ARHAI Scotland

Antimicrobial Resistance and Healthcare Associated Infection

NHS National Services Scotland

Rapid review of the literature – Respirators in health and care settings for the prevention of COVID-19 transmission

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Background

An open letter to UK government from almost 1500 healthcare workers (HCWs), teachers and other members of the public,[1] as well as a recent open letter to Public Health England from the British Medical Association,[2] outlined concerns regarding the current UK infection prevention and control (IPC) recommendation of wearing an FRSM for the care of suspected and/or confirmed COVID-19 patients, out with aerosol generating procedures (AGPs).

BMA authors highlight that they wish to ensure staff are protected from aerosol transmission of COVID-19 through wider provision and use of respiratory protective equipment (RPE), however, no citations are provided[2] and currently the evidence to support predominant airborne transmission of COVID-19 is limited.[3] The BMA state that PHE guidance was originally driven by PPE supply, and that now supply is no longer an issue, wider use of respirators should be implemented.[2] They also state that the WHO has modified its guidance such that where respirators are available, they should be considered for wider use, but this guidance has not been found. The BMA state that *"effective and adequate PPE will […] provide protection to patients in reducing nosocomial infections"*, however, this would only be the case if respirators were applied for patient use.[2] Further to this, they outline that *"many female doctors have reported struggling to find respirator masks that pass fit testing"*, an issue which would not be resolved through wider respirator use.[2]

In both letters, authors indicate that in areas where higher grade RPE is currently recommended, there is evidence indicating lower infection rates amongst staff.[1, 2] The authors postulate that this correlates with increased aerosol protection provided by higher-grade PPE and increased air exchanges. In the BMA letter no citations are provided to support this and the papers cited to support these conclusions in the NHS FreshAir letter have numerous limitations including testing practices between community and the study's HCW population being different, issues regarding power of studies and the value of serological testing.[1, 2] An ARHAI Scotland rapid review on health care worker COVID-19 infection acquisition rates is currently underway.

The BMA and NHS FreshAir group request that UK guidance be changed, with a recommendation that FFP respirators be worn for all care of suspected and/or confirmed COVID-19 patients.[1, 2]

Historically there has been a clear dichotomy in the literature regarding droplet and aerosol transmitted pathogens. Droplets have been categorised as particles ≥5µm which settle within 2 metres of the source and are mitigated by fluid resistant barriers whereas aerosols are categorised as being <5µm, can travel over longer distances and are small enough to penetrate non-filtering materials.[4, 5] Over time this dichotomy has been challenged with researchers outlining that a range of particle sizes will be produced by infected patients when speaking, coughing, sneezing etc.[4-7] The key question, however, still lies in the pathogen's main mode of transmission. Although aerosols and small droplet particles may be produced, transmission is dependent on the infectious dose carried within these particles.

Upon examination of the evidence, a multitude of health organisations have surmised that COVID-19 is likely to be predominantly spread via contact and droplet transmission routes.[8-11]

The ARHAI infection prevention and control rapid review which is updated on a monthly basis indicates that currently there is no clear evidence of airborne transmission being the main route of transmission of SARS-CoV-2, however, limited evidence for longer distance, air-mediated transmission, under specific circumstances, has been identified.[3]

Current guidance for most countries recommends use of contact and droplet precautions with fluid resistant surgical masks (FRSMs) to be worn by all health and care setting staff when caring for patients where COVID-19 infection is suspected or confirmed.[8-12] However, in light of isolated reports of transmission within the community which closely reflect features of airborne respiratory infection transmission and uncertainties regarding the transmissibility of new COVID-19 variants,[13] the question has been raised (as demonstrated by the BMA and NHS FreshAir letters)[1, 2] as to whether respirators would provide better protection and reduced HCW COVID-19 infection rates if used more widely for non-AGP healthcare provision. This also necessitates an analysis of the evidence regarding the suitability of valved and non-valved respirators as forms of source control.

Objectives

The following research questions were considered:

- What is the evidence for extension of respirator use by HCWs beyond AGPs to reduce nosocomial transmission of COVID-19 infection?
- What is the evidence for use of respirators as a form of source control?
- What are the current recommendations for respirator use in both UK health and care settings and other developed nation health and care settings in association with COVID-19?

Methodology

For details of the search strategy see Appendix 1. As this was a rapid review, evidence was critiqued by a single reviewer, but not formally graded with the use of an appraisal tool.

Results

What is the evidence for extension of respirator use by HCWs beyond AGPs to reduce nosocomial transmission of COVID-19 infection?

As part of the first version of this review, 413 articles were identified with 47 included based on a first screen and 13 based on the second. Of the 13 articles which were assessed in more detail, 4 were systematic reviews,[14-17] 2 rapid reviews,[18, 19] 2 experimental studies,[20, 21] 2 case-control studies [22, 23] (1 of which was excluded),[23] 1 retrospective cohort study which was excluded,[24] 1 case report which was excluded [25] and 1 meta-sub analysis of historical RCT data [26] which was also excluded.

In the second update of this review, 139 articles were identified with 53 included based on a first screen and 9 based on the second. Of the 9 articles which were assessed in more detail, 1 was a rapid review, [27] 3 were observational survey studies (all of which were excluded), [28-30] 2 were experimental comparative studies[31,

[32] (1 of which was excluded),[32] 1 was a meta-analysis (which was excluded)[33] and 1 was a systematic review.[34]

Laboratory and experimental studies consistently demonstrate that surgical masks are not suitable for filtering out small aerosols and that FFP respirators are superior for this purpose.[20, 21, 31, 35-37] However, in relation to protection against predominantly droplet spread respiratory viral infections, based on current limited evidence where the two mask types are compared, this does not appear to translate over to a difference in HCW infection rates within the clinical environment.

Historically a number of randomised clinical trials have been conducted to compare rates of influenza among healthcare workers following the use of either a surgical mask or N95 respirator.[38-44] Whilst one reported a statistically significant difference in efficacy of the N95 respirators versus the surgical masks,[38] most did not [39, 40] or only found a difference under specific circumstances such as evaluation of an alternative secondary outcome (bacterial colonisation in place of laboratory confirmed influenza) [41-43] or continuous use of an N95 respirator compared to targeted use which again was linked to the secondary outcome of clinical respiratory illness rather than laboratory confirmed viral infection.[44] One trial also assessed seasonal coronavirus infection rates but was likely underpowered.[26]

These RCTs were all assessed as having a high risk of bias, ill-defined control arms, specificity towards influenza (with none evaluating COVID-19 outcomes), poor monitoring of adherence and lack of applicability to UK healthcare settings, especially as (excluding *Radonovich et al's* study which utilised type IIR masks)[39] types of masks cannot be established (e.g. type I, II or IIR) and were compared to N95 respirators (equivalent to FFP2 respirators) which are not recommended for use in UK health and care settings.

Multiple rapid and systematic reviews, both recent [15, 17, 18, 27, 34, 45, 46] and historic, [35, 47-50] have evaluated the N95 and surgical mask comparative clinical trials described above, in an attempt to ascertain the potential benefit of respirators versus FRSMs for protection of HCWs against predominantly droplet transmitted respiratory viral infections. Most of the studies identified in these reviews were evaluated as part of a recent 2019 Health Protection Scotland RPE literature review update. All of these reviews, including a recent Cochrane review,[46] have surmised that there is

inconclusive evidence to suggest that N95 respirators are superior to surgical masks when treating patients with predominantly droplet spread respiratory infections.

One recent rapid review used a small, specific sub-group analysis to support a potential beneficial effect of respirators over surgical masks.[19] Four RCTs were included, all of which had previously been assessed as part of the 2019 HPS RPE literature review and as part of multiple other systematic reviews.[19] For two of the clustered RCTs, which assessed clinical respiratory infection (CRI) as an outcome, meta-analysis showed that N95 respirators meaningfully reduced the risk of developing CRI compared to surgical masks (RR 0.43, CI 0.29-0.64), with low quality of evidence.[19] For one of these trials it was only continuous use of respirators compared to surgical masks which showed a significant difference in CRI[44] and it is important to note that CRI does not equate to laboratory confirmed infection. CRI in both trials was defined as two or more respiratory symptoms or one respiratory symptom and a systemic symptom self-reported by HCWs.[38, 44] The 2011 trial appears to have been underpowered which is perhaps why it was given less weight in the meta-analysis, however, the surgical masks used appear to be different in each trial with one classed as fluid resistant and the other not which invalidates the meta-analysis due to significant study heterogeneity.[38, 44]

In Ueki et al's experimental, comparative study, mannequins, nebulisers and ventilators were used to assess the protective effect of cotton, surgical or N95 masks against SARS-CoV-2 aerosolised particles when worn for protection and/or as a form of source control.[31] The nebuliser particle size percentages exhaled were as follows: <3 µm 20%, 3-5 µm 40%, >5-8 µm, 40%. Particles were exhaled continuously to simulate a mild cough at a flow speed of 2 m/s for 20 min.[31] Viral loads and viral particles that passed through the masks were measured by use of a plaque assay and quantitative real-time reverse transcription PCR (qRT-PCR), respectively. A distance of 50cm between mannequin heads (compared to 25cm), without masks, reduced viral load at the receiver to 45% and a distance of 100cm reduced viral load to 31% (compared to 25cm).[31] The 'receiver' wearing a surgical mask reduced viral titre (from an uncovered source at 50cm) to 53% although this was not a quantitatively significant reduction. A non-fit tested N95 mask, worn by the 'receiver', reduced viral titre to 43% although again, this was not a quantitatively significant reduction.[31] An N95 mask which had been sealed/taped to the face of the 'receiver',

reduced viral titre to 21% which was a quantitatively significant reduction, although this likely does not reflect results of in-vivo fit testing. When surgical masks were worn by both receiver and source, viral titre was reduced to 29% which was a quantitative significant reduction (p=<0.05).[31] When the source wore a surgical mask and receiver wore an N95 mask, viral titres were reduced to 31% (p=<0.05). This study provides evidence for the ability of surgical masks and N95 masks to block the path of SARS-CoV-2 viral particles.[31] However, without knowing the infectious dose of the virus and based on the experimental nature of the study it is difficult to draw solid conclusions on their meaningful protective effect and any differences based on mask types. Authors found that protective efficiency was significantly higher when masks were worn by both the virus 'spreader' and 'receiver', suggesting a synergistic effect.[31]

A recent case-control study with a significant number of limitations suggested that FFP respirators may provide greater protection against HCW COVID-19 infection but due to its numerous limitations, it is not recommended that this study be used in isolation to support recommendations.[22] In this study, 244 HCW cases with laboratory-confirmed COVID-19 were compared with 886 HCW controls who had remained 'healthy throughout the pandemic' based on self-assessment.[22] The study involved HCWs from 67 countries meaning that local community/nosocomial transmission rates would have been highly variable as well as local infection control policies. Non-AGP medical mask use was not consistently associated with HCP COVID-19, but HCP infection was more likely with prolonged continuous contact (≥45 mins) while not wearing a respirator (adjusted OR 2.3 vs. 0.8 when respirator used).[22] Authors concluded that medical masks are likely adequate during most non-AGP contact with COVID-19 patients, but respirators might be considered if prolonged close contact is anticipated.[22]

In a recent review, Chu et al included studies of any design, in any setting, to assess the protective effects of eye protection, physical distancing and mask wearing.[16] Chu et al identified 30 studies which focused on the association between use of various types of face masks and respirators by HCWs, patients, or both with virus transmission.[16] Most of these studies would have been excluded as part of the recent RPE HPS literature review update due to the majority reporting on bundled interventions, including different components of PPE and distancing.[16] Authors state

that association with protection from infection was more pronounced with N95 or similar respirators (aOR 0·04, 95% CI 0·004 to 0·30) compared with other masks (aOR 0·33, 95% CI 0·17 to 0·61) which they describe as a moderate credibility subgroup effect.[16] However, the associated p-value is 0.090, which would be considered non-significant. In the context of the research questions in this rapid review, one also cannot ascertain the frequency or pattern of AGPs performed in the settings in these studies.

A Canadian clinical trial assessing respirator/mask use and COVID-19 infection in HCWs is currently underway and due to be published in April 2021.[51]

What is the evidence for use of respirators as a form of source control?

To answer this research question all references from the first two updates were re-screened and reviewed with additional grey literature searching. Nineteen articles were identified; one expert opinion piece,[52] three in-vitro observational studies,[53-55] one narrative review[56] and three in-vivo observational studies[57-59] were excluded. The eleven remaining in-vitro observational studies, all of which were included, assessed the efficacy of N95 (FFP2) respirator use as a form of source control.[31, 60-69].

In Johnson et al's observational study nine subjects with clinical and laboratory confirmed influenza infection coughed whilst wearing different mask types; surgical masks were compared with non-fit tested standard N95 respirator masks.[60] Participants coughed 5 times for each intervention/control onto a petri dish which was held 20cm from their mouths.[60] Intervention and control phases included; 1) a 'before cough' with no mask, 2) a cough with an N95 respirator, 3) a cough with a surgical mask and 4) an 'after cough' with no mask.[60] Steps 2 and 3 were randomised. Surgical and N95 masks appeared to be equally effective in filtering influenza, given that no influenza could be detected by RT-PCR in any of the 9 participants for either mask, however, there were 4 out of 18 occasions where influenza was not detected during either control cough phase which infers methodological limitations regarding study design.[60] This study was limited by a very small sample size, influenza specificity, an unknown surgical mask type and lack of assessment of the effect of wearing a mask for longer than approximately 5 minutes.

This study provides initial evidence that surgical masks may be comparable to N95 respirators for the purpose of source control, however, due to the significant limitations further research is needed.[60]

In a similar study to Johnson et al's, Asadi et al conducted an *in vitro* experimental study comparing the efficacies of a number of masks, including non-valved N95 respirators and surgical masks, at reducing aerosol particle emission rates when 10 healthy human participants were breathing, speaking, and coughing.[61] When wearing no mask, the median particle emission rate was 0.31 particles/s.[61] This was significantly reduced (approx. 6-fold) by the wearing a surgical mask or N95 respirator (0.06 and 0.07 particles per second respectively).[61] When talking without a mask, the median emission rate was 2.77 particles/s.[61] Both surgical masks and N95 respirators significantly decreased emission rates to 0.18 and 0.36 particles/s, respectively.[61] During coughing without a mask a median of 10.1 particles/s were produced, wearing surgical masks significantly reduced the median emission rate to 2.44 particles/s, and wearing an N95 reduced the median emission rate to 6.15 particles/s, however this was not statistically significant.[61] Although limited by a small sample size and mask specificity, the findings of this study suggest that using both surgical masks and N95 (unvalved) masks significantly reduce the outward emission of particles during breathing and talking, with surgical masks also significantly reducing the rate when coughing.[61]

Hui et al looked at visual smoke dissemination (oil-based smoke particles, measuring less than 1 µm in diameter) using a mannequin that simulated coughing, wearing no mask, a surgical mask or an N95 respirator (non-valved).[62] Coughing bouts were generated by short bursts of oxygen flow at 650, 320, and 220L/min to simulate normal, mild and poor coughing efforts.[62] Dispersal distances were significantly reduced by wearing a surgical mask (30.0 +/- 3.4 cm) or a non-valved N95 respirator (15.1 +/- 2.7 cm), p=0.001.[62] This study although experimental in nature, does provide evidence that surgical masks and N95 respirators most likely significantly reduce distances of forwardly dispersed cough plumes when worn by patients.[62]

Five studies were similar in their design; two mannequin heads were placed at set distances apart within a chamber (one 'source' and one 'receiver' attached to nebulisers or oxygen lines) with filtration and exposure to particles measured when

mouth openings were covered with different mask types at either source, receiver or both.[31, 63, 67-69] Four of the studies involved dispersal of radiolabelled wet aerosols[63, 67-69] and one used SARS-CoV-2 aerosolised particles.[31]

In Ueki et al's study, SARS-CoV2 particles had a broad range of sizes (<3 μm 20%, 3-5 μm 40%, >5-8 μm, 40%) 'exhaled' by the source at a flow speed of 2 m/s for 20 min within a chamber with 0 air changes per hour (ACH).[31] The 'source' wearing a surgical mask reduced viral titre (Log_{10}PFU) detected at the 'receiver' (50cm away) to 27% compared to the control (no masks), whereas the N95 mask at source reduced it to 5% and a 'fit tested' N95 meant virus was undetectable at the receiver, however, fit tested equated to application of tape at the borders of the mask, which does not reflect clinical practice.[31] This study although limited by its in-vitro nature, and failure to specify exact surgical mask type, suggests that at close range (50cm) with no air changes per hour, a non-valved respirator is a suitable means of source control when compared to a surgical mask.[31]

Studies by Diaz et al, Patel et al, Mansour et al and Skaria and Smaldone were highly similar in their designs.[63, 67-69] All mannequins were placed at approximately 3 feet apart with measurements taken over 8-10 minutes within environments of 6 ACH (some at both 0ACH and 6ACH).[63, 67-69] The mean diameter of radiolabelled wet particles did not differ significantly between studies (~0.95μm-1.5μm).[63, 67-69] Respirators were all N95 and surgical masks met type IIR standards. [63, 67-69] Mansour et al were unique in their choice of soft malleable resuscitation heads to better replicate the *in vivo* fit of masks.[69]

In Diaz et al's study, at the source, a non-valved N95 respirator resulted in significantly greater filtration averaging 35.7% in comparison with a tight fitting surgical mask 14.8% and a loose fitting surgical mask 6.07% (captured by the mask).[63] In Skaria et al's study an N95 mask at source was able to filter 84.47% of particles.[68] In comparison, the secure fit surgical mask and natural fit surgical mask filtered 49.21% and 22.7% of particles respectively.[68] In Mansour et al's study, at the source, N95 mask filtration averaged 77.06% in comparison with 37.03% for the tight surgical mask and 13.18% for the natural fitting surgical mask.[69]

The above studies show the superior filtration efficacy of an N95 respirator at source, however, in both Diaz et al and Mansour et al's study, significantly greater filtration

with the N95 did not correlate with a significant reduction in receiver exposure.[63, 69] Loose or tight surgical masks or N95 respirators at the source consistently resulted in very low exposure percentages of 0.003-0.006% which suggests deflection was a dominant factor and that differences in filtration efficacy at the source do not directly correlate with degree of exposure at the 'receiver'.[63, 69] In Mansour et al's study, with a naturally fitting surgical mask, 0.00637% of maximum exposure was observed (a protection factor (PF) of 214), a tightly fitted surgical mask and N95 mask placed on the source resulted in similar small exposure percentages at the receiver; 0.00023% (PF 5,850) and 0.0019% (PF 7,174) respectively.[69]

In Patel et al's study percentage of exhaled particles detected at the receiver was measured when the 'source' was 'breathing' or 'coughing'.[67] Patel et al found that when coughing (a series of 1.5L breaths generating a peak flow of 5.2L/sec), a mask or respirator on the source was statistically superior to a mask or unsealed respirator on the receiver in all environments.[67] In experiments whereby both source and receiver replicated tidal breathing, in an environment with zero air changes, a naturally fitting surgical mask on the source reduced exposure at the receiver to approximately 60%, a secure fit surgical mask reduced it to ~25% and an N95 to ~10%.[67] Both the secure fit surgical mask and N95 mask reductions were statistically significant.[67] When masks were trialled on receivers, only the N95 mask sealed with Vaseline resulted in a statistically significant drop in exposure.[67] This eludes to the superior effect of source control over receiver protection. When ACH was increased to 6, all masks at source were more effective, demonstrating the importance of environmental ventilation, with the naturally fitting surgical mask reducing exposure to ~20%, the secure fit surgical mask reducing it to ~15% and the N95 to ~10%.[67] Skaria and Smaldone similarly found that exposure at the receiver was 21% when the naturally fitting surgical mask was placed on the source, 16% when the secure fit surgical mask was used and 6% when an N95 mask was used.[68] In line with Patel et al's findings, Mansour et al's study found that any mask applied to the source mannequin resulted in significant reductions in exposure, whereas on the receiver, only a Vaseline sealed N95 respirator mask provided statistically significant protection.[69]

Exposure percentages based on source mask types at the receiver, are similar in the studies by Patel et al and Skaria et al,[67, 68] however, they are markedly reduced,

although comparable to each other, in both Mansour et al's and Diaz et al's studies.[63, 69] The reason for this is unclear as all four studies are similar in design and execution.

All of these studies demonstrate the importance of source control and suggest that a surgical mask placed on the source or spreader of infectious particles is potentially more important and effective than any mask worn by the exposed receiver during an interaction. These studies also suggest that a non-valved respirator should not be strictly precluded from use as a form of source control, if required.

Guidance

Most guidance does not refer to respirators at all when discussing source control, only medical masks or cloth face coverings.[9, 10, 12, 70-74] Some CDC guidance represents an exception to this where it states that a respirator without an exhalation valve should be worn when both source control and respiratory protection are required.[66, 75]

Historically the Scottish National Infection Prevention and Control Manual (NIPCM) has not recommended the use of respirators for source control as they are not tested in line with standards for this purpose and sufficient evidence did not support their use in this manner. The 2019 NIPCM RPE literature review states that "due to the nature of the FFP respirator filtration, which filters incoming air and not expelled air, it is not suitable for an infectious patient to wear an FFP respirator.[76, 77]

Valved respirators

International guidance is consistent in its recommendation that valved respirators should not be used for source control as they allow the expulsion of un-filtered air on exhalation.[11, 75, 78-83]

There is conflicting guidance regarding the appropriateness of covering a valved respirator with a surgical mask. Both the CDC and The British Association of Oral and Maxillofacial surgeons advise that if only a respirator with an exhalation valve is available, a surgical mask that does not interfere with the respirator fit, should be used to cover the exhalation valve.[66, 84] However, in contrast to this, WHO *"does not recommend the use of a medical mask in combination with a respirator to extend the*

use of a respirator, or to ensure source control when using a respirator with an unfiltered exhalation valve".[82]

Certain studies have assessed the efficacy and appropriateness of valved respirators as a form of source control. Verma et al visualised tracers composed of droplets of distilled water and glycerin (estimated to be less than 10µm) expelled through the mouth opening of a mannequin using laser sheets.[64] Authors found that an N95 mask equipped with an exhalation valve resulted in a large number of droplets passing through the exhale valve unfiltered, which authors concluded significantly reduced its effectiveness as a means of source control.[64] They also observed that a non-valved N95 respirator when compared to a surgical mask showed comparable minimal leakage, however, this was a qualitative visual observation.[64]

The National Institute for Occupational Safety and Health (NIOSH) recently tested the source control filtration efficacy of 13 valved filtering face piece (FFP) respirators.[65] They also tested a selection of other mask types including surgical masks and cloth face coverings.[65] Six replicates of each test were performed within a controlled chamber system which featured a different valved FFP respirator type, different airflow rate (25, 55 or 85L/min) and different valve covering mitigation measure (surgical tape placed over the valve on the inside of the mask, a surgical mask worn over the exterior of the mask or an ECG pad placed over the valve on the inside of the mask).[65] For all three valve covering mitigation strategies particle penetration ranged from <1% to 55% with significant variation seen both between FFPs and on multiple testing of the same FFP.[65] Considering the median penetration at 85 Lpm, penetration was 31% for the control; 23% for the masked-over mitigation; 5% for the taped mitigation and 2% for the ECG pad mitigation.[65] It is important to note the in-vitro nature of the experiment with a single small particle size of 0.35µm having been used.[65] The authors conclude that *"even unmitigated FFPs with an exhalation valve can help to provide some degree of source control"* and even go onto say that this may be comparable to the source control provided by a surgical mask, as these respirators would be more consistent in their filtration levels, as expulsion of particles would be less influenced by surgical mask side gaps.[65] However, this conclusion seems premature as penetration of particles through the

surgical mask ranged from 1-17% in this study versus <1-55% in the valved respirator.[65]

What are the current recommendations for respirator use in both UK health and care settings and other developed nations in association with COVID-19?

Seven guidance documents from six healthcare organisations; Public Health England[9], European Centre for Disease Prevention and Control[81], Centers for Disease Control and Prevention[71], World Health Organization[8], Australian Government[11] and the Government of Canada[10] were reviewed as part of the first version of this rapid review.

In the second update, it was ascertained that some WHO[8], PHE[9], Australian Government[11], Canadian Government[10] and ECDC guidance[81] had remained unchanged. The CDC[71] had updated their guidance and 15 guidance documents were newly incorporated into the review. [12, 70, 72, 85-96]

CDC guidance recommends (E) that an FFP2/N95 respirator be worn for the routine care of suspected or confirmed COVID-19 infected patients with the ECDC advising that FFP2/FFP3 respirators should be used as minimum respiratory protection with an FFP3 respirator being worn when performing AGPs with these cases.[72] However, the guidelines then state that surgical or procedural masks may be worn if FFPs are unavailable, whilst acknowledging that this has limitations and risks.[71, 72, 81] Further contradiction can be identified in other ECDC guidance[81] where it is advised that HCWs, caring for residents of care homes with respiratory infection/symptoms, should wear a medical mask or an FFP2 respirator if available.[81]

ECDC guidance generally contradicts its recommendation of respirators for non-AGP care by outlining the weak evidence for non-AGP based COVID-19 aerosol transmission. It cites two systematic reviews[16, 47] when stating that *"with the exception of AGPs, it is unclear whether respirators provide better protection than medical masks against other coronaviruses and respiratory viruses such as influenza"*.[81]

The CDC do not provide citations to support their recommendation for an N95 respirator for routine care and in fact, express a clear stance on the doubtful role of

airborne transmission as a predominant route of COVID-19 infection spread in other publications.[7] In a scientific brief, last updated in October 2020, CDC authors outline that *"the epidemiology of SARS-CoV-2 indicates that most infections are spread through close contact, not airborne transmission"*.[7] They state that data indicates COVID-19 has a comparable transmission pattern to that of other respiratory pathogens predominantly spread by larger droplets and close contact and that greater secondary attack rates with a higher R number would have been observed for a pathogen predominantly spread via the true airborne route.[7] Overall, they conclude that *"there is no evidence of efficient spread (i.e., routine, rapid spread) to people far away or who enter a space hours after an infectious person was there".*[7] The CDC do outline that under specific circumstances such as those of prolonged exposure and poor ventilation within enclosed spaces, longer range air-mediated transmission of COVID-19 may occur.[7]

In cases where prioritisation of RPE is needed, the ECDC[81] advise that a rational approach would involve *"prioritising use of respirators for care activities involving a higher perceived risk of transmission, such as during AGPs or in intensive care*". Similarly, the CDC advise that respirators be prioritized for situations where *"respiratory protection is most important"* and for the care of patients with airborne transmitted pathogens.[71]

In line with ECDC guidance,[81] the CDC recommend that for the collection of diagnostic respiratory samples, HCWs should wear an N95 or higher-level respirator (facemask if a respirator is not available), eye protection, gloves, and a gown.[71] The ECDC aligns with this recommendation in the context of swabbing being conducted in an enclosed space, but advise that for outdoor testing, an FRSM is suitable. Neither the CDC[71] nor ECDC[81] provide specific evidentiary support for these recommendations.

The CDC recommend N95 respirators for routine care of suspected or confirmed COVID-19 cases, within hospital[71] and care homes[86] however, some respirator guidance is given for the care of patients who do not have defined suspected or confirmed COVID-19 infection but, in light of estimated levels and patterns of transmission within the community, may merit respirator use by HCWs, based on the risk of asymptomatic carriage.[71] The CDC state that in areas of moderate to

substantial[a] community transmission, for patients without symptoms or a history of COVID-19 case contact, standard precautions are recommended with addition of eye protection and a face mask but an N95 respirator is required for AGPs or surgical procedures that generate aerosols from areas such as the nose and throat, oropharynx or respiratory tract.[71] They go on to state that in areas of minimal to no[b] community transmission HCWs are advised to *"continue to adhere to Standard and Transmission-Based Precautions, including use of eye protection and/or an N95 or equivalent or higher-level respirator based on anticipated exposures and suspected or confirmed diagnoses",* essentially reflecting a 'business as usual approach'.[71]

a. Substantial community transmission was defined by the CDC as 'Large scale community transmission, including communal settings (e.g., schools, workplaces).' Minimal to moderate community transmission is defined as 'Sustained transmission with high likelihood or confirmed exposure within communal settings and potential for rapid increase in cases'. There is no definition for moderate to substantial transmission provided.[71]

b. No to minimal community transmission was defined by the CDC as 'Evidence of isolated cases or limited community transmission, case investigations underway; no evidence of exposure in large communal setting'.[71]

WHO[8], PHE[9], Australian Government[11], Canadian Government[10] and New Zealand Government guidance[12] recommends a surgical mask and eye protection for routine care contact with suspected or confirmed COVID-19 cases, however, very little supportive evidence is cited for this recommendation. WHO[8] states that COVID-19 has been detected in the air of health and care settings where AGPs are not being performed via PCR, but infectious virus has not been cultured from these samples and that predominant droplet transmission is supported by both *Chu et al.'s* 2020 systematic review[16] and a multitude of other studies. However, more recent WHO guidance contains some contradictory text.[94] Authors state that respirators are recommended *"primarily for settings where AGPs are performed; however, if health workers prefer them and they are sufficiently available and cost is not an issue, they could also be used during care for COVID-19 patients in other settings".*[94]

In a recent New Zealand government media briefing, officials outlined that PPE guidance surrounding 'managed isolation and quarantine' areas was changing.[88] They advised that respirators are now recommended for workers in scenarios where they cannot maintain a 2 metre physical distance from confirmed/suspected cases.[88] Evidence to support this change in guidelines has not been cited, and instead seems to be based on a precautionary approach to PPE due to concerns around airborne transmission.[88] These changes do not appear to have, as of yet, filtered through to other New Zealand guidance documents and contradict other New Zealand guidance where WHO guidance is cited on rational use of PPE in relation to their recommendation for use of surgical mask during routine care of suspected/confirmed COVID-19 cases.[12]

In all encountered guidance, respirators were advised for AGPs, with slight variation in the list of procedures classified as such, and with some sources incorporating a risk assessment element. Canadian guidance[10] advises the use of N95 respirators for AGPs but also makes reference to potential AGPs based on uncertain evidence. For these procedures, the guidance states that *"selection of PPE should be informed by point of care risk assessment that considers the risk that each individual patient will cough or sneeze in association with the procedure, and balances patient and HCW safety"* which may be challenging for HCWs to implement in practice.[10] WHO advise that respirators should be worn in surgery for confirmed/suspected COVID-19 cases if AGPs are expected or if the procedure involves anatomic regions where viral loads of the virus may be higher (e.g. nose, oropharynx, respiratory tract) and can be worn under the same circumstances for unknown COVID-19 status cases.[8] Australian government [11, 89-92] guidance makes it clear that N95 respirators are not recommended out with AGP care, however, does outline specific situations/settings where a HCW may wish to consider wearing one due to general limited evidence. Australian guidance outlines that HCWs may wish to use respirators in emergency departments, residential care facilities or in-patient facilities

a) For the care of suspected/confirmed COVID-19 cases under the following circumstances:

- *"Settings where there are a high density of COVID-infected patients, particularly in wards or cohorted areas without optimal ventilation and where prolonged episodes of care are required".*[90]
- *"For the clinical care of patients who have cognitive impairment, are unable to cooperate or exhibiting challenging behaviours".*[90, 91]
- *"Where there are high numbers of suspected or confirmed COVID-19 patients AND a risk of challenging behaviours and/or unplanned aerosol-generating procedures".*[90, 91]
- For aged care home residents in areas with significant community transmission (based on local/jurisdictional guidance).[93]

b) For the care of patients, not suspected or confirmed to have COVID-19 infection, in areas of significant community transmission, under the following circumstances:

- *"Where there are high numbers of suspected or confirmed COVID-19 patients/residents AND a risk of challenging behaviours and/or unplanned aerosol-generating procedures (e.g. including intermittent use of high flow oxygen). In these situations, use of a* [particulate filter respirator] *(PFR), for up to four hours, if tolerated, will avoid the need for frequent changes of face covering".*[90]

It is also stated in Australian guidance that a *"PFR should be used for active airway management procedures"*.[90] New Zealand Government guidance clearly states that respirators are not required for collecting nasopharyngeal and throat swabs, as they are not considered by their organisation to be AGPs[12] whereas Australian guidance states that *"If you need to collect a specimen with an AGP, for example sputum induction, you should wear a PFR".*[92] Although Australian guidance[11] advocates use of respirators in a wide range of additional circumstances out with AGPs, their guidance still supports the concept of poor evidence of aerosol transmission through citing a narrative review by *Conly et al.*[4] and stating that *"there is little clinical or epidemiological evidence that airborne transmission of SARSCoV-2, at distances greater than 1.5 m, occurs frequently"*.[89]

WHO supports the concept of respirators for 'AGP hot spots', for example in *"intensive care units, where AGPs are frequently performed, the health worker may choose to wear a particulate respirator throughout his or her shift, in areas of*

community transmission".[8] PHE guidance no longer clearly denotes the need for respirators in 'AGP hot spots' eg. ICUs, but does suggest their continued relevance via the following statement: *"Consideration may need to be given to the application of airborne precautions where the number of cases of COVID-19 requiring AGPs increases and patients/individuals cannot be managed in single or isolation rooms".*[9]

Recent changes to public face mask guidance in some European countries has been observed. Details of these changes are currently only available from media reports with no accompanying supportive cited evidence and with a reflection of these changes remaining unobserved within general European or International guidance sources. The ECDC does state, in relation to risks associated with the new UK variant, that mitigation strategies should be strengthened with implementation of potentially stricter non-pharmaceutical interventions (NPIs) and that authorities should be communicating and engaging with the population to encourage compliance.[97]

The German government have outlined that *"medical masks (so-called surgical masks, or KN95/N95 or FFP2 masks) offer greater protection than normal cloth masks, which are not subject to any standards with regard to their effectiveness".*[98] Based on this and their concerns over spread of the new UK variant within Germany, a precautionary approach has been taken with a new obligation to wear a medical mask when using public transport and in shops.[98] The German government have also now advised that FFP2 mask should be worn by all staff in care homes who have contact with residents.[98] In contrast to general German government guidance, the state of Bavaria are enforcing the use of N95 respirators in shops and on public transport.[99]

The French government have mandated that citizens wear single-use masks which meet surgical FFP1 mask specifications or higher in all public places meaning homemade/cloth masks are no longer suitable in these settings and, in Austria, the government have advised the population to wear FFP2 masks in shops and on public transport from the 25th of January 2021.[99]

In contrast to the European guidance outlined above, CDC guidance specifies that the public should *"not use surgical masks and respirators that are meant for healthcare workers* [as] *surgical masks and respirators are critical supplies that*

should be reserved for healthcare workers and other medical first responders to prevent supply shortages".[83]

In conclusion, recent changes to European guidance are varied and do not appear to be evidence-based but rather precautionary in nature.

Conclusion

There is currently no strong evidence to support a recommendation that non-valved respirators should not be used for source control. The weak in-vitro evidence to date suggests that non-valved respirators are comparable, if not superior to surgical masks as a source control measure. However, there is no evidence to support a change in recommendations based on current transmission rate evidence. It is important to note that efficacy of source control depends on a variety of factors beyond the in-vitro filtration capabilities measured at source, including deflection of particles/respiratory plume, face mask fit and ventilation.

Limited evidence suggests that valved respirators should not be used for source control and this is supported by numerous sources of international guidance.

Overall, evidence of a superior protective effect of respirators compared to surgical masks for non-AGP direct care of COVID-19 infected patients is extremely limited and this is currently reflected in conflicting developed country HCW respirator guidance. All recent systematic and/or rapid reviews are consistent in their findings that the value of respirators over surgical masks for prevention of nosocomial transmission of predominantly droplet transmitted respiratory infection is uncertain. No COVID-19 clinical trials are currently available and all SARS/MERS based evidence is observational in nature. Evidence is clouded by bundled infection control approaches, community transmission, poor descriptions of mask types (with a focus on comparison to FFP2 rather than FFP3 respirators) and an unclear distinction between AGP and non-AGP care.

Evidence for aerosol/air mediated longer-range transmission of COVID-19 infection is weak and, if occurring, may be specifically associated with AGPs/enclosed spaces/poor ventilation. In line with current guidance, HCWs should already be wearing respirators when carrying out AGPs on suspected or confirmed COVID-19

cases, i.e. those patients which fall into the amber and red pathways. However, Scottish IPC guidance does state that, based on a personal PPE risk assessment, *"when prevalence is high, and where staff have concerns about potential exposure to themselves,* [HCWs] *may choose to wear an FFP3 respirator rather than an FRSM when performing an AGP on a low-risk pathway patient"*.[74]

The decision to recommend the use of respirators for the care of suspected or confirmed COVID-19 cases, within Scottish health and care settings, beyond the performance of AGPs, lies not only in assessment of the limited evidence base but a decision on whether the precautionary principle should be implemented.

There are a number of important factors to consider when assessing the potential role of wider respirator use on nosocomial transmission rates. Greater use of respirators may compromise supply for those HCWs performing higher risk aerosol generating procedures. Respirators cannot be worn by patients or visitors due to fit testing requirements meaning that patient-to-patient nosocomial transmission rates would likely be unaffected by any change to respirator recommendations. Respirators when worn by HCWs are subject to the same compliance issues as other forms of PPE and there is evidence from Scottish outbreak reporting that a number of behavioural and compliance issues, including community-based activities, (rather than inappropriateness of healthcare-based PPE provisions) may be impacting upon HCW nosocomial transmission rates.[3]

Based on experimental studies where respirators and masks are compared in terms of their capacity to provide protection or source control, it is recommended that patients should be strongly encouraged to wear surgical masks to reduce the risk of transmission associated with the non-AGP care of unmasked patients. Limited current evidence demonstrates the significant value of the synergistic protective effect when surgical masks are worn by both HCW and patient.

Further research is needed in the form of comparative clinical trials regarding the use of respirators (FFP2 or FFP3) versus surgical masks for the non-AGP care of suspected or confirmed COVID-19 infected patients, with laboratory confirmed healthcare worker COVID-19 infection as a primary outcome.

Appendix 1

The following search strategy was processed in OVID Embase and Medline databases on the 21st of September 2020 and again on the 8th of January 2021. Studies were included if they compared the protective effect of respirators versus surgical masks in the treatment of patients infected with predominantly droplet transmitted respiratory infections within the health and care setting. On the 25th of January search results were reviewed to incorporate studies where respirators were evaluated as a form of source control. Additional grey literature searches of online resources was also carried out.

1. respirator.mp.
2. respirators.mp.
3. FFP*.mp.
4. filtering face piece.mp.
5. filtering facepiece.mp.
6. N95.mp.
7. respiratory protective equipment.mp.
8. RPE.mp.
9. exp respiratory protective devices/
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. exp infection/
12. exp infection control/
13. exp disease transmission, infectious/
14. 11 or 12 or 13
15. 10 and 14
16. limit 15 to english language
17. limit 16 to humans
18. limit 17 to covid-19

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