER GROUPS

Protective barrier enclosures
US FDA has revoked its emergency license for barrier enclosures devices in August 2020 and now recommends the use of enclosures with suction devices in keeping with

emerging objective evidence. "Protective barrier enclosures (with or without negative pressure) should never be a replacement for using PPE. Any protective barrier enclosure should be removed if it impedes the HCP's ability to perform a medical procedure on a patient." EUA has been issued for specific barrier enclosures with negative pressure [11].

Physical barriers for public spaces
WHO: "Use physical barriers to reduce exposure to the COVID-19 virus, such as glass or plastic windows. This approach can be implemented in areas of the healthcare setting where patients will first present, such as triage areas, the registration desk at the emergency department or at the pharmacy window where medication is collected" [12].

CDC recommends the following:
1. Placing a barrier (e.g., sneeze guard) between employees and customers [13].
2. "Where possible, establish physical barriers between bus transit operators and passengers. Use strip curtains, plastic barriers, or similar materials to create impermeable dividers or partitions" [14].
3. "Install physical barriers, such as sneeze guards and partitions, particularly in areas where it is difficult for individuals to remain at least 6 feet apart. Barriers can be useful at reception areas, distribution counters, and other areas where remaining at least 6 feet apart is difficult" [15] [16].
4. When social distancing can not be maintained: additional control measures: Using physical barriers (e.g., plexiglass or similar materials, other impermeable dividers or partitions) to separate staff and students from each other in classrooms or other shared spaces [17].

US Dept of Labor Occupational Safety and Health Administration (OSHA): "Installing plexiglass, stainless steel, or other barriers between workers, such as on assembly lines, or between workers and customers, such as at points of sale" [18].

The National Sanitation Foundation (NSF) and U.S. Food and Drug Administration (FDA) requires that all food on display is protected by cases or sneeze guards [3].

RESEARCH GAPS
There is a lack of clinical studies on COVID-19 infection rates among persons using the various protective physical barriers.

There are 3 registered clinical trials in ClinicalTrials.gov on the efficacy of aerosol boxes [19, 20, 21]. One trial plans to assess health care worker contamination [20].

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Q15. Should surfaces be disinfected to prevent COVID-19 infection?

As of 30 June 2021

RECOMMENDATION

We recommend the practice of cleaning and disinfecting surfaces using the appropriate disinfecting chemical agents such as 0.5% sodium hypochlorite solution (bleach) or 70% alcohol to prevent COVID-19 infection. (*Low certainty of evidence; Strong recommendation*)

For high touch surfaces and high traffic areas, such as in the workplace, disinfection should be done before shift, intermittently during, and after the shift.

For household disinfection, once daily disinfection on high touch surfaces is recommended.

Consensus Issues

The panel noted that alcohol is actually recommended for use on skin but is now also being used in the environment because of its accessibility. As for sodium hypochlorite solution, the DOH Department Memorandum 2020-0157 ("Guidelines on Cleaning and Disinfection in Various Settings as an Infection Prevention and Control Measure Against COVID-19") provides instructions on its dilution and appropriate use.

KEY FINDINGS

No randomized controlled studies were found directly addressing this question. Indirect evidence from a rapid systematic review of 7 studies, 5 laboratories, 1 case control, and 1 experimental provided data on the effects of cleaning products on SARS-CoV-2 inactivation. Indirect evidence from laboratory studies showed that SARS-CoV-2 is inactivated by common disinfectants within 1 minute when used according to their manufacturer's specifications and precautionary measures. However, disinfectants such as 0.1% sodium hypochlorite and 70% alcohol are potential irritants to the skin, ocular tissue, and respiratory tract and should be handled with proper protection and precaution.

INTRODUCTION

Transmission of COVID-19 occurs directly through droplet transmission via close contact (within 1 meter) of an infected person or through fomites in the immediate environment or surfaces. [2] Exposure to virus happens in everyday activities when using elevators, riding public transportation, dining at restaurants, spending time indoors such as workplaces and malls, walking through corridors and using common facilities like toilets and office pantries [1]. The SARS-CoV-2 virus has been found to survive on various surfaces from several hours (gloves) to up to 9 days (plastics) at room temperature [3,4,5]. Higher temperatures (>30°C) and relative humidity in buildings, hospitals and homes also affect its viability [4]. Initial reviews established the efficiency of inactivating coronaviruses, i.e., MERS-CoV, human coronavirus, SARS-CoV, using 0.1% sodium hypochlorite or 62-71% ethanol within 1-minute exposure time [3,5]; however, evidence focused on SARS-CoV-2 needs to be established.

REVIEW METHODS

A systematic search was conducted in various electronic research databases (MEDLINE, Google Scholar, Medline, Cochrane CENTRAL, HERDIN), pre-print databases (Chinaxiv.org, Medrxiv, biorxiv.org), trial registries (clinicaltrials.gov, EU, Canada, IISRCTN, China, ANZ, Brazil, Germany, Japan, Korea, India, the Netherlands and Pan Africa). We also checked for recommendations and evidence summaries from the USPSTF, NICE, WHO, EU, Australian and Canadian Preventive Task Forces, DOH and PSMID.

We initially looked for randomized clinical trials, controlled clinical trials, and systematic reviews of clinical trials. The search was expanded to include observational studies. Free text and MeSH terms related to “disinfecting or cleaning surfaces”, “disinfection,” “disinfect*,” “cleaning agents,” “detergents,” and “non-pharmacologic interventions,” were used.

RESULTS

No direct evidence from randomized clinical trials were found assessing the efficacy of disinfecting surfaces in preventing COVID-19 infection. Indirect evidence was obtained from a rapid systematic review of 7 studies on environmental cleaning in the prevention of COVID-19 infection. These studies included 5 laboratory tests and an experimental and a case-control study both done in hospital settings. The chemicals or disinfecting techniques used were ethanol (n=1), household bleach (n=3), hydrogen peroxide (n=2), aldehydes (n=1), chlorine dioxide (n=2), and UV irradiation (n=1). Only one study that used hydrogen peroxide tested hospital rooms where COVID-19 patients were admitted. Five laboratory-based studies took samples from various surfaces such as hospital equipment, in patient areas, gowns, and protective equipment, while one study tested wastewater.

The studies revealed that all products, with the right concentration and proper protocol, were effective in inactivating the coronavirus. Free chlorine and free iodine were found to be more effective than chlorine dioxide and iodine detergent, respectively [6].

Disinfectants are known to cause irritation of the skin and mucosa and are corrosive to the respiratory and digestive tracts (Appendix 1). Sodium hypochlorite may cause skin and ocular irritation gastric burns. Ethanol used in hand sanitizers may cause central nervous system and gastrointestinal irritation, and respiratory arrest [7]. Hydrogen peroxide is highly flammable and can also cause air embolism [8]. Because of its widespread use, recent concerns have also been raised on its effect on urban and marine wildlife [10,11].

RECOMMENDATIONS FROM OTHER GROUPS

The CDC recommends regularly disinfecting and cleaning in shared spaces if there is increased risk of infection from touching surfaces. This is emphasized in areas where there are widespread community transmission as well as in healthcare facilities [12].

WHO recommends identifying high-traffic areas and high-touch surfaces that should be cleaned with soap and water followed by disinfection using sodium hypochlorite (1000 ppm) or 70%-90% alcohol. They emphasized the importance of regularly training the staff on safe chemical handling and appropriate protective equipment [13].

The Canadian National Collaborating Center for Environmental Health further advises using pre-mixed disinfecting cleaner products instead of mixing separate products, to avoid creating dangerous by-products [14].

The DOH, in its April 2020 Memorandum No. 2020-0157, recommended cleaning and disinfecting surfaces at least once daily using 0.5% sodium hypochlorite solution (5000 ppm) while other disinfectant solutions such as ammonium chloride, phenols and hydrogen peroxide should be used according to the manufacturer's specifications. Furthermore, employees are encouraged to conduct surface disinfection in their work stations before the start of the shift, intermittently during shift and at the end of the shift. Food manufacturing shall use alternative disinfectants such as chlorine solution for food safety and Good Manufacturing Practices [15].

NICE, NIH, Australian NCCETF and the USPSTF did not have any recommendations on disinfecting surfaces.

RESEARCH GAPS

There were no ongoing clinical trials or studies on disinfecting surfaces for COVID-19 prevention found in the clinical trial registries. The effectiveness of disinfectants in reducing viral loads and inactivating viruses has been well established in the past. This knowledge precludes any clinical trials to provide direct evidence on its role in the prevention of COVID-19 and can be said to be moot and academic.

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Appendix 1. Disinfecting products and their health effects from prolonged exposure

Product	*Active Ingredient*	*Area of Application*	*Concentration (%)*	*Exposure Time (minutes)*	*Occupational Exposure Limit*[a] *(ppm)*	*Health Effects from Prolonged Exposure*
Household Bleach	Sodium hypochlorite	Surfaces	5.25-6.15	1-10	0.5 (per 15-minutes)	Skin, ocular irritation, and gastric burns
	Hypochlorous acid	Surfaces	0.017-0.046	10	0.5 (per 15-minutes)	
	Glycolic acid	Surfaces	11.185	10	Not found	Chemical burns to respiratory track
	Peroxyacetic acid	Surfaces	2.38-15	1	0.4 (per 15-minutes)[b]	Burns of the skin and eyes
	Quaternary Ammonium compounds (quats)	Surfaces	0.05-0.2	0.5-10	Not found	Mild to severe irritation of the skin and mucous membranes
	Octanoic acid	Surfaces	0.099-3.05	2	Not found	Skin irritation, scales, and scabs
Alcohol	Ethanol	Surfaces	60-80	0.5-1	1,000	Irritation of the respiratory tract and effects on the central nervous system
	L-lactic acid	Surfaces	0.19-1.77	5-10	Not found	Eye and skin irritation
	Citric acid	Surfaces	2.5-4.9	5	5 mg/m^3	Eye and skin irritant
	Hydrogen peroxide	Surfaces	0.39-27.5	5	1	Burns of the skin and eyes
Hand sanitizer	Benzalkonium chloride (quats)	Hands	0.12<	3-10		Skin irritation if prolonged contact
Hand sanitizer	Ethanol	Hands	60-95	0.5-1	1,000	Irritation of the respiratory tract and effects on the central nervous system

[a]The National Institute for Occupational Safety and Health recommended exposure limits for up to a 10-hour time weighted average.
[b]American Conference of Governmental Hygienists.
Abbreviation: ppm, parts per million.

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