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Appendix 2. List of hospitals participating in the study and physicians in charge

	Name of hospital	Institution	State	Country
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2	Centro Medico Luis Adolfo López Mateos	ISSSTE	Mexico City	Mexico
3	Centro Médico Nacional 20 de Noviembre	ISSSTE	Mexico City	Mexico
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10	Hospital Materno de Celaya	SSA	Guanajuato	Mexico
11	Hospital Juárez de México	SSA	Mexico City	Mexico
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13	Hospital General Tuxtepec	SSA	Oaxaca	Mexico
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23	Hospital General Regional No. 251	IMSS	Mexico City	Mexico
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25	Unidad Médica de Alta Especialidad “Adolfo Ruiz Cortines”	IMSS	Veracruz	Mexico
26	Hospital Comunitario de Ocuituco	SSA	Morelos	Mexico
27	Hospital Rural No. 1 San Felipe Ecatepec	IMSS	Chiapas	Mexico

* IMMS: Mexican Social Security Institute

* ISSSTE: Government Workers’ Social Security and Services Institute

* SSA: Secretariat of Health (*Secretaría de Salud*)

* IESS: Ecuadorian Social Security Institute

Appendix 3. Chest CT assessment using the CO-RADS* categorical assessments scheme to evaluate suspicion of COVID-19

Category	Level of COVID-19 suspicion	Chest CT findings
CO-RADS 1	Very low	Normal or non-infectious abnormalities
CO-RADS 2	Low	Abnormalities consistent with infections other than COVID-19
CO-RADS 3	Indeterminate	Unclear whether COVID-19 is present
CO-RADS 4	High	Abnormalities suspicious for COVID-19
CO-RADS 5	Very high	Typical COVID-19
CO-RADS 6	Proven	RT-PCR + for SARS-CoV-2

*CO-RADS: COVID-19 Reporting and Data System.

Appendix 4. Calculation of FiO_2 based on type of supplemental oxygen delivery device used.

Oxygen therapy	Flow (L/min)	* FiO_2 (%)
Nasal cannula	1	24 %
	2	28 %
	3	32 %
	4	36 %
	5	40 %
	6	44 %
Non-rebreather mask	10-15	80-95 %
High-flow nasal cannula	Flows up to 60	*Up to 100%

* FiO_2 : Fraction of inspired oxygen.

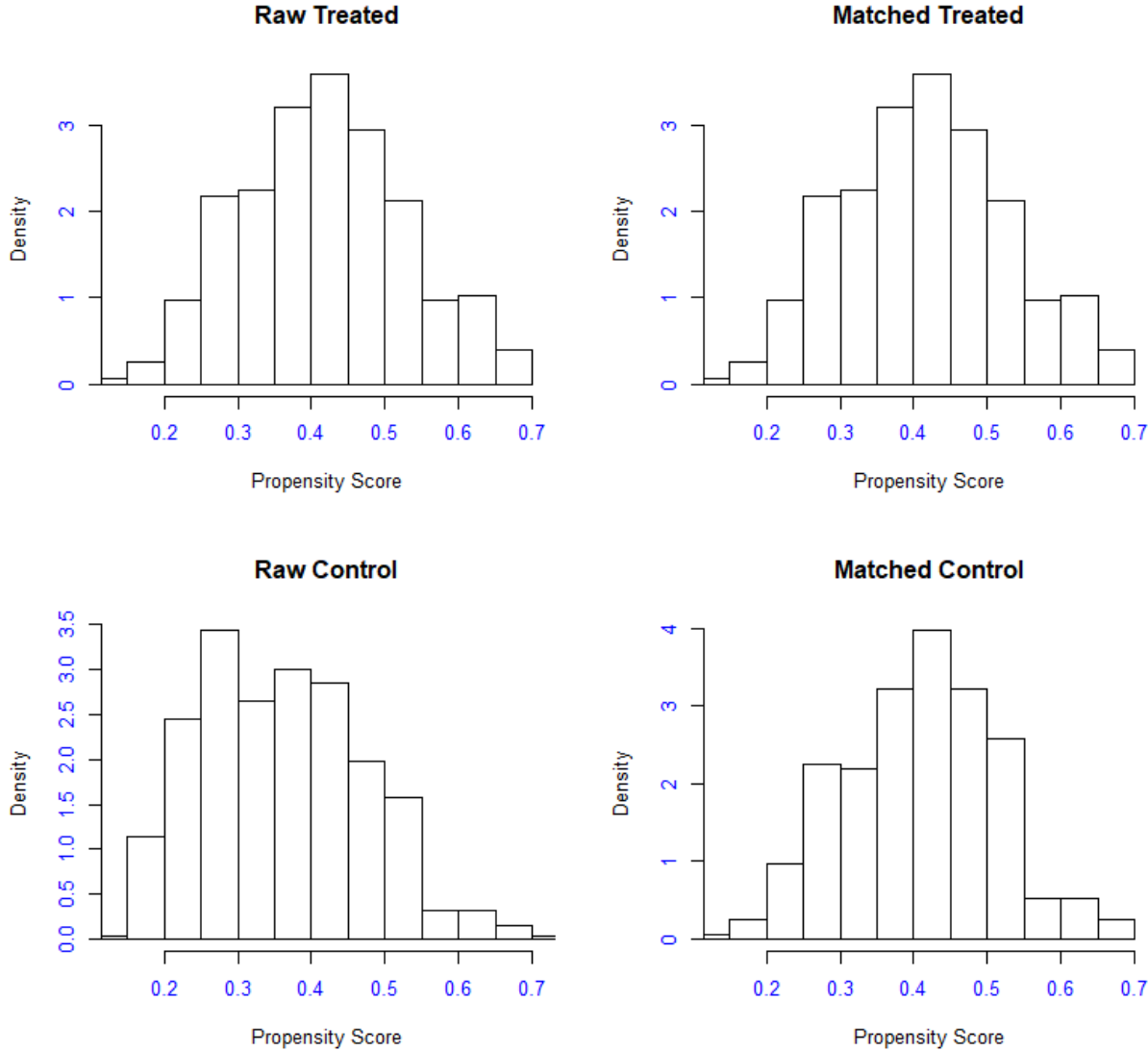
Appendix 5. Sample size calculation.

Sample size was calculated to determine the difference between two independent proportions with the formula:

$$\text{Subjects per group} = \frac{[Z_{\alpha}\sqrt{2P(1-P)} + Z_{\beta}\sqrt{P_1(1-P_1) + P_2(1-P_2)}]^2}{(P_1 - P_2)^2}$$

Where Z_{α} at 95% (two-sided) was 1.96; Z_{β} at 90%, was 1.282; P_1 was 0.23 for the number of patients with oxygen therapy who were intubated during in-hospital stay, according to Argenziano MG, et al. 2020. Considering a clinically significant reduction of 1% in the incidence of orotracheal intubation, P_2 was estimated to be 0.13 for the number of patients in prone position intubated during in-hospital stay. P was the pondered measure of the two proportions, being equal to 0.18. Hence, the calculated sample size was 309 subjects per group. Calculations were performed with the G*Power v.3.1.9.7 software.

Appendix 6. Density functions before and after propensity score matching of patients in the awake prone (treated) and awake supine (control) cohorts.



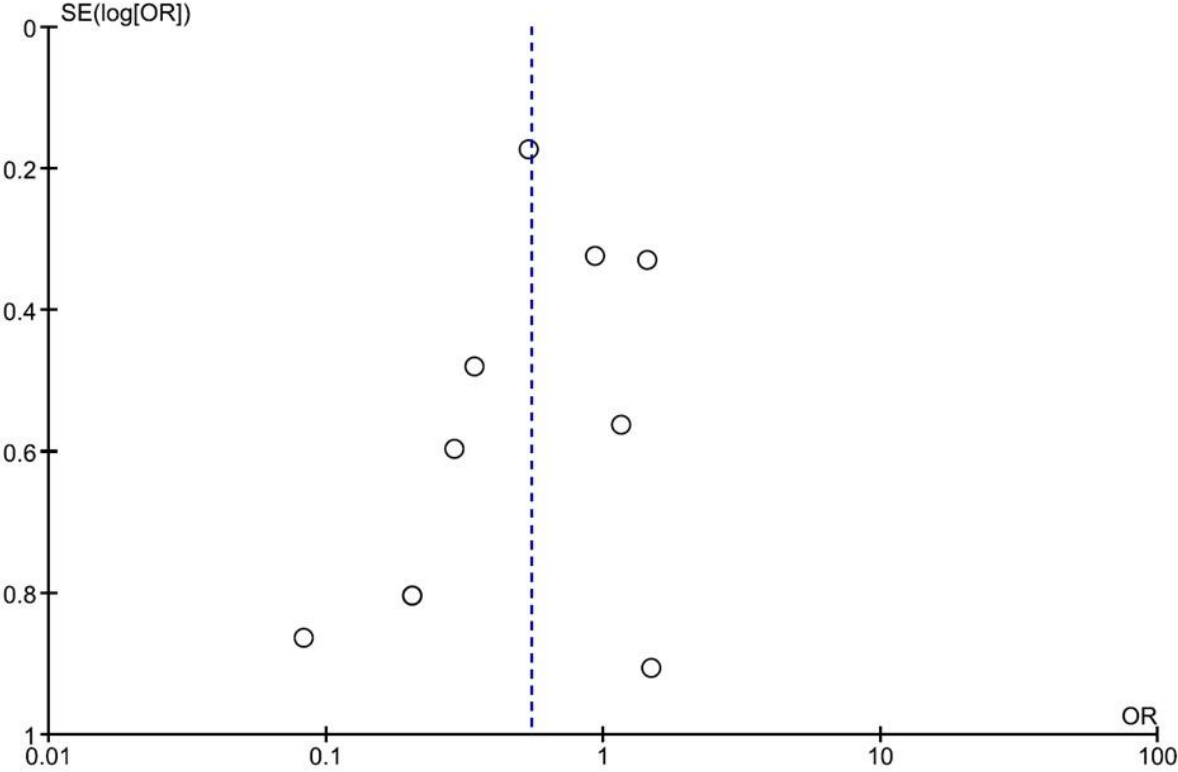
Appendix 7. Search strategy

We searched MEDLINE and EMBASE through OVID, PubMed, BioRxiv and MedRxiv for research on COVID-19 published until 8 June 2021. We used the publicly available COVID-19 Living Evidence on COVID-19 dataset [32]. Search terms for the search strategy were: ('severe acute respiratory syndrome coronavirus 2' [supplementary concept] OR 'COVID-19' [supplementary concept] OR 'coronavirus' OR 'HCoV' OR 'nCoV' OR '2019 nCoV' OR 'covid' OR 'covid19' OR 'severe acute respiratory syndrome coronavirus 2' OR 'SARS-CoV-2' OR 'SARS-CoV 2' OR 'SARS coronavirus 2') AND (prone) AND (awake). The following filters were applied for study design: case series, case-control study, cohort study, trial, other, or unclassified. Studies were chosen regardless of language, provided an abstract in English was available, and if the study included and clearly differentiated patients undergoing awake prone positioning from those in awake supine position, as well as intubation rates for both groups.

Appendix 8. Orotracheal intubation risk and mortality risk in patients with a positive SARS-CoV-2 test (excluding patients in whom diagnostic testing was not performed) managed with awake prone positioning, adjusted for confounding variables, in both the unmatched and the propensity-score matched cohort.

	Unmatched			Matched		
	OR (95% CI)	p value	E-Value	OR (95% CI)	p value	E-Value
Model for intubation^a						
Awake prone	0.18 (0.12-0.28)	<0.0001	3.19	0.20 (0.12-0.32)	<0.0001	2.93
Model for mortality^b						
Awake prone	0.23 (0.15-0.35)	<0.0001	2.77	0.23 (0.14-0.37)	<0.0001	2.67
<p>a: Model adjusted for age, sex [men], ICU attention, diabetes, systemic arterial hypertension, obesity, heart disease, cancer, chronic kidney disease, pre-prone SpO₂/FiO₂ ratio, supplemental oxygen delivery device, ceftriaxone, enoxaparin, tocilizumab, oseltamivir, and systemic steroids. Goodness of fit: Hosmer-Lemeshow $X^2=11.6$, p=0.2 AUC=0.84, 95%CI:0.81-0.88, p<0.0001</p> <p>b: Model adjusted for age, sex [men], ICU attention, diabetes, systemic arterial hypertension, obesity, heart disease, pre-prone SpO₂/FiO₂ ratio, supplemental oxygen delivery device, ceftriaxone, enoxaparin, tocilizumab, oseltamivir, and systemic steroids. Goodness of fit: Hosmer-Lemeshow $X^2=12.7$, p=0.1 AUC=0.80, 95%CI:0.77-0.84, p<0.0001</p>						

Appendix 9. Funnel Plot



Abbreviations

PaO₂: partial arterial pressure of oxygen, SpO₂: peripheral arterial oxygen saturation, PaO₂/FiO₂: arterial partial pressure of oxygen /fraction of inspired oxygen, PaCO₂: arterial partial pressure of carbon dioxide, RR: respiratory rate, NIV: non-invasive ventilation, HFNC: high-flow nasal cannula, ARDS: Acute respiratory distress syndrome, COVID-19: coronavirus disease, STROBE: Strengthening the Reporting of Observational studies in Epidemiology, AP: awake prone, CO-RADS: COVID-19 Reporting and Data System, IQR: interquartile range, SD: standard deviation, OR: odds ratio, CI: confidence interval, Ppl: pleural pressure, TPP: Transpulmonary pressure, V/Q: ventilation-perfusion.