### *Table 1.* **Evidence Profile for NIV Compared With IMV for Patients With COVID-19 and Acute Hypoxemic Respiratory Failure <<AU: Please add all relevant reference numbers to the table.>>**

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| **Variable** | **Certainty Assessment** | | | | | | | **Findings** | **Certainty** | **Importance** |
|  | **Studies, *n*** | **Study Design** | **Risk of Bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other Considerations** |  |  |  |
| Mortality (follow-up, 90 d to unknown) | 3 | Observational | Not serious\* | Serious† | Not serious‡ | Not serious | None§ | NIV and IMV may have similar effects, but the exact comparative effect is uncertain. There were 103 patients analyzed in 1 study on COVID-19, showing an HR of 1.61 (95% CI, 0.84–3.09), and 303 patients with MERS (adjusted OR, 0.61 [CI, 0.23–1.60]) and 493 patients with SARS patients (adjusted OR, 0.36 [CI, 0.16–0.78]). Ten additional eligible studies in patients with COVID-19 presented only unadjusted results.|| | ⨁◯◯◯ Very low | Critical |
| Need for invasive ventilation (follow -up time not defined) | 1 | Observational | Not serious | Not serious | Not serious | Serious¶ | None | OR, 0.36 (CI, 0.16–0.78); 493 patients with SARS | ⨁◯◯◯ Very low | Critical |
| Risk for virus transmission to HCWs through AGPs (including intubation, airway suctioning, close contact through nasopharyngeal swabs) (assessed with multiple methods, including infection) | 25 | Observational | Serious\*\* | Not serious | Not serious†† | Not serious | None | Studies published before 2010 in patients with SARS suggested that NIV (2 cohort studies; OR, 3.1 [CI, 1.4–6.8), manipulation of a BiPAP mask (1 cohort study; OR, 6.2, [CI, 2.2–18 1]), and manual ventilation before intubation (1 cohort study; OR, 2.8 [CI, 1.3–6.4]) increased the odds of transmission. Eight studies also assessed tracheal intubation as the AGP and reported an unadjusted increase in the odds of transmission: pooled OR, 6.6 (CI, 2.3–18.9) across 4 cohort studies and 6.6 (CI, 4.1–10.6) across 4 case–control studies. There were no comparative studies in COVID-19, but 2 studies evaluating NIV in COVID-19 (58, 61) reported unadjusted rates of transmission to HCW. Thirteen additional studies in COVID-19 and MERS described the risk for transmission from procedures including intubation and mechanical ventilation, but these studies were not adjusted. The risk seems to be increased from both NIV and IMV, but the comparative risk is uncertain.‡‡§§ | ⨁◯◯◯ Very low | Critical |

AGP = aerosol-generating procedure; BiPAP = bilevel positive airway pressure; COVID-19 - coronavirus disease 2019; CPAP = continuous positive airway pressure; HCW = health care worker; HR = hazard ratio; IMV = invasive mechanical ventilation; MERS = Middle East respiratory syndrome; NIV = noninvasive ventilation; OR = odds ratio; RR = risk ratio; SARS = severe acute respiratory syndrome.

\* Studies were nonrandomized and were evaluated by using the Newcastle-Ottawa Scale. We did not rate down further, although only unadjusted studies were available for patients with COVID-19 and at higher risk of bias, but we placed emphasis on the evidence at lower risk of bias.

† The 3 studies reported widely different point estimates. They could not be meta-analyzed; 1 study in patients with COVID-19 reported an HR that could not be converted to an OR or an RR because of high baseline event rates. Although we could not evaluate the degree of overlap in CIs across the 3 studies (because of the use of different effect measures), 2 of the studies had CIs that appeared nonoverlapping; therefore, we rated down for inconsistency.

‡ We did not rate down for indirectness for the association between NIV and IMV in patients with SARS or MERS, because the viruses that cause these diseases belong to the same family as that which causes COVID-19. However, the pathophysiology may differ, and future studies may change this judgment. We also did not rate down for intervention indirectness, although NIV can be applied in many different ways. Here, we referred to BiPaP and CPAP, including CPAP with helmets.

|| In the only study from Italy, Duca and associates (26) reported a higher death rate in patients receiving helmet CPAP or other NIV compared with IMV. Wang and colleagues (29) found low rates of rescue invasive ventilation in patients receiving NIV or high-flow oxygen via nasal cannula. Wu and associates (31) reported a mortality rate greater than 60% in the NIV group and of 100% in the IMV group. We did not calculate effect estimates, given the high risk for confounding and selection bias as well as other potential biases in these studies.

¶ Total number of patients and events borderline low despite statistical significance.

\*\* We rated down for risk of bias because most relevant studies largely presented unadjusted results

‡‡ All studies published before 2020 were performed in patients with SARS or MERS. There were 4 studies in patients with COVID-19 that demonstrated a risk for transmission associated with AGP. We did not rate down for indirectness.

§§ Five studies published after 2010 reported on the number of staff who performed AGPs and who were infected. Three of these studies found no cases of transmission to HCWs in the following AGPs: bronchoscope-guided endotracheal intubation through nasal insertion; airway suction, nebulizer treatment, sputum induction, bronchoscopy, and intubation; or nasopharyngeal swab. The fourth study showed a 11% infection rate among anesthetists who had direct contact with patients with COVID-19 who received oxygen via nasal cannula. The fifth study reported on a nurse administrator who contracted MERS-CoV infection after being present in the intensive care unit during 2 simultaneous cardiac resuscitations and having face-to-face contact with a febrile HCW. Four additional laboratory studies support the risk for transmission of coronavirus from AGPs.

### *Table 2.* **Evidence Profile for NIV Compared With No Mechanical Ventilation for Patients With COVID-19 and Acute Hypoxemic Respiratory Failure<<AU: Please add all relevant reference numbers to the table.>>**

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| **Variable** | **Certainty Assessment** | | | | | | | **Findings** | **Certainty** | **Importance** |
|  | **Studies, *n*** | **Study Design** | **Risk of Bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other Considerations** |  |  |  |
| Mortality (follow-up, 90 d to unknown for 1 study) | 2\* | Observational | Not serious† | Not serious | Not serious \* | Not serious ‡ | None § | NIV may reduce the risk for death compared with no mechanical ventilation. There were 2 studies in 187 patients (1 RCT in 60 patients, with 3 events in 30 patients in the no mechanical ventilation group and 0 events in 30 patients in the NIV group; 1 cohort study with 127 patients, with an OR of 0.21 (95% CI, 0.09–0.47). | ⨁⨁◯◯ Low | Critical |
| Risk for virus transmission to HCWs through AGPs (including intubation, airway suctioning, close contact through nasopharyngeal swabs) | 6 | Observational | Not serious | Not serious|| | Not serious\* | Not serious | None § | NIV may increase the risk for transmission of COVID-19 to HCWs. In SARS and MERS, NIV (2 cohort studies; OR, 3.1 [CI, 1.4–6.8]), manipulation of a BiPAP mask (1 cohort study; OR, 6.2 [CI, 2.2–18 1]) and manual ventilation before intubation (1 cohort study; OR, 2.8 [CI, 1.3–6.4]) also showed increased odds of transmission. Two studies evaluating NIV in COVID-19 (Ng and colleagues [58] and Heinzerling and associates [61]) reported cases of transmission to HCWs. ¶ | ⨁⨁◯◯ Low | Critical |

AGP = aerosol-generating procedure; BiPAP = bilevel positive airway pressure; COVID-19 - coronavirus disease 2019; CPAP = continuous positive airway pressure; HCW = health care worker; MERS = Middle East respiratory syndrome; NIV = noninvasive ventilation; OR = odds ratio; RCT = randomized controlled trial; SARS = severe acute respiratory syndrome.

\* We did not rate down for population indirectness, because the viruses that cause SARS and MERS belong to the same family as that which causes COVID-19. However, the pathophysiology may differ, and future studies may change this judgment. We also did not rate down for intervention indirectness, although NIV can be applied in many different ways. Here we referred to BiPaP and CPAP, including CPAP with helmets.

† One study was an RCT (at some risk of bias due to imbalances in baseline characteristics) and 1 was a nonrandomized study, evaluated by using the Newcastle-Ottawa Scale without major concern for risk of bias. We did not rate down further, although only unadjusted studies were available for patients with COVID-19 and at higher risk of bias. This is because there is no convincing evidence yet that NIV would have different effects on COVID-19 compared with SARS and MERS.

‡ There was 1 RCT and 1 cohort study. The RCT had only 3 events in 60 patients. We did not rate down for imprecision, but noted that a total of 187 patients will lead to somewhat imprecise estimates. There also is evidence from RCTs summarized in our review of systematic reviews that supported the findings and, therefore, was not rated down for imprecision.

§ The effect is large, considering the thresholds set by GRADE, assuming that the OR translates into similar magnitudes of relative risk estimates. Although the effect was large, given residual concerns about risk of bias, we did not rate up because of some concerns about imprecision (GRADE suggests rating up for large effect if the effects were precise).

|| Studies reported differences in the risk for transmission, but owing to poor reporting, we could not identify reasons for differences in transmission. We did not rate down for inconsistency because the variability of the effect is beyond a threshold of concern that leads to similar interpretation at the systematic review level. The final rating of inconsistency should depend on an actual decision threshold set by decision makers or guideline development group.

¶ Four additional studies published after 2010 reported on the number of staff who performed AGPs and who became infected. Three of these studies found no cases of transmission to HCWs with the following AGPs: bronchoscope-guided endotracheal intubation through nasal insertion; airway suction, nebulizer treatment, sputum induction, bronchoscopy, and intubation; or nasopharyngeal swab. The fourth study showed a 11% infection rate among anesthetists who had direct contact with patients with COVID-19 who received oxygen via nasal cannula. Yet, 6 additional laboratory studies support the risk for transmission of coronavirus from AGPs.

## *Table 3.* **Recommendations From Various Organizations Regarding NIV<<AU: Please add all relevant reference numbers to the table.>>**

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| **Organization** | **Document** | **Country** | **Date** | **HFNC Recommended?** | **BiPAP Recommended?** | **CPAP Recommended?** | **Risk to Staff** |
| American Association for Respiratory Care: <https://www.aarc.org/resources/professional-documents/guidance-documents/> | Guidance Document: SARS CoV-2 | United States | 2020 | Yes; HFNC over NIPPV in acute hypoxemic respiratory failure despite conventional oxygen | No comment | No—not recommended owing to high failure rate; can be used with close monitoring if HFNC not available | No comment |
| Australian and New Zealand Intensive Care Society (ANZICS): <https://www.anzics.com.au/coronavirus-guidelines/> | ANZICS COVID-19 Guidelines: Version 1 | Australia and New Zealand | 16 March 2020 | Yes, recommended where staff have airborne PPE for hypoxia and negative pressure room | No—NIV not recommended unless atypical presentation, such as COPD, and staff have airborne PPE and a negative pressure room | No—NIV not recommended unless atypical presentation, such as COPD, and staff have airborne PPE and a negative pressure room | High risk for aerosolization with NIV; recommends airborne PPE and a negative pressure room |
| European Society of Intensive Care Medicine and the Society of Critical Care Medicine 2020: <https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19> | Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults With Coronavirus Disease 2019 (COVID-19) | International | 28 March 2019 | Yes, recommended over conventional oxygen and NIVVP, for hypoxemia despite conventional oxygen therapy | Selected patients, for a trial of NIPPV if HFNC not available; uncertain of the evidence for helmet CPAP; close monitoring | Selected patients, for a trial of NIPPV if HFNC unavailable; uncertain of the evidence for helmet CPAP; close monitoring | Suggests fitted respirator masks and negative pressure rooms |
| ICM Anaesthesia: <https://icmanaesthesiacovid-19.org/critical-care-preparation-and-management-in-the-covid-19-pandemic> | Critical Care Preparation and Management in the COVID-19 Pandemic | United Kingdom | 17 March 2020 | No—should be avoided; no survival benefit compared with conventional oxygen therapy, and the risk for environmental viral contamination | No comment | Use for short periods, with a well-fitting mask; may be a bridge to IMV or the ceiling of care | Risk for aerosolization with HFNC |
| Jin et al, *Military Medical Research*: <https://mmrjournal.biomedcentral.com/track/pdf/10.1186/s40779-020-0233-6> | A Rapid Advice Guideline for the Diagnosis and Treatment of 2019 Novel Coronavirus (2019-nCoV) Infected Pneumonia (Standard Version) | International | 6 February 2020 | Yes, if patient is in ARDS despite conventional oxygen therapy |  | Can be considered in selected patients; high failure rate in MERS; trial of 1 h | Recommends aerosol precautions |
| National COVID-19 Clinical Evidence Taskforce: <https://covid19evidence.net.au/> | Management of Patients With Severe to Critical COVID-19 Disease | Australia | 16 April 2020 | Yes; considered when patient cannot maintain Sao2 ≥92% with standard oxygen delivery despite conventional oxygen delivery | No Comment | No—in patients with hypoxemia associated with COVID-19 disease, do not routinely use NIV; can be considered in certain clinical scenarios | Recommends HFNC in negative pressure rooms, rooms with only patients with COVID-19, and adequate staff protection |
| NHS England: <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/specialty-guide-NIV-respiratory-support-and-coronavirus-v3.pdf> | Guidance for the Role and Use of Non-invasive Respiratory Support in Adult Patients With COVID-19 (Confirmed or Suspected): Version 3 | United Kingdom | 6 April 2020 | No—not recommended, owing to lack of efficacy and risk for onward spread | Not usually needed, reserved for those with hypercapnic acute on chronic ventilatory failure | Yes; NIV preferred but should not replace early intubation; if trialled, monitor every 30 min; can be used as bridge to intubation | Risk with HFNC |
| UpToDate: <https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-critical-care-issues> | Coronavirus Disease 2019 (COVID-19): Critical Care and Airway Management issues | International | 1 March 2020 | Decision on HFNC or NIV should be made by balancing the risks and benefits to the patient, the risk for exposure in HCWs, and best use of resources; this approach should be reassessed as new data become available |  | Decision on HFNC or NIV should be made by balancing the risks and benefits to the patient, the risk for exposure in HCWs, and best use of resources; this approach should be reassessed as new data become available | Risk for aerosolization above 6 L; NIV carries risk for aerosolization |
| World Health Organization:  <https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected> | Clinical Management of Severe Acute Respiratory Infection When COVID-19 Disease Is Suspected | International | 13 March 2020 | Selected patients, trial of 1 h, reduces need for intubation, close monitoring needed, may be used in mild to moderate hypercapnia | Selected patients | Selected patients, close monitoring; risks include delayed intubation, large tidal volumes, and injurious transpulmonary pressures | Uncertain risk for aerosolization; airborne precautions should be used |

AGP = aerosol-generating procedure; ARDS = acute respiratory distress syndrome; BiPAP = bilevel positive airway pressure; COPD = chronic obstructive pulmonary disease; COVID-19 - coronavirus disease 2019; HCW = health care worker; HFNC = high-flow oxygen by nasal cannula; IMV = invasive mechanical ventilation; MERS = Middle East respiratory syndrome; NIPPV = noninvasive positive-pressure ventilation; NIV = noninvasive ventilation; PPE = personal protective equipment; SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2.