Supplemental Material

Manuscript Title: Promoting evidence-based practice in acute respiratory distress syndrome: a systematic review

Author list:
Shewit P. Giovanni, MD, MS
Ann L. Jennerich, MD, MS, ATSF
Tessa L. Steel, MD, MPH
Sharukh Lokhandwala, MD, MS
Waleed Alhazzani, MBBS, MS, FRCPC
Curtis H. Weiss, MD, MS
Catherine L. Hough, MD, MS

e-Appendix 1: Search strategies

1) PubMed:

("quality improvement" OR "quality improvements" OR quality of health care[mh] OR toolkit* OR tool[tiab] OR tools[tiab] OR "decision support" OR "decision supports" OR decision support techniques[mh] OR clinical decision making[mh] OR reminder[tw] OR reminders[tw] OR checklist* OR aid[tiab] OR aids[tiab] OR adhere* OR implement* OR utiliz*[tw] OR protocol* OR guideline[tw] OR guidelines[tw] OR guideline[pt] OR practice guideline[pt] OR guideline adherence[mh] OR guidelines as topic[mh] OR clinical protocols[mh] OR patient-centered care[mh] OR comprehensive health care[mh] OR recommendation*[tiab] OR consensus[tw] OR pathway* OR evidence[tw])

AND
(low tidal volume* OR lower tidal volume* OR "low tidal ventilation" OR limit tidal volume* OR tidal volume[mh] OR lung protect* OR lpv*[tiab] OR ltv*[tiab] OR neuromuscular blocking agents[mh] OR "neuromuscular blockade" OR "neuromuscular blockades" OR "neuromuscular block" OR "neuromuscular blocks" OR neuromuscular blocker* OR "neuromuscular blocking" OR neuromuscular nondepolarizing agents[pa] OR prone position[mh] OR prone[tiab] OR proning[tiab])

AND
(acute lung injury[mh] OR lung injury[mh:noexp] OR adult respiratory distress syndrome[mh] OR ards[tiab] OR acute respiratory distress syndrome*[tiab] OR adult respiratory distress syndrome*[tiab])

AND
2002:2021[pdat] AND english[la]

2) Embase:

('quality improvement':ti,ab,de OR 'quality improvements':ti,ab,de OR 'health care quality'/exp OR toolkit:ti,ab,de OR toolkits:ti,ab,de OR tool:ti,ab OR tools:ti,ab OR 'decision support':ti,ab,de OR 'decision supports':ti,ab,de OR 'decision support system'/exp OR 'clinical decision making'/exp OR reminder:ti,ab,de OR reminders:ti,ab,de OR checklist:ti,ab,de OR checklists:ti,ab,de OR aid:ti,ab OR aids:ti,ab OR adhere* OR implement* OR utiliz* OR protocol* OR guideline* OR 'practice guideline'/exp OR 'protocol compliance'/exp OR 'clinical protocol'/exp OR 'patient centered':ti,ab,de OR 'patient centeredness':ti,ab OR 'patient care'/exp OR recommendation* OR consensus:ti,ab,de OR pathway* OR evidence:ti,ab,de)

AND

('low tidal volume*' OR 'lower tidal volume*' OR 'low tidal ventilation' OR 'limit tidal volume*' OR 'tidal volume'/exp OR 'lung protect*' OR lpv*:ti,ab OR ltv*:ti,ab OR 'neuromuscular blocking agent'/exp OR 'neuromuscular blockade*' OR 'neuromuscular block*' OR 'neuromuscular blocker*' OR 'neuromuscular blocking' OR 'prone position'/exp OR 'prone positioning'/exp OR prone:ti,ab,de OR proning:ti,ab,de)

AND
('acute lung injury'/exp OR 'lung injury'/de OR 'adult respiratory distress syndrome'/exp OR ards:ti,ab OR 'acute respiratory distress syndrome' OR 'adult respiratory distress syndrome*")

AND [2002-2021]/py

AND [english]/lim

3) CINAHL:
(quality improvement OR MH "Quality of Health Care+" OR toolkit* OR tool OR tools OR decision support OR MH "Decision Support Techniques+" OR MH "Decision Making, Clinical" OR reminder OR checklist* OR "aid" OR "aids" OR adhere* OR implement* OR utiliz* OR protocol* OR guideline OR MH "Guideline Adherence" OR critical path OR MH "Practice Guidelines" OR MH "Protocols+" OR MH "Patient Centered Care" OR patient centered OR patient centeredness OR MH "Patient Care+" OR recommendation OR consensus OR pathway* OR evidence)

AND
(low tidal volume OR lower tidal volume OR low tidal ventilation OR limit tidal volume OR MH "Tidal Volume" OR lung protect* OR lpv* OR ltv* OR MH "Neuromuscular Blocking Agents+" OR neuromuscular blockade OR neuromuscular block OR neuromuscular blocker OR neuromuscular blocking OR MH "Prone Position" OR prone OR proning)

AND

(MH "Acute Lung Injury+" OR MH "Lung Injury" OR MH "Respiratory Distress Syndrome, Acute" OR ards OR acute respiratory distress syndrome* OR adult respiratory distress syndrome*)

AND
PY 2002-2021 AND LA English

4) Cochrane:

#1 (quality improvement* or toolkit or toolkits or tool or tools or decision support* or reminder or reminders or checklist or checklists or aid or aids or adhere* OR implement* or utiliz* or protocol* or guideline* or recommendation* or consensus or pathway* or evidence):ti,ab,kw (Word variations have been searched)
#2 MeSH descriptor: [Decision Support Techniques] explode all trees
#3 MeSH descriptor: [Quality of Health Care] explode all trees
#4 MeSH descriptor: [Clinical Decision-Making] explode all trees
#5 MeSH descriptor: [Guideline Adherence] explode all trees
#6 MeSH descriptor: [Clinical Protocols] explode all trees
#7 MeSH descriptor: [Patient-Centered Care] explode all trees
#8 MeSH descriptor: [Comprehensive Health Care] explode all trees
#9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10 low tidal volume* OR lower tidal volume* OR low tidal ventilation OR limit tidal volume* or lung protect* or lpv* OR ltv* or neuromuscular blockade* or neuromuscular block* OR neuromuscular blocker* OR "neuromuscular blocking" or prone or proning
#11 MeSH descriptor: [Tidal Volume] explode all trees
#12 MeSH descriptor: [Neuromuscular Blocking Agents] explode all trees
#13 MeSH descriptor: [Prone Position] explode all trees
#14 #10 or #11 or #12 or #13
#15 #9 and #14
#16 MeSH descriptor: [Acute Lung Injury] explode all trees
#17 MeSH descriptor: [Lung Injury] this term only
#18 MeSH descriptor: [Respiratory Distress Syndrome, Adult] explode all trees
#19 ards or acute respiratory distress syndrome* or adult respiratory distress syndrome*
#20 #16 or #17 or #18 or #19
#21 #15 and #20

e-Appendix 2: GRADE assessment

Question: Does the presence of practice guides (protocols, policies, aids, checklists) compared to no practice guides increase the adherence to, or implementation of LTVV in mechanically ventilated patients with ARDS?
Setting: Emergency department, Intensive care unit
Bibliography: Belda 2004, Birkhoelzer 2019, Fuller 2017, Kalb 2014, Nota 2016, Wolthuis 2005, Wolthuis 2007

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Adherence with low tidal volume ventilation									
5	observational studies	serious [a]	not serious	serious [b]	serious [c]	none	**Wolthius 2007:** Comparing pre- to post-intervention at the same study site, the percentage of data points with VT > 10 mL/kg PBW declined from 49% to 3%, and the number of observations with VT > 8 mL/kg PBW decreased from 86% to 28% (n=20). **Kalb 2014:** Adherence to Vt < 6.5 ml/kg IBW in patients with documented ARDS/ALI was 23% pre-intervention (41/178) and 37% post-intervention (177/474) (p<0.005). **Nota 2016:** Adherence to TV <6.5 cc/kg PBW was higher after introduction of the intervention (increase in adherence of 29.4% [IQR, 19.3%–39.5%] from baseline). There was a a postintervention linear trend of 0.23% (IQR, –0.11% to 0.58%) improvement per month. **Fuller 2017:** For patients with ARDS in the ED, LPV use increased from 11.1% pre-intervention (n=44) to 61.5% post-intervention (n=21), p<0.01. Post-intervention, LPV in the ICU increased from 11.4% to 35.3%, p<0.01. The ED intervention was a significant predictor of receipt of ICU LPV (OR 3.41, 95% CI 1.15 – 10.1, p=0.03). **Birkhoelzer 2019:** Pre-intervention, ventilated patients (n=77) received VT< 8 ml/kg IBW 68.2% of the time (1464/2148 hours). Post-intervention, ventilated patients (n=60) received VT< 8 ml/kg IBW 81% of the time (1491/1843 hours).	⊕◯◯◯ VERY LOW	CRITICAL
Mean or median tidal volume									
4	observational studies	serious [d]	not serious	not serious	serious [e]	none	**Belda 2004:** Following a clinician-education intervention, patient with ARDS (N=45) were less likely to receive high tidal volume ventilation (mean day-3 VT 10.3 ± 2.3 mL/kg before vs 8.9 ± 1.7 mL/kg after, p=0.02). **Wolthuis 2005:** In patients with ALI/ARDS mean tidal volumes were 9.9±2.2 ml/kg PBW before the intervention (n=24) and 8.2±1.8 ml/kg PBW after (n=21) (p=0.013). **Wolthuis 2007:** Mean VT was 7.6 mL/kg PBW (95% CI 6.5– 8.7) at the intervention site compared to 10.3 mL/kg PBW at site not receiving the intervention (95% CI 9.5–11.0). **Fuller 2017:** For patients with ARDS in the ED, pre-intervention median tidal volumes were 8.0 mL/kg PBW (IQR 7.1 – 9.1) compared to 6.4 mL/kg PBW (IQR 6.1 – 6.8) post-intervention. Post-intervention, ICU tidal volume decreased from median 8.1 mL/kg PBW (IQR 7.3 – 9.1) to 7.0 (IQR 6.2 – 8.4), p<0.01.	⊕◯◯◯ VERY LOW	CRITICAL
Mortality									
3	observational studies	serious [f]	not serious	serious [g]	serious [h]	none	**Belda 2004:** Comparing pre- and post-intervention groups, hospital mortality was 43% before the intervention vs 50% after the intervention, p=0.77. **Kalb 2014:** ICU mortality ratio (using APACHE IV predictions) was 0.94 pre-implementation vs 0.65 (p <0.03) in the last reported post-implementation assessment. Hospital mortality did not show significant change during the study. **Fuller 2017:** The intervention was associated with a reduction in mortality from 54.8% (102/186) to 39.5% (17/43). After multivariable logistic regression, OR 0.36, 95% CI 0.16 – 0.82, p=0.02.	⊕◯◯◯ VERY LOW	IMPORTANT
Ventilator utilization									

2	observational studies	serious [i]	not serious	serious [g]	not serious	none	**Kalb 2014:** Mean ventilator duration range - the number of days of mechanical ventilation/APACHE IV predicted days of mechanical ventilation - was 1.08 pre-intervention and 0.92 post-intervention (mean −15.8% decrease, p<0.05). **Fuller 2017:** Ventilator-free days were higher in the intervention group than in the pre-intervention group (11.6 ± 10.8 vs. 7.7 ± 9.9 days, p=0.03).	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval

Explanations

a. Wolthuis 2007 pooled data from intervention and control arms. Fixed effects included in the regression model were study, sample time, and the interaction between study and sample time. No adjustment for other potential confounders. Nota 2016, unclear if adjusted for potential confounders in the primary analysis, no discussion of auto-correlation related to interrupted time-series analysis. Neither Kalb 2014 nor Birkhoelzer 2019 accounted for potential confounders or differences related to site.
b. In Nota 2016 and Birkhoelzer 2019, outcome was not reported by disease state. Results include data on patients without ARDS.
c. Wolthuis 2007, Fuller 2017 with few participants per group.
d. Belda 2004 did not adjust for potential confounders. Wolthius 2005 made no adjustment for potential confounders or study site. Wolthuis 2007 pooled data from intervention and control arms. Fixed effects included in the regression model were study, sample time, and the interaction between study and sample time. No adjustment for other potential confounders. Fuller 2017 did not adjust for potential confounders.
e. Belda 2004, Wolthuis 2005 and 2007, Fuller 2017 with few participants per group.
f. Belda 2004 did not adjust for potential confounders. Kalb 2014 did not account for potential confounders or differences related to site.
g. In Kalb 2014, outcome was not reported by disease state. Results include data on patients without ARDS.
h. In Belda 2004 and Kalb 2014, unclear number of mortality events. Fuller 2017 with few events.
i. Kalb 2014 did not account for potential confounders or differences related to site. Fuller 2017 did not adjust for potential confounders.

Question: Does the presence of practice guides (protocols, policies, aids, checklists and/or props) compared to no practice guides increase the adherence to, or implementation of prone position therapy in mechanically ventilated patients with ARDS?
Setting: Intensive care unit
Bibliography: Luedike 2015, Gallo de Moraes 2020

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Application of prone positioning									
1	observational studies	serious [a]	not serious	not serious	serious [b]	none	**Luedike 2015:** Prone positioning was applied in 7% of cases in 2013 (n = 2/15). In 2014, after implementation of an ARDS standard operating procedure, early prone positioning was applied in 73% of cases (n = 24/33) (2013 vs 2014, p<0.05).	⨁◯◯◯ VERY LOW	CRITICAL
Time to initiation of prone positioning from onset of severe ARDS									
1	observational studies	serious [a]	not serious	not serious	serious [b]	none	**Gallo de Moraes 2020:** Among patients who were placed in the prone position (n=28), time from hypoxemia to initiation of prone positioning was shorter after protocol implementation (42.2 hours before vs. 16.3 hours, p=0.007).	⨁◯◯◯ VERY LOW	CRITICAL
Mortality									
2	observational studies	serious [a]	not serious	not serious	serious [c]	none	**Luedike 2015:** There was no significant difference in 28- and 180-day mortality in patients with ARDS after implementation of the ARDS standard operating procedure. **Gallo de Moraes 2020:** There was no significant difference in ICU- or hospital mortality in patients with ARDS after implementation of an ARDS management protocol.	⨁◯◯◯ VERY LOW	IMPORTANT
Length of stay									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
1	observational studies	serious [a]	not serious	not serious	serious [b]	none	**Gallo de Moraes 2020:** Among patients with severe ARDS, there was no significant difference in hospital or ICU length of stay after implementation of an ARDS management protocol (n=112 pre-protocol and 122 post-protocol). Among a subgroup of patients with severe ARDS who were placed in the prone position (n=28), there was no significant difference in hospital length of stay after protocol implementation, whereas ICU length of stay was shorter after protocol implementation (14.3 days vs. 6 days, p=0.03).	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval

Explanations

a. No adjustment for potential confounders.
b. Few participants, few events.
c. Few participants, unclear number of deaths in Luedike.