

COVID-19 Scientific Advisory Group

Rapid Evidence Report

Key Research Question: In awake non-intubated patients with SARS-COV-2 pneumonia who are being cared for in acute care facilities, is prone positioning safe and/or effective at improving patient outcomes?

Context

- Prone Positioning is a non-pharmacological therapy for hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS) where patients lay on their stomach rather than their back (Kallet et al. 2015, Scholten et al. 2017)
- Prone positioning intubated and mechanically ventilated patients with moderate-severe ARDS within an intensive care unit (ICU) is a proven life-saving intervention.
 - The PROSEVA trial demonstrated a 16% absolute risk reduction in mortality (number needed to treat of 6 to save one life) for patients with moderate-severe ARDS when patients were prone positioned for 16 hours or longer at a time (Guerin et al. 2013).
 - Although many patients demonstrated an improvement in oxygenation in PROSEVA when in the prone position, this improvement had no association with the survival benefit demonstrated. The effect was likely mediated through a reduction in ventilator induced lung injury not improved oxygenation (Albert et al. 2014)
- Prone positioning non-intubated patients has gained attention as a potential treatment through small case reports and uncontrolled case series, social media, and conventional media reports.
- Awake prone positioning non-intubated patients has been attempted on hospital wards outside of the ICU in the Calgary zone without a formal protocol or a detailed evaluation of the risks and benefits.
- These guidelines are intended for clinicians who may be responsible for patients with hypoxemic respiratory failure who are hospitalized and not yet requiring the ICU.

Key Messages from the Evidence Summary

- While awake prone positioning of non-intubated patients admitted with acute hypoxemic respiratory failure secondary to COVID-19 may improve oxygen saturation levels, its effect on clinical outcomes such as hospital survival, intubation or need for ICU admission has not been defined.
- The risks of awake prone positioning in non-intubated patients with acute hypoxemic respiratory failure secondary to COVID-19 have not been established, but previous studies in patients with ARDS raise concerns about aspiration, hemodynamic instability, pressure ulcers, cardiac arrest, and delayed intubation.
- Careful assessment of patient indications and contraindications, as well as the identification of the appropriate care setting is required prior to consideration for awake prone positioning of patients admitted with COVID-19.

Committee Discussion

The committee achieved consensus on the recommendation. It was acknowledged that some small case series, without adequate controls, had shown improvements in short-term oxygenation, but that information on adverse events was not provided. It was noted that proning is a well-established practice for ARDS in intubated patients cared for in ICUs and that it is associated with improved survival in ICUs. However, it was acknowledged that this could not be extrapolated to proning in awake patients outside the ICU without further trials in this specific population, in part because of lack of information on who awake proning should be used in, how long it should be used for, and the frequency of adverse events. It was noted that nursing protocols would be required to enable safe care of patients undergoing proning on medical wards. The committee felt that where available, patients for whom proning is considered should be enrolled in clinical trials that are starting in Alberta. For patients being

considered for awake prone positioning outside of a clinical trial, some practical considerations are offered including which patients might be considered, as well as ensuring nursing protocols are available to monitor patients.

Recommendations

1. The efficacy and safety of awake prone positioning of non-intubated COVID-19 patients with hypoxemic respiratory failure is not established and hence this practice is not recommended for routine application in this population of patients. Ongoing clinical trials (some of which are active in Alberta) should inform the best utility of this practice in the future.

Practical Considerations

1. If being considered for awake prone positioning outside of a clinical trial, COVID-19 patients should be assessed:
 - a. to determine their ability to communicate and co-operate with procedures, rotate to front and adjust position independently and to confirm an absence of anticipated airway issues.
 - b. to rule out absolute contraindications including respiratory distress ($RR \geq 35$, $PaCO_2 \geq 48$, accessory muscle use), immediate need for intubation, hemodynamic instability ($SBP < 90\text{mmHg}$) or arrhythmia, agitation or altered mental status, unstable spine/thoracic injury/recent abdominal surgery
 - c. to rule out relative contraindications: facial injury, neurological issues (e.g. frequent seizures), morbid obesity, pregnancy (2/3rd trimesters), pressure sores / ulcers
2. If awake prone positioning for COVID-19 patients is being considered for use outside of a clinical trial, health systems should be assessed to identify the required setting including equipment, staffing, and monitoring required.
3. If awake prone positioning for COVID-19 patients is being considered for use outside of critical care, a pathway should be developed to characterize required training, monitoring, documentation and outcomes measurement and include appropriate thresholds for discontinuation and escalation to the next level of care.

Strength of Evidence

1. The strength of the evidence to support awake prone positioning of non-intubated COVID-19 patients with hypoxemic respiratory failure on the hospital ward with the goal of improving oxygen saturations is **WEAK**.
2. The strength of the evidence to support the effectiveness of awake prone positioning of non-intubated COVID-19 patients with hypoxemic respiratory failure on a hospital ward with the goal of improving patient survival, reducing the need for intubation, or reducing hospital length of stay is **UNDETERMINED** due to lack of randomized control trials as well as a lack of standardized description of risks and their quantification.

Limitations of this review

This review is limited by several things:

1. COVID-19 is a novel disease and thus limited studies exist on the use of non-pharmacological therapies such as awake prone positioning. Current available literature for COVID-19 includes only several case reports and a single prospective cohort study that did not describe a standardized proning procedure and /or include any safety outcomes or a control group.
2. Studies using awake prone positioning in non-COVID19 patients are limited to case reports or small prospective and retrospective case series which were heterogeneous in design, had methodologically biases, and lacked appropriate control groups.

Summary of Evidence

A total of eleven studies (including four prospective case series, five retrospective case series, and two case reports) with 141 patients in total describe the use of awake prone positioning for hypoxemic respiratory failure. Five of these studies (n=91 patients, 2 case reports and 3 prospective case series) report on the use of awake prone positioning in SARS-COV-2 patients. Studies are summarized in tables 1 and 2.

Appraisal of notable studies:

The Caputo et al. (2020) study presents a prospective cohort of 50 consecutive SARS-COV-2 patients treated with awake prone positioning in the emergency department. The study is presented with a limited narrative description of the patients with no tables or figures within the article. The median time patients were observed in the emergency department was 29 minutes. The authors describe an increase in oxygen saturation from 84% to 94% when patients were in the prone position for 5 minutes while on either 5L/min nasal prongs or a non-rebreather. 36% of patients (n=18) were intubated during their hospital stay, with 26% (n=13) intubated within 24 hours of prone positioning and 14% (n=7) requiring intubation within 60 minutes of prone positioning. The dose (duration) of prone positioning is not clearly defined or described. Adverse events of prone positioning are not described. There was no description of a control arm. The authors propose their findings are hypothesis generating.

The Ding et al. (2020) study presents a prospective cohort of 20 consecutive patients with ARDS treated with awake prone positioning. All the patients in this study were admitted to the ICU and were placed on either high flow nasal cannula or non-invasive ventilation. Prone positioning was applied a minimum of twice per day for a minimum of 30 minutes per session, with an average of 2 hours per session. Patients with high flow nasal cannula or non-invasive ventilation in combination with prone positioning were observed to have an overall improvement in their PaO₂:FiO₂ ratio. 45% of patients required intubated (9 of 20 patients). Only one safety outcome was formally assessed – the ability to tolerate prone positioning. Two patients did not tolerate prone positioning and two patients had worsening PaO₂:FiO₂ when prone positioning was combined with non-invasive ventilation.

The Scaravelli et al. (2015) study presents a retrospective cohort of 15 patients over 6 years with acute hypoxemic respiratory failure who were prone positioned. In total 43 prone positioning sessions were performed, with a median of 2 (1-3) per patient. The median duration of prone positioning per session was 3 (2-4) hours and the longest session lasted 8 hours. Two patients were intubated and two patients died without being intubated. It is unclear from the description if intubation was not offered to the patients who died without being intubated. Adverse events were not described.

Two recent case series from single centers in France and Italy (**Elharrar et al, 2020** and **Sartini et al, 2020**) were published in JAMA (May 15, 2020) describing the tolerance and short term oxygenation benefits of awake prone positioning in patients with COVID-19 being treated for acute hypoxemic respiratory failure with oxygen via NP or in those who require NIV. Both studies were performed outside of the ICU and ER setting on hospital wards. Both studies demonstrated tolerance of prone positioning in a majority of patients. Short term improvements in oxygenation were observed while in the prone position in most patients and there were modest rates for intubation or other important clinical outcomes. Any improvements in comfort or oxygenation were not sustained when the patients returned to the supine position.

An editorial published in the same issue, (**Telius et al, 2020**) describes the current theories for how prone positioning could reduce lung injury in ARDS. The editorial describes the two articles as suggesting some benefit in case series and cautions that although patients had an improvement in oxygenation during prone positioning, the small number of patients, short study duration and the lack of control groups are major study limitations and the results should be interpreted with caution. The authors suggest larger more rigorous studies will be required to support any generalizability. They made specific reference to the need for clinicians to “closely monitor patients for whom prone positioning is used for tolerance and response and aim to prevent delayed intubation and controlled mechanical ventilation when necessary.”

Table 1 – Characteristics of Studies Examining Awake Prone Positioning in Non-intubated Hypoxemic Respiratory Failure Patients

Author	Study Dates	Study Type	No. of pts	Inclusion Criteria	Exclusion Criteria	Setting	Oxygen Delivery Mode	Prone Positioning Protocol	Study Outcome	Safety Outcomes reported
COVID-19 patients										
Elharrar (2020)	2020	Prospective cohort	24	Hypoxemia, CT chest consistent with COVID-19 and posterior lesions	Requiring intubation, altered consciousness	Medical unit	NP, facemask, HFNC	Single episode, no goal duration	Proportion of patients with PaO ₂ increase ≥20% from supine to PP	Yes
Sartini (2020)	2020	Cross-sectional survey	15	Hypoxemia (SpO ₂ <94%), FiO ₂ >0.6 and CPAP 10 cm H ₂ O	-	Medical Unit	NIV	Not standardized	PaO ₂ :FiO ₂ , RR, patient comfort with NIV	No
Caputo (2020)	2020	Prospective cohort	50	Hypoxemia (SpO ₂ <90%)	NIV use, DNR order	ED	NP or facemask	Not Standardized	SpO ₂ 5 minutes after PP, intubation rate within 24hrs	No
Elkattawy (2020)	2020	Case report	1	Hypoxemia	-	Medical unit	NP	Not Standardized	-	No
Slessarev (2020) ¹	2020	Case report	1	Hypoxemia	-	ICU	HFNC	Not Standardized	-	No
Non-COVID-19 patients										
Ding (2020)	2018-2019	Prospective cohort	20	ARDS (Berlin criteria) on NIV with CPAP 5 cm H ₂ O and PaO ₂ :FiO ₂ <200	Requiring intubation	ICU	HFNC or NIV	>30 minutes, 2 times daily for 3 days	Intubation rate, change in PaO ₂ :FiO ₂	Yes
Perez-Nieto (2020)	2017-2018	Retrospective cohort	6	ARDS (Berlin criteria) non-infections ARDS, and PaO ₂ :FiO ₂ <100	-	ICU	HFNC or NIV	2-3 hours, 2 times daily for 2 days	-	No
Scaravilli (2015)	2009-2014	Retrospective Cohort	15	PaO ₂ :FiO ₂ <300, and undergone one PP without intubation	-	ICU	NP, HFNC or NIV	Not Standardized	Change in PaO ₂ :FiO ₂	Yes
Feltracco (2012)	-	Retrospective Cohort	3	Post lung transplant, and hypoxemia	-	ICU	HFPV	Not Standardized	-	No
Feltracco (2009)	-	Retrospective Cohort	2	Post lung transplant, and hypoxemia	-	ICU	NIV	Not Standardized	-	No
Valter (2003)	-	Retrospective Cohort	4	Hypoxemia	-	ICU	NIV	Not Standardized	-	No

Abbreviations: ARDS, acute respiratory distress syndrome; CPAP, continuous positive airway pressure; CT, computed tomography; DNR, do not resuscitate; ED, emergency department; FiO₂, fraction of inhaled oxygen; HFNC, high-flow nasal cannula; ICU, intensive care unit; NIV, non-invasive ventilation; NP, nasal prongs; PaO₂, partial pressure of arterial oxygen; PP, prone position; RR, respiratory rate; SpO₂, oxygen saturation

Table 2 - Physiological and Clinical Outcomes of Patients Receiving Awake Prone Positioning

Author	Supine Oxygenation, mean (SD), median [IQR]	Prone Position Oxygenation, mean (SD), median [IQR]	Resp Rate, breaths/min	Intubation Rate, No. (%)	Daily Duration of Prone Position, hours	Adverse Events
COVID-19 patients						
Elharrar (2020)	PaO ₂ 72.8 (14.2)	PaO ₂ 91 (27.3) 75% had <20% increase PaO ₂	-	5/24 (20.8)	63% ≥3	42% backpain 17% tolerated < 1 hour 17% required intubation within 72 hours
Sartini (2020)	PaO ₂ :FiO ₂ 58-117**	PaO ₂ :FiO ₂ 114-122**	Supine: 21-31** PP: 18-27**	1/15 (6.6)	Median 3 (IQR, 1-6)	1 death (7%)
Caputo (2020)	SpO ₂ 84% [75-90]	SpO ₂ 94% [90-95]	-	13/50 (26.0)	-	8% required intubation within 30 minutes
Elkattawy (2020)	SpO ₂ 94%, 4 L/min NP	SpO ₂ 95%, room air	-	-	12	None
Slessarev (2020)	PaO ₂ :FiO ₂ 100**	PaO ₂ :FiO ₂ 250**	-	0/1 (0)	17	Nosebleed
Non-COVID-19 patients						
Ding (2020)	PaO ₂ :FiO ₂ 95 (22) / 102 (15)*	PaO ₂ :FiO ₂ 130 (35) / 113 (25)*	-	9/20 (45.0)	Mean (SD) Unintubated 1.8 (0.7), Intubated 1.9 (1.4)	2 non-tolerant
Perez-Nieto (2020)	PaO ₂ :FiO ₂ 80 [67-91]	PaO ₂ :FiO ₂ 116 [101-131]	-	2/6 (33.3)	-	None
Scaravilli (2015)	PaO ₂ :FiO ₂ 127(49)	PaO ₂ :FiO ₂ 186 (72)	Mean (SD) Supine: 26 (10) PP: 25 (11)	2/15 (13.3)	Median 3 (IQR, 2-4)	No displaced catheters, pressure sores, neuropathies, vomiting, change in hemodynamics or vasopressors use 2/15 patients non-tolerant 3/15 patients died without intubation: 2 patients placed on ECMO prior to intubation, and 1 patient changed goals of care
Feltracco (2012)	-	-	-	0/1 (0)	2-3	None
Feltracco (2009)	FiO ₂ 0.80	FiO ₂ 0.60	-	0/1 (0)	6-8	None
Valter (2003)	FiO ₂ 0.70 [0.60-0.70]	FiO ₂ 0.40 [0.30-0.50]	Median (IQR): Supine: 31 (26-38) PP: 20 (18-21)	0/1 (0)	2-5	None

* High flow nasal cannula success/failure, ** Range estimated from figure
Abbreviations: ECMO, extracorporeal membrane oxygenation; FiO₂, fraction of inhaled oxygen; IQR, interquartile range; PaO₂, partial pressure of arterial oxygen; PP, prone position; SD, standard deviation; SpO₂, oxygen saturation.

Research Question - In awake non-intubated patients with SARS-COV-2 pneumonia who are being cared for in acute care facilities, is prone positioning safe and/or effective at improving patient outcomes?

1. While awake prone positioning non-intubated ward patients may improve oxygen saturation levels, its effect on clinical outcomes such as hospital survival, intubation or need for ICU admission remain undefined. This is primarily due to the lack of rigorously conducted randomized control trials to allow comparison between the intervention and usual care. Some additional points to note are as follows:
 - o Studies reported to date were primarily conducted in a highly monitored setting (ie ICU or ED)
 - o Two studies and one case report trialed awake prone positioning on general hospital wards.
 - o The dose (duration of prone positioning) remains highly variable and is not standardized.
 - o The majority of patients are on high flow nasal cannula or non-invasive ventilation.
 - o Many studies did not include COVID-19 patients.

2. The risks of awake prone positioning non-intubated ward patients (which could include unintentional removal of intravenous lines/catheters, aspiration, hemodynamic instability, pressure ulcers, cardiac arrest, and delayed intubation) remain undefined with the exception of intolerance to prone positioning, musculoskeletal pain and nosebleeds.
 - Reporting of safety or adverse events was not standardized and largely retrospective.
3. Routine awake prone positioning of non-intubated COVID-19 patients with hypoxemic respiratory failure should not be offered outside of a clinical trial given the unknown clinical benefits and potential for significant risk.
 - Two clinical trials locally are launching that offer the opportunity for patients to participate (CORONA and COVI-PRONE)

Evolving Evidence

Several international multicenter trials are launching to examine the use of awake prone positioning. In the Calgary zone, the following two trials will be available:

COVI-PRONE – Examining the use of awake prone positioning in non-intubated COVID-19 patients with hypoxemic respiratory failure who are candidates for the ICU based on their goals of care (R1/R2).

CORONA - Examining the use of awake prone positioning in non-intubated COVID-19 patients with hypoxemic respiratory failure who are not candidates for the ICU based on their goals of care (R3/M1/M2).

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Date report submitted to committee: May 15, 2020

Date of first assessment: May 19, 2020

(If applicable) Date of re-assessment:

Authorship and Committee Members

This report was written by Ken Parhar¹, Jason Weatherald², and Kevin Solverson², and scientifically reviewed by Elizabeth Mackay, Andrew MacRae, Brandie Walker, Brian Holroyd (external reviewer), Dan Zuege³ (external reviewer), and Ron Spice (external reviewer). The full Scientific Advisory Group was involved in discussion and revision of the document: Braden Manns (co-chair), Lynora Saxinger (co-chair), John Conly, Alexander Doroshenko, Shelley Duggan, Nelson Lee, Elizabeth MacKay, Andrew MacRae, Jeremy Slobodan, James Talbot, Brandie Walker, and Nathan Zelyas.

Conflicts of Interest

1 - Primary investigator – TheraPPP study, Venting Wisely, PRONTO studies involving implementation science and improving the use of prone positioning for moderate-severe ARDS in the ICU. Co-Primary investigator for COVI-PRONE and CORONA examining the use of awake prone positioning in COVID-19 respiratory failure

2 - Co-Primary investigator for COVI-PRONE and CORONA examining the use of awake prone positioning in COVID-19 respiratory failure

3 – Co-investigator - TheraPPP study, Venting Wisely, PRONTO studies involving implementation science and improving the use of prone positioning for moderate-severe ARDS in the ICU. Co-Primary investigator for COVI-PRONE and CORONA examining the use of awake prone positioning in COVID-19 respiratory failure

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COVID-19 Scientific Advisory Group Rapid Evidence Report

Appendix

List of Abbreviations

AHS: Alberta Health Services

COVID-19: Coronavirus Disease-2019

SAG: Scientific Advisory Group

Literature Search

A literature search was conducted by Nicole Loroff from Knowledge Resources Services (KRS) within the Knowledge Management Department of Alberta Health Services. No publication date was applied to retrieve relevant literature not specific to COVID-19. Databases and grey literature sources searched include: MEDLINE (Ovid), PubMed, Trip PRO, Cochrane Library, LitCOVID, WHO COVID-19 Research Database, Centre for Evidence-Based Medicine (CEBM), National Institute for Health and Care Excellence (NICE), medRxiv, BMJ Best Practice, Cambridge Coronavirus Free Access Collection, Google Scholar and Google. The citation tracking method was applied in Google Scholar. Briefly, the search strategy involved combinations of keywords and subject headings including:

- SARS-Cov-2 or COVID-19 or coronavirus
- Awake prone positioning
- Other potentially relevant respiratory conditions identified by the primary writer

The full search strategy is listed in the Search Strategy section below.

Articles identified by KRS in their search were initially screened by title against the PICOS statement listed in Table 1 below. 38 articles were identified by KRS with references and abstracts provided for further review. 29 were excluded from the review in accordance with the inclusion/exclusion criteria stated below.

Table 1. Inclusion and exclusion criteria for results of the literature search

Population	Patients with hypoxemic respiratory failure who are not intubated.
Intervention	Prone positioning
Comparison	Usual management (supine position)
Outcome	Including but not limited to: Clinical (intubation rates or survival), physiological (oxygen saturations), hospital resource utilization (length of stay in ICU or hospital), adverse events
Settings	Hospitalized patient

Critical Evaluation of the Evidence

Table 2. Narrative overview of the literature included in this review.

	Description
Volume	3 prospective cohort studies were included, 1 case series, 5 retrospective observational studies were included, 2 case reports were included
Quality	Low quality with small numbers and single centers without control groups and poor description of inclusion/exclusion or outcomes measured. Limited numbers of patients with COVID-19. Limited description of intervention regarding duration. Limited description of harms.
Applicability	Differences in volume of patients and capacity for ICU and intubation and different public health interventions. Differences in health care systems and implementation of guidelines and pathways. Very few studies of patients being treated with Prone Positioning on Medical Units.
Consistency	Consistent results suggesting improvements in oxygenation

Search Strategy

Database(s): **Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily** 1946 to May 06, 2020

#	Searches	Results
1	exp Coronavirus/ or exp Coronavirus Infections/ or coronaviru*.mp. or "corona virus*".mp. or ncov*.mp. or n-cov*.mp. or "novel cov".mp. or COVID-19.mp. or COVID19.mp. or COVID-2019.mp. or COVID2019.mp. or SARS-CoV-2.mp. or SARSCoV-2.mp. or SARSCoV2.mp. or SARSCoV19.mp. or SARS-Cov-19.mp. or SARSCov-19.mp. or SARSCoV2019.mp. or SARS-Cov-2019.mp. or SARSCov-2019.mp. or "severe acute respiratory syndrome coronaviru*".mp. or "severe acute respiratory syndrome cov 2".mp. or "2019 ncov".mp. or 2019ncov.mp.	22252
2	Patient Positioning/	6295
3	Prone Position/	3976
4	prone position*.mp.	7526
5	(prone adj2 position*).mp.	7953
6	(proned or proning or self-proning).mp.	78
7	2 or 3 or 4 or 5 or 6	13624
8	1 and 7	12
9	Respiratory Distress Syndrome, Adult/	19171
10	Severe Acute Respiratory Syndrome/	4568
11	SARS Virus/	3016
12	Middle East Respiratory Syndrome Coronavirus/	1033
13	Influenza A Virus, H1N1 Subtype/	15117
14	exp Pneumonia/	92786
15	"acute respiratory distress syndrome".mp.	12832
16	"acute respiratory syndrome".mp.	8780
17	(ARDS or SARS or SARS-CoV or MERS or MERS-CoV or H1N1 or pneumonia or influenza).mp.	273859
18	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	291373

19	7 and 18	1098
20	limit 19 to english language	953
21	(non-intubat* or nonintubat* or "not intubat*" or non-ventilat* or nonventilat* or "not ventilat*" or conscious or awake or tubeless).mp.	78151
22	20 and 21	25
23	limit 20 to "all adult (19 plus years)"	343
24	limit 23 to "reviews (best balance of sensitivity and specificity)"	44
25	7 and 21	256
26	limit 25 to english language	236
27	limit 26 to "all adult (19 plus years)"	108

PubMed

#	Searches	Results
1	"coronavirus"[MeSH Terms] OR "coronavirus infections"[MeSH Terms] OR "coronaviru*" [Title/Abstract] OR "corona virus"[Title/Abstract] OR "ncov*" [Title/Abstract] OR "n cov*" [Title/Abstract] OR "novel cov*" [Title/Abstract] OR "COVID-19"[Title/Abstract] OR "COVID19"[Title/Abstract] OR "COVID-2019"[Title/Abstract] OR "COVID2019"[Title/Abstract] OR "SARS-COV-2"[Title/Abstract] OR "SARSCOV-2"[Title/Abstract] OR "sarscov2" [Title/Abstract] OR "SARSCOV19"[Title/Abstract] OR "sars cov 19" [Title/Abstract] OR "severe acute respiratory syndrome cov 2"[Title/Abstract] OR "2019 ncov"[Title/Abstract] OR "2019ncov"[Title/Abstract] OR "severe acute respiratory disease"[Title/Abstract]	28763
2	"prone position"[MeSH Terms] OR "patient positioning"[MeSH Terms] OR "prone position*" [Title/Abstract] OR "prone n2 position*" [Title/Abstract] OR "proned"[Title/Abstract] OR "proning"[Title/Abstract] OR "self-proning"[Title/Abstract]	13707
3	1 and 2	24
4	limit 3 to english language	21
5	"respiratory distress syndrome, adult"[MeSH Terms] OR "severe acute respiratory syndrome"[MeSH Terms] OR "SARS virus"[MeSH Terms] OR "middle east respiratory syndrome coronavirus"[MeSH Terms] OR "influenza a virus, h1n1 subtype"[MeSH Terms] OR "pneumonia"[MeSH Terms] OR "acute respiratory distress syndrome"[Title/Abstract] OR "acute respiratory syndrome"[Title/Abstract] OR "ARDS"[Title/Abstract] OR "SARS"[Title/Abstract] OR "SARS-CoV"[Title/Abstract] OR "MERS"[Title/Abstract] OR "MERS-CoV"[Title/Abstract] OR "H1N1"[Title/Abstract] OR "pneumonia"[Title/Abstract] OR "influenza"[Title/Abstract]	284352
6	2 and 5	1112
7	limit 6 to english language	967
8	"non intubat*" [Title/Abstract] OR "nonintubat*" [Title/Abstract] OR "not intubat*" [Title/Abstract] OR "non ventilat*" [Title/Abstract] OR "nonventilat*" [Title/Abstract] OR "not ventilat*" [Title/Abstract] OR "conscious" [Title/Abstract] OR "awake" [Title/Abstract] OR "tubeless" [Title/Abstract]	71756
9	7 and 8	20
10	limit 7 to "all adult (19 plus years)"	342
11	limit 10 to "review"	41
12	2 and 8	220
13	limit 12 to english language	205
14	limit 13 to "all adult (19 plus years)"	92

TRIP Pro/Google Scholar/Google

("covid-19" OR coronavirus OR COVID19 OR "corona virus" OR ncov OR "n-cov" OR "covid-2019" OR covid2019 OR "SARS-COV-2" OR "sarscov-2" OR sarscov2 OR sarscov19 OR "sars-cov-19" or "sarscov-19" OR sarscov2019 OR "sars-cov-2019" OR "severe acute respiratory syndrome") AND (prone position or proned or prone positioning or proning or self-proning) from:2020

("acute respiratory distress syndrome" or "acute respiratory syndrome" or ARDS or SARS or SARS-CoV or MERS or MERS-CoV or H1N1 or pneumonia or influenza) AND (prone position or proned or prone positioning or proning or self-proning) AND (non-intubat* or nonintubat* or nonventilat* or non-ventilat* or conscious or awake or tubeless)

(non-intubat* or nonintubat* or nonventilat* or non-ventilat* or conscious or awake or tubeless) AND (prone position or proned or prone positioning or proning or self-proning)

LitCovid/ WHO COVID-19 Database/Cochrane Library/Centre for Evidence-Based Medicine (CEBM)/National Institute for Health and Care Excellence (NICE)/medRxiv/BMJ Best Practice/Cambridge Coronavirus Free Access Collection
(prone or prone position or proned or proning or prone positioning or self-proning)

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