

Pediatric Mechanical Ventilation: Applying Data from Adults to Kids

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Adult Mechanical Ventilation

- ◆ Numerous clinical studies (ARDS Network)
- ◆ Focus on ALI / ARDS
- ◆ Large, prospective, multicenter RCTs
 - low tidal volume ventilation
 - PEEP management
 - fluid management
 - corticosteroids

Pediatric Mechanical Ventilation

- ◆ 'Large', prospective RCTs
 - exogenous surfactant
 - prone positioning
- ◆ Otherwise, 'definitive' data lacking.
 - low tidal volume ventilation
 - PEEP management
 - fluid management
 - corticosteroids
 - etc., etc.

Pediatric Mechanical Ventilation



Why are pediatric data lacking?

- ◆ Pediatric ALI / ARDS
 - Data from the initial PALISI weaning study
 - 9 North American PICUs for 6 mos
 - 6,403 total PICU admissions
 - 1,096 (17.1%) required mechanical ventilation for > 24 hrs
 - 701 (64%) met exclusion criteria
 - Eligible: 395 (6.2% of total admissions)
 - Mortality = 1.6%

Randolph, AJRCCM, 2003.


Feasibility of Clinical Trials

- ◆ 6,403 total PICU admissions
- ◆ 1,096 pts ventilated > 24 hrs

	Enrolled pts (n=303)
Bronchiolitis	81
Pneumonia	48
ARDS	23
Pulm edema / effusion	8
PPHN	5
Chest trauma	4
Other	20

Randolph, AJRCCM, 2003.

Characteristics of Peds MV



CHEST

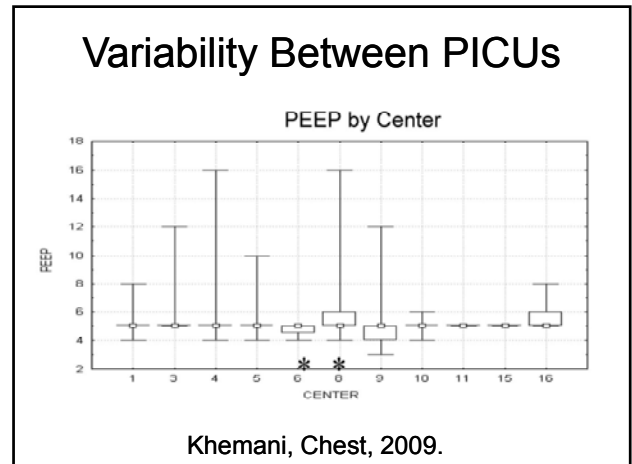
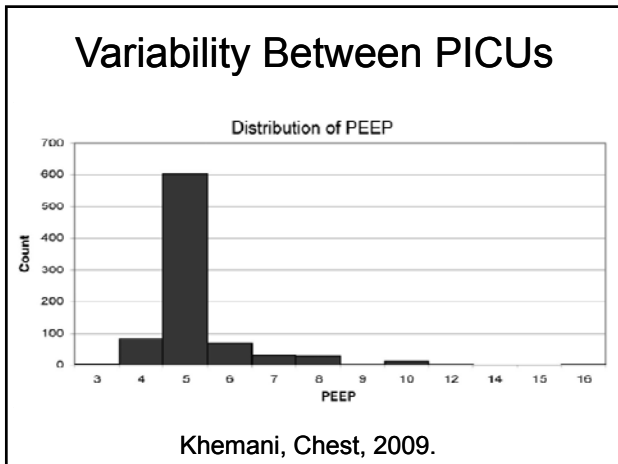
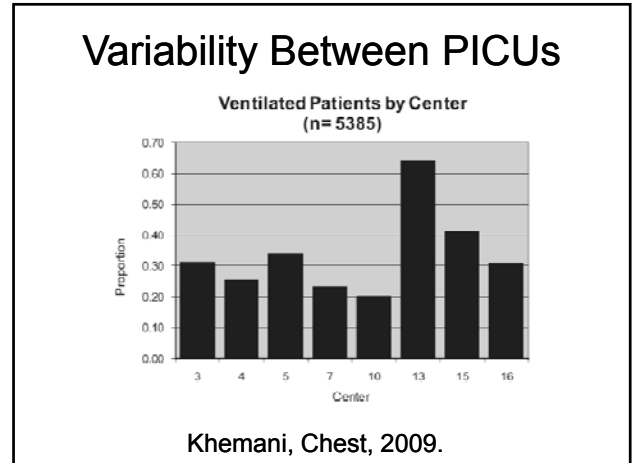
Original Research

CRITICAL CARE MEDICINE

Characteristics of Children Intubated and Mechanically Ventilated in 16 PICUs

Bobinder G. Khemani, MD, MScI; Barry P. Markowitz, MD, MPH; and Martha A. Q. Curley, PhD, RN

Khemani, Chest, 2009.




- ### Looking to the adult world for data....
- ◆ Acute lung injury / ARDS
 - ◆ Large, prospective, multicenter, RCTs
 - low tidal volume ventilation
 - PEEP management
 - fluid management
 - corticosteroids

Low Tidal Volume Ventilation

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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*

6 ml/kg for Pediatrics?

- ◆ ARDS Network low tidal volume study
 - definitive study
 - only intervention to conclusively reduce mortality for adult ALI / ARDS
- ◆ Currently, extrapolate data from adult ALI / ARDS or rely on clinical experience.

ARDS Network, New Engl J Med, 2000.

Study Details

VARIABLE	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	GROUP RECEIVING LOWER TIDAL VOLUMES
Ventilator mode	Volume assist-control	Volume assist-control
Initial tidal volume (ml/kg of predicted body weight)	12	6
Plateau pressure (cm of water)	≤50	≤30
Ventilator rate setting, needed to achieve a pH goal of 7.3 to 7.45 (breaths/min)	6-35	6-35
Ratio of the duration of inspiration to the duration of expiration	1:1-1:3	1:1-1:3
Oxygenation goal	PaO ₂ , 55-80 mm Hg, or SpO ₂ , 88-95%	PaO ₂ , 55-80 mm Hg, or SpO ₂ , 88-95%

ARDS Network, New Engl J Med, 2000.

Low Tidal Volume

VARIABLE	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	P VALUE
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15±11	12±11	0.006

ARDS Network, New Engl J Med, 2000.

Are we injuring lungs??

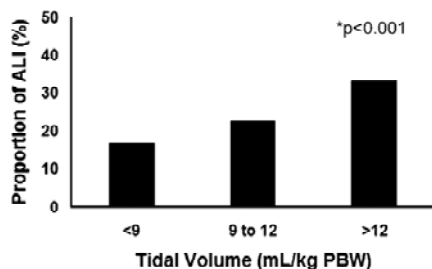
Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation*

Ognjen Gajic, MD; Saqib I. Dara, MD; Jose L. Mendez, MD; Adebola O. Adesanya, MD; Emir Festic, MD; Sean M. Caples, MD; Rimki Rana, MD; Jennifer L. St. Sauver, PhD; James F. Lymp, PhD; Bekelc Afessa, MD; Rolf D. Hubmayr, MD

Crit Care Med 2004 Vol. 32, No. 9

Normal Lungs to Start

↑ Vt → increased likelihood to develop ALI



Gajic, Crit Care Med, 2004.

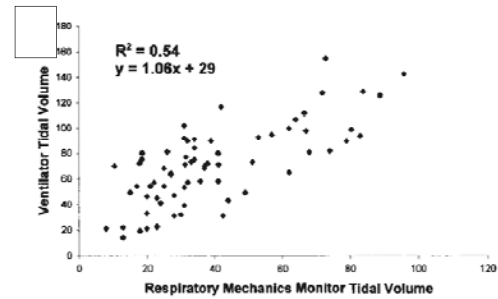
Low Tidal Volume Ventilation

- ◆ Low Vt ventilation
 - definitively reduces mortality in adult patients
 - protects against development of ALI
- ◆ Adverse effects have not been reported.
- ◆ Sedation requirements are not increased.
- ◆ Bottom line
 - Limiting alveolar distension saves lives.
 - Can we obtain pediatric data?
 - If so, would the results be different?

Low Tidal Volumes for Pediatrics

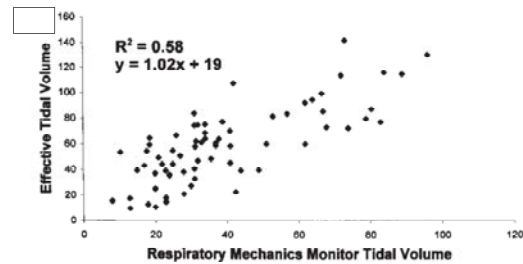
- ◆ Special populations
 - neonates, esp. premature infants
 - congenital heart disease
 - increased intracranial pressure
- ◆ Ideal body weight
 - on-line calculations for ≥ 1 yr of age
- ◆ Where should you measure tidal volume?

Tidal Volume Measurements in Peds



Cannon, AJRCCM, 2000.

Tidal Volume Measurements in Peds



Cannon, AJRCCM, 2000.

Low Tidal Volume Data in Pediatrics??

- ◆ Can we obtain low tidal volume data in infants and children with ALI / ARDS?
- ◆ Would it be ethical to conduct such a study?
- ◆ Study groups? 6 vs. 12? 4 vs. 8? 3 vs. 6?
- ◆ Equipoise?
- ◆ Age cohorts? (Infants, children, teens)
- ◆ Where (how) should Vt be measured?
- ◆ What about pts with normal lungs?

PEEP

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 22, 2004 VOL. 351 NO. 4

Higher versus Lower Positive End-Expiratory Pressures
in Patients with the Acute Respiratory Distress Syndrome

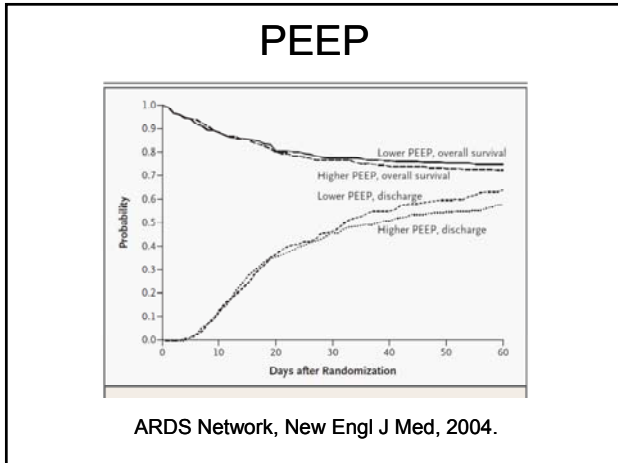
The National Heart, Lung, and Blood Institute ARDS Clinical Trials Network*

ALVEOLI (Assessment of Low tidal Volume and elevated End-exp. volume to Obviate Lung Injury)

Lower PEEP group													
FiO ₂	0.3	0.4	0.5	0.5	0.5	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18-24
Higher-PEEP group (before protocol change to use higher levels of PEEP)													
FiO ₂	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5-0.8	0.8	0.9	1.0		
PEEP	5	8	12	14	16	16	18	18	20	22	22-24		
Higher-PEEP group (after protocol changed to use higher levels of PEEP)													
FiO ₂	0.3	0.3	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0				
PEEP	12	14	14	16	18	20	22	22	22-24				

- ◆ 'Lower' PEEP → not 'Low' PEEP
- ◆ V_T 6 mL/kg PBW
- ◆ SpO₂, PaO₂, and compliance improved with ↑ PEEP
- ◆ Stopped at 549 pts for futility
- ◆ No safety concerns

ARDS Network, New Engl J Med, 2004.



PEEP

Table 4. Main Outcome Variables.*

Outcome	Lower-PEEP Group	Higher-PEEP Group	P Value
Death before discharge home (%)†			
Unadjusted	24.9	27.5	0.48
Adjusted for differences in baseline covariates	27.5	25.1	0.47
Breathing without assistance by day 28 (%)	72.8	72.3	0.89
No. of ventilator-free days from day 1 to day 28‡	14.5±10.4	13.8±10.6	0.50
No. of days not spent in intensive care unit from day 1 to day 28	12.2±10.4	12.3±10.3	0.83
Barotrauma (%)§	10	11	0.51
No. of days without failure of circulatory, coagulation, hepatic, and renal organs from day 1 to day 28	16±11	16±11	0.82

ARDS Network, New Engl J Med, 2004.

Ventilation Strategy Using Low Tidal Volumes, Recruitment Maneuvers, and High Positive End-Expiratory Pressure for Acute Lung Injury and Acute Respiratory Distress Syndrome

	Fraction of Inspired Oxygen (F _i O ₂)							
	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Control ARDS ranges, cm H ₂ O	5	5.5	6-7	7	8-14	11	14-18	18-24
Low open ventilation PEEP ranges, cm H ₂ O	5-10	10-14	14-20	20	20	20	20	20-24
Before protocol change	5-10	10-14	14-20	20	20	20-22	22	22-24
After protocol change	5-10	10-14	14-20	20	20	20-22	22	22-24

- ◆ Target V_T 6 mL/kg PBW
- ◆ CTL (n=508): P_{plat} ≤ 30 cm H₂O (VCV), 'lower' PEEP
- ◆ Intervention (n=475): P_{plat} ≤ 40 cm H₂O (PCV), recruitment maneuvers, initial PEEP 20 cm H₂O
- ◆ No significant difference in hospital mortality

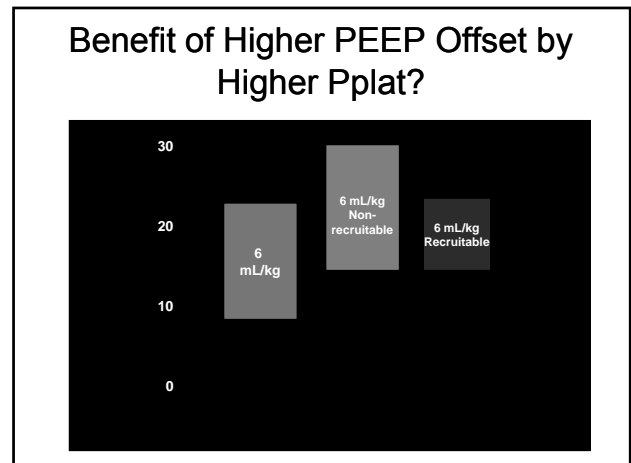
Meade, JAMA, 2008.

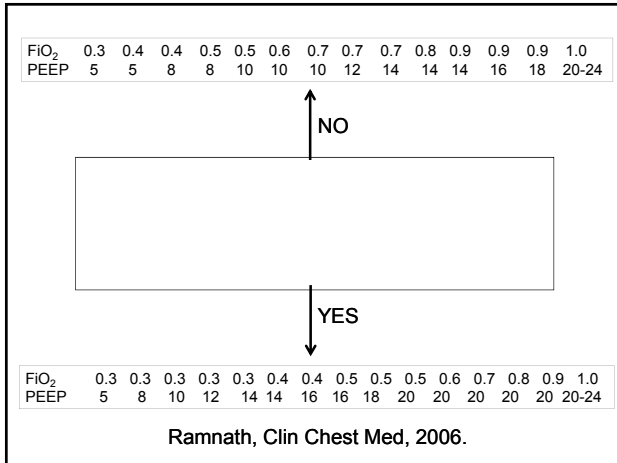
Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome

- ◆ Target V_T 6 mL/kg PBW
- ◆ CTL (n=382): low PEEP (5-9 cm H₂O) minimal distension strategy
- ◆ Intervention (n=385): PEEP set to achieve P_{plat} 28-30 cm H₂O (recruitment strategy); PEEP 16±3 cm H₂O on day 1
- ◆ No significant difference in mortality, but improved lung function, ↓ LOV, and ↓ organ failure

Mercat, JAMA, 2008.

- ### Why did these studies fail to show a mortality benefit?
- 1) Inadequate statistical power
 - 2) Higher PEEP does not help
 - 3) PEEP strategies were incorrect
 - 4) Harm from higher P_{plat} offsets benefit of PEEP
 - 5) Unknown



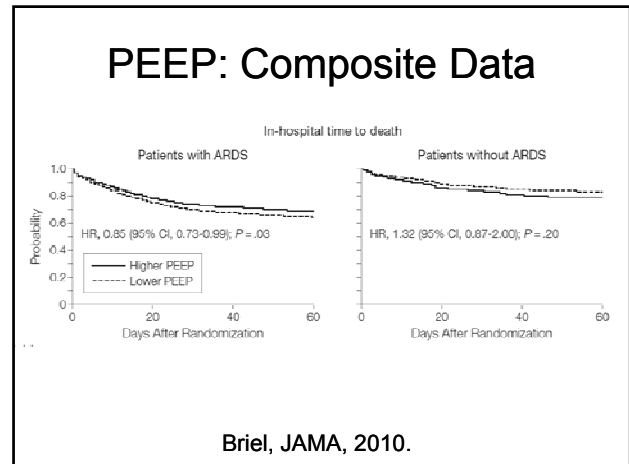
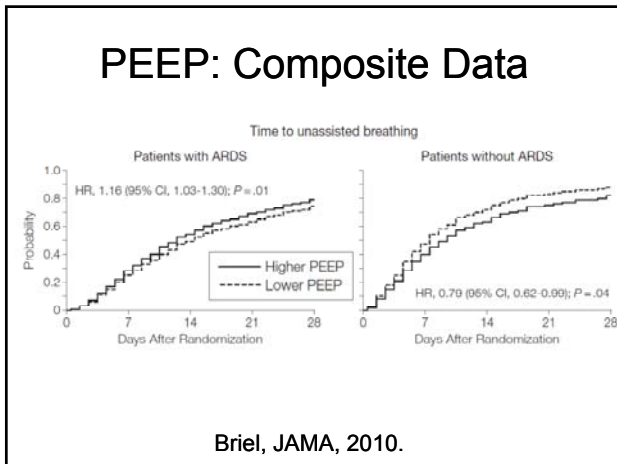


PEEP: Definitive Data?

Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome: Systematic Review and Meta-analysis

Matthias Briel; Maureen Meade; Alain Mercat; et al.
JAMA. 2010;303(9):865-873 (doi:10.1001/jama.2010.218)

Data Extraction Data from 2299 individual patients in 3 trials were analyzed using uniform outcome definitions. Prespecified effect modifiers were tested using multi-variable hierarchical regression, adjusting for important prognostic factors and clustering effects.



- ### PEEP for Pediatrics
- ◆ Can we obtain definitive data? Sample size?
 - ◆ Are the ARDS Network PEEP-FiO₂ tables too aggressive for neo-peds?
 - ◆ Age / weight cohorts?
 - ◆ Congenital heart disease?
 - ◆ Would 'PEEP phobia' inhibit a study?
 - ◆ Outcome measures?
 - ◆ Would this study be best performed after a peds low TV study?

FACTT

The NEW ENGLAND JOURNAL of MEDICINE

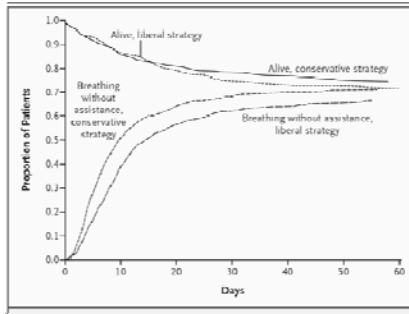
ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

ARDS Network, New Engl J Med, 2006.

FACTT



ARDS Network, New Engl J Med, 2006.

FACTT

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28 [†]	14.6±0.5	12.1±0.5	<0.001
ICU-free days [‡]			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001

ARDS Network, New Engl J Med, 2006.

Table 3. Main Outcome Variables.^a

Outcome	Conservative Strategy	Liberal Strategy	P Value
Organ-failure-free days^{†‡}			
Days 1 to 7			
Cardiovascular failure	3.9±0.1	4.2±0.1	0.04
CNS failure	3.4±0.2	2.9±0.2	0.02
Renal failure	5.5±0.1	5.6±0.1	0.45
Hepatic failure	5.7±0.1	5.5±0.1	0.12
Coagulation abnormalities	5.6±0.1	5.4±0.1	0.23
Days 1 to 28			
Cardiovascular failure	19.0±0.5	19.1±0.4	0.85
CNS failure	18.8±0.5	17.2±0.5	0.03
Renal failure	21.5±0.5	21.2±0.5	0.59
Hepatic failure	22.0±0.4	21.2±0.5	0.18
Coagulation abnormalities	22.0±0.4	21.5±0.4	0.37
Dialysis to day 60			
Patients (%)	10	14	0.06
Days	11.0±1.7	10.9±1.4	0.96

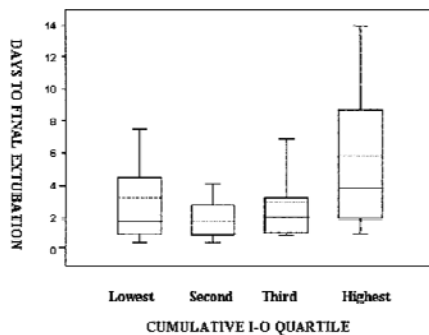
ARDS Network, New Engl J Med, 2006.

Feature Article—Continuing Medical Education Article

Cumulative fluid intake minus output is not associated with ventilator weaning duration or extubation outcomes in children*

Adrienne G. Randolph, MB, BS, MS MSc; Peter W. Forbes, MA; Rainer G. Gedeit, MD; John H. Arnold, MD; Randall G. Wetzel, MB, BS, MS; Peter M. Luckett, MD; Mary E. O'Neil, MPH; Shekhar T. Venkataraman, MD; Kathleen L. Meert, MD; Ira M. Cheifetz, MD, FCCM, FAAHC; Peter N. Cox, MChB; James H. Hanson, MD; for the Pediatric Acute Lung Injury & Sepsis Investigators (PALISI) Network

Pediatr Crit Care Med 2005 Vol. 6, No. 6



Randolph, Pediatr Crit Care Med, 2006.

Fluid Management for Pediatrics

- ◆ Do we under- or over-diuresis our pts?
- ◆ Control group?
- ◆ Target for fluid management? CVP?
- ◆ Equipoise?
- ◆ Could we even agree on a protocol?

Steroids

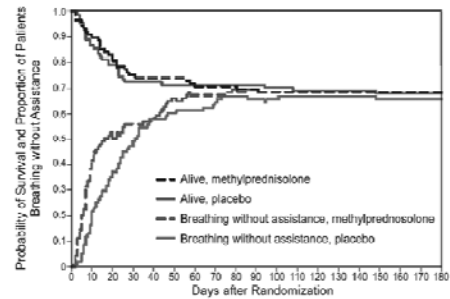
The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2006 VOL. 354 NO. 16

Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

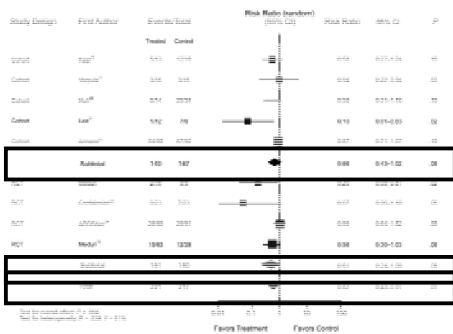
The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network^a

Steroids for 'Persistent' ARDS



ARDS Network, New Engl J Med, 2006.

Steroids



Tang, Crit Care Med, 2009.

Steroids for Pediatrics

- ◆ Steroids are commonly used in the peds world? But, what about for ALI / ARDS?
- ◆ If so, how much and when?
- ◆ Will this topic ever reach the top of the 'to study' list?

Pediatric Mechanical Ventilation

- ◆ Clearly need more neo-peds RCTs!
- ◆ Often need more data to determine efficacy than safety.
- ◆ If an approach is safe but unknown to alter outcome, is it reasonable to proceed?
- ◆ Uncontrolled variables: knowledge, experience, & support available in an individual ICU.

Looking to the Future....

- ◆ With coordinated efforts among multiple children's hospitals, more data are on the horizon....
 - exogenous surfactant
 - sedation management for ALI / ARDS
 - risks / benefits of transfusions
 - influenza (vaccine effectiveness, antivirals, immune response)
 - glucose management
- ◆ And, keep in mind....