#### **CRITICALLY APPRAISED TOPIC**

#### FOCUSED CLINICAL QUESTION

In premature infants (<32 weeks gestation) on mechanical ventilation, does supine, lateral, or prone positioning promote better oxygen saturation (PaO2 or SpO2 or lung volume)?

#### AUTHOR

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#### **CLINICAL SCENARIO**

A child is born early at 28 weeks old. The lungs are the last major organ system to develop, meaning premature infants born before 32 weeks of gestation often struggle to maintain adequate oxygen levels. As a result, they are often put on mechanical ventilation. The amount of lines and tubes coming from a premature infant can often limit the diversity of positions in which they are placed. The infant is may be placed in positions that make nursing care easiest. Since improving oxygenation is often the final step to medical stabilization for the infant and our primary goal with mechanically ventilation, is there a position that is more effective for adequate oxygenation than other positions?

#### SUMMARY OF SEARCH

[Best evidence appraised and key findings]

Current literature supports prone positioning a superior for short-term improvements and stabilization in oxygenation and respiration. When prone is not possible quarter prone and lateral positions are seen as a favourable alternative. The studies selected (Wu 2015 and Hough 2012) support this finding. There were small-to-moderate effect sizes indicating improvements in oxygenation (as measured by arterial blood gases and SpO2) and lung mechanics (measured by tidal volume and lung compliance) in prone position when compared to supine. The effect sizes and results do not guarantee that every preterm infant will respond positively. In conclusion, positioning in prone is a safe, alternative, non-pharmacological method to improve oxygenation in preterm infants on CPAP. It does not guarantee improvements but should still be considered as a strategy for improving oxygenation and stabilizing preterm infants receiving mechanical ventilation.

#### **CLINICAL BOTTOM LINE**

Prone positioning had moderate evidence supporting it as the superior position for improving oxygenation in preterm infants receiving mechanical ventilation via CPAP.

This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor

The above information should fit onto the first page of your CAT

#### SEARCH STRATEGY

Terms used to guide the search strategy						
Patient/Client Group	Patient/Client GroupIntervention (or Assessment)		<u><b>O</b></u> utcome(s)			
"premature infant"	"respiration"	"Position"	"oxygenation"			
"neonate"	"ventilation"	"prone"	"SpO2"			
"neonat""	"positive airway pressure"	"supine"	"lung volume"			
"infant"	"CPAP"	"lateral"	"respiration"			
"newborn"			"breathing"			

# Final search strategy (history):

Show your final search strategy (full history) from PubMed. Indicate which "line" you chose as the final search strategy.

- 1. (((neonate) OR (neonat\*)) OR (premature infant)) OR (newborn); 890.912 results
- 2. (((ventilat\*) OR (respirat\*)) OR (positive airway pressure)) OR (CPAP); 1,215,948 results
- 3. ((position\*) OR (supine)) OR (prone); 696,990 results
- (((((neonate) OR (neonat\*)) OR (premature infant)) OR (newborn)) AND ((((ventilat\*) OR (respirat\*)) OR (positive airway pressure)) OR (CPAP))) AND (((position\*) OR (supine)) OR (prone)); 1,750 results
- 5. (((oxygen\*) NOT (craniosynostosis)) NOT (skin)) NOT (kangaroo); 726,548 results
- ((((((neonate) OR (neonat\*)) OR (premature infant)) OR (newborn)) AND ((((ventilat\*) OR (respirat\*)) OR (positive airway pressure)) OR (CPAP))) AND (((position\*) OR (supine)) OR (prone))) AND ((((oxygen\*) NOT (craniosynostosis)) NOT (skin)) NOT (kangaroo)); 387 results
- ((((((neonate) OR (neonat\*)) OR (premature infant))) AND ((((ventilat\*) OR (respirat\*)) OR (positive airway pressure)) OR (CPAP))) AND (((position\*) OR (supine)) OR (prone))) AND ((((oxygen\*) NOT (craniosynostosis)) NOT (skin)) NOT (kangaroo)); 375 results
- (((((((neonat\*)) OR (premature infant))) AND ((((ventilat\*) OR (respirat\*)) OR (positive airway pressure)) OR (CPAP))) AND (((position\*) OR (supine)) OR (prone))) AND ((((oxygen\*) NOT (craniosynostosis)) NOT (skin)) NOT (kangaroo)); 295 results
- (((((((neonat\*)) OR (premature infant))) AND ((((ventilat\*) OR (positive airway pressure)) OR (CPAP))) AND (((position\*) OR (supine)) OR (prone))) AND ((((oxygen\*) NOT (craniosynostosis)) NOT (skin)) NOT (kangaroo)); 177 results
- Search: (((((((infant) OR (neonate)) OR (premature infant)) AND ((((venilat\*) OR (respirat\*)) OR (positive airway pressur)) OR (breath\*))) AND (position)) AND (((prone) OR (supine)) OR (lateral)) ) NOT (kangaroo)) NOT (maternal) Filters: Randomized Controlled Trial, Humans, English, Newborn: birth-1 month, Infant: birth-23 months. Results: 53
- 11. (((((((neonat\*)) OR (premature infant))) AND ((((ventilat\*) OR (positive airway pressure)) OR (CPAP))) AND (((position\*) OR (supine)) OR (prone))) AND ((((oxygen\*) NOT (craniosynostosis)) NOT (skin)) NOT (kangaroo)) Filters: Newborn: birth-1 month, Infant: birth-23 months, from 2005 – 2020. 88 Results
- 12. Search: ((((((infant) OR (neonate)) OR (premature infant)) AND ((((venilat\*) OR (respirat\*)) OR (positive airway pressur)) OR (breath\*))) AND (position)) AND (((prone) OR (supine)) OR (lateral)) ) NOT (kangaroo)) NOT (maternal) Filters: Meta-Analysis, Systematic Review, Humans, English, Newborn: birth-1 month, Infant: birth-23 months. Results: 9

In the table below,	show how ma	ny results you	ı got from y	<i>our search</i>	from each	database you
searched.						

Databases and Sites Searched	Number of results	Limits applied, revised number of results (if applicable)
PubMed	See Above	<ul> <li>Revised to include supine, prone, lateral positions</li> <li>Revised to exclude craniosynostosis, kangaroo and skin contact, and maternal care</li> </ul>

		<ul> <li>Revised to narrow to specifically a neonatal and premature population instead of a broader infant population</li> <li>Restricted the publication years to 2005-2020 to excluded outdated information. Restricted the subjects to newborns and infants to exclude children over 23 months old.</li> </ul>
CINAHL	19	<ul> <li>Restricted to: peer review reviews, articles, humans, English, newborns (0- 1month), publication years (2005-2020)</li> </ul>
Web of Science	759 4 highly cited in the field	<ul> <li>Restricted document type to articles or reviews (excluded book chapters, etc)</li> <li>Restricted publication years to 2005-2020</li> <li>Sorted by relevance to get the most relevant articles first.</li> <li>Significant crossover with PubMed results.</li> </ul>

# **INCLUSION and EXCLUSION CRITERIA**

# **Inclusion Criteria**

- Premature infants born at 36 weeks or earlier
- Mechanical ventilation due to lung underperformance, poor oxygenation, or respiratory distress syndrome.
- Outcome measures of PaO2, SpO2, lung volume, vitals, or episodes of apnoea.
- Assessment of effect of at least one of the following: prone, quarter prone, lateral, quarter lateral, or supine positioning.

# **Exclusion Criteria**

- Post-term infants, children, or adults.
- Infants having received or receiving surgical procedures.
- Procedural care during assessment, such as heel sticks, diaper changes, feeding, and suctioning.
- Infants suffering neonatal abstinence syndrome.
- Infants with diagnosed cardiovascular or heart abnormalities.
- Infants with any neurological or sensory condition or abnormalities.
- Infants with congenital malformations.
- Assessment of kangaroo care or skin-to-skin contact care positioning on respiration. Handles must be in NICU isolettes
- Subjects may not be under any pharmacological treatment during the time of the study (no opioids, sedatives, etc.)

# **RESULTS OF SEARCH**

## Summary of articles retrieved that met inclusion and exclusion criteria

For each article being considered for inclusion in the CAT, score for methodological quality on an appropriate scale, categorize the level of evidence, indicate whether the relevance of the study PICO to your PICO is high/mod/low, and note the study design (e.g., RCT, systematic review, case study).

Author (Year)	Risk of bias (quality score)*	Level of Evidence**	Relevance	Study design
Chang (2002)	PEDro Scale: 9/11	18	7/10	RCT with a cross-over design
Utario (2017)	PEDro Scale: 9/11	18	5/10	RCT with a cross-over design
Brunherotti (2014)	PEDro Scale: 9/11	1B	8/10 all premies, all on CPAP but small N with some lost to follow up	RCT with a cross-over design
Santos (2017)	Downs and Black Checklist 19/29	3 Downgraded from level 2B for lack of description on methods, follow-up, and confounding factors.	5/10, some infants required sedation eventually,	Quasi-experimental
Wu (2015)	PEDro Scale: 9/11	18	8/10	RCT
Hough (2012)	PEDro Scale: 9/11	18	8/10	RCT with cross-over design
Gouna (2013)	PEDro Scale: 8/11	18	7/10	RCT with cross-over design
Rivas Fernandez (2016)	AMSTAR 11/11	1A	8/10 little differentiation for premies	Systematic Review

\*Indicate tool name and score

\*\*Use Portney & Watkins Table 16.1 (2009); if downgraded, indicate reason why

#### **BEST EVIDENCE**

The following 2 studies were identified as the 'best' evidence and selected for critical appraisal. Rationale for selecting these studies were:

- Hough et al. There are two different measures, one of lung volume and the other of oxygenation. There is a control group of healthy, spontaneous breathing infants and a crossover design assessing 3 separate positions for each infant.
- Wu et al. There was a supine group and a group that alternated supine and prone every four hours to assess the change when the infants were experimental group was in prone vs supine. The outcome measures are appropriate to what I am looking for.
- > Both the studies are relevant to my PICO question and have a high level of evidence (1B).

# (1) Description and appraisal of "Effect of Change of Mechanical Ventilation Position on the Treatment of Neonatal Respiratory Failure" by Jiebin Wu (2015)

#### Aim/Objective of the Study/Systematic Review:

To use different positions of mechanical ventilation to treat neonatal respiratory failure as an alternate strategy to prone position or supine position to assess for improvement in oxygenation and reduced complications.

#### **Study Design**

[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

This was a randomized control trial assessing the effects of supine against alternating supine and prone positioning for improved oxygenation and reduced complications in preterm infants with respiratory failure. 67 infants were randomized into two groups, with 33 infants placed in the supine position group and 34 in the alternate position group. Infants were randomly allocated and the statistician who analysed the data was blinded to allocation, but the administrators and data collectors were not blind to the treatments applied. Children in dorsal position group were in dorsal position, with the head and shoulder at an elevation of 30 °; the children in alternate position groups were in dorsal position for 4 hour and in prone position for next 4 hour alternately. The two groups did not display any statistically significant differences at baseline.

Monitoring data was assessed at 8 hours and 1§ hours. The monitoring data at 8 and 16 h in dorsal position group and alternate position group included ventilator-associated parameters, such as FiO2, PIP, PEEP, and RR; blood air monitoring parameters: PaO2and PaCO2, and oxygenation index (OI = PaO2/FiO2); and monitoring mechanics of lung: pulmonary dynamic compliance (Cdy), tidal volume (VT), and minute volume (MV). Cdy, VT, and MV were normalized to organ weight. The drawl time in dorsal position group and alternate position group, PaCO2and PaO2at 1 h after drawl.

## Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

All subjects were treated in the neonatal intensive unit of Xuzhou Central Hospital between February 2012 and August 2013.

#### **Participants**

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

Participants were 67 neonatal infants treated at the hospital. All infants had a birthweight below 2.7kg and met the diagnostic criteria of neonatal respiratory failure. Inclusion criteria was a confirmed diagnosis of respiratory failure by a MD. Exclusion criteria was a severe thoracic deformity, unstable hemodynamic, increased intracranial pressure, acute hemmorrhage, pneumothorax, intolerance to prone positioning, and patients with rapidly deteriorating vitals on prone position.

All subjects received oral trachea cannula, with the excessive length of the trachea cannula removed to reduce dead space. Fabian neonatal/pediatric ventilator or Drager Babylag 8000 ventilator was used with mechanical ventilation model: synchronized intermittent mandatory ventilation model (SIMV) (pressure control) ? PEEP. Initial adjustment parameters were PIP 15–20 cm H2O(1 cm H2O = 0.098 kPa), FiO240–60 %, PEEP 4–6 cm H2O, respiratory rate 40–50 times/min, and inspiratory duration 0.3–0.5 s. Ventilation was performed by flow triggering, and autonomous respiration was reserved.

The supine position group had 33 cases, 18 male, 15 females. The average birthweight was 2.1kg with a standard deviation of .58kg. Prior to intervention the average respiration rate was 62.95 times per minute, the average PaO2 was 48.32 mmHg, and the average PaCO2 was 58.36mmHg.

The alternate position group had 34 cases, 16 male, 18 females. The average birthweight was 2.2kg with a standard deviation of 0.64kg. Prior to intervention the average respiration rate was 63.82 times per minute, the average PaO2 was 47.23 mmHg, and the average PaCO2 was 59.06mmHg. There was difference in variables between the two groups at baseline was not statistically significant.

There were three cases of drawl failure, including one death in the supine position group. There were two cases of drawl failure, including one death in the alternate position group. For these infant's data is available for measures assessed while on mechanical ventilation, but they were excluded in data collection for mechanical ventilation withdrawal and PaO2 and PaCO2 in the hour after mechanical ventilation withdrawal.

# Intervention Investigated

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

#### Control

There was no control group receiving no treatment of a placebo treatment, but the supine position group was considered a "control" for this study because there was no change in position from the initial position the infant was placed in. Children in this group were placed in supine with the head and shoulder elevated at 30 degrees. The infants were placed in this position for all 16 hours of ventilation time and for the hour after ventilatory weaning and withdrawal. All treatment was completed in isolettes at the NICU of the hospital.

#### Experimental

The experimental group was a group of infants that alternated supine and prone positioning. Infants were placed in supine for 4 hours and prone for 4 hours. In supine infants were placed in supine with the head and shoulder elevated at 30 degrees. The specific procedure for prone position: the neonate was in prone position, with the head toward one side to avoid oppression of trachea cannula. Head and shoulder were maintained at an elevation of 30 °, and the trunk and lower extremities in a prone position. Special attention was paid to avoid accidental drawl of the trachea cannula and the stomach tube while moving in prone position so as to prevent arteriovenous disjunction. Monitoring data was taken at 8 and 16 hours and in the hour after ventilation weaning and ventilator withdrawal.

#### **Outcome Measures**

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

During ventilation FiO2, PIP, PEEP, RR, PaO2, PaCO2, oxygenation index (OI=PaO2/FiO2), pulmonary dynamic compliance (Cody), tidal volume (VT), minute volume (MV) were measured at 8 and 16 hours. At 1 hour after ventilator withdrawal PaCO2 and PaO2 were measured. Ventilator parameters were assessed by the ventilator itself. All measures were recorded by a researcher at the hospital. All measurement data was expressed in mean  $\pm$  standard deviation, and a t test was sued for inter-group comparison, the enumeration data were represented by % and X<sup>2</sup> test was used of intergroup comparison. P <0.05 indicated statistically significant difference.

Parameter	Time (hours)	Supine Position Group (n=33)	Alternate Position Group (n=34)	т	Р
FiO2	8 hours	$0.40 \pm 0.05$	$0.39 \pm 0.04$	0.905	>0.05
	16 hours	$0.41 \pm 0.03$	$0.40 \pm 0.04$	1.155	>0.05
PIP (cm H2O)	8 hours	$19.28 \pm 4.81$	$20.63 \pm 3.39$	1.331	>0.05
	16 hours	$20.18 \pm 4.74$	$20.83 \pm 5.25$	0.531	>0.05
PEEP (cm H2O)	8 hours	$4.98 \pm 0.38$	$5.12 \pm 0.56$	1.194	>0.05
	16 hours	$5.23 \pm 1.07$	$5.18 \pm 0.59$	0.238	>0.05
RR (times/min)	8 hours	$48.28 \pm 7.81$	$47.73 \pm 6.83$	0.307	>0.05
	16 hours	$47.97 \pm 6.77$	$46.87 \pm 6.46$	0.681	>0.05

Ventilator Associated Parameters<sup>1</sup> (mean  $\pm$  standard deviation)

(Note: all data in the table above was taken directly from the original article)

Oxygenation and Lung Mechanic Indicators<sup>1</sup> (mean  $\pm$  standard deviation)

Indicators	Time (h)	Supine Position Group (n= 33)	Alternate Position Group (n=34)	Т	Ρ
PaO2 (mmHg)	8 hours	$60.13 \pm 8.95$	$65.29 \pm 7.62$	2.544	<0.05
	16 hours	$62.22 \pm 10.83$	$67.52 \pm 9.31$	2.150	<0.05
OI (mm Hg)	8 hours	$150.16 \pm 20.51$	$166.95 \pm 25.57$	2.981	<0.05
	16 hours	$152.23 \pm 22.45$	$169.59 \pm 20.28$	3.323	<0.05
PaCO2 (mm	8 hours	$49.26 \pm 6.76$	$48.24 \pm 8.91$	0.527	>0.05
Hg)	16 hours	$43.57 \pm 8.73$	$44.82 \pm 8.66$	0.588	>0.05
Cody (ml/Cm	8 hours	$0.36 \pm 0.07$	$0.43 \pm 0.08$	3.807	<0.05
H2O)	16 hours	$0.40 \pm 0.09$	$0.46 \pm 0.11$	2.439	<0.05
VT (mL)	8 hours	$5.53 \pm 1.13$	$6.27 \pm 1.08$	2.741	<0.05
	16 hours	$5.61 \pm 1.15$	$6.58 \pm 1.37$	3.134	<0.05
MV (mL/min)	8 hours	$243.61 \pm 25.79$	$251.12 \pm 20.44$	1.323	>0.05
	16 hours	$248.08 \pm 25.35$	$257.14 \pm 21.87$	1.568	>0.05

(Note: all data in the table above was taken directly from the original article)

Drawl Time, PaCO2/PaO2 at 1 hours after drawl<sup>1</sup> (mean  $\pm$  standard deviation)

Group	Case number	Duration of Mechanical Ventilation (days)	PaCO2 (mm Hg)	PaO2 (mm Hg)
Supine Position Group	32	$4.19 \pm 1.46$	44.03 ± 3.43	57.13 ± 5.64
Alternate Position Group	33	3.98 ± 1.63	42.95 ± 4.28	58.35 ± 4.66
t		0.547	1.120	0.952
Р		>0.05	>0.05	>0.05

(Note: all data in the table above was taken directly from the original article)

# **Main Findings**

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. You may summarize results in a table but you must explain the results with some narrative.]

Differences in ventilator-associated parameters at 8 and 16 hours were not statistically significant. PaO2 and OI at 8 hours and 16 hours was higher in the alternate position group and these results were statistically significant. This implies that alternating positions while on mechanical ventilation can result in better oxygenation. Tidal volume and pulmonary dynamic compliance differences were also statistically significant, indicating that alternating position can improve lung dynamics in premature infants. PaCO2 differences were no statistically significant between the groups.

The last table indicates that there were three cases of mechanical withdrawal failure in the supine group (including one death) and two cases in the alternate group (including one death.) The infants who died before weaning off the mechanical ventilation were not included data for drawl time or partial gas pressures after weaning. The differences in drawl time, PaCO2 after drawl, and PaO2 after drawl were not statistically significant. It is important to note that even though the results were not statistically significant for these parameters, the alternate position group did display slightly superior results. The objective of this study was

to assess parameters while infants were on the ventilator, and more thorough research is needed about the effects of ventilatory positioning after infants wean off mechanical ventilation.

## **Original Authors' Conclusions**

[Paraphrase as required. If providing a direct quote, add page number]

PaO2, OI, VT, and Cody at 8 and 16 hours were higher in the alternate position groups and the results were statistically significant.<sup>1</sup> This implies that oxygenation and respiratory mechanics were superior in the alternate position group when compared to the supine group. This is in agreement with previous literature on the nature of neonatal lung and thoracic mechanics and the effect of ventilation in prone. Alternating positions is also beneficial for common neonatal treatments such as backslapping, suctioning, and skin care.<sup>1</sup> Therefore, alternating prone and supine is beneficent to preterm neonates receiving mechanical ventilation.

## **Critical Appraisal**

# Validity

[Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.]

The article scores an 8/11 on the PEDro scale assessing the validity of randomized control trials. While groups were similar at baseline there was no blinding of therapists administering the therapy or assessors measuring outcomes. Additionally, some subjects were excluded from withdrawal data which may have slightly skewed results. The lack of blinding indicates that there is room for bias in interpretation and collection of results. The general consensus of literature is that prone positioning is superior for oxygenation and lack of blinding may cause confirmation bias. Additionally, the study did assess respiration rate and blood arterial gases at baseline and found no differences between groups. This means that the differences in the oxygenation between the two groups can be attributed to effects of positioning. The internal validity was also accurate as the study had excellent inclusion and external criteria that made it relevant to the clinical questions. In conclusion, with the exception of blinding the study offers an acceptable level of internal and external validity and is appropriate to apply to the clinical scenario.

#### Interpretation of Results

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

Alternating prone and supine positioning provides short-term improvements in oxygenation and lung mechanics that are beneficial for preterm infants on mechanical ventilation. At 16 hours the effect sizes of PaO2 (0.52), OI (0.81), VT (0.77), and Cdy (0.60) ranged from medium to large. This indicates the alternate positioning was moderately effective in improving these parameters in preterm infants with a moderate degree of clinical certainty. Prone positioning can improve oxygenation and lung mechanics in the short term, which can help with vital stabilization and mechanical ventilation weaning. The alternate position group did display a slightly smaller duration of mechanical ventilation and improved blood arterial gas markers after weaning off the ventilation, but these results were not statistically significant. This implies that more research is needed in the long-term effect of positioning during mechanical ventilation and the effects on the infant's oxygenation and respiratory mechanics after ventilator withdrawal. There was also a limitation to the study as the groups were not measured during the 4-hour periods where the alternate group was in supine, meaning there is no way to know whether the improvements in oxygenation

# **Applicability of Study Results**

[Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.]

In a clinical scenario, alternating prone and supine positioning every 4 hours can improve short term oxygenation and respiratory mechanics. Alternating infants every 4 hours is a practical and low-cost way to improve oxygenation and help with respiratory stability. Alternate positioning is also beneficial for other medical treatments the neonate may receive while on mechanical ventilation. Short-term improvements in oxygenation and respiratory mechanics can help with vitals stabilization and could lead to earlier ventilatory weaning and reduced NICU stays. The long-term effects of alternate positioning still need to be researched, but results indicate there may be slight improvement in oxygenation post-ventilator and in duration of mechanical ventilation. Overall evidence supports alternate positioning for preterm infants on mechanical ventilation as a safe, practical, cost-effective intervention to improve short-term oxygenation and lung mechanics.

## Aim/Objective of the Study/Systematic Review:

To use electrical impedance tomography (EIT) to measure the effect of body positioning on regional ventilation distribution and regional filling characteristics of the lung in preterm infants on CPAP and with a group of spontaneously breathing preterm infants.

## **Study Design**

[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

A randomized crossover study to investigate the effect of body position on regional ventilation distribution in preterm infants on CPAP compared with spontaneously breathing healthy preterm infants. The three positions used were supine, quarter prone (right side uppermost) and prone (head turned to the left.) The order of the three different body positions was randomized by concealed random allocation. Outcome measures were recorded 30 minutes after each position change.

CPAP respiratory support was delivered using infant nasal CPAP cannula (Hudson RCI, Temecula, CA) with a Bubble CPAP delivery system BC151 (Fischer and Paykel Healthcare, Auckland, New Zealand) using pressures of 6-8 cm H2O. The control group of spontaneously breathing infants were free of any respiratory impairments and never required any respiratory support.

Electrical impedance tomography was used to measure regional ventilation distribution and lung filling. Three consecutive recordings of 1 min each were taken 30 minutes after each position change. Impedance amplitudes for the anterior, posterior, right, and left side of the lung were measured. Global inhomogeneity index was also measured to indicate the homogeneity of tidal volume distribution in the lung. Phase angle was also used to investigate regional differences in lung-filling characteristics. A positive phase angle indicates the region of interest leads inspiratory filling in relation to the global lung. A negative phase angle indicates the region of interest lags behind. Other measures included SpO2, FiO2, respiratory rate, and heart rate. The SpO2/FiO2 ration was also calculated. Oxygen saturation was manually recorded at the time of each EIT recording using a bedside cardiorespiratory monitor.

#### Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

The neonatal intensive care unit at the Mater Mother's Hospital, South Brisbane, Australia.

#### Participants

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

There were a total of 32 infants included in the study. 24 preterm infants on CPAP and 6 spontaneously breathing healthy preterm infants. Inclusion criteria were infants aged 32 weeks of gestation or younger with a body weight of >750g. Exclusion criteria was cardiopulmonary instability, recent surgery, lung collapse, air leak syndrome, musculoskeletal congenital deformation, and poor skin integrity. All infants on CPAP were being managed for respiratory distress syndrome.

There were some significant differences between the control (spontaneously breathing) and CPAP group. Both birthweight and study weight were statistically significantly lower in the CPAP group. Gestational age was also significantly lower in the CPAP group. However, there was no statistically significant difference in postnatal age between the two groups. There were no dropouts or subject's loss to follow-up.

# **Intervention Investigated**

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

#### Control

6 preterm infants spontaneously breathing, mean birth weight 1816 g, mean gestational age 32.0 weeks. The infants followed the same protocol as the experimental group. Each infant was randomly allocated to one of the following positions to start: supine, quarter prone, or prone. The infant was placed in each position for an unspecified amount of time, and the order of the three positions was randomized by concealed random allocation. Outcome measures were assessed 30 minutes after each position change.

#### Experimental

24 preterm infants receiving CPAP respiratory support for respiratory distress. Mean birth weight 1151g and mean gestational age 28.7 weeks. Each infant was randomly allocated to one of the following positions to start: supine, quarter prone, or prone. The infant was placed in each position for an unspecified amount of time, and the order of the three positions was randomized by concealed random allocation. Outcome measures were assessed 30 minutes after each position change.

#### **Outcome Measures**

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

Electrical impedance tomography was used to measure regional ventilation distribution and lung filling. Three consecutive recordings of 1 min each were taken 30 minutes after each position change. Impedance amplitudes for the anterior, posterior, right, and left side of the lung were measured. Global inhomogeneity index was also measured to quantify tidal volume distribution within the lung. Phase angle was also used to investigate regional differences in lung-filling characteristics. A positive phase angle indicates the region of interest leads inspiratory filling in relation to the global lung. A negative phase angle indicates the region of interest lags behind. Other measures included SpO2, FiO2, respiratory rate, and heart rate. The SpO2/FiO2 ration was also calculated.

# **Main Findings**

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. Use a table to summarize results if possible.]

There was no significant interactions between sequence order, position, and region on phase angle in infants on CPAP. There was a significant interaction between position and region of interest phase angle, but there was no main effect of position for either healthy infants or the infants on CPAP. For both groups, irrespective of position, there were significant effects of position on lung amplitude, with a higher amplitude in the posterior lung over anterior and right side over left. Infants on CPAP also had significantly higher global inhomogeneity index across all positions compared to the controls, with no statistically significant effect of sequence or position. The higher inhomogeneity index indicates increases in pulmonary impedance in the lungs.

For oxygenation and positioning, there was increased respiration rate in supine compared to quarter prone and prone for infants on CPAP. Infants on CPAP also had better SpO2/FiO2, which is an indication of oxygenation. This agrees with previous studies that have suggest oxygenation is improved in prone compared to supine.

Overall there was no effect of body position on regional ventilation distribution in terms of amplitude and global homogeneity in the infants on CPAP. Healthy preterm infants saw an increase in the quarter prone position and prone position when compared to supine.

	Supine Mean	Supine SEM	Prone Mean	Prone SEM	Quarter Prone Mean	Quarter Prone SEM
FiO2	0.23	0.01	0.22	0.01	0.22	0.00
SpO2 (%)	96.72	0.59	97.18	0.43	97.93	0.43
SpO2/FiO2	431.96	13.08	443.78	12.17	449.81	8.42

Oxygenation Data for Preterm Infants on CPAP<sup>2</sup>

Respiratory	67.02	4.44	59.88	3.76	57.60	3.75	
Rate							l
(breaths/min)							J

(Note: all data in the table above was taken directly from the original article)

Oxygenation Data for Spontaneously Breathing Controls<sup>2</sup>

	Supine Mean	Supine SEM	Prone Mean	Prone SEM	Quarter Prone Mean	Quarter Prone SEM
FiO2	0.21	NA	0.21	NA	0.21	NA
98.75	98.75	0.43	98.01	0.66	98.69	0.45
SpO2/FiO2	470.24	2.03	466.72	3.16	469.97	2.15
Respiratory Rate (breaths/min)	55.83	5.03	59.22	5.12	53.92	4.96

(Note: all data in the table above was taken directly from the original article)

# **Original Authors' Conclusions**

[Paraphrase as required. If providing a direct quote, add page number]

Ventilation in preterm infants is not gravity-dependent but follows an anatomical pattern. Positioning had little impact on regional ventilation distribution on both spontaneously breathing preterm infants and infants in CPAP. Infants on CPAP also had significantly higher global inhomogeneity index across all positions when compared to the controls, indicating increased lung impedance. Positioning had no statistically significant effects on oxygenation in spontaneously breathing preterm infants. Quarter prone and prone positioning demonstrated significantly improved oxygenation statistics while also having statistically significant decreased respiration rate than supine. This overall implies that positioning other than supine can be beneficial in improving oxygenation and respiration values.

# **Critical Appraisal**

# Validity

[Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.]

This study scored 8/11 on the PEDro scale to assess internal and external validity of randomized control trials. The study had appropriate inclusion and external criteria which established internal validity. For external validity there were some gaps in blinding. There was not any blinding among therapy administrators or individuals measuring outcomes. The lack of blinding indicates that there is room for bias in interpretation and collection of results. The general consensus of literature is that prone positioning is superior for oxygenation and lack of blinding may cause confirmation bias. There was also a lack of information about who assessed outcomes or when they were assessed. There was no information about how long the infants spent in each position. Both of these are major errors that make the results difficult to apply to preterm infants in a clinical situation. There was also a major difference in the control (spontaneously breathing group) and the CPAP group. The spontaneously breathing group had significantly higher bodyweight than the CPAP group. Weight is a sign of development and this indicates that the differences between the groups may not be an accurate assessment since the control and intervention group are not equal at baseline. Overall the internal validity is excellent but there are missing details and problems with the control group that make this study difficult to apply to a clinical population.

# **Interpretation of Results**

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

There is an overall difference in regional lung amplitude in both the CPAP and control group, indicating that regional lung volume differences are independent of CPAP use and position. There were differences in oxygenation and positioning in infants on CPAP. Quarter prone and prone positioning had significantly improved oxygenation and respiration rate compared with supine for infants on CPAP. There was a small effect size for SpO2 between prone and supine (0.22) and a moderate effect size for quarter prone (0.47). The same was true of SpO2/FiO2 with effect sizes of 0.20 and 0.33 respectively. There were small-to-moderate effect sizes for prone (0.35) and quarter prone (0.46) compared to supine in respiration rate as well. The effect sizes and improvements in oxygenation indicate that there is an association between prone and quarter prone and improved oxygenation in preterm infants on CPAP. There is no effect of positioning on regional lung volumes.

# **Applicability of Study Results**

[Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.]

The results concerning global lung volume indicate the regional ventilation volume does not change with positioning. The results concerning oxygenation parameters indicate there is small-to-moderate improvements in oxygenation with quarter prone and prone positioning for preterm infants on CPAP. The results of the study indicate that using quarter prone or prone as an alternate to supine positioning for mild-to-moderate improvements in oxygenation or preterm infants on CPAP. The results indicate that the changes while clinically significant, may only indicate mild improvements for our clinical scenario. The results indicate that positioning infants with poor oxygenation in prone or quarter prone as compared to supine may yield mild benefits, but that these are not guaranteed. The long-term effects of alternate positioning still needs to be researched, but evidence supports alternate positioning for preterm infants on mechanical ventilation as a safe, practical, cost-effective intervention to improve oxygenation.

# SYNTHESIS AND CLINICAL IMPLICATIONS

[Synthesize the results, quality/validity, and applicability of the two studies reviewed for the CAT. Future implications for research should be addressed briefly. Limit: 1 page.]

The studies assessed concluded that prone position is superior for oxygenation with small-to-moderate effect sizes. In the Wu, 2015 study the results for oxygenation and lung dynamic parameters ranged from medium to large. This indicates the alternate positioning was moderately effective in improving these parameters in preterm infants with a moderate degree of clinical certainty. Prone positioning can improve oxygenation and lung mechanics in the short term, which can help with vital stabilization and mechanical ventilation weaning. The alternate position group did display a slightly smaller duration of mechanical ventilation and improved blood arterial gas markers after weaning off the ventilation, but these results were not statistically significant. In the Hough, 2012 study quarter prone and prone positioning had significantly improved oxygenation and respiration rate compared with supine for infants on CPAP. The results had only small-to-moderate effect sizes as well. The effect sizes and improved oxygenation indicate that there is an association between prone and quarter prone and improved oxygenation in preterm infants on CPAP. There is no effect of positioning on regional lung volumes.

The overall assessment of validity indicates excellent internal validity, as both studies assess oxygenation in preterm infants on mechanical ventilation with well-defined exclusion and inclusion criteria. There was also a lack of blinding among assessors and intervention -administrators. This is common in physical therapy studies because of the nature of interventions and assessment. However, it does leave room for bias. There was also issues in the Hough, 2012 study about intervention parameters and significant differences in the control and intervention groups at baseline. This makes it more difficult to generalize the results of this study to the study population. Despite all of these errors, both studies scored relatively high on the PEDro scale, indicating an acceptable level of external validity.

The studies have different levels of applicability to clinical populations. The Wu, 2015 study provided details on intervention protocols at a level that makes replication in a clinical scenario feasible. Precise positioning, ventilator, and assessment details were provided and can be replicated in a hospital setting. The Hough, 2012 study is less feasible to replicate. The implications from both of these studies, along with others assessed in initial articles that met inclusion and external criteria for this CAT, is to further establish a universal positioning protocol to improve oxygenation. Another direction for research is to continue with high-quality randomized control trials assessing the effects of specific positioning protocols on preterm infants with comparable control groups. Current systematic reviews<sup>3</sup> of positioning on oxygenation in preterm infants. There is a need for high-quality, low bias randomized control trials further examining these effects.

# REFERENCES

[List all references cited in the CAT]

Bibliography

- Wu J, Zhai J, Jiang H, et al. Effect of change of mechanical ventilation position on the treatment of neonatal respiratory failure. *Cell Biochem Biophys*. 2015;72(3):845-849. doi:10.1007/s12013-015-0547-2
- 2. Hough JL, Johnston L, Brauer SG, Woodgate PG, Pham TMT, Schibler A. Effect of body position on ventilation distribution in preterm infants on continuous positive airway pressure. *Pediatr Crit Care Med*. 2012;13(4):446-451. doi:10.1097/PCC.0b013e31822f18d9
- 3. Rivas-Fernandez M, Roqué I Figuls M, Diez-Izquierdo A, Escribano J, Balaguer A. Infant position in neonates receiving mechanical ventilation. *Cochrane Database Syst Rev.* 2016;11:CD003668. doi:10.1002/14651858.CD003668.pub4