Federatie
Medisch
Specialisten

Leidraad
Buikligging bij patiënten met COVID-19 en niet-invasieve beademing of ‘high flow nasal oxygen’ toediening

Samenstelling van de werkgroep

De werkgroep is samengesteld om een leidraad te formuleren over buikligging bij patiënten met COVID-19 en niet-invasieve beademing of 'high flow nasal oxygen' toediening. Alle werkgroepleden zijn door de wetenschappelijke verenigingen gemandateerd voor deelname aan deze werkgroep.

Samenstelling van de werkgroep:
Dr. L.M. van den Toorn, longarts, NVALT, voorzitter
Drs. M. Groenendijk, longarts-intensivist, NVALT
Prof. dr. J.G. van der Hoeven, internist-intensivist, NVIC
Prof. dr. L.M.A. Heunks, longarts-intensivist, NVIC
Drs. N. Voesten, anesthesioloog-intensivist, NVA
Prof. dr. P.W.B. Nanayakkara, internist, NIV
Drs. A.J. Meinders, internist-intensivist, NIV

Met ondersteuning van
Dr. J.C. Maas, adviseur, Kennisinstituut van de Federatie Medisch Specialisten
Dr. S.N. Hofstede, senior adviseur, Kennisinstituut van de Federatie Medisch Specialisten

Disclaimer

Algemeen
De werkgroep bestaande uit afvaardiging vanuit de NVALT, NVIC, NIV en NVA heeft de grootst mogelijke zorg besteed aan de inhoud van deze leidraad. Desondanks accepteren zij geen aansprakelijkheid voor eventuele onjuistheden in dit document, voor enigerlei schade of voor andersoortige gevolgen die voortvloeien uit of samenhangen met het gebruik van deze leidraad.

Looptijd
Deze leidraad is geldig vanaf 18 februari 2021.

Deze leidraad kan tussentijds worden bijgewerkt en/of gewijzigd. De meest actuele versie is de versie die staat op de website van de Federatie Medisch Specialisten.

Inhoudsopgave

Samenstelling van de werkgroep 2
Disclaimer 2
Leidraad 4

Leidraad

Uitgangsvraag
Wat is de meerwaarde van buikligging bij patiënten met COVID-19 die niet-invasieve toediening van een hoge concentratie zuurstof krijgen?

Inleiding
Voor geïntubeerde patiënten met een ARDS beeld met een PaO2/FiO2 <150mmHg leidt beademing in buikligging tot een afname in mortaliteit. Op fysiologische gronden is het redelijk aan te nemen dat dit ook geldt voor ARDS ten gevolge van SARS-CoV-2. De inmiddels uitgebreid opgedane ervaring hiermee lijkt in dezelfde richting te wijzen. Mogelijk heeft buikligging ook een positief effect bij COVID-19 patiënten met non-invasieve respiratoire ondersteuning, bij voorbeeld in de vorm van high flow nasal oxygen (HFNO) toediening.

Search and select
A systematic review of the literature was performed to answer the following question:
What is the (non)-effectiveness of prone position versus no prone position in patients with COVID-19 on supplementary oxygen who are not (yet) intubated?

P: Patients with COVID-19 on supplementary oxygen who are not (yet) intubated
I: Prone positioning
C: No prone positioning
O: Course of the disease, admission ICU, mortality

Relevant outcome measures
The expertise group considered course of the disease, admission to ICU and mortality as a critical outcome measures for decision making.

A priori, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined a RD of 5% or an HR or RR or OR >1.05 and <0.95 as a minimal clinically (patient) important difference.

Search and select (Methods)
The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until October 29, 2020. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 442 hits. Studies were selected based on the following criteria: RCTs, cohort studies or case-control studies comparing proning with no proning in the treatment of patients COVID-19 on supplementary oxygen who are not (yet) intubated. Studies with n (intervention group) <10 were excluded. 67 studies were initially selected based on title and abstract screening. After reading the full text, 64 studies were excluded (see the table with reasons for exclusion under the tab Methods), and three studies were included.

Results

No randomised trials were found that compared proning to no proning in patients with COVID-19 receiving supplementary oxygen but not yet intubated (awake proning), but three cohort studies (Ferrando, 2020; Halifax, 2020; Padrao, 2020) were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of literature

Description of studies

Ferrando (2020) compared the use high-flow nasal oxygen with awake prone position with high-flow nasal oxygen only. The study included 199 patients with peripheral oxyhemoglobin saturation (SpO2) <93% with a non-rebreather face mask at 15 L/min. 55 patients were pronated during high-flow nasal oxygen treatment.

Hallifax (2020) compared proning to not proning in patients with COVID-19 who are receiving supplementary oxygen but not yet intubated (awake proning). The study included 155 patients who were transferred to high dependency unit if there was an increasing oxygen requirement, or an absolute oxygen requirement of: either FiO2 ≥40% or ≥8L/min via face mask. Awake proning was attempted in 30 of the 48 patients (62.5%). Proning was not attempted in 18 patients, because they were deemed too unstable, were being managed as end-of-life care, were mobilising independently and able to sit out of bed and therefore deemed too well to benefit, were admitted prior to commencement of routine proning or were unable to tolerate prone position. Successful (full) proning, defined as at least 2 hours in the prone position, twice a day for two consecutive days, was achieved in 11 of the 30 patients (36.7%), and semiproning in 17 (56.7%) patients. Two (6.7%) patients declined proning after initial attempt.

Padrao (2020) compared patients using supplemental oxygen with a flow rate ≥ 3 L/min in awake prone position with patients using supplemental oxygen decline prone position in a retrospective cohort study(n=109). 57 patients received supplemental oxygen in an awake prone position and 109 patients did not.

Results

Course of the disease

Ferrando (2020) and Padrao (2020) reported adjusted hazard ratio's. Results are shown in table 1. Studies showed conflicting results. Padro (2020) showed a clinical relevant adjusted effect in favor of the proned group, but Ferrando 2020) did not find a clinical relevant effect.

Table 1: adjusted effects sizes proning vs. no proning.

Study	**Adjusted effect size (95%CI), p**	**Adjustment parameters**
Ferrando, 2020	HR: 1.002 (0.531-1.890), p=0.99	age, sex, obesity, nonrespiratory sequential organ failure assessment severity score, APACHE II, Creactive protein, days from symptoms onset to high-flow nasal therapy start, respiratory rate, and peripheral oxyhemoglobin saturation

Padrao, 2020	HR: 0.90 (0.55-1.49), p=0.69)	age, SpO2/FIO2 ratio, respiratory rate and obesity status

Admission to ICU
Padrao (2020) reported ICU admission after 15 days. 82% of the patients in the proning group and 72% of the patients of the non-proning group were admitted to the ICU. The higher unadjusted odds ratio (1.14, 95%CI: 0.96-1.34, p=0.183) in favor of the non-proning group was clinically relevant.

Mortality
Ferrando (2020, ICU mortality), Halifax (2020, 28-day mortality) and Padrao (2020, 15 day mortality) reported adjusted effect sizes regarding mortality. Results are shown table 2. Studies showed conflicting results. Ferrando (2020) showed a clinical relevant adjusted effect in favor of the non-proned group, while Halifax (2020) and Padrao (2020) found a clinical relevant effect in favor of the proned group.

Table 2: adjusted effects sizes proning vs. no proning.

Study	**Adjusted effect size (95%CI), p**	**Adjustement parameters**
Ferrando, 2020	HR: 2.411 (0.556 - 10.442), p=0.23	age, sex, obesity, nonrespiratory sequential organ failure assessment severity score, APACHE II, Creactive protein, days from symptoms onset to high-flow nasal therapy start, respiratory rate, and peripheral oxyhemoglobin saturation
Halifax, 2020	OR: 0.06 (0.01 - 0.55), p=0.031	age, clinical frailty score and FiO2 requirement at the start of respiratory therapy
Padrao, 2020	OR: 0.50 (0.15 – 1.65), p=0.26	age, SpO2/FIO2 ratio, respiratory rate and obesity status

<u>Level of evidence of the literature</u>
Course of the disease (intubation)
The level of evidence regarding the outcome measure intubation started as low as it was based on observational studies and was downgraded to very low because of study limitations (selection bias), conflicting results (inconsistency) and the small number of included patients (imprecision).

ICU admission
The level of evidence regarding the outcome measure ICU admission started as low as it was based on an observational study and was downgraded to very low because of study limitations (selection bias) and the small number of included patients (imprecision).

Mortality
The level of evidence regarding the outcome measure mortality started as low as it was based on observational studies and was downgraded to very low because of study limitations (selection bias), conflicting results (inconsistency) and the small number of included patients (imprecision).

Conclusions

Very low GRADE	It is uncertain whether there may be a difference in intubation rates between proned and non-proned patients who are receiving supplementary oxygen but not yet intubated (awake proning). *Source: Ferrando, 2020; Padrao, 2020*

Very low GRADE	The evidence suggests that proned patients who are receiving supplementary oxygen but not yet intubated (awake proning) have a higher risk to be admitted to the ICU after 15 days than non-proned patients, but the evidence is very uncertain. *Source: Padrao, 2020*

Very low GRADE	It is uncertain whether there may be a difference in mortality in proned patients who are receiving supplementary oxygen but not yet intubated (awake proning) compared to non-proned patients. *Source: Ferrando, 2020; Halifax, 2020; Padrao, 2020*

Overwegingen – van bewijs naar aanbeveling
<u>Voor- en nadelen van de interventie en de kwaliteit van het bewijs</u>
Er zijn geen RCT's gevonden die buikligging versus geen buikligging tijdens niet-invasieve zuurstoftoediening onderzochten bij patiënten met COVID-19. Er zijn drie studies die het effect van buikligging tijdens non-invasieve beademing hebben onderzocht ten aanzien van intubatie, IC-opname en mortaliteit. Echter, door de studieopzet (risk of bias) en het zeer geringe aantal patiënten is de overall bewijskracht zeer laag, waardoor er op basis van deze studies geen conclusies kunnen worden getrokken.

Hoewel buikligging bij wakkere patiënten die niet invasief worden beademd niet routinematig wordt ingezet, zijn er anekdotische en niet gecontroleerde observaties dat deze interventie zou kunnen bijdragen aan het voorkomen van intubatie en IC opname. Veel van deze observaties zijn afkomstig uit low-income landen zoals India en Suriname. Door de beperkte middelen in deze landen zijn deze ervaringen waarschijnlijk beperkt te vertalen naar de Nederlandse situatie. Diverse internationale instanties hebben adviezen opgenomen in hun COVID behandel protocollen over buikligging bij niet invasief beademende patiënten. Daar het gaat om een interventie die op fysiologische gronden effectief zou kunnen zijn, is verder gerandomiseerd hoog volume onderzoek noodzakelijk om te bepalen wat de plaats zou kunnen zijn in de behandeling van COVID-19 pneumonie. Zoals ook bij buikligging bij mechanische beademde patiënten verbetert mogelijk de oxygenatie bij niet invasief beademde patiënten in buikligging. Het is echter niet bewezen dat deze eventuele verbetering ook leidt tot een betere overleving of minder frequente intubatie. Het overlevingsvoordeel bij geïntubeerde patiënten met ARDS is niet het gevolg van de verbeterde oxygenatie maar van de de longprotectieve beademings strategie die VILI

(ventilator induced lung injury) voorkomt. Of wakkere buikligging bij niet geïntubeerde patiënten naast een betere oxygenatie ook de ademarbeid verminderd en daarmee uitputting en mogelijk SILI (Self Induced Lung Injury) voorkomt zal verder onderzoek moeten uitwijzen. Hierbij dienen tevens aspecten rond veiligheid en tolerantie voldoende aandacht te hebben. Waarschijnlijk is het moment van starten essentieel voor het eventuele succes, waar patiënten die reeds dreigend respiratoir insufficiënt zijn geen baat zullen hebben en mogelijk door uitgestelde intubatie en mechanische ventilatie zelfs potentieel achteruit zullen gaan. Gerandomiseerd onderzoek zal moeten aantonen of vroeg gestarte self proning ook in een omgeving met voldoende middelen invasieve beademing kan voorkomen. Op dit moment zijn deze onderzoeken gaande en zullen de resultaten daarvan bovenstaande overwegingen helpen beantwoorden (NCT04402879, NCT04383613, NCT04383613, NCT04350723, NCT04365959, NCT04347941).

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Buikligging wordt door niet geïntubeerde patiënten wisselend ervaren. De tot heden bekende data tonen een goede acceptatie van de interventie. Hierbij is naar de ervaring van meerdere ervaren behandelaren wel veel aandacht nodig voor de begeleiding van patiënten. Deze begeleiding dient praktisch en angst reducerend te zijn daar de interventie met name in het begin als oncomfortabel ervaren kan worden. Veiligheid en veiligheidsgevoel dienen optimaal geborgd te zijn door getraind personeel en goede monitoring. Ook dient het beoogde effect van de interventie duidelijk te zijn en geobjectiveerd te worden. Hoe dit dient te gebeuren is onderwerp van verder onderzoek.

Kosten (middelenbeslag)

Hoewel buikligging gepaard gaat met meer kosten dan conventionele behandeling, zijn de uiteindelijke kosten afhankelijk van de effectiviteit van de behandeling. Deze effectiviteit is op dit moment onvoldoende bekend. Wanneer IC opname uitgesteld of voorkomen zou kunnen worden door deze interventie, zal naast het kosten aspect ook de mogelijke schaarste aan IC-capaciteit een rol spelen in de acceptatie van buikligging op een verpleegafdeling.

Aanvaardbaarheid, haalbaarheid en implementatie

Wanneer buikligging bij niet geïntubeerde patiënten wenselijk is, zal dit moeten geschieden in een veilige omgeving. Dit houdt tenminste in dat er goed geschoold personeel is dat in staat is de respiratoire conditie van de patiënt adequaat te monitoren. Dit zal dus in een ziekenhuis dienen te gebeuren. Er zullen goede afspraken moeten zijn over de voortgang van de behandeling. Het effect van de behandeling dient steeds te worden geëvalueerd en bij verslechtering van de patiënt dient escalatie naar een meer intensieve behandeling en monitoring niet te worden vertraagd. Goede afspraken tussen behandelaren zoals bijvoorbeeld longartsen en intensivisten, en frequent overleg zijn essentieel wanneer deze behandeling buiten de IC zou plaatsvinden.

Aanbeveling

Aanbeveling-1

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

De werkgroep is van mening dat voor buikligging bij niet invasief beademde patiënten op dit moment het bewijs ontbreekt om een aanbeveling te doen ten aanzien van het al dan niet toepassen hiervan. Er is te weinig bewijs voor de werkzaamheid en veiligheid om de therapie buiten trial verband te gebruiken.

Pas geen buikligging toe bij niet-invasieve beademing, met uitzondering van toepassing in onderzoeksverband.

Literatuur

Hallifax RJ, Porter BM, Elder PJ, Evans SB, Turnbull CD, Hynes G, Lardner R, Archer K, Bettinson HV, Nickol AH, Flight WG, Chapman SJ, Hardinge M, Hoyles RK, Saunders P, Sykes A, Wrightson JM, Moore A, Ho LP, Fraser E, Pavord ID, Talbot NP, Bafadhel M, Petousi N, Rahman NM; Oxford Respiratory Group. Successful awake proning is associated with improved clinical outcomes in patients with COVID-19: single-centre high-dependency unit experience. BMJ Open Respir Res. 2020 Sep;7(1):e000678. doi: 10.1136/bmjresp-2020-000678. PMID: 32928787; PMCID: PMC7490910.

Ferrando C, Mellado-Artigas R, Gea A, Arruti E, Aldecoa C, Adalia R, Ramasco F, Monedero P, Maseda E, Tamayo G, Hernández-Sanz ML, Mercadal J, Martín-Grande A, Kacmarek RM, Villar J, Suárez-Sipmann F; COVID-19 Spanish ICU Network. 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. Crit Care. 2020 Oct 6;24(1):597. doi: 10.1186/s13054-020-03314-6. PMID: 33023669; PMCID: PMC7537953.

Padrão EM, Valente FS, Besen BA, Rahhal H, Mesquita PS, de Alencar JC, da Costa MG, Wanderley AP, Emerenciano DL, Bortoleto FM, Fortes JC, Marques B, de Souza SF, Marchini JF, Neto RA, de Souza HP; COVIDTEAM. Awake prone positioning in COVID-19 hypoxemic respiratory failure: exploratory findings in a single-center retrospective cohort study. Acad Emerg Med. 2020 Oct 27. doi: 10.1111/acem.14160. Epub ahead of print. PMID: 33107664.

Evidence tables

Research question: What is the (non)-effectiveness of prone position versus no prone position in patients with COVID-19 on supplementary oxygen who are not (yet) intubated?

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison / control (C) [3]	Follow-up	Outcome measures and effect size [4]	Comments
Fernando, 2020	Type of study: multi-centre prospective cohort study with inclusion from March 12th 2020 to June 9th 2020 Setting and Country: 36 hospitals, Spain/Andorra Funding and conflicts of interest: Funding: Instituto de Salud Carlos III, Madrid, Spain #CB06/06/1088; #PI16/00049; #PI18/01611; #PI19/00141) Competing interests: The	Inclusion criteria: (1) age ≥ 18 years, (2) confirmed SARS-CoV-2 infection from a respiratory tract sample using PCR-based tests, (3) no previous invasive MV or NIV use before starting HFNO, and (4) peripheral oxyhemoglobin saturation (SpO2) <93% with a non-rebreather face mask at 15 L/min. Exclusion criteria: Patients with nonconfirmed SARS-CoV-2 infection	Describe intervention (treatment/procedure/test): patients who received high-flow nasal oxygen therapy + awake prone positioning, not further defined	Describe control (treatment/procedure/test): patients who only received high-flow nasal oxygen therapy	Length of follow-up: Until June 28th, 2020 Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): Intubation unadjusted sample I: n=22 (40%) C: n=60 (41.7%) p=0.481 HR: 0.879 (95%CI: 0.531-1.435), p=0.60 adjusted sample: I: 35.0% C: 37.3% P=0.824 HR: 1.002 (0.531-1.890), p=0.99 Time from HFNO start to intubation: unadjusted sample (median (IQR) I: 2.0 (1-	*"Awake-PP was indicated by medical criteria and was not uniformly defined and protocolized for the study."* *Authors conclusion: We found that this combined approach did not reduce the risk of intubation, but could increase the risk of delaying intubation. In the current study, awake-PP did not affect 28-day mortality.*

	authors declare that they have no competing interests.	according to WHO guidance and patients with no data on ventilation strategies <u>N total at baseline</u>: I: n=55 C: n=144 <u>Important prognostic factors</u>[2]: *age (range):* I: 60.0 (54.0-70.0) C: 63.0 (55.0-71.0) *Sex:* I: 24.1% emale C: 27.3% female Groups comparable at baseline? No substantial imbalances in patients' demographics, vital signs, arterial blood gases, and laboratory findings at baseline were				3)days C: 1.0 (1-2.5) days p=0.055 adjusted sample: I: 4.1 days C: 2.0 days p=0.054 <u>Discharge from ICU</u> unadjusted sample I: n=41 /49 (83%) C: 105/122 (86%) p=0.427 adjusted sample I: 80% C: 90.8% p=0.18 <u>ICU length of stay:</u> Unadjusted sample median (IQR) I: 8.0 (5-14) days C: 7.5 (4-14) days p=0.27 Adjusted sample: I: 11.4 days C: 11.6 days p=0.95 <u>Mortality 28-day</u> unadjuste	

		observed . In both samples, PaO2/FiO2 was significantly higher in the HFNO + awake-PP group.				d sample I: 8/49 (16.3%) C: 17/122 (13.9%) HR: 1.046 (0.402, 2.722), p=0.92 Adjusted sample: I: 20% C: 9.2% HR: 2.411 (95%CI: 0.556-10.442), p=0.23 Logistic models were fitted to predict treatment at baseline using the following variables as predictors of treatment: age, sex, obesity, nonrespiratory sequential organ failure assessment severity score, APACHE II, Creactive protein, days from symptoms onset to	

						high-flow nasal therapy start, respiratory rate, and peripheral oxyhemoglobin saturation	
Hallifax, 2020	Type of study: single-centre retrospective cohort study Setting and country: HDU at John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust (OUHNFT) Funding and conflicts of interest: The paper was not directly funded by any grant or funding body. RJ Hallifax and CD Turnbull are	Inclusion criteria: Patients were transferred to HDU if there was an increasing oxygen requirement, or an absolute oxygen requirement of: either FiO2 ≥40%or ≥8L/min via mask face. Referrals were made from medical wards or directly from the emergency department and all transfers were approved by a respiratory consultant.	Describe intervention (treatment/procedure/test): CPAP therapy, proning and starting respiratory therapy when on moderate oxygen therapy. 'Successful' proning was defined as at least 2 hours in the prone position, twice a day for two consecutive days. Awake proning in the HDU was set up and began on the 6 April 2020, 2 weeks after the first cases in our institution, and in response to anecdotal reports of success. Oxygen requirement prior to commencement of respiratory support was defined as moderate (FiO2 ≤60%) or high (FiO2 >60%).	Describe control (treatment/procedure/test): 'Unsuccessful' proning	Length of follow-up: admission Loss-to-follow-up: Intervention: N (%) Reasons (describe) Control: N (%) Reasons (describe) Incomplete outcome data: Intervention: N (%) Reasons (describe) Control: N (%)	Outcome measures and effect size (include 95%CI and p-value if available): OR for mortality Unsuccessful proning: ref Successful proning: 0.06 (95% CI 0.00 to 0.80) Full proning mortality 0/11, 0.0%; non-full proning mortality 12/19, 63.2% *Multilevel logistic regression, model includes	*Authors' conclusion* The mortality of patients with COVID-19 requiring respiratory support is considerable. Data from our cohort of patients managed on a respiratory HDU providing CPAP and respiratory physiotherapy support to enable awake proning show an association with successful awake

	Academic clinical Lecturers in Respiratory Medicine funded by the National Institute for Health Research (NIHR). NM Rahman, ID Pavord and N Petousi are funded by the NIHR Oxford Biomedical Research Centre. Competing interests: None declared	Patients were not transferred to HDU if they were rapidly deteriorating and required immediate ICU admission, or if they were deemed to be for ward-based care. Decisions about ceilings of care and escalation to the HDU were made within an agreed ethical framework, and on the basis of clinical need and suitability for escalation. There was no resource limitation. <u>Exclusion criteria</u>: - <u>N total at baseline</u>: Awake proning was attempted			Reasons (describe)	age, clinical frailty score, Oxygen therapy prior to respiratory support, CPAP only/ CPAP transfer onto HFNO	proning and improved outcomes in patients receiving non-invasive respiratory support

		in 30/48 (62.5%) patients. Proning was not attempted in 18 patients: 7 (38.9%) were deemed too unstable or were being managed as end-of-life care, 5 (27.7%) were mobilising independently and able to sit out of bed and therefore deemed too well to benefit, 3 (16.7%) were admitted prior to commencement of routine proning, and 2 (11.1%) were unable to tolerate prone position. Successful (full) proning was achieved in					

		11/30 (36.7%), and semipronin g in 17 (56.7%) patients. Two (6.7%) patients declined proning after initial attempt. <u>Important prognostic factors</u>[2]: *Overall (n=48)* *age ± SD:* 69 (54-80) *Sex:* 32 male/ 16 female Groups comparabl e at baseline? Uncelear					
Padrao 2020	Type of study: single centre retrospecti ve cohort study with Setting and Country: Hospital das Clínicas da Faculdade de Medicina da Universida de de São	<u>Inclusion criteria</u>: (1) age > 18 years-old; (2) confirmed or suspected COVID-19; (3) spontaneo us breathing (i.e., not on invasive mechanical ventilation) ;	Describe intervention (treatment/proced ure/test): awake prone positioning	Describe control (treatment/proced ure/test): Patients who declined to undergo awake prone positioning were not excluded from the cohort and were included in the control group.	<u>Length of follow-up</u>: 15 days <u>Loss-to-follow-up</u>: Not reported <u>Incompl ete outcome data</u>: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): <u>Intubation</u> number of intubation s I: 33 (48%) C: 53 (49%) HR: 1.21 (95%CI: 0.78-1.88),	*Authors conclusio n:* *the exposure to awake prone positionin g in patients with suspected or confirmed COVID-19 with hypoxemi c respirator*

	Paulo, Brasil Funding and conflicts of interest: Funding: no funding Competing interests: The authors declare that they have no competing interests.	(4) respiratory rate ≥ 24 ipm; and (5) using supplemental oxygen with a flow rate ≥ 3 L/min. The patients had to have a positive RT-PCR for SARS-CoV-2 from analysis of nasopharyngeal, oropharyngeal swab or tracheal secretion specimens and/or suggestive clinical findings and typical lung CT scan. <u>Exclusion criteria</u>: (1) patients intubated in other hospitals and referred to the HCFMUSP or patients intubated within one hour of arrival to the emergency				p=0.39 adjusted HR: 0.89 (0.54-1.48), p=0.67) Discharged alive after 15 days: I: 23 (40%) C: 43 (39%) no statistics reported No oxygen therapy after 15 days: I: 5 (9%) C: 10(9%) RR: 0.93 (0.29-3.06), p=0.91 adjusted RR: 0.55 (0.14-2.12), p=0.39 Oxygen by mask or nasal cannula after 15 days: I: 12 (21%) C: 13 (12%) RR: 1.73 (0.68-4.39), p=0.25 adjusted RR: 2.62 (0.87-	*y failure was not associated with reduced intubation rates in our cohort. However, the technique is associated with improved physiologic parameters and the confidence intervals could not exclude neither a beneficial nor a harmful effect of the therapy.*

		department; (2) hemodynamic instability (defined as mean arterial pressure (MAP) <65mmHg and use of vasopressors to achieve MAP > 65mmHg); (3) recent abdominal surgery; (4) acute hypercapnic respiratory failure; (5) unstable fractures; (6) pregnancy; or (7) other contraindication to the prone position, as judged by the treating physician and documented in the medical record. Patients with a discussion of limitation of organ support (do-not-				7.86), p=0.086 Non-invasie ventilation or HFNC after 15 days: I: 1 (2%) C: 5 (5%) RR: 0.37 (0.04, 3.39), p=0.38) adjusted RR 0.26 (0.02-3.3), p=0.30 Mechanical ventilation after 15 days: I: 10 (18%) C: 16 (15%) RR: 1.17 (0.46-2.99), p=0.75) Adjusted RR: 1.05 (0.36-3.07), p=0.92 Dead after 15 days: I: 6 (11%) C: 22 (20%) RR: 0.51 (0.18-1.44), p=0.202 adjusted RR: 0.50 (0.15	

		intubate order) were also excluded. <u>N total at baseline</u>: I: n=57 C: n=109 <u>Important prognostic factors</u>[2]: *age (SD):* I: 51.8 (13) C: 61.4 (13.6) *Sex:* I: 70% M C: 66% M Groups comparable at baseline? Overall, the groups were comparable and represent a cohort with acute hypoxemic respiratory failure with a low burden of extra-pulmonary organ dysfunctions. The exceptions were age and SpO2/FIO2 ratio,				– 1.65), p=0.26 ICU admission I; 47 (82%) C: 79 (72%) RR: 1.41 (0.96-1.34) p=0.183 adjusted risk ratios accounting for age, SpO2/FIO2 ratio, respiratory rate and obesity status.	

		which were lower, while respiratory rate was higher in the prone positioning group.					

Notes:

1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Risk of bias table for intervention studies (observational: non-randomized clinical trials, cohort and case-control studies)

Study reference (first author, year of publication)	**Bias due to a non-representative or ill-defined sample of patients?**[1] (unlikely/likely/unclear)	**Bias due to insufficiently long, or incomplete follow-up, or differences in follow-up between treatment groups?**[2] (unlikely/likely/unclear)	**Bias due to ill-defined or inadequately measured outcome ?**[3] (unlikely/likely/unclear)	**Bias due to inadequate adjustment for all important prognostic factors?**[4] (unlikely/likely/unclear)
Ferrando, 2020	Likely (*"Awake-PP was indicated by medical criteria and was not uniformly defined and protocolized for the study.")*	Unlikely	Unlikely	Unlikely
Hallifax, 2020	Likely	Unlikely	Unlikely	Unlikely
Padrao, 2020	Likely ("Patients who declined to undergo awake prone positioning were not excluded from the cohort and were included in the control group")	Likely (follow-up ended after 15 days, while treatment was not finished)	Unlikely	Unlikely (Likely for ICU admission)

1. Failure to develop and apply appropriate eligibility criteria: a) case-control study: under- or over-matching in case-control studies; b) cohort study: selection of exposed and unexposed from different populations.
2. Bias is likely if: the percentage of patients lost to follow-up is large; or differs between treatment groups; or the reasons for loss to follow-up differ between treatment groups; or length of follow-up differs between treatment groups or is too short. The risk of bias is unclear if: the number of patients lost to follow-up; or the reasons why, are not reported.

3. Flawed measurement, or differences in measurement of outcome in treatment and control group; bias may also result from a lack of blinding of those assessing outcomes (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has “soft” (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
4. Failure to adequately measure all known prognostic factors and/or failure to adequately adjust for these factors in multivariate statistical analysis.

Table of excluded studies

Author and year	Reason for exclusion
Bastoni, 2020	See not-graded studies
Bell, 2020	SR, only not-graded studies included
Bower, 2020	Comment
Caputo, 2020	No comparison
Carsetti, 2020	Does not fit PICO (intubated patients)
Chad, 2020	Narratieve review
Cohen, 2020	Narrative review, <10 included patients
Coppo, 2020	No comparison
Damarla, 2020	No comparison
Despres, 2020	<10 included patients
Dondorp, 2020	Narrative review
Elharrar, 2020	Does not fit PICO (outcome)
Foy 2020	Does not fit PICO (outcome)
Golestani-Eraghi, 2020	No comparison
Guenancia, 2020	No comparison
Kolkova 2020	<10 included patients
Lindahl, 2020	Narrative review
Longhini, 2020	Narrative review
McNicholas, 2020	Narrative review
Munshi, 2020	Narrative review
Ng, 2020	No comparison
Paul, 2020	Narrative review, <10 included patients
Prasad, 2020	Narrative review
Rao, 2020	Does not fit PICO (non-COVID patients)
Raoof 2020	Narrative review
Retucci, 2020	Does not fit PICO (outcome)
Sen, 2020	Narrative review
Shukla, 2020	No comparison
Sinha, 2020	Narrative review
Solverson, 2020	No comparison
Sun, 2020	Narrative review
Taboada, 2020	<10 included patients
Taboada, 2020	No comparison
Telias, 2020	Narrative review
Thompson, 2020	No comparison
Tolcher, 2020	Narrative review
Trembley, 2020	Does not fit PICO (intubation instead of pronin)
Tu, 2020	<10 included patients
Vibert, 2020	<10 included patients
Westafer, 2020	Narrative review
Winck, 2020	Narrative review
Winearls, 2020	No comparison
Xu 2020	No comparison
Zhu, 2020	<10 included patients
Zochios, 2020	Narrative review
Anand 2020	SR review: included studies reported no comparison
Aroroa, 2020	Narrative review

Asghar, 2020	Does not fit pico (invasive vs nonivasive)
Bell, 2020	No comparison
Gupta, 2020	Editorial
Lee, 2020	Does not fit pico (invasive mv)
Magalhaes, 2020	Narrative review
Mahmoodpoor, 2020	No comparison
Makkar, 2020	Narrative review
Mukhtar, 2020	Does not fit pico (no proning)
Ng, 2020	Comment
Paternoster, 2020	No comparison
Pooni, 2020	Narrative review
Raoof, 2020	Narrative review
Rippo-gallardo, 2020	No comparison
Sardesi, 2020	No experiment
Sartini, 2020	No comparison
Taboada, 2020	No comparison
Wheaterald, 2020	SR review: Zhang 2020 excluded as it was unclear whether patient received supplemental oxygen. Other included studies reported no comparison

Literature search strategy

Richtlijn: COVID-19	
Uitgangsvraag: Buikligging noninvasieve beademing	
Database(s): Ovid/Medline, Embase	Datum: 6-10-2020,7-10-2020, 29-10-2020
Periode: nvt	Talen: nvt
Literatuurspecialist: Ingeborg van Dusseldorp	

Toelichting en opmerkingen:

29-10-2020

De term noninvasive ventilation toegevoegd. Deze term was bij de opzet van de eerste zoekstrategie niet meer meegenomen omdat de bovenliggende term artificial ventilation werd geschrapt uit de strategie. Non-invasive ventilation werd wel meegenomen als title, abstract, keyword maar daarmee werd noninvasive niet gevonden.

7-10-2020

De term respiratory insufficiency en de term breathing disorders toegevoegd, omdat volgend artikel niet werd aangetroffen in het resultaat. Thompson AE, Ranard BL, Wei Y, et al. Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. JAMA Intern Med. 2020 Jun 17 [Epub ahead of print].
Het missende aantal (78 referenties) is toegevoegd aan Rayyan.
Daarnaast het tekstwoord prone verder beperkt tot prone near/3 disorder* omdat prone ook: vatbaar betekent en vaak wordt gebruikt.

6-10-2020

De vraag is op twee manieren benaderd:
Algorithme en (noninvasieve) beademing en COVID-19
OF
Buikligging en (noninvasieve) beademing en COVID-19

Het sleutelartikel wordt gevonden.
Optimizing respiratory care in coronavirus disease-2019: A comprehensive, protocolized, evidence-based, algorithmic approach.
Sinha S; Sardesai I; Galwankar SC; Nanayakkara PWB; Narasimhan DR; Grover J; Anderson HL 3rd; Paladino L; Gaieski DF; Somma SD; Stawicki SP.
International Journal of Critical Illness and Injury Science. 10(2):56-63, 2020 Apr-Jun.

Zoekopbrengst

Datum	EMBASE	OVID/MEDLINE	Ontdubbeld
6-10-2020	188	104	230
7-10-2020	271	164	344
29-10-2020	347	212	442

Zoekverantwoording

Ovid/Medline 29-10-2020

1 ((exp Coronavirus/ or Coronavirus Infections/ or pneumonia virus*.ti,ab,kf. or cov.ti,ab,kf.) and ((outbreak or wuhan).ti,ab,kf. or novel.af. or '19'.ti,ab,kf. or '2019'.ti,ab,kf. or epidem*.af. or epidemy.af. or epidemic*.af. or pandem*.af. or new.ti,ab,kf.)) or (coronavirus* or 'corona virus*' or ncov or '2019ncov' or 'covid19' or "covid 19" or "sars cov 2" or 'sars2' or "ncov 2019" or "sars coronavirus 2" or "sars corona virus 2" or "severe acute respiratory syndrome cov 2" or "severe acute respiratory syndrome cov2" or "severe acute respiratory syndrome cov*").ti,ab,kf. (81784)
2 limit 1 to dt="20191201-20220101" (69146)
3 exp prone position/ or prone.ti,ab,kf. or proning.ti,ab,kf. or exp algorithms/ or algorithm*.ti,ab,kw. (550215)
4 1 and 3 (1662)
5 exp airway management/ or respiratory care.ti,ab,kf. or airway management.ti,ab,kf. or exp respiratory therapy/ or respiratory therapy.ti,ab,kf. or exp oxygen inhalation therapy/ or o2 administration.ti,ab,kf. or o2 therapy.ti,ab,kf. or oxygen administration.ti,ab,kf. or oxygen inhalation therapy.ti,ab,kf. or oxygen insufflation.ti,ab,kf. or oxygen therapy.ti,ab,kf. or oxygen treatment.ti,ab,kf. or high flow nasal cannula*.ti,ab,kf. or hfnc.ti,ab,kf. or non-invasive ventilation.ti,ab,kf. or noninvasive ventilation.ti,ab,kf. or non-invasive positive pressure ventilation.ti,ab,kf. or noninvasive positive pressure ventilation.ti,ab,kf. or nasal intermittent positive pressure ventilation.ti,ab,kf. or nippv.ti,ab,kf. or bipap.ti,ab,kf. or bilevel positive airway pressure.ti,ab,kf. or cpap.ti,ab,kf. or continuous positive airway pressure.ti,ab,kf. or non rebreather.ti,ab,kf. or non rebreathing.ti,ab,kf. or nrb.ti,ab,kf. or nrbm.ti,ab,kf. or low flow nasal cannula.ti,ab,kf. or invasive mechanical ventilation.ti,ab,kf. or optiflow.ti,ab,kf. or vapotherm.ti,ab,kf. or exp respiration disorders/ or respiration deficiency.ti,ab,kf. or respiration disturbance.ti,ab,kf. or respiration failure.ti,ab,kf. or respiration insufficiency.ti,ab,kf. or respiratory deficiency.ti,ab,kf. or respiratory disturbance.ti,ab,kf. or respiratory dysfunction.ti,ab,kf. or respiratory failure.ti,ab,kf. or respiratory insufficiency.ti,ab,kf. or respiratory tract insufficiency.ti,ab,kf. (341535)
6 exp algorithms/ or algorithm*.ti,ab,kw. (474065)
7 1 and 3 and 5 (212)

Ovid/Medline 7-10-2020

1 ((exp Coronavirus/ or Coronavirus Infections/ or pneumonia virus*.ti,ab,kf. or cov.ti,ab,kf.) and ((outbreak or wuhan).ti,ab,kf. or novel.af. or '19'.ti,ab,kf. or '2019'.ti,ab,kf. or epidem*.af. or epidemy.af. or epidemic*.af. or pandem*.af. or new.ti,ab,kf.)) or (coronavirus* or 'corona virus*' or ncov or '2019ncov' or 'covid19' or "covid 19" or "sars cov 2" or 'sars2' or "ncov 2019" or "sars coronavirus 2" or "sars corona virus 2" or "severe acute respiratory syndrome cov 2" or "severe acute respiratory syndrome cov2" or "severe acute respiratory syndrome cov*").ti,ab,kf. (71724)
2 limit 1 to dt="20191201-20220101" (59001)
3 exp prone position/ or prone.ti,ab,kf. or proning.ti,ab,kf. or exp algorithms/ or algorithm*.ti,ab,kw. (549853)
4 1 and 3 (1397)
5 exp airway management/ or respiratory care.ti,ab,kf. or airway management.ti,ab,kf. or exp respiratory therapy/ or respiratory therapy.ti,ab,kf. or exp oxygen inhalation therapy/ or o2 administration.ti,ab,kf. or o2 therapy.ti,ab,kf. or oxygen administration.ti,ab,kf. or oxygen inhalation therapy.ti,ab,kf. or oxygen insufflation.ti,ab,kf. or oxygen therapy.ti,ab,kf. or oxygen

treatment.ti,ab,kf. or high flow nasal cannula*.ti,ab,kf. or hfnc.ti,ab,kf. or non-invasive ventilation.ti,ab,kf. or non-invasive positive pressure ventilation.ti,ab,kf. or nasal intermittent positive pressure ventilation.ti,ab,kf. or nippv.ti,ab,kf. or bipap.ti,ab,kf. or bilevel positive airway pressure.ti,ab,kf. or cpap.ti,ab,kf. or continuous positive airway pressure.ti,ab,kf. or non rebreather.ti,ab,kf. or non rebreathing.ti,ab,kf. or nrb.ti,ab,kf. or nrbm.ti,ab,kf. or low flow nasal cannula.ti,ab,kf. or invasive mechanical ventilation.ti,ab,kf. or optiflow.ti,ab,kf. or vapotherm.ti,ab,kf. or exp respiration disorders/ or respiration deficiency.ti,ab,kf. or respiration disturbance.ti,ab,kf. or respiration failure.ti,ab,kf. or respiration insufficiency.ti,ab,kf. or respiratory deficiency.ti,ab,kf. or respiratory disturbance.ti,ab,kf. or respiratory dysfunction.ti,ab,kf. or respiratory failure.ti,ab,kf. or respiratory insufficiency.ti,ab,kf. or respiratory tract insufficiency.ti,ab,kf. (340550)

6 1 and 3 and 5 (164)

Ovid/Medline 6-10-2020

1 "Optimizing respiratory care in coronavirus disease-2019".fc_titl. (1)

2 ((exp Coronavirus/ or Coronavirus Infections/ or pneumonia virus*.ti,ab,kf. or cov.ti,ab,kf.) and ((outbreak or wuhan).ti,ab,kf. or novel.af. or '19'.ti,ab,kf. or '2019'.ti,ab,kf. or epidem*.af. or epidemy.af. or epidemic*.af. or pandem*.af. or new.ti,ab,kf.)) or (coronavirus* or 'corona virus*' or ncov or '2019ncov' or 'covid19' or "covid 19" or "sars cov 2" or 'sars2' or "ncov 2019" or "sars coronavirus 2" or "sars corona virus 2" or "severe acute respiratory syndrome cov 2" or "severe acute respiratory syndrome cov2" or "severe acute respiratory syndrome cov*").ti,ab,kf. (71723)

3 limit 2 to dt="20191201-20220101" (59001)

4 exp prone position/ or prone.ti,ab,kf. or proning.ti,ab,kf. or exp algorithms/ or algorithm*.ti,ab,kw. (549799)

5 2 and 4 (1397)

6 exp airway management/ or respiratory care.ti,ab,kf. or airway management.ti,ab,kf. or exp respiratory therapy/ or respiratory therapy.ti,ab,kf. or exp oxygen inhalation therapy/ or o2 administration.ti,ab,kf. or o2 therapy.ti,ab,kf. or oxygen administration.ti,ab,kf. or oxygen inhalation therapy.ti,ab,kf. or oxygen insufflation.ti,ab,kf. or oxygen therapy.ti,ab,kf. or oxygen treatment.ti,ab,kf. or high flow nasal cannula*.ti,ab,kf. or hfnc.ti,ab,kf. or non-invasive ventilation.ti,ab,kf. or non-invasive positive pressure ventilation.ti,ab,kf. or nasal intermittent positive pressure ventilation.ti,ab,kf. or nippv.ti,ab,kf. or bipap.ti,ab,kf. or bilevel positive airway pressure.ti,ab,kf. or cpap.ti,ab,kf. or continuous positive airway pressure.ti,ab,kf. or non rebreather.ti,ab,kf. or non rebreathing.ti,ab,kf. or nrb.ti,ab,kf. or nrbm.ti,ab,kf. or low flow nasal cannula.ti,ab,kf. or invasive mechanical ventilation.ti,ab,kf. or optiflow.ti,ab,kf. or vapotherm.ti,ab,kf. (171354)

7 2 and 4 and 6 (104)

8 1 and 8 (1)

Embase 29-10-2020

No.	Query	Results
#24	#20 OR #23	**347**
#23	#22 NOT #20	**38**
#22	#17 AND #18 AND #21	**78**
#21	'breathing disorder'/exp	**358134**
#20	#17 AND #18 AND #19	**233**

No.	Query	Results
#19	'oxygenation'/exp OR 'oxygen therapy'/exp OR 'high flow nasal cannula'/exp OR 'high flow oxygen therapy'/exp OR 'high flow nasal oxygen therapy'/exp OR 'non invasive positive pressure ventilation'/exp OR 'nasal intermittent positive pressure ventilation'/exp OR 'invasive mechanical ventilation'/exp OR 'noninvasive ventilation'/exp OR 'o2 administration':ti,ab,kw OR 'o2 therapy':ti,ab,kw OR 'oxygen administration':ti,ab,kw OR 'oxygen inhalation therapy':ti,ab,kw OR 'oxygen insufflation':ti,ab,kw OR 'oxygen therapy':ti,ab,kw OR 'oxygen treatment':ti,ab,kw OR 'high flow nasal cannula*':ti,ab,kw OR hfnc:ti,ab,kw OR 'non-invasive ventilation':ti,ab,kw OR 'non-invasive positive pressure ventilation':ti,ab,kw OR 'nasal intermittent positive pressure ventilation':ti,ab,kw OR nippv:ti,ab,kw OR bipap:ti,ab,kw OR 'bilevel positive airway pressure':ti,ab,kw OR cpap:ti,ab,kw OR 'continuous positive airway pressure':ti,ab,kw OR 'non rebreathing valve'/exp OR 'non rebreather':ti,ab,kw OR 'non rebreathing':ti,ab,kw OR nrb:ti,ab,kw OR nrbm:ti,ab,kw OR 'low flow nasal cannula':ti,ab,kw OR 'invasive mechanical ventilation':ti,ab,kw OR optiflow:ti,ab,kw OR vapotherm:ti,ab,kw OR 'respiration control'/exp OR 'airway control':ti,ab OR 'airway management':ti,ab OR 'breathing control':ti,ab OR 'breathing regulation':ti,ab OR 'respiration control':ti,ab OR 'respiration regulation':ti,ab OR 'respiratory control':ti,ab OR 'respiratory regulation':ti,ab OR 'respiratory failure'/exp OR 'respiration deficiency':ti,ab OR 'respiration disturbance':ti,ab OR 'respiration failure':ti,ab,kw OR 'respiration insufficiency':ti,ab,kw OR 'respiratory deficiency':ti,ab,kw OR 'respiratory disturbance':ti,ab,kw OR 'respiratory dysfunction':ti,ab,kw OR 'respiratory failure':ti,ab,kw OR 'respiratory insufficiency':ti,ab,kw OR 'respiratory tract insufficiency':ti,ab,kw OR 'noninvasive ventilation':ti,ab,kw	**300391**
#18	('coronavirus disease 2019'/exp OR (('coronavirinae'/exp OR 'coronavirus infection'/de OR coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'pneumonia virus*':ti,ab,kw OR cov:ti,ab,kw OR ncov:ti,ab,kw) AND (outbreak:ti,ab,kw OR wuhan:ti,ab,kw)) OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR ((coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw) AND 2019:ti,ab,kw) OR 'sars cov 2':ti,ab,kw OR sars2:ti,ab,kw OR 'coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'ncov 2019':ti,ab,kw OR ncov:ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars corona virus 2':ti,ab,kw OR 'severe acute respiratory syndrome cov 2':ti,ab,kw OR 'severe acute respiratory syndrome cov2':ti,ab,kw) AND [2019-2020]/py	**59139**
#17	'prone position'/exp OR ((prone NEAR/3 position*):ti,ab,kw) OR proning:ti,ab,kw OR 'algorithm'/exp OR algorithm*:ti,ab,kw	**532776**

Embase 7-10-2020

No.	Query	Results
#8	#4 OR #7	**271**
#7	#6 NOT #4	**38**
#6	#1 AND #2 AND #5	**78**
#5	'breathing disorder'/exp	**358134**
#4	#1 AND #2 AND #3	**233**

No.	Query	Results
#3	'oxygenation'/exp OR 'oxygen therapy'/exp OR 'high flow nasal cannula'/exp OR 'high flow oxygen therapy'/exp OR 'high flow nasal oxygen therapy'/exp OR 'non invasive positive pressure ventilation'/exp OR 'nasal intermittent positive pressure ventilation'/exp OR 'invasive mechanical ventilation'/exp OR 'o2 administration':ti,ab,kw OR 'o2 therapy':ti,ab,kw OR 'oxygen administration':ti,ab,kw OR 'oxygen inhalation therapy':ti,ab,kw OR 'oxygen insufflation':ti,ab,kw OR 'oxygen therapy':ti,ab,kw OR 'oxygen treatment':ti,ab,kw OR 'high flow nasal cannula*':ti,ab,kw OR hfnc:ti,ab,kw OR 'non-invasive ventilation':ti,ab,kw OR 'non-invasive positive pressure ventilation':ti,ab,kw OR 'nasal intermittent positive pressure ventilation':ti,ab,kw OR nippv:ti,ab,kw OR bipap:ti,ab,kw OR 'bilevel positive airway pressure':ti,ab,kw OR cpap:ti,ab,kw OR 'continuous positive airway pressure':ti,ab,kw OR 'non rebreathing valve'/exp OR 'non rebreather':ti,ab,kw OR 'non rebreathing':ti,ab,kw OR nrb:ti,ab,kw OR nrbm:ti,ab,kw OR 'low flow nasal cannula':ti,ab,kw OR 'invasive mechanical ventilation':ti,ab,kw OR optiflow:ti,ab,kw OR vapotherm:ti,ab,kw OR 'respiration control'/exp OR 'airway control':ti,ab OR 'airway management':ti,ab OR 'breathing control':ti,ab OR 'breathing regulation':ti,ab OR 'respiration control':ti,ab OR 'respiration regulation':ti,ab OR 'respiratory control':ti,ab OR 'respiratory regulation':ti,ab OR 'respiratory failure'/exp OR 'respiration deficiency':ti,ab OR 'respiration disturbance':ti,ab OR 'respiration failure':ti,ab,kw OR 'respiration insufficiency':ti,ab,kw OR 'respiratory deficiency':ti,ab,kw OR 'respiratory disturbance':ti,ab,kw OR 'respiratory dysfunction':ti,ab,kw OR 'respiratory failure':ti,ab,kw OR 'respiratory insufficiency':ti,ab,kw OR 'respiratory tract insufficiency':ti,ab,kw	**294987**
#2	('coronavirus disease 2019'/exp OR (('coronavirinae'/exp OR 'coronavirus infection'/de OR coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'pneumonia virus*':ti,ab,kw OR cov:ti,ab,kw OR ncov:ti,ab,kw) AND (outbreak:ti,ab,kw OR wuhan:ti,ab,kw)) OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR ((coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw) AND 2019:ti,ab,kw) OR 'sars cov 2':ti,ab,kw OR sars2:ti,ab,kw OR 'coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'ncov 2019':ti,ab,kw OR ncov:ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars corona virus 2':ti,ab,kw OR 'severe acute respiratory syndrome cov 2':ti,ab,kw OR 'severe acute respiratory syndrome cov2':ti,ab,kw) AND [2019-2020]/py	**59139**
#1	'prone position'/exp OR ((prone NEAR/3 position*):ti,ab,kw) OR proning:ti,ab,kw OR 'algorithm'/exp OR algorithm*:ti,ab,kw	**532776**

Embase 6-10-2020

No.	Query	Results
#5	#3 AND #4	**188**
#4	'oxygenation'/exp OR 'oxygen therapy'/exp OR 'high flow nasal cannula'/exp OR 'high flow oxygen therapy'/exp OR 'high flow nasal oxygen therapy'/exp OR 'non invasive positive pressure ventilation'/exp OR 'nasal intermittent positive pressure ventilation'/exp OR 'invasive mechanical ventilation'/exp OR 'o2 administration':ti,ab,kw OR 'o2 therapy':ti,ab,kw OR 'oxygen administration':ti,ab,kw OR 'oxygen inhalation therapy':ti,ab,kw OR 'oxygen insufflation':ti,ab,kw OR 'oxygen therapy':ti,ab,kw OR 'oxygen treatment':ti,ab,kw	**190268**

No.	Query	Results
	OR 'high flow nasal cannula*':ti,ab,kw OR hfnc:ti,ab,kw OR 'non-invasive ventilation':ti,ab,kw OR 'non-invasive positive pressure ventilation':ti,ab,kw OR 'nasal intermittent positive pressure ventilation':ti,ab,kw OR nippv:ti,ab,kw OR bipap:ti,ab,kw OR 'bilevel positive airway pressure':ti,ab,kw OR cpap:ti,ab,kw OR 'continuous positive airway pressure':ti,ab,kw OR 'non rebreathing valve'/exp OR 'non rebreather':ti,ab,kw OR 'non rebreathing':ti,ab,kw OR nrb:ti,ab,kw OR nrbm:ti,ab,kw OR 'low flow nasal cannula':ti,ab,kw OR 'invasive mechanical ventilation':ti,ab,kw OR optiflow:ti,ab,kw OR vapotherm:ti,ab,kw OR 'respiration control'/exp OR 'airway control':ti,ab OR 'airway management':ti,ab OR 'breathing control':ti,ab OR 'breathing regulation':ti,ab OR 'respiration control':ti,ab OR 'respiration regulation':ti,ab OR 'respiratory control':ti,ab OR 'respiratory regulation':ti,ab	
#3	#1 AND #2	**502**
#2	('coronavirus disease 2019'/exp OR (('coronavirinae'/exp OR 'coronavirus infection'/de OR coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'pneumonia virus*':ti,ab,kw OR cov:ti,ab,kw OR ncov:ti,ab,kw) AND (outbreak:ti,ab,kw OR wuhan:ti,ab,kw)) OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR ((coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw) AND 2019:ti,ab,kw) OR 'sars cov 2':ti,ab,kw OR sars2:ti,ab,kw OR 'coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'ncov 2019':ti,ab,kw OR ncov:ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars corona virus 2':ti,ab,kw OR 'severe acute respiratory syndrome cov 2':ti,ab,kw OR 'severe acute respiratory syndrome cov2':ti,ab,kw) AND [2019-2020]/py	**59139**
#1	'prone position'/exp OR prone:ti,ab,kw OR proning:ti,ab,kw OR 'algorithm'/exp OR algorithm*:ti,ab,kw	**622576**