intubated early. Furthermore, outcome data on patients who are treated with HFNC initially, specifically nonurgent patients, indicate reduced rates of endotracheal intubation without any significant difference in mortality when compared with conventional oxygen therapy in both coronaviruse induced acute respiratory distress syndrome (2) and typical patients with acute respiratory distress syndrome (3). These reports suggest that a strategy of HFNC first in nonurgent patients could reduce ventilator use further if employed at the outset. In our intensive care unit, we favor a strategy that combines the use of HFNC, NIV (when heart failure or obstructive lung disease is present), and IMV in a sequential manner. We believe, the key to success with this approach is an early and standardized assessment of noninvasive device failure by monitoring work of breathing, respiratory rate and using standardized assessment tools such as the ROX index (4). In contrast, the study referenced by the authors pointing to the potential harm of HFNC in nonurgent patients is a retrospective observational study that considers failure when patients desaturate on maximum fraction of inspired oxygen, become hypercapnic, or develop metabolic acidosis and shock, potentially too late for fostering optimal outcomes (5).

Although we appreciate this important study that attempts to help with the allocation of scarce resources, we fear the conclusion that favors early mechanical ventilation may be premature. We kindly ask the authors to elucidate further how nonurgent patients were defined and point estimates derived. A sensitivity analysis using HFNC outcomes from available meta-analyses would be desirable. Particularly at a time when the critical care community is mired in a hot debate regarding the benefits of earlier intubation to prevent lung injury (6), we believe these are important points to clarify because they might have significant adverse public policy impact.

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Reply: Optimal Respiratory Assistance Strategy for Patients with COVID-19

From the Authors:

Hatipoğlu and colleagues raise two main questions in their letter: Who exactly are "nonurgent" patients? And how should our findings that a strategy of high-flow nasal cannula (HFNC) coupled with early invasive mechanical ventilation (MV) for patients with coronavirus disease (COVID-19)–associated acute respiratory distress syndrome (ARDS) be interpreted for use in clinical medicine and public health?

Our definition of "nonurgent" patients as "those clinicians would feel are at high risk of needing MV, but do not need it urgently (akin to those enrolled in trials of HFNC pre-MV)" is, admittedly, vague. To better conceptualize who these patients are, we direct readers to the parameters used to describe them (Table 1 in our manuscript [1]): 5% will die and 65% will deteriorate without the institution of HFNC or MV (the remaining 30% will recover without advanced respiratory support and leave the hospital alive), and, as a group, they will exist on simple supplemental oxygen (low-flow nasal cannula or face mask) for, on average, 20 hours before their death, deterioration, or recovery occurs. What does that look like? Assuming those who recover stay in the hospital for 2 days, those who die or deteriorate will last only 8 hours without either HFNC or MV. Put simply, these are not patients who are stable on low-flow nasal cannula; rather, without access to HFNC or MV (or noninvasive positive-pressure ventilation), more than two-thirds will deteriorate or die in short order. Although we agree a careful, protocolized approach to escalating respiratory support may be successful in safely avoiding MV in many of these patients, some will worsen and require MV urgently. And although the evidence is admittedly imperfect, we cannot ignore the potential harm associated with delaying intubation for those who eventually need it.

In interpreting our findings, it is important to remember that our simulation assesses the impacts of different respiratory support allocation strategies on the *population*, not the individual. Model inputs represent estimates of population averages determined from available literature on non–COVID-19 ARDS (including, as suggested by Hatipoğlu and colleagues, "HFNC outcomes from available metaanalyses") adjusted by clinician experience with COVID-19. Model outcomes include cumulative deaths across a

population and days when that population does not have access to a ventilator. Our model is not capable of assessing the impact of initiating HFNC (or performing early intubation for MV) on individual patients, each with their own unique disease trajectory and risk for decompensation.

Our work is not intended to promote a public policy mandating use of early MV when available supply exceeds a threshold of 10% of total capacity and HFNC otherwise. Rather, it is meant to demonstrate that given our best understanding of the potential benefits and harms of each device in COVID-19–associated ARDS, a strategy inclusive of both devices is preferable. Early in the epidemic, many sites avoided use of HFNC; neither this approach nor one of complete avoidance of early intubation for all "nonurgent" patients is optimal. Clinician judgment coupled with close monitoring of patients' responses to chosen strategies will always play into deciding which "nonurgent" patients get HFNC (and/or noninvasive positive-pressure ventilation) and which get early intubation. Our simulation is valuable in that it suggests that including HFNC in clinicians' arsenals and allowing for early intubation when MV supply allows is reasonable and will likely result in the best outcomes for the population as a whole.

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