

Supplementary Table 1. Summary of findings from included COVID-19 studies

Study Details	Study Design	Case numbers	Study Population	Intervention	Outcome Measure(s)	Summary of Findings	Study Limitations
Bastoni et al (2020), Italy	Case Series	10 patients	Non-intubated patients undergoing helmet CPAP for respiratory failure secondary to confirmed COVID-19 pneumonia	PP while continuing helmet CPAP plus low dose morphine infusion (to assist with compliance)	<ul style="list-style-type: none"> PaO₂/FIO₂ one hour after commencing PP Point-of-care lung US signs 	<ul style="list-style-type: none"> 4 patients were unable to tolerate PP In 6 patients who were able to PP, median PaO₂/FIO₂ improved from 68+/-5 to 97+/-8 mmHg Lung US showed no difference in B line quantity and distribution 	<ul style="list-style-type: none"> No comparator group Small sample size Limited documentation
Burton-Pappal (2020), England	Retrospective, single centre, Observational Cohort Study	33	Non-intubated patients who were COVID-19 positive and who required additional respiratory support beyond oxygen therapy (P/F ratio <200)	NIV (either CPAP or BiPAP) + encouragement to PP depending on tolerability	<ul style="list-style-type: none"> Intubation PaO₂/FIO₂ ratio RR HR ICU Length of Stay (LOS) Hospital LOS Mortality 	<ul style="list-style-type: none"> 7/20 patients required intubation Mean PaO₂/FIO₂ ratio improved by 28.7mmHg Patients who were subsequently intubated demonstrated lower tolerance of PP and significantly poorer response to PP in terms of oxygenation RR and HR were unchanged For those who avoided intubation, ICU LOS was 5 days and Hospital LOS was 11 days All patients survived to hospital discharge 	<ul style="list-style-type: none"> No comparator group Small sample size Retrospective Non-representative population (ie most patients aged <60)
Caputo, et al (2020), USA	Prospective observational cohort study (convenience sample)	50	Non-intubated patients with suspected COVID-19 with hypoxia on arrival at the Emergency Department despite supplemental O ₂	PP without change in FIO ₂ / O ₂ delivery device	<ul style="list-style-type: none"> Change in SpO₂ before and 5 minutes after PP Requirement for intubation within 24 hours 	<ul style="list-style-type: none"> Median SpO₂ <ul style="list-style-type: none"> at triage: 80% after application of supplemental O₂: 84% after 5 minutes of PP: 94% 13 patients (24%) failed to improve or maintain SpO₂ and required intubation within 24 hours 	<ul style="list-style-type: none"> No comparator group Questionable clinical relevance of SpO₂ at 5 minutes after PP
Cohen et al, (2020), Israel	Case series	2	Non-intubated patients with Type 1 Respiratory failure secondary to COVID-19 pneumonia	PP	<ul style="list-style-type: none"> Oxygenation (SpO₂) RR 	<ul style="list-style-type: none"> Both patients demonstrated marked improvement in SpO₂ within 10-30 minutes after commencing PP One of the patients exhibited a significant reduction in RR with PP 	<ul style="list-style-type: none"> No comparator group Small sample size Marked variation in PP protocols
Coppo et al (2020), Italy	Prospective Cohort study (convenience sample)	47	Non-intubated patients Age 18-75 COVID-19 positive	PP for at least 3 hours. O ₂ not changed if possible <ul style="list-style-type: none"> Helmet CPAP 44 Reservoir mask 9 Venturi mask 3 	<ul style="list-style-type: none"> PaO₂/FIO₂ ratio <ul style="list-style-type: none"> prior to PP 10min after PP commenced 1hour after moved back to supine PaCO₂ change Intubation rate Comfort 	<ul style="list-style-type: none"> Oxygenation improved by >50% 10min after PP Oxygenation improvement not statistically significant once supine position resumed No difference in accessory muscle use, dyspnea or PaCO₂ Responders to treatment had PP initiated earlier in their hospital stay Higher CRP and LDH levels correlated to lower PF ratios No difference in intubation rate between those who responded to PP and those who did not respond 	<ul style="list-style-type: none"> No comparator group Significant selection bias to data provided Exclusion criteria broad and subjective (eg NYHA class-2, BNP > double normal, had contraindication as decided by the attending physician) 610 eligible patients did not participate Adverse events not recorded Excluded 9 patients based on poor tolerance Excluded a patient based on age after intervention was performed

Damarla et al (2020), USA	Case series	10	Non-intubated adult patients who were COVID-19 positive with rapidly increasing O ₂ requirements or increased work of breathing (WOB) Admission to ICU Either on HFNP or NP alone	Patients asked to alternate between prone and supine 2 hourly during the day and sleep in prone position as tolerated	<ul style="list-style-type: none"> Change in SpO₂ and RR 1 hour after initial PP compared to pre prone. Incidence of intubation within two weeks of first PP 28 day follow up 	<ul style="list-style-type: none"> Oxygenation improved following PP. Median SpO₂ at 1 hour increased from 94% to 98%. WOB improved with median RR reduced from 31 to 22. No adverse events recorded. 8/10 patients did not require intubation 7/10 did not require escalation of respiratory care All patients had been discharged home at 28 day follow up 	<ul style="list-style-type: none"> No comparator group Small sample size Measures of patient dyspnea and comfort not collected Data on patient adherence to PP not collected after 1st episode One patient also enrolled in trial remdesivir v placebo
Despres et al (2020), France	Case series	6	Non-intubated patients who were COVID-19 positive with rapidly worsening dyspnea and oxygenation (SpO ₂ <92% despite O ₂ ≥ 5L/min)	PP with either HFNC or conventional O ₂ therapy (COT) Duration >1 hour and was maintained depending on tolerance and repeated as necessary	<ul style="list-style-type: none"> PaO₂/FIO₂ ratio Need for intubation Subjective dyspnea 	<ul style="list-style-type: none"> 9 sessions total assessed of PP in 6 patients 4/9 were with HFNC 5/9 were with COT PaO₂/FIO₂ ratio improved after 4 sessions (3 HFNP, 1 COT) 3/6 patients intubated All patients described subjective enhancement of dyspnea with PP 	<ul style="list-style-type: none"> No comparator group Small sample size
Dong, et al (2020), China	Retrospective cohort study	25	Non-intubated COVID-19 patients with PaO ₂ /FIO ₂ <300, RR ≥ 30 or SpO ₂ < 93% *Included patients receiving O ₂ via nasal prongs, O ₂ masks, HFNC, NIV masks *Of 48 patients identified in cross-sectional survey, 23 were excluded for reasons including inter-hospital transfer, intolerance of treatment protocol or rapid improvement resulting in exit from treatment protocol at <5days	PP *Duration determined by severity: a) PaO ₂ /FIO ₂ <200 and bilateral chest infiltrates on CT: 10h/day b) All other patients: 4h/day *For patients not tolerating PP for prescribed length of time, Lateral Position was prescribed	<ul style="list-style-type: none"> Mortality Need for intubation 	<ul style="list-style-type: none"> All 25 patients survived None required intubation 	<ul style="list-style-type: none"> No comparator group Small sample size Retrospective Missing data Not peer reviewed Selection bias
Elharrar, et al (2020), France	Prospective, single centre, observational cohort study	24	Non-intubated patients with acute respiratory failure secondary to COVID-19	PP without change in O ₂ delivery device	<ul style="list-style-type: none"> Patient tolerance ≥ 1h, ≥ 3h Proportion of "Responders" (PaO₂ increase ≥ 20% before vs during PP) Variation PaO₂ or PaCO₂ before vs during PP Proportion of "persistent responders" (PaO₂ increase ≥ 20% before PP vs 6-12h after supination) Complications 10 day follow up 	<ul style="list-style-type: none"> Patient tolerance: <ul style="list-style-type: none"> - 4 did not tolerate for ≥ 1hour - 5 tolerated for 1-3 hours - 15 tolerated for ≥ 3 hours Responders: 6 patients (25% of total, 40% of those who tolerated ≥ 3hours) Persistent Responders: 3 patients Complications: <ul style="list-style-type: none"> - 10 patients reported back pain during PP - No major complications 10 day follow-up: <ul style="list-style-type: none"> - 5 patients required intubation and mechanical ventilation 	<ul style="list-style-type: none"> No comparator group Small sample size Outcome measures of questionable clinical significance

Elkattawy, et al (2020), USA	Case Report	1	Non-intubated patient with acute respiratory failure secondary to COVID-19	PP with O2 via nasal cannulae	<ul style="list-style-type: none"> Tolerance Oxygenation 	<ul style="list-style-type: none"> PP was well tolerated for 12 hours Patient exhibited significant improvement in oxygenation and secretion clearance 	<ul style="list-style-type: none"> No comparator group Small sample size
Froelich et al (2020), France	3 case reports	3	Non-intubated patients with Confirmed COVID-19	Various position: semi-sitting in bed sitting in chair, supine, left and right lateral, PP and PP ergonomically supported Oxygen: Mask 15L/min + NP 6L/min	<ul style="list-style-type: none"> Vital signs Dyspnoea 	<ul style="list-style-type: none"> Placing the most affected part of the lung on top had the best result 2/3 tolerated prone positions with significant increases in SpO2 in the ergonomically supported PP (1 patient tolerated <30min) 	<ul style="list-style-type: none"> No comparator group Small sample size Poor tolerance with only 1 >30min Limited measurements of useful data No comparator group
Gallardo et al (2020), Italy	Case Series	13	Patients with moderate to severe ARDS secondary to COVID-19 (PaO2:FIO2 ratio <150) who were undergoing Helmet CPAP	PP initiated when PaO2:FIO2 <150 and maintained as long as tolerated (range 2-3.5 hours)	<ul style="list-style-type: none"> PaO2:FIO2 ratio Complications 	<ul style="list-style-type: none"> 12/13 patients exhibited a significant improvement in PaO2:FIO2 ratio No complications were recorded 	<ul style="list-style-type: none"> No comparator group Small sample size Retrospective
Jena et al (2020), India	Case Report	1	Non-intubated patient with type I respiratory failure secondary to COVID-19	O2 therapy continuing via NRBM combined with PP for 30min every 2 hours during the day and continuously overnight *Total: 12 hours/day	<ul style="list-style-type: none"> Oxygenation 	<ul style="list-style-type: none"> Patient demonstrated a progressive improvement in mean oxygenation over 2 days after commencing the PP protocol 	<ul style="list-style-type: none"> No comparator group Small sample size
Lawton et al (2020), UK	Retrospective observational cohort study	559	Consecutive patients with COVID-19 admitted to Bradford Royal Infirmary, UK prior to 21 May 2020	Treatment algorithm utilising escalating O2 therapy *PP for 30 minutes 2x/day was encouraged in conjunction with the commencement of mask CPAP on the ward	<ul style="list-style-type: none"> ICU admission Intubation Hospital Mortality ICU Mortality *Comparisons were made against ISARIC database 	<ul style="list-style-type: none"> 40 patients were admitted to ICU and 27 patients were intubated (*Based on ISARIC data, expected numbers were 92 requiring ICU admission and 55 requiring intubation) Hospital Mortality was 33.3% (compared to 38.6% for ISARIC) ICU Mortality was 54.5% (ISARIC: 53.7%) 	<ul style="list-style-type: none"> No true comparator group Retrospective PP played a relatively minor role in the treatment algorithm and was not reported in detail in the findings Early commencement of CPAP was the main intervention Study population not representative of general UK (though likely skewed towards more severe disease due to higher comorbidities and low socio-economic status)
Ng et al (2020), Singapore	Case series	10	Non-intubated patients who were COVID-19 positive and requiring O2 in ward setting. *Excluded if FIO2 ≥50%	PP 1 hr per session, 5 sessions/day, spaced 3 hours apart during awake hours	<ul style="list-style-type: none"> Haemodynamics and SpO2 at 0, 30 and 60 mins from start of each session 	<ul style="list-style-type: none"> 3 patients required increased oxygen support in ICU 1 patient intubated and subsequently died All able to tolerate PP protocol 	<ul style="list-style-type: none"> No comparator group Small sample size Rates of intubation compared a retrospective group of patients but no data provided 8 patients initiated on other therapies (eg lopinavir/ritonavir)

Paul et al (2020), USA	Case Series	2	Non-intubated patients with Type I respiratory failure secondary to COVID-19 *Patient 2 deteriorated post extubation	PP accompanied by low dose alprazolam to manage anxiety and enhance tolerance	• Oxygenation	• Both patients exhibited marked improvement in oxygenation and decrease in O ₂ requirements within hours of pronation • Neither patient required subsequent intubation • Both were subsequently discharged from the ICU	• No comparator group • Small sample size
Retucci et al, (2020), Italy	Prospective, Pilot Observational Study	26	Consecutive patients with Type I respiratory failure secondary to COVID-19 who were already undergoing Helmet CPAP	Trial of PP (if lung impairment was bilateral) or Lateral Positioning (if lung impairment was unilateral - good lung down)	• A-a Gradient • RR • Dyspnoea • SBP • Patient comfort *Measured: - Prior to PP/LP - 1 hour after commencing PP/LP - 45 minutes after resuming semi-recumbent position *Each trial was designated as "success" or "fail" according to pre-designated criteria for the above measures	• Total of 39 trials (12 PP, 27 LP) were conducted • 6 trials were designated "successful" • 15 trials were designated "failed" • 2 patients were unable to tolerate PP/LP • 7 patients were intubated • 2 patients died	• No comparator group • Small sample size • Arbitrary designation of success/fail criteria (eg decrease in A-a Gradient >20%)
Xu, et al (2020), China	Case Series	10	Non-intubated patients with acute respiratory failure secondary to COVID-19 (PaO ₂ /FiO ₂ <300 mmHg)	Management bundle including: • HFNC • PP>16h/d • Antiviral drug • Negative volume balance • Corticosteroid	• Respiratory parameters measured each day for 3 days, before and after PP - PaO ₂ /FiO ₂ ratio - PaCO ₂ • Intubation	• After PP: - Slight increase in median PaCO ₂ - Significant increase in PaO ₂ /FiO ₂ • None of the patients progressed to critical illness / required intubation	• No comparator group • Small sample size • Retrospective
Sartini, et al (2020), Italy	Prospective observational study *Selected by cross-sectional survey	15	Non-intubated patients with acute respiratory failure secondary to COVID-19, limited response to NIV in supine position	PP+NIV *Duration and frequency was individualised	• Respiratory parameters *data collected: - before NIV+PP - during NIV+PP (1 hour after start) - 1 hour after NIV+PP ending • Patient comfort (numerical rating scale) • 14 day follow-up	• Respiratory rate: all patients had a reduction during and after pronation • SpO ₂ and PaO ₂ /FiO ₂ ratio: - all patients had improvement during pronation - 12/15 patients had improvement after pronation • Comfort: - 11/15 patients reported improvement during pronation - 13/15 patients reported improvement after pronation - 2/15 reported no change • At 14 days: - 9 patients discharge home - 1 improved and ceased pronation - 3 continued pronation - 1 intubated - 1 died	• No comparator group • Small sample size • Intervention compares PP+NIV to supine position with no NIV - therefore does not isolate PP as a variable • Non-standardised protocol • Observation study only • Selection bias: didn't include those patients who failed NIV in PP or those that were intubated or died before selection date.
Sztajnbock, et al (2020), Brazil	Case Series	2	Non-intubated patients with acute respiratory failure secondary to COVID-19	PP without change in O ₂ delivery device (non-rebreather 10L)	• Oxygenation • Dyspnoea	• Both exhibited dramatic improvements in symptoms and oxygenation • Neither patient required intubation	• No comparator group • Small sample size

Thompson et al (2020), USA	Case series	29	Non-intubated patients who were COVID-19 positive with Severe respiratory failure <ul style="list-style-type: none"> RR >30 SpO2 <-93% despite O2 (15L/min by Non-rebreather mask or 6L/min by NP) 	PP as long as tolerated up to 24 hours/day. Minimum 1 hour	<ul style="list-style-type: none"> Change in SpO2 before and 1 hour after initiation of PP 	<ul style="list-style-type: none"> 4 refused any PP attempt and were immediately intubated Median improvement in SpO2 1 hour after PP was 7%. 19/25 had improved SpO2 12/25 required intubation 	<ul style="list-style-type: none"> No comparator group Small sample size
Tu et al (2020), China	Pilot study Case series	9	Non-intubated patients who were COVID-19 positive receiving O2 via HFNC <ul style="list-style-type: none"> *PaO2/FiO2 <150mmHg 	Twice daily PP procedures	Pre and post PP measurements of: <ul style="list-style-type: none"> PaO2 PaCO2 SaO2 pH Intubation	<ul style="list-style-type: none"> Median duration of PP was 2 hours. IQR 1-4hours SaO2 and PaO2 increased post PP 2 required intubation (1 extubated day 8, 1 ECMO) 	<ul style="list-style-type: none"> No comparator group Small sample size No time points of when post PP measurements were taken
Whittemore et al (2020), UK	Case Report	1	Non-intubated 60 year old male with Type I respiratory failure secondary to COVID-19	Prolonged PP > 18 hours/ day	<ul style="list-style-type: none"> Oxygenation 	<ul style="list-style-type: none"> Marked and rapid improvement in oxygenation occurred with each resumption of PP 	<ul style="list-style-type: none"> No comparator group Small sample size