

Research Articles
Research
Making Sense of It All

Kansas Respiratory Care Society
April 10, 2015
Wichita, KS



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Learning Objectives

- Getting started
 - Literature review
 - Hierarchy and grading
 - Orientation and organization
- Article components with critical evaluation
 - Title
 - Abstract
 - Introduction
 - Methods
 - Results
 - Discussion/Conclusion

Research



Literature Review

- Common Databases
 - Medline via PubMed – Medical Science
 - PsychInfo – Social/Behavioral Science
 - Google Scholar – accesses many databases
- Ask your librarian
 - Best resources
 - Search terms

Research



Develop Clinical Question

	Topic	Clinical Question
P	Population	Population or clinical problem of interest
I	Intervention (New treatment)	Exposure, test, or treatment
C	Comparison (Standard treatment)	What you think the intervention is better or worse than
O	Outcome	Of interest (to patient)

Mayer D. (2004). *Essential Evidence-Based Medicine*. New York: Cambridge University Press.

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The New England Journal of Medicine

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VOLUME 342

MAY 4, 2000

NUMBER 18



VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

ABSTRACT

Background Traditional approaches to mechanical ventilation use tidal volumes of 10 to 15 ml per kilogram of body weight and may cause stretch-induced lung injury in patients with acute lung injury and the acute respiratory distress syndrome. We therefore conducted a trial to determine whether ventilation with lower tidal volumes would improve the clinical outcomes in these patients.

Methods Patients with acute lung injury and the acute respiratory distress syndrome were enrolled in a multicenter, randomized trial. The trial compared traditional ventilation treatment, which involved an initial tidal volume of 12 ml per kilogram of predicted

THE mortality rate from acute lung injury and the acute respiratory distress syndrome¹ is approximately 40 to 50 percent.²⁻⁴ Although substantial progress has been made in elucidating the mechanisms of acute lung injury,⁵ there has been little progress in developing effective treatments.

Traditional approaches to mechanical ventilation use tidal volumes of 10 to 15 ml per kilogram of body weight.⁶ These volumes are larger than those in normal subjects at rest (range, 7 to 8 ml per kilogram), but they are frequently necessary to achieve normal values for the partial pressure of arterial carbon diox-



Orientation to Article

	Topic	ARDS Network
P	Population	Patients with acute lung injury and ARDS
I	Intervention	Ventilation with lower tidal volume
C	Comparison	Traditional ventilation treatment
O	Outcome	In-hospital mortality Ventilator free days (1 – 28 days)
D	<i>Design</i>	<i>Multi-center randomized trial</i>

Adapted from Mayer D. (2004). *Essential Evidence-Based Medicine*. Cambridge University Press: New York.

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Initial Evaluation



VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH
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THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

- Title
 - Mini abstract
- Abstract
 - Brief summary
 - Introduction
 - Methods
 - Results
 - Discussion/Conclusion

Research



ARDSNet (2000) Lower Tidal Volumes

Population

outcomes in these patients.

Methods Patients with acute lung injury and the acute respiratory distress syndrome were enrolled in a multicenter, randomized trial. The trial compared traditional ventilation treatment, which involved an initial tidal volume of 12 ml per kilogram of predicted body weight and an airway pressure measured after a 0.5-second pause at the end of inspiration (plateau pressure) of 50 cm of water or less, with ventilation with a lower tidal volume, which involved an initial tidal volume of 6 ml per kilogram of predicted body weight and a plateau pressure of 30 cm of water or less. The first primary outcome was death before a patient was discharged home and was breathing without assistance. The second primary outcome was the number of days without ventilator use from day 1 to day 28.



ARDSNet (2000) Lower Tidal Volumes

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Intervention



ARDSNet (2000) Lower Tidal Volumes

Comparison

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ARDSNet (2000) Lower Tidal Volumes

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Outcomes

Research



ARDSNet (2000) Lower Tidal Volumes

Findings

was the number of days without ventilator use from day 1 to day 28.

Results The trial was stopped after the enrollment of 861 patients because mortality was lower in the group treated with lower tidal volumes than in the group treated with traditional tidal volumes (31.0 percent vs. 39.8 percent, $P=0.007$), and the number of days without ventilator use during the first 28 days after randomization was greater in this group (mean [\pm SD], 12 ± 11 vs. 10 ± 11 ; $P=0.007$). The mean tidal volumes on days 1 to 3 were 6.2 ± 0.8 and 11.8 ± 0.8 ml per kilogram of predicted body weight ($P<0.001$), respectively, and the mean plateau pressures were 25 ± 6 and 33 ± 8 cm of water ($P<0.001$), respectively.

Conclusions In patients with acute lung injury and the acute respiratory distress syndrome, mechanical ventilation with a lower tidal volume than is traditionally used results in decreased mortality and increases the number of days without ventilator use. (N Engl J Med 2000;342:1301-8.)

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Literature Review Matrix

Pub date	Author	Design	Population	Intervention	Comparison	Outcome(s)	Findings	Notes	Reference
2000	ARDSNet	MC RT	<ul style="list-style-type: none"> • N=861 • Intubated • Receiving MV • Acute lung injury • ARDS 	Lower tidal volume	Traditional ventilation treatment	<ul style="list-style-type: none"> • In-hospital mortality (breathing without assistance) • Number of vent free days 	MV with lower tidal volume <ul style="list-style-type: none"> • decreased IH mortality • increased vent free days 		
2015	Rialp et al.	Repeated Crossover	<ul style="list-style-type: none"> • N= 14 • Intubated • RTW 	CO ² Response Test	Repeated CO ² Response Test	<ul style="list-style-type: none"> • Consistency ICC • Agreement ANOVA 	<ul style="list-style-type: none"> • Good correlation • Good agreement 		

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Level of Evidence Pyramid





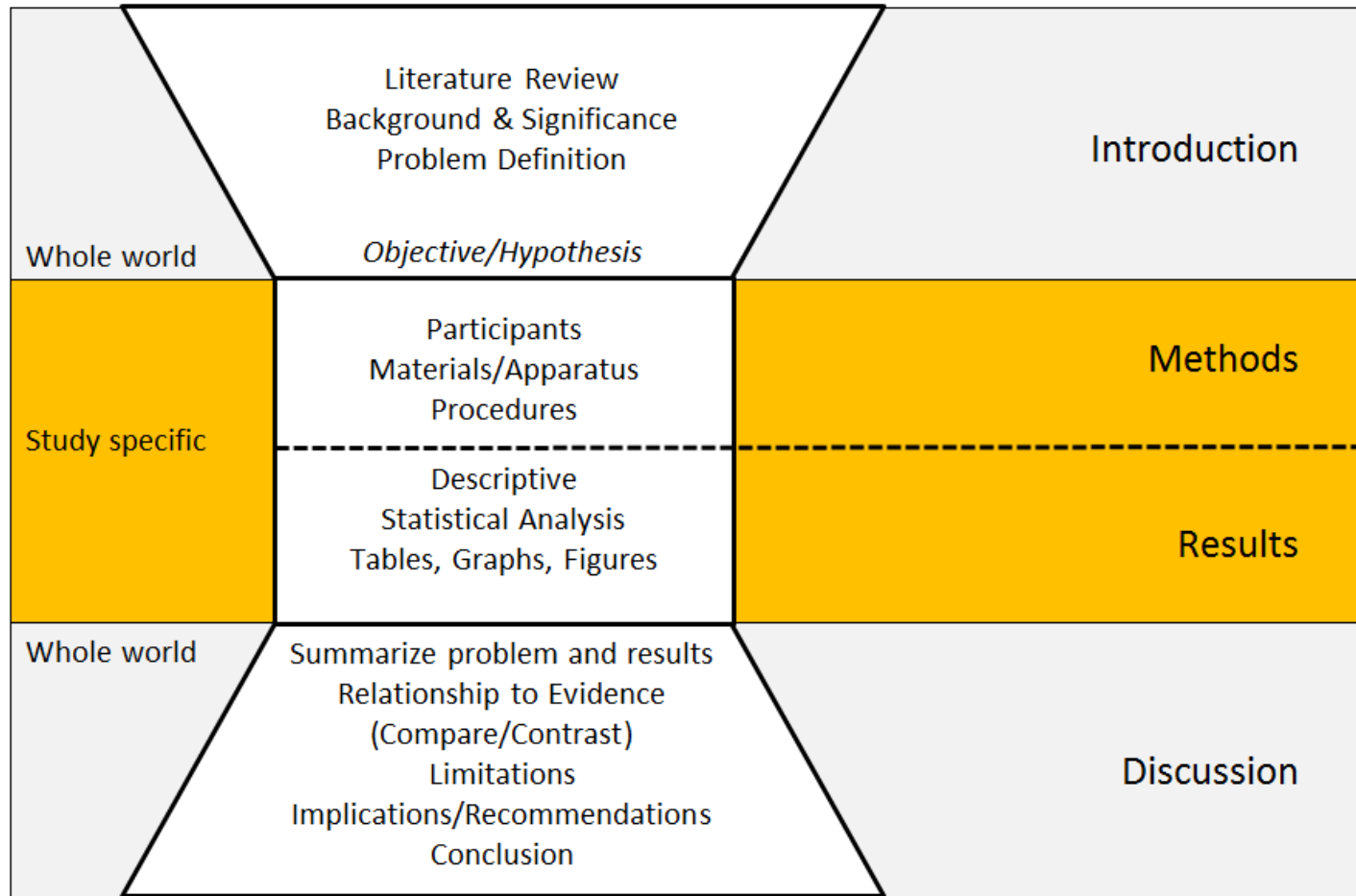
Classification of Levels of Evidence

Level	Therapy/Prevention, Aetiology/Harm
1a	Systematic review (with homogeneity) of RCTs
1b	Individual RCT (with narrow Confidence Interval)
1c	All or none (ie all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)
2c	"Outcomes" Research or ecologic studies (studies of group ch ^{ics})
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual Case-Control Study
4	Case-series (and poor quality cohort and case-control studies)
5	Expert opinion or based on physiology, bench research or "first principles"

Research



Structure





Introduction: *Purpose*

- Review of previous research
 - Current citations
 - Critical evaluation (identify problems)
 - Identify gaps in research
 - Ex. Unexamined populations?
- Demonstrates logic of hypothesis and study design

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Introduction

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VOLUME 342

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THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

- Mortality rate from acute lung injury
- Traditional approach
 - Necessary for partial pressure of arterial carbon dioxide and PH
 - May cause disease due to excessive distention and release inflammatory mediators which may cause organ damage
- Lower tidal volumes
 - May reduce injurious lung distention and release of inflammatory mediators
 - May cause respiratory acidosis and decrease arterial oxygenation
- Conflicting results from randomized trials
- *Goal: use of lower tidal volumes improve clinical outcomes*

Research



Introduction: *Critically Evaluate*

- Problem narrowly defined
- Only one side of issue presented
- Key articles/authors missing
- Gaps in knowledge not critically evaluated
- No distinction between research findings
 - Opinions
 - Theory proposal
- Does not provide support for
 - For hypothesis and/or research question
 - Need for study

Research



Methods: *Purpose*

- Information to understand, critique and replicate
 - Participants: characteristics of subjects
 - Procedures: testing situation and design
 - Materials/Apparatus: characteristics of testing materials and equipment
 - Statistical analysis
- Define limitations

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Methods

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Topic	ARDS Network
Participants	Inclusion: Intubated, receiving MV Edema; No pulmonary capillary wedge pressure Exclusion: time, age, other trials, pregnant, disease, contraindications, other confounding factors; unwilling to participate
Procedures	Randomization Ventilator procedures Monitoring for organ/system failure
Materials Apparatus	Times and calibration of vent settings Patient data Assessment of compliance
Statistics	Baseline: Students t-test; Fishers' exact test Outcomes: ANCOVA or Wilcoxin's test Mortality: Chi-square P values two-way Logarithm transformation



Methods: *Critically Evaluate*

- Artificial or limited settings
- Recruitment and sampling
 - Inclusion & exclusion
 - Sampling method appropriate (generalizability)
 - Sample size adequate overall and in each group
 - Equality of groups
- Measurement and collection techniques
 - Un-validated or unreliable instruments
 - Data accuracy (objective and subjective)
 - Duration of intervention & follow-up
- Statistics
 - Appropriateness of test/assumption violations
 - Missing data/Outliers
- Limitations not addressed in article

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Results: *Purpose*

- Describe the findings statistically
 - Describe population
 - Express results of statistical tests
 - (p-values, confidence intervals, effect sizes)
 - Narrative highlights tables/figures
 - Validity/reliability statistics
- May visually present results
 - Tables
 - Graphs
 - Figures

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Results

TABLE 2. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	GROUP RECEIVING LOWER TIDAL VOLUMES (N=432)	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES (N=429)
Age (yr)	51±17	52±18
Female sex (%)	40	41
Race or ethnic group (%)		
White	75	71
Black	16	19
Hispanic	5	7
Other or unknown	4	3
APACHE III score†	81±28	84±28
PaO ₂ :FiO ₂	138±64	134±58‡
PaO ₂ :FiO ₂ ≤200 (%)	82	85
Tidal volume (ml)§	676±119	665±125
Minute ventilation (liters/min)	13.4±4.3¶	12.7±4.3
No. of nonpulmonary organ or system failures	1.8±1.1	1.8±1.0
Lung injury (%)		
Pneumonia	33	36
Sepsis	27	26
Aspiration	15	14
Trauma	13	9
Other causes	10	11
Multiple transfusions	2	3

*Plus-minus values are means ±SD. Because of rounding, not all percentages total 100. PaO₂ denotes partial pressure of arterial oxygen, and FiO₂ fraction of inspired oxygen.

†APACHE III denotes Acute Physiology, Age, and Chronic Health Evaluation. Scores can range from 0 to 299, with higher scores indicating more severe illness.³⁴

‡Data were missing for one patient.

§Data were available for 300 patients in the group treated with lower tidal volumes and for 290 patients in the group treated with traditional tidal volumes.

¶P=0.01.

||Organ and system failures were defined as described in the Methods section.

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Results

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- Mortality rate
 - Traditional=39.8%; lower=31.0%; $p=0.007$
- Vent-free days
 - Significantly higher in lower volume (Table 4)
- Organ/system failure free days
 - Significantly lower in lower volume; $p=0.006$
- Neuro-muscular blocking drugs days
 - No significant difference
- Interleukin-6 concentrations
 - Significantly lower in lower volume; $p<0.001$

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Results

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VOLUME 342

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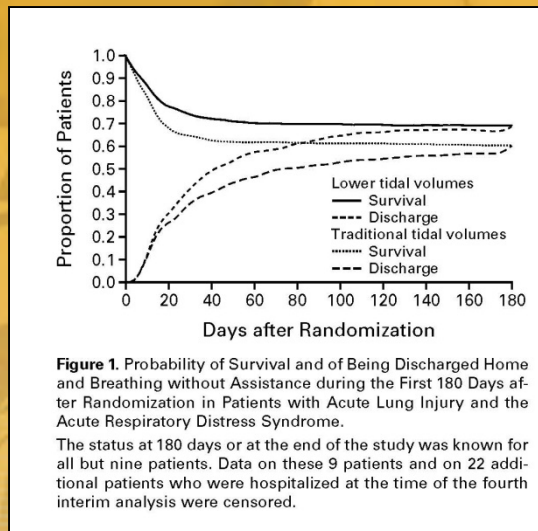
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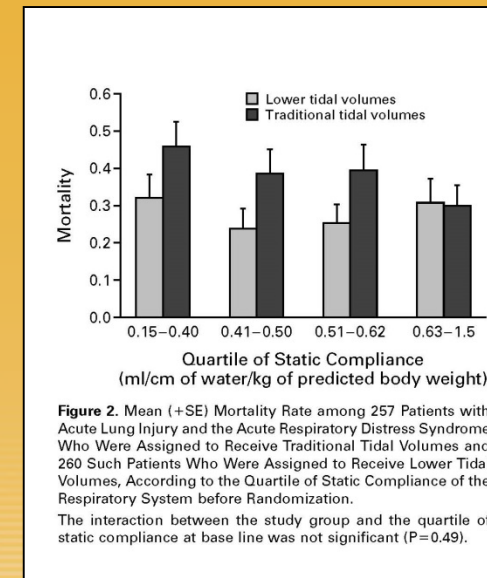
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Probability of Survival (Figure 1)



Quartile of Static Compliance (Figure 2)



Research



Results: *Critically Evaluate*

- Groups not comparable
 - Baseline (not adjusted when appropriate)
- Statistics
 - Inappropriate test(s)
 - Violation of assumptions
 - Data not corrected if appropriate
- Limitations of significance testing
 - Statistically significant vs. clinically important
- Does not make sense; *get statistical help*

Research



Discussion: *Purpose*

- Summarize purpose and results
- Describe the meaning of findings
- Compare/contrast results in terms of previous literature
- Identify limitations
 - Discuss reliability/validity of measurements
- Evaluate generalizability of results
- Make recommendations based on findings
- Connect to practice
- Suggest future research
- Draw appropriate conclusions

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Discussion

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- Recap primary results
 - Mortality was reduced by 22%
 - Vent-free days greater in lower tidal volume
 - Reductions in interleukins
- Consistent with previous literature
 - Experiments in animals and humans
- Explanation
 - Differences in tidal volumes
 - Previous studies not able to detect difference
 - Treatment of acidosis

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Discussion

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THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

- Further explanation
 - Acidosis as caused by excessive stretch
 - Increased positive end-expiration & reduced stretch could be beneficial
 - Barotrauma equal in both groups; consistent with previous literature
 - Similarity in vent-free days in survivors may be due to reduced mortality in lower tidal volume
- Conclusion
 - Treatment designed to prevent excessive stretch resulted in improvement in several important outcomes

Research



Discussion: *Critically Evaluate*

- Results discussed in terms of Intro citations
- Specific implication discussed
- Alternative interpretations of data not explored
- Causality not interpreted cautiously
- Under/overstating conclusions
- Limitations not discussed
- Distinction between speculation and data-based conclusions
- Generalizability

Research



Additional Considerations

- Citations
 - Current (2000, range of citations 1966 – 1999)
 - Seminal
- Organized, cohesive and readable
- Is the research likely to
 - help in decision making?
 - inspire additional research?
- Does the report extend the boundaries of our knowledge on a topic, especially our understanding of relevant theories?

Research



Thank You!

- Any questions

Research



References

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