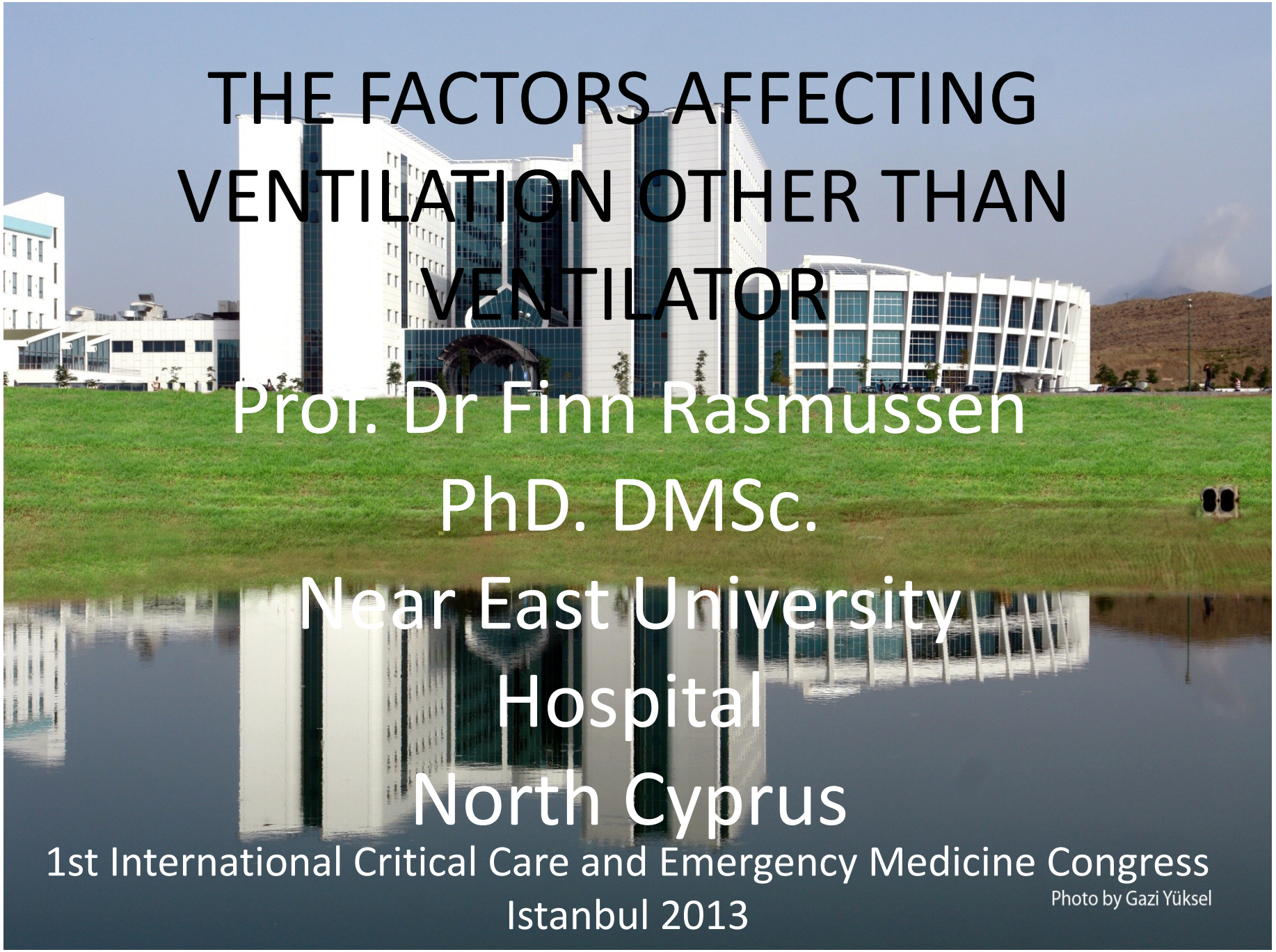

THE FACTORS AFFECTING VENTILATION OTHER THAN VENTILATOR

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1st International Critical Care and Emergency Medicine Congress
Istanbul 2013

Photo by Gazi Yüksel

Conflicts of Interest

- None

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation

- **The Ventilator Bundle**
  - **Benefits from position (semi recumbent position)**
  - **Sedation**
  - **ulcer disease prophylaxis, and deep venous thrombosis prophylaxis**
- **Physiotherapy/Rehabilitation**
- **Endotracheal Tubes** (Silver-Coated + continuous aspiration of the subglottis secretions)
- **Oral Rinse/ Selective Decontamination**
- **Prone position in ARDS**
- **Neuromuscular blockers**
- **Exogenous surfactant, iNO**
- **Extra-corporeal membrane oxygenation (ECMO)**

THE FACTORS AFFECTING VENTILATION OTHER THAN VENTILATOR

What to measure?

Important proxy marker for ventilation:

- Mortality
- Mechanical ventilation
  - Intubation rate
  - Duration of mechanical ventilation
- Duration of stay
  - ICU

Annals of Internal Medicine. 1986;10

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

- **The Ventilator Bundle**
  - **Benefits from position (semi recumbent position)**
  - Sedation
- Physiotherapy
- Oral Rinse/ Selective Decontamination
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- Prone position in ARDS
- Neuromuscular blockers
- Benefit from exogenous surfactant, iNO or iEPO
- Extra-corporeal membrane oxygenation (ECMO)

Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial

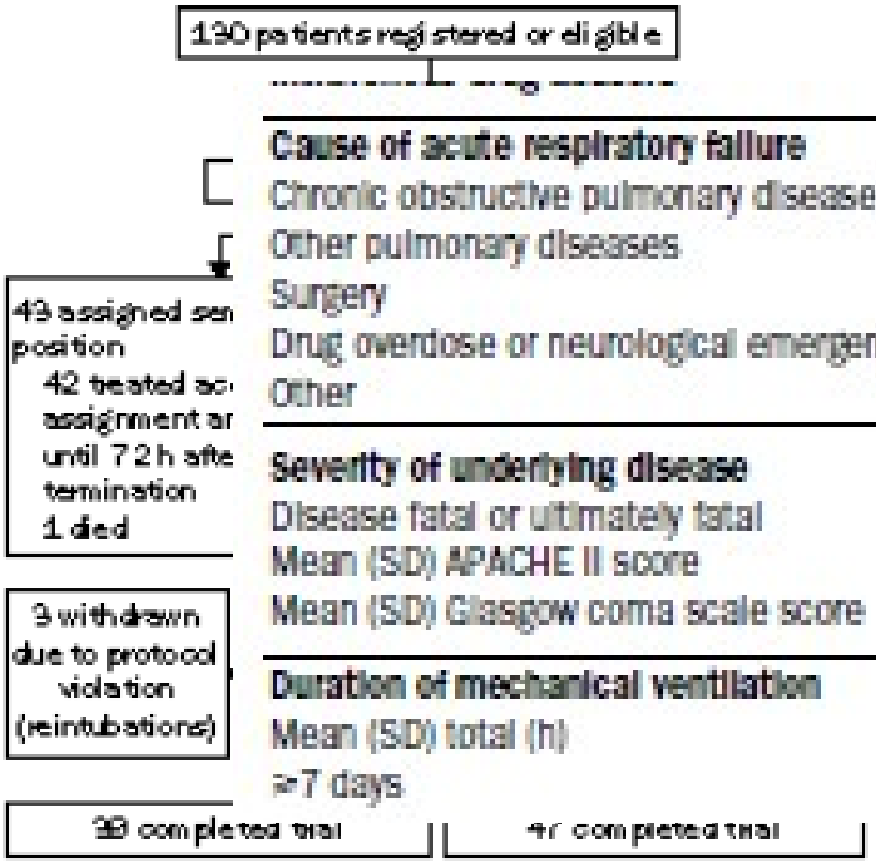
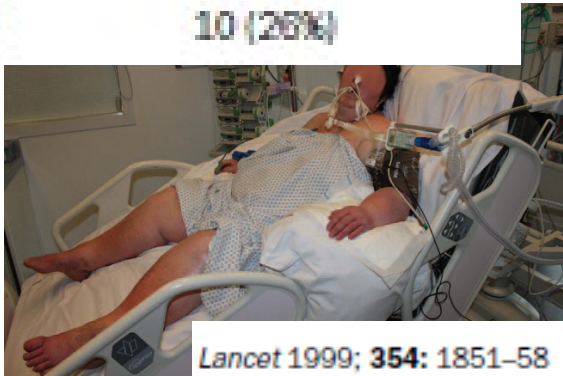


Figure 1: **Trial profile**

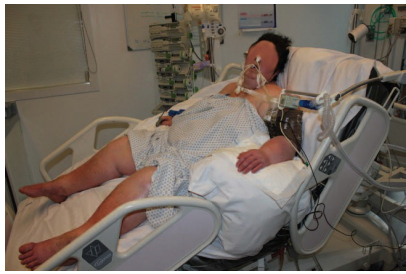
	Supine (n=47)	Semirecumbent (n=39)
Cause of acute respiratory failure		
Chronic obstructive pulmonary disease	16 (34%)	13 (33%)
Other pulmonary diseases	12 (26%)	8 (21%)
Surgery	6 (13%)	7 (18%)
Drug overdose or neurological emergency	3 (6%)	5 (13%)
Other	10 (21%)	6 (15%)
Severity of underlying disease		
Disease fatal or ultimately fatal	44 (94%)	31 (80%)
Mean (SD) APACHE II score	23·8 (6·1)	21·3 (6·0)
Mean (SD) Glasgow coma scale score	9·4 (4·3)	10·3 (4·2)
Duration of mechanical ventilation		
Mean (SD) total (h)	171 (167)	145 (149)
≥7 days	18 (38%)	10 (26%)



Patients were randomly allocated to either semirecumbent (45°) or supine body positon (0°)

Lancet 1999; **354:** 1851–58

Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial



The incidence rate of clinically suspected pneumonia:

Semi recumbent group 10.9 per 1000 ventilator days

Supine body position 41.2 per 1000 ventilator days

p=0.003

The incidence rate of microbiologically confirmed pneumonia:

Semi recumbent group 7.3 per 1000 ventilator days

Supine body position 28.4 per 1000 ventilato

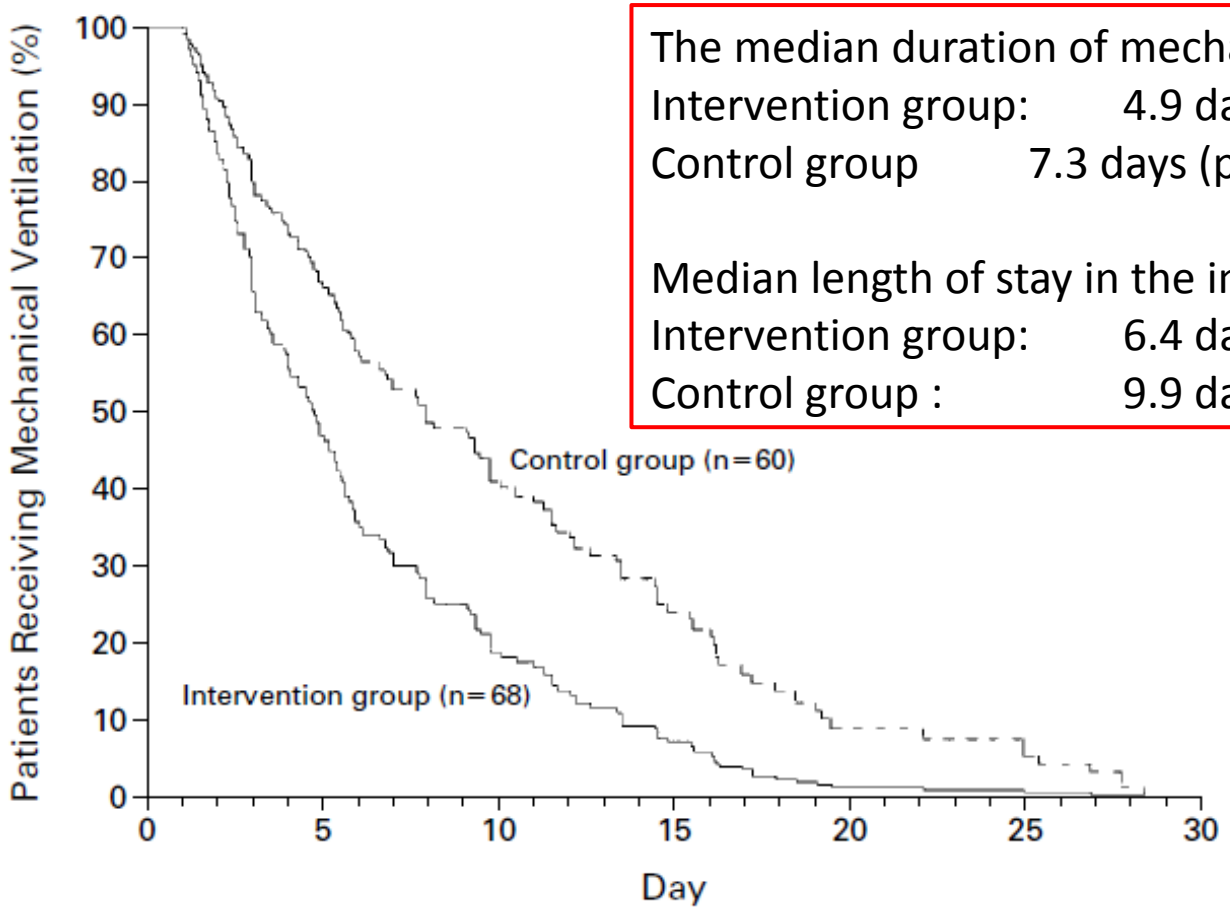
Lancet 1999; **354:** 1851–58

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

- The Ventilator Bundle
  - Benefits from position (semi recumbent position)
  - **Sedation**
- Physiotherapy/Rehabilitation
- Oral Rinse/ Selective Decontamination
- Endotracheal Tubes (Silver-Coated + continuous aspiration of the subglottis secretions)
- Prone position in ARDS
- Neuromuscular blockers
- Exogenous surfactant, iNO or iEPO
- Extra-corporeal membrane oxygenation (ECMO)

DAILY INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION



The median duration of mechanical ventilation:
Intervention group: 4.9 days
Control group 7.3 days (p=0.004),

Median length of stay in the intensive care:
Intervention group: 6.4 days
Control group : 9.9 days (p=0.02)

Figure 1. Kaplan–Meier Analysis of the Duration of Mechanical Ventilation, According to Study Group. After adjustment for base-line variables (age, sex, weight, APACHE II score, and type of respiratory failure), mechanical ventilation was discontinued earlier in the intervention group than in the control group (relative risk of extubation, 1.9; 95 percent confidence interval, 1.3 to 2.7; P<0.001).

(N Engl J Med 2000;342:1471-7.)

Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

	Intervention group (n=167)	Control group (n=168)
Age (years)	60 (48 to 71)	64 (51 to 75)
Sex (female)	77 (46%)	83 (49%)
APACHE II score	26 (21 to 33)	26·5 (21 to 31)
SOFA score	9 (6 to 11)	8 (6 to 11·5)
Diagnosis on admission to intensive care		
Sepsis/acute respiratory distress syndrome	79 (47%)	87 (52%)
Myocardial infarction/congestive heart failure	22 (13%)	29 (17%)
Chronic obstructive pulmonary disease/asthma	17 (10%)	12 (7%)
Altered mental status	18 (11%)	12 (7%)
Hepatic or renal failure	9 (5%)	5 (3%)
Malignancy	3 (2%)	2 (1%)
Alcohol withdrawal	1 (1%)	1 (1%)
Other*	18 (11%)	20 (12%)
RASS on first study day	−4 (−5 to −2)	−4 (−5 to −2)
Sedation before enrolment		
Benzodiazepines (mg)†	8 (4 to 34)	10 (2 to 41)
Opiates (μg)‡	815 (184 to 4380)	850 (142 to 4685)
Propofol (mg)	5102 (2340 to 9720)	3248 (1455 to 7420)
Time from admission to enrolment (days)	2·2 (1·1 to 3·9)	2·2 (1·1 to 3·9)

Data are n (%) or median (IQR). APACHE II=acute physiology and chronic health evaluation II. RASS=Richmond agitation-sedation scale. SAT=spontaneous awakening trial. SBT=spontaneous breathing trial. SOFA=sequential organ failure assessment. *Including gastrointestinal bleeding, metabolic disarray, haemoptysis, pulmonary embolism, and status epilepticus. †Expressed in lorazepam equivalents.[34] ‡Expressed in fentanyl equivalents.[34]

Table 1: **Baseline characteristics**

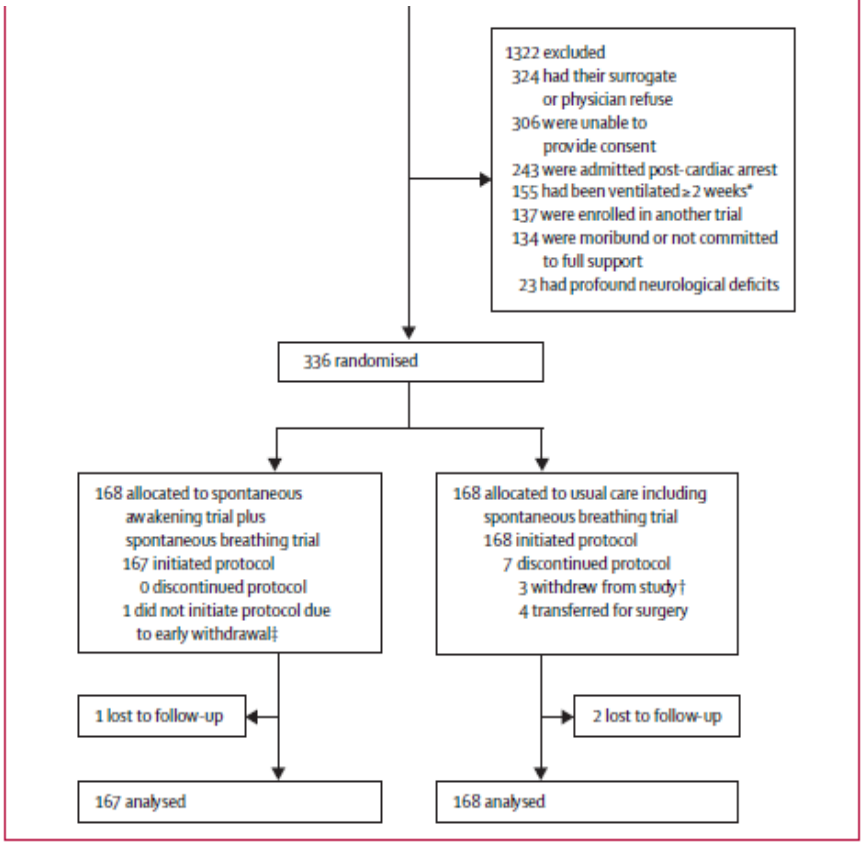


Figure 2: **Trial profile**

The primary endpoint was time breathing without assistance

Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

	Intervention group (n=167)	Control group (n=168)	p value
Ventilator-free days*			
Mean	14·7 (0·9)	11·6 (0·9)	0·02
Median	20·0 (0 to 26·0)	8·1 (0 to 24·3)	
Time to discharge (days)			
From intensive care	9·1 (5·1 to 17·8)	12·9 (6·0 to 24·2)	0·01
From hospital	14·9 (8·9 to 26·8)	19·2 (10·3 to NA)†	0·04
28-day mortality	47 (28%)	58 (35%)	0·21
1-year mortality	74 (44%)	97 (58%)	0·01
Duration of brain dysfunction (days)			
Coma	2 (0 to 4)	3 (1 to 7)	0·002
Delirium	2 (0 to 5)	2 (0 to 6)	0·50
RASS at first successful SBT	−1 (−3 to 0)	−2·5 (−4 to 0)	0·0001
Complications			
Any self-extubation	16 (10%)	6 (4%)	0·03
Self-extubation requiring reintubation‡	5 (3%)	3 (2%)	0·47
Reintubation‡	23 (14%)	21 (13%)	0·73
Tracheostomy	21 (13%)	34 (20%)	0·06

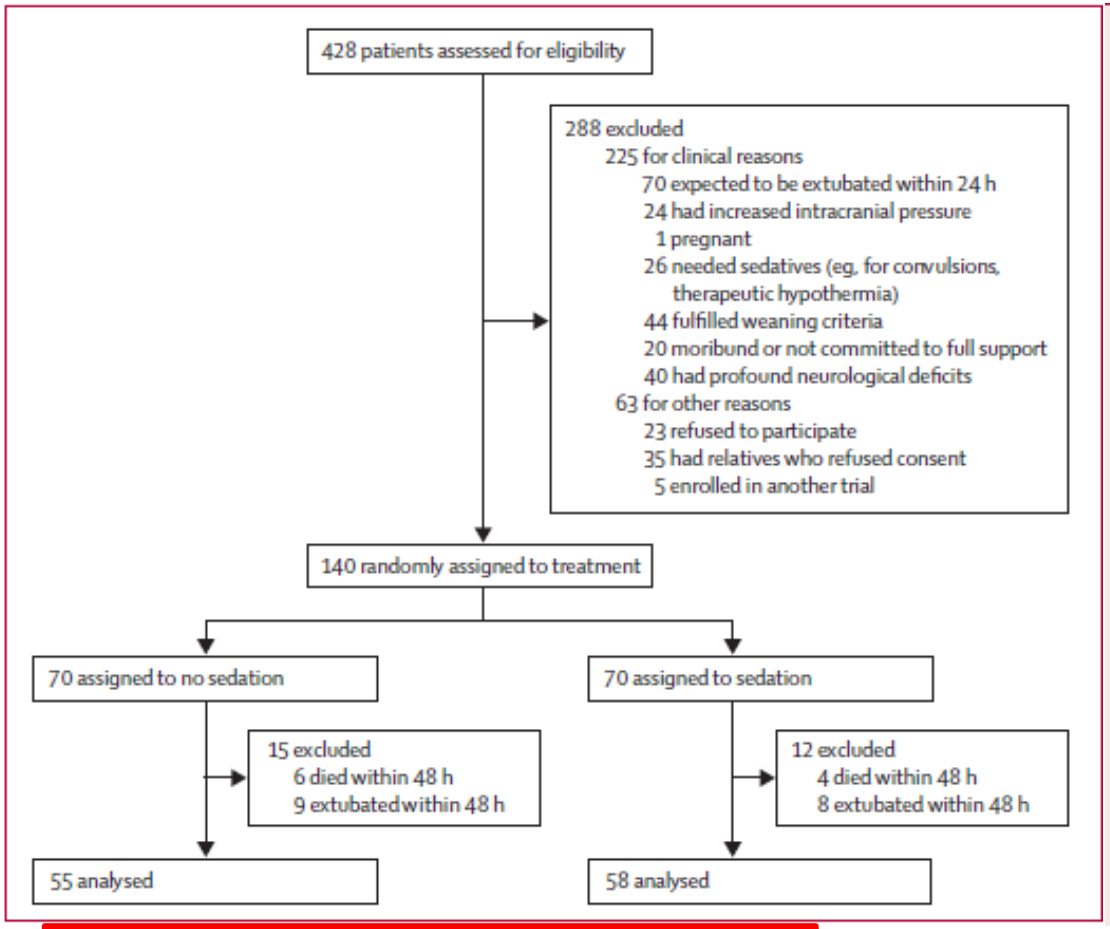
Data are mean (SD), n (%), or median (IQR). RASS=Richmond agitation-sedation scale. SAT=spontaneous awakening trial. SBT=spontaneous breathing trial. *Ventilator-free days from study day 1 to 28. †Greater than 25% of patients in the SBT group remained in the hospital at study day 28. ‡Reintubation within 48 hours of extubation.

Table 3: **Main outcomes**

For every seven patients treated with the intervention, one life was saved (number needed to treat was 7.4 (4.2-35.5).

A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial

Thomas Strøm, Torben Martinussen, Palle Toft



	No sedation (n=55)	Sedation (n=58)
Age (years)	67 (54–74)	65 (54–74)
Women	13 (24%)	24 (41%)
Weight (kg)	80·0 (74·0–92·0)	78·5 (70·0–91·0)
APACHE II	26 (19–30)	26 (22–31)
SAPS II	46 (36–56)	50 (43–63)
SOFA (at day 1)	7·5 (5·0–11·0)	9·0 (5·5–11·0)
Diagnosis at admission to intensive care unit		
Respiratory disorder*	26 (47%)	27 (47%)
Sepsis	15 (27%)	19 (33%)
Pancreatitis	2 (4%)	3 (5%)
Peritonitis	0	1 (2%)
Gastro-intestinal bleeding	5 (9%)	0
Liver and biliary disease	2 (4%)	0
Trauma	2 (4%)	3 (5%)
Other	3 (5%)	5 (9%)

Data are in number (%) or median (IQR). APACHE II=acute physiology and chronic health evaluation. SAPS II=simplified acute physiology score. SOFA=sequential organ-failure assessment. *Pneumonia, chronic obstructive pulmonary disease, and asthma.

Table 1: **Baseline characteristics on admission to the intensive care unit**

The primary outcome:
Number of days without mechanical ventilation in a 28-day period

A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial

Thomas Strøm, Torben Martinussen, Palle Toft

Mortality was increased in the group receiving sedation, but the difference compared with the group receiving no sedation did not reach significance. The occurrence of agitated delirium was increased in the group receiving no sedation.

study is limited by being single centre and unblinded, which holds a risk of bias.

The generalisability of results is limited by the fact that we had a standard nurse to patient ratio of 1:1, which is not possible in many intensive care units, and we used an extra person to calm patients, although this person was seldom needed and was used for very short periods.

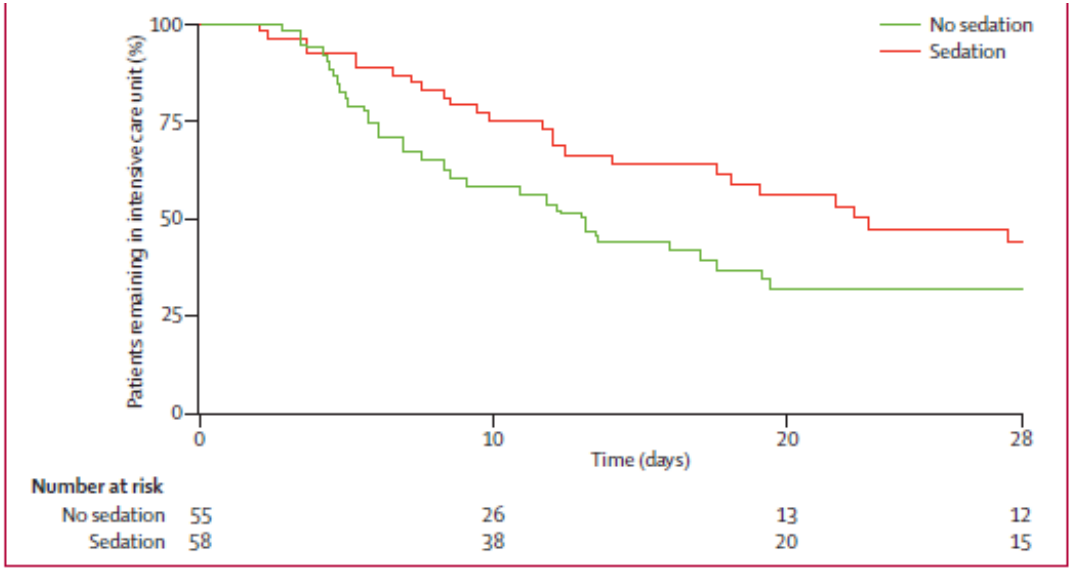


Figure 2: Kaplan-Meier plot of length of stay in the intensive care unit and number at risk from admission to 28 days

Days without ventilation:

Intervention: 13.8 days

Interrupted sedation : 9.6 days (p=0.01)

Further, 18% of the intervention group did not tolerate the no sedation strategy.

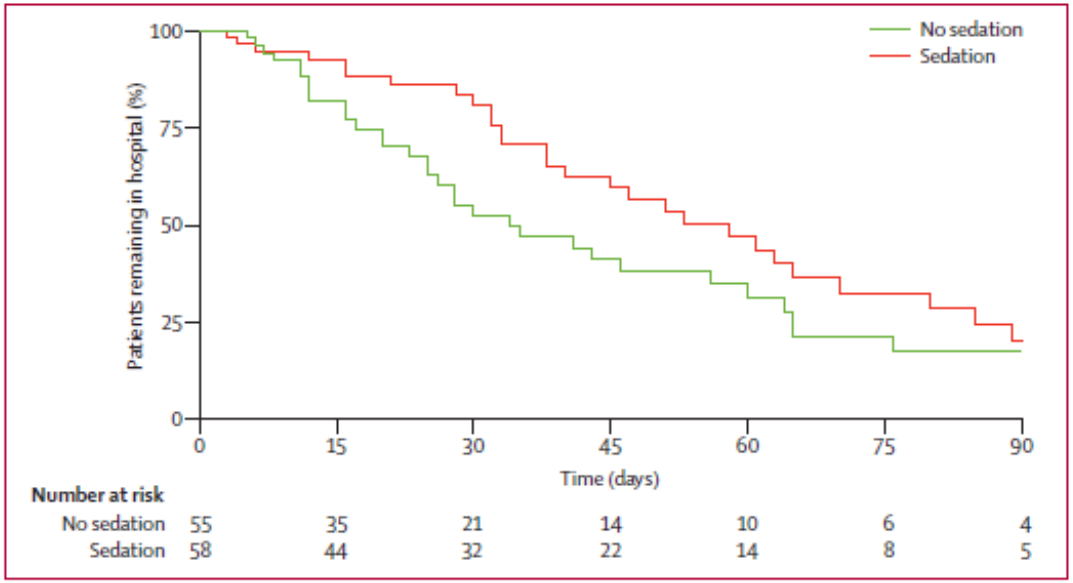


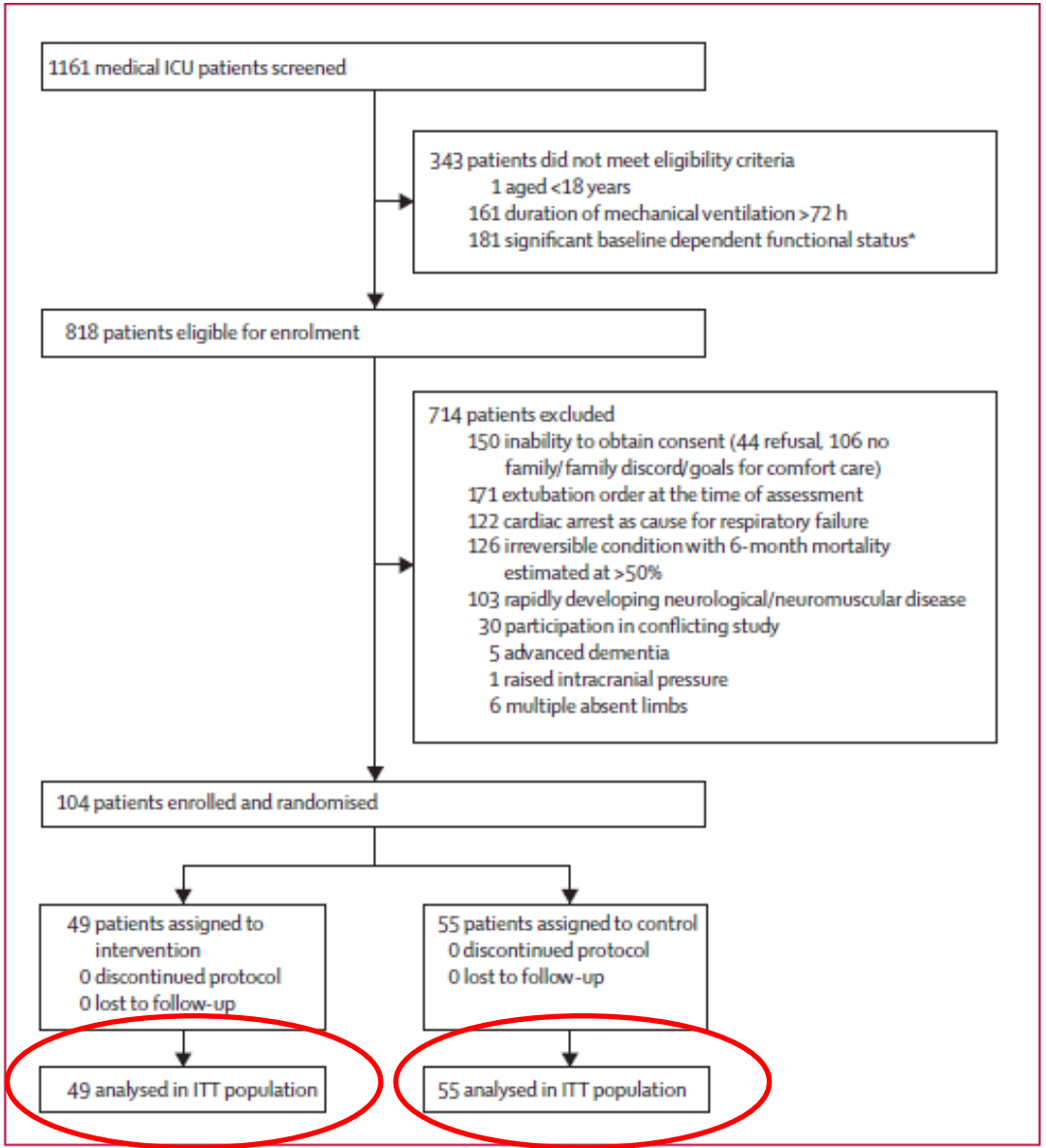
Figure 3: Kaplan-Meier plot of length of stay in hospital and number at risk from admission to 90 days

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

- The Ventilator Bundle
  - Benefits from position (semi recumbent position)
  - Sedation
  - ulcer disease prophylaxis, and deep venous thrombosis prophylaxis
  - More ?
- **Physiotherapy /Rehabilitation**
- Oral Rinse/ Selective Decontamination
- Endotracheal Tubes (Silver-Coated + continuous aspiration of the subglottis secretions)
- Prone position in ARDS
- Neuromuscular blockers
- Benefit from exogenous surfactant, iNO or iEPO

Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial



The primary endpoint:

Number of patients returning to independent functional status at hospital discharge

(was defined as the ability to perform six activities of daily living and the ability to walk independently.)

Secondary endpoints:

Ventilator-free days during the first 28 days of hospital stay.

Duration of delirium

Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial

	Intervention (n=49)	Control (n=55)	p value
Return to independent functional status at hospital discharge	29 (59%)	19 (35%)	0·02
ICU delirium (days)	2·0 (0·0–6·0)	4·0 (2·0–7·0)	0·03
Time in ICU with delirium (%)	33% (0–58)	57% (33–69)	0·02
Hospital delirium (days)	2·0 (0·0–6·0)	4·0 (2·0–8·0)	0·02
Hospital days with delirium (%)	28% (26)	41% (27)	0·01
Barthel Index score at hospital discharge	75 (7·5–95)	55 (0–85)	0·05
ICU-acquired paresis at hospital discharge	15 (31%)	27 (49%)	0·09
Ventilator-free days*	23·5 (7·4–25·6)	21·1 (0·0–23·8)	0·05
Duration of mechanical ventilation (days)	3·4 (2·3–7·3)	6·1 (4·0–9·6)	0·02
Duration of mechanical ventilation, survivors (days)	3·7 (2·3–7·7)	5·6 (3·4–8·4)	0·19
Duration of mechanical ventilation, non-survivors (days)	2·5 (2·4–5·5)	9·5 (5·9–14·1)	0·04
Length of stay in ICU (days)	5·9 (4·5–13·2)	7·9 (6·1–12·9)	0·08
Length of stay in hospital (days)	13·5 (8·0–23·1)	12·9 (8·9–19·8)	0·93
Hospital mortality	9 (18%)	14 (25%)	0·53

Data are n (%), median (IQR), or mean (SD). ICU=intensive care unit. *Ventilator-free days from study day 1 to day 28. Barthel Index scale 0–100, APACHE II scale 0–71.

Table 3: Main outcomes according to study group

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

- The Ventilator Bundle
  - Benefits from position (semi recumbent position)
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- Endotracheal Tubes (Silver-Coated + continuous aspiration of the subglottis secretions)
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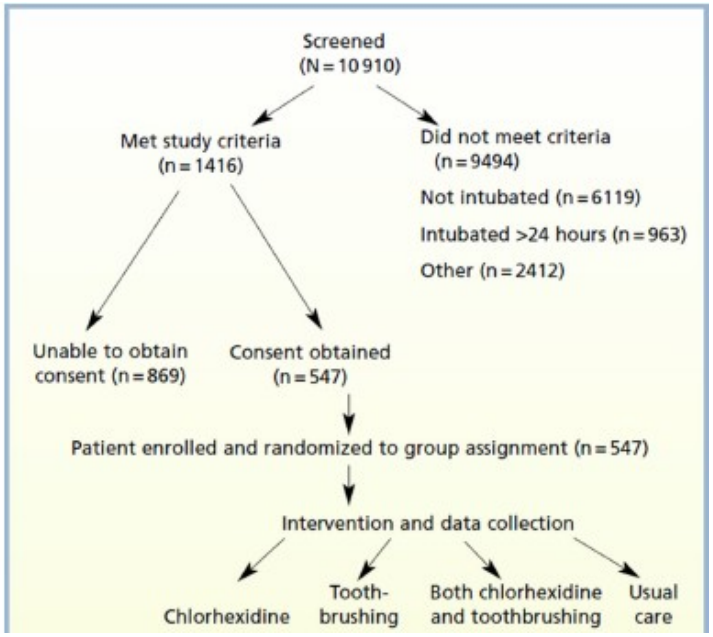
- Benefit from exogenous surfactant, iNO or iEPO

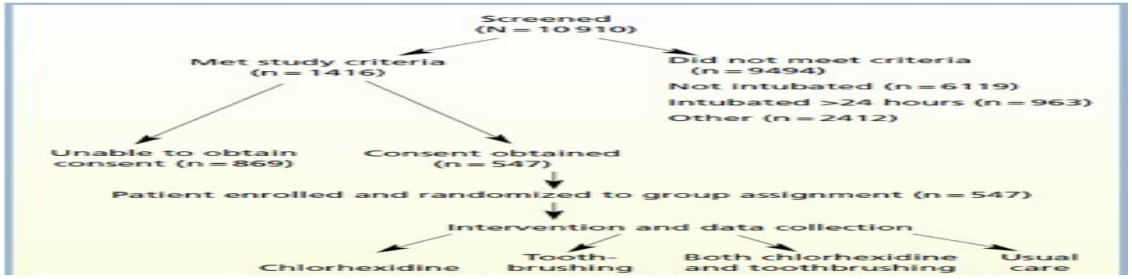
Am J Crit Care. 2009 September ; 18(5): 428–438. doi:10.4037/ajcc2009792.

CHLORHEXIDINE, TOOTHBRUSHING, AND PREVENTING VENTILATOR-ASSOCIATED PNEUMONIA IN CRITICALLY ILL ADULTS



Primary end points:

1. Incidence of ventilator-associated pneumonia (VAP)



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CHLORHEXIDINE, TOOTHBRUSHING, AND PREVENTING VENTILATOR-ASSOCIATED PNEUMONIA IN CRITICALLY ILL ADULTS

Comparison of baseline and day 3 outcomes by treatment

Outcomes	All patients (n = 192) Day 1	Day 3	*pa*	Patients without pneumonia at baseline (n = 87) Day 1	Day 3	*pb*
Clinical Pulmonary Infection Score, mean (SD)						
Chlorhexidine			.29			.02[c]
Yes	5.36 (2.17)	5.26 (2.44)		3.56 (1.29)	4.36 (2.11)	
No	5.70 (2.35)	5.78 (2.20)		3.36 (1.16)	5.36 (2.08)	
Toothbrushing			.95			.30
Yes	5.66 (2.38)	5.58 (2.34)		3.49 (1.30)	5.02 (2.28)	
No	5.41 (2.16)	5.48 (2.33)		3.43 (1.17)	4.66 (2.01)	
Pneumonia, %						
Chlorhexidine			.13			.006[c]
Yes	51.1	41.3		—[d]	24	
No	58.0	55.0		—	52	
Toothbrushing			.86			.54
Yes	55.7	49.5		—	40	
No	53.7	47.4		—	36	

Conclusions—Chlorhexidine, but not toothbrushing, reduced early ventilator-associated pneumonia in patients without pneumonia at baseline.

Am J Crit Care. 2009 September ; 18(5): 428–438. doi:10.4037/ajcc2009792.

CHLORHEXIDINE, TOOTHBRUSHING, AND PREVENTING VENTILATOR-ASSOCIATED PNEUMONIA IN CRITICALLY ILL ADULTS

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To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

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  - More ?
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- Prone position in ARDS
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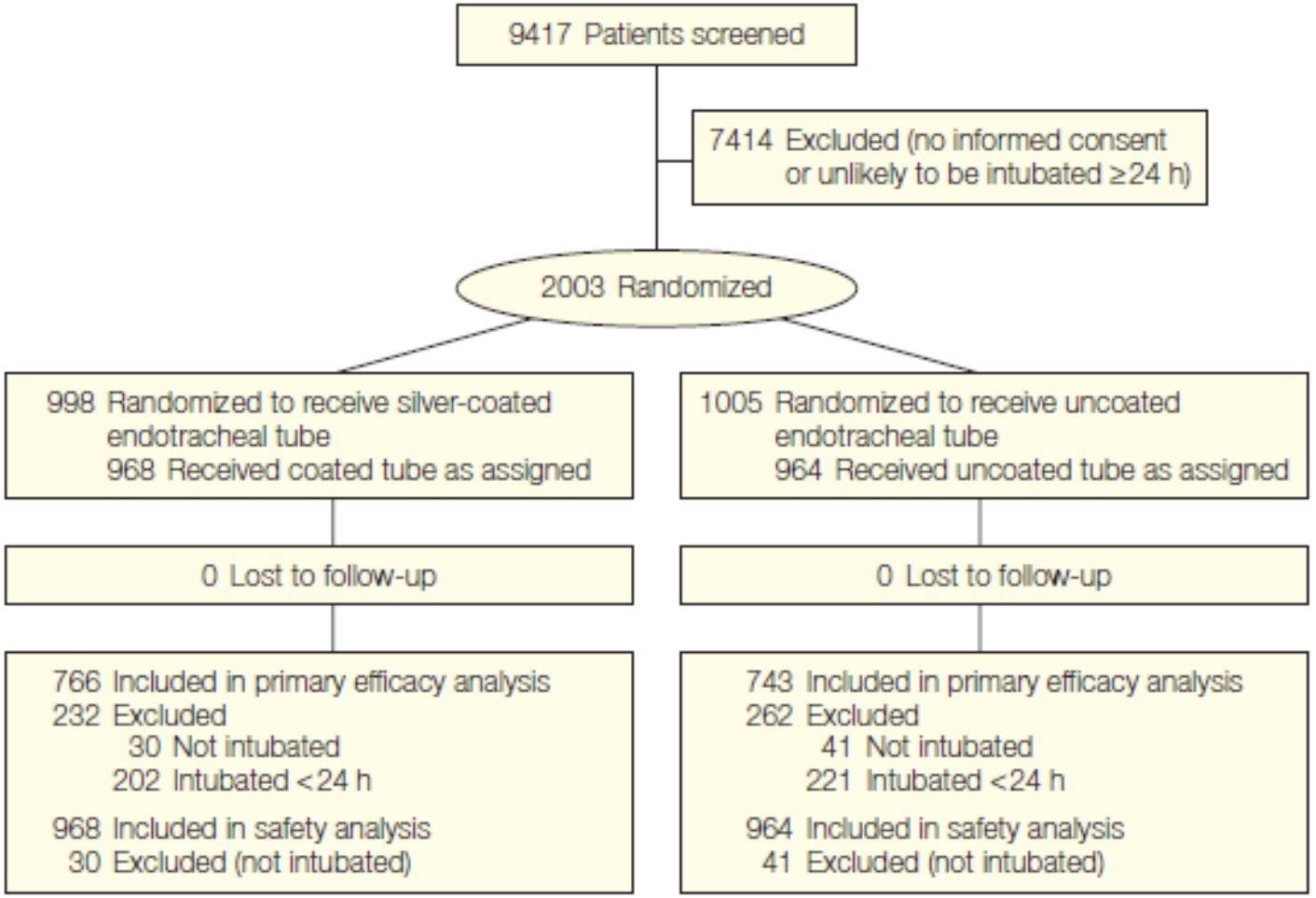
Silver-Coated Endotracheal Tubes and Incidence of Ventilator-Associated Pneumonia

The NASCENT Randomized Trial



JAMA. 2008;300(7):805-813

Silver-Coated Endotracheal Tubes and Incidence of Ventilator-Associated Pneumonia

The NASCENT Randomized Trial

Table 2. Incidence of Microbiologically Confirmed Ventilator-Associated Pneumonia (VAP)[a]

	Evaluable Patients With VAP, No./Total (%) [95% CI]			
	Silver-Coated Tube	Uncoated Tube	RR Reduction, % (95% CI)	*P* Value
VAP at any time				
Intubated ≥24 h	37/766 (4.8) [3.4-6.6]	56/743 (7.5) [5.7-9.7]	35.9 (3.6-69.0)	.03
All intubated	37/968 (3.8) [2.7-5.2]	56/964 (5.8) [4.4-7.5]	34.2 (1.2-67.9)	.04
VAP within 10 d of intubation				
Intubated ≥24 h	27/766 (3.5) [2.3-5.1]	50/743 (6.7) [5.0-8.8]	47.6 (14.6-81.9)	.005
All intubated	27/968 (2.8) (1.9-4.0)	50/964 (5.2) (3.9-6.8)	46.2 (12.6-81.1)	.007

JAMA. 2008;300(7):805-813

Scope of the talk

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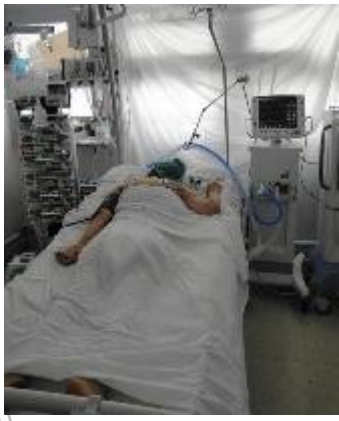
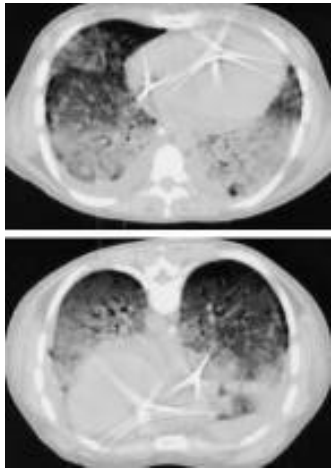




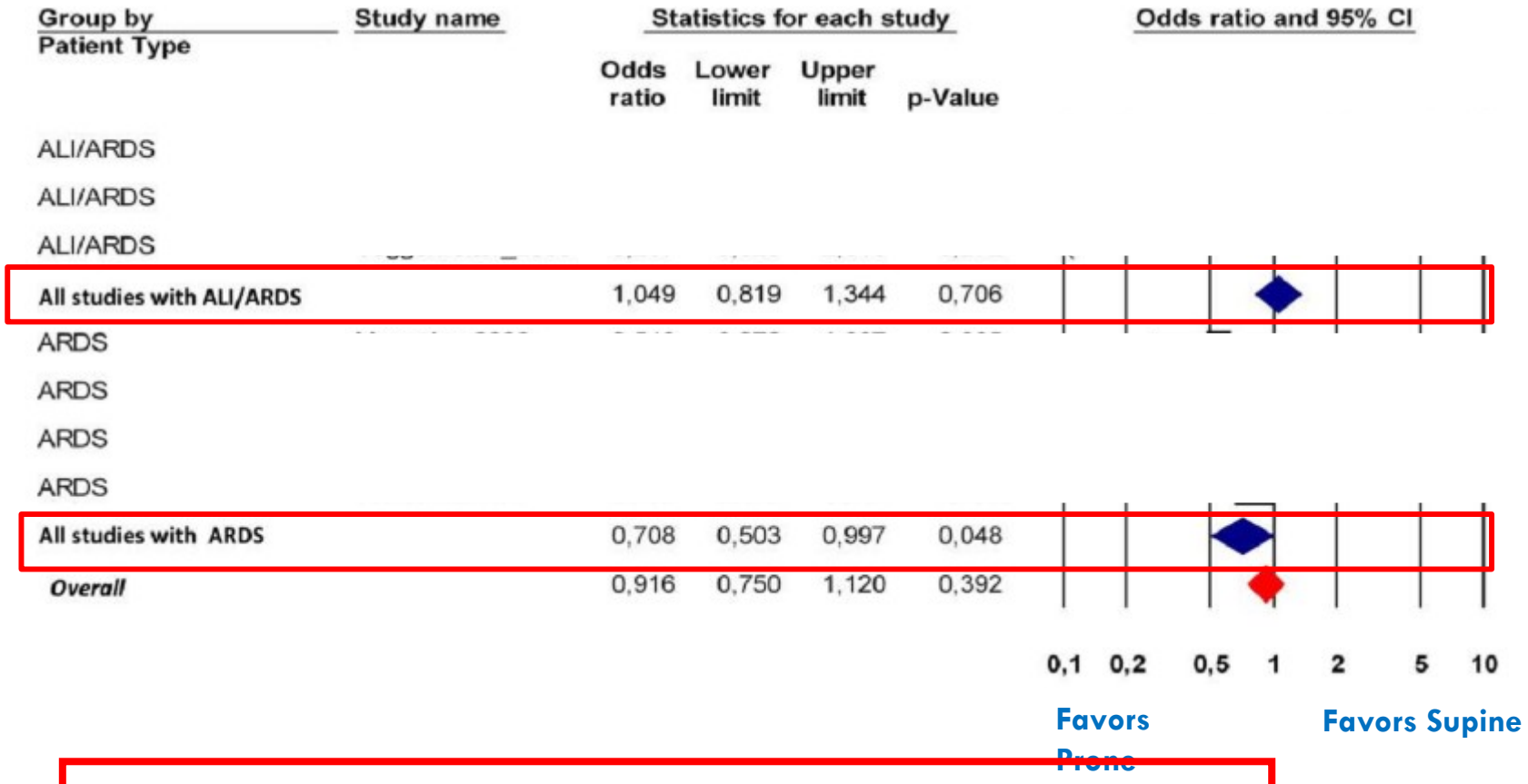
Abroug et al. Critical Care 2011, 15:R6
http://ccforum.com/content/15/1/R6

CRITICAL CARE

RESEARCH Open Access

An updated study-level meta-analysis of randomised controlled trials on proning in ARDS and acute lung injury

Fekri Abroug[1*], Lamia Ouanes-Besbes[1], Fahmi Dachraoui[1], Islem Ouanes[1], Laurent Brochard[2,3,4]



Long duration of ventilation in prone position seem to reduces ICU mortality when only ARDS patients are considered

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D., Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D., Christian Bengler, M.D., Jack Richecoeur, M.D., Marc Gainnier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaele Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*

Table 2. Ventilator Settings, Respiratory-System Mechanics, and Results of Arterial Blood Gas Measurements at the Time of Inclusion in the Study.*

Variable	Supine Group (N=229)	Prone Group (N=237)
Tidal volume (ml)	381±66	384±63
Tidal volume (ml per kg of PBW)	6.1±0.6	6.1±0.6
Respiratory frequency (breaths per min)	27±5	27±5
PEEP (cm of water)	10±4	10±3
F_{IO_2}	0.79±0.16	0.79±0.16
$Pplat_{RS}$ (cm of water)	23±5	24±5
Cst_{RS} (ml per cm of water)	35±15	36±23
Pao_2 (mm Hg)	80±18	80±19
Pao_2:F_{IO_2} (mm Hg)	100±20	100±30
$Paco_2$ (mm Hg)	52±32	50±14
Arterial pH	7.30±0.10	7.30±0.10
Plasma bicarbonate (mmol per liter)†	25±5	25±5

Mul

prospective,

N Engl J Med. 2013 Jun 6;368(23):2159-68.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prone Positioning in Severe Acute Respiratory Distress Syndrome

Jean-Chris
Thierry
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Rapha

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M.D.,
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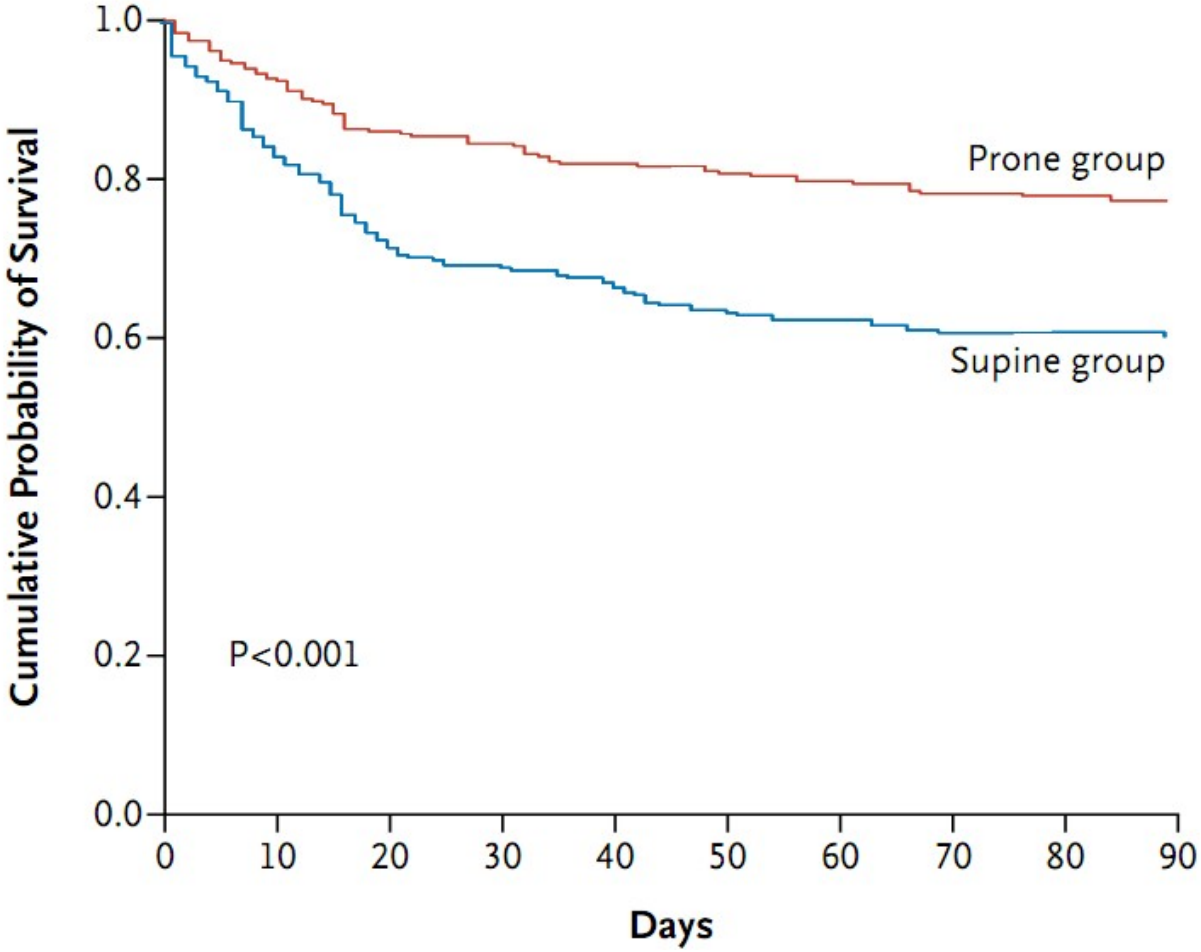


In patients with severe ARDS:
Early application of prolonged prone-positioning sessions significantly decreased 28-day and 90-day mortality.

N Engl J Med. 2013 Jun 6;368(23):2159-68.

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

- The Ventilator Bundle
  - Benefits from position (semi recumbent position)
  - Sedation
  - ulcer disease prophylaxis, and deep venous thrombosis prophylaxis
  - More ?
- Physiotherapy
- Endotracheal Tubes (Silver-Coated + continuous aspiration of the subglottis secretions)
- Oral Rinse
- Prone position in ARDS
- **Neuromuscular blockers**
- Benefit from exogenous surfactant, iNO

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 SEPTEMBER 16, 2010 VOL. 363 NO. 12

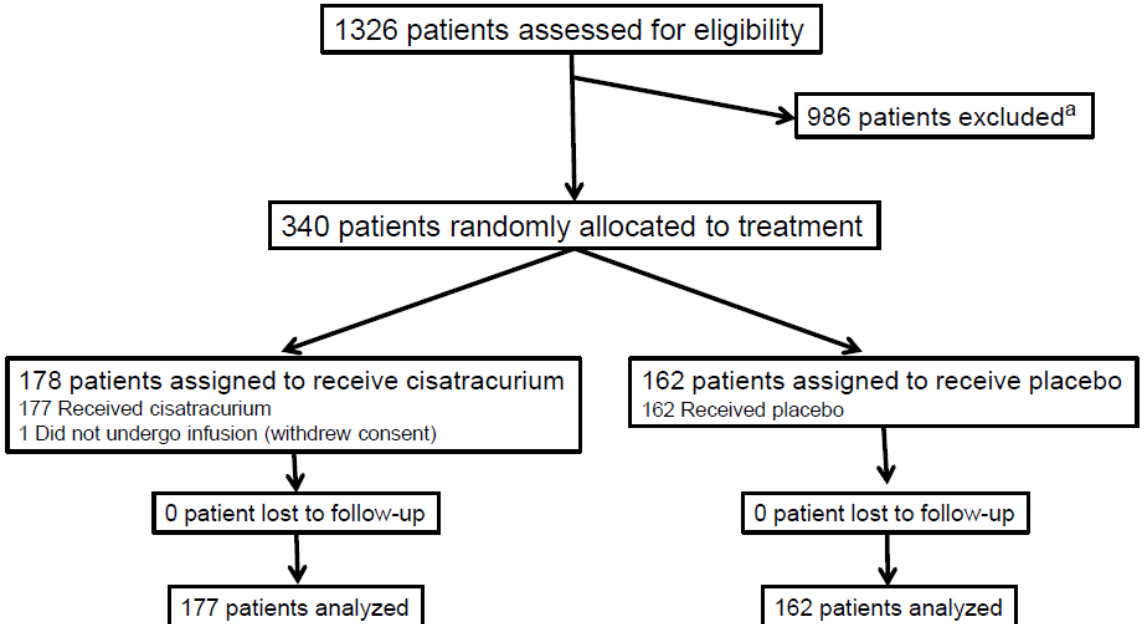
Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D.,

Multicenter, double-blind trial

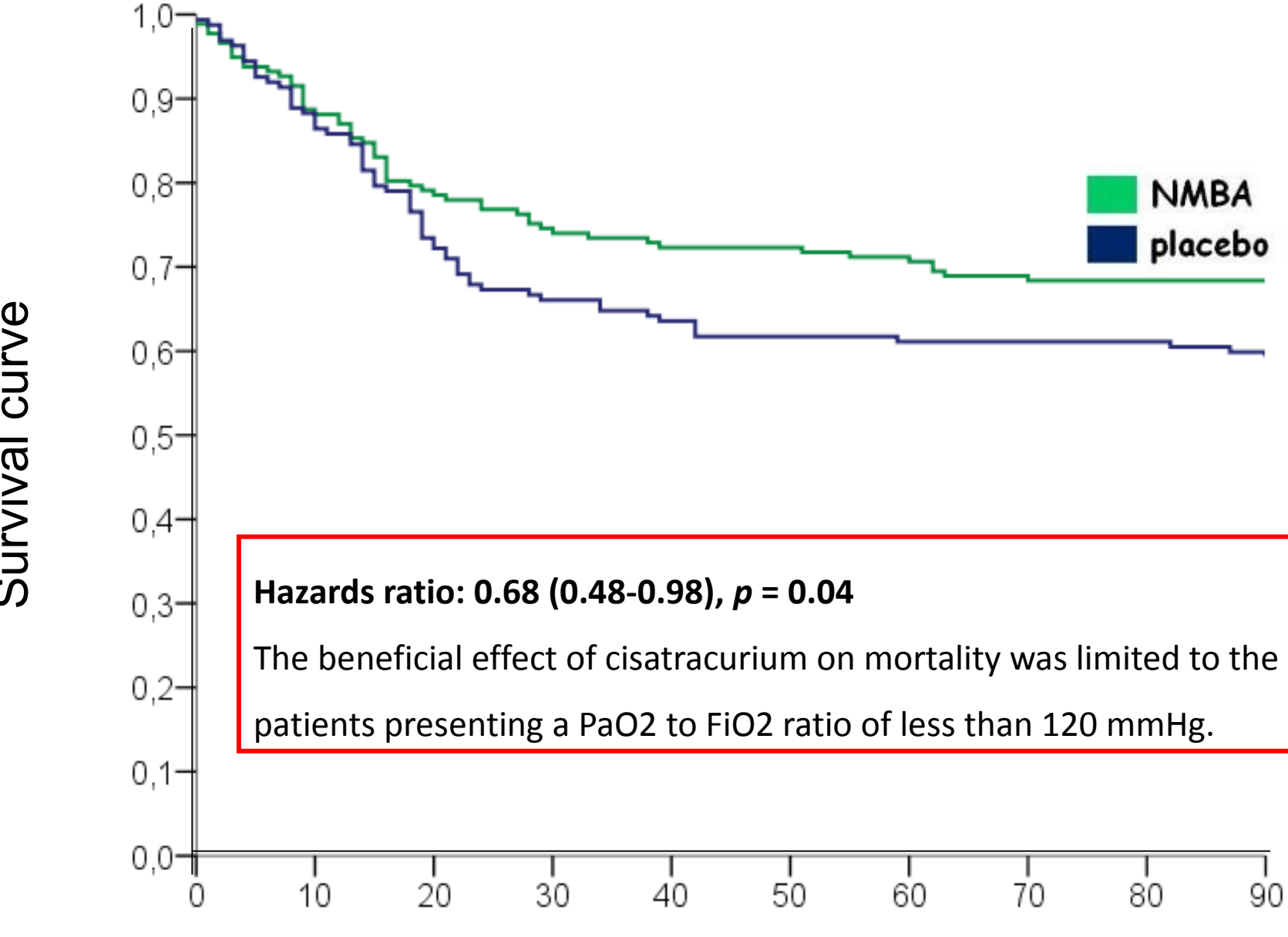
Intervention group:
48-h continuous cisatracurium infusion
(bolus of 15 mg i.v., then 37.5 mg/h infusion for 48 h)

Severe ARDS defined as:
Within the previous 48 h
(PaO2 to FiO2 ratio <150 mmHg with PEEP of at least 5 cm H2O.)



Papazian L, Forel JM, Gacouin A, Penot-Ragon C, Perrin G, Loundou A, Jaber S, Arnal JM, Perez D, Seghboyan JM, Constantin JM, Courant P, Lefrant JY, Guérin C, Prat G, Morange S, Roch A, ACURASYS Study Investigators: **Neuromuscular blockers in early acute respiratory distress syndrome.** *N Engl J Med* 2010, **363**:1107–1116.

In patients with severe ARDS, early administration of a neuromuscular blocking agent improved the adjusted 90-day survival and increased the time off the ventilator without increasing muscle weakness.



Hazards ratio: 0.68 (0.48-0.98), *p* = 0.04

The beneficial effect of cisatracurium on mortality was limited to the patients presenting a PaO2 to FiO2 ratio of less than 120 mmHg.

Perrin G, Loundou A, Jaber M, Courant P, Lefrant JY, Study Investigators: ory distress syndrome. N

Scope of the talk

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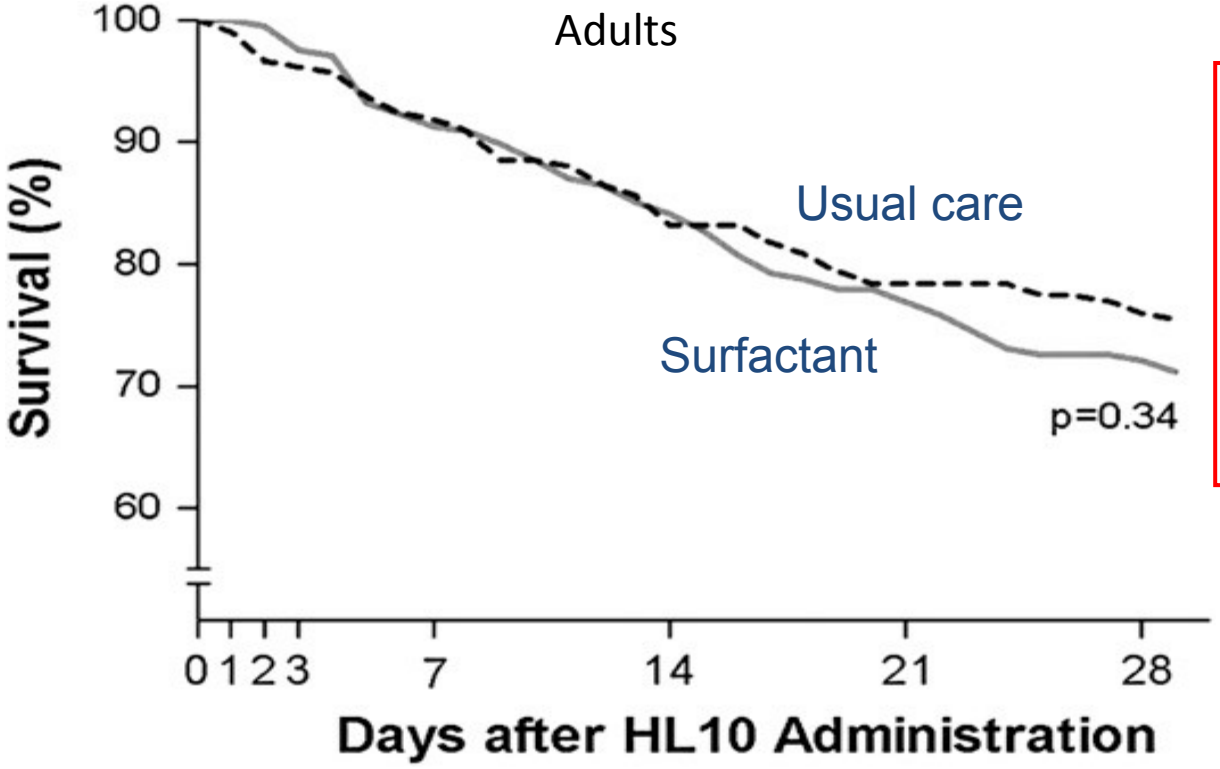
- Prone position in ARDS
- Neuromuscular blockers
- **Benefit from exogenous surfactant, iNO**

Exogenous Natural Surfactant for Treatment of Acute Lung Injury and the Acute Respiratory Distress Syndrome

Jozef Kesecioglu[1], Richard Beale[2], Thomas E. Stewart[3], George P. Findlay[4], Jean-Jacques Rouby[5], Laurent Holzapfel[6], Peter Bruins[7], Edmee J. Steenken[8], Ole K. Jeppesen[8], and Burkhard Lachmann[9]

Surfactant replacement therapy is crucial in the management of neonatal respiratory failure but the best preparation, optimal dose and timing of administration at different gestations is not completely clear. Neonatology 2013;103(4):353-68.



Instillation of a large bolus of exogenous natural porcine surfactant HL 10 in patients with ALI and ARDS did not improve outcome and showed a trend toward increased mortality and adverse effects

Am J Respir Crit Care Med Vol 180. pp 989–994, 2009

Analysis 2.5. Comparison 2 Mortality: INO versus control (bias assessment), Outcome 5 Mortality: sensitivity analysis based on sample size calculation & early stopping.

Review: Inhaled nitric oxide for acute respiratory distress syndrome (ARDS) and acute lung injury in children and adults

Comparison: 2 Mortality: INO versus control (bias assessment)

Outcome: 5 Mortality: sensitivity analysis based on sample size calculation & early stopping

Study or subgroup	INO n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Adequate				
Cuthbertson 2000	8/15	7/15		1.14 [0.56, 2.35]
Dellinger 1998	35/120	17/57		0.98 [0.60, 1.59]
Mehta 2001	4/8	3/6		1.00 [0.35, 2.88]
Michael 1998	11/20	9/20		1.22 [0.65, 2.29]
Payen 1999	53/98	53/105		1.07 [0.82, 1.39]
Taylor 2004	54/165	53/167		1.03 [0.75, 1.41]
Subtotal (95% CI)	**426**	**370**		**1.05 [0.89, 1.25]**
Total events: 165 (INO), 142 (Control)				
Heterogeneity: Chi² = 0.40, df = 5 (P = 1.00); I² = 0.0%				
Test for overall effect: Z = 0.59 (P = 0.56)				
2 Inadequate or unclear				
Day 1997	1/12	2/12		0.50 [0.05, 4.81]
Dobyns 1999	22/53	24/55		0.95 [0.61, 1.47]
Gerlach 2003	3/20	4/20		0.75 [0.19, 2.93]
Ibrahim 2007	9/15	8/15		1.13 [0.60, 2.11]
Lundin 1999	48/93	38/87		1.18 [0.87, 1.61]
Park 2003	8/17	2/6		1.41 [0.41, 4.87]
Schwebel 1997	0/9	0/10		0.0 [0.0, 0.0]
Troncy 1998	9/15	8/15		1.13 [0.60, 2.11]
Subtotal (95% CI)	**234**	**220**		**1.08 [0.87, 1.34]**
Total events: 100 (INO), 86 (Control)				
Heterogeneity: Chi² = 1.57, df = 6 (P = 0.95); I² = 0.0%				
Test for overall effect: Z = 0.72 (P = 0.47)				
Total (95% CI)	**660**	**590**		**1.06 [0.93, 1.22]**
Total events: 265 (INO), 228 (Control)				
Heterogeneity: Chi² = 2.03, df = 12 (P = 1.00); I² = 0.0%				
Test for overall effect: Z = 0.90 (P = 0.37)				
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.85), I² = 0.0%				

0.01 0.1 1 10 100

Favours experimental Favours control

/ distress syndrome
dren and adults

rol, Outcome 5 PaO2/FiO2 difference

iNO cannot be recommended for patients with acute hypoxemic respiratory failure.

	Weight	Mean Difference
CI		IV,Random,95% CI
	35.7 %	29.00 [5.02, 52.98]
	11.9 %	26.00 [-32.13, 84.13]
	52.4 %	56.20 [44.80, 67.60]
	100.0 %	**42.90 [20.57, 65.23]**

0 100

urs INO

Scope of the talk

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- The Ventilator Bundle
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  - ulcer disease prophylaxis, and deep venous thrombosis prophylaxis
  - More ?
- Physiotherapy
- **Endotracheal Tubes** (Silver-Coated + continuous aspiration of the subglottis secretions)
- Oral Rinse
- Prone position in ARDS
- Benefit from exogenous surfactant, iNO
- **Extra-corporeal membrane oxygenation (ECMO)**

Extra-corporeal membrane oxygenation (ECMO)

VENO-VENOUS ECMO

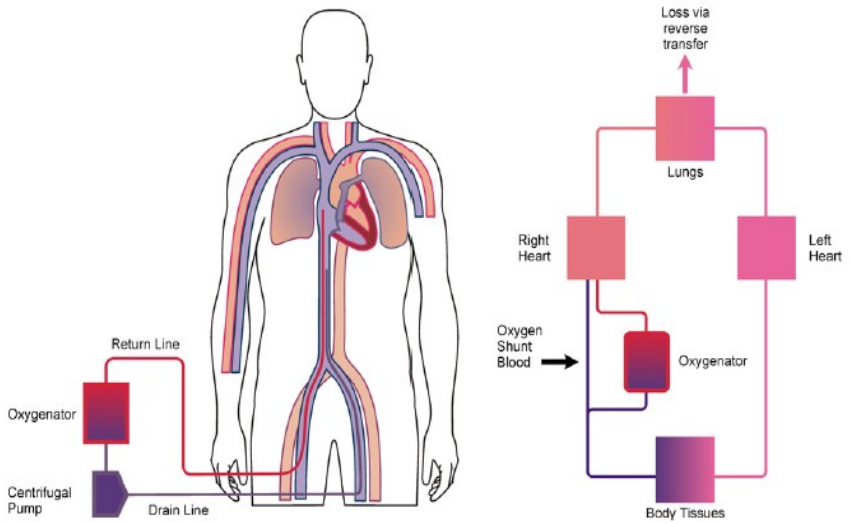


Fig. 4. Schematic diagram of veno-venous extracorporeal membrane oxygenation circuit.

According to the extracorporeal life support organization (ELSO):

'ECMO initiation should be considered:

In hypoxic respiratory failure when the risk of mortality is 50% or greater.

Identified by PaO2/FiO2 less than 150mmHg on FiO2 greater than 90% and/or Murray score 2–3.

According to the extracorporeal life support organization (ELSO) :

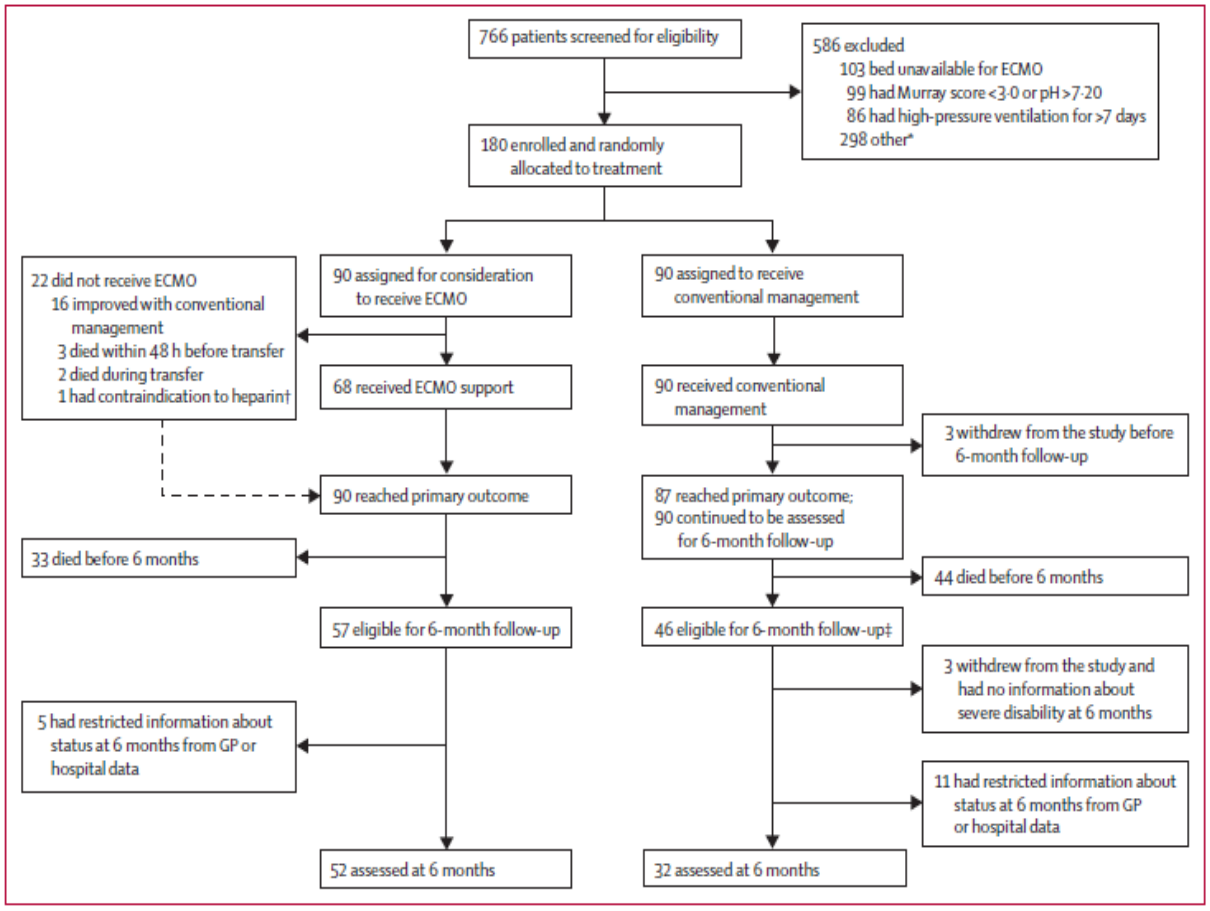
ECMO is indicated:

Risk of mortality exceeds 80%.

PaO2/FiO2 is less than 80 on FiO2 greater than 90% and Murray score is 3–4'.

Curr Opin Crit Care 2012, 18:99–104 Injury (2012), http://dx.doi.org/10.1016/j.injury.2012.11.017

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial



The primary outcome measure was death or severe disability at 6 months after randomization

Intent-to-treat analysis was used for survival and cost analysis

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

	ECMO group (n=90)*	Conventional management group (n=90)	Relative risk (95% CI, p value)
Death or severe disability at 6 months	NA	NA	0·69 (0·05–0·97, 0·03)†
No	57 (63%)	41 (47%)‡	NA
Yes	33 (37%)	46 (53%)‡	NA
No information about severe disability	0	3 (3%)§	NA
Died at ≤6 months or before discharge	NA	NA	0·73 (0·52–1·03, 0·07)
No	57 (63%)	45 (50%)	NA
Yes	33 (37%)	45 (45%)	NA
Severe disability			
No	57 (63%)	41 (46%)	NA
Yes	0	1 (1%)	NA

The CESAR trial showed a 16%

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

The study was limited by:

The absence of a Standardised treatment protocol in the conventional

management group.

The single referral centre.

Scope of the talk

To provide a comprehensive understanding of some non-ventilatory determinants to improve ventilation/outcome

- Staff (Communication + Nursery)
- The Ventilator Bundle
  - Benefits from position (semi recumbent position)
  - Sedation
  - ulcer disease prophylaxis, and deep venous thrombosis prophylaxis
  - More ?
- Physiotherapy
- Endotracheal Tubes (Silver-Coated + continuous aspiration of the subglottis secretions)
- Oral Rinse
- Prone position in ARDS
- Neuromuscular blockers

Adequate Oxygen therapy

Oxygen is a drug.

Clinically, the primary indication for supplemental oxygen is to reverse hypoxemia

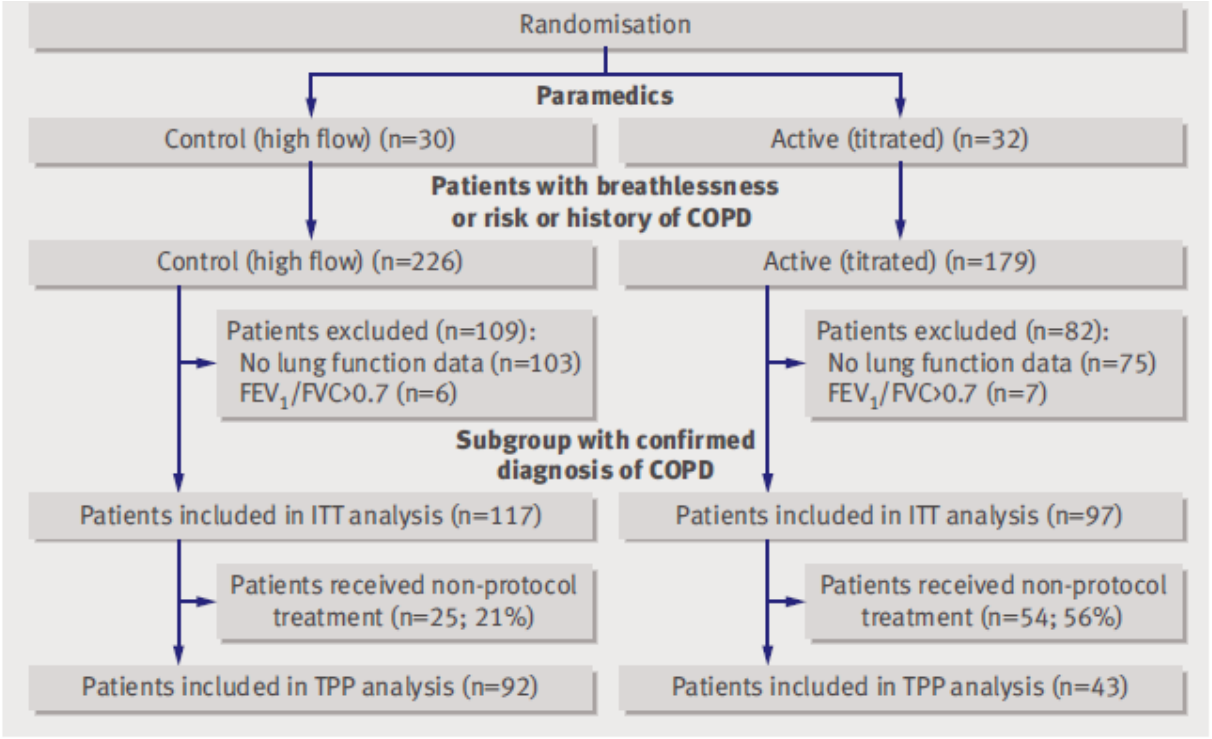
Oxygen saves lives when used appropriately to correct hypoxaemia and is an essential component in resuscitation of the critically ill

Historically, high levels of oxygen were given to all patients with dyspnoea and critical illness
34% of ambulance patients receive oxygen during transit and 15–17% of hospital inpatients will be receiving oxygen at any given time

No evidence of benefit exists for administering oxygen in patients who are normoxaemic (normal arterial oxygen levels) or very mildly hypoxaemic

Intensive Care Med (2011) 37:1–3 DOI 10.1007/s00134-010-2034-y
Thorax 2008; 63: Suppl. 6, vi1–vi68.

Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial



Flow of participants through study. COPD=chronic obstructive pulmonary disease; FEV_1=forced expiratory volume in one second; FVC=forced vital capacity; ITT=intention to treat; TPP=treatment per protocol

Titrated oxygen treatment by paramedics to achieve arterial oxygen saturations between 88% and 92%

Patients with breathlessness and a history or risk of chronic obstructive pulmonary disease

Main outcome measure Prehospital or in-hospital mortality.

BMJ 2010;341:c5462doi:10.1136/bmj.c5462

Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial

Table 3 | Intention to treat analysis. Values are numbers (percentages) unless stated otherwise

	Control (high flow oxygen)	Active (titrated oxygen)	Treatment effect	P value
Mortality				
All patients	21/226 (9)	7/179 (4)	0.42 (0.20 to 0.89)*	0.02
Confirmed COPD	11/117 (9)	2/97 (2)	0.22 (0.05 to 0.91)*	0.04
Incidence of ventilation				
All patients	19/213 (9)	13/166 (8)	0.88 (0.45 to 1.72)*	0.70
Non-invasive ventilation	7	8		
Invasive ventilation	12	5		
Confirmed COPD	15/105 (14)	8/84 (10)	0.67 (0.29 to 1.54)*	0.34
Non-invasive ventilation	6	5		
Invasive ventilation	9	3		

Arterial oxygen saturations between 88% and 92%, reduced the risk of death from respiratory failure by 58% for all patients and 78% for COPD and number needed to harm of 14

BMJ 2010;341:c5462doi:10.1136/bmj.c5462

Should Stroke Victims Routinely Receive Supplemental Oxygen?

A Quasi-Randomized Controlled Trial

Hypothesis:

Breathing 100% oxygen for the first 24 hours after an acute stroke would not reduce mortality, impairment, or disability.

The study shows that Oxygen

Stroke patients in the treatment group received 100% oxygen at atmospheric pressure at a rate of 3 liters per minute through a nasal catheter for 24 hours after they entered the hospital.

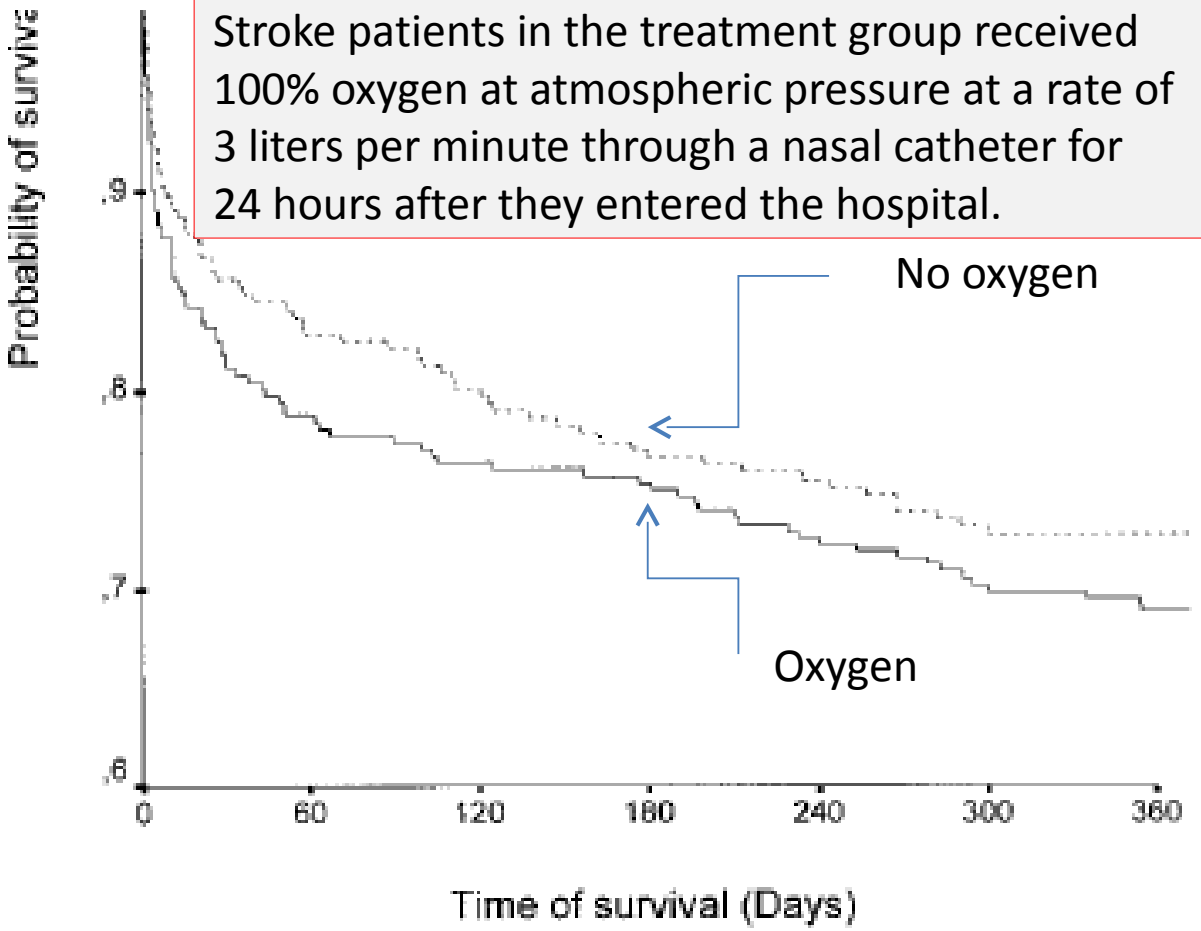


Figure 2. Kaplan-Meier estimated time of survival, by treatment group (n=550). The solid line indicates the oxygen group; the dashed line, the control group.

Stroke. 1993;24:2035-2047

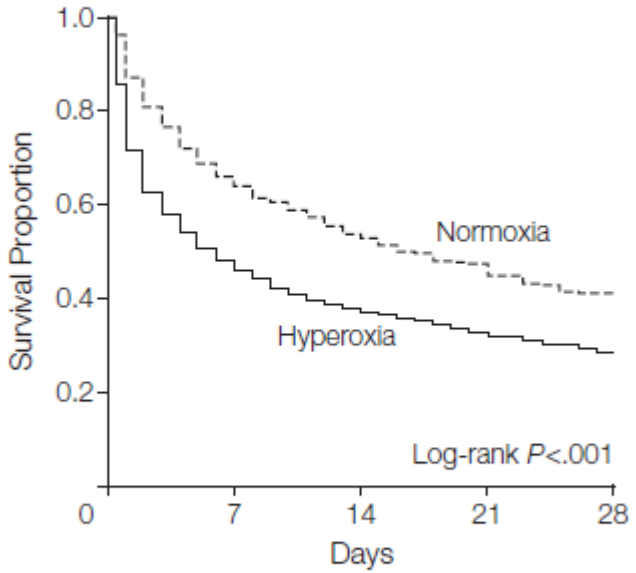
Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality

Critical care database of intensive care units (ICUs) at 120 US hospitals between 2001 and 2005

Patient inclusion criteria were age older than 17 years, nontraumatic cardiac arrest, cardiopulmonary resuscitation within 24 hours prior to ICU arrival, and arterial blood gas analysis performed within 24 hours following ICU arrival

Patients were divided into 3 groups defined a priori based on PaO2 on the first arterial blood gas values obtained in the ICU.

Figure. In-Hospital Death Between Hyperoxia and Normoxia



JAMA. 2010;303(21):2165-2171

Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality

Table 5. Multiple Logistic Regression Model With In-Hospital Mortality as the Dependent Variable[a]

Variable	OR (95% CI)	*P* Value
Age decile	1.1 (1.1-1.2)	<.001
Emergency department origin	1.5 (1.3-1.7)	<.001
Nonindependent functional status at admission	1.3 (1.1-1.4)	<.001
Chronic renal failure	1.6 (1.3-1.9)	<.001
Active chemotherapy	2.8 (1.8-4.6)	<.001
High heart rate in ICU[b]	1.9 (1.7-2.1)	<.001
Hypotension at ICU arrival[c]	2.1 (1.9-2.3)	<.001
Hypoxia exposure	1.3 (1.1-1.5)	.009
Hyperoxia exposure	1.8 (1.5-2.2)	<.001

Abbreviations: CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

[a] Event rates (mortality) for each variable and for the relevant reference group appear in eTable 2 at http://www.jama.com. The following variables were removed from the model because of nonsignificance: female sex, OR, 1.1 (95% CI, 1.0-1.2; *P*=.29); chronic respiratory disease, OR, 1.3 (95% CI, 1.0-1.6; *P*=.05); human immunodeficiency virus, OR, 1.9 (95% CI, 1.0-3.7; *P*=.06); and requiring inotropic therapy, OR, 1.1 (95% CI, 0.9-1.3; *P*=.19).

[b] Indicates the highest value for first 24 hours in the ICU (1=exceeds median; 0=median or lower).

[c] Defined as any systolic blood pressure of less than 90 mm Hg within 1 hour of ICU arrival.[14]

Suggests that both hypoxemia and hyperoxemia are associated with increased mortality and disposition.

Paradoxically: Giving too much oxygen at the time of an acute infarction may worsen Oxygen delivery to the cardiac muscle

JAMA. 2010;303(21):2165-2171

High-concentration versus titrated oxygen therapy in ST-elevation myocardial infarction: A pilot randomized controlled trial

A randomized controlled trial (n= 136)

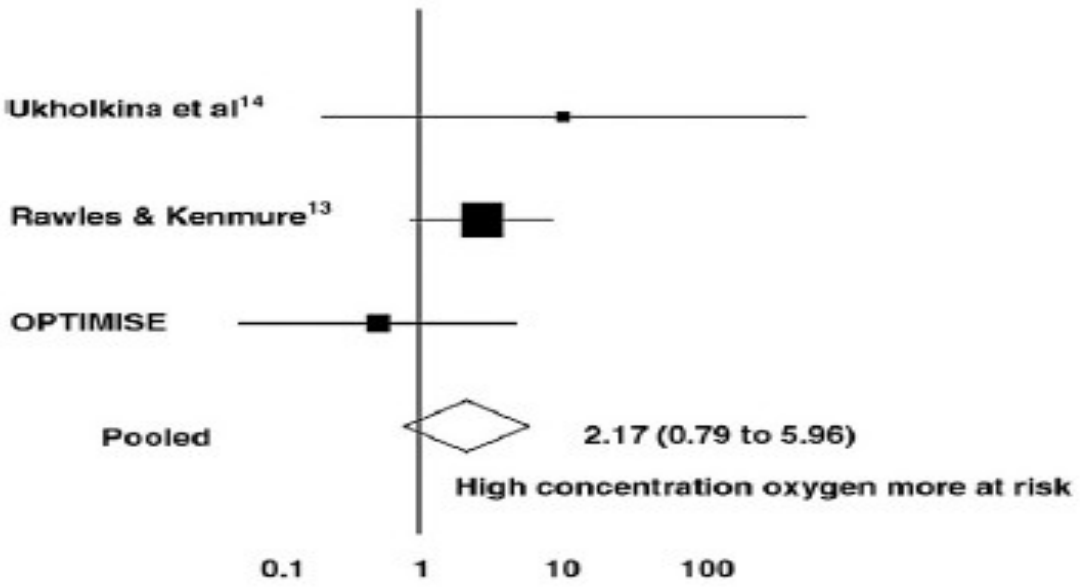
The first STEMI uncomplicated by cardiogenic shock or marked hypoxia were

randomized to receive high-concentration (6 L/min via medium concentration mask) or

Titrated Oxygen (to achieve oxygen saturation 93%-96%) for 6 hours after presentation.

The main outcome variables:
30-day mortality
Infarct size assessed by troponin T level at 72 hours

Figure 3



Am Heart J 2012;163:168-75.)

Prof. Dr Finn Rasmussen PhD. DMSc. Near East University Hospital North Cyprus