# Evidence Search Service Results of your search request

## Proning self-ventilating patients with COVID-19

**ID of request:** 26155  
**Date of request:** 17th November, 2020  
**Date of completion:** 17th November, 2020

If you would like to request any articles or any further help, please contact:  Sarah Rudd at [Sarah.Rudd@nbt.nhs.uk](mailto:Sarah.Rudd@nbt.nhs.uk)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: Proning self-ventilating patients with COVID-19. Sarah Rudd. (17th November, 2020). BRISTOL, UK: North Bristol Library and Information Service.

**Sources searched**  
EMBASE (1)  
EMCARE (2)  
Google (2)  
Intensive Care Society (1)  
MEDLINE (31)

**Date range used** (5 years, 10 years): 2020   
**Limits used** (gender, article/study type, etc.): -   
**Search terms and notes** (full search strategy for database searches below):

Time spent - 2 hours

For more information about the resources please go to: <https://link.nbt.nhs.uk/Interact/Pages/Section/Default.aspx?Section=3527>.

## Summary of Results

Results include a 2015 Cochrane review on proning patients which is referenced in the University Hospitals Birmingham guideline.

Additional guidance comes from [ICS Guidance for Prone Positioning of the Conscious COVID Patient 2020](file:///\\northbristol.local\home\user\Draft%20searches\index.php%3fPageID=literature_search_request_assigned&RequestID=26155) from the Intensive Care Society.

There is a range of original research all from this year.

If you would like any additional information please let me know.

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## A. Systematic Reviews

#### Cochrane Database of Systematic Reviews

**Prone position for acute respiratory failure in adults** (2015)

Bloomfield, R., Noble, D., Sudlow, A.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=94a2933fa94a493aeede6c9d776d9187)

Authors' conclusions We found no convincing evidence of benefit nor harm from universal application of PP in adults with hypoxaemia mechanically ventilated in intensive care units (ICUs). Three subgroups (early implementation of PP, prolonged adoption of PP and severe hypoxaemia at study entry) suggested that prone positioning may confer a statistically significant mortality advantage. Additional adequately powered studies would be required to confirm or refute these possibilities of subgroup benefit but are unlikely, given results of the most recent study and recommendations derived from several published subgroup analyses. Meta‐analysis of individual patient data could be useful for further data exploration in this regard. Complications such as tracheal obstruction are increased with use of prone ventilation. Long‐term mortality data (12 months and beyond), as well as functional, neuro‐psychological and quality of life data, are required if future studies are to better inform the role of PP in the management of hypoxaemic respiratory failure in the ICU.

## B. Institutional Publications

#### Intensive Care Society

**ICS Guidance for Prone Positioning of the Conscious COVID Patient 2020** (2020)

Peter Bamford, Andrew Bentley, Jane Dean, David Whitmore and Noamaan Wilson-Baig

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b7c2f9931758d89904e9e97d33590263)

#### University Hospitals Birmingham NHS Foundation Trust

**C093 - PRONING IN THE WARD-BASED AWAKE SELF VENTLIATING PATIENT WITH COVID-19** (2020)

Dr Shyam Madathil (and respiratory colleagues at UHBFT)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d2cb2bc164a929e874c906d25661f587)

To advise Clinicians on how to prone awake patients on the ward who are self ventilating in the management of COVID19

## C. Original Research

1. **A need for prone position CPR guidance for intubated and non-intubated patients during the COVID-19 pandemic.**  
   Barker Joseph Resuscitation 2020;151:135-136.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d1fadb4884c4e9b76f448658f092c8af)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=37c8c295429302a96b064c81bb699cee)

1. **Awake prone positioning does not reduce the risk of intubation in COVID-19 treated with high-flow nasal oxygen therapy: a multicenter, adjusted cohort study.**  
   Ferrando Carlos Critical care (London, England) 2020;24(1):597.

BACKGROUNDAwake prone positioning (awake-PP) in non-intubated coronavirus disease 2019 (COVID-19) patients could avoid endotracheal intubation, reduce the use of critical care resources, and improve survival. We aimed to examine whether the combination of high-flow nasal oxygen therapy (HFNO) with awake-PP prevents the need for intubation when compared to HFNO alone.METHODSProspective, multicenter, adjusted observational cohort study in consecutive COVID-19 patients with acute respiratory failure (ARF) receiving respiratory support with HFNO from 12 March to 9 June 2020. Patients were classified as HFNO with or without awake-PP. Logistic models were fitted to predict treatment at baseline using the following variables: age, sex, obesity, non-respiratory Sequential Organ Failure Assessment score, APACHE-II, C-reactive protein, days from symptoms onset to HFNO initiation, respiratory rate, and peripheral oxyhemoglobin saturation. We compared data on demographics, vital signs, laboratory markers, need for invasive mechanical ventilation, days to intubation, ICU length of stay, and ICU mortality between HFNO patients with and without awake-PP.RESULTSA total of 1076 patients with COVID-19 ARF were admitted, of which 199 patients received HFNO and were analyzed. Fifty-five (27.6%) were pronated during HFNO; 60 (41%) and 22 (40%) patients from the HFNO and HFNO + awake-PP groups were intubated. The use of awake-PP as an adjunctive therapy to HFNO did not reduce the risk of intubation [RR 0.87 (95% CI 0.53-1.43), p = 0.60]. Patients treated with HFNO + awake-PP showed a trend for delay in intubation compared to HFNO alone [median 1 (interquartile range, IQR 1.0-2.5) vs 2 IQR 1.0-3.0] days (p = 0.055), but awake-PP did not affect 28-day mortality [RR 1.04 (95% CI 0.40-2.72), p = 0.92].CONCLUSIONIn patients with COVID-19 ARF treated with HFNO, the use of awake-PP did not reduce the need for intubation or affect mortality.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cbaa31eaa0cd53b8dd4a40d661f3194a)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6ff0bc521b28c4a71204663982a125db)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8fffc4bf8d6cae6d2648c0a175418a05)

1. **Awake prone positioning for non-intubated oxygen dependent COVID-19 pneumonia patients.**  
   Ng Ziqin The European respiratory journal 2020;56(1):No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ecc5005985058430c0800aa2ac8f73b4)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=3beb0f0c87592d2ca738a858329f2664)

1. **Awake prone positioning of hypoxaemic patients with COVID-19: protocol for a randomised controlled open-label superiority meta-trial.**  
   Tavernier Elsa BMJ open 2020;10(11):e041520.

INTRODUCTIONProne positioning (PP) is an effective first-line intervention to treat patients with moderate to severe acute respiratory distress syndrome (ARDS) receiving invasive mechanical ventilation, as it improves gas exchanges and reduces mortality. The use of PP in awake spontaneous breathing patients with ARDS secondary to COVID-19 was reported to improve oxygenation in few retrospective trials with small sample size. High-level evidence of awake PP for hypoxaemic patients with COVID-19 patients is still lacking.METHODS AND ANALYSISThe protocol of this meta-trial is a prospective collaborative individual participant data meta-analysis of randomised controlled open label superiority trials. This design is particularly adapted to a rapid scientific response in the pandemic setting. It will take place in multiple sites, among others in USA, Canada, Ireland, France and Spain. Patients will be followed up for 28 days. Patients will be randomised to receive whether awake PP and nasal high flow therapy or standard medical treatment and nasal high flow therapy. Primary outcome is defined as the occurrence rate of tracheal intubation or death up to day 28. An interim analysis plan has been set up on aggregated data from the participating research groups.ETHICS AND DISSEMINATIONEthics approvals were obtained in all participating countries. Results of the meta-trial will be submitted for publication in a peer-reviewed journal. Each randomised controlled trial was registered individually, as follows: NCT04325906, NCT04347941, NCT04358939, NCT04395144 and NCT04391140.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a3bfe492afc76e736950a8fa8d77cb4c)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=19f969d8a8d578a5ce9868516bd54662)

1. **Conscious prone positioning during non-invasive ventilation in COVID-19 patients: experience from a single centre.**  
   Burton-Papp Helmi C. F1000Research 2020;9:859.

Critically ill patients admitted to hospital following SARS-CoV-2 infection often experience hypoxic respiratory failure and a proportion require invasive mechanical ventilation to maintain adequate oxygenation. The combination of prone positioning and non-invasive ventilation in conscious patients may have a role in improving oxygenation. The purpose of this study was to assess the effect of prone positioning in spontaneously ventilating patients receiving non-invasive ventilation admitted to the intensive care.  Clinical data of 81 patients admitted with COVID 19 pneumonia and acute hypoxic respiratory failure were retrieved from electronic medical records and examined. Patients who had received prone positioning in combination with non-invasive ventilation were identified. A total of 20 patients received prone positioning in conjunction with non-invasive ventilation. This resulted in improved oxygenation as measured by a change in PaO 2/FiO 2 (P/F) ratio of 28.7 mmHg while prone, without significant change in heart rate or respiratory rate. Patients on average underwent 5 cycles with a median duration of 3 hours. There were no reported deaths, 7 of the 20 patients (35%) failed non-invasive ventilation and subsequently required intubation and mechanical ventilation. In our cohort of 20 COVID-19 patients with moderate acute hypoxic respiratory failure, prone positioning with non-invasive ventilation resulted in improved oxygenation. Prone positioning with non-invasive ventilation may be considered as an early therapeutic intervention in COVID-19 patients with moderate acute hypoxic respiratory failure.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2c67d9bc796748fb6b9a7a1c99980cc5)

1. **Conscious Proning: An Introduction of a Proning Protocol for Nonintubated, Awake, Hypoxic Emergency Department COVID-19 Patients.**  
   Jiang Lynn G. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine 2020;27(7):566-569.

The novel coronavirus, or COVID-19, has rapidly become a global pandemic. A major cause of morbidity and mortality due to COVID-19 has been the worsening hypoxia that, if untreated, can progress to acute respiratory distress syndrome (ARDS) and respiratory failure. Past work has found that intubated patients with ARDS experience physiological benefits to the prone position, because it promotes better matching of pulmonary perfusion to ventilation, improved secretion clearance, and recruitment of dependent areas of the lungs. We created a systemwide multi-institutional (New York-Presbyterian Hospital enterprise) protocol for placing awake, nonintubated, emergency department patients with suspected or confirmed COVID-19 in the prone position. In this piece, we describe the background literature and the approach we have taken at our institution as we care for a high burden of COVID-19 cases with respiratory symptoms.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8bc68bd1a2d95977ee77c41cdd0baad3)

1. **COVID-19 Care in India: Evolving Paradigms from Public Health to Critical Care.**  
   Joshi Shashank R. The Journal of the Association of Physicians of India 2020;68(10):56-58.

Covid-19 pandemic in India has rapidly grown though we have a low case fatality rate, high recovery rate and large population is asymptomatic or presymptomatic. Public health measures to close the tap across the country need hypervigilance and follow simple dictum of aggressive testing, tracing and isolation. The covid cases need an early diagnosis with treat and care model. Most can be managed with home isolation under telemedicine supervision with oxygen saturation screening by a simple six minute walk test. Hospitalised cases have emerging evidence in different therapies from antivirals, steroids, immunologic to heparins but high flow oxygen, prone position and supportive care remains the cornerstone in critical care with nursing and nutrition. Vaccine research is ongoing but currently only social vaccine can mitigate the pandemic. Covid appropriate behaviour of Masking, sanitisation and physical distancing with immune modulating behaviour like adequate sleep, digital detox for two hour and clean well ventilated environment is the key with breathing exercises including yoga and positive mental health and avoidance of crowds the only vaccine to live with covid -19 today.

1. **Critically Ill Patients with COVID-19: A Narrative Review on Prone Position.**  
   Qadri Syeda Kashfi Pulmonary therapy 2020;:No page numbers.

INTRODUCTIONProne position is known to improve mortality in patients with acute respiratory distress syndrome (ARDS). The impact of prone position in critically ill patients with coronavirus disease of 2019 (COVID-19) remains to be determined. In this review, we describe the mechanisms of action of prone position, systematically appraise the current experience of prone position in COVID-19 patients, and highlight unique considerations for prone position practices during this pandemic.METHODSFor our systematic review, we searched PubMed, Scopus and EMBASE from January 1, 2020, to April 16, 2020. After completion of our search, we became aware of four relevant publications during article preparation that were published in May and June 2020, and these studies were reviewed for eligibility and inclusion. We included all studies reporting clinical characteristics of patients admitted to the hospital with COVID-19 disease who received respiratory support with high-flow nasal cannula, or noninvasive or mechanical ventilation and reported the use of prone position. The full text of eligible articles was reviewed, and data regarding study design, patient characteristics, interventions and outcomes were extracted.RESULTSWe found seven studies (total 1899 patients) describing prone position in COVID-19. Prone position has been increasingly used in non-intubated patients with COVID-19; studies show high tolerance and improvement in oxygenation and lung recruitment. Published studies lacked a description of important clinical outcomes (e.g., mortality, duration of mechanical ventilation).CONCLUSIONSBased on the findings of our review, we recommend prone position in patients with moderate to severe COVID-19 ARDS as per existing guidelines. A trial of prone position should be considered for non-intubated COVID-19 patients with hypoxemic respiratory failure, as long as this does not result in a delay in intubation.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d45219500718a0cda3c40caa444aa513)

1. **Current and evolving standards of care for patients with ARDS**  
   Menk M. Intensive Care Medicine 2020;:No page numbers.

Care for patients with acute respiratory distress syndrome (ARDS) has changed considerably over the 50 years since its original description. Indeed, standards of care continue to evolve as does how this clinical entity is defined and how patients are grouped and treated in clinical practice. In this narrative review we discuss current standards - treatments that have a solid evidence base and are well established as targets for usual care - and also evolving standards - treatments that have promise and may become widely adopted in the future. We focus on three broad domains of ventilatory management, ventilation adjuncts, and pharmacotherapy. Current standards for ventilatory management include limitation of tidal volume and airway pressure and standard approaches to setting PEEP, while evolving standards might focus on limitation of driving pressure or mechanical power, individual titration of PEEP, and monitoring efforts during spontaneous breathing. Current standards in ventilation adjuncts include prone positioning in moderate-severe ARDS and veno-venous extracorporeal life support after prone positioning in patients with severe hypoxemia or who are difficult to ventilate. Pharmacotherapy current standards include corticosteroids for patients with ARDS due to COVID-19 and employing a conservative fluid strategy for patients not in shock; evolving standards may include steroids for ARDS not related to COVID-19, or specific biological agents being tested in appropriate sub-phenotypes of ARDS. While much progress has been made, certainly significant work remains to be done and we look forward to these future developments.<br/>Copyright &#xa9; 2020, Springer-Verlag GmbH Germany, part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f04de928c7c9f642fc6cce0b14e07577)

1. **Early Self-Proning in Awake, Non-intubated Patients in the Emergency Department: A Single ED's Experience During the COVID-19 Pandemic.**  
   Caputo Nicholas D. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine 2020;27(5):375-378.

OBJECTIVEProlonged and unaddressed hypoxia can lead to poor patient outcomes. Proning has become a standard treatment in the management of patients with ARDS who have difficulty achieving adequate oxygen saturation. The purpose of this study was to describe the use of early proning of awake, non-intubated patients in the emergency department (ED) during the COVID-19 pandemic.METHODSThis pilot study was carried out in a single urban ED in New York City. We included patients suspected of having COVID-19 with hypoxia on arrival. A standard pulse oximeter was used to measure SpO2 . SpO2 measurements were recorded at triage and after 5 minutes of proning. Supplemental oxygenation methods included non-rebreather mask (NRB) and nasal cannula. We also characterized post-proning failure rates of intubation within the first 24 hours of arrival to the ED.RESULTSFifty patients were included. Overall, the median SpO2 at triage was 80% (IQR 69 to 85). After application of supplemental oxygen was given to patients on room air it was 84% (IQR 75 to 90). After 5 minutes of proning was added SpO2 improved to 94% (IQR 90 to 95). Comparison of the pre- to post-median by the Wilcoxon Rank-sum test yielded P = 0.001. Thirteen patients (24%) failed to improve or maintain their oxygen saturations and required endotracheal intubation within 24 hours of arrival to the ED.CONCLUSIONAwake early self-proning in the emergency department demonstrated improved oxygen saturation in our COVID-19 positive patients. Further studies are needed to support causality and determine the effect of proning on disease severity and mortality.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=92be4509e27b11b923c6350835bf10eb)

1. **Effectiveness of prone positioning in non-intubated ICU patients with moderate to severe ARDS by COVID-19.**  
   Taboada Manuel Anesthesia and analgesia 2020;:No page numbers.

BACKGROUNDIn the treatment for severe acute respiratory distress syndrome (ARDS) from Coronavirus Disease 2019 (COVID-19), the World Health Organization (WHO) recommends prone positioning (PP) during mechanical ventilation for periods of 12-16 hours per day to potentially improve oxygenation and survival. In this prospective observational study, we evaluated the ability of long PP sessions to improve oxygenation in awake ICU patients with moderate or severe ARDS due to COVID-19.METHODSThe study was approved by the ethics committee of Galicia (code No. 2020-188), and all patients provided informed consent. In this case series, awake patients with moderate or severe ARDS by COVID-19 admitted to the Intensive Care Unit (ICU) at University Hospital of Santiago from March 21 to April 5, 2020 were prospectively analyzed. Patients were instructed to remain in PP as long as possible, until the patient felt too tired to maintain that position. Light sedation was administered with dexmedetomidine. The following information were collected: number and duration of PP sessions, StO2 and blood gases before, during and following a PP session, need of mechanical ventilation, duration of ICU admission and ICU outcome. Linear mixed effects models (LMM) were fit to estimate changes from baseline with a random effect for patient.RESULTSSeven patients with moderate or severe ARDS by COVID 19 were included. All patients received at least one PP session. A total of 16 PP sessions were performed in the 7 patients during the period study. The median duration of PP sessions was 10 hours. Dexmedetomidine was used in all PP sessions. Oxygenation increased in all sixteen sessions performed in the seven patients. The ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FiO2) significantly increased during PP (change from baseline and CI 97.5%: 110 [19; 202]) and after PP, albeit not significantly (change from baseline and CI 97.5%: 38 [-9.2; 85]) compared with previous supine position. Similarly, tissue oxygenation underwent a small improvement during PP (change from baseline and CI 97.5%: 2.6% [0.69; 4.6]) without significant changes after PP. Two patients required intubation. All patients were discharged from the ICU.CONCLUSIONSWe found that PP improved oxygenation in ICU patients with COVID-19 and moderate or severe ARDS. PP was relatively well tolerated in our patients and may be a simple strategy to improve oxygenation trying to reduce patients in mechanical ventilation and the length of stay in the ICU, especially in COVID-19 pandemic.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fafa65d3293d5391584b1aa534bb6ac0)

1. **Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study.**  
   Coppo Anna The Lancet. Respiratory medicine 2020;8(8):765-774.

BACKGROUNDThe COVID-19 pandemic is challenging advanced health systems, which are dealing with an overwhelming number of patients in need of intensive care for respiratory failure, often requiring intubation. Prone positioning in intubated patients is known to reduce mortality in moderate-to-severe acute respiratory distress syndrome. We aimed to investigate feasibility and effect on gas exchange of prone positioning in awake, non-intubated patients with COVID-19-related pneumonia.METHODSIn this prospective, feasibility, cohort study, patients aged 18-75 years with a confirmed diagnosis of COVID-19-related pneumonia receiving supplemental oxygen or non-invasive continuous positive airway pressure were recruited from San Gerardo Hospital, Monza, Italy. We collected baseline data on demographics, anthropometrics, arterial blood gas, and ventilation parameters. After baseline data collection, patients were helped into the prone position, which was maintained for a minimum duration of 3 h. Clinical data were re-collected 10 min after prone positioning and 1 h after returning to the supine position. The main study outcome was the variation in oxygenation (partial pressure of oxygen [PaO2]/fractional concentration of oxygen in inspired air [FiO2]) between baseline and resupination, as an index of pulmonary recruitment. This study is registered on ClinicalTrials.gov, NCT04365959, and is now complete.FINDINGSBetween March 20 and April 9, 2020, we enrolled 56 patients, of whom 44 (79%) were male; the mean age was 57·4 years (SD 7·4) and the mean BMI was 27·5 kg/m2 (3·7). Prone positioning was feasible (ie, maintained for at least 3 h) in 47 patients (83·9% [95% CI 71·7 to 92·4]). Oxygenation substantially improved from supine to prone positioning (PaO2/FiO2 ratio 180·5 mm Hg [SD 76·6] in supine position vs 285·5 mm Hg [112·9] in prone position; p<0·0001). After resupination, improved oxygenation was maintained in 23 patients (50·0% [95% CI 34·9-65·1]; ie, responders); however, this improvement was on average not significant compared with before prone positioning (PaO2/FiO2 ratio 192·9 mm Hg [100·9] 1 h after resupination; p=0·29). Patients who maintained increased oxygenation had increased levels of inflammatory markers (C-reactive protein: 12·7 mg/L [SD 6·9] in responders vs 8·4 mg/L [6·2] in non-responders; and platelets: 241·1 × 103/μL [101·9] vs 319·8 × 103/μL [120·6]) and shorter time between admission to hospital and prone positioning (2·7 days [SD 2·1] in responders vs 4·6 days [3·7] in non-responders) than did those for whom improved oxygenation was not maintained. 13 (28%) of 46 patients were eventually intubated, seven (30%) of 23 responders and six (26%) of 23 non-responders (p=0·74). Five patients died during follow-up due to underlying disease, unrelated to study procedure.INTERPRETATIONProne positioning was feasible and effective in rapidly ameliorating blood oxygenation in awake patients with COVID-19-related pneumonia requiring oxygen supplementation. The effect was maintained after resupination in half of the patients. Further studies are warranted to ascertain the potential benefit of this technique in improving final respiratory and global outcomes.FUNDINGUniversity of Milan-Bicocca.

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1. **Guidance and Patient Instructions for Proning and Repositioning of Awake, Nonintubated COVID-19 Patients.**  
   Bentley Suzanne K. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine 2020;:No page numbers.

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1. **High-Flow, Noninvasive Ventilation and Awake (Nonintubation) Proning in Patients With Coronavirus Disease 2019 With Respiratory Failure.**  
   Raoof Suhail Chest 2020;158(5):1992-2002.

The coronavirus disease 2019 pandemic will be remembered for the rapidity with which it spread, the morbidity and mortality associated with it, and the paucity of evidence-based management guidelines. One of the major concerns of hospitals was to limit spread of infection to health-care workers. Because the virus is spread mainly by respiratory droplets and aerosolized particles, procedures that may potentially disperse viral particles, the so-called "aerosol-generating procedures" were avoided whenever possible. Included in this category were noninvasive ventilation (NIV), high-flow nasal cannula (HFNC), and awake (nonintubated) proning. Accordingly, at many health-care facilities, patients who had increasing oxygen requirements were emergently intubated and mechanically ventilated to avoid exposure to aerosol-generating procedures. With experience, physicians realized that mortality of invasively ventilated patients was high and it was not easy to extubate many of these patients. This raised the concern that HFNC and NIV were being underutilized to avoid intubation and to facilitate extubation. In this article, we attempt to separate fact from fiction and perception from reality pertaining to the aerosol dispersion with NIV, HFNC, and awake proning. We describe precautions that hospitals and health-care providers must take to mitigate risks with these devices. Finally, we take a practical approach in describing how we use the three techniques, including the common indications, contraindications, and practical aspects of application.

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1. **Is the Prone Position Helpful during Spontaneous Breathing in Patients with COVID-19?**  
   Telias I. JAMA - Journal of the American Medical Association 2020;323(22):2265-2267.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ff6cf7edcecd2714ce7d8325c9e60ad3)

1. **Physiotherapy Care of Patients with Coronavirus Disease 2019 (COVID-19) - A Brazilian Experience.**  
   Righetti Renato Fraga Clinics (Sao Paulo, Brazil) 2020;75:e2017.

Some patients with coronavirus disease (COVID-19) present with severe acute respiratory syndrome, which causes multiple organ dysfunction, besides dysfunction of the respiratory system, that requires invasive procedures. On the basis of the opinions of front-line experts and a review of the relevant literature on several topics, we proposed clinical practice recommendations on the following aspects for physiotherapists facing challenges in treating patients and containing virus spread: 1. personal protective equipment, 2. conventional chest physiotherapy, 3. exercise and early mobilization, 4. oxygen therapy, 5. nebulizer treatment, 6. non-invasive ventilation and high-flow nasal oxygen, 7. endotracheal intubation, 8. protective mechanical ventilation, 9. management of mechanical ventilation in severe and refractory cases of hypoxemia, 10. prone positioning, 11. cuff pressure, 12. tube and nasotracheal suction, 13. humidifier use for ventilated patients, 14. methods of weaning ventilated patients and extubation, and 15. equipment and hand hygiene. These recommendations can serve as clinical practice guidelines for physiotherapists. This article details the development of guidelines on these aspects for physiotherapy of patients with COVID-19.

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1. **Posicao prona em pacientes em ventilacao espontanea com insuficiencia respiratoria por COVID-19: Relato de casoProne position in patients in spontaneous ventilation with respiratory failure by COVID-19: Case report**  
   Dos Anjos J.L.M. Revista Pesquisa em Fisioterapia 2020;10(3):537-542.

INTRODUCTION: The Prone Position (PP) is generally used in cases of Acute Respiratory Insufficiency (IRPA), in patients with Acute Respiratory Distress Syndrome (ARDS) and in invasive mechanical ventilation, in order to improve oxygenation, but it can be used useful in cases of mild IRPA, using the need for invasive mechanical ventilation and complications associated with the ventilator. <br/>OBJECTIVE(S): To describe or report the case of using the prone position (PP) in patients with spontaneous ventilation with mild respiratory failure secondary to COVID-19. <br/>METHOD(S): this is a case of a patient diagnosed with COVID-19, with an IRPA level, with dyspnea, cough, hypoxemia and desaturation, which includes treatment techniques that use a prone position protocol for two hours, twice a day for the entire hospital stay. <br/>RESULT(S): The patient presented hypoxemia (SpO2-94% and PO2-62.9), associated with a food (Borg 6) on admission, having received improvements in food (Borg 4) and 96% saturation in pulse oximetry after 24 hours from the beginning of the protocol and after 48 hours it improves the gasometric and SpO2 and PaO2 values of 96.5% and 80.6 mmHg, respectively. <br/>CONCLUSION(S): The prone position in patients on spontaneous ventilation, with respiratory failure secondary to COVID-19 is safe and can be used as adjunctive therapy to treatment in this patient profile.<br/>Copyright &#xa9; 2020, BAHIANA - School of Medicine and Public Health. All rights reserved.

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1. **Prone position in ARDS patients: why, when, how and for whom.**  
   Guérin Claude Intensive care medicine 2020;:No page numbers.

In ARDS patients, the change from supine to prone position generates a more even distribution of the gas-tissue ratios along the dependent-nondependent axis and a more homogeneous distribution of lung stress and strain. The change to prone position is generally accompanied by a marked improvement in arterial blood gases, which is mainly due to a better overall ventilation/perfusion matching. Improvement in oxygenation and reduction in mortality are the main reasons to implement prone position in patients with ARDS. The main reason explaining a decreased mortality is less overdistension in non-dependent lung regions and less cyclical opening and closing in dependent lung regions. The only absolute contraindication for implementing prone position is an unstable spinal fracture. The maneuver to change from supine to prone and vice versa requires a skilled team of 4-5 caregivers. The most frequent adverse events are pressure sores and facial edema. Recently, the use of prone position has been extended to non-intubated spontaneously breathing patients affected with COVID-19 ARDS. The effects of this intervention on outcomes are still uncertain.

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1. **Prone positioning and high-flow oxygen improved respiratory function in a 25-week pregnant woman with COVID-19.**  
   Vibert Florence European journal of obstetrics, gynecology, and reproductive biology 2020;250:257-258.

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1. **Prone Positioning for Pregnant Women With Hypoxemia Due to Coronavirus Disease 2019 (COVID-19).**  
   Tolcher Mary Catherine Obstetrics and gynecology 2020;136(2):259-261.

The coronavirus disease 2019 (COVID-19) pandemic has prompted expanded use of prone positioning for refractory hypoxemia. Clinical trials have demonstrated beneficial effects of early prone positioning for acute respiratory distress syndrome (ARDS), including decreased mortality. However, pregnant women were excluded from these trials. To address the need for low-cost, low-harm interventions in the face of a widespread viral syndrome wherein hypoxemia predominates, we developed an algorithm for prone positioning of both intubated and nonintubated pregnant women. This algorithm may be appropriate for a wide spectrum of hypoxemia severity among pregnant women. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is responsible for the clinical manifestations of COVID-19. This syndrome can manifest as severe pneumonia complicated by hypoxemia and ARDS. Given the current global COVID-19 pandemic, with a large number of ARDS cases, there is renewed interest in the use of prone positioning to improve oxygenation in moderate or severe hypoxemia. Among the populations who can benefit from prone positioning are pregnant women experiencing severe respiratory distress, as long as the physiologic changes and risks of pregnancy are taken into account.

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1. **Prone Positioning in Awake, Nonintubated Patients With COVID-19 Hypoxemic Respiratory Failure.**  
   Thompson Alison E. JAMA internal medicine 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=83fef36261503f803dfbea447731995a)

1. **Prone Positioning in Awake, Nonintubated Patients With COVID-19: Necessity Is the Mother of Invention.**  
   Sarma Aartik JAMA internal medicine 2020;:No page numbers.

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1. **Prone Positioning in Non-Intubated Patients With COVID-19 Outside of the Intensive Care Unit: More Evidence Needed.**  
   Ripoll-Gallardo Alba Disaster medicine and public health preparedness 2020;:1-3.

The coronavirus disease (COVID-19) pandemic has brought the Italian National Health System to its knees. The abnormally high influx of patients, together with the limited resources available, has forced clinicians to make unprecedented decisions and provide compassionate treatments for which little or no evidence is yet available. This is the case for the use of noninvasive positive pressure ventilation and continuous airway pressure ventilation, combined with prone position in patients with COVID-19 and acute respiratory distress syndrome treated outside of intensive care units. In our article, we comment on the evidence available, so far, and provide a brief summary of data collected at our health institution in Piedmont, Italy.

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1. **Prone positioning in non-intubated patients with COVID-19: raising the bar.**  
   Munshi Laveena The Lancet. Respiratory medicine 2020;8(8):744-745.

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1. **Prone positioning in patients treated with non-invasive ventilation for COVID-19 pneumonia in an Italian emergency department.**  
   Bastoni Davide Emergency medicine journal : EMJ 2020;37(9):565-566.

We report the experience of prone ventilation in selected patients treated with helmet non-invasive ventilation (NIV) continuous positive airway pressure (CPAP) for acute respiratory failure in COVID-19 pneumonia. Preliminary results showed an improvement in the PaO2 value and PaO2/FiO2 ratio after 1 hour of prone ventilation. No variation of the lung ultrasound pattern before and after prone ventilation has been detected. At the time of writing, we attempted proning with helmet NIV CPAP in 10 patients. In 4 out of 10 patients, the attempt failed due to lack of compliance of the patient, scarce pain control even with ongoing treatment and refusal by the patient to prone positioning.

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1. **Prone Positioning of Nonintubated Patients with COVID-19.**  
   Damarla Mahendra American journal of respiratory and critical care medicine 2020;202(4):604-606.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0ba85ea8a22cccf07677dc39f6cbe054)

1. **Prone positioning to improve oxygenation and relieve respiratory symptoms in awake, spontaneously breathing non-intubated patients with COVID-19 pneumonia.**  
   Sztajnbok Jaques Respiratory medicine case reports 2020;30:101096.

Emergency departments are facing an unprecedented challenge in dealing with patients who have coronavirus disease 2019 (COVID-19). The massive number of cases evolving to respiratory failure are leading to a rapid depletion of medical resources such as respiratory support equipment, which is more critical in low- and middle-income countries. In this context, any therapeutic and oxygenation support strategy that conserves medical resources should be welcomed. Prone positioning is a well-known ventilatory support strategy to improve oxygenation levels. Self-proning can be used in the management of selected patients with COVID-19 pneumonia. Here, we describe our experience with two COVID-19-positive patients who were admitted with respiratory failure. The patients were successfully managed with self-proning and noninvasive oxygenation without the need for intubation.

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1. **Proning in Non-Intubated (PINI) in Times of COVID-19: Case Series and a Review.**  
   Paul Vishesh Journal of intensive care medicine 2020;35(8):818-824.

It has been well known for decades that prone positioning (PP) improves oxygenation. However, it has gained widespread acceptance only in the last few years since studies have shown significant survival benefit. Many centers have established prone ventilation in their treatment algorithm for mechanically ventilated patients with severe acute respiratory distress syndrome (ARDS). Physiologically, PP should also benefit awake, non-intubated patients with acute hypoxemic respiratory failure. However, proning in non-intubated (PINI) patients did not gain any momentum until a few months ago when the Coronavirus disease 2019 (COVID-19) pandemic surged. A large number of sick patients overwhelmed the health care system, and many centers faced a dearth of ventilators. In addition, outcomes of patients placed on mechanical ventilation because of COVID-19 infection have been highly variable and often dismal. Hence, increased focus has shifted to using various strategies to prevent intubation, such as PINI. There is accumulating evidence that PINI is a low-risk intervention that can be performed even outside intensive care unit with minimal assistance and may prevent intubation in certain patients with ARDS. It can also be performed safely at smaller centers and, therefore, may reduce the patient transfer to larger institutions that are overwhelmed in the current crisis. We present a case series of 2 patients with acute hypoxemic respiratory failure who experienced significant improvements in oxygenation with PP. In addition, the physiology of PP is described, and concerns such as proning in obese and patient's anxiety are addressed; an educational pamphlet that may be useful for both patients and health care providers is provided.

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1. **Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit.**  
   Sartini Chiara JAMA 2020;323(22):2338-2340.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=41e8fd13c195d73586090c183d409ca1)

1. **The POSITIONED Study: Prone Positioning in Nonventilated Coronavirus Disease 2019 Patients-A Retrospective Analysis.**  
   Jagan Nikhil Critical care explorations 2020;2(10):e0229.

Given perceived similarities between coronavirus disease 2019 pneumonia and the acute respiratory distress syndrome, we explored whether awake self-proning improved outcomes in coronavirus disease 2019-infected patients treated in a rural medical center with limited resources during a significant local coronavirus disease 2019 outbreak.DesignRetrospective analysis of prospectively collected clinical data.SettingSingle-center rural community-based medical center in Grand Island, NE.PatientsOne hundred five nonintubated, coronavirus disease-infected patients.InterventionsNone.Measurements and Main ResultsAfter patients were educated on the benefits of awake self-proning, compliance was voluntary. The primary outcome was need for intubation during the hospital stay; secondary outcomes included serial peripheral capillary oxygen saturation measured by pulse oximetry to the Fio2 ratios, in-hospital mortality, and discharge disposition. Of 105 nonintubated, coronavirus disease-infected patients, 40 tolerated awake self-proning. Patients who were able to prone were younger and had lower disease severity. The risk of intubation was lower in proned patients after adjusting for disease severity using Sequential Organ Failure Assessment scores (adjusted hazard ratio, 0.30; 95% CI, 0.09-0.96; p = 0.043) or Acute Physiology and Chronic Health Evaluation II scores (adjusted hazard ratio, 0.30; 95% CI, 0.10-0.91; p = 0.034). No prone patient died compared with 24.6% of patients who were not prone (p < 0.001; number needed to treat = 5; 95% CI, 3-8). The probability of being discharged alive and peripheral capillary oxygen saturation measured by pulse oximetry to the Fio2 ratios were statistically similar for both groups.ConclusionsAwake self-proning was associated with lower mortality and intubation rates in coronavirus disease 2019-infected patients. Prone positioning appears to be a safe and inexpensive strategy to improve outcomes and spare limited resources. Prospective efforts are needed to better delineate the effect of awake proning on oxygenation and to improve patients' ability to tolerate this intervention.

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1. **Tolerability and safety of awake prone positioning COVID-19 patients with severe hypoxemic respiratory failure.**  
   Solverson Kevin Canadian journal of anaesthesia = Journal canadien d'anesthesie 2020;:No page numbers.

PURPOSEProne positioning of non-intubated patients with coronavirus disease (COVID-19) and hypoxemic respiratory failure may prevent intubation and improve outcomes. Nevertheless, there are limited data on its feasibility, safety, and physiologic effects. The objective of our study was to assess the tolerability and safety of awake prone positioning in COVID-19 patients with hypoxemic respiratory failure.METHODSThis historical cohort study was performed across four hospitals in Calgary, Canada. Included patients had suspected COVID-19 and hypoxic respiratory failure requiring intensive care unit (ICU) consultation, and underwent awake prone positioning. The duration, frequency, tolerability, and adverse events from prone positioning were recorded. Respiratory parameters were assessed before, during, and after prone positioning. The primary outcome was the tolerability and safety of prone positioning.RESULTSSeventeen patients (n = 12 ICU, n = 5 hospital ward) were included between April and May 2020. The median (range) number of prone positioning days was 1 (1-7) and the median number of sessions was 2 (1-6) per day. The duration of prone positioning was 75 (30-480) min, and the peripheral oxygen saturation was 91% (84-95) supine and 98% (92-100) prone. Limitations to prone position duration were pain/general discomfort (47%) and delirium (6%); 47% of patients had no limitations. Seven patients (41%) required intubation and two patients (12%) died.CONCLUSIONSIn a small sample, prone positioning non-intubated COVID-19 patients with severe hypoxemia was safe; however, many patients did not tolerate prolonged durations. Although patients had improved oxygenation and respiratory rate in the prone position, many still required intubation. Future studies are required to determine methods to improve the tolerability of awake prone positioning and whether there is an impact on clinical outcomes.

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1. **Transport of a Nonintubated Prone Patient with Severe Hypoxemic Respiratory Failure Due to COVID-19.**  
   Boomhower James Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors 2020;:1-4.

With the COVID-19 pandemic, healthcare systems have been facing an unprecedented, large-scale respiratory disaster. Prone positioning improves mortality in severe hypoxemic respiratory failure, including COVID-19. While this is effective for intubated patients with moderate-to-severe ARDS, it has also been shown to be beneficial for non-intubated patients. Critical care transport (CCT) has become an essential component of combating COVID-19, frequently transporting patients to receive advanced respiratory therapies and distribute patients in concert with available resources. With increasing awake proning, CCT teams may encounter patients supported in the prone position. Historically, transporting in the prone position has not been embraced due to substantial risks of desaturation during transport. In this case report, we describe the first known report of transporting a non-intubated, critically ill COVID-19 patient in the prone position.

1. **Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure.**  
   Elharrar Xavier JAMA 2020;323(22):2336-2338.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bf6803d2f43e2b4ae1d8daf3f4b9e94f)

1. **Voluntary Prone Position for Acute Hypoxemic Respiratory Failure in Unintubated Patients.**  
   Rao Shoma V. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine 2020;24(7):557-562.

Severe hypoxemic respiratory failure is frequently managed with invasive mechanical ventilation with or without prone position (PP). We describe 13 cases of nonhypercapnic acute hypoxemic respiratory failure (AHRF) of varied etiology, who were treated successfully in PP without the need for intubation. Noninvasive ventilation (NIV), high-flow oxygen via nasal cannula, supplementary oxygen with venturi face mask, or nasal cannula were used variedly in these patients. Mechanical ventilatory support is offered to patients with AHRF when other methods, such as NIV and oxygen via high-flow nasal cannula, fail. Invasive mechanical ventilation is fraught with complications which could be immediate, ranging from worsening of hypoxemia, worsening hemodynamics, loss of airway, and even death. Late complications could be ventilator-associated pneumonia, biotrauma, tracheal stenosis, etc. Prone position is known to improve oxygenation and outcome in adult respiratory distress syndrome. We postulated that positioning an unintubated patient with AHRF in PP will improve oxygenation and avoid the need for invasive mechanical ventilation and thereby its complications. Here, we describe a series of 13 patients with hypoxemic respiratory of varied etiology, who were successfully treated in the PP without endotracheal intubation. Two patients (15.4%) had mild, nine (69.2%) had moderate, and two (15.4%) had severe hypoxemia. Oxygenation as assessed by PaO2/FiO2 ratio in supine position was 154 ± 52, which improved to 328 ± 65 after PP. Alveolar to arterial (A-a) O2 gradient improved from a median of 170.5 mm Hg interquartile range (IQR) (127.8, 309.7) in supine position to 49.1 mm Hg IQR (45.0, 56.6) after PP. This improvement in oxygenation took a median of 46 hours, IQR (24, 109). Thus, voluntary PP maneuver improved oxygenation and avoided endotracheal intubation in a select group of patients with hypoxemic respiratory failure. This maneuver may be relevant in the ongoing novel coronavirus disease pandemic by potentially reducing endotracheal intubation and the need for ventilator and therefore better utilization of critical care services.How to cite this articleRao SV, Udhayachandar R, Rao VB, Raju NA, Nesaraj JJJ, Kandasamy S, et al. Voluntary Prone Position for Acute Hypoxemic Respiratory Failure in Unintubated Patients. Indian J Crit Care Med 2020;24(7):557-562.

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| 18. | EMBASE | (10 AND 13 AND 17) | 3 |
| 19. | EMCARE | (prone OR proning OR proned).ti,ab | 21795 |
| 20. | EMCARE | (covid\* OR coronavirus\* OR 2019-nCoV OR COVID-19 OR COVID19 OR SARS-CoV-2 OR coronavirus\* OR coronovirus\* OR coronavirinae\* OR Coronavirus\* OR Coronovirus\* OR Wuhan\* OR Hubei\* OR Huanan OR "2019-nCoV" OR 2019nCoV OR nCoV2019 OR "nCoV-2019" OR "COVID-19" OR COVID19 OR "CORVID-19" OR CORVID19 OR "WN-CoV" OR WNCoV OR "HCoV-19" OR HCoV19 OR CoV OR "2019 novel\*" OR Ncov OR "n-cov" OR "SARS-CoV-2" OR "SARSCoV-2" OR "SARSCoV2" OR "SARS-CoV2" OR SARSCov19 OR "SARS-Cov19" OR "SARSCov-19" OR "SARS-Cov-19" OR Ncovor OR Ncorona\* OR Ncorono\* OR NcovWuhan\* OR NcovHubei\* OR NcovChina\* OR NcovChinese\*).ti,ab | 23407 |
| 21. | EMCARE | exp CORONAVIRINAE/ | 2797 |
| 22. | EMCARE | (20 OR 21) | 24299 |
| 23. | EMCARE | ("self-ventilat\*").ti,ab | 13 |
| 24. | EMCARE | (spontaneous ADJ2 breath\*).ti,ab | 2017 |
| 25. | EMCARE | (spontaneous ADJ2 ventilat\*).ti,ab | 836 |
| 26. | EMCARE | (23 OR 24 OR 25) | 2687 |
| 27. | EMCARE | (19 AND 22 AND 26) | 2 |
| 28. | CINAHL | (prone OR proning OR proned).ti,ab | 13328 |
| 29. | CINAHL | (covid\* OR coronavirus\* OR 2019-nCoV OR COVID-19 OR COVID19 OR SARS-CoV-2 OR coronavirus\* OR coronovirus\* OR coronavirinae\* OR Coronavirus\* OR Coronovirus\* OR Wuhan\* OR Hubei\* OR Huanan OR "2019-nCoV" OR 2019nCoV OR nCoV2019 OR "nCoV-2019" OR "COVID-19" OR COVID19 OR "CORVID-19" OR CORVID19 OR "WN-CoV" OR WNCoV OR "HCoV-19" OR HCoV19 OR CoV OR "2019 novel\*" OR Ncov OR "n-cov" OR "SARS-CoV-2" OR "SARSCoV-2" OR "SARSCoV2" OR "SARS-CoV2" OR SARSCov19 OR "SARS-Cov19" OR "SARSCov-19" OR "SARS-Cov-19" OR Ncovor OR Ncorona\* OR Ncorono\* OR NcovWuhan\* OR NcovHubei\* OR NcovChina\* OR NcovChinese\*).ti,ab | 26441 |
| 30. | CINAHL | COVID-19/ OR CORONAVIRUS/ | 11025 |
| 31. | CINAHL | (29 OR 30) | 28684 |
| 32. | CINAHL | ("self-ventilat\*").ti,ab | 16 |
| 33. | CINAHL | (spontaneous ADJ2 breath\*).ti,ab | 1322 |
| 34. | CINAHL | (spontaneous ADJ2 ventilat\*).ti,ab | 560 |
| 35. | CINAHL | (32 OR 33 OR 34) | 1718 |
| 36. | CINAHL | (28 AND 31 AND 35) | 1 |
| 37. | Medline | (prone OR proning OR proned).ti,ab | 77676 |
| 38. | Medline | (covid\* OR coronavirus\* OR 2019-nCoV OR COVID-19 OR COVID19 OR SARS-CoV-2 OR coronavirus\* OR coronovirus\* OR coronavirinae\* OR Coronavirus\* OR Coronovirus\* OR Wuhan\* OR Hubei\* OR Huanan OR "2019-nCoV" OR 2019nCoV OR nCoV2019 OR "nCoV-2019" OR "COVID-19" OR COVID19 OR "CORVID-19" OR CORVID19 OR "WN-CoV" OR WNCoV OR "HCoV-19" OR HCoV19 OR CoV OR "2019 novel\*" OR Ncov OR "n-cov" OR "SARS-CoV-2" OR "SARSCoV-2" OR "SARSCoV2" OR "SARS-CoV2" OR SARSCov19 OR "SARS-Cov19" OR "SARSCov-19" OR "SARS-Cov-19" OR Ncovor OR Ncorona\* OR Ncorono\* OR NcovWuhan\* OR NcovHubei\* OR NcovChina\* OR NcovChinese\*).ti,ab | 88937 |
| 39. | Medline | exp CORONAVIRUS/ OR exp CORONAVIRUS INFECTIONS/ | 51251 |
| 40. | Medline | (38 OR 39) | 97513 |
| 41. | Medline | (nonintubated OR "non-intubated" OR "noninvasive ventilat\*" OR "non-invasive ventilat\*").ti,ab | 6517 |
| 42. | Medline | (37 AND 40 AND 41) | 37 |
| 43. | Medline | ("high flow oxygen").ti,ab | 493 |
| 44. | Medline | (37 AND 40 AND 43) | 8 |

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