Prone positioning for patients with hypoxic respiratory failure related to COVID-19

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Pneumonia is the most common reason for admission to hospital among patients with coronavirus disease 2019 (COVID-19), and many such patients will require supplemental oxygen.[1] Severe pneumonia can result in acute hypoxic respiratory failure necessitating supplemental oxygen therapy or respiratory support with mechanical ventilation. Severe acute respiratory failure may result in acute respiratory distress syndrome (ARDS) — a form of noncardiogenic pulmonary edema precipitated by a direct (e.g., pneumonia) or indirect (e.g., pancreatitis) injury. The mainstays of the management of ARDS are treating the underlying precipitant and supportive care, which includes mechanical ventilation with every effort to mitigate ventilator-associated lung injury. Ventilation in the prone position is a technique that has been employed and evaluated over the past 3 decades among patients who are mechanically ventilated for all severities of ARDS, with the greatest benefits seen among those with moderate to severe ARDS, for which it is now considered standard of care.[2]

During the COVID-19 pandemic, as health care systems scrambled to accommodate the surge in patients with acute respiratory failure, reports emerged of the potential benefit of prone positioning of patients with COVID-19 who were hypoxic and not intubated.[1] The findings of several observational studies suggested that prone positioning may improve oxygenation among patients on both low-flow (e.g., nasal prong oxygen) and higher-flow oxygen delivery devices (e.g., high-flow nasal cannula) not yet receiving mechanical ventilation.[1,3–7] We discuss prone positioning, its physiologic mechanisms, who may be eligible to receive it, accumulating evidence related to its effectiveness among patients with hypoxic respiratory failure related to COVID-19 pneumonia and potential harms of the procedure. By summarizing the available literature available to guide clinicians in the use of prone positioning for this population (Box 1), we also draw attention to important areas of future investigation.

Box 1: Evidence used in this review

We conducted a MEDLINE search of all English-language articles published between Jan. 1, 2020, and Sept. 14, 2020, for the words or phrases “prone position” or “prone positioning” in the context of the treatment of coronavirus disease 2019 (COVID-19).

KEY POINTS

- Prone positioning has been widely adopted into standard practice for patients with severe acute respiratory distress syndrome who are mechanically ventilated based on high-quality evidence.
- Prone positioning in patients with hypoxic respiratory failure who are awake, spontaneously breathing and not intubated is possible in noncritical care settings; evidence has emerged of its use in the management of patients with coronavirus disease 2019 (COVID-19) pneumonia, showing potential for improved oxygenation and decreased dyspnea.
- Studies have not yet provided clinicians with tools to predict which patients with COVID-19 are most likely to improve with prone positioning, nor have they proven whether prone positioning is able to delay or avoid the need for invasive ventilation or shown a mortality benefit.
- Prone positioning for patients who are mechanically ventilated comes with risks related to dislodgement of endotracheal tubes and access lines, which are reduced for awake, nonventilated patients; however, risks related to pressure may be mitigated as patients who are awake can change position independently.
- Randomized controlled trials are needed to better understand the benefits and adverse effects of prone positioning in patients with COVID-19 who are breathing spontaneously.

What is prone positioning and how does it affect lung function?

In the setting of severe ARDS, ventilation in the supine position results in gravitational forces that may increase pulmonary edema and atelectasis in dependent (posterior) lung zones. Abdominal organs displace the posterior diaphragm superiorly, exacerbating posterior lung collapse.[8] Defective hypoxic pulmonary vasoconstriction may also contribute to ventilation/perfusion (V/Q) mismatch.[9]

Prone positioning refers to positioning a patient face down onto their anterior chest and abdomen to take advantage of physiologic changes that can result in improved oxygenation through decreased V/Q mismatch and, potentially, decreased lung injury. In the prone position, expansion of the anterior chest wall is restricted, resulting in a more homogeneous chest wall compliance (Figure 1), and gravitational forces on lung parenchyma enable greater recruitment of the posterior zones, allowing for a greater proportion of alveoli to participate in gas exchange. A more equal distribution of stress forces onto the lungs by the diaphragm also occurs in the prone position, which may help reduce lung injury both during mechanical ventilation and while breathing spontaneously.[8,10] The position also enhances the inferior movement of the diaphragm, which relieves compression on atelectatic posterior lung zones, increasing lung recruitability.[10,11] Prone positioning has relatively little effect on a patient's lung perfusion, however, as most blood flow is directed to posterior lung zones while both supine and prone.[9] The result is improved V/Q matching, a decrease in the shunt fraction and improved oxygenation.

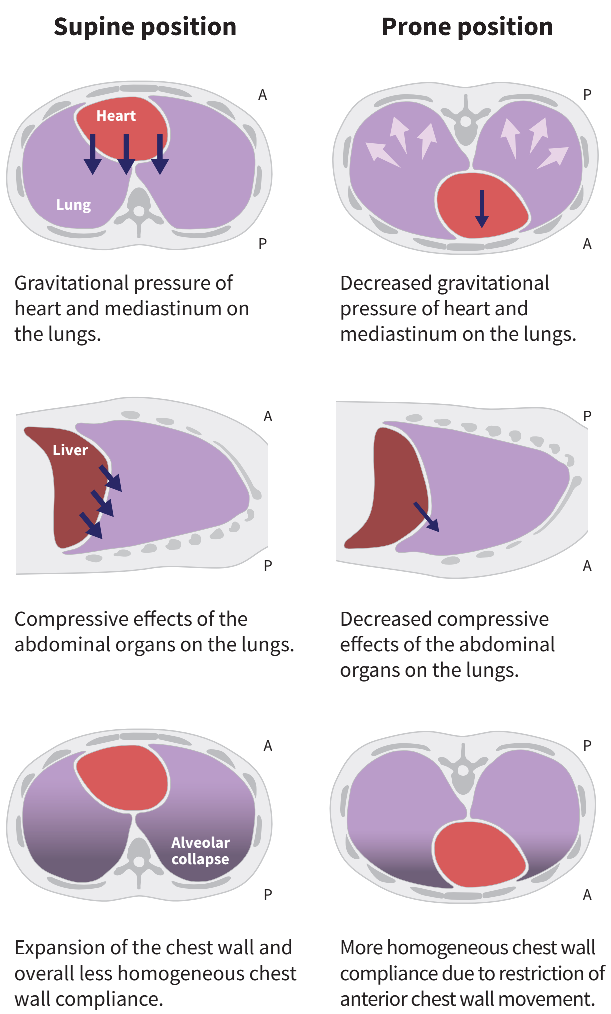

Figure 1: A comparison of some physiological effects of supine (left) and prone (right) positioning. In the prone position, reduced force from other organs is applied to the lungs, which allows for improved lung compliance and therefore improved relation between ventilation and perfusion of the lungs. Top panel: Dark blue arrows indicate the direction of the force exerted on the lungs by the heart. Middle panel: Arrows indicate the direction of the force exerted on the lungs by the abdominal organs. For prone positioning, less force from these organs is applied to the lungs, which allows for improved lung compliance by decreasing the force it needs to expand against. Bottom panel: Graded shading represents lung perfusion with darker shade representing greater ventilation/perfusion mismatch owing to alveolar collapse posteriorly in the supine position (reduced in the prone patient as this position allows for more even chest expansion). Note: A = anterior, P = posterior. Modified from the original figure created by Mike Fralick and Saba Manzoor by Émilie Lacharité.

How should patients be placed in the prone position?

Turning a patient with an endotracheal tube and other indwelling devices from the supine to prone position is a process that must be managed meticulously. Because most patients are heavily sedated and usually medically paralyzed to facilitate ventilation, 3 or more trained staff are needed to turn the patient in a coordinated fashion.[12]

During the COVID-19 pandemic, some institutions have attempted prone positioning among patients with hypoxia who are awake and not intubated, either in the emergency department or inpatient units. For patients who are not intubated, many of the risks associated with placement in the prone position are mitigated (e.g., displacement of an endotracheal tube). The process is easier if patients can turn without physical assistance; however, especially for the initial episode of prone positioning, a staff member should be present to ensure that connection of oxygen tubing, intravenous lines and any other tubing (e.g., Foley catheter) are maintained during repositioning. Access to continuous oxygen plethysmography and close monitoring of the respiratory rate is advantageous to ensure that the patient does not deteriorate clinically and to facilitate the monitoring of respiratory status among patients enrolled in research studies.

Appropriate cushioning with pillows or rolled blankets under pressure points, such as the patient's upper chest and pelvis, can increase comfort and tolerability of the prone position, and potentially mitigate increased intra-abdominal pressure that can transfer to the lungs. Patients who are breathing spontaneously can alter their head and arm position at least every 2 hours to avoid pressure injuries.[12]

Who is eligible for prone positioning?

Before the COVID-19 pandemic, prone positioning was used mainly for patients with severe ARDS who were being ventilated mechanically.[13] Among patients with COVID-19 who are breathing spontaneously and not intubated, observational data suggest that prone positioning might improve oxygenation in those who can tolerate the position. Several randomized controlled trials (RCTs) are underway to investigate the effectiveness of prone positioning in both patients requiring low-flow supplemental oxygen in a ward-based setting (Clinical Trials nos. NCT04383613, NCT04402879, NCT04517123) and patients with more severe respiratory failure that requires higher-flow oxygen support (Clinical Trials nos. NCT04350723, NCT04543760).

Placement in the prone position should be avoided for patients who are breathing spontaneously but may require imminent intubation (e.g., those with a reduced level of consciousness or worsening hypoxia despite maximal supplemental oxygen) or those with anatomic contraindications to prone positioning as identified by the established ARDS literature (e.g., facial trauma; recent abdominal, thoracic or spine surgery; recent pacemaker insertion; or unstable spine or pelvic fractures).[1,4,12,14]

Little is known about the effects of prone positioning during pregnancy on the fetus, as pregnant patients are frequently excluded from trials (a practice recently challenged during the COVID-19 pandemic[15]), although a previous case report described successful prone positioning for a pregnant patient who was critically ill with viral pneumonia.[16] A protocol and guide for prone positioning based on expert opinion was recently developed for clinicians caring for obstetrical patients,[17] and successful use of prone positioning for a pregnant patient with COVID-19 has been documented in a case report.[18]

For whom is prone positioning effective?

Patients with ARDS

Prone positioning has been evaluated since the 1970s as part of the management of patients with ARDS.[13] Among patients with moderate-to-severe ARDS, prolonged prone positioning (at least 12 h/d) has been found to reduce mortality and is now the standard of care in the management of these patients.[2,13] Ventilation in the prone position is thought to decrease ventilator-associated lung injury through greater uniformity in the distribution of tidal volume, which leads to less nonphysiologic strain on the lungs. A large multicentre RCT published in 2013 involving 474 participants in France found that ventilation of patients with moderate-to-severe ARDS (arterial partial pressure of oxygen/fractional concentration of oxygen in inspired air [Pao_2/Fio_2] < 150 mm Hg) who were placed in the prone position for 16 hours per day was associated with an improved 28-day mortality compared with being positioned in the supine position (hazard ratio 0.39, 95% confidence interval [CI] 0.25–0.63).[12] A meta-analysis of 8 RCTs that pooled data across 2129 patients with ARDS who were mechanically ventilated subsequently showed that patients with moderate-to-severe ARDS who were randomly assigned to prone positioning for at least 12 hours per day had a lower mortality rate (risk ratio [RR] 0.74, 95% CI 0.56–0.99) than those ventilated in the supine position.[13]

Prone positioning has been attempted in patients with ARDS related to COVID-19 and, although there is debate about whether there are unique physiologic attributes associated with ARDS related to COVID-19,[19,20] some guidelines (e.g., Surviving Sepsis Campaign) recommend that prone positioning be considered for patients with severe ARDS related to COVID-19 because prone positioning is known to be beneficial in the setting of severe ARDS.[21–23]

Patients who are not intubated

Before the COVID-19 pandemic, prone positioning was infrequently used in the management of patients with hypoxic respiratory failure who were not intubated. A 2015 single-centre retrospective cohort study evaluated the response of 15 patients who received a total of 43 prone-positioning procedures. Most participants (n = 13) had a diagnosis of pneumonia and, during 42% of the procedures, noninvasive ventilation was used. Participants' hypoxia significantly improved while prone (supine Pao_2/Fio_2 mean 127 [standard deviation (SD) 49] mm Hg, prone Pao_2/Fio_2 mean 186 [SD 72] mm Hg; $p < 0.05$), although there was no sustained improvement when patients were returned to the supine position.[7]

A multicentre prospective cohort study examined the effect of combining prone positioning with either noninvasive ventilation or high-flow nasal cannula in 20 participants who were awake, 11 of whom had viral pneumonia.[4] A stepwise approach was used to add prone positioning to either an oxygen-delivery system based on clinical response of the patient or to switch between noninvasive ventilation and high-flow nasal cannula. Baseline hypoxia in patients was not reported, although all patients met the criteria for ARDS. The authors found improved oxygenation when prone positioning was added to high-flow nasal cannula but not to noninvasive ventilation and, although 11 participants avoided intubation, the study found a nonsignificant increase in patients with severe ARDS who required intubation and mechanical ventilation.[4]

The literature to guide the use of prone positioning in patients with acute respiratory failure related to COVID-19 who are breathing spontaneously and not intubated comprises case reports, case series and observational studies.[1,3,4,6,7,14] The large number of patients with COVID-19 worldwide has led to the evaluation of prone positioning outside of the intensive care unit (ICU): in emergency departments, medical wards and repurposed surgical floors.

Based on the available observational evidence (summarized in Table 1), prone positioning in this patient population appears to improve oxygenation for many patients.[1,3,6,7,28–32] For example, one prospective nonrandomized study involving 50 patients who received prone positioning in the emergency department showed improved oxygenation within 5 minutes of placement, although 36% required intubation within about 72 hours.[6] Noninvasive ventilation and prone positioning were used concurrently in one small cross-sectional study involving 15 participants with COVID-19 and were shown to improve oxygenation, including 80% of participants who had sustained improvement after being returned to the supine position.[3] A retrospective cohort study reviewed the outcomes for 24 patients in a respiratory unit who received continuous positive airway pressure (CPAP) in conjunction with prone positioning and found that, although addition of CPAP did not significantly increase arterial oxygen saturation, the combination of CPAP and prone positioning did (mean arterial oxygen saturation at baseline 94% (SD 3%) and after prone positioning 96% (SD 2%; $p < 0.05$).[25] This improvement was sustained 1 hour after participants were returned to the supine position.[25] A prospective cohort study involving 56 patients who received prone positioning in either the emergency department, medical ward or monitored unit[24] showed that prone positioning was feasible in 84% of participants and improved oxygenation significantly, although this did not persist when patients were returned to the supine position. In a small, prospective single-centre study in France, use of a single episode of prone positioning was shown to have good tolerability but improved oxygenation for only 25% of participants, with half of those who responded showing persistent improvement.[1] However, lack of randomization in these studies means that the benefits observed may be because of prone positioning, selection bias or confounding by indication.

Table 1: Summary of evidence for prone positioning in patients with coronavirus disease 2019 who are not intubated

Study	Study design	Study population	Primary outcome(s)	Location	Oxygen support	Prone protocol	Main finding(s)
Caputo et al.[6]	Single-centre prospective cohort study	*n* = 50 Baseline Spo_2 before PP: median 84% (IQR 75%–90%)	Change in oxygenation (Spo_2), rate of intubation in first 24 h of presentation to ED	ED	NRB (38 of 50 patients, 76%) or HFNC (12 of 50 patients, 24%)	Five minutes of PP without change in oxygen delivery	• Spo_2 after a single episode of 5 min PP: median 94% (IQR 90%–95%) • Eighteen of 50 patients (36%) intubated within about 72 h of presentation
Elharrar et al.[1]	Prospective before–after study, single centre	*n* = 24 Baseline Pao_2: mean 72.8 (SD 14.2) mm Hg	Increase in Pao_2 ≥ 20% of baseline	Medical ward	16 of 24 patients (67%) on NC < 4 L/min; 8 of 25 patients (33%) on NC ≥ 4 L/min or HFNC	Single episode of PP; duration determined by comfort	• Six of 24 patients (25%) had the primary outcome • No persistent response to PP once in supine position again • Fifteen of 24 patients (63%) able to tolerate PP for > 3 h
Sartini et al.[3]	Single-centre cross-sectional study	*n* = 15 Baseline Pao_2/Fio_2: mean 157 (SD 43) mm Hg	Change in oxygenation and respiratory vital signs	Medical ward	NIV	Cycles of PP: median 2 (IQR 1–3) for a median duration of 3 (IQR 1–6) h	• All patients had improvement in RR, Pao_2/FIo_2 during PP* • Twelve of 15 patients (80%) had improvement in oxygenation after PP* • Eleven of 15 patients (73%) had improvement in comfort during PP
Coppo et al.[24]	Single-centre prospective cohort study	*n* = 56 Baseline Pao_2/Fio_2: mean 180.5 (SD 76.6) mm Hg	Change in supine Pao_2/Fio_2 after episode of PP	Medical ward, ED, HDU	CPAP (44 of 56 patients, 79%), reservoir mask (9 of 56 patients, 16%), Venturi mask (3 of 56 patients, 5%)	Minimum 3 h, up to 8 h depending on comfort; 25 patients maintained > 3 h	• Improved oxygenation while in PP: mean Pao_2/Fio_2 285.5 (SD 112.9) • Nonsignificant improvement in oxygenation after PP in 50% of participants
Winearls et al.[25]	Single-centre retrospective cohort study	*n* = 24 Baseline Pao_2/Fio_2 on CPAP: mean 143 (SD 73) mm Hg	Change in respiratory vital signs, tolerance and duration of PP	HDU	CPAP	PP initiated median 30 (IQR 7–99) h after CPAP; mean duration of PP in first 24 h: 8 (SD 5) h, continued for 10 (SD 5) d	• Significant increase in Pao_2/Fio_2 with PP and CPAP: mean 252 (SD 87) mm Hg, $p < 0.01$; increase sustained 1 h after PP stopped • Two patients not able to tolerate PP because of discomfort
Solverson et al.[26]	Multicentre retrospective cohort study	*n* = 17 Baseline Pao_2/Fio_2: median 152 (IQR 97–233) mm Hg	Tolerance of PP, physiologic and clinical outcomes	Medical ward, ICU	NC, NRB, HFNC	Median no. of daily PP sessions 2 (IQR 1–6) with a median duration of 75 (IQR 30–480) min for first session	• Decreased respiratory rate and improved oxygenation while in PP • 35% (*n* = 6) of patients stopped PP after ≤ 60 min because of musculoskeletal pain or general discomfort
Ferrando et al.[27]	Multicentre prospective cohort study	*n* = 199; 144 patients received only HFNC and 55 received HFNC + PP	Physiologic and clinical outcomes, including intubation risk	ICU	HFNC	PP was considered only if duration was > 16 h/d, regardless of the no. of sessions	• Significant increase in Pao_2/Fio_2 for combination of HFNC + PP • Trend toward delay in intubation for patients receiving HFNC + PP; no difference in intubation rates between groups

Note: CPAP = continuous positive airway pressure, ED = emergency department, Fio_2 = fractional concentration of oxygen in inspired air, HDU = high dependency unit, HFNC = high-flow nasal cannula, ICU = intensive care unit, IQR = interquartile range, NC = nasal cannula, NIV = noninvasive ventilation, NRB = nonrebreather high-flow oxygen mask, Pao_2 = arterial partial pressure of oxygen, PP = prone positioning, RR = respiratory rate, SD = standard deviation, Spo_2 = peripheral oxygen saturation of hemoglobin.
*Exact data not available.

REVIEW

Evidence that prone positioning decreases the need for intubation is lacking. Some observational studies have shown that prone positioning results in a decreased respiratory rate,[3,28] which may lessen patients' risk of developing self-inflicted lung injury,[3,10] although extrapolating from this surrogate outcome should be done with caution.[1,3,6,7] Among patients with mild or moderate ARDS who were intubated or received short (< 12 h daily) durations of prone positioning, improved oxygenation did not correlate with a mortality benefit.[13] Furthermore, evidence about the persistence of improvement in oxygenation once patients who are spontaneously breathing return to the supine position is not consistent,[1,3,6,11,24,25,28] which suggests that RCTs that examine clinical outcomes among patients with COVID-19 who receive prone positioning are needed. Despite these deficiencies in evidence, the Intensive Care Society in the United Kingdom has released guidance based on expert opinion that encourages the use of prone positioning for patients who are not intubated because of its ease of application and potential benefits.[33]

What are the potential harms of prone positioning?

Among patients with ARDS who are mechanically ventilated, potential adverse events from prone positioning arise mostly when turning patients to the prone position (owing to tube or line dislodgment) and from sequalae of prolonged static positioning in patients who are unable to move (including pressure wounds, pressure neuropathy or neurapraxia and facial edema).[13] Most of these risks are substantially reduced in patients who are spontaneously breathing and not intubated because they are able to shift position as required for comfort.

Although patient discomfort can be a limiting factor in the use of prone positioning or can lead to its early cessation, proper positioning and cushioning of pressure points may lead to better tolerance.[1,4,7,11,31] A Canadian prospective cohort study involving 4 hospitals in Calgary evaluated the safety and tolerability of prone positioning of patients who were not intubated on both the medical ward and in the ICU.[26] The study reported that 17 participants received a median of 2 (range 1–6) sessions of prone positioning for a median of 75 (range 30–480) minutes. Time spent prone was limited by back or shoulder pain (n = 2, 12%), general discomfort (n = 6, 35%) and delirium (n = 1, 6%). Eight patients (47%) had no tolerability problems. There were otherwise no serious adverse events.[26]

Whether prolonged prone positioning in patients with COVID-19 who are awake and not intubated increases the risk for venous thromboembolic disease is an important consideration, because observational studies have shown COVID-19 to be associated with an increased risk of venous thrombosis.[34] The published studies of prone positioning in nonintubated patients have sparsely reported on its harms.

If prone positioning delays rather than prevents intubation, it may increase rates of emergent intubation, which carries its own risks. A 2020 multicentre cohort study across 36 hospitals in Spain and Andorra found that use of prone positioning with high-flow nasal cannula did not reduce the risk of intubation (RR 1.002, 95% CI 0.531–1.890; p = 0.99).[27] This study also showed a nonsignificant trend of increasing time to intubation (2.0 v. 4.1 d, p = 0.054), which raises concern for potential harm caused by delayed intubation.[27]

What questions remain?

Studies have not yet provided clinicians with tools to predict which patients are most likely to improve; characterized the relative benefits of prone positioning, high-flow nasal cannula and noninvasive intubation (both independently and when combined); determined the optimal "dose" of prone positioning; or, most critically, proven whether prone positioning is able to delay or avoid the need for invasive ventilation. It is not known whether prone positioning can reduce health care costs because studies of its cost-effectiveness are lacking. Although it appears that prone positioning can be implemented outside of critical care settings with minimal cost, it may be associated with increased use of personal protective equipment (PPE) if several health care workers need to assist with prone positioning. However, if the intervention is shown in future studies to decrease admissions to critical care units, this could translate into substantial cost savings. Even if mechanical ventilation is delayed or avoided, this may not lead to improved patient outcomes; therefore, identifying patients who are not likely to benefit from a trial of nonintubated prone positioning will be crucial. Rigorous RCTs will be essential in addressing these questions.

What are the logistical considerations for using prone positioning during the COVID-19 pandemic?

Prone positioning of patients with COVID-19 on medical wards may become a more common practice in an effort to prevent mechanical ventilation if critical care resources become overwhelmed. As modelling studies have indicated this may be a risk for Canadian hospitals if public interventions are not followed,[35,36] hospitals should therefore develop or adopt guidance on prone positioning and support rapid knowledge translation and training of clinical staff. As an example, Doussot and colleagues described the creation of a dedicated prone-positioning team at a regional hospital in France.[37] Surgeons, nurses, physiotherapists and other clinicians volunteered to receive training that included incorporation of a checklist, simulation and proper PPE education.[37]

Conclusion

Prone positioning has been widely adopted into standard practice for patients with severe ARDS who are mechanically ventilated based on robust RCT evidence. However, since the COVID-19 pandemic has overwhelmed some health systems around the globe, leading to intensive care resources becoming strained, prone positioning for patients who are breathing spontaneously and not intubated is an attractive intervention because of its easy administration in many care settings and sound physiologic rationale. Although the current evidence base to support the use of prone positioning is of low quality, many RCTs are currently underway that are likely to provide answers to questions regarding its clinical benefit, safety profile and possible cost-effectiveness. Good evidence to guide patient selection and timing of starting and stopping prone positioning is needed.

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Competing interests: Michael Fralick is a Co-principal investigator for the COVID-PRONE study (ClinicalTrials.gov no. NCT04383613). He is also is a consultant for Pine Trees Health, a start-up company developing a CRISPR-based diagnostic test for coronavirus disease 2019. Kevin Venus and Laveena Munshi are members of the steering committee of the COVID-PRONE study. No other competing interests were declared.

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