Transmission of SARS-CoV-2 in healthcare workers caring for patients with severe or critical COVID-19 on supportive ventilation

A rapid evidence review

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Declarations of Interests

None declared.

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Protocol/Topic Registration:

This rapid evidence review was registered with the National Collaborating Centre for Methods and Tools (NCCMT) (https://www.nccmt.ca/covid-19/covid-19-evidence-reviews/429).

Abbreviations

AGP	aerosol generating procedures
BiPAP	bilevel positive airway pressure
CPAP	continuous positive airway pressure
HCW	healthcare worker
HFNC	high flow nasal cannula
HFNO	high flow nasal oxygen
IMV	invasive mechanical ventilation
MA	meta-analysis
MERS	middle east respiratory syndrome
NIV	noninvasive mechanical ventilation
NMA	network meta-analysis
RR	rapid review
SARS	severe acute respiratory syndrome
SR	systematic review
WHO	World Health Organization

KEY FINDINGS

We located no comparative studies reporting exposure or transmission of SARS-CoV-2 in healthcare workers caring for hospitalized patients with severe or critical COVID-19 on supportive ventilation.

Instead, we summarized findings from 10 studies reporting the incidence of SARS-CoV-2 transmission to healthcare workers caring for patients with severe or critical COVID-19 on supportive ventilation. We also considered the use of personal protective equipment (mask, eye protection, gown, shield etc.) by healthcare workers exposed to patients on supportive ventilation.

In this rapid evidence review, we found ten descriptive studies reporting the incidence of transmission of SARS-CoV-2 to healthcare workers caring for patients with COVID-19 on high flow nasal oxygen, noninvasive ventilation (BiPAP, CPAP) or who were present for intubation procedures.

When appropriate PPE was not used by healthcare workers, there was documented transmission of SAR-CoV-2 to healthcare workers. None of the studies reported transmission to healthcare workers when appropriate PPE was described and used. Studies that reported appropriate PPE protections generally described use of global droplet precautions, surgical masks or N95 respirators along with eye protection/facial shields, gowns or aprons, hair protection, and gloves for any patient contact.

Rapid evidence review approach for the direct PICO

Research question

In healthcare workers (HCW) caring for patients with severe or critical COVID-19 on supportive ventilation, to what extent is the risk of nosocomial SARS-CoV-2 infection in HCW, higher with high flow nasal oxygen (HFNO), continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV) when compared to invasive mechanical ventilation (IMV)?

Methods overview

We conducted a rapid review of the evidence for noninvasive ventilation strategies and implemented the population, intervention, comparator, outcomes (PICO) framework to formulate the research question (Table 1):

Table 1: PICO framework

Population	Healthcare workers[a] caring for hospitalized patients with severe or critical COVID-19 and acute hypoxemic respiratory failure
Intervention	Provision of care/direct exposure to hospitalized patients with COVID-19 and acute hypoxemic respiratory failure on: • High flow nasal oxygen • Continuous positive airway pressure (facemask or helmet) • Noninvasive ventilation via facemask (or other non-helmet interfaces including nasal, oronasal, and full facial mask) • Noninvasive ventilation via helmet
Comparators	Provision of care/direct exposure to hospitalized patients with COVID-19 and acute hypoxemic respiratory failure on: • Invasive mechanical ventilation
Outcomes	Nosocomial SARS-CoV-2 infection in (or transmission to) healthcare workers
Eligible study designs	Systematic/rapid reviews to identify eligible trials, randomized controlled trials

a - May include, but are not restricted to, doctors, nurses, residents, therapists, technologists, or housekeepers.

Table 2 provides a summary of the methods used for this rapid evidence assessment. Where methods were not feasible due to a lack of eligible studies, deviations from the planned approach are noted.

Table 2: Summary of Methods

Search (systematic/rapid reviews)	Systematic/rapid reviews used to identify eligible trials Targeted search of COVID-19 meta-databases • WHO COVID-19 database • Living Overviews of Evidence (L.OVE) platform • COVID-END inventory of best evidence syntheses for clinical management Original search executed May 2-3, 2021 with alerts continued to December 19, 2021
Search (primary studies)	Top-up of recent primary studies published since date of last systematic/rapid review search • WHO COVID-19 register • Cochrane COVID-19 register • Clinicaltrials.gov • International Clinical Trials Registry Platform[a] Original search executed May 19, 2021 with alerts continued to December 19, 2021
Screening and selection	Single reviewer screened records using Covidence When they met the population, intervention, comparator, outcome: • Completed comparative primary studies from systematic/rapid reviews were included in this review • Completed comparative primary studies identified during the top-up search were included in this review <u>Protocol deviation:</u> As no completed comparative studies were located in the search, descriptive studies reporting incidence of healthcare worker transmission of SAR-CoV-2 associated with exposure to supportive ventilation interventions were included
Data tabulation	Single reviewer with checking by a second reviewer Study characteristics and reported outcome data for individual studies carried forward from the systematic/rapid reviews where possible or extracted *de novo*
Quality/ROB	As no completed comparative studies were located in the search, and incidence studies were summarized, no risk of bias or study quality assessments were completed
Synthesis	Descriptive. Meta-analysis as planned (pairwise for healthcare worker infection or transmission) was not feasible as no comparative studies were included
Summary of findings	Summary of Findings tables were not feasible

Involvement of citizen partners	Reviewed population, intervention, comparator, outcome and provided input. Co-produce a patient-specific knowledge translation product

a: Planned but not executed due to availability of the database during the period of this rapid review.

Rapid evidence review findings for the direct PICO

We located three relevant systematic reviews[1-5] reporting exposure or transmission of SARS-CoV-2 in healthcare workers caring for hospitalized patients with severe or critical COVID-19 on supportive ventilation. No eligible comparative studies were identified.

We summarized findings from ten descriptive studies[6-15] **reporting the incidence of SARS-COV-2 transmission to healthcare workers caring for patients with severe or critical COVID-19 on supportive ventilation.** In addition, we considered the appropriate use of personal protective equipment (mask, eye protection, gown, shield etc.) by healthcare workers exposed to patients on supportive ventilation.

Identified systematic reviews and rapid reviews

We searched for systematic reviews and rapid reviews published between January 1, 2020 and May 19, 2021 and screened 728 records. Search alerts were maintained until December 19, 2021.

A total of three eligible systematic reviews (SRs) reported in five[1-5] records were included. No eligible rapid reviews were identified.

Schünemann et al. (2020) is a living systematic review presenting four different streams of evidence related to ventilation techniques and COVID-19, including transmission to HCW in Stream 4[4]. The review did not update Stream 4 as part of the living updates. Authors considered a variety of evidence for aerosol-generating procedures (AGPs) including noninvasive ventilation (NIV), high-flow nasal oxygen (HFNO) and mechanical ventilation approaches. Studies of severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS) and pandemic influenzas were also eligible for inclusion and may provide informative indirect evidence relevant to this rapid evidence review. Based on the totality of the evidence for the AGPs, evidence showed heterogeneous effects for the transmission of SARS-CoV-2 to HCWs from AGPs, and authors concluded that "*these findings need to be interpreted with great caution, owing to a probable confounding effect of personal protective equipment (PPE) use and variable methods and reporting*"[4].

Two additional systematic reviews by Chan et al. (2021) and Cournoyer et al. (2021) assessed the risk of coronavirus transmission to HCW performing AGPs[1,2]. Both included studies of SARS, MERS and SARS-CoV-2. Chan et al. also considered the potential benefits of PPE during AGPs and considered studies of coronavirus 1 and 2. Author conclusions noted that "*specific AGPs (endotracheal intubation, NIV) are high risk for the transmission of SARS and SARS-CoV-2 from patients to healthcare workers. Personal protective equipment (N95 masks, gowns, gloves) reduce the odds of contracting SARS and SARS-CoV-2*"[1]. Cournoyer et al. concluded that "Being exposed or performing an intubation, bag-valve-mask ventilation, and NIV were associated with an increased risk of infection"[2].

No eligible comparative studies were identified after screening the included studies from the three included SRs.

Results from the top-up search

We conducted a top-up search for primary studies published between July 11, 2020[1] and May 19, 2021 and maintained search alerts until December 19, 2021. A total of 2,746 records were screened.

No eligible comparative studies were identified in the top-up search.

Evidence from available studies

As no eligible comparative studies were identified, **we summarized the available data for healthcare worker transmission of SARS-CoV-2 from ten descriptive reports and case-contact investigations[6-15]**. Records were included if they reported the exposure of healthcare workers to any supportive ventilation interventions in the PICO. Records that summarized broad exposure to aerosol generating procedures without detail pertaining to the specific ventilation supports in the PICO were not included or summarized.

Table 3 provides an overview of key study descriptors, including the HCW populations involved, ventilation support exposures, use of PPE, laboratory testing for SARS-CoV-2, and any risk of bias assessments carried forward from the originating SR (where applicable). Of the two studies with risk of bias assessment using the Newcastle Ottawa Scale carried forward from the systematic review, there were concerns about selection and comparability in one study by Ng et al. (2020) and exposure in comparability in Heinzerling et al. (2020). No *de novo* risk of bias assessments were conducted.

Many of the studies report case-contact investigations where a patient(s) entered hospital and received care prior to a positive test for SARS-COV-2. In many cases, and notably in those documented early in the pandemic during the winter and spring of 2020, HCW did not have appropriate PPE when supportive ventilation procedures were used. The studies predominantly tested only symptomatic HCWs, and not all exposed HCWs, likely missing cases of transmission to asymptomatic HCWs. Studies early in the pandemic may have tested HCWs too soon or too late after their exposure to index cases, however some studies did report multiple testing over 14 or 15 days[9,11,12].

Table 4 provides a summary of HCW exposure to noninvasive and invasive ventilation supports of interest according to the stated appropriateness of PPE use for all studies. **Eight of ten studies[6-15] reported HCW exposure to patients receiving endotracheal intubation or intubation[6-13]**. Off these, one study reported that none of the 72 HCWs interviewed had exposure to the only ventilation support relevant to the PICO (endotracheal intubation)[13]. A total of **four studies reported HCWs exposed to noninvasive ventilation support[8,9,11,14]**, **and one reported HCW exposure to HFNO[15]**. One study reported “ventilation” support without noting whether it was invasive or noninvasive[12]. Very few details are provided in the studies about specific type of noninvasive ventilation, although BiPAP and CPAP were specified in one study[8]. None of the studies reported specific use of facemask or helmet noninvasive ventilation.

[1] The date of the most recent search from the Schünemann et al. (2020) systematic review.

None of the studies reported any SARS-CoV-2 transmission to HCWs wearing appropriate PPE[9,11]. Studies that reported appropriate PPE generally described global use of droplet precautions, surgical masks or N95 respirator masks along with eye protection and/or facial sheilds, gowns or aprons, hair protection, and gloves.

Three of the four studies including HCWs caring for patients with COVID-19 while on supportive ventilation without appropriate PPE[6,8,14] reported at least one or more instances of SARS-CoV-2 transmission to the HCWs (endotracheal intubation, n=1 study; intubation, n=1 study; NIV, n=2 studies). Not all studies reported PPE use in enough detail for the appropriateness or percentage of time used to be ascertained or assessed[7,12,13,15].

None of the studies reported or tested for any specific SARS-CoV-2 variants of concern (e.g. delta or omicron by common name), although the studies were mostly reporting data from the early or mid-stages of the pandemic. Only one study reported the overall vaccination status of the HCWs and data from 2021.

Table 3: Summary of included studies for COVID-19 patients using supportive ventilation

Study; Country	Design/Setting	Period of Evaluation	Population	Assessment of PPE	Laboratory tests	Risk of bias
Ng et al., 2020[11] Singapore	Case-contact investigation; Hospital (ICU)	February 2020	41 HCWs responsible for caring for patient with severe pneumonia before confirming diagnosis of SARS-CoV-2 HCWs were exposed to AGPs (endotracheal intubation, extubation, noninvasive ventilation, and exposure to aerosols in an open circuit) for at least 10 minutes at less than 2 metres from the index patient	Yes on surgical mask or N-95 masks	Nasopharyngeal swab for PCR assay testing (day 1,2,4,5,14)	5/9[a]; concern related to selection and comparability
Heinzerling et al., 2020[8] CA, USA	Case-contact investigation; Hospital	February 2020	37 HCWs who were in contact with a confirmed case of SARS-CoV-2 (including 3 with positive results) to a variety of ventilation supports	HCWs only used gloves and/or face masks.	Nasopharyngeal and oropharyngeal specimens for real-time RT-PCR testing	6/9[a]; concern related to comparability and exposure
Liu et al., 2020[9] Wuhan, China	Cross-sectional study; Hospital	January-April 2020	420 HCWs (116 doctors, 304 nurses) deployed to Wuhan for 6 to 8 weeks to deliver care to patients with severe or critical COVID-19 and were involved in at least one AGP (tracheal intubation, noninvasive mechanical ventilation, gastric intubation, sputum aspiration, aerosol inhalation, tracheostomy/care, throat swab collection.)	HCWs were provided with appropriate PPE, including protective suits, surgical or N95 masks, gloves, hair covers, goggles, face shields, and gowns or aprons	Serologic SARS-CoV-2 testing with nucleic acid (Day 1, 7, 14) and IgM or IgG antibody tests	Not assessed

Study; Country	Design/Setting	Period of Evaluation	Population	Assessment of PPE	Laboratory tests	Risk of bias
Lucar et al., 2020[10] MS, USA	Case-contact investigation; Hospital (prolonged orthopedic surgical intervention)	March 2020	11 HCW exposed to trauma patient during hospitalization and 6+ hour surgery which included endotracheal intubation without appropriate PPE.	Routine surgical PPE changed to COVID-19 PPE mid-surgery when case suspected	Nasopharyngeal specimens; RT-PCR testing of single symptomatic HCW only (timing of test not reported); other 10 HCW not tested.	Not assessed
Periyasamy et al., 2020[12] Malaysia	Case-contact investigation; Hospital (ED and ICU exposure)	February-March 2020	25 HCW exposed to AGPs by severe pneumonia patient who later tested positive for SARS-CoV-2. Procedures included nebulizer therapy, endotracheal intubation, invasive ventilation, and tracheal suctioning.	Surgical or N95 masks and “different levels of PPE”	Nasopharyngeal specimens; RT-PCR testing at day 1,9,13,15	Not assessed
Bays et al., 2020[6] USA	Case-contact investigation with active case-finding; Hospital (oncology, ICU)	February-March 2020	145 HCW exposed to AGPs (endotracheal intubation) for 2 patients (case 1 and 2) without appropriate PPE. * Focus on Case 2 (oncology patient) as Case 1 patient covered in Heinzerling et al. 2020[8].	“PPE without airborne or droplet protection”	Nasopharyngeal specimens; RT-PCR. No asymptomatic testing.	Not assessed
Ran et al., 2020[13] Wuhan, China	Retrospective cohort; Hospital	December 2019-January 2020	72 HCW classified by high and low risk exposures to patients with COVID-19, including some to tracheal intubation.	Varied. A total of 49 categorized as ‘improper PPE”, but no details of use during ventilation support.	RT-PCR. No other details provided.	Not assessed.
Chatterjee et al., 2020[7]	Case-control investigation (Interviews at day	May 2020	378 symptomatic HCW who tested positive on RT-PCR following hospital work (along with 373 who	Varied. Approximately 20% reported “never using PPE” and mask	RT-PCR	Not assessed.

Study; Country	Design/Setting	Period of Evaluation	Population	Assessment of PPE	Laboratory tests	Risk of bias
India	7 to discover exposure status); Hospital		tested negative). Includes doctors, nurses, auxiliary midwives housekeeping staff, security, and other (undescribed). AGPs were considered, including intubation.	type was not differentiated between surgical, N95 etc.		
Al Lawarti et al. 2021[14] Oman	Case-contact investigation; Hospital (HDU)	July 2020	38 HCW exposed to COVID-19 patient who received 48 hours of NIV prior to diagnosis of COVID-19 and implementation of appropriate contact and airborne isolation precautions.	Not while NIV administered for first 48 hours.	RT-PCR	Not assessed.
Rhee at al. 2022 (online first July 2021)[15] MA, USA	Case-contact investigation; Hospital (ICU)	April 2021	52 HCW exposed, including 12 directly exposed, to a highly symptomatic, but undiagnosed COVID-19 patient in the ICU receiving HFNO in a positive pressure room.	Universal masking surgical) policy with standard precautions including eye protection for all patient encounters; patient was unmasked during all encounters.	RT-PCR ≥ day 3, not all staff tested.	Not assessed.

RT-PCR= Reverse transcription polymerase chain reaction; PCR= polymerase chain reaction; HCW=healthcare worker; ED=emergency department; AGP=aerosol generating procedures; ICU=intensive care unit; HDU=high-dependency unit; BiPAP=bilevel positive airway pressure; CPAP=continuous positive airway pressure; PPE=personal protective equipment; NIV=noninvasive ventilation; HFNO=high flow nasal oxygen

a: assessed from the Schünneman et al. SR based on assessment with the Newcastle-Ottawa Scale.

Table 4: HCW Transmission data by study

Study; Country	Ventilation support exposure	HCW exposed to patient on ventilation support	Transmission of SARS-CoV-2 to HCW wearing appropriate PPE	Transmission of SARS-CoV-2 to HCW without appropriate PPE
Ng et al., 2020[11] Singapore	Endotracheal intubation	10/41 (4 surgical mask, 6 N95 mask)	0	NA
	NIV (ICU or HDU)	25/41 (25 surgical mask, 0 N95 mask)	0	NA
Heinzerling et al., 2020[8] CA, USA *Of 141 exposed HCW, interviewed n=37 for exposures.	NIV (BiPAP, CPAP)	6/37	NA	2
	Intubation, performed or assisted	2/37	NA	1
	Intubation, present in room	11/37	NA	0
Liu et al., 2020[9] Wuhan, China	Tracheal intubation	98/116 doctors 0/304 nurses	0[a]	NA
	Noninvasive mechanical ventilation	0/116 doctors 227/304 nurses	0[a]	NA
Lucar et al., 2020[10] MS, USA	Endotracheal intubation	3/11	NA	0[b]
Periyasamy et al., 2020[12] Malaysia	Ventimask, nebulizer or oral suctioning (with surgical mask)	15/25	0	
	Intubation (with N95 mask)	3/25	0	
	Ventilation (with surgical mask)	4/25	0	
	Ventilation (with N95 mask)	3/25	0	
Bays et al., 2020[6]	Endotracheal intubation[c]	7/145	NA	4

Study; Country	Ventilation support exposure	HCW exposed to patient on ventilation support	Transmission of SARS-CoV-2 to HCW wearing appropriate PPE	Transmission of SARS-CoV-2 to HCW without appropriate PPE
USA				
Ran et al., 2020[13] Wuhan, China	Tracheal intubation	0/72[d]	NA	
Chatterjee et al., 2020[7] India	Endotracheal intubation	31/751	22	
Al Lawarti et al. 2021[14] Oman	NIV	38/38	NA	33 (7 doctors 26 nurses)[e]
Rhee at al. 2022 (online first July 2021)[15] MA, USA	HFNO	52/52 had circular room pod (distance) exposure	0[f]	
	HFNO	12/52 had direct care exposure	0[f]	

NA = no applicable; HCW=healthcare worker; ICU=intensive care unit; HDU=high-dependency unit; BiPAP=bilevel positive airway pressure; CPAP=continuous positive airway pressure; PPE=personal protective equipment; NIV=noninvasive ventilation; HFNO=high flow nasal oxygen

a: Zero symptoms in any HCW also noted in study.
b: One of three HCW became symptomatic a few hours after assisting with the intubation, but tested negative.
c: The HCW performing the procedure wore a surgical mask without eye protection. The other 6 HCWs wore neither masks nor eye protection.
d: None of HCWs in the study had participated in tracheal intubations, and no other NIV are described.
e: There may be one additional positive case in a paramedic, but reporting is not clear enough to elucidate this conclusively.
f: Study notes universal masking and an 84% HCW vaccination rate.

Conclusions

There are no comparative clinical studies reporting the risk of transmission of SARS-CoV-2 in healthcare workers caring for hospitalized patients with severe or critical COVID-19 on supportive ventilation.

Three included systematic reviews broadly conclude that aerosol generating procedures for patients, including supportive ventilation strategies, increase the risk of SARS, MERS and SARS-CoV-2 transmission to healthcare workers. Endotracheal intubation and noninvasive ventilation are specifically noted to increase risk in two of the systematic reviews.

In this rapid evidence review, we found ten descriptive studies reporting the incidence of transmission of SARS-CoV-2 to healthcare workers caring for patients with COVID-19 on high flow nasal oxygen, noninvasive ventilation (BiPAP, CPAP) or who were present for intubation procedures. When appropriate PPE was not used by healthcare workers, there was transmission of SAR-CoV-2 to healthcare workers. None of the studies reported transmission to healthcare workers when appropriate PPE was described and used. Studies that reported appropriate PPE protections generally described use of global droplet precautions, surgical masks or N95 respirators along with eye protection/facial shields, gowns or aprons, hair protection, and gloves.

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