



# Physiopathology of difficult weaning

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*Service de Médecine Intensive et Réanimation*  
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*Inserm U1042*



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## **Non Financial support for congress**

- Hill-Rom
- Dräger

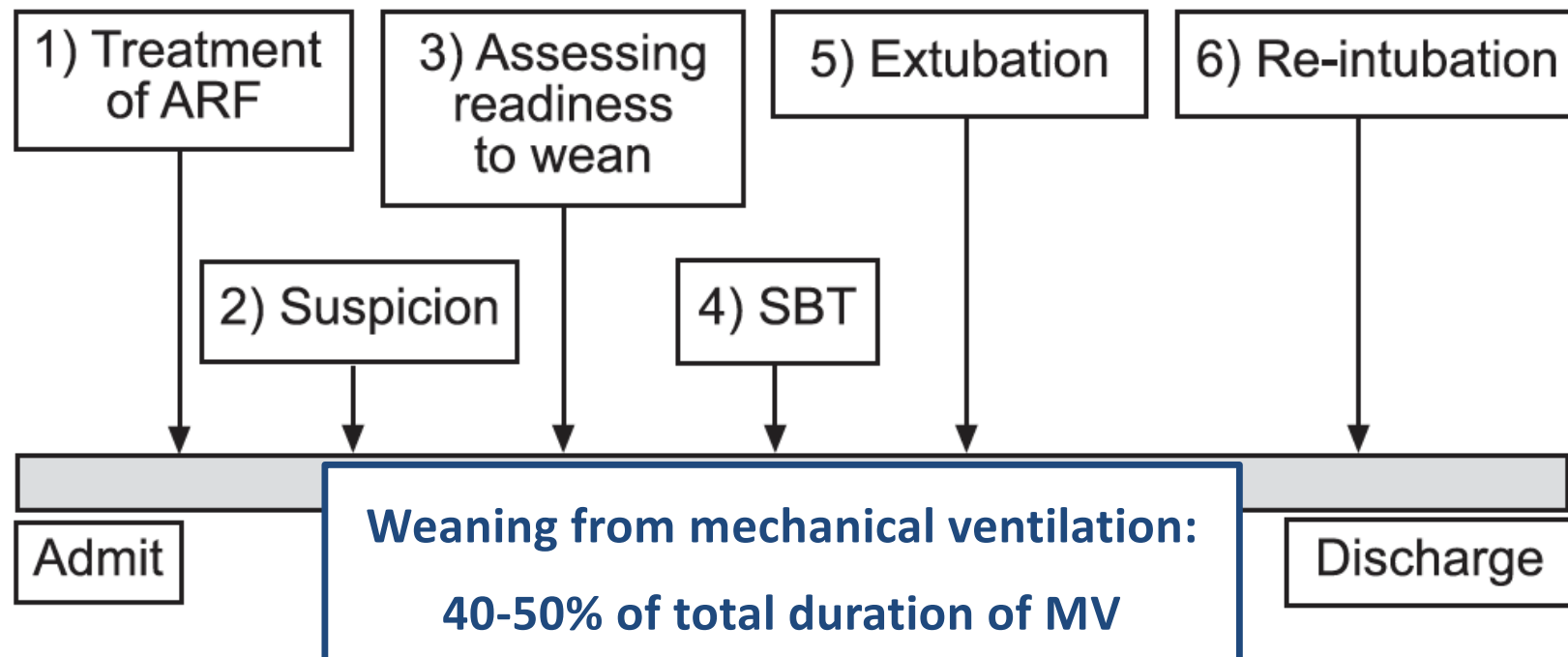
## **Fees for speaker:**

- Covidien
- Lilly oncology
- Boehringer Ingelheim
- Pfizer

# Weaning from mechanical ventilation

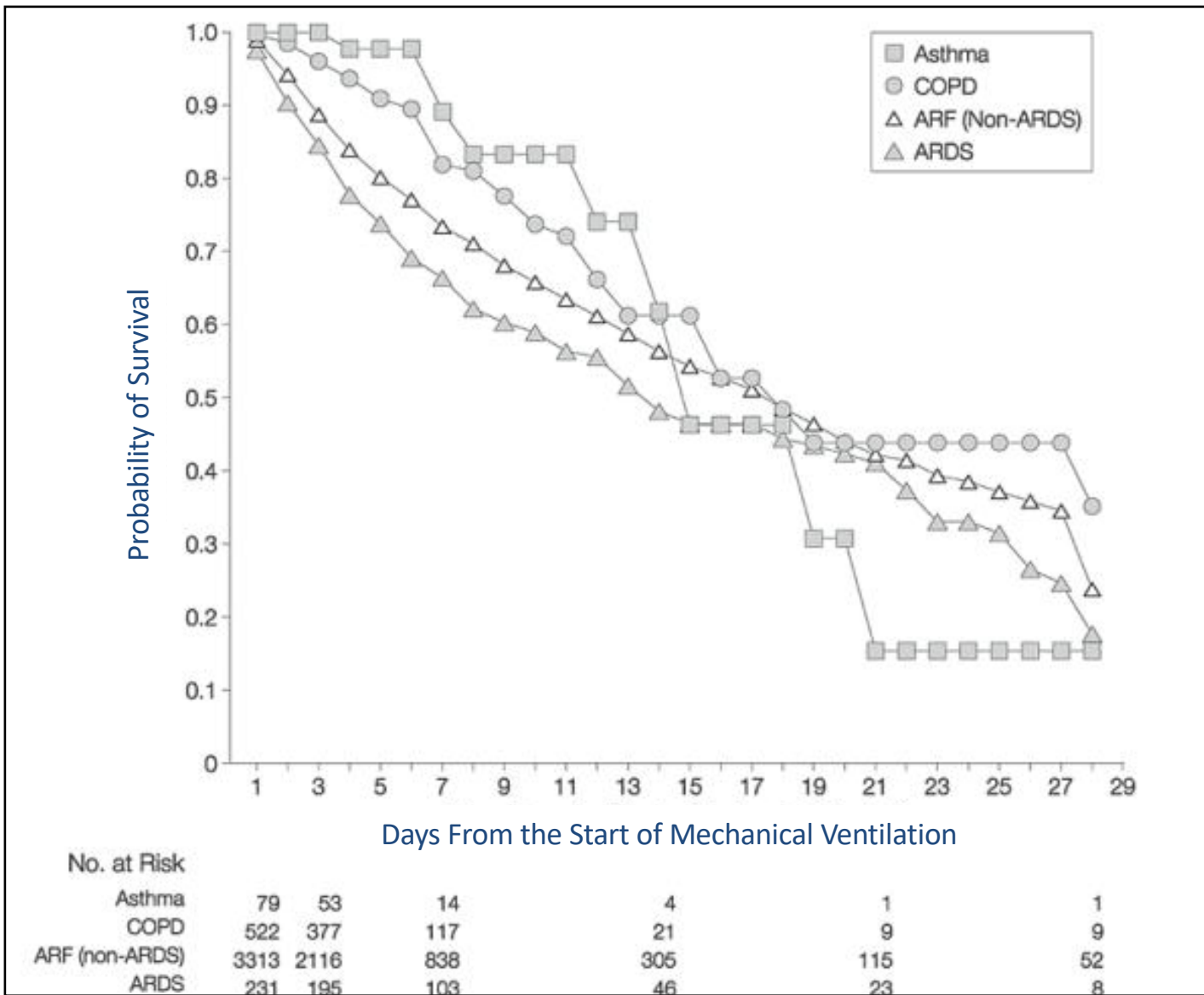
J-M. Boles<sup>\*</sup>, J. Bion<sup>#</sup>, A. Connors<sup>¶</sup>, M. Herridge<sup>+</sup>, B. Marsh<sup>§</sup>, C. Melot<sup>f</sup>, R. Pearl<sup>\*\*</sup>,  
H. Silverman<sup>###</sup>, M. Stanchina<sup>¶¶</sup>, A. Vieillard-Baron<sup>++</sup>, T. Welte<sup>§§</sup>

ERJ 2007

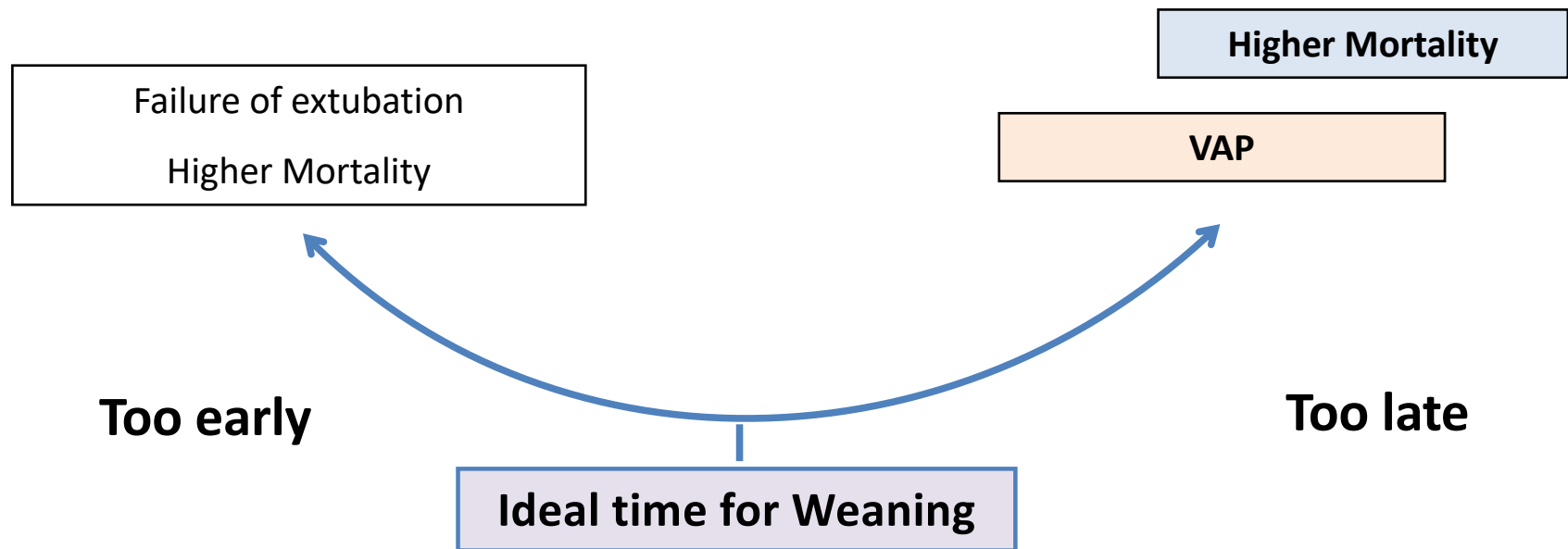


**Characteristics and Outcomes in Adult Patients Receiving Mechanical Ventilation: A 28-Day International Study.**

**Mortality is associated with duration of Mechanical Ventilation**



# Weaning = Challenge



## Difficult weaning : which definition ?

**2005:** National Association  
for Medical Direction of  
Respiratory Care  
“the need for more than **21**  
**consecutive days** of MV for  
more than **6 h/day**”



**Weaning according to New  
Definition (WIND) study  
(2016)**

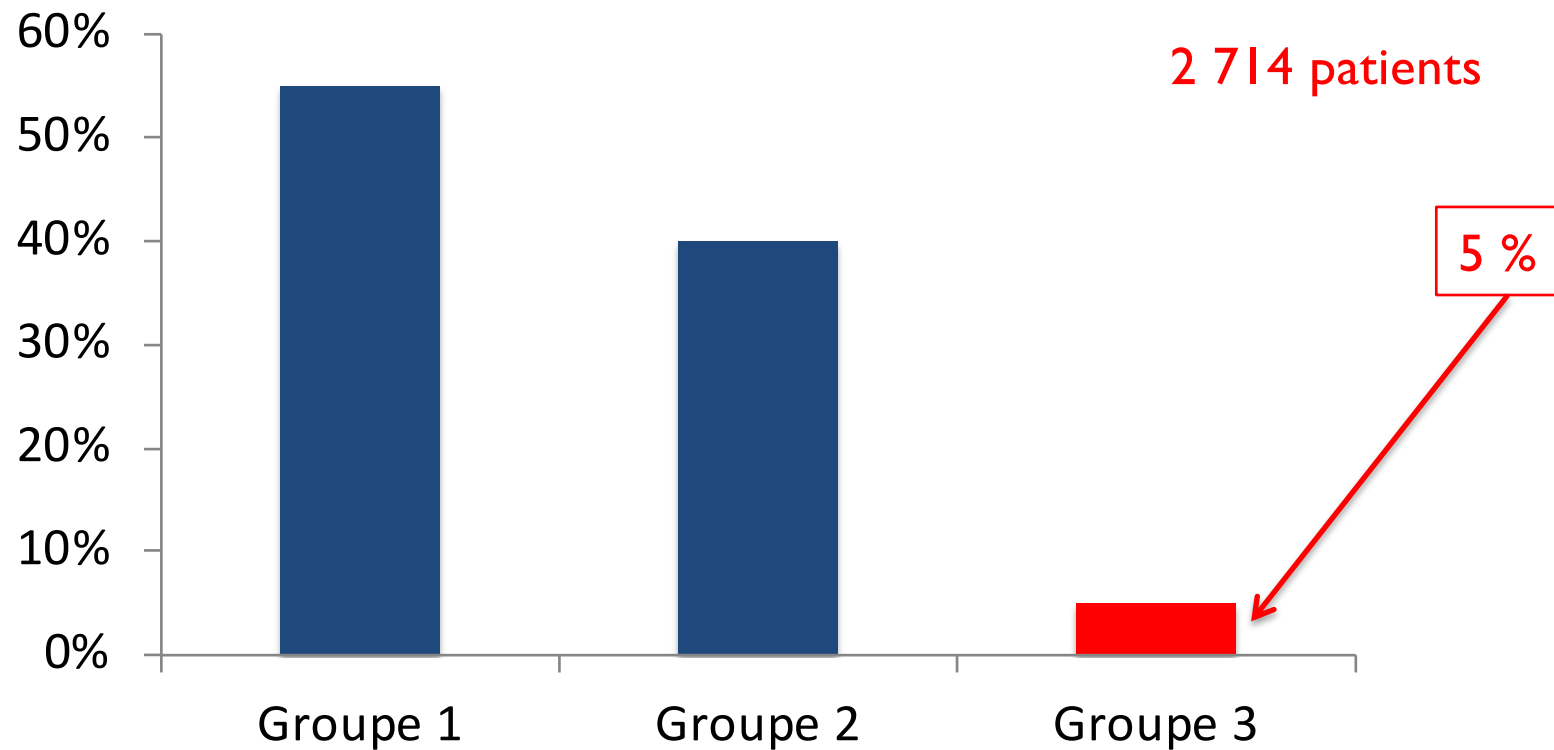
“successful extubation after  
**more than three SBTs** or  
taking **more than seven  
days**”

**2007:** European  
Respiratory Society (ERS)  
Task Force  
“the need of more than **7**  
**days of weaning** after the  
first spontaneous  
breathing trial (**SBT**)”

# Characteristics and Outcomes of Ventilated Patients According to Time to Liberation from Mechanical Ventilation

Oscar Peñuelas<sup>1,2</sup>, Fernando Frutos-Vivar<sup>1,2</sup>, Cristina Fernández<sup>3</sup>, Antonio Anzueto<sup>4</sup>, Scott K. Epstein<sup>6</sup>, Carlos Apezteguía<sup>7</sup>, Marco González<sup>8</sup>, Nicolas Nin<sup>1,2</sup>, Konstantinos Raymondos<sup>9</sup>, Vinko Tomicic<sup>10</sup>, Pablo Desmery<sup>11</sup>, Yaseen Arabi<sup>12</sup>, Paolo Pelosi<sup>13</sup>, Michael Kuiper<sup>14</sup>, Manuel Jibaja<sup>15</sup>, Dimitros Matamis<sup>16</sup>, Niall D. Ferguson<sup>5</sup>, and Andrés Esteban<sup>1,2</sup> for the Ventila Group\*

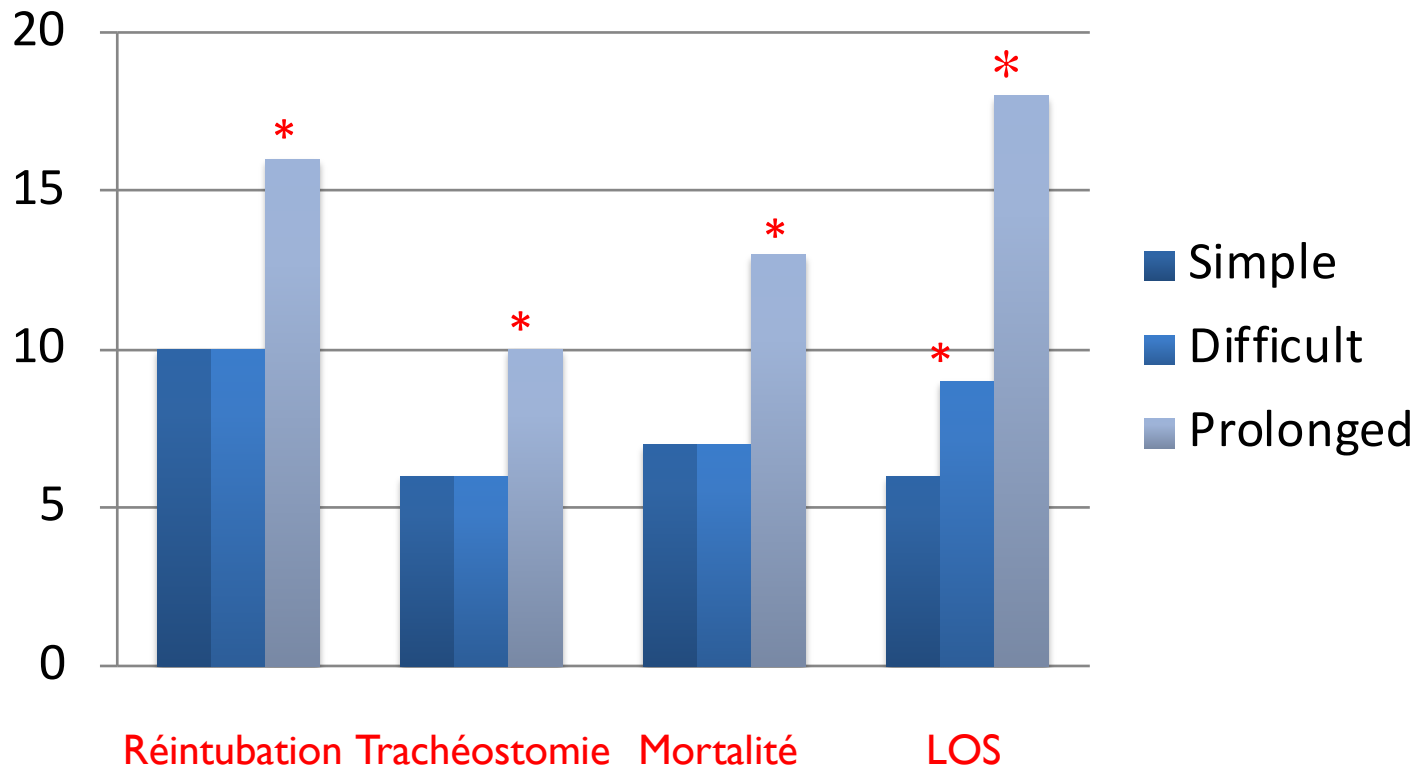
Am J Respir Crit Care Med Vol 184. pp 430–437, 2011



# Characteristics and Outcomes of Ventilated Patients According to Time to Liberation from Mechanical Ventilation

Oscar Peñuelas<sup>1,2</sup>, Fernando Frutos-Vivar<sup>1,2</sup>, Cristina Fernández<sup>3</sup>, Antonio Anzueto<sup>4</sup>, Scott K. Epstein<sup>6</sup>, Carlos Apezteguía<sup>7</sup>, Marco González<sup>8</sup>, Nicolas Nin<sup>1,2</sup>, Konstantinos Raymondos<sup>9</sup>, Vinko Tomicic<sup>10</sup>, Pablo Desmery<sup>11</sup>, Yaseen Arabi<sup>12</sup>, Paolo Pelosi<sup>13</sup>, Michael Kuiper<sup>14</sup>, Manuel Jibaja<sup>15</sup>, Dimitros Matamis<sup>16</sup>, Niall D. Ferguson<sup>5</sup>, and Andrés Esteban<sup>1,2</sup> for the Ventila Group\*

Am J Respir Crit Care Med Vol 184. pp 430–437, 2011



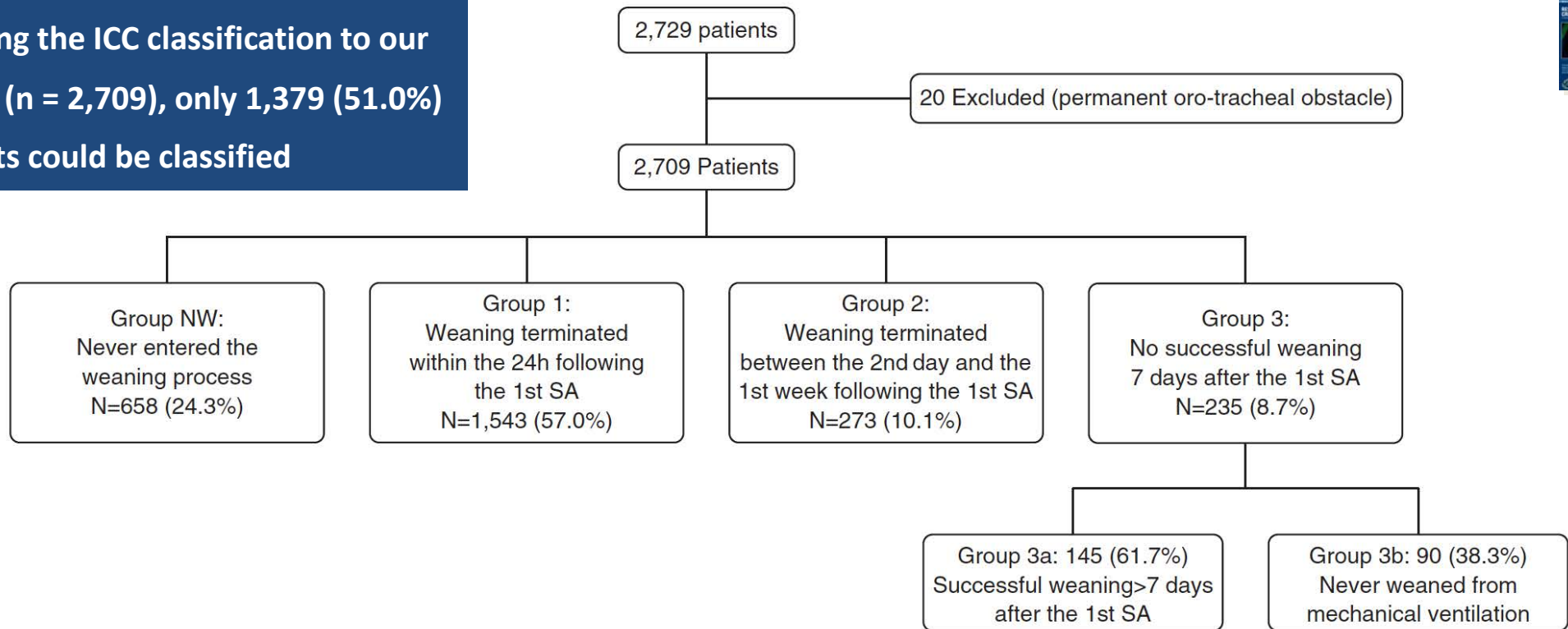


# Epidemiology of Weaning Outcome according to a New Definition

The WIND Study

Béduneau et al. AJRCCM 2017

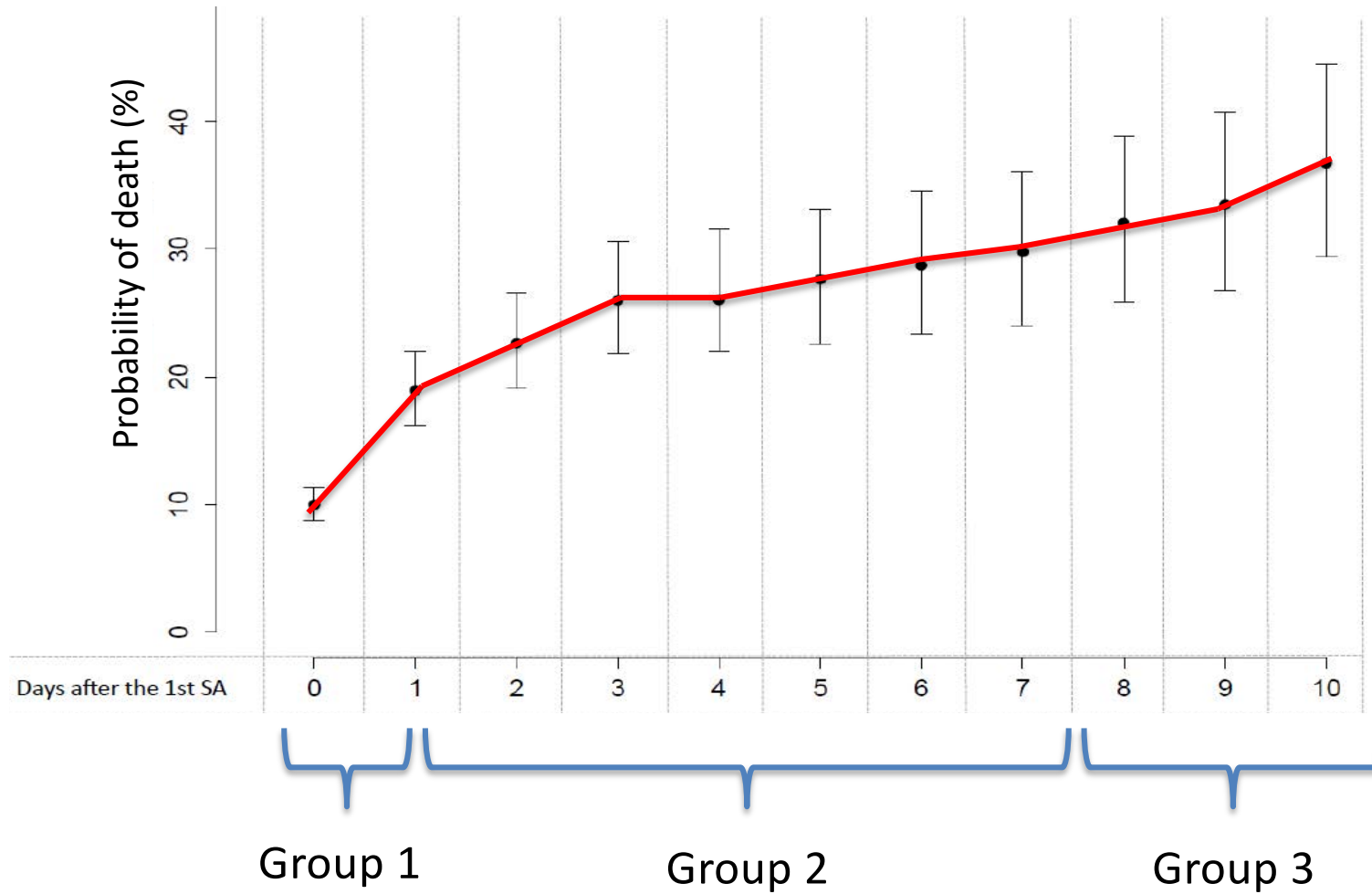
Applying the ICC classification to our cohort (n = 2,709), only 1,379 (51.0%) patients could be classified



# Epidemiology of Weaning Outcome according to a New Definition

The WIND Study

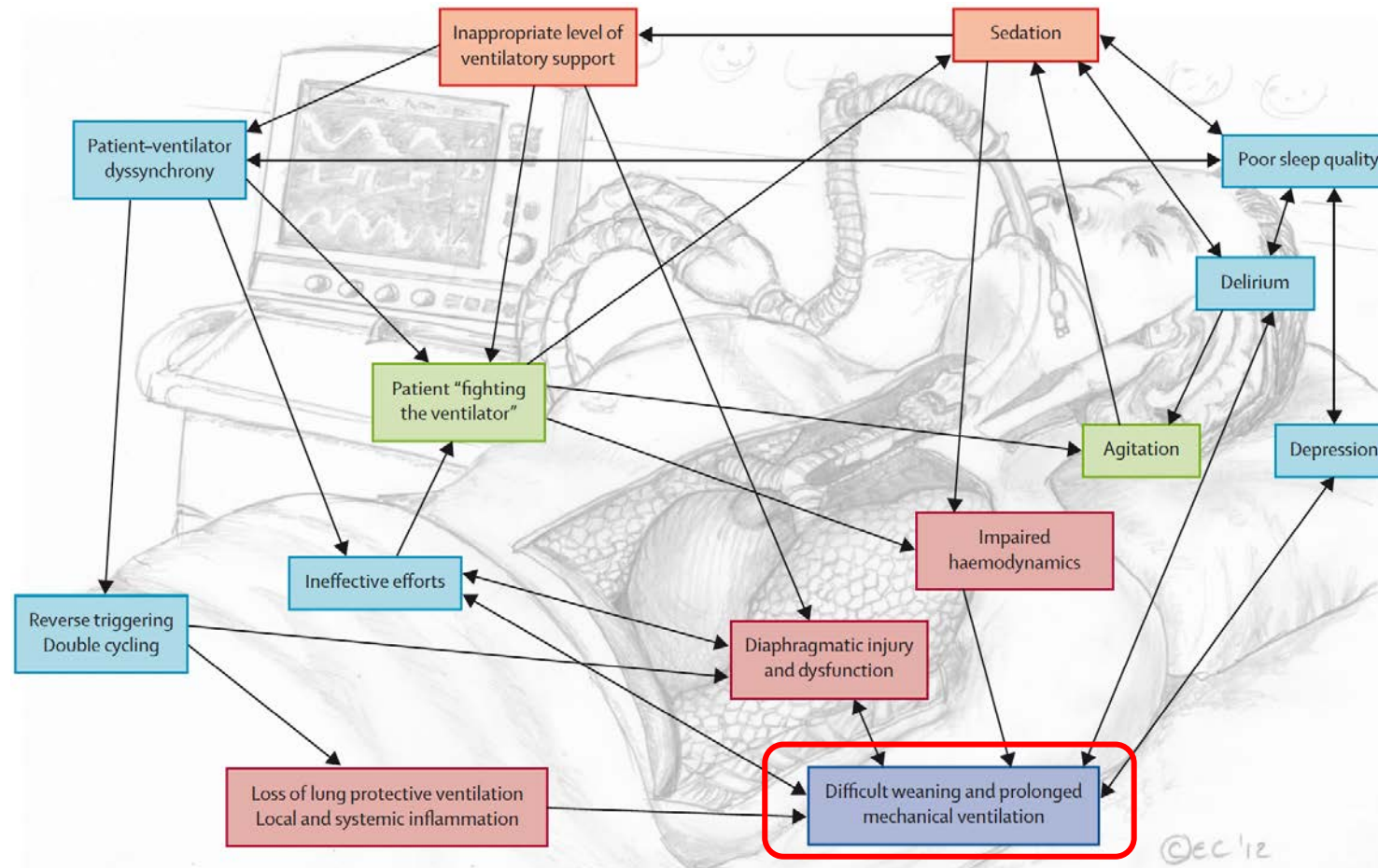
Béduneau et al. AJRCCM 2017



# Clinical challenges in mechanical ventilation

Ewan C Goligher, Niall D Ferguson, Laurent J Brochard

Lancet 2016



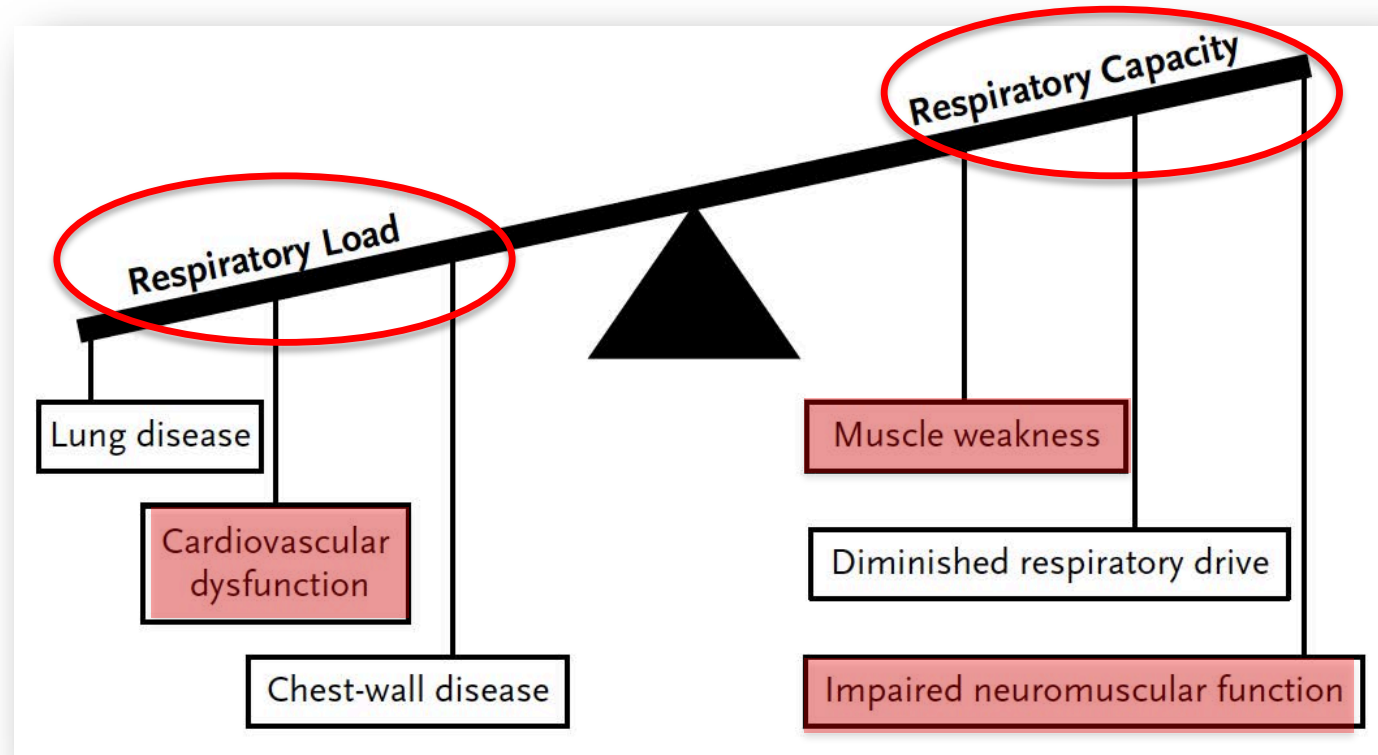
**TABLE 4** Common pathophysiologies and their incidence, which may impact on the ability to wean a patient from mechanical ventilation

Pathophysiology	Consider
<b>Respiratory load</b>	<p>Increased work of breathing: inappropriate ventilator settings</p> <p>Reduced compliance: pneumonia (ventilator-acquired); cardiogenic or noncardiogenic oedema; pulmonary fibrosis; pulmonary haemorrhage; diffuse pulmonary infiltrates</p> <p>Airway bronchoconstriction</p> <p>Increased resistive load</p> <p>    During SBT: endotracheal tube</p> <p>    Post-extubation: glottic oedema; increased airway secretions; sputum retention</p>
<b>Cardiac load</b>	<p>Cardiac dysfunction prior to critical illness</p> <p>Increased cardiac workload leading to myocardial dysfunction: dynamic hyperinflation; increased metabolic demand; unresolved sepsis</p>
<b>Neuromuscular</b>	<p>Depressed central drive: metabolic alkalosis; mechanical ventilation; sedative/hypnotic medications</p> <p>Central ventilatory command: failure of the neuromuscular respiratory system</p> <p>Peripheral dysfunction: primary causes of neuromuscular weakness; CINMA</p>
<b>Neuropsychological</b>	<p>Delirium</p> <p>Anxiety, depression</p>
<b>Metabolic</b>	<p>Metabolic disturbances</p> <p>Role of corticosteroids</p> <p>Hyperglycaemia</p>
<b>Nutrition</b>	<p>Overweight</p> <p>Malnutrition</p>
<b>Anaemia</b>	<p>Ventilator-induced diaphragm dysfunction</p>

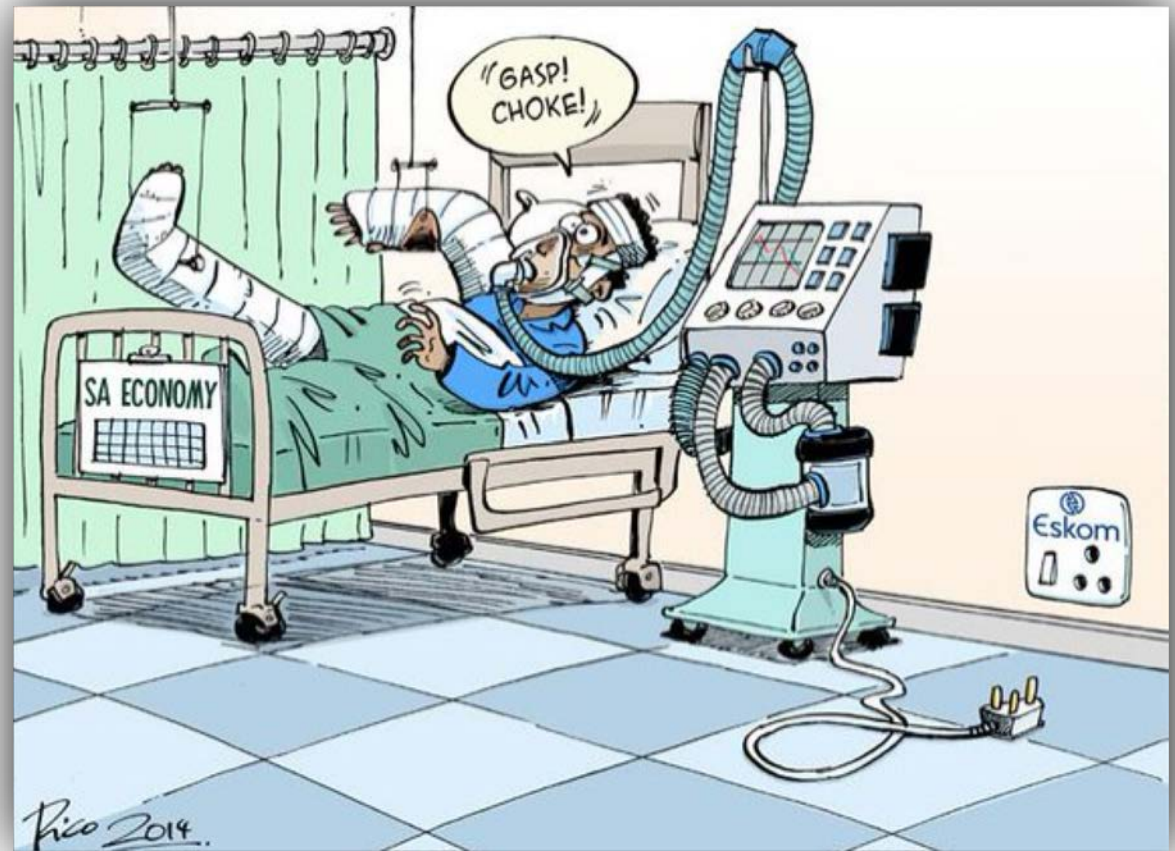
# Weaning Patients from the Ventilator

N Engl J Med 2012;367:2233-9.

John F. McConville, M.D., and John P. Kress, M.D.

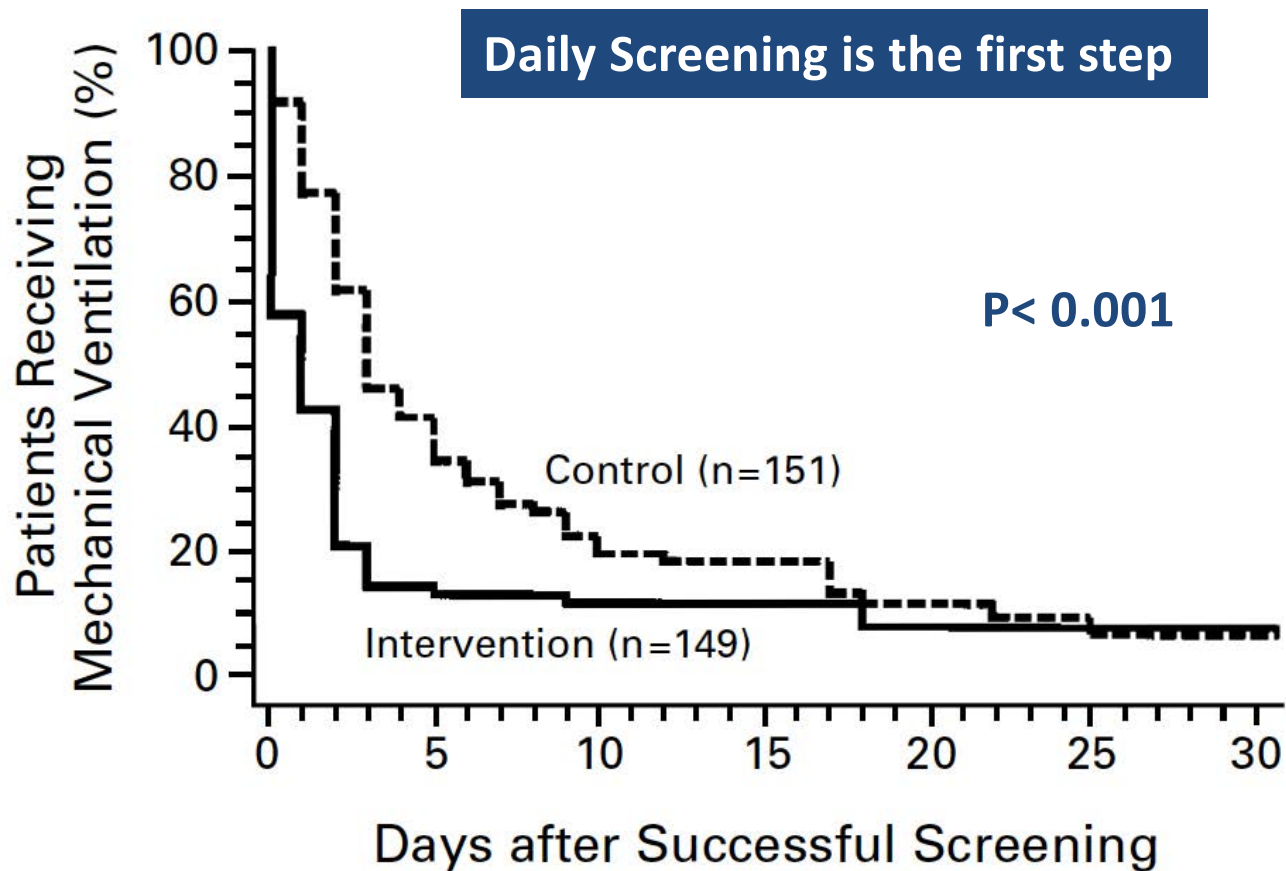


Sevrage  
possible mais  
non identifié



# EFFECT ON THE DURATION OF MECHANICAL VENTILATION OF IDENTIFYING PATIENTS CAPABLE OF BREATHING SPONTANEOUSLY

N=300 Patients



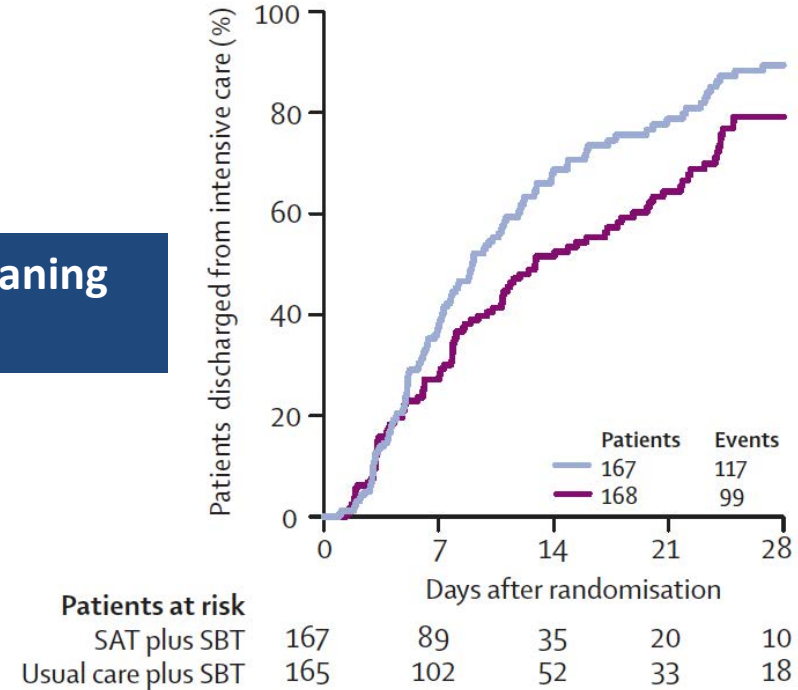
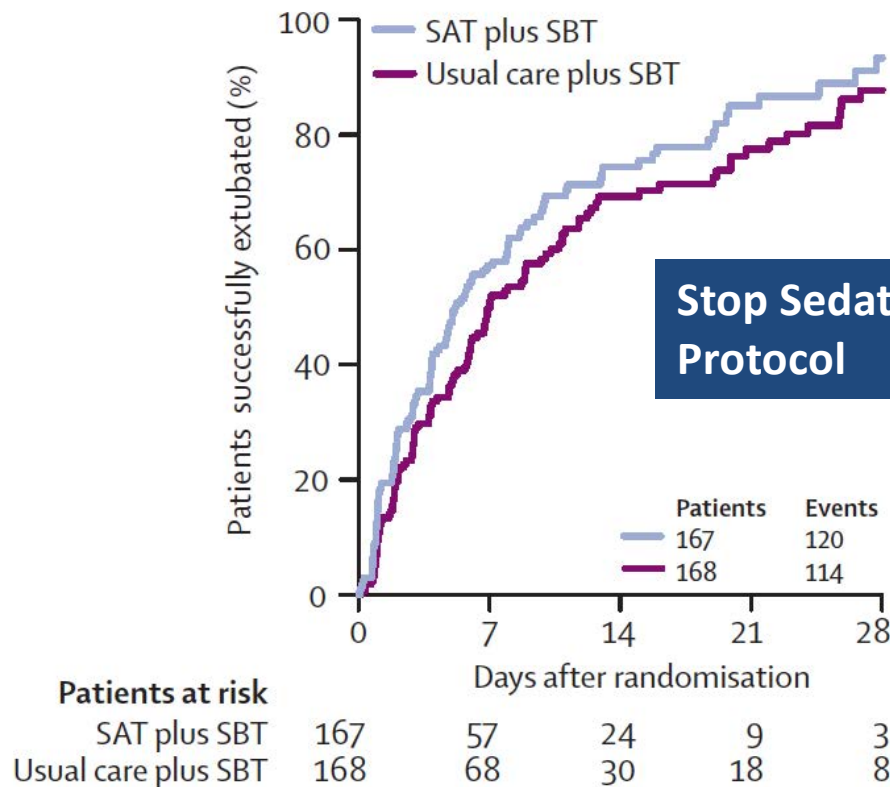
## Intervention Group

- 1) A daily screening of respiratory function
- 2) A 2-hour trial of spontaneous Breathing
- 3) Notification of the physician of the successful results



Ely W et al. NEJM 1996

# 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



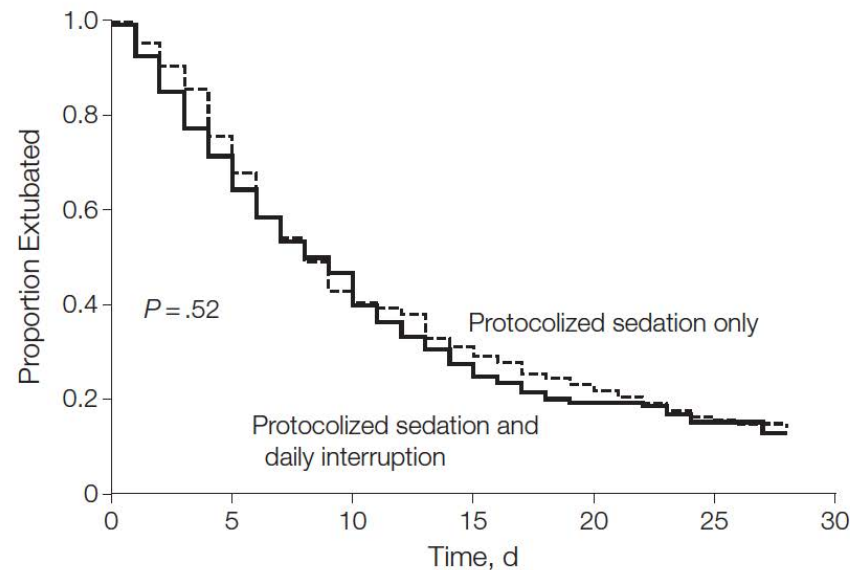
Girard T et al. Lancet 2008



# Daily Sedation Interruption in Mechanically Ventilated Critically Ill Patients Cared for With a Sedation Protocol

A Randomized Controlled Trial

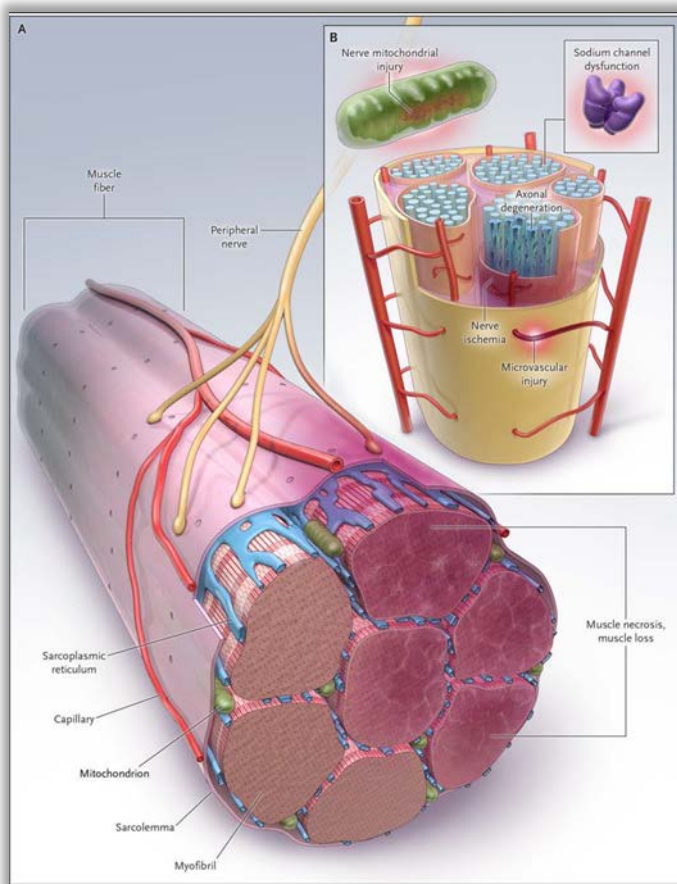
**Figure 2.** Kaplan-Meier Curves for Time to Successful Extubation



**N=430 Patients**

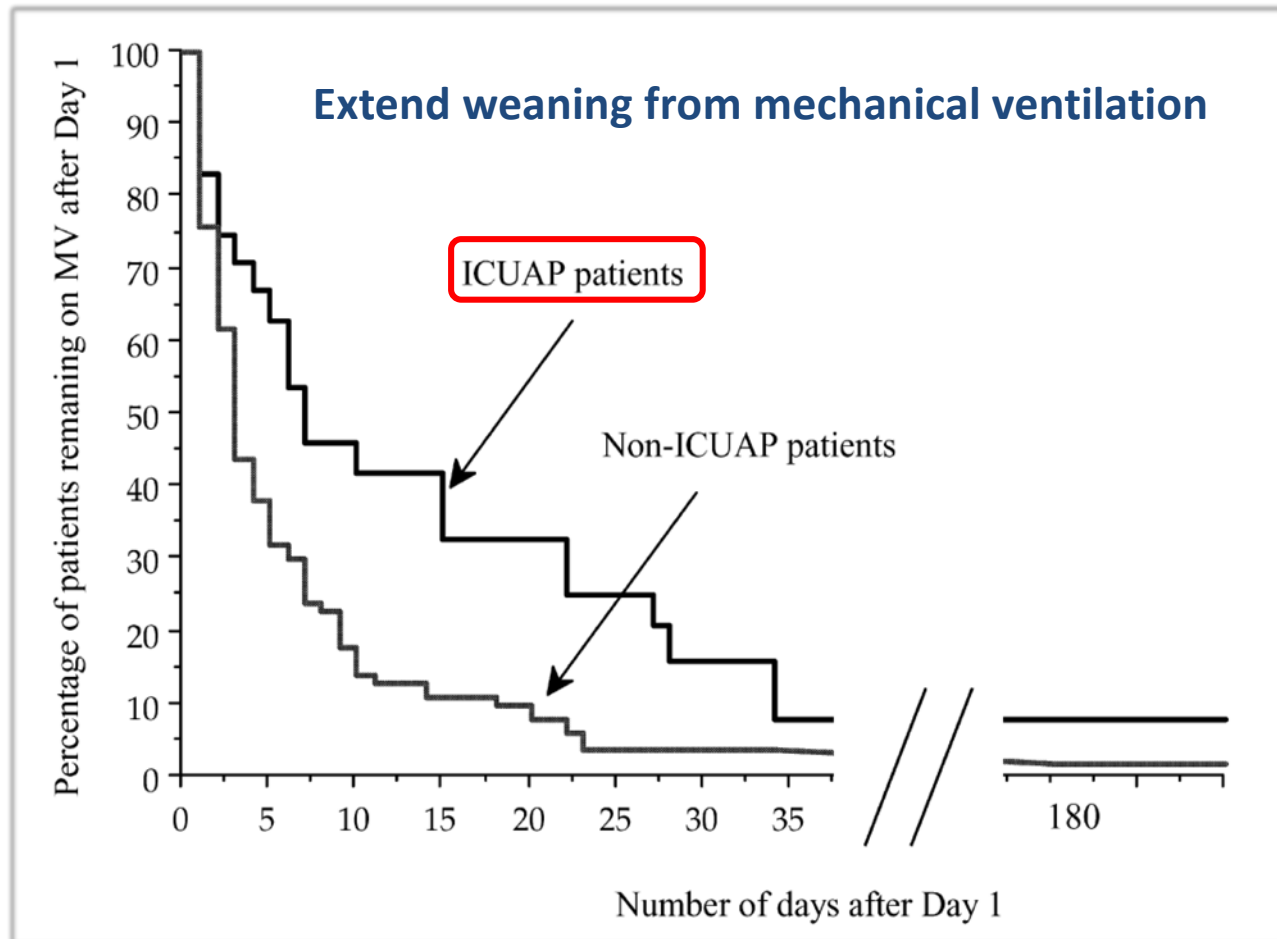
No. at risk						
Protocolized sedation only	209	146	72	49	34	23
Protocolized sedation and daily interruption	214	140	81	42	28	16

# ICU-Acquired Weakness and Recovery from Critical Illness



The reported incidence of ICU-acquired weakness ranges from 25 to 100%

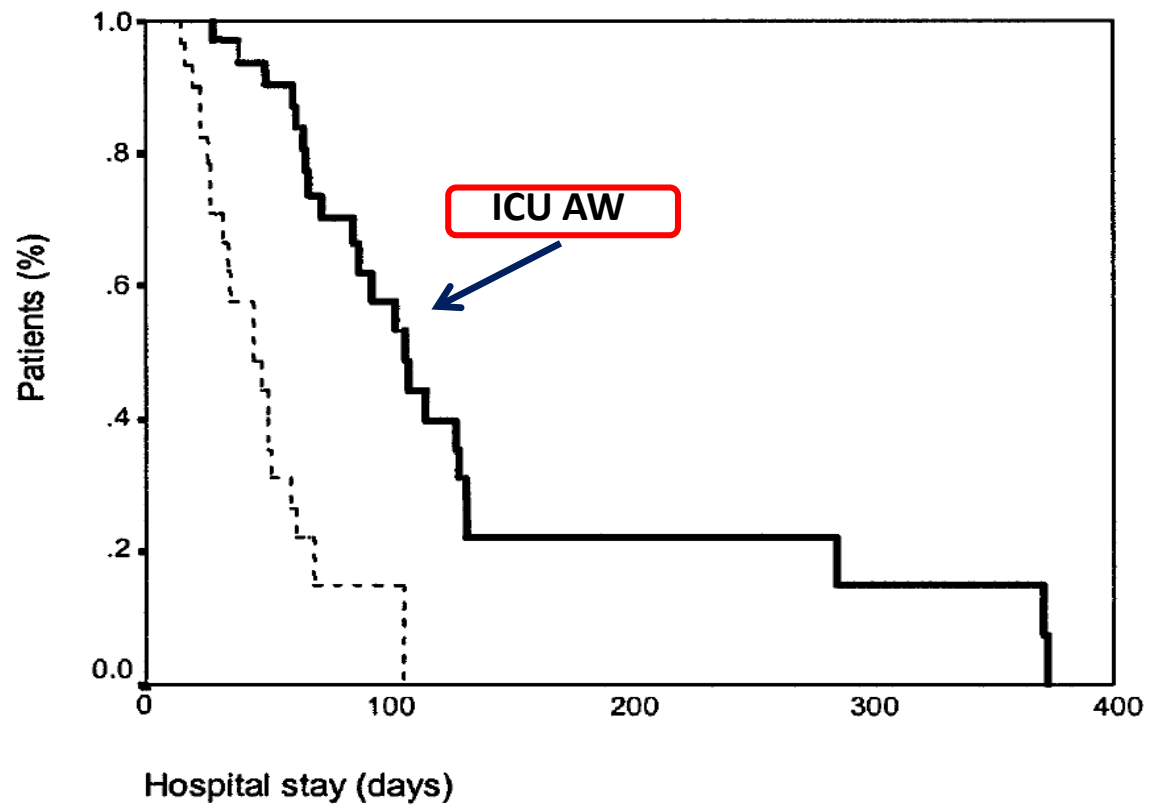
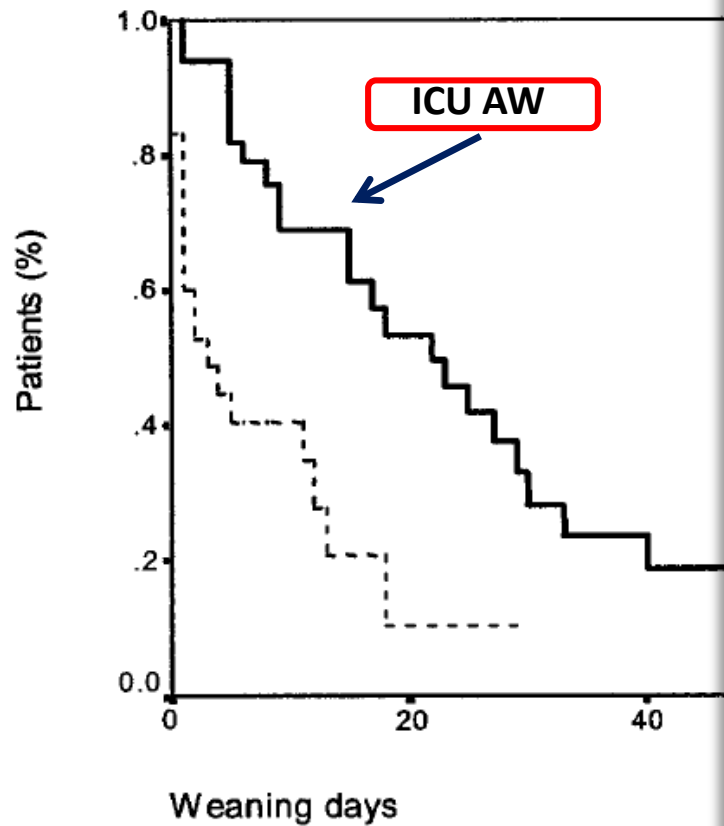
# Does ICU-acquired paresis lengthen weaning from mechanical ventilation?



# Effect of critical illness polyneuropathy on the withdrawal from mechanical ventilation and the length of stay in septic patients\*



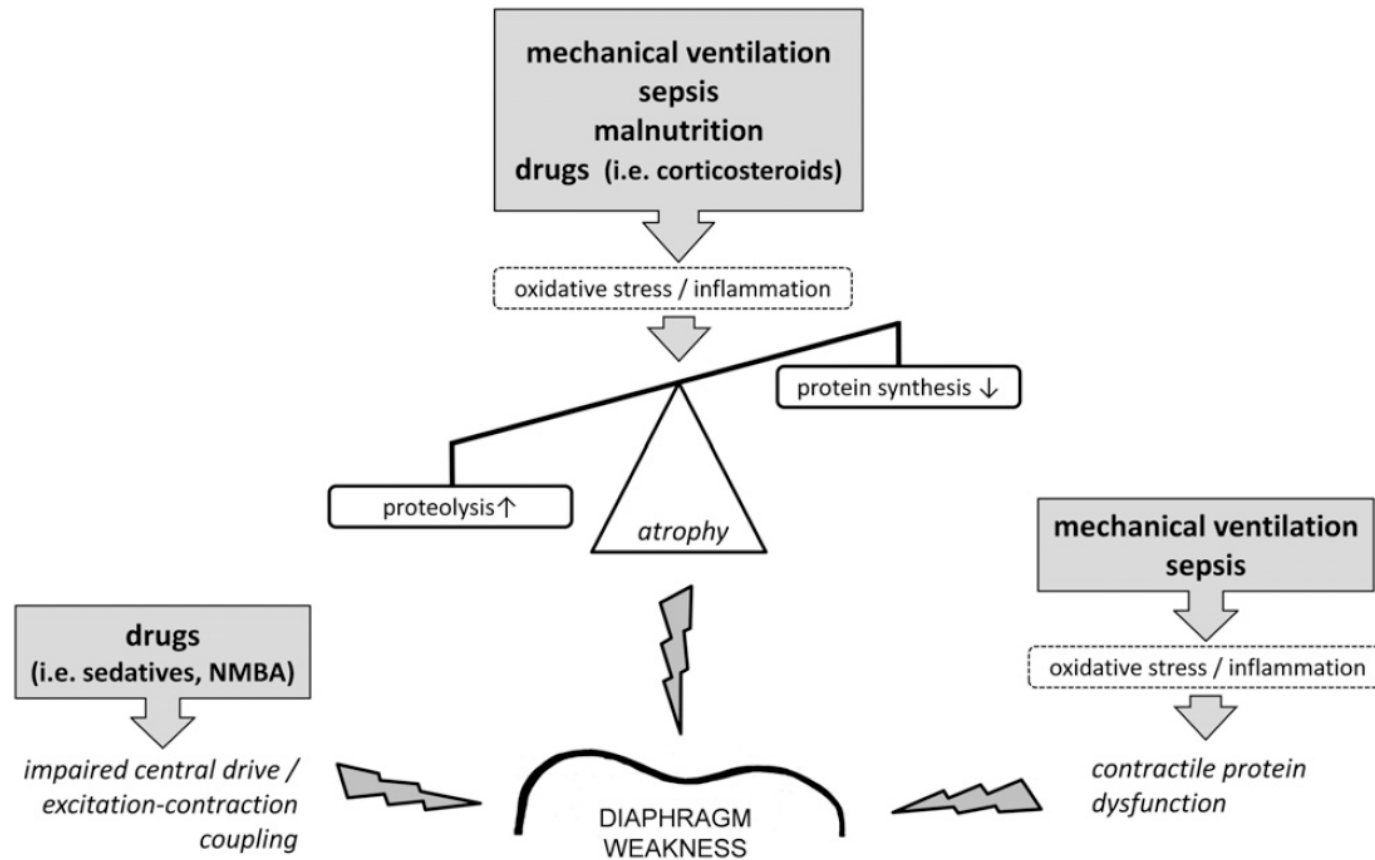
Garnacho-Montero et al. 2005



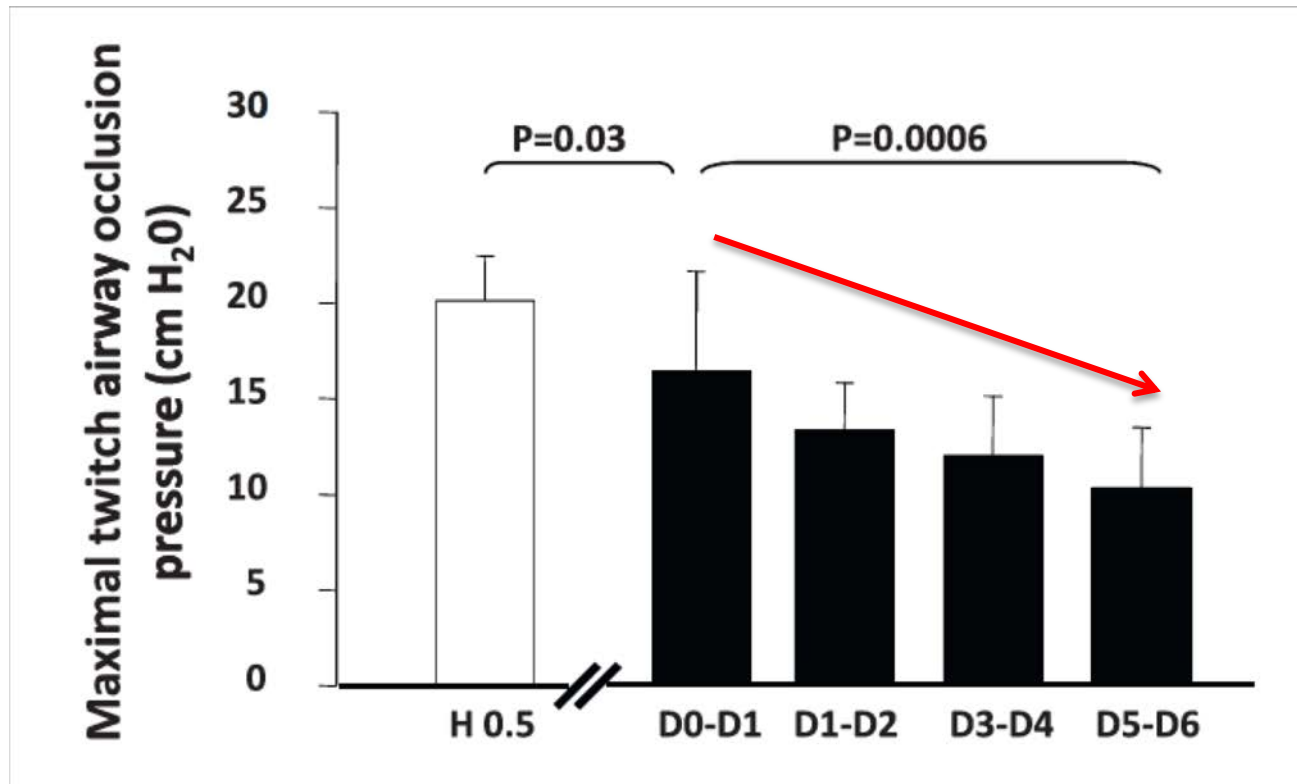
# Monitoring of the Respiratory Muscles in the Critically Ill

Jonne Doorduyn<sup>1</sup>, Hieronymus W. H. van Hees<sup>2</sup>, Johannes G. van der Hoeven<sup>1</sup>, and Leo M. A. Heunks<sup>1</sup>

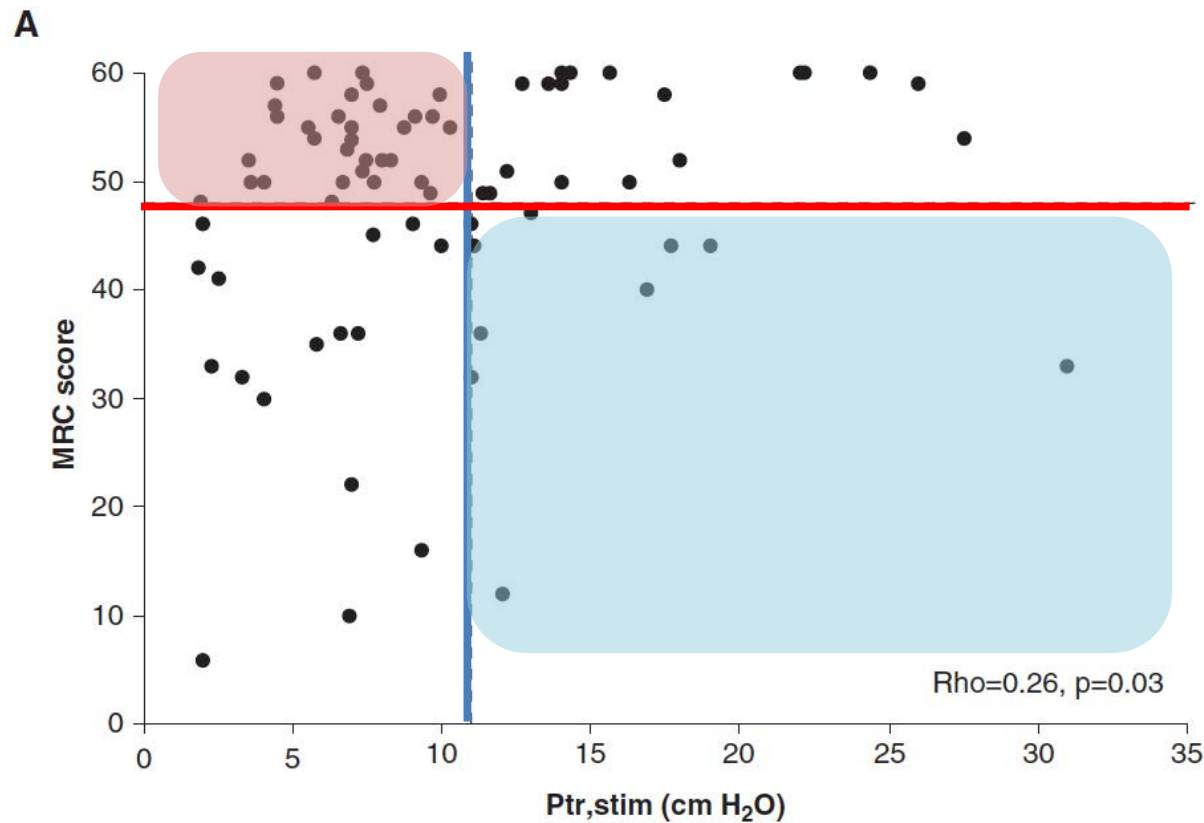
2013



# Rapidly Progressive Diaphragmatic Weakness and Injury during Mechanical Ventilation in Humans



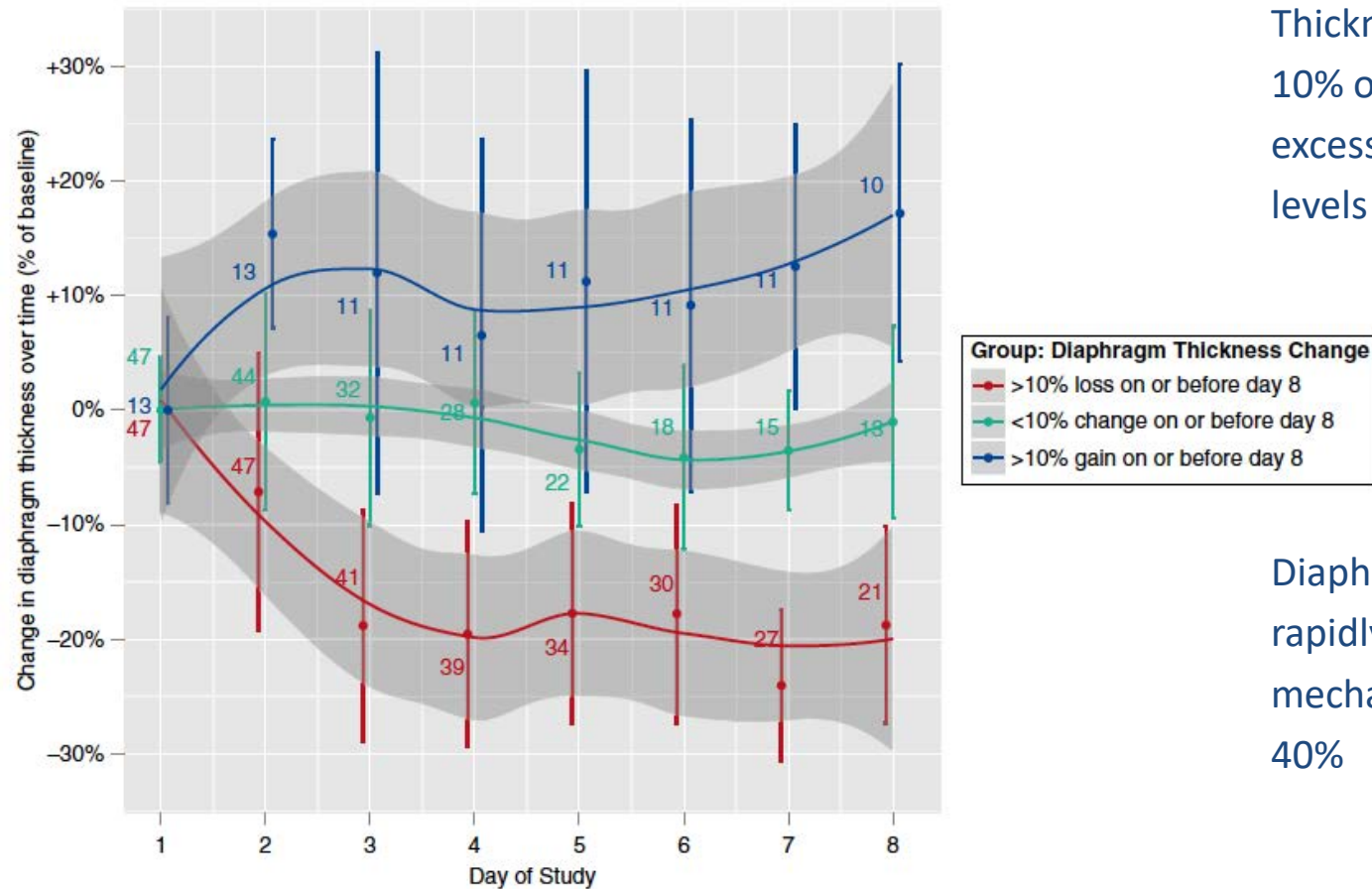
# Coexistence and Impact of Limb Muscle and Diaphragm Weakness at Time of Liberation from Mechanical Ventilation in Medical Intensive Care Unit Patients



76 patients at their first weaning attempt:  
63% had diaphragm dysfunction, 34% had limb muscle weakness and 21% had both

# Evolution of Diaphragm Thickness during Mechanical Ventilation

## Impact of Inspiratory Effort



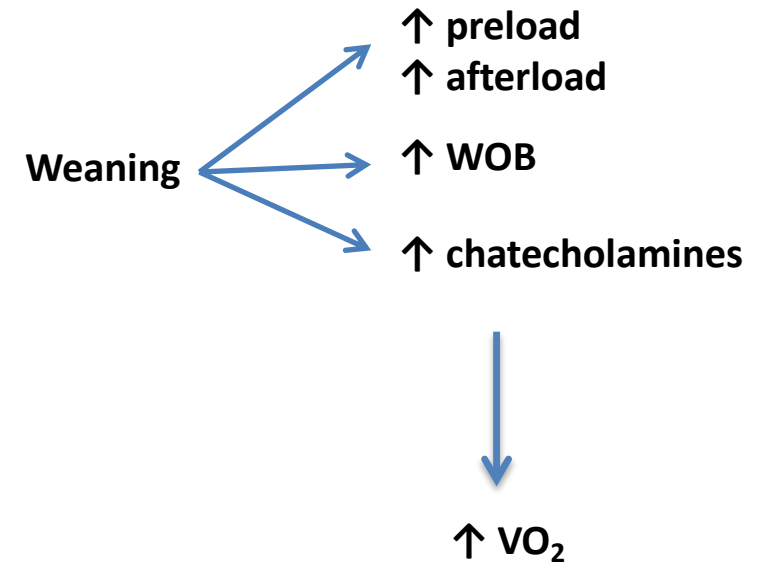
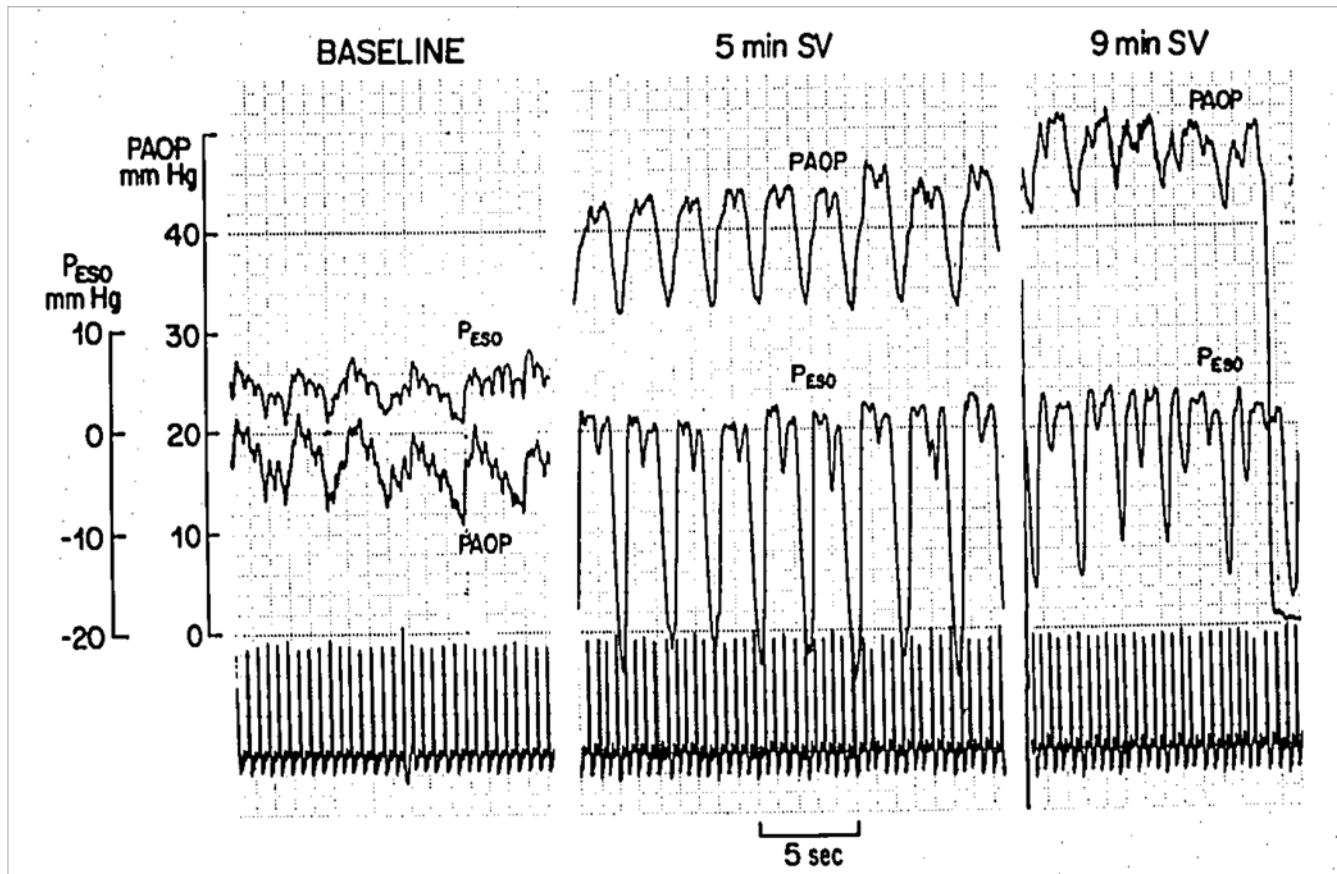
Thickness increases in approximately 10% of patients in association with excess inspiratory effort and lower levels of ventilatory support

Diaphragm thickness decreases rapidly during the first several days of mechanical ventilation in more than 40%



# Acute Left Ventricular Dysfunction during Unsuccessful Weaning from Mechanical Ventilation

Lemaire et al. Anesthesiology 1988



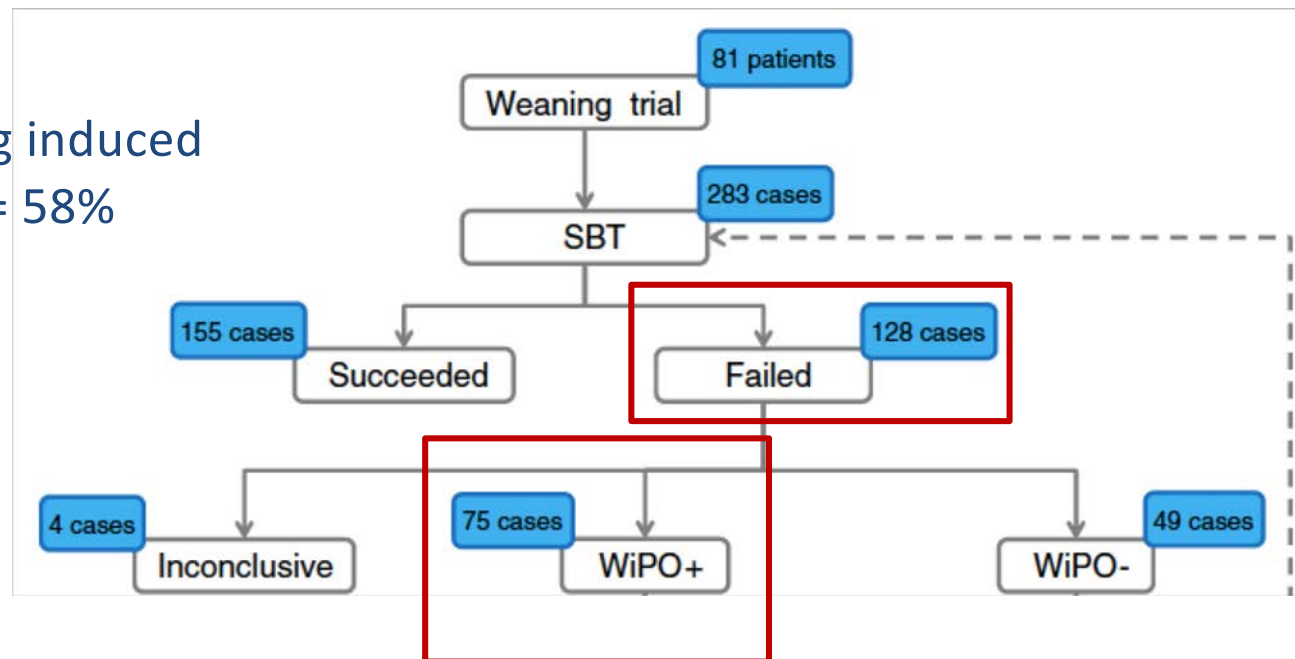
# Cardiac dysfunction induced by weaning from mechanical ventilation: incidence, risk factors, and effects of fluid removal



Critical Care

Jinglun Liu<sup>1,2,3,4†</sup>, Feng Shen<sup>1,2,3,5†</sup>, Jean-Louis Teboul<sup>1,2,3</sup>, Nadia Anguel<sup>1,2,3</sup>, Alexandra Beurton<sup>1,2,3</sup>, Nadia Bezaz<sup>1,2,3</sup>, Christian Richard<sup>1,2,3</sup> and Xavier Monnet<sup>1,2,3\*</sup>

Incidence of weaning induced cardiac dysfunction = 58%



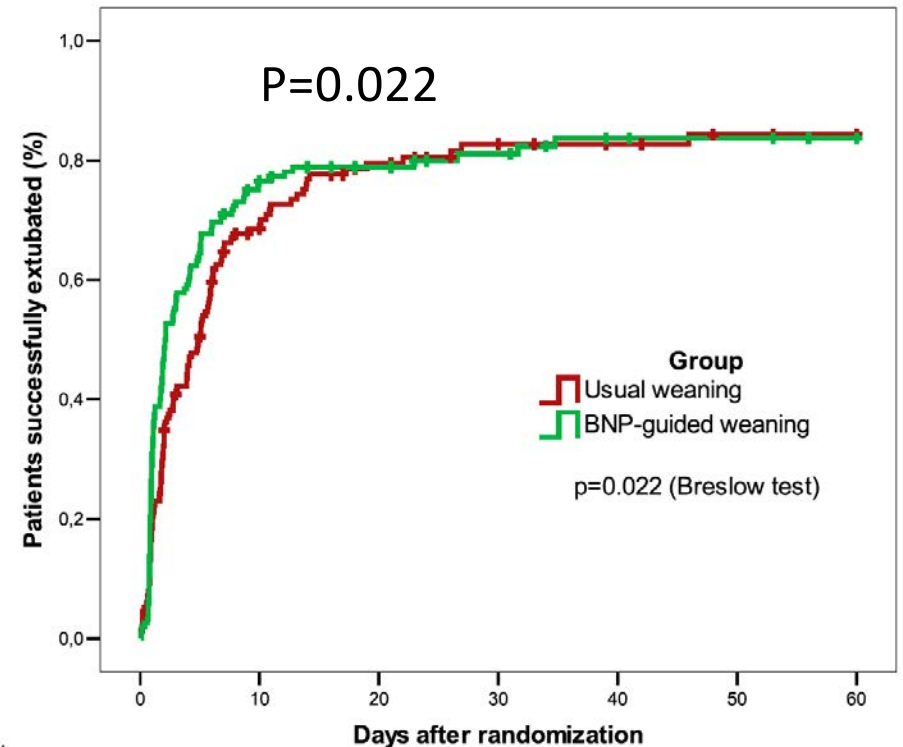
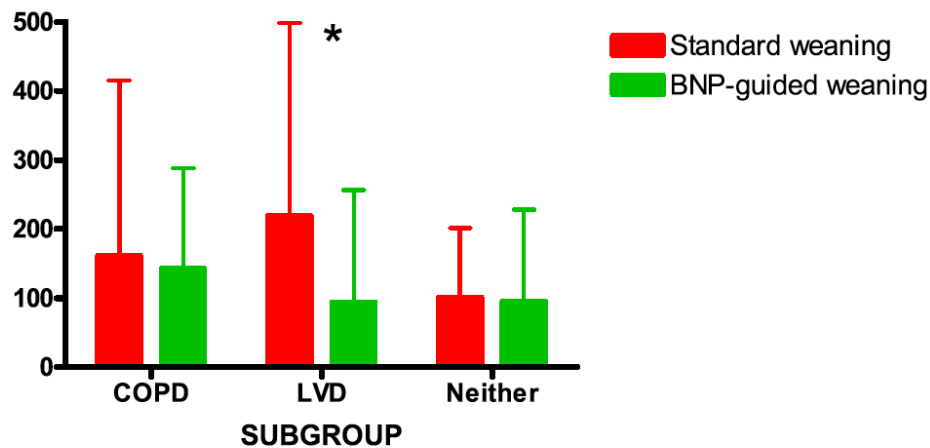
# Natriuretic Peptide–driven Fluid Management during Ventilator Weaning

A Randomized Controlled Trial



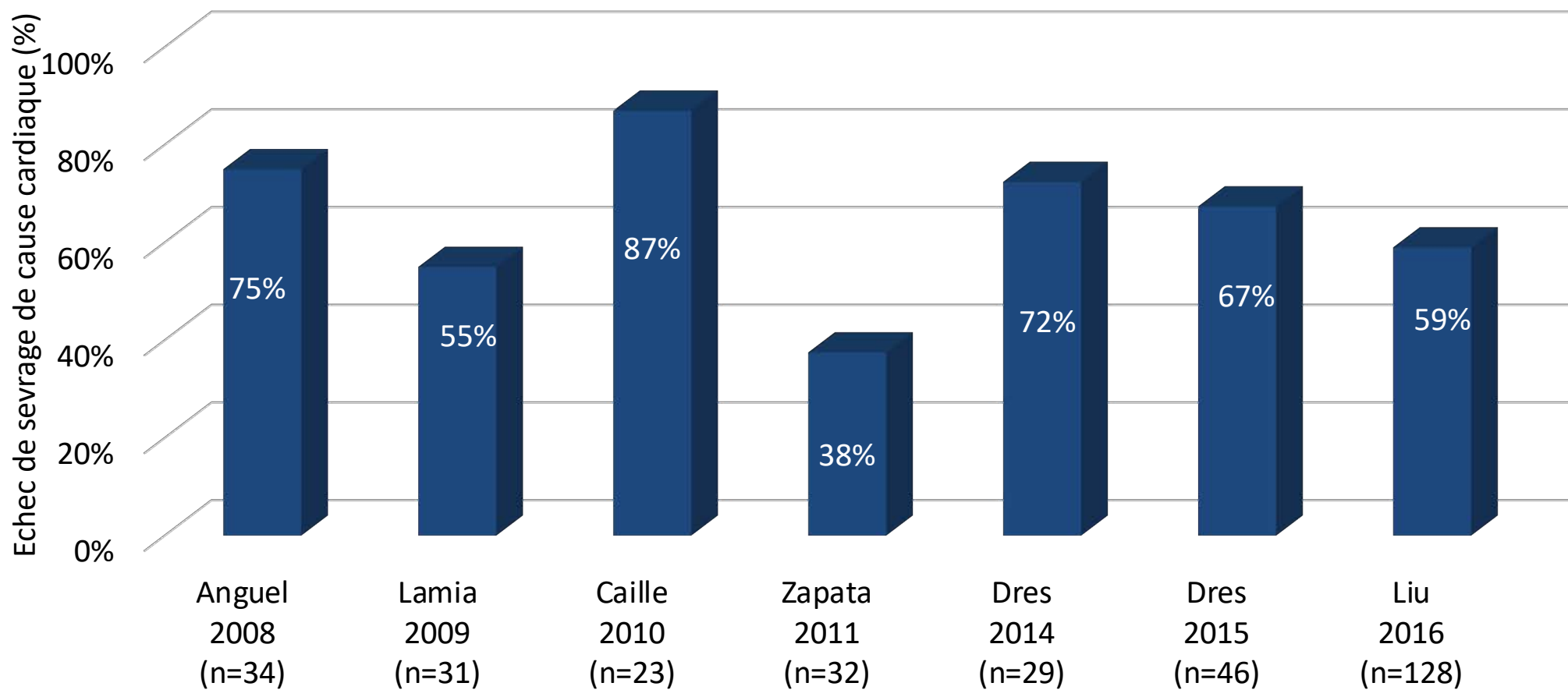
Mekontso-Dessap et al. AJRCCM 2012

Time to successful weaning

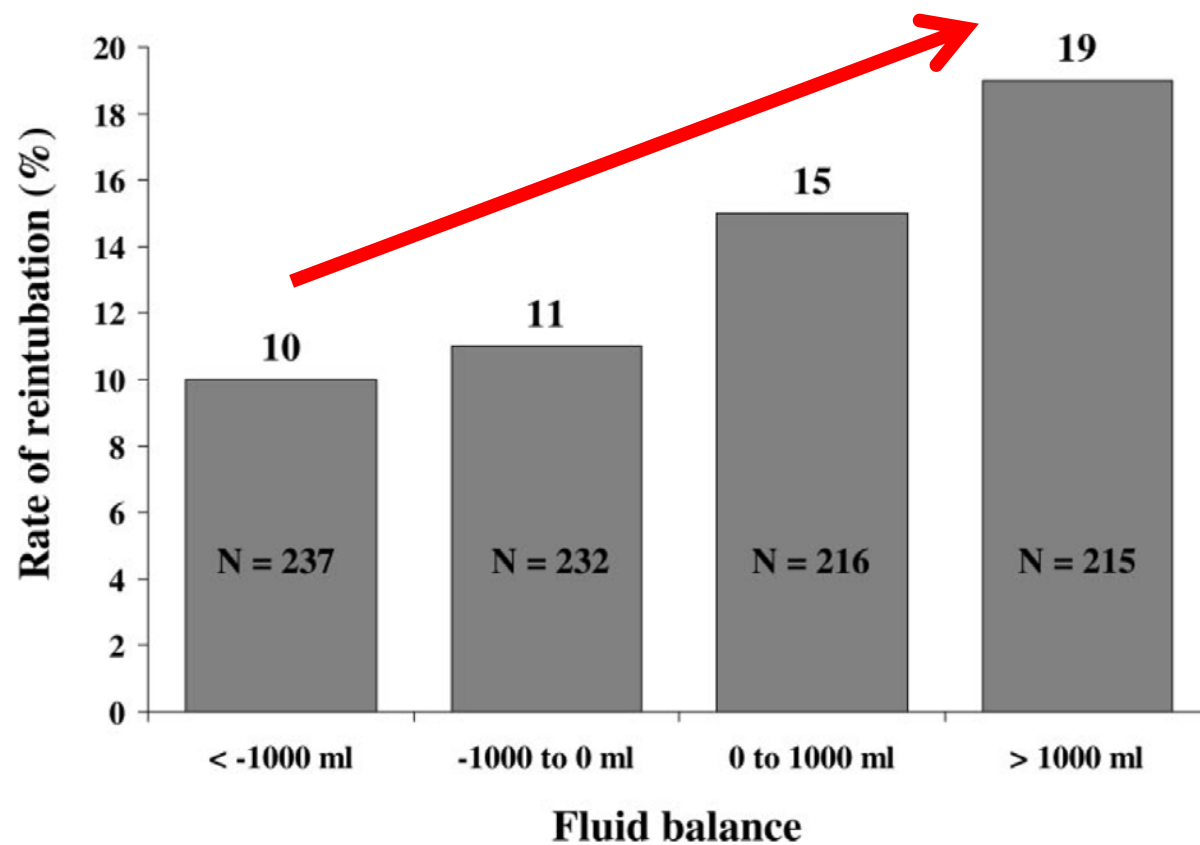


Number at risk	0	10	20	30	40	50	60
Usual care	152	39	22	15	12	9	6
BNP-guided	152	32	21	16	11	10	8

# Incidence de l'OAP au cours du sevrage



# Risk Factors for Extubation Failure in Patients Following a Successful Spontaneous Breathing Trial\*



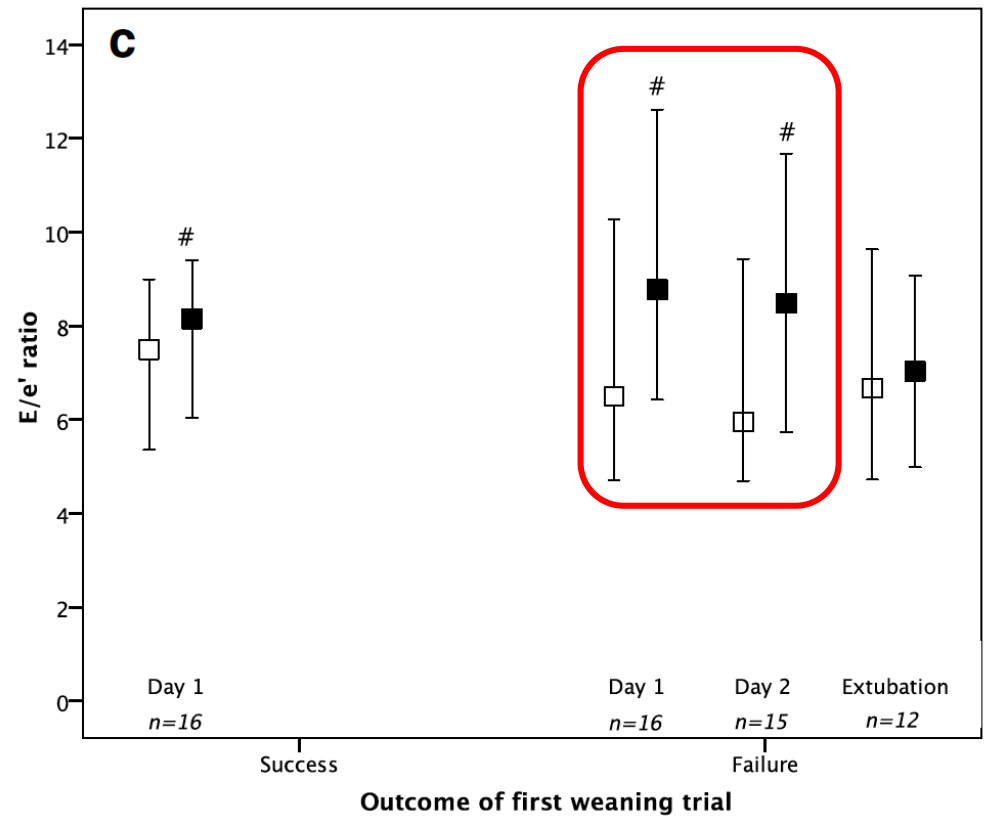
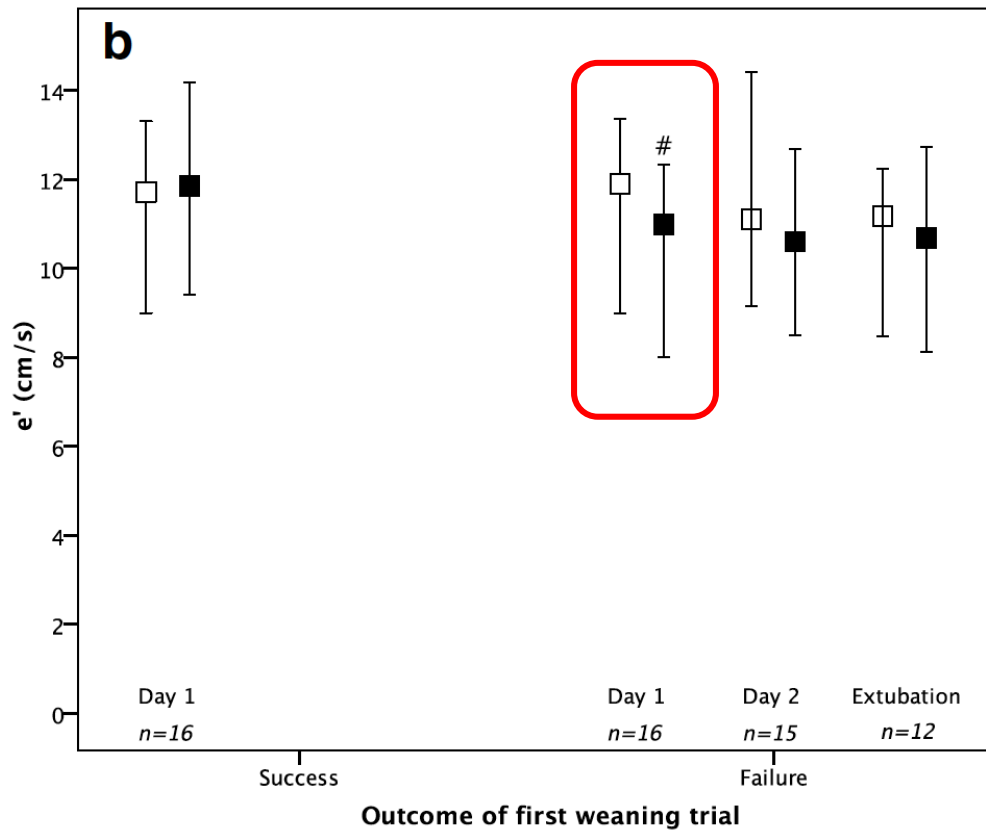
N=900 Patients

121 Extubation Failure

# Cardiac function during weaning failure: the role of diastolic dysfunction

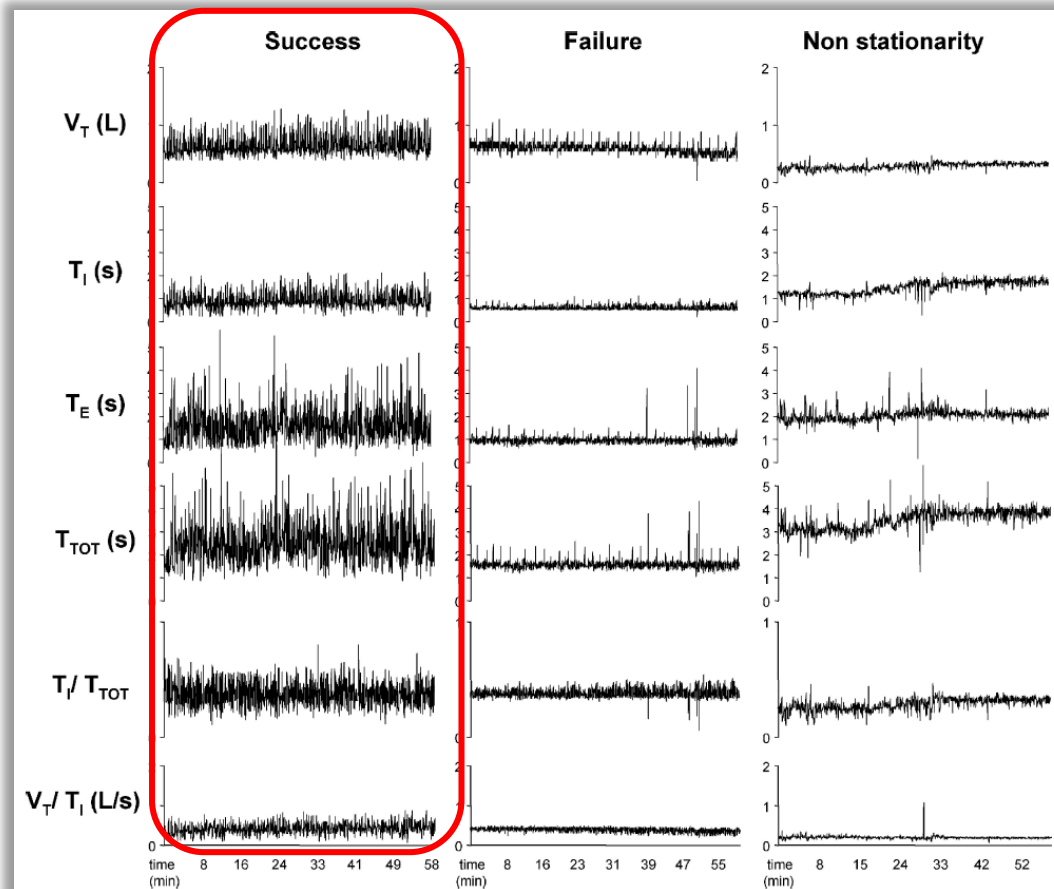
Annals of Intensive Care  
Roche-campo et al. 2017

N=67



# Reduced breathing variability as a predictor of unsuccessful patient separation from mechanical ventilation\*

Wysocki et al. 2006



51 patients – 46 analyzed

Variability is a main characteristic of ventilation

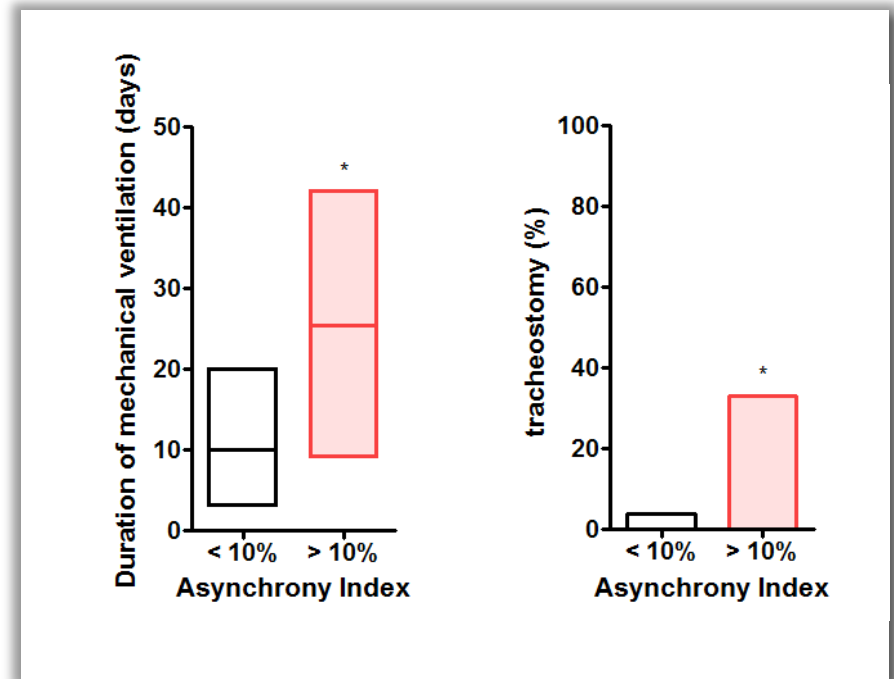
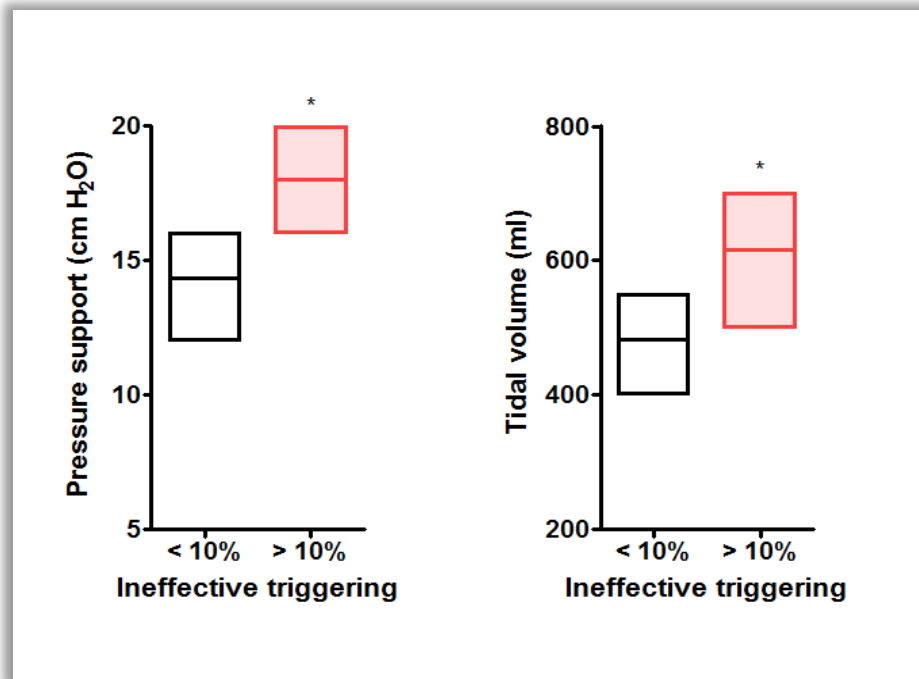




Arnaud W. Thille  
Pablo Rodriguez  
Belen Cabello  
François Lellouche  
Laurent Brochard

## Patient-ventilator asynchrony during assisted mechanical ventilation

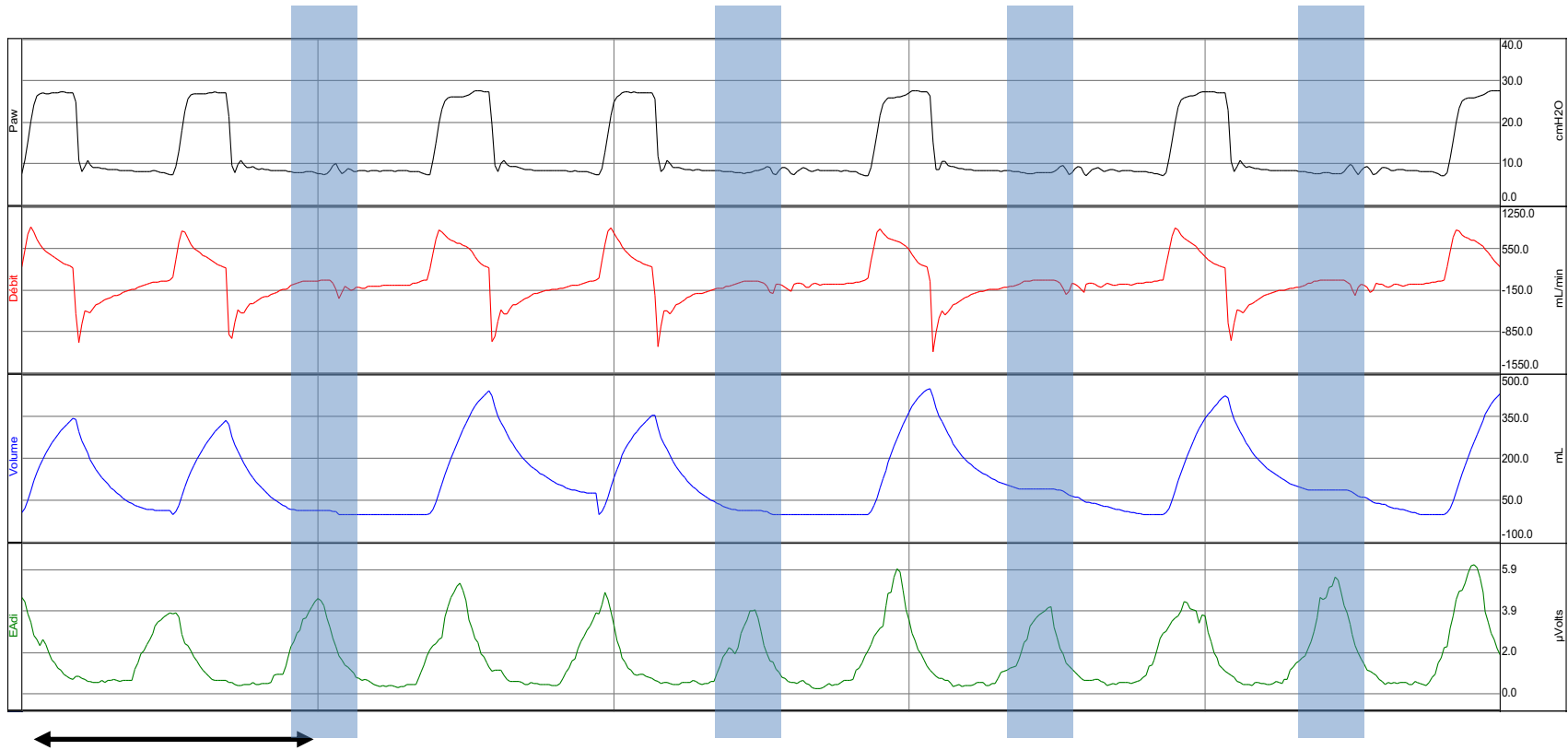
62 patients under mechanical ventilation: 24% presented an asynchrony index higher than 10%





# Over-Assistance

PSV 160%



4 sec

# Mechanical Ventilation–induced Diaphragm Atrophy Strongly Impacts Clinical Outcomes



Gohliger et al. AJRCCM (2018) 197; 204-213

Over assistance – Diaphragm atrophy

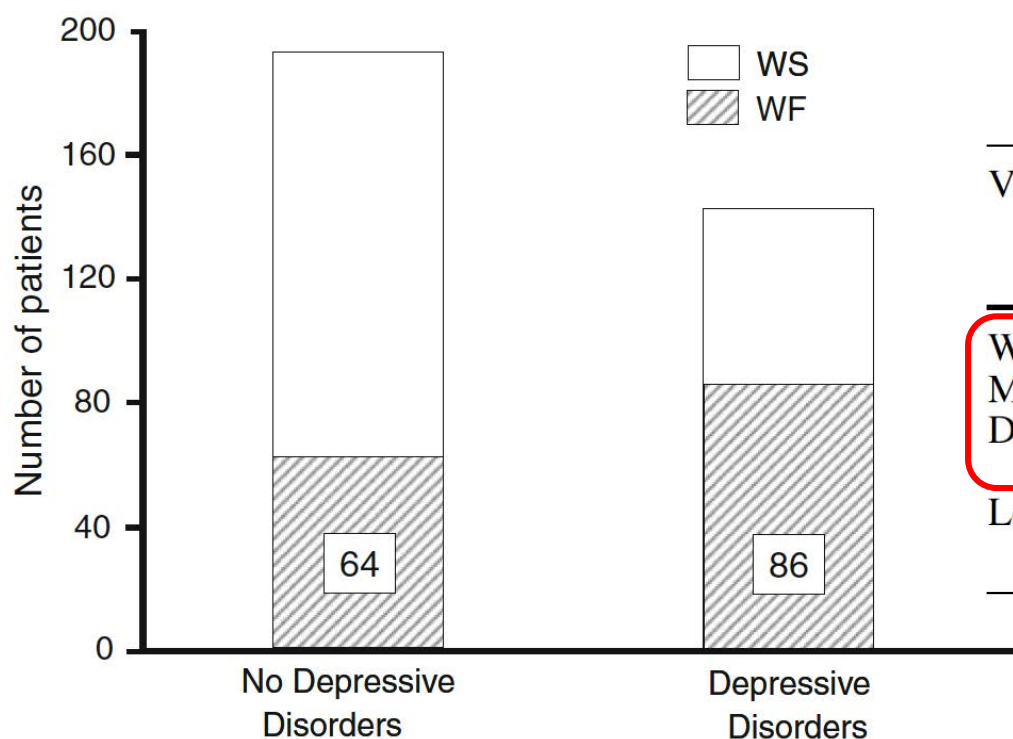
Under-assistance – Strong effort

Outcome	Initial Change in Diaphragm Thickness during First Week of Ventilation Patients with $\geq 2$ Measurements ( $n = 191$ )			Statistical Comparisons Adjusted Count Ratio or Adjusted Odds Ratio (95% CI)*	
	$\geq 10\%$ Decrease in Thickness ( $n = 78$ ; 41%)	$< 10\%$ Change in Thickness ( $n = 66$ ; 35%)	$\geq 10\%$ Increase in Thickness ( $n = 47$ ; 24%)	$\geq 10\%$ Decrease in Thickness vs. $< 10\%$ Change in Thickness	$\geq 10\%$ Increase in Thickness vs. $< 10\%$ Change in Thickness
Ventilator-free days to Day 60	46 (0–53)	51 (0–55)	37 (0–51)	0.77 (0.59–1.00)	0.91 (0.67–1.22)
Duration of ventilation (in ICU survivors), d	9 (5–17) <sup>†</sup>	5 (4–9)	10 (6–22) <sup>†</sup>	1.69 (1.28–2.24)	1.38 (1.00–1.90)
Duration of ICU admission (in ICU survivors), d	12.5 (7–21) <sup>†</sup>	8 (5–12)	14 (7–24) <sup>†</sup>	1.71 (1.29–2.27)	1.31 (0.94–1.83)
Duration of hospitalization (in hospital survivors), d	29 (16–58) <sup>†</sup>	22 (11–51)	30 (17–65)	1.44 (1.01–2.05)	1.23 (0.71–1.60)
Complications of acute respiratory failure, $n$ (%) <sup>‡</sup>	49 (64) <sup>†</sup>	31 (48)	31 (67) <sup>†</sup>	3.00 (1.34–6.72)	1.84 (0.77–4.43)
Reintubation, $n$ (%)	16 (21) <sup>†</sup>	5 (8)	12 (26) <sup>†</sup>	3.55 (1.14–11.05)	3.24 (0.97–10.88)
Tracheostomy, $n$ (%)	20 (26) <sup>†</sup>	7 (11)	11 (23)	3.58 (1.29–9.97)	2.11 (0.66–6.70)
Mechanical ventilation >14 d, $n$ (%)	27 (35) <sup>†</sup>	14 (21)	20 (43) <sup>†</sup>	2.97 (1.26–6.97)	2.16 (0.87–5.40)
Readmission to ICU during same hospital admission, $n$ (%)	5 (7)	9 (15)	9 (20)	0.78 (0.21–2.84)	2.32 (0.70–7.67)
Death in ICU, $n$ (%)	19 (24)	12 (18)	11 (23)	1.55 (0.61–3.95)	1.28 (0.45–3.65)
Death in hospital, $n$ (%)	28 (37)	21 (3)	17 (37)	1.66 (0.73–3.76)	0.94 (0.38–2.34)

Optimal assistance

# Depressive disorders during weaning from prolonged mechanical ventilation

Intensive Care Med (2010) 36:828–835



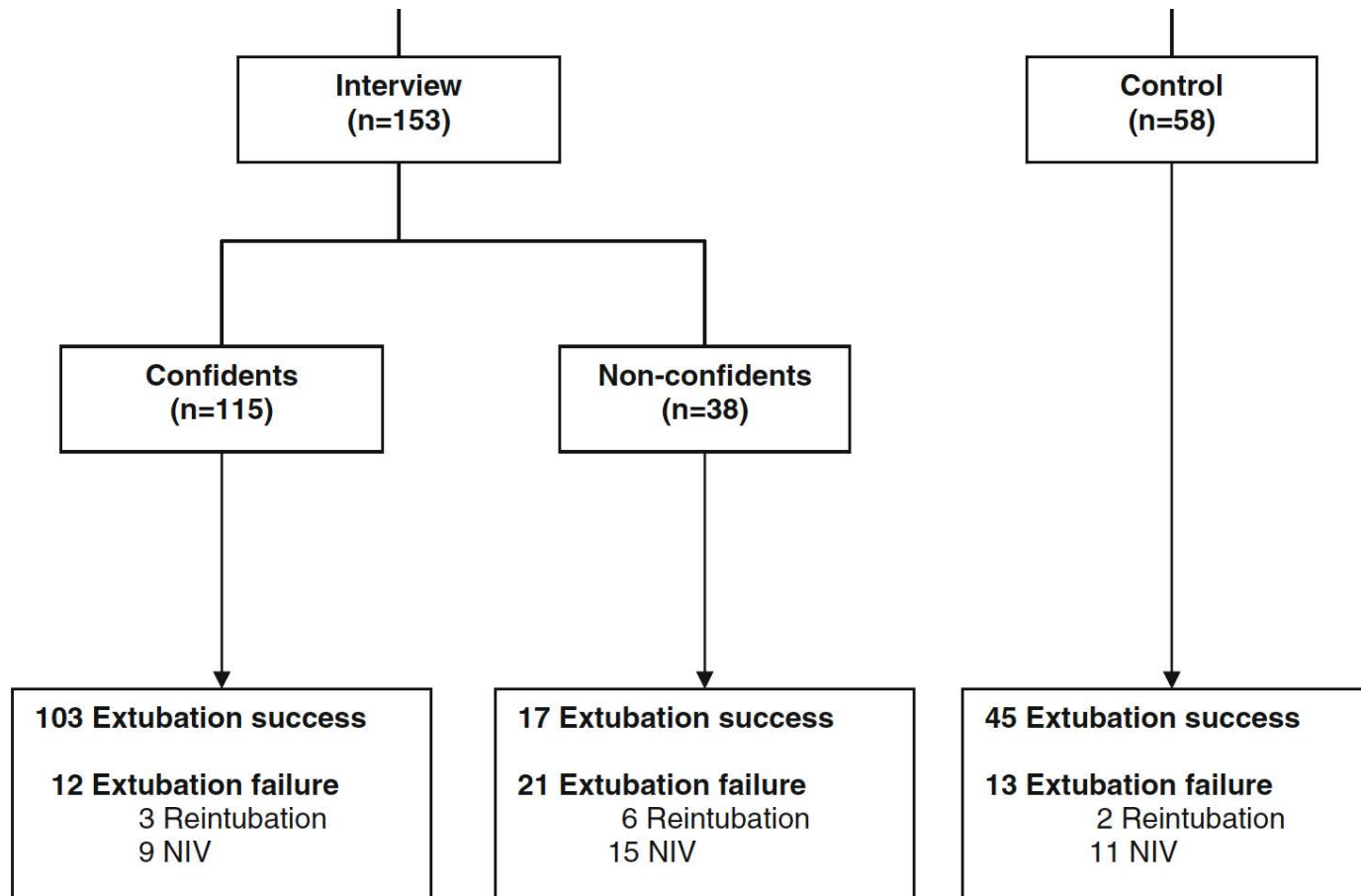
**N=336**

Variable	No depressive disorders ( <i>n</i> = 194)	Depressive disorders ( <i>n</i> = 142)	<i>P</i> value
Weaning failure (%)	33.0	60.6	0.0001
Mortality (%)	10.3	23.9	0.0008
Duration of MV at RMLH, days, median (IOR)	13 (5–38)	24 (8–41)	0.007
Length of stay at RMLH, days, median (IQR)	33 (24–42)	35 (23–46)	0.55

**Depressive disorders= 42%**

Jubran et al. ICM 2010

# Patients' prediction of extubation success

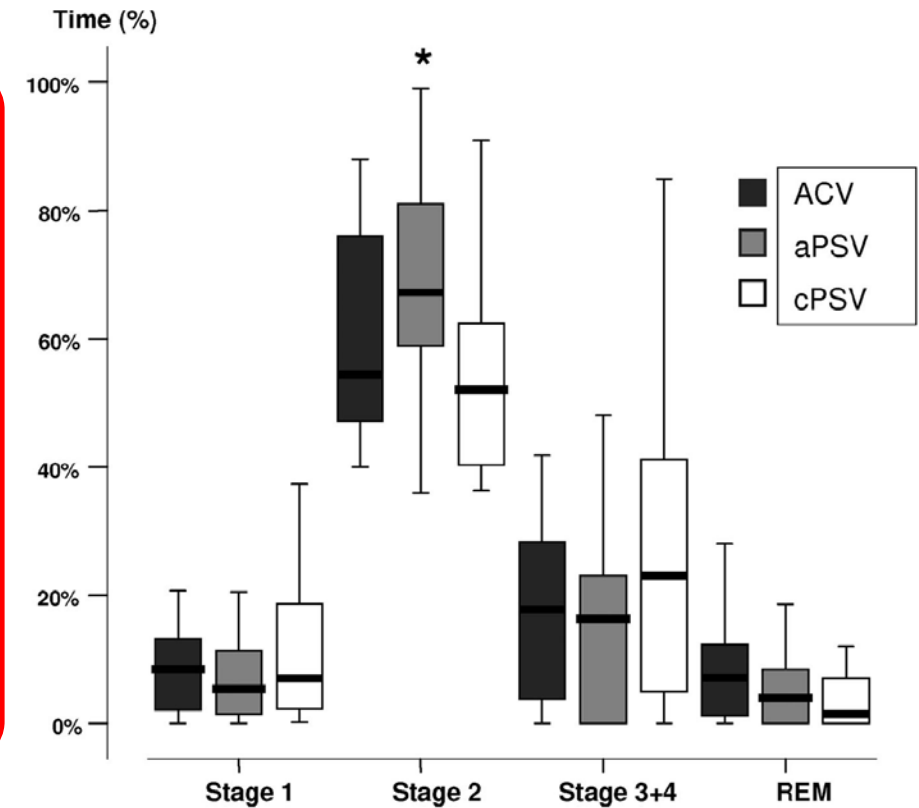


# Sleep quality in mechanically ventilated patients: Comparison of three ventilatory modes

Cabello B et al. CCM 2008

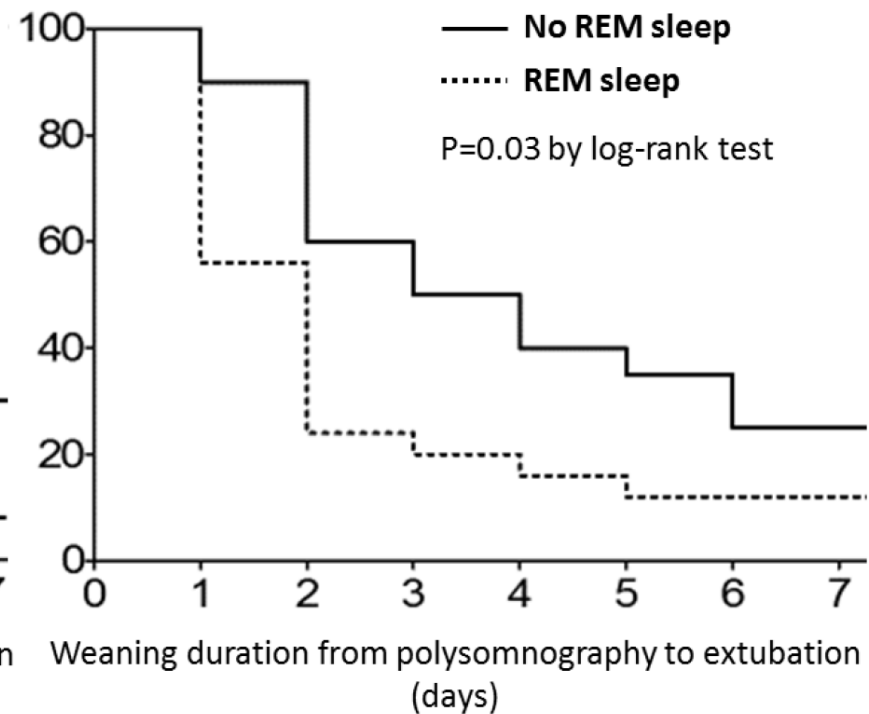
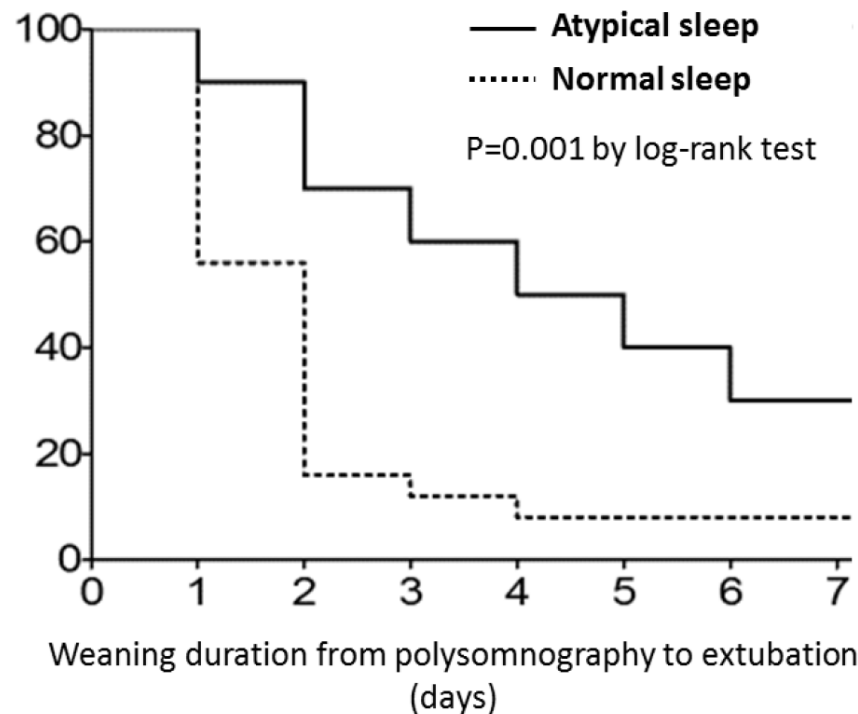
Table 2. Sleep architecture and fragmentation during the study (18 hours)

Patient, N	Stage 1, %	Stage 2, %	Stage 3 and 4, mins	Rapid Eye Movement, %	Fragmentation Index
1	2	83	102	1	15
2	1	64	119	18	25
3	5	57	246	10	35
4	8	68	73	0	41
5	10	66	98	7	41
6	7	64	67	13	53
7	8	48	91	7	37
8	1	51	178	13	67
9	17	49	63	15	20
10	10	47	119	12	19
11	4	49	300	11	29
12	3	88	54	0	11
13	15	41	151	11	51
14	16	74	31	5	14
15	8	79	35	2	23
Median [25–75th percentiles]	8 [3–11]	63 [48–74]	98 [63–151]	10 [2–13]	29 [19–41]



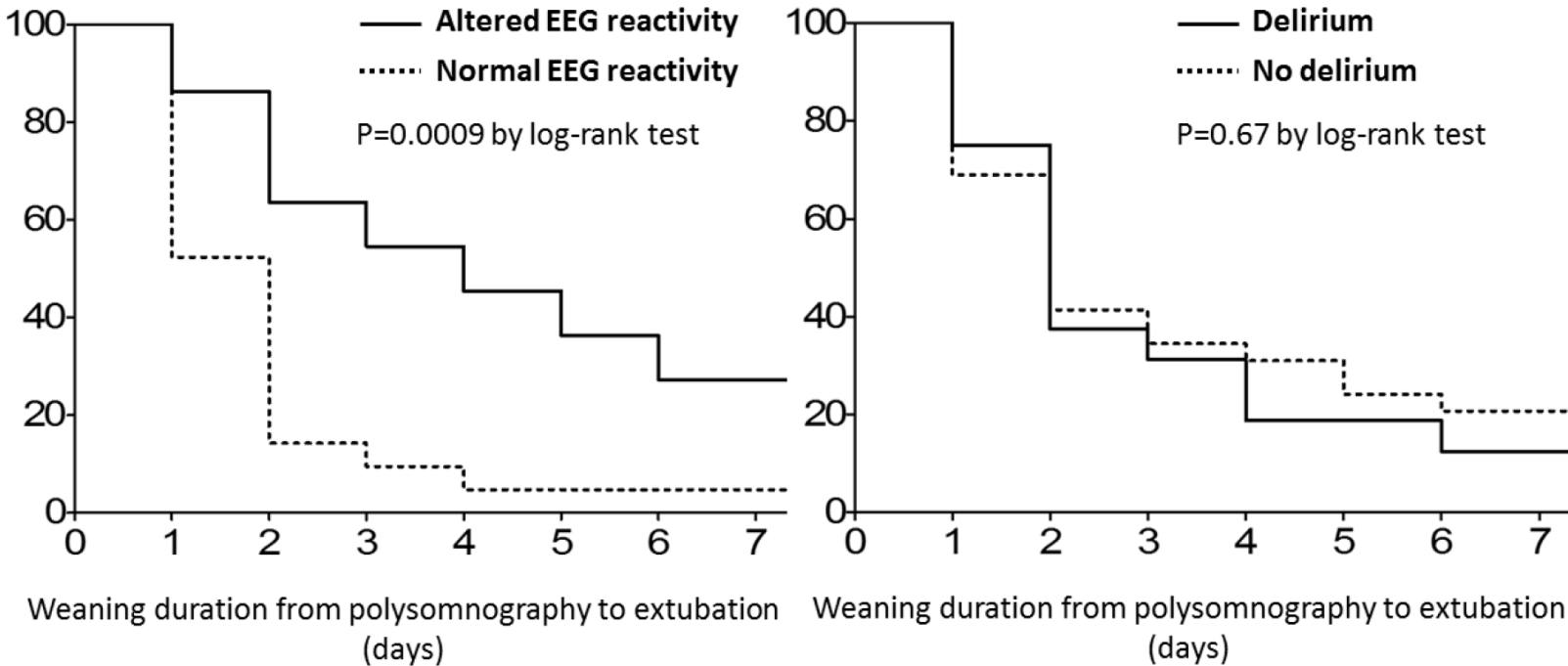
# Impact of sleep alterations on weaning duration in mechanically ventilated patients: a prospective study

Thille AW et al. ERJ 2018



# Impact of sleep alterations on weaning duration in mechanically ventilated patients: a prospective study

Thille AW et al. ERJ 2018



# Delirium and Circadian Rhythm of Melatonin During Weaning From Mechanical Ventilation

## An Ancillary Study of a Weaning Trial

Mekontso Dessap *et al.* Chest 2015

Outcome	Mental Status at Initiation of Weaning <sup>a</sup>		P Value
	Normal (n = 24)	Delirious (n = 43)	
Time to first extubation, h			.086
Median (IQR)	27.5 (21.7-62.0)	49.7 (21.4-137.6)	
Mean (SD)	43.0 (29.6)	111.7 (176.6)	
Time to successful extubation, h			.086
Median (IQR)	27.4 (21.1-72.2)	51.0 (21.9-143.5)	
Mean (SD)	56.4 (59.3)	164.8 (255.3)	
Ventilator-free days from randomization to d 28			.044
Median (IQR)	26.6 (23.7-27.1)	23.1 (0.8-27.1)	
Mean (SD)	23.5 (7.6)	17.7 (11.5)	
Ventilator-free days from randomization to d 60			.027
Median (IQR)	58.6 (55.7-59.1)	54.4 (25.2-58.9)	
Mean (SD)	52.9 (16.4)	41.7 (23.8)	



# Delirium and Circadian Rhythm of Melatonin During Weaning From Mechanical Ventilation

## An Ancillary Study of a Weaning Trial

Mekontso Dessap *et al.* Chest 2015

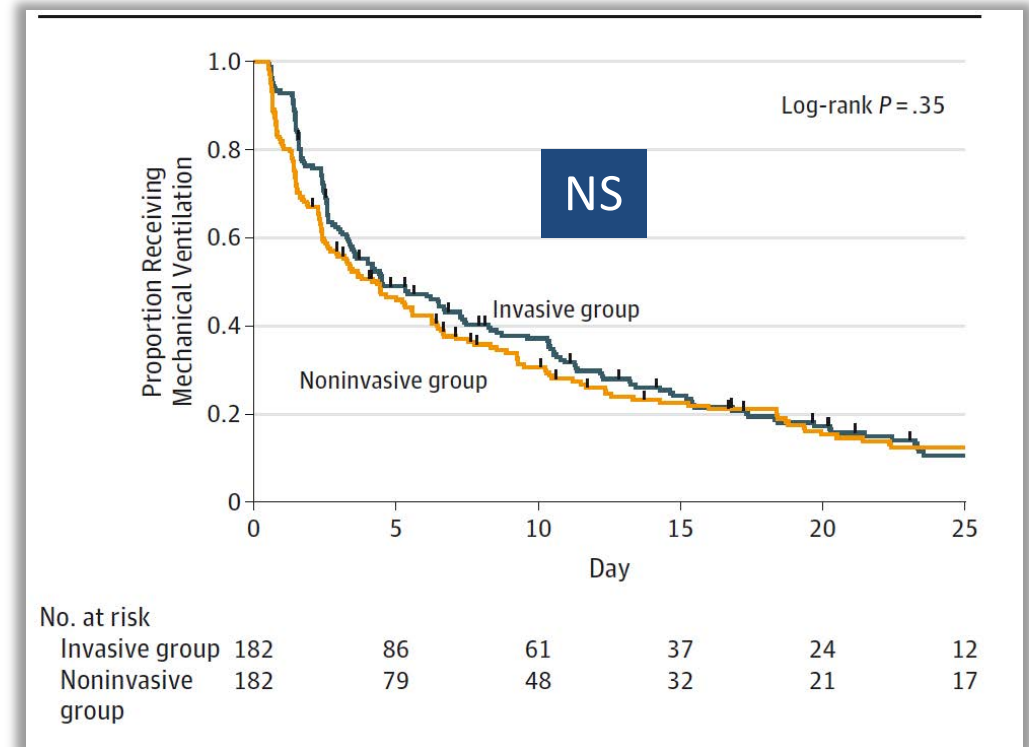
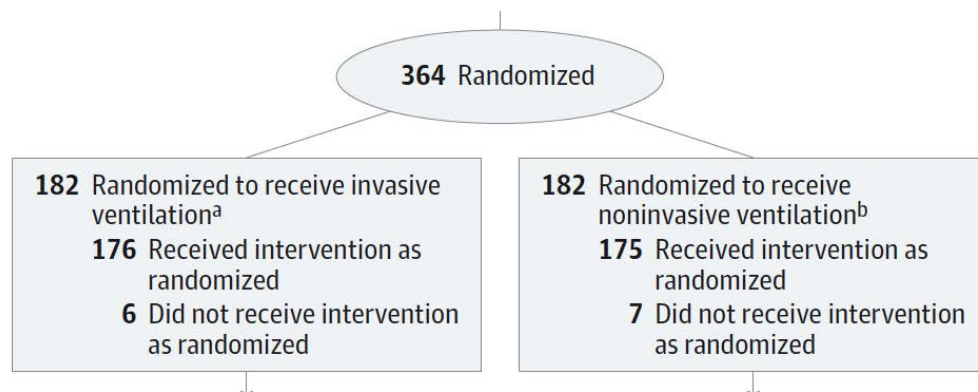
Respiratory function			
Respiratory worsening requiring a return to assist-control ventilation	5 (20.8)	21 (48.8)	.024
Ventilator-associated pneumonia	2 (8.3)	13 (30.2)	.039
Ventilator-associated complication	1 (4.2)	11 (25.6)	.044
Need for noninvasive ventilation after extubation	11 of 23 (47.8)	16 of 38 (42.1)	.663
Reintubation within 72 h after extubation	3 of 23 (13.0)	6 of 38 (15.8)	> .99
Tracheostomy	1 (4.2)	5 (11.6)	.408
Cardiovascular function			
Need for fluid loading	7 (29.2)	23 (53.5)	.055
Need for catecholamine infusion	9 (37.5)	21 (48.8)	.371
Neurologic function			
Need for continuous sedation because of clinical worsening	2 (8.3)	30 (69.8)	< .001
Need for continuous analgesia because of clinical worsening	1 (4.2)	24 (55.8)	< .001

# Effect of Protocolized Weaning With Early Extubation to Noninvasive Ventilation vs Invasive Weaning on Time to Liberation From Mechanical Ventilation Among Patients With Respiratory Failure

## The Breathe Randomized Clinical Trial

Perkins et al. 2018

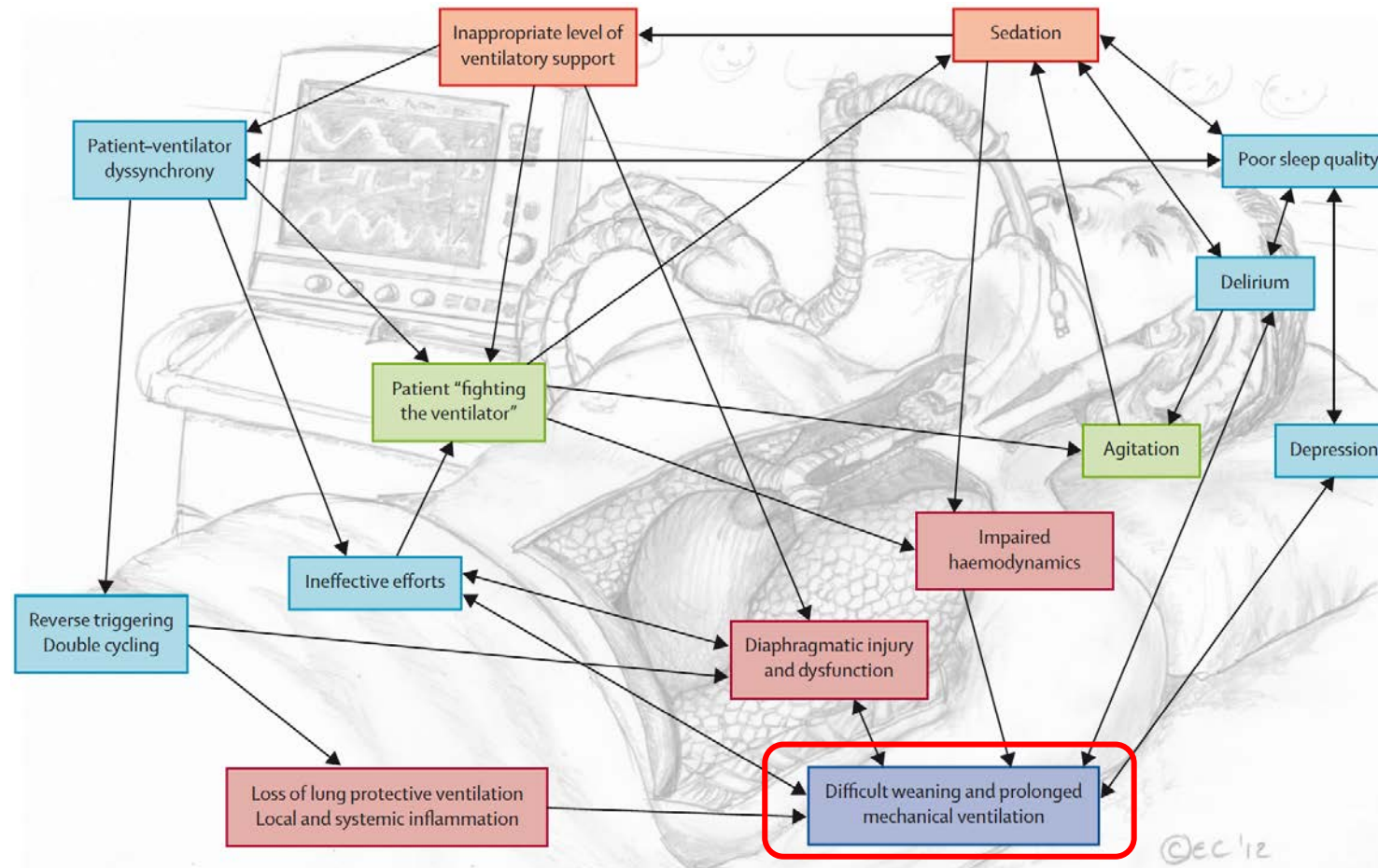
**JAMA | Original Investigation**

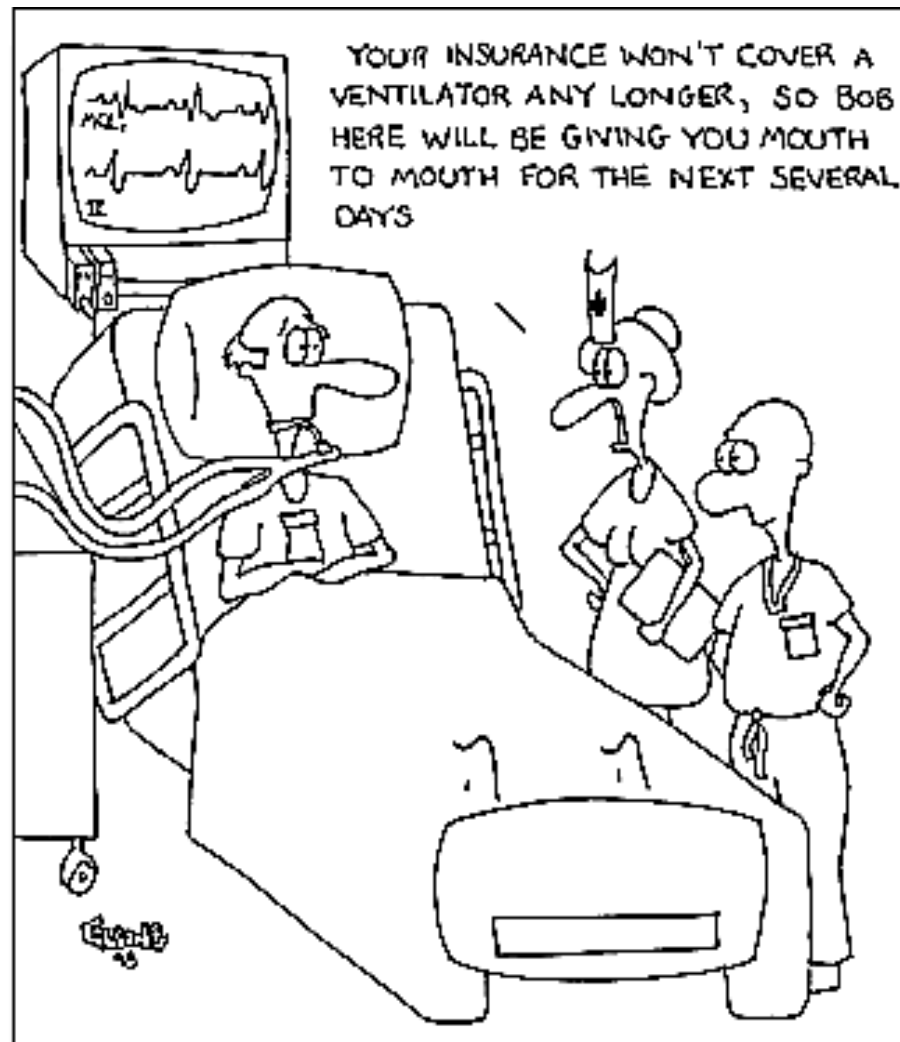


# Clinical challenges in mechanical ventilation

Ewan C Goligher, Niall D Ferguson, Laurent J Brochard

Lancet 2016







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