PNEUMOLOGIA 2018

Milano, 14 – 16 giugno 2018 · Centro Congressi Palazzo delle Stelline

10.30 - 11.00 **Lettura** VMNI: quando serve e quando è giusto fermarsi *Stefano Nava (Bologna)*

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Conflict of Interest

I have affiliations with, special interests, or have conducted business with the following companies that in context with this presentation might possibly constitute a real or perceived conflict of interest:

- Philips (speaking fee and advisory board)
- Resmed (speaking fee and travel grants)
- Breas (advisory board)
- Fisher and Paykel (research grant and speaking fee)

Punto 1. =QUANDO SERVE ?

Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

Bram Rochwerg[1], Laurent Brochard[2,3], Mark W. Elliott[4], Dean Hess[5], Nicholas S. Hill[6], Stefano Nava[7] and Paolo Navalesi[8] (members of the steering committee); Massimo Antonelli[9], Jan Brozek[1], Giorgio Conti[9], Miquel Ferrer[10], Kalpalatha Guntupalli[11], Samir Jaber[12], Sean Keenan[13,14], Jordi Mancebo[15], Sangeeta Mehta[16] and Suhail Raoof[17,18] (members of the task force)

Do we need Guidelines and an EBM process ?

Probably to minimize the bias of large variabily in dealing with similar issue

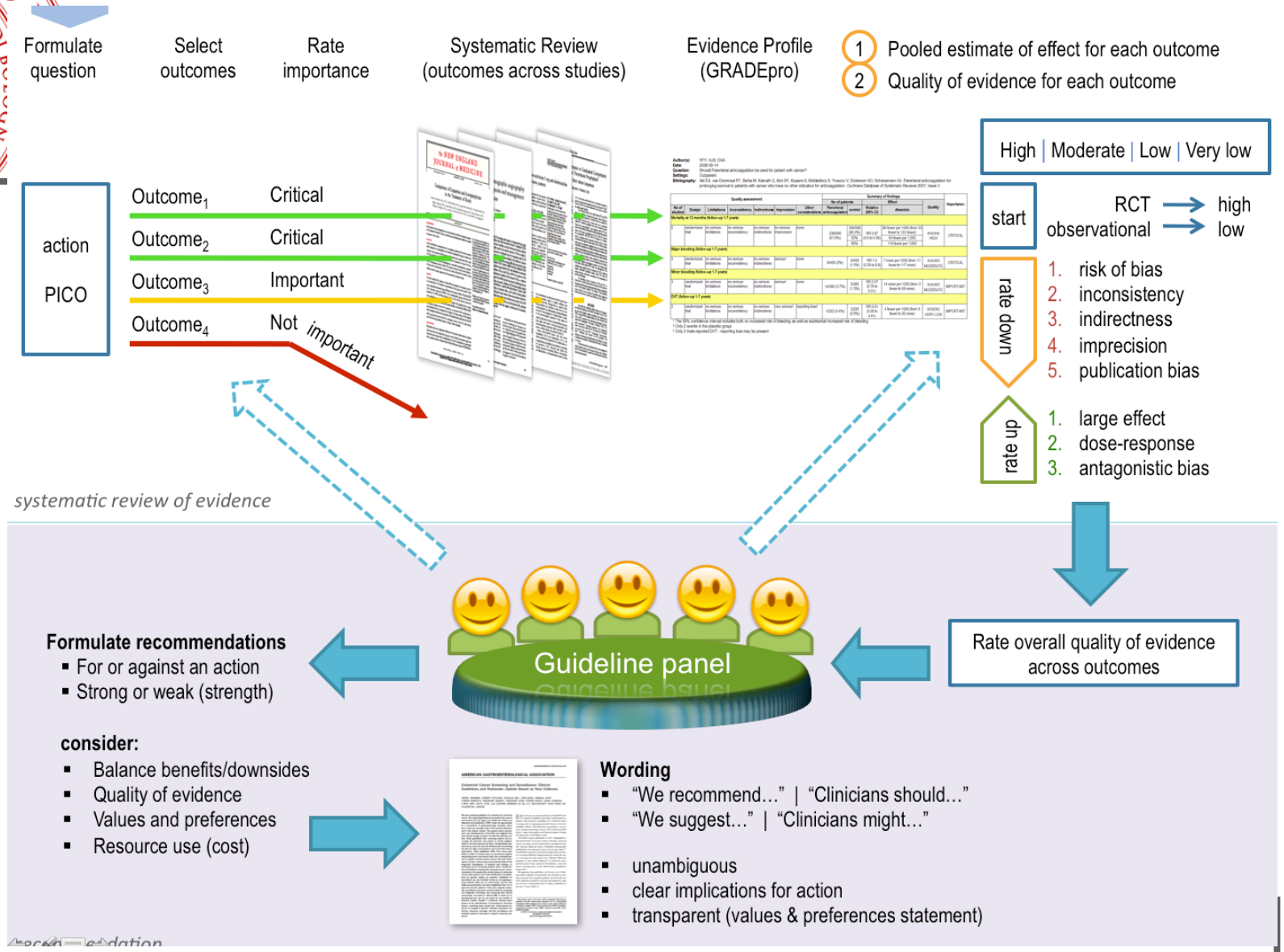
The example of WEANING

“Weaning” according to Rubens

“Weaning” according to Tricia KLINE

“Weaning” according to Diego RIVERA

PICO= Population-Intervention–Comparison-Outcome



The “easiest” one:

THE CASE of COPD

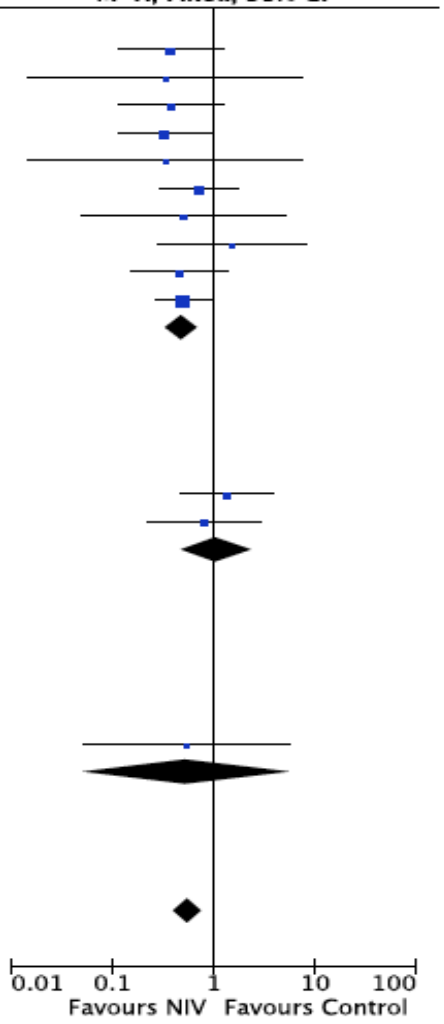
Mortality

TASK FORCE REPORT
ERS/ATS GUIDELINES

Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

Bram Rochwerg[1], Laurent Brochard[2,3], Mark W. Elliott[4], Dean Hess[5], Nicholas S. Hill[6], Stefano Nava[7] and Paolo Navalesi[8] (members of the steering committee); Massimo Antonelli[9], Jan Brozek[3], Giorgio Conti[9], Miquel Ferrer[10], Kalpalatha Guntupalli[11], Samir Jaber[12], Sean Keenan[13,14], Jordi Mancebo[15], Sangeeta Mehta[16] and Suhail Raoof[17,18] (members of the task force)

Study or Subgroup	NIV Events	NIV Total	Standard Medical Care Events	Standard Medical Care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Compared to standard of care						
Avdeev 1998	3	26	9	29	9.7%	0.37 [0.11, 1.23]
Bardi 2000	0	15	1	15	1.7%	0.33 [0.01, 7.58]
Bott 1993	3	26	9	30	9.5%	0.38 [0.12, 1.27]
Brochard 1995	4	43	12	42	13.8%	0.33 [0.11, 0.93]
Celikel 1998	0	15	1	15	1.7%	0.33 [0.01, 7.58]
Chen 2005	12	171	7	71	11.3%	0.71 [0.29, 1.73]
Dikensoy 2002	1	17	2	17	2.3%	0.50 [0.05, 5.01]
Khilnani 2010	3	20	2	20	2.3%	1.50 [0.28, 8.04]
Martin 2000	3	12	6	11	7.1%	0.46 [0.15, 1.40]
Plant 2000	12	118	24	118	27.3%	0.50 [0.26, 0.95]
Subtotal (95% CI)		**463**		**368**	**86.8%**	**0.49 [0.34, 0.70]**
Total events	41		73			
Heterogeneity: $Chi^2 = 3.46$, df = 9 (P = 0.94); $I^2 = 0\%$						
Test for overall effect: Z = 3.89 (P = 0.0001)						
1.1.2 Compared to MV						
Conti 2002	6	23	5	26	5.3%	1.36 [0.48, 3.86]
Jurjevic 2009	4	78	5	78	5.7%	0.80 [0.22, 2.87]
Subtotal (95% CI)		**101**		**104**	**11.0%**	**1.07 [0.48, 2.39]**
Total events	10		10			
Heterogeneity: $Chi^2 = 0.40$, df = 1 (P = 0.53); $I^2 = 0\%$						
Test for overall effect: Z = 0.16 (P = 0.87)						
1.1.3 Patients with ARF who are not acidotic						
Barbe 1996	0	10	0	10		Not estimable
Keenan 2005	1	25	2	27	2.2%	0.54 [0.05, 5.59]
Subtotal (95% CI)		**35**		**37**	**2.2%**	**0.54 [0.05, 5.59]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.52 (P = 0.61)						
Total (95% CI)		**599**		**509**	**100.0%**	**0.55 [0.40, 0.77]**
Total events	52		85			
Heterogeneity: $Chi^2 = 6.98$, df = 12 (P = 0.86); $I^2 = 0\%$						
Test for overall effect: Z = 3.58 (P = 0.0003)						
Test for subgroup differences: $Chi^2 = 3.02$, df = 2 (P = 0.22), $I^2 = 33.7\%$						



COPD Evidence Profile

How much can we trust the evidence?

What is the evidence?

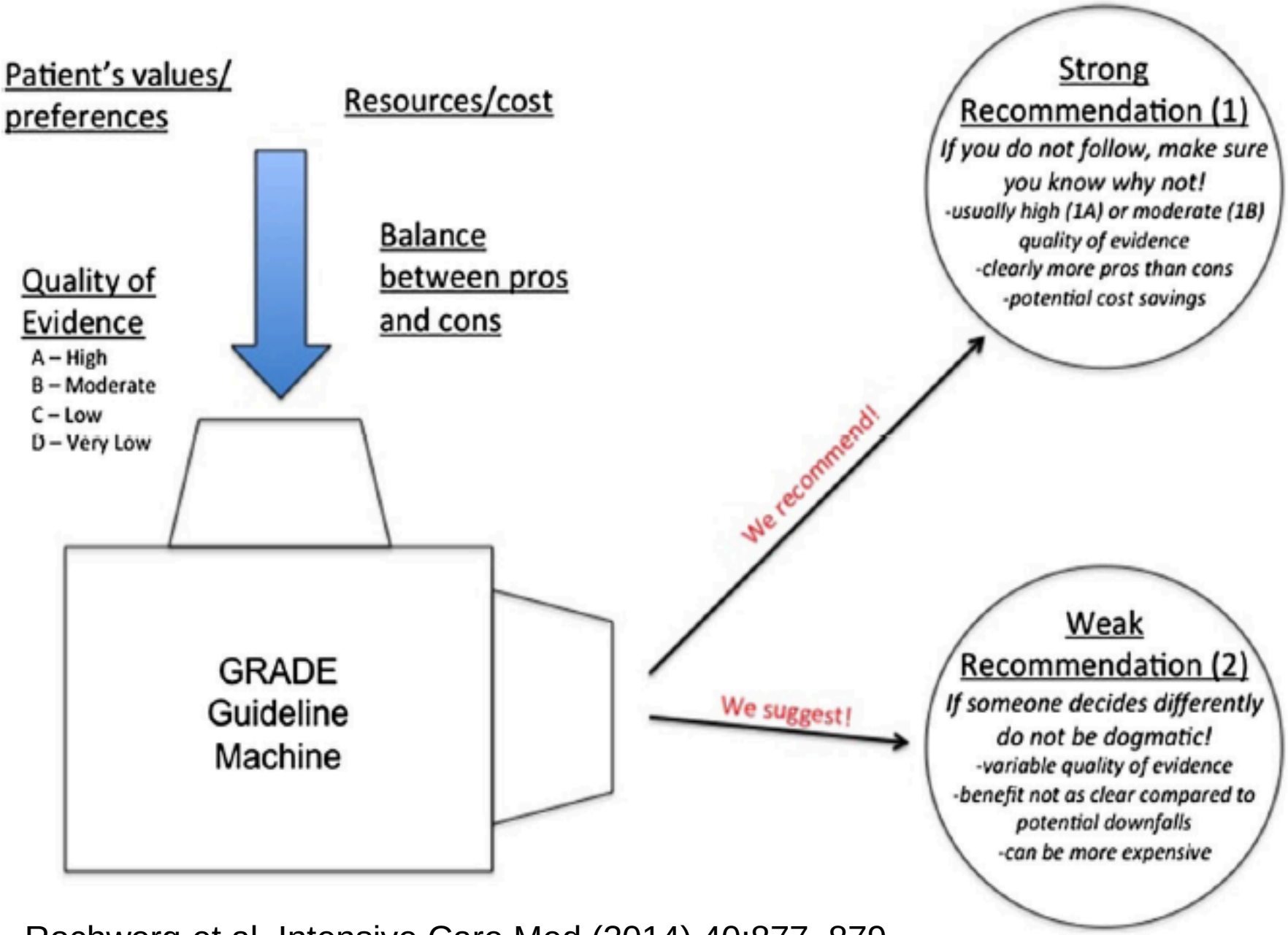
Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NIV	supplemental oxygen	Relative (95% CI)	Absolute (95% CI)		
Mortality												
14	RCTs	not serious	not serious	not serious	not serious	strong association	52/599 (8.7%)	85/609 (14.0%)	**RR 0.63** (0.46 to 0.87)	**52 fewer per 1,000** (from 18 fewer to 75 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Lack of blinding of intervention.
b. Variable definition used across studies.

From Evidence to Recommendation..



Rochwerg et al. Intensive Care Med (2014) 40:877–879

COPD Recommendation

"We recommend bilevel NIV for patients with acute respiratory failure leading to acute or acute on chronic respiratory acidosis, (pH ≤ 7.35) due to COPD exacerbation (strong recommendation, high certainty in the evidence)"

COPD: New from Previous Guidelines

"We recommend a trial of bilevel NIV in patients considered to require ETI and mechanical ventilation, unless the patient is immediately deteriorating (strong recommendation, moderate certainty in the evidence)"

“Slam Dunks”

- Strong Recommendation for Initiation
  - Acute exacerbation of COPD with hypercarbia
  - Cardiogenic pulmonary edema

Pre-hospital CPE

Intubation

Favours NIV

1.2.3 Pre-hospital						
Ducros 2011	3	107	6	100	4.5%	0.45 [0.11, 1.86]
Frontin 2011	2	60	3	62	2.1%	0.68 [0.11, 4.21]
Plaissance 2007	6	63	16	61	10.9%	0.30 [0.11, 0.82]
Roessler 2012	1	24	6	25	4.2%	0.14 [0.02, 1.25]
Thompson 2008	7	35	17	34	10.2%	0.25 [0.09, 0.73]
Subtotal (95% CI)		**289**		**282**	**31.8%**	**0.31 [0.17, 0.55]**
Total events	19		48			

Heterogeneity: $Chi^2 = 1.67$, $df = 4$ ($P = 0.80$); $I^2 = 0\%$

Test for overall effect: $Z = 3.94$ ($P < 0.0001$)

"We suggest that CPAP or bilevel NIV be used for patients with acute respiratory failure due to CPE in the pre-hospital setting (conditional recommendation, low certainty of evidence)"

Punto 2. = QUANDO POTREBBE SERVIRE

Conditional Recommendation For	No recommendation	Conditional Recommendation Against
Immunocompromised patients with resp failure	Asthma Exacerbation	Post-extubation respiratory failure
Postoperative resp failure	De novo Respiratory Failure	
Palliative care associated dyspnea	Pandemic Viral Illness	
Chest trauma (lung contusion)		
Prophylaxis post-extubation in high risk		
Weaning from MV in COPD patients		

Conditional Recommendation For	No recommendation	Conditional Recommendation Against
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Chest trauma (lung contusion)		
Prophylaxis post-extubation in high risk		
Weaning from MV in COPD patients		

Palliative Care

- NIV in patients with respiratory failure receiving palliative care?
  - NIV improved dyspnea – lowered Borg scale by 0.89 points (95% CI 0.79-0.99)
  - NIV decreased opioid requirement – 32.4mg less morphine equivalents (95% CI 17.4-47.4)

"We suggest offering NIV to dyspnoeic patients for palliation in the setting of terminal cancer or other terminal conditions. (Conditional recommendation, moderate certainty of evidence)"

Conditional Recommendation For	No recommendation	Conditional Recommendation Against
Immunocompromised patients with resp failure	Asthma Exacerbation	Post-extubation respiratory failure
Postoperative resp failure	De novo Respiratory Failure	
Palliative care associated dyspnea	Pandemic Viral Illness	
Chest trauma (lung contusion)		
Prophylaxis post-extubation in high risk		
Weaning from MV in COPD patients		

Chest Trauma

Outcome	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	NIV	supplemental oxygen	Relative (95% CI)	Absolute (95% CI)	Quality
Mortality	4	RCT	not serious	not serious	not serious	serious	5/86 (5.8%)	11/93 (11.8%)	**RR 0.55** (0.22 to 1.41)	53 fewer per 1000 (from 48 more to 92 fewer)	⊕⊕⊕○ MODERATE
Intubation	2	RCT	serious	not serious	not serious	not serious	4/31 (12.9%)	15/36 (41.7%)	**RR 0.21** (0.06 to 0.74)	329 fewer per 1000 (from 108 fewer to 392 fewer)	⊕⊕⊕○ MODERATE
ICU LOS	4	RCT	serious	not serious	not serious	not serious	80	82	not estimable	MD **2.47 lower** (3.45 lower to 1.5 lower)	⊕⊕⊕○ MODERATE
Nosocomial Pneumonia	3	RCT	serious	not serious	serious	not serious	11/79 (13.9%)	29/83 (34.9%)	**RR 0.29** (0.13 to 0.64)	248 fewer per 1000 (from 126 fewer to 304 fewer)	⊕⊕○○ LOW

Chest Trauma

- Heterogenous population
  - Severity of illness, rib # vs flail chest, other injuries
- Various comparators
  - Supplemental oxygen vs invasive ventilation

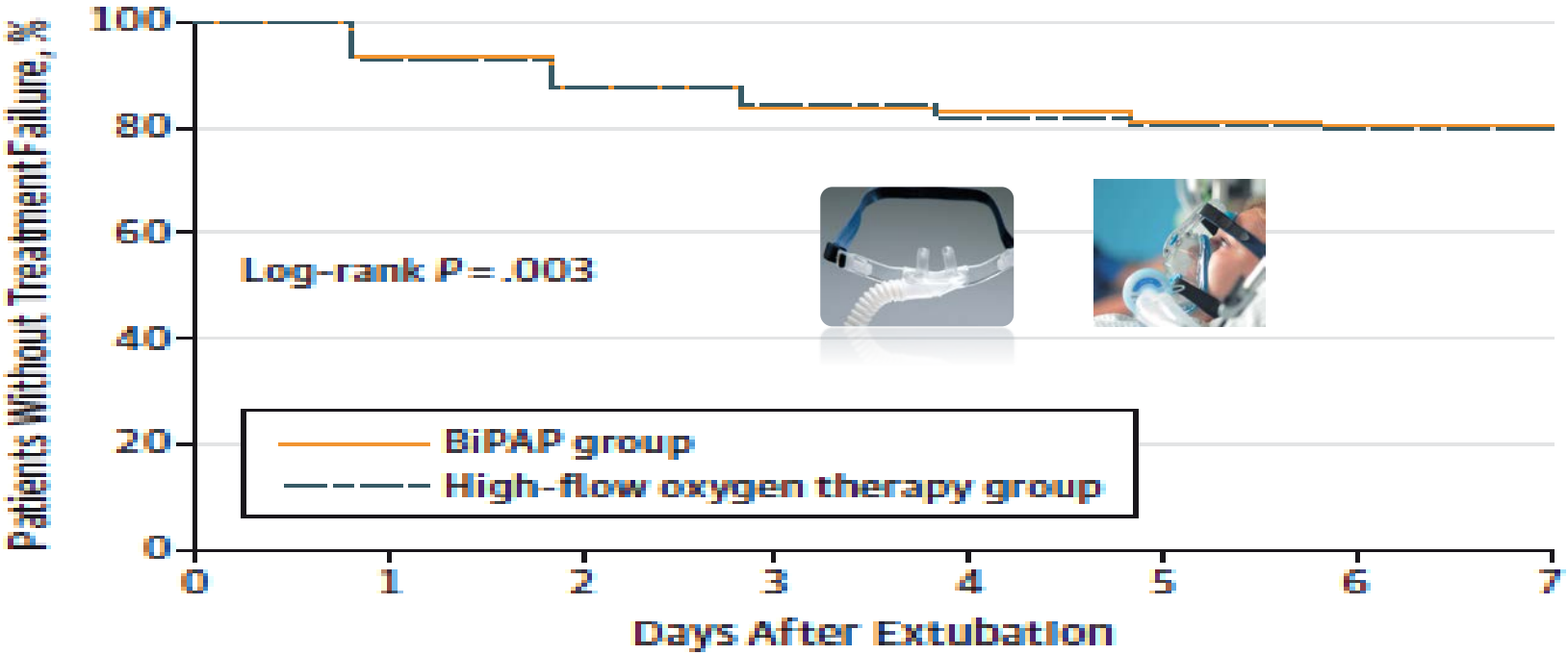
"We suggest NIV for chest trauma patients with ARF. (Conditional recommendation, moderate certainty of evidence)"

Conditional Recommendation For	No recommendation	Conditional Recommendation Against
Immunocompromised patients with resp failure	Asthma Exacerbation	Post-extubation respiratory failure
Postoperative resp failure	De novo Respiratory Failure	
Palliative care associated dyspnea	Pandemic Viral Illness	
Chest trauma (lung contusion)		
Prophylaxis post-extubation in high risk		
Weaning from MV in COPD patients		

High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery

A Randomized Clinical Trial

Stephan JAMA 2015



Postoperative RF

- Heterogenous type of surgical procedures
  - Abdominal, Thoracic, Cardio-Thoracic
  - CPAP and NIV used
  - Different comparator (i.e. standard O_2 and HOF)
  - Surgical complications such as anastomotic leak or intra-abdominal sepsis should be addressed first

"We suggest NIV for postoperative patients with ARF. (Conditional recommendation, moderate certainty of evidence)"

Punto 3. =QUANDO FERMARSI

Prophylaxis in COPDE

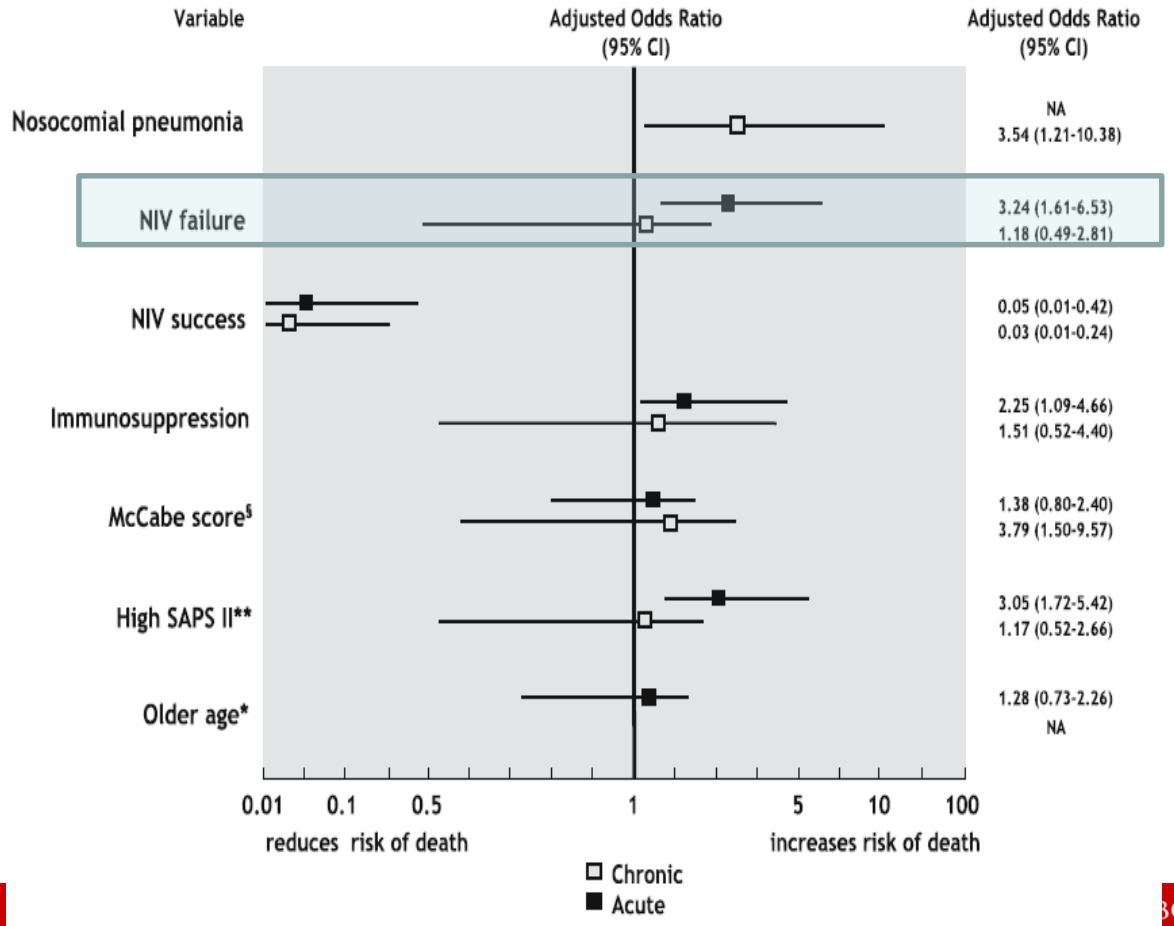
"We suggest NIV not be used in patients with hypercapnia who are not acidotic in the setting of a COPD exacerbation (conditional recommendation, low certainty in the evidence)"

Intensive Care Med (2006) 32:1756–1765
DOI 10.1007/s00134-006-0324-1

ORIGINAL

Alexandre Demoule
Emmanuelle Girou
Jean-Christophe Richard
Solenne Taille
Laurent Brochard

Benefits and risks of success or failure of noninvasive ventilation



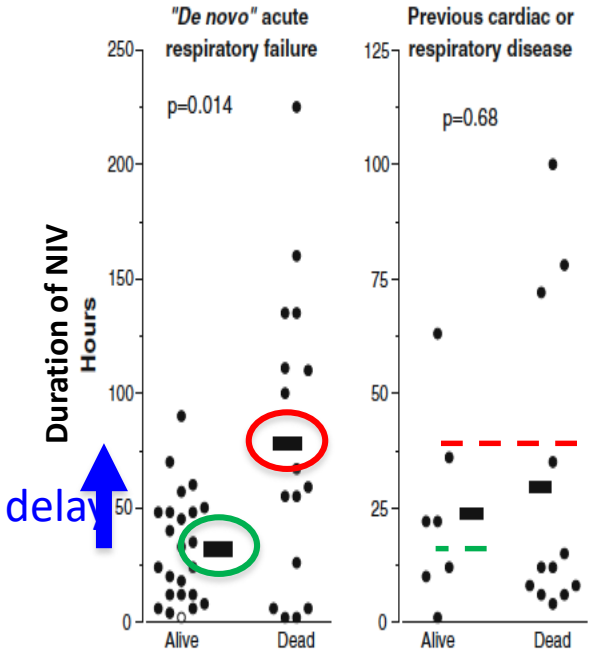
Delayed intubation increases mortality

Intensive Care Med (2012) 38:458-466
DOI 10.1007/s00134-012-2475-6

ORIGINAL

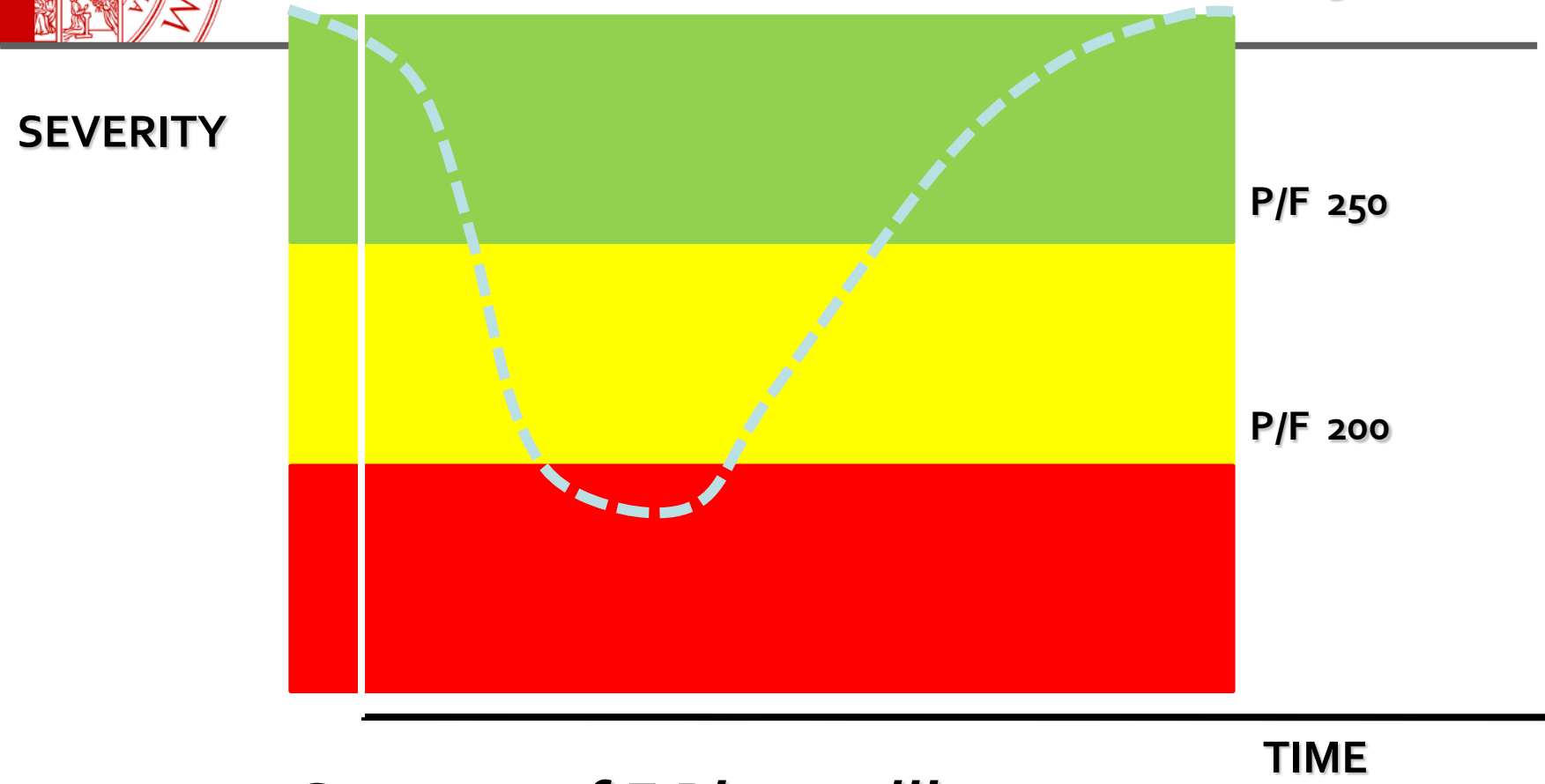
Andres Carrillo
Gumersindo Gonzalez-Diaz
Miquel Ferrer
Maria Elena Martinez-Quintana
Antonia Lopez-Martinez
Noemi Llamas
Maravillas Alcazar
Antoni Torres

Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure



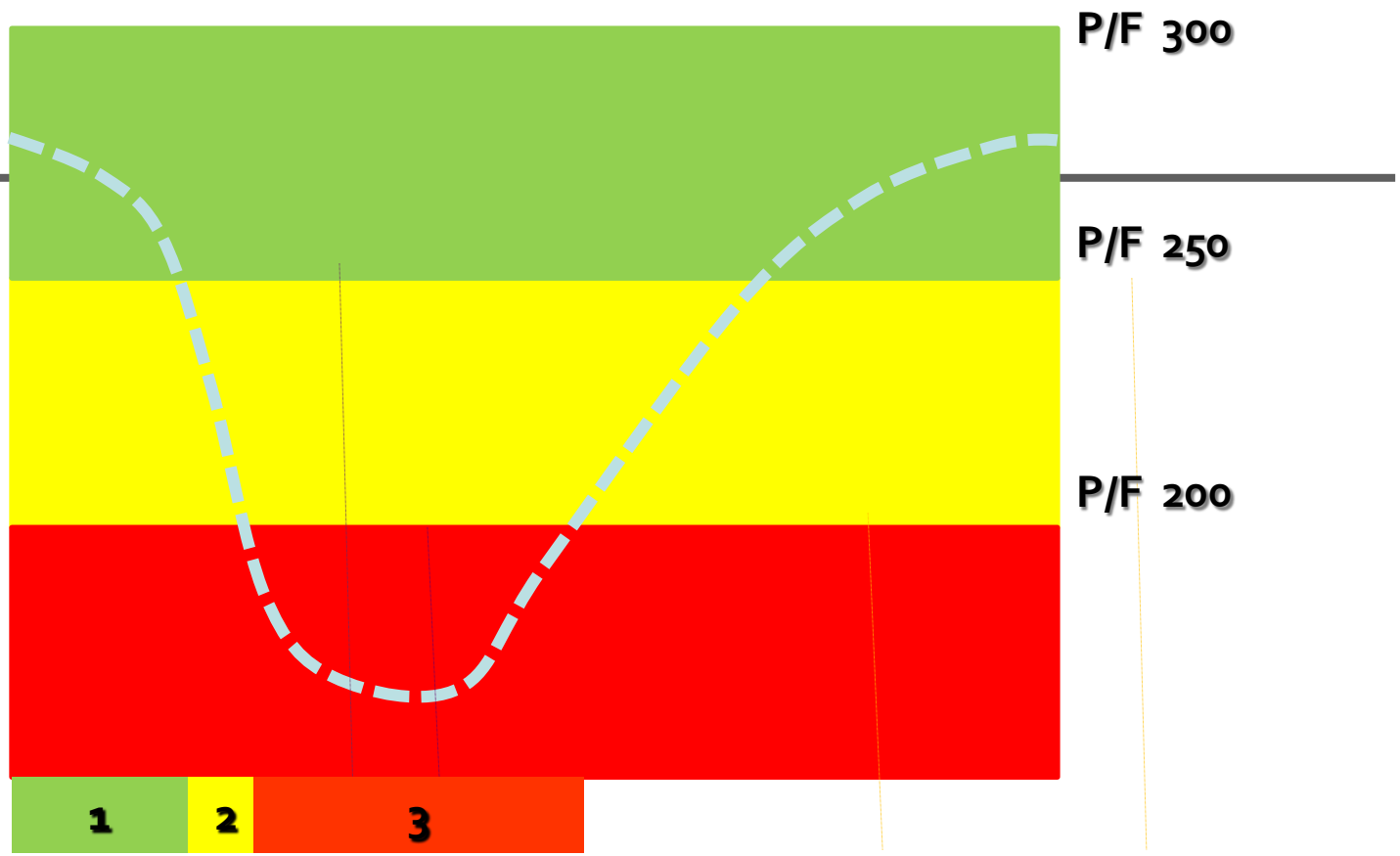
Carrillo A et al. Intensive Care Med 2012;38:458-466

Time course



Courtesy of F.Rizzonelli

TIMING and LOCATION



1: PREVENT ARF	1: WARD
2: AVOID intubation	2: HIGH DEPENDENCY
3: ALTERNATIVE to intubation	3: ICU or HIGH DEPENDENCY UNIT

Noninvasive Ventilation in Severe Hypoxemic Respiratory Failure

A Randomized Clinical Trial

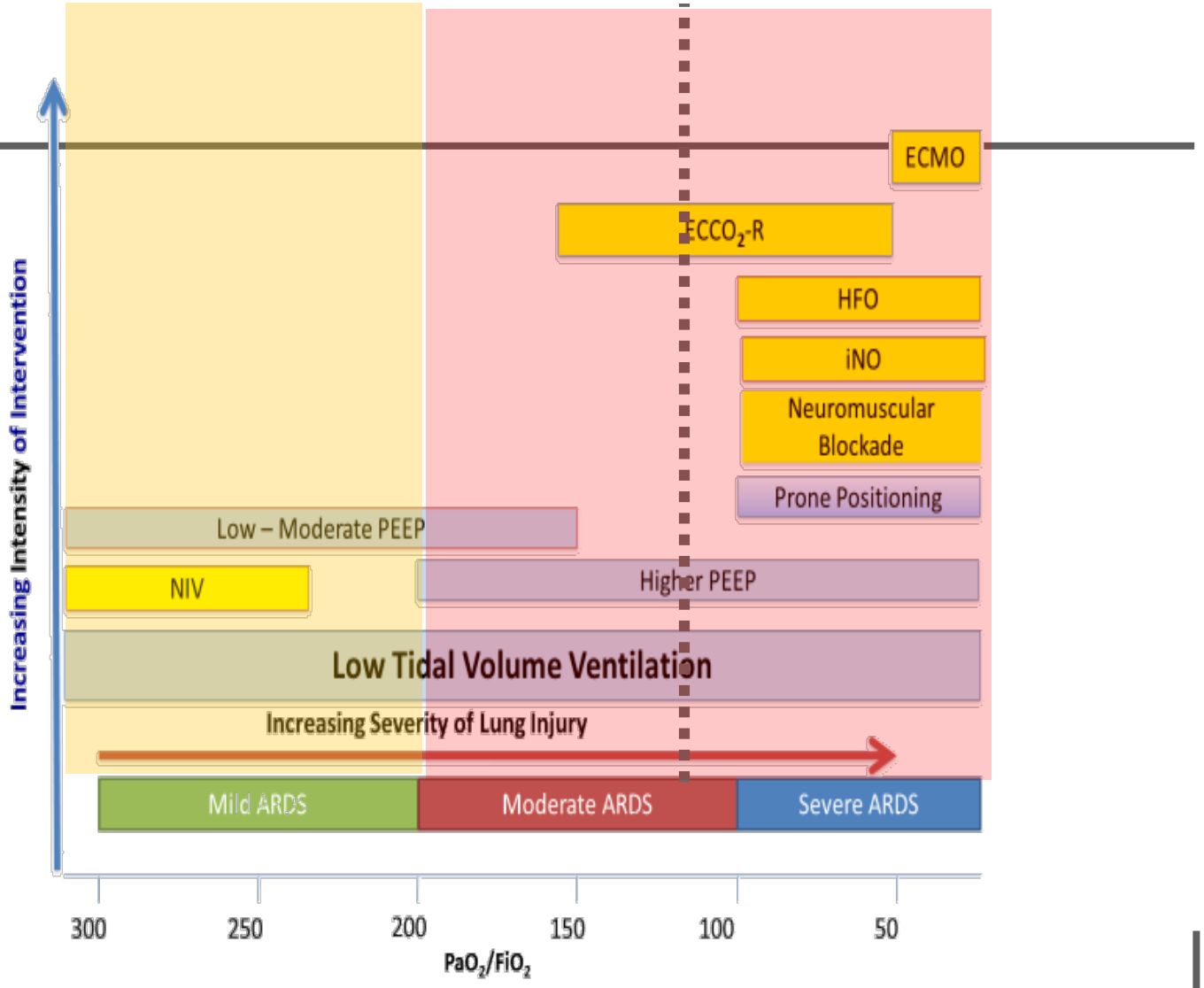
Am J Respir Crit Care Med Vol 168. pp 1438–1444, 2003

Miquel Ferrer, Antonio Esquinas, Miguel Leon, Gumersindo Gonzalez, Antonio Alarcon, and Antoni Torres

TABLE 3. MULTIVARIATE ANALYSES OF RISK FACTORS FOR INTUBATION*

	Adjusted Odds Ratio	95% CI	p Value
Noninvasive ventilation†	0.20	0.07–0.58	0.003
Cardiogenic pulmonary edema†	0.14	0.04–0.56	0.005
ARDS	28.5	3.2–249.8	0.003

ARDS is associated with an high risk of NIV failure



Noninvasive Ventilation of Patients with Acute Respiratory Distress Syndrome

Insights from the LUNG SAFE Study

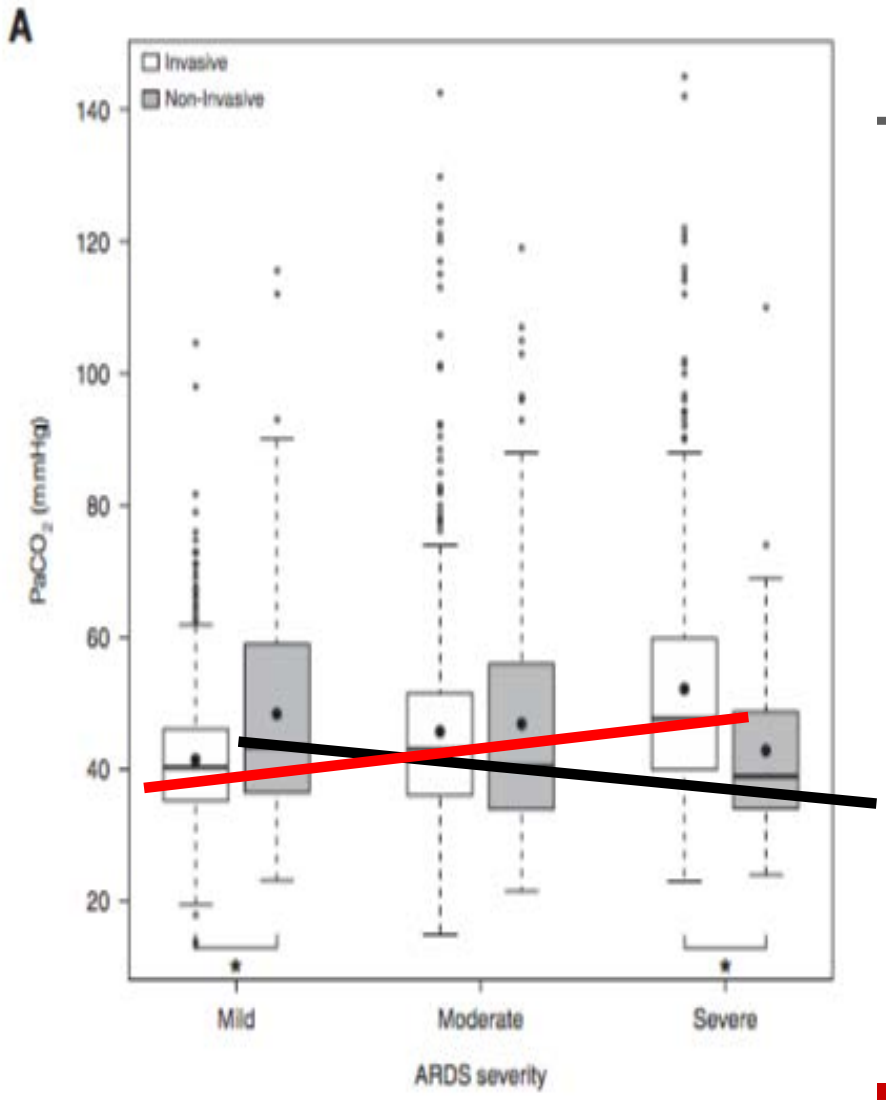
	ARDS, Mild		ARDS, Moderate		ARDS, Severe		ARDS		*P* Value within NIV	*P* Value within Invasive-MV
	NIV	Invasive-MV	NIV	Invasive-MV	NIV	Invasive-MV	NIV	Invasive-MV		
N	119	714	232	1,106	85	557	436	2,377	—	—

NIV use % 17%. 21%. 15%

	ARDS-NIV (without Treatment Limitations)		*P* Value
	Success	Failure	
Patients, n (%)			0.001
All	218 (62.5)	131 (37.5)	
Mild ARDS	77 (77.8)	22 (22.2)	
Moderate ARDS	105 (57.7)	77 (42.3)	
Severe ARDS	36 (52.9)	32 (47.1)	
Male, n (%)	129 (59.2)	80 (61.1)	0.727
Age, median (IQR)	66.5 (52 to 78)	63.0 (53 to 74)	0.081
ICU mortality, n (%)			
All	23 (10.6)	56 (42.7)	<0.001
Patients with Pa_{O_2}/FI_{O_2} ratio <150 mm Hg	13 (14.6)	36 (45.0)	<0.001
Patients with Pa_{O_2}/FI_{O_2} ratio ⩾150 mm Hg	10 (7.8)	20 (39.2)	<0.001
Hospital mortality, n (%)	35 (16.1)	59 (45.4)	<0.001

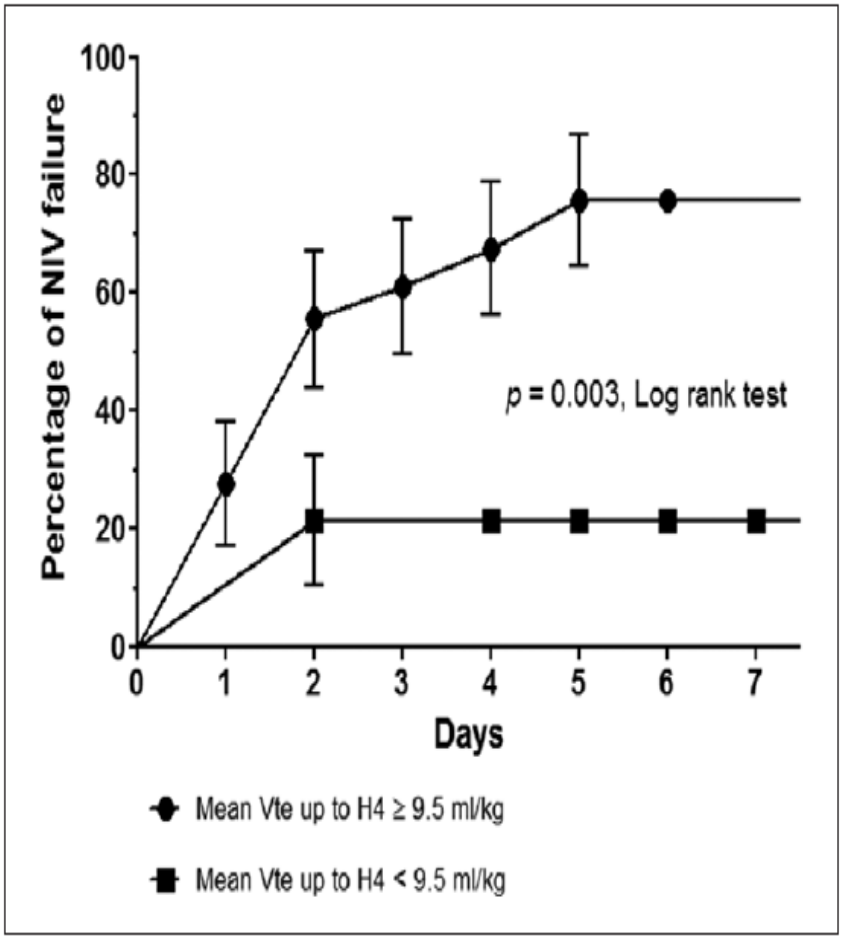
Noninvasive Ventilation of Patients with Acute Respiratory Distress Syndrome

Insights from the LUNG SAFE Study



Failure of Noninvasive Ventilation for De Novo Acute Hypoxemic Respiratory Failure: Role of Tidal Volume

Guillaume Carteaux, MD[1,2,3]; Teresa Millán-Guilarte, MD[4]; Nicolas De Prost, MD, PhD[1,2,3]; Keyvan Razazi, MD[1,2,3]; Shariq Abid, MD, PhD[3]; Arnaud W. Thille, MD, PhD[5]; Frédérique Schortgen, MD, PhD[1,3]; Laurent Brochard, MD[3,6,7]; Christian Brun-Buisson, MD[1,2,8]; Armand Mekontso Dessap, MD, PhD[1,2,3]



62 patients, 47 with ARDS. In patients with p/f<200, Vt is Good predictor prediction for NIV failure

Mechanisms of VILI: role of transpulmonary pressure (P_L)

$$P_L = Paw - Ppl$$

(ventilator)(muscles)

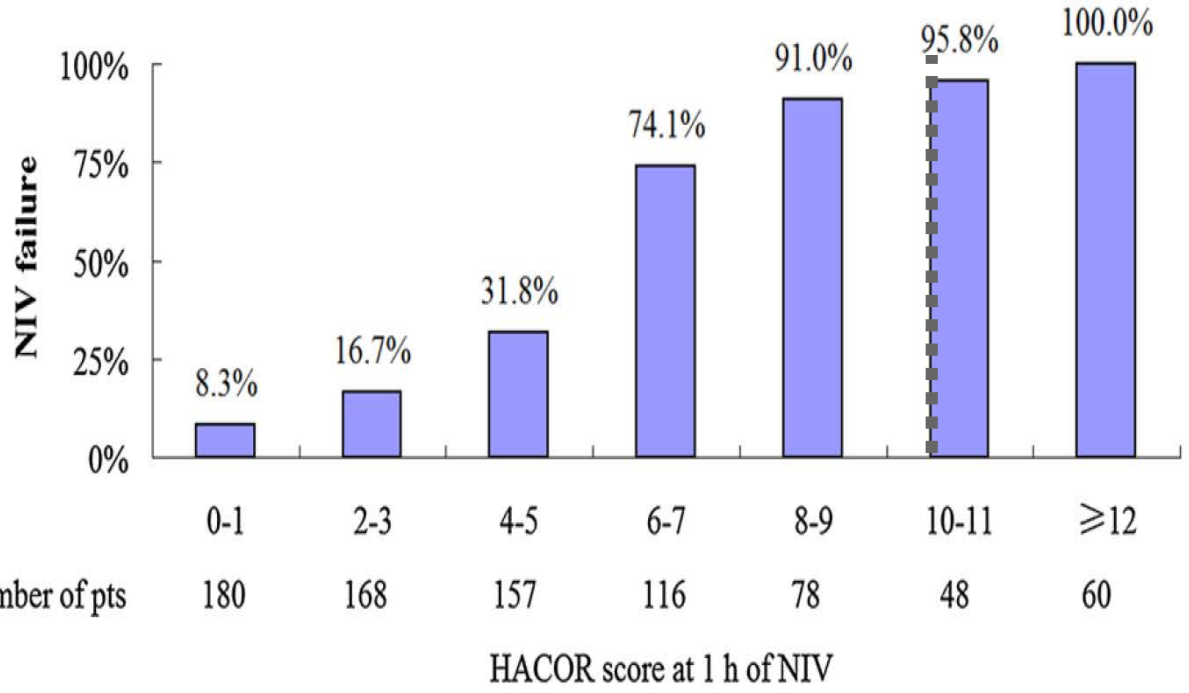
Unfortunately end inspiratory transpulmonary pressure is impossible to know during NIV, despite it can surrogated by dynamic transpulmonary pressure, whose measurement however requires esophageal baloon and is not clinically feasible in all patients

Intensive Care Med
DOI 10.1007/s00134-016-4601-3

ORIGINAL

Assessment of heart rate, acidosis, consciousness, oxygenation, and respiratory rate to predict noninvasive ventilation failure in hypoxemic patients

Jun Duan*, Xiaoli Han, Linfu Bai, Lintong Zhou and Shicong Huang



Question 5: Should NIV be used in de novo ARF?

De novo respiratory failure refers to respiratory failure occurring without prior chronic respiratory disease.

Most patients in this category have hypoxaemic respiratory failure, usually defined as significant hypoxaemia (arterial oxygen tension/inspiratory oxygen fraction ratio (PaO2/FIO2) ⩽200), tachypnoea (respiratory rate >30–35 breaths·min–1) and a non-COPD diagnosis

Question 5: Should NIV be used in de novo ARF?

Specific risks have been described with NIV and there is not enough evidence to recommend its use.

Further research is needed and this question requires reappraisal in the future.

Considering that some studies have identified populations likely to succeed with NIV, a trial of NIV might be offered to a patient with hypoxaemic respiratory failure, community-acquired pneumonia or early ARDS if they are being managed by an experienced clinical team, are carefully selected are closely monitored in the ICU, reassessed early after starting NIV and intubated promptly if they are not improving.

CONCLUSIONS

The “new” guidelines emphasized the role of NIV as first line treatment for:

ARF due to COPD exacerbation with pH<7.35 and CPE, even outside the hospital GO FOR IT !

“New” conditional recommendation for:
Post operative respiratory failure – palliative care – chest trauma – prophylaxis of post extubation failure in high risk patients
YOU MAY USE IT !

ARDS and DE NOVO ARF: PROBABLY STOP IT !

IN THIS TASK FORCE 100% MAN !