Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

coronavirus disease 2019 in this population was very low, making it completely different from that enrolled by Hamed et al.[1]

In conclusion, the two aforementioned studies underline the critical importance of the population being examined. It is key that BAL and less invasive methods be compared prospectively in a cohort of consecutive patients with suspected SARS-Cov-2 infection who have been enrolled based on criteria decided beforehand, preferably across a wide spectrum of disease severity. This would allow us to decide reliably when it is clinically useful to perform an invasive procedure that, in this specific setting, implies organizational complexity and risks to the health-care staff.

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Response

To the Editor:

We note with interest the letter from Trisolini et al in response to our recent report of nasopharyngeal-lung gradient in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among critically ill patients.[1] They draw attention to the apparently contrasting findings of Geri et al,[2] who found that BAL in patients who are not ventilated with hypoxemic respiratory failure with negative nasopharyngeal polymerase chain reaction (PCR) for SARS-CoV-2 identified only two additional cases of coronavirus disease 2019 (COVID-19). In our report, we noted that 33% of patients with positive deep lung samples (BAL or endotracheal aspirate) had negative nasopharyngeal PCR.[1] Our finding of both false-negative nasopharyngeal swabs and higher viral load in the lungs is consistent with other reports. Wang et al[3] noted a significantly higher positivity rate for BAL (93%) compared with a nasal swab (63%), findings which were replicated in a recent metanalysis of seven diagnostic studies[4] that included those of Wang et al.[3]

We believe the key to understanding these apparently divergent results lies in the differences in the populations that were examined. Our study and those analyzed by Bwire et al[4] included only patients with PCR-confirmed COVID-19 and examined viral detection at different sites, whereas Geri et al[2] investigated patients with undifferentiated respiratory failure. Our study included patients who were admitted at the peak of the first wave of the pandemic in the United Kingdom, and the ICUs that were involved were largely or completely occupied by patients with COVID-19, whereas the prevalence in centers in the study by Geri et al[2] was 21%. Furthermore, all patients had sufficiently severe respiratory failure to merit admission to ICU, and all but one were receiving ventilatory support. Finally, 40% of the patients in the study of Geri et al had no evidence of viral pneumonitis on CT scans. Overall, it appears the divergent results arise from differing pretest probabilities of infection. With a relatively low pretest probability, it is perhaps unsurprising that Geri et al[2] detected only an additional 2.5% cases by bronchoscopy. We do not believe this invalidates the use of deep lung samples to investigate undifferentiated severe respiratory failure, especially as we enter the influenza season in the northern hemisphere. Sampling of the distal lungs can aid the identification of both SARS-CoV-2 and other viral or bacterial pathogens, although the relative roles of

endotracheal aspirate and BAL in this setting remain to be determined. When the implications of any study are being interpreted, it is vital to consider the population sampled and to be wary of applying findings to populations that were not well represented in the study under consideration.

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Decrease Dead Space Prior to Calling the ECMO!

To the Editor:

We have read with interest the article by Bullen et al[1] in the September 2020 issue of *CHEST*. The authors provide the example of a patient with severe ARDS and respiratory acidosis leading to veno-venous extracorporeal membrane oxygenation (VV-ECMO) and propose a detailed algorithm to select patients requiring VV-ECMO. In this algorithm, one important step is missing. The optimization of lung-protective ventilation should include minimization of the dead space. The total dead space includes the instrumental dead space (comprising the heat and moisture exchanger, catheter mount, several connectors, and the endotracheal tube), in addition to the anatomical dead space and alveolar dead space (Fig 1). The dead space reduces CO_2 removal, and this effect is particularly relevant when low or very low tidal volumes (TVs) (≤ 6 mL/kg predicted body weight [PBW]) are set in association with a high or very high respiratory rate (RR) (≥ 25 breaths/min),[2] which is usually the case in patients with severe ARDS who are potential candidates for ECMO. The impact of instrumental dead space has been shown previously when moderately reduced TV and moderately increased RR were used. In the study by Prat et al,[3] the $Paco_2$ went from 80.3 mm Hg to 63.6 mm Hg after reducing the instrumental dead space from 120 mL to 0 mL in 10 patients with ARDS. The mean TV was 6.9 mL/kg, and the mean RR was 20 breaths/min.

More recently, Richard et al[4] found that 88% of the patients had a TV < 5.25 mL/kg PBW and two-thirds of the patients with ARDS could receive ultraprotective ventilation (mean TV < 4.2 mL/kg PBW) without extracorporeal CO_2 removal when mechanical ventilation management was optimized. Optimization comprised a reduction of the dead space (by replacing the heat and moisture exchanger by a heated humidifier and by removing useless connectors such as the catheter mount) and with high RR. The maximal reduction of the dead space is now a recommendation for managing patients with ARDS.[5] However, it would be acceptable to use ECMO or extracorporeal CO_2 removal if $Paco_2$ remained too high (after minimizing the dead space) to further