not included in the study (data not shown). In addition, the exposure–outcome effect estimates may be further impacted because of unmeasured confounding; however, covariates in the final model reflect those that have been previously described to be associated with NTM acquisition. Finally, our study only evaluated incident NTM isolation in CF rather than NTM lung disease (as this was a rare event); however, NTM isolation alone is an important clinical endpoint in CF.

The potential increased risk of NTM conferred by VDD may have important clinical consequence for the management of individuals with CF. More frequent monitoring of vitamin D concentrations and targeted attempts at aggressive repletion—especially in those who are significantly deficient—may warrant investigation as to whether they would reduce the risk of NTM infection. Further prospective studies with larger populations are warranted to better define the relationship between VDD and the risk of NTM infection and disease in CF.

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Optimal Respiratory Assistance Strategy for Patients with COVID-19

To the Editor:

We read with interest the study by Gershengorn and colleagues on the impact of high flow nasal cannula (HFNC) use on clinical outcomes and allocation of invasive mechanical ventilators (IMVs) among patients with coronavirus disease (COVID-19) related acute hypoxemic respiratory failure (AHRF) (1). The authors apply computer simulation to determine the utility of HFNC as part of several treatment strategies in improving outcomes and invasive mechanical ventilator availability. The authors conclude that the best strategy is one that employs early intubation of patients who do not need IMV urgently but incorporates HFNC oxygen therapy when mechanical ventilator inventory falls below 10% of capacity. Although incorporating HFNC oxygen therapy into the treatment of patients with COVID- 19 related respiratory failure makes intuitive and scientific sense, we question the promotion of early intubation for patients who do not require such intervention at the time of initial assessment.

The authors define "nonurgent" patients as those clinicians would feel are at high risk of needing IMV but do not need it urgently. These are the patients who would be managed with alternative means of respiratory assistance such as noninvasive ventilation (NIV) and HFNC oxygen treatment in practice and also in clinical trials. Consequently, by definition, we have no outcome data on how such patients would have done had they been

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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

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