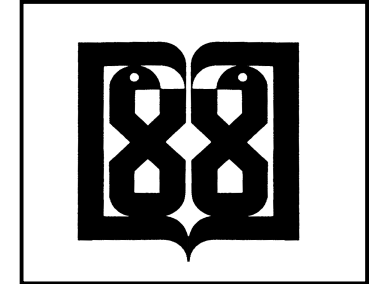


# تهویه غیر تهاجمی بعد از جداسازی از دستگاه تهویه مکانیکی

**NIV after liberation of )  
(mechanical ventilation**

**دکتر علیرضا باقری**

فوق تخصص ریه، استادیار دانشگاه علوم پزشکی تهران





## The use of NIV immediately following extubation

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Service  
Henry Ford Hospital

Associate Professor of Medicine  
Wayne State University School of  
Medicine

# Educational Objectives

- To learn about the clinical outcomes that may be improved by the use of non-invasive ventilation post-extubation.
- To become familiar with the population that may benefit from non-invasive ventilation following extubation.
- To understand the contraindications and risks to using non-invasive ventilation post-extubation.

# Case Presentation

150/58 HR=99 RR=24 T=37.4

Intubated/sedated

Cardiac rhythm irr. irr.

↓ breath sounds, + edema

Foley, ET tube, NG

PRVC, FiO2=0.4, set rate 12, PEEP=5

Passes SBT



| Lab Test          | Patient Value       | Normal Range   |
|-------------------|---------------------|----------------|
| Sodium            | 150 mmol/L          | 135-145 mmol/L |
| Potassium         | 4.0 mmol/L          | 3.5-5.0 mmol/L |
| Carbon dioxide    | 33 mmol/L           | 21-35 mmol/L   |
| Creatinine        | 1.88 mg/dL          | <1.13 mg/dL    |
| ALT               | 518 IU/L            | <40 IU/L       |
| AST               | 284 IU/L            | <35 IU/L       |
| BNP               | 1091 pg/mL          | <50 pg/mL      |
| White blood count | 6.3 K/uL            | 3.8-10.6 K/uL  |
| Hemoglobin        | 12.8 g/dL           | 13.5-17.0 g/dL |
| Platelet count    | 140 K/uL            | 150-450 K/uL   |
| pH                | 7.35                |                |
| pO <sub>2</sub>   | 74 mm Hg (room air) |                |
| PCO <sub>2</sub>  | 58.2 mm Hg          |                |



# سوال ۱: استفاده از NIV بعد از اکستوباسیون لوله تراشه برای این بیمار با کدام عاقبت (outcome) همراه است؟

آ) عواقب و نتایج بالینی مهم با استفاده از NIV تغییری نمی کند.

ب) احتمال اینتوباسیون مجدد (re-intubation) کم می شود ولی مرگ و میر کوتاه مدت (short-term mortality) فرقی نمی کند.

پ) طول مدت بستری در آیسیو (ICU length) تغییری نمی کند ولی مرگ و میر کوتاه مدت کمتر می شود.

ت) احتمال اینتوباسیون مجدد کم می شود و مرگ و میر کوتاه مدت هم کمتر می شود.



# Liberation From Mechanical Ventilation in Critically Ill Adults



Executive Summary of an Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline

Gregory A. Schmidt, MD, FCCP; Timothy D. Girard, MD; John P. Kress, MD, FCCP; Peter E. Morris, MD, FCCP; Daniel R. Ouellette, MD, FCCP; Waleed Alhazzani, MD; Suzanne M. Burns, RN, MSN, ACNP, RRT; Scott K. Epstein, MD, FCCP; Andres Esteban, MD, PhD; Eddy Fan, MD, PhD; Miguel Ferrer, MD, PhD;

- *Question 1: In acutely hospitalized patients ventilated more than 24 h, should the spontaneous breathing trial (SBT) be conducted with or without inspiratory pressure augmentation?*
- *Question 2: In acutely hospitalized patients ventilated for more than 24 h, do protocols attempting to minimize sedation compared with approaches that do not attempt to minimize sedation impact duration of ventilation, duration of ICU stay, and short-term mortality (60 days)?*
- *Question 3: In high-risk patients receiving mechanical ventilation for more than 24 h who have passed an SBT, **does extubation to preventive noninvasive ventilation (NIV) compared with no NIV have a favorable effect on duration of ventilation, ventilator-free days, extubation success (liberation > 48 h), duration of ICU stay, short-term mortality (60 days), or long-term mortality?***



- *Question 4: Should acutely hospitalized adults who have been mechanically ventilated for >24 h be subjected to protocolized rehabilitation directed toward early mobilization or no protocolized attempts at early mobilization?*
- *Question 5: Should acutely hospitalized adults who have been mechanically ventilated for > 24 h be managed with a ventilator liberation protocol or no protocol?*
- *Question 6: Should a cuff leak test (CLT) be performed prior to extubation of mechanically ventilated adults? Should systemic steroids be administered to adults who fail a CLT prior to extubation?*





## Liberation From Mechanical Ventilation in Critically Ill Adults



Executive Summary of an Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline

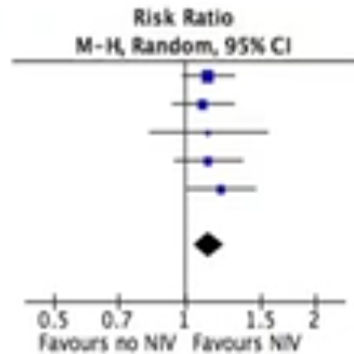
### Liberation Guidelines: PICO Question #3

- **Population:**
  - High-risk patients receiving MV > 24 hours who have passed an SBT.
- **Intervention:**
  - Immediate NIV
- **Comparator:**
  - No NIV
- **Outcomes:**
  - Extubation success, ICU LOS, short- and long-term mortality

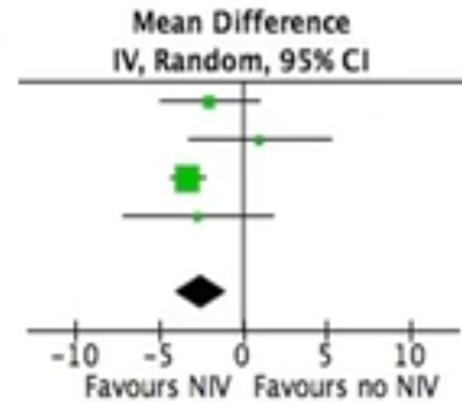


عواقب و نتایج بالینی مهم با استفاده از NIV تغییری نمی کند.

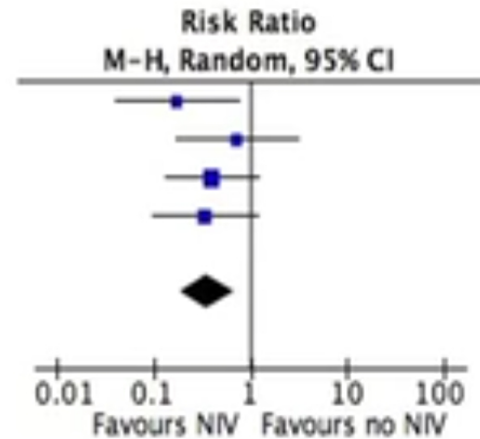
Outcome: Extubation



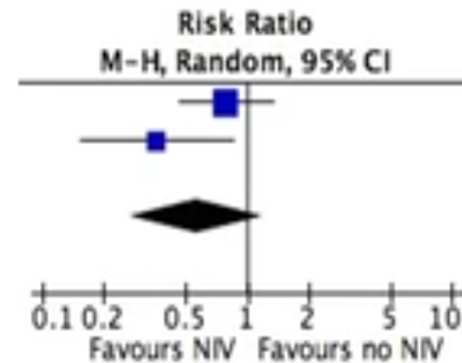
Outcome: ICU  
LOS



Outcome: Short-term  
Mortality



Outcome:  
Long-term  
Mortality

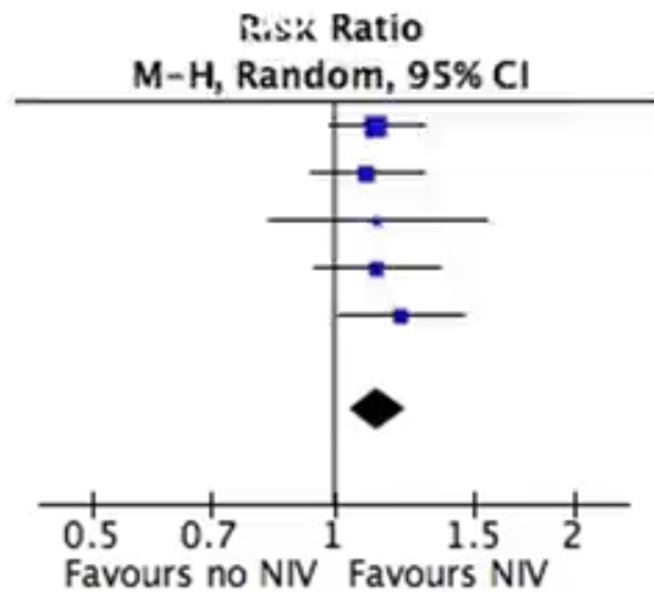




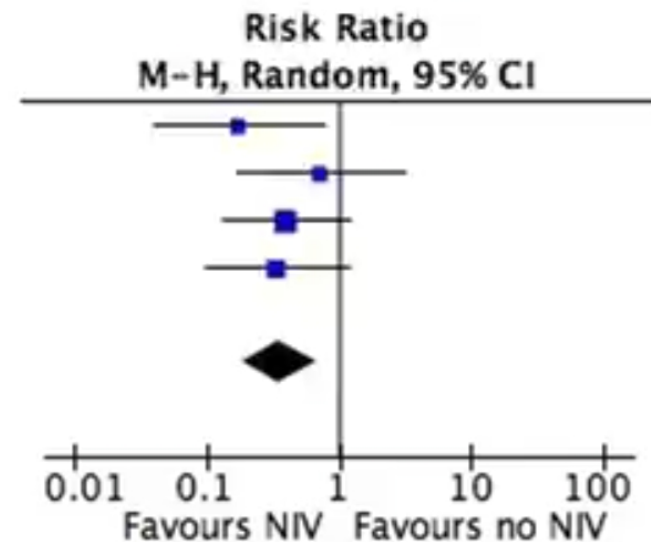


احتمال اینتوباسیون مجدد (re-intubation) کم می شود ولی مرگ و میر کوتاه مدت (short-term mortality) فرقی نمی کند.

### Outcome: Extubation



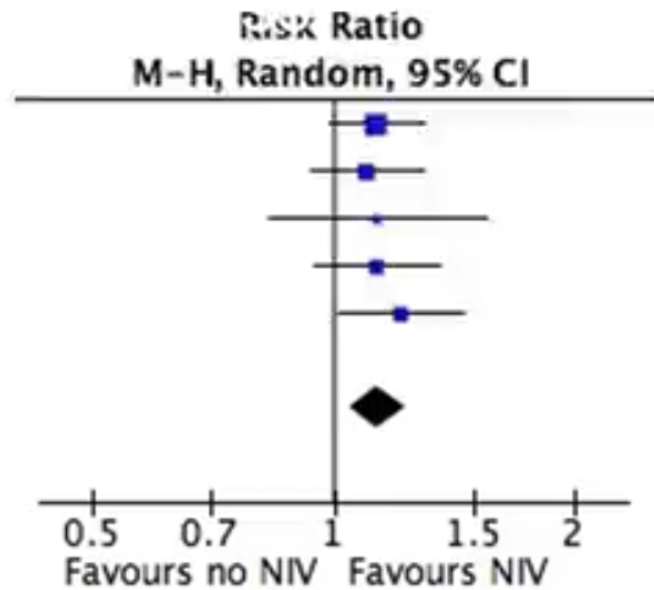
### Outcome: Short-term Mortality



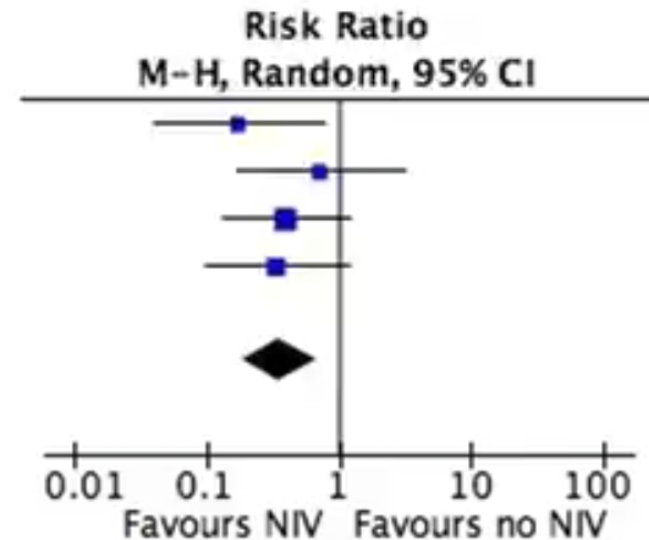


✓ احتمال اینتوباسیون مجدد (re-intubation) کم می شود و مرگ و میر کوتاه مدت (short-term mortality) هم کاهش می یابد.

### Outcome: Extubation



### Outcome: Short-term Mortality





## سوال ۲: بهترین گزینه برای استفاده از NIV بعد از اکستوباسیون لوله تراشه کدام یک از موارد زیر است؟

آ) آقای ۷۰ ساله که ۷ روز قبل بدلیل تشدید حاد COPD اینتوبه شده، **spont Mode** را تحمل می کند و شرایط رهایی از ونتیلاتور را دارد.

ب) آقای ۳۰ ساله که ۴۸ ساعت قبل بدلیل نارسایی تنفسی حاد ناشی از مسمومیت با مواد مخدر اینتوبه شده است و شرایط رهایی از ونتیلاتور را دارد.

پ) خانم ۸۰ ساله که ۵ روز قبل بدلیل سپسیس و عفونت ادراری اینتوبه شده، فعلا سپسیس کنترل شده، هایپرکاپنه ندارد، **spont Mode** را تحمل می کند و شرایط رهایی از ونتیلاتور را دارد.

ت) خانم ۶۰ ساله که ۵ روز قبل بدلیل سپسیس و COVID19 اینتوبه شده ، ادم و هایپرکاپنه ندارد و شرایط رهایی از ونتیلاتور را دارد.



following risk factors for respiratory failure after extubation: (1) age greater than 65 yr, (2) cardiac failure as the cause of intubation, or (3) increased severity, assessed by an Acute Physiology and Chronic Health Evaluation (APACHE)-II (16) score exceeding 12 on the day of extubation (1). Patients with tracheotomy were not screened for the study.

Ferrer et al. Am J Respir Crit Care Med  
2006

with chronic respiratory disorders, intubated for 48 h or more, who tolerated a spontaneous breathing trial through a T-piece after recovery of their disease, with hypercapnic respiratory failure ( $\text{PaCO}_2 > 45$  mm Hg) on spontaneous breathing, were deemed eligible for the study. We did not

Ferrer et al. Lancet 2009

Other studies: “at risk”, mean age 72,  
“COPD”

- In studies of preventive NIV, there was heterogeneity in defining the high-risk patient. Risk factors included:

- ❖ *older age*

- ❖ *comorbidities : COPD or CHF*

- ❖ *hypercapnia during the SBT*

**Studies heterogeneous  
for at risk population:  
Consider chronic  
respiratory acidosis,  
COPD, “CHF”, severity of  
illness**



## سوال ۲: بهترین گزینه برای استفاده از NIV بعد از اکستوباسیون لوله تراشه کدام یک از موارد زیر است؟

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## سوال ۳: کدام یک از گزینه های زیر در مورد خطرات و موارد منع استفاده از NIV بعد از اکستوباسیون لوله تراشه صحیح است؟

(آ) در اسیدوز تنفسی استفاده از NIV منع شده است . (contraindication)

(ب) در بیمارانی که همراهی و تحمل استفاده از NIV را ندارند (uncooperative)، با افزایش آرام بخشی (sedation) ممکن است درمان با NIV ادامه یابد .

(پ) در بیماران با شکستگی صورت، استفاده از NIV بعد از اکستوباسیون لوله تراشه با کمک ماسک های با مواد سیلیکون نرم قابل انجام است .

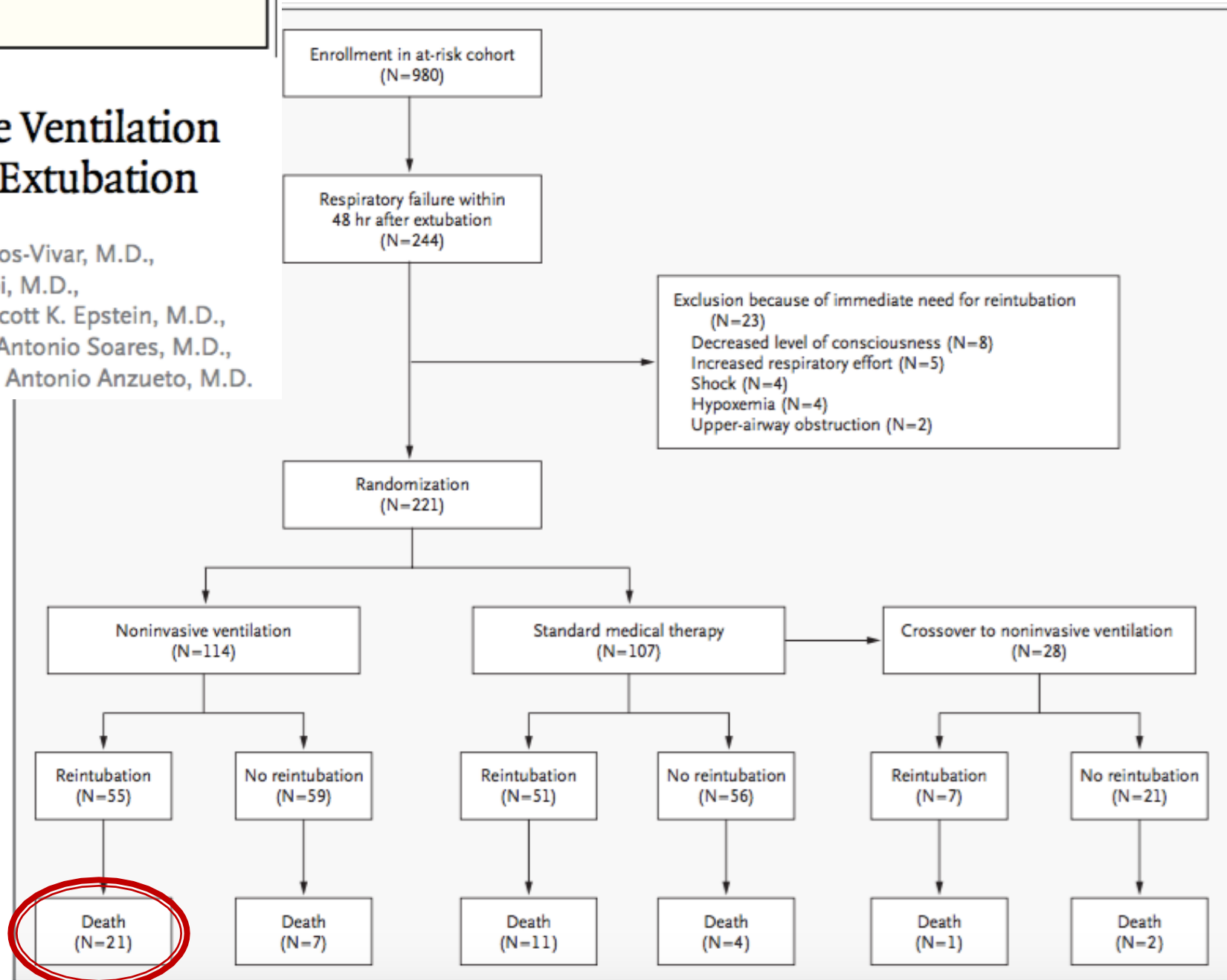
(ت) تاخیر در استفاده از NIV بعد از اکستوباسیون لوله تراشه (شروع NIV از زمانی که بیمار دیسترس تنفسی پیدا کند) به نسبت مراقبت های استاندارد (اکسیژن کمکی و ..) عواقب و نتایج بدتری خواهد داشت





# Noninvasive Positive-Pressure Ventilation for Respiratory Failure after Extubation

Andrés Esteban, M.D., Ph.D., Fernando Frutos-Vivar, M.D.,  
Niall D. Ferguson, M.D., Yaseen Arabi, M.D.,  
Carlos Apezteguía, M.D., Marco González, M.D., Scott K. Epstein, M.D.,  
Nicholas S. Hill, M.D., Stefano Nava, M.D., Marco-Antonio Soares, M.D.,  
Gabriel D'Empaire, M.D., Inmaculada Alía, M.D., and Antonio Anzueto, M.D.





# چرا NIV در این مطالعه موثر نبود؟

- 1) *experience of the health care team using the technique..*
- 2) *timing of the initiation of NIV..*
- 3) *study population ..*

**Table 4.** Reasons for Reintubation, as Defined in the Protocol Guidelines, According to Study Group.

| Reason  | Non-invasive Ventilation (N=55)<br>no. (%) | Standard Medical Therapy (N=51)<br>no. (%) | P Value |
|---|--|--|---------|
| Lack of improvement in signs of muscle fatigue                  | 25 (45)                                    | 23 (45)                                    | 0.97    |
| Hypoxemia   | 9 (16)                                     | 15 (29)                                    | 0.11    |
| Copious secretions  | 5 (9)                                      | 6 (12)                                     | 0.65    |
| Lack of improvement in pH or partial pressure of carbon dioxide | 8 (15)                                     | 3 (6)                                      | 0.13    |
| Changes in mental status  | 4 (7)                                      | 2 (4)                                      | 0.45    |
| Hypotension   | 4 (7)                                      | 2 (4)                                      | 0.45    |

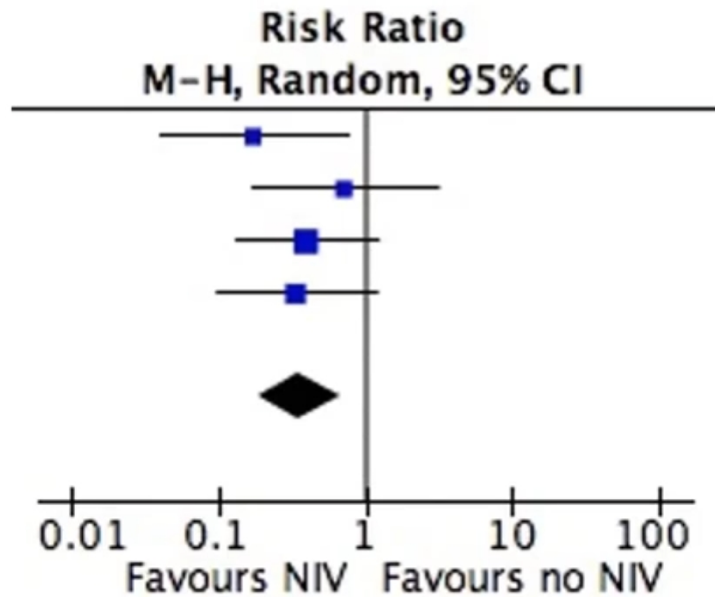
**Table 1.** Baseline Characteristics of the Patients, According to Study Group.\*

| Characteristic                                     | Non-invasive Ventilation (N=114) | Standard Medical Therapy (N=107) | P Value |
|--|----------------------------------|----------------------------------|---------|
| Age — yr   | 61±17                            | 58±19                            | 0.25    |
| Female sex — no. (%)                               | 47 (41)                          | 47 (44)                          | 0.68    |
| Simplified Acute Physiology Score II on admission† | 37±13                            | 36±10                            | 0.77    |
| Reason for initiation of mechanical ventilation    |                                  |                                  | 0.65    |
| Acute respiratory failure — no. (%)                |                                  |                                  |         |
| Pneumonia  | 28 (25)                          | 20 (19)                          |         |
| Postoperative respiratory failure                  | 20 (18)                          | 23 (21)                          |         |
| Sepsis   | 13 (11)                          | 11 (10)                          |         |
| Trauma   | 11 (10)                          | 7 (7)                            |         |
| Cardiac failure                                    | 8 (7)                            | 12 (11)                          |         |
| Acute respiratory distress syndrome                | 4 (4)                            | 8 (7)                            |         |
| Other  | 12 (11)                          | 10 (9)                           |         |
| Acute-on-chronic respiratory failure — no. (%)     |                                  |                                  |         |
| Chronic obstructive pulmonary disease              | 14 (12)                          | 9 (8)                            |         |
| Asthma   | 1 (1)                            | 3 (3)                            |         |
| Neuromuscular disease — no. (%)                    | 3 (3)                            | 4 (4)                            |         |



# استفاده فوری از NIV در برابر استفاده تاخیری از NIV:

**Imm. NIV; 4 studies**



**Delayed; Esteban et al**

- Mortality 25% in NIV versus 14% in standard therapy

Outcome: Short-term Mortality



# موارد منع استفاده از تهویه غیر تهاجمی

• منع مطلق:

✓ ایست تنفسی

✓ عدم امکان چفت کردن ماسک

• منع نسبی:

• ناپایداری بالینی:

• شوک

• ایسکمی قلبی یا آریتمی کنترل نشده

• ترشحات تنفسی زیاد

• خونریزی گوارشی فوقانی کنترل نشده

• عدم همکاری بیمار، بیقراری

• عدم امکان حفاظت از راه هوایی

• اختلال بلع

• نارسایی چند ارگان (دو یا بیشتر..)

• جراحی اخیر راه هوایی یا گوارشی فوقانی



## سوال ۳: کدام یک از گزینه های زیر در مورد خطرات و موارد منع استفاده از NIV بعد از اکستوباسیون لوله تراشه صحیح است؟

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(پ) در بیماران با شکستگی صورت، استفاده از NIV بعد از اکستوباسیون لوله تراشه با کمک ماسک های با مواد سیلیکون نرم قابل انجام است .

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## Liberation Guidelines: PICO Question #3

- **Population:**
  - High-risk patients receiving MV > 24 hours who have passed an SBT.
- **Intervention:**
  - Immediate NIV
- **Comparator:**
  - No NIV
- **Outcomes:**
  - Extubation success, ICU LOS, short- and long-term mortality

Ouellette et al. CHEST 2017; 151:166-180

## *CHEST/ATS Recommendation*

**3. For patients at high risk for extubation failure who have been receiving mechanical ventilation for more than 24 h and who have passed an SBT, we recommend extubation to preventive NIV (Strong Recommendation, Moderate Quality Evidence).**





## E 2 ] Summary of Recommendations

| Recommendation  | Strength of Recommendation | Certainty of Evidence (ie, Quality of Evidence) |
|---|----------------------------|---|
| 1. For acutely hospitalized patients ventilated more than 24 h, we suggest that the initial SBT be conducted with inspiratory pressure augmentation (5-8 cm H <sub>2</sub> O) rather than without (T-piece or CPAP) | Conditional                | Moderate certainty in the evidence              |
| 2. For acutely hospitalized patients ventilated for more than 24 h, we suggest protocols attempting to minimize sedation  | Conditional                | Low certainty in the evidence                   |
| 3. For patients at high risk for extubation failure who have been receiving mechanical ventilation for more than 24 h and who have passed an SBT, we recommend extubation to preventive NIV                         | Strong                     | Moderate certainty in the evidence              |
| 4. For acutely hospitalized patients who have been mechanically ventilated for > 24 h, we suggest protocolized rehabilitation directed toward early mobilization  | Conditional                | Low certainty in the evidence                   |
| 5. We suggest managing acutely hospitalized patients who have been mechanically ventilated for > 24 h with a ventilator liberation protocol   | Conditional                | Low certainty in the evidence                   |
| 6a. We suggest performing a CLT in mechanically ventilated adults who meet extubation criteria and are deemed at high risk for PES  | Conditional                | Very low certainty in the evidence              |
| 6b. For adults who have failed a CLT but are otherwise ready for extubation, we suggest administering systemic steroids at least 4 h before extubation; a repeated CLT is not required                              | Conditional                | Moderate certainty in the evidence              |



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

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

### *Question 10: Should NIV be used in ARF following extubation from invasive mechanical ventilation?*

- treating post-extubation respiratory failure ?

OR

- preventing respiratory failure from developing at all ?



### ***Question 10a: Should NIV be used to prevent respiratory failure post-extubation?***

The benefits of early application of NIV soon after extubation have been assessed in unselected patients (*i.e.* any patients after planned extubation) and in at-risk patients. For most included studies, at-risk included patients >65 years or those with underlying cardiac or respiratory disease.

#### ***Recommendations***

We suggest that NIV be used to prevent post-extubation respiratory failure in high-risk patients post-extubation. (Conditional recommendation, low certainty of evidence.)

We suggest that NIV should not be used to prevent post-extubation respiratory failure in non-high-risk patients. (Conditional recommendation, very low certainty of evidence.)

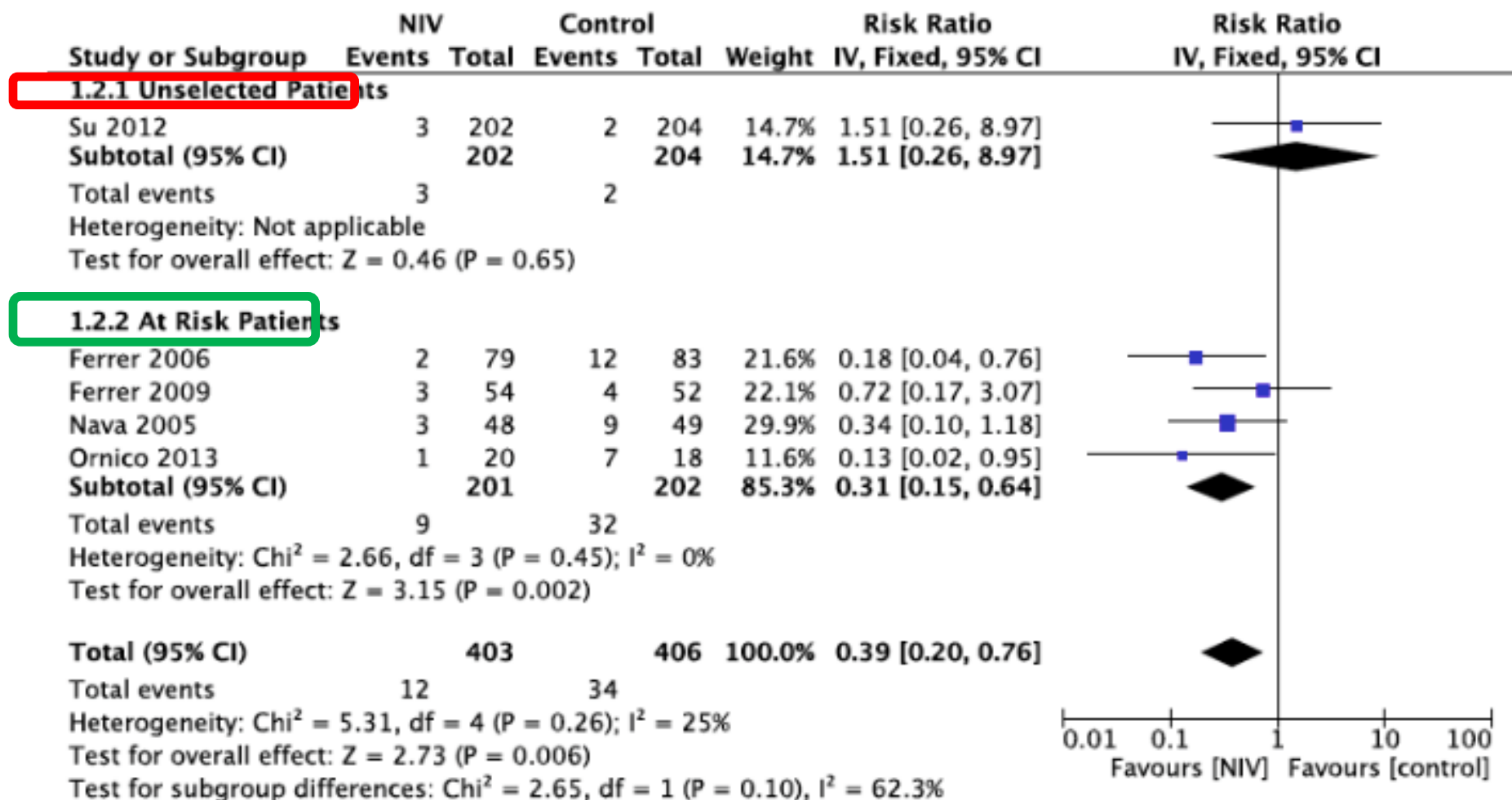
some inconsistencies regarding the criteria for considering patients at high risk of extubation failure. Recent work reports that patients >65 years and with underlying cardiac or respiratory disease are at high risk for extubation failure with a re-intubation rate >30% if both comorbidities are present and >20% if one of the two is present [122]. Early NIV after planned extubation decreases both intubation rate and mortality in patients at high risk of extubation failure. Patients with an unplanned extubation are a higher risk group and further studies should specifically address the use of NIV in this group.





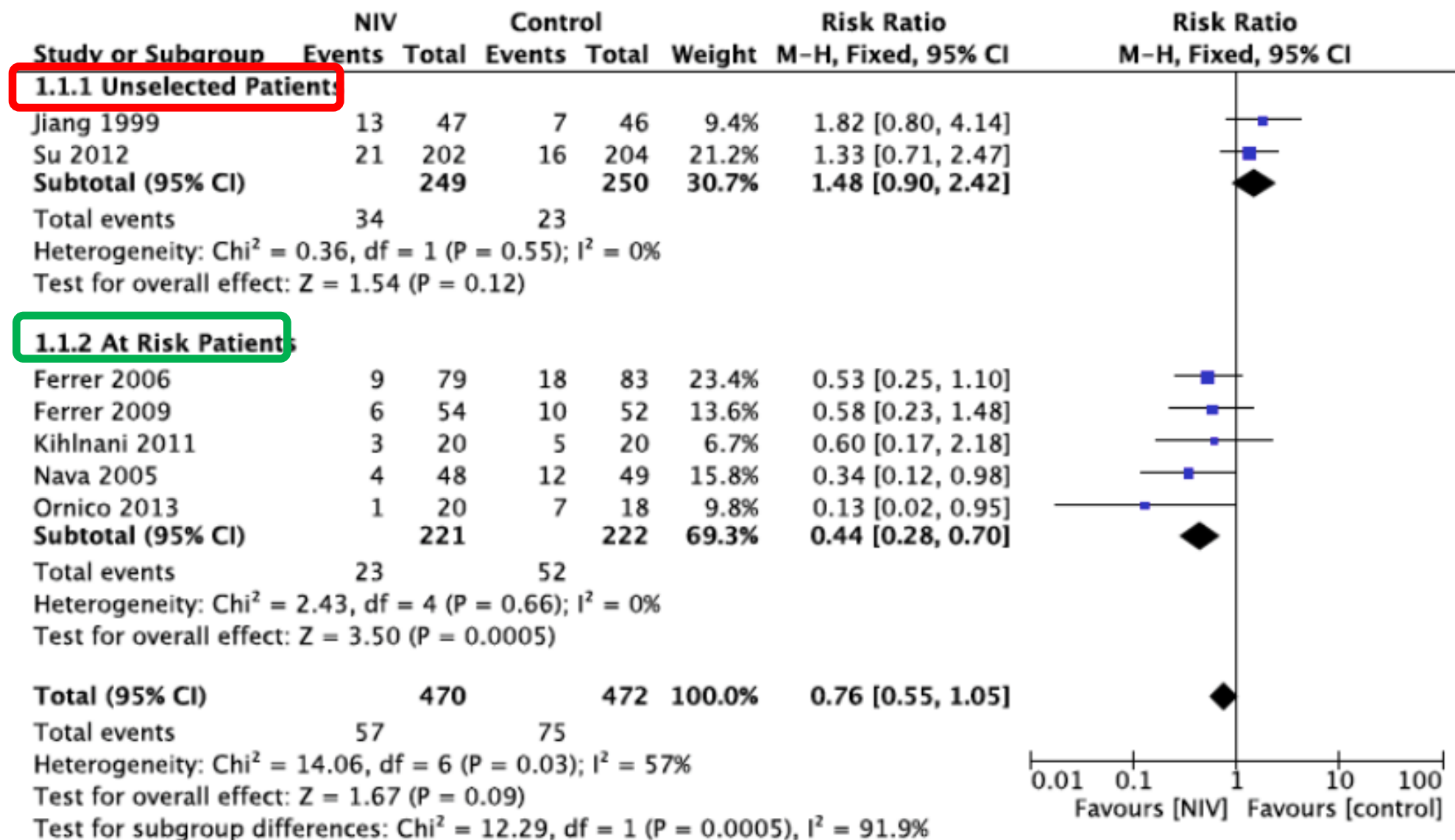
## Question #10a: Should NIV be used in the prevention of respiratory failure post extubation?

### Mortality





## Re-Intubation





### Question 10b: Should NIV be used in the treatment of respiratory failure that develops post-extubation?

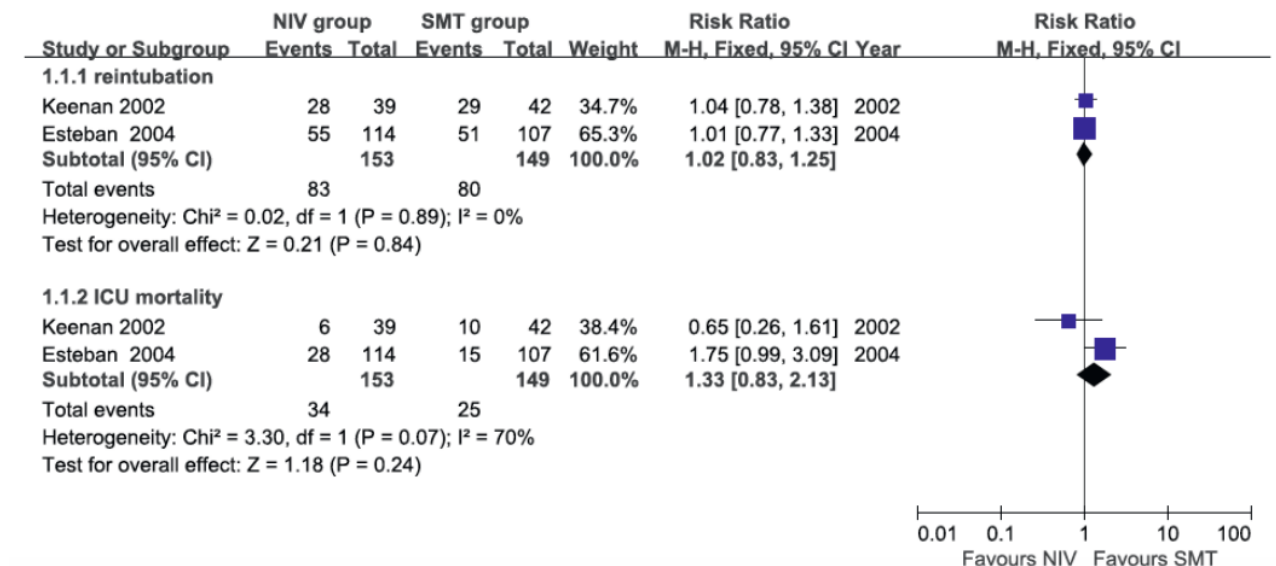
Following the positive findings of case series and case-control studies, two RCTs compared NIV with conventional treatment (oxygen therapy) in patients who developed respiratory failure after planned extubation [123, 124].

#### Recommendation

We suggest that NIV should not be used in the treatment of patients with established post-extubation respiratory failure. (Conditional recommendation, low certainty of evidence.)

#### Question #10b: Should NIV be used in the treatment of respiratory failure post extubation?

Mortality & Re-intubation







- NIV is a strategy to allow earlier extubation in selected patients : acute-on-chronic respiratory failure (hypercapnic RF or AECOPD).
- But with considerations :

Table 4. Subjects Deemed at Risk for Extubation Failure in the Studies by Nava et al<sup>21</sup> and Ferrer et al<sup>22</sup>

| Nava                                  | Ferrer  |
|---------------------------------------|---|
| Hypercapnia                           | Age > 65 y                                    |
| Congestive heart failure              | Cardiac failure as the cause of intubation    |
| Ineffective cough                     | Increased severity, assessed by an            |
| Excessive tracheobronchial secretions | APACHE-II score > 12 on the day of extubation |
| More than 1 failed SBT                |   |
| More than 1 comorbid condition        |   |
| Upper-airway obstruction              |   |

## The Role of Noninvasive Ventilation in the Ventilator Discontinuation Process

Dean R Hess PhD RRT FAARC

- The criteria to initiate an SBT must be satisfied.
- The upper airway should be patent.
- The patient should be able to clear secretions (with or without assistance).
- The patient should be a good candidate for NIV; able to tolerate the interface.
- The patient should be able to breathe spontaneously long enough to allow mask and ventilator adjustments.
- *Extubation to NIV is discouraged if the patient would be technically difficult to reintubate.*



2006  
NY, US

# Noninvasive ventilation for prevention of post-extubation respiratory failure in obese patients

A.A. El Solh\*, A. Aquilina\*, L. Pineda\*, V. Dhanvantri\*, B. Grant\*<sup>#</sup> and P. Bouquin\*

- 62 (**BMI > 35**) , after SBT:
  - ✓ 1) BiPAP (initial I: 12 E:4 titrated to RR < 25 & SpO2> 90%)
  - 2) O2 + physiotherapy ..
- Respiratory failure: > 1h ..
  - pH < 7.35 & ↑ PCO2 > 20%
  - SpO2 < 90%
  - ↓ consciousness
  - respiratory muscle fatigue
  - Sever delirium, agitation
  - Secretion not cleared

|                               | NIV       | Conventional therapy | p-value |
|-------------------------------|-----------|----------------------|---------|
| Subjects n                    | 62        | 62                   |         |
| Respiratory failure           | 6 (10)    | 16 (26)              | 0.03    |
| Reintubation                  | 6 (10)    | 13 (21)              | 0.14    |
| Causes of respiratory failure |           |                      |         |
| Hypoxia                       | 2 (3)     | 3 (5)                |         |
| Hypercapnia                   | 2 (3)     | 9 (15)               |         |
| Respiratory muscle fatigue    | 1 (2)     | 2 (3)                |         |
| Haemodynamic instability      | 0         | 1 (2)                |         |
| Inability to clear secretions | 0         | 1 (2)                |         |
| Delirium                      | 1 (2)     | 0                    |         |
| Hospital-acquired pneumonia   | 3 (5)     | 9 (15)               | 0.13    |
| Bloodstream infection         | 2 (3)     | 5 (8)                | 0.44    |
| ICU stay days                 | 11.8±7.9  | 18.2±11.2            | <0.001  |
| Hospital stay days            | 20.6±10.6 | 26.0±11.3            | 0.007   |
| Hospital mortality            | 8 (13)    | 15 (24)              | 0.17    |

Eur Respir J 2006; 28



# Effect of Postextubation High-Flow Nasal Oxygen With Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation Among Patients at High Risk of Extubation Failure

A Randomized Clinical Trial

Arnaud W. Thille, MD, PhD,<sup>1,2</sup> Grégoire Muller, MD,<sup>3</sup> Arnaud Gacouin, MD,<sup>4</sup> Rémi Coudroy, MD,<sup>1,2</sup> Maxens Decavèle, MD,<sup>5</sup> Romain Sonnevile, MD, PhD,<sup>6</sup> François Beloncle, MD,<sup>7</sup> Christophe Girault, MD,<sup>8</sup> Laurence Dangers, MD,<sup>9</sup> Alexandre Lautrette, MD, PhD,<sup>10</sup> Séverin Cabasson, MD,<sup>11</sup> Anahita Rouzé, MD,<sup>12</sup> Emmanuel Vivier, MD,<sup>13</sup> Anthony Le Meur, MD,<sup>14</sup> Jean-Damien Ricard, MD, PhD,<sup>15</sup> Keyvan Razazi, MD,<sup>16</sup> Guillaume Barberet, MD,<sup>17</sup> Christine Lebert, MD,<sup>18</sup> Stephan Ehrmann, MD, PhD,<sup>19</sup> Caroline Sabatier, MD,<sup>20</sup> Jeremy Bourenne, MD,<sup>21</sup> Gael Pradel, MD,<sup>22</sup> Pierre Bailly, MD,<sup>23</sup> Nicolas Terzi, MD, PhD,<sup>24</sup> Jean Dellamonica, MD, PhD,<sup>25</sup> Guillaume Lacave, MD,<sup>26</sup> Pierre-Éric Danin, MD,<sup>27</sup> Hodanou Nanadougmar, MD,<sup>28</sup> Aude Gibelin, MD,<sup>29</sup> Lassane Zanre, MD,<sup>30</sup> Nicolas Deye, MD, PhD,<sup>31</sup> Alexandre Demoule, MD, PhD,<sup>5</sup> Adel Maamar, MD,<sup>4</sup> Mai-Anh Nay, MD,<sup>3</sup> René Robert, MD, PhD,<sup>1,2</sup> Stéphanie Ragot, PharmD, PhD,<sup>2</sup> and Jean-Pierre Frat, MD<sup>1,2</sup>, for the HIGH-WEAN Study Group and the REVA Research Network

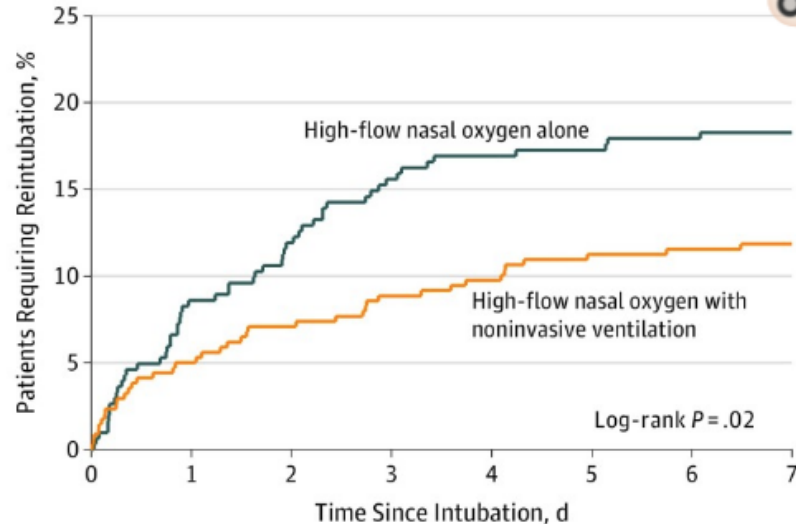
2019  
France

- 641(out of 3121) high risk reintubation (> 65 y, chronic heart or lung)

1) HFNO: flow> 50 l/m, SpO2> 92%, > 2d

✓ 2) Immediately PSV:5 + PEEP: 5-10, >12h/d

AND HFNO in intervals



|                         |     |     |     |     |     |     |     |     |
|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| No. at risk             |     |     |     |     |     |     |     |     |
| High-flow nasal oxygen  |     |     |     |     |     |     |     |     |
| Alone                   | 302 | 276 | 265 | 253 | 248 | 246 | 244 | 243 |
| With                    | 339 | 321 | 314 | 308 | 305 | 294 | 292 | 291 |
| noninvasive ventilation |     |     |     |     |     |     |     |     |

HFNO

NIV +HFNO

## Primary Outcome

|                       |         |         |                      |     |
|-----------------------|---------|---------|----------------------|-----|
| Reintubation at day 7 | 55 (18) | 40 (12) | -6.4 (-12.0 to -0.9) | .02 |
|-----------------------|---------|---------|----------------------|-----|

## Secondary Outcomes

|   |         |         |                      |     |
|---|---------|---------|----------------------|-----|
| Postextubation respiratory failure at day 7 | 88 (29) | 70 (21) | -8.5 (-15.2 to -1.8) | .01 |
|---|---------|---------|----------------------|-----|

## Reintubation

|         |         |        |                     |     |
|---------|---------|--------|---------------------|-----|
| At 48 h | 36 (12) | 24 (7) | -4.8 (-9.6 to -0.3) | .04 |
|---------|---------|--------|---------------------|-----|

|         |         |        |                      |      |
|---------|---------|--------|----------------------|------|
| At 72 h | 47 (16) | 30 (9) | -6.7 (-11.9 to -1.7) | .009 |
|---------|---------|--------|----------------------|------|

|                        |         |         |                      |      |
|------------------------|---------|---------|----------------------|------|
| Up until ICU discharge | 59 (20) | 41 (12) | -7.4 (-13.2 to -1.8) | .009 |
|------------------------|---------|---------|----------------------|------|

## Length of stay, median (IQR), days

|        |              |              |                   |     |
|--------|--------------|--------------|-------------------|-----|
| In ICU | 11 (7 to 19) | 12 (7 to 19) | 0.5 (-1.6 to 2.6) | .55 |
|--------|--------------|--------------|-------------------|-----|

|             |               |               |                   |     |
|-------------|---------------|---------------|-------------------|-----|
| In hospital | 23 (15 to 39) | 25 (15 to 42) | 2.3 (-1.4 to 6.1) | .31 |
|-------------|---------------|---------------|-------------------|-----|

## Mortality

|        |        |        |                    |     |
|--------|--------|--------|--------------------|-----|
| In ICU | 26 (9) | 21 (6) | -2.4 (-6.7 to 1.7) | .25 |
|--------|--------|--------|--------------------|-----|

|             |         |         |                   |     |
|-------------|---------|---------|-------------------|-----|
| In hospital | 46 (15) | 54 (16) | 0.7 (-5.0 to 6.3) | .80 |
|-------------|---------|---------|-------------------|-----|

|           |         |         |                   |     |
|-----------|---------|---------|-------------------|-----|
| At day 28 | 33 (11) | 39 (12) | 0.6 (-4.4 to 5.5) | .82 |
|-----------|---------|---------|-------------------|-----|

|           |         |         |                    |     |
|-----------|---------|---------|--------------------|-----|
| At day 90 | 65 (21) | 62 (18) | -3.2 (-9.5 to 2.9) | .30 |
|-----------|---------|---------|--------------------|-----|

## Exploratory Outcomes

|  |         |         |                      |     |
|--|---------|---------|----------------------|-----|
| Patients meeting reintubation criteria during ICU stay | 65 (22) | 49 (14) | -7.1 (-13.1 to -1.1) | .02 |
|--|---------|---------|----------------------|-----|

|                                  |         |         |                      |     |
|----------------------------------|---------|---------|----------------------|-----|
| Mortality or reintubation in ICU | 64 (21) | 51 (15) | -6.2 (-12.2 to -0.2) | .04 |
|----------------------------------|---------|---------|----------------------|-----|

|                                   |            |            |                     |     |
|-----------------------------------|------------|------------|---------------------|-----|
| Mortality of reintubated patients | 21/59 (36) | 11/41 (27) | -8.8 (-25.7 to 9.9) | .35 |
|-----------------------------------|------------|------------|---------------------|-----|

2019 Oct 1

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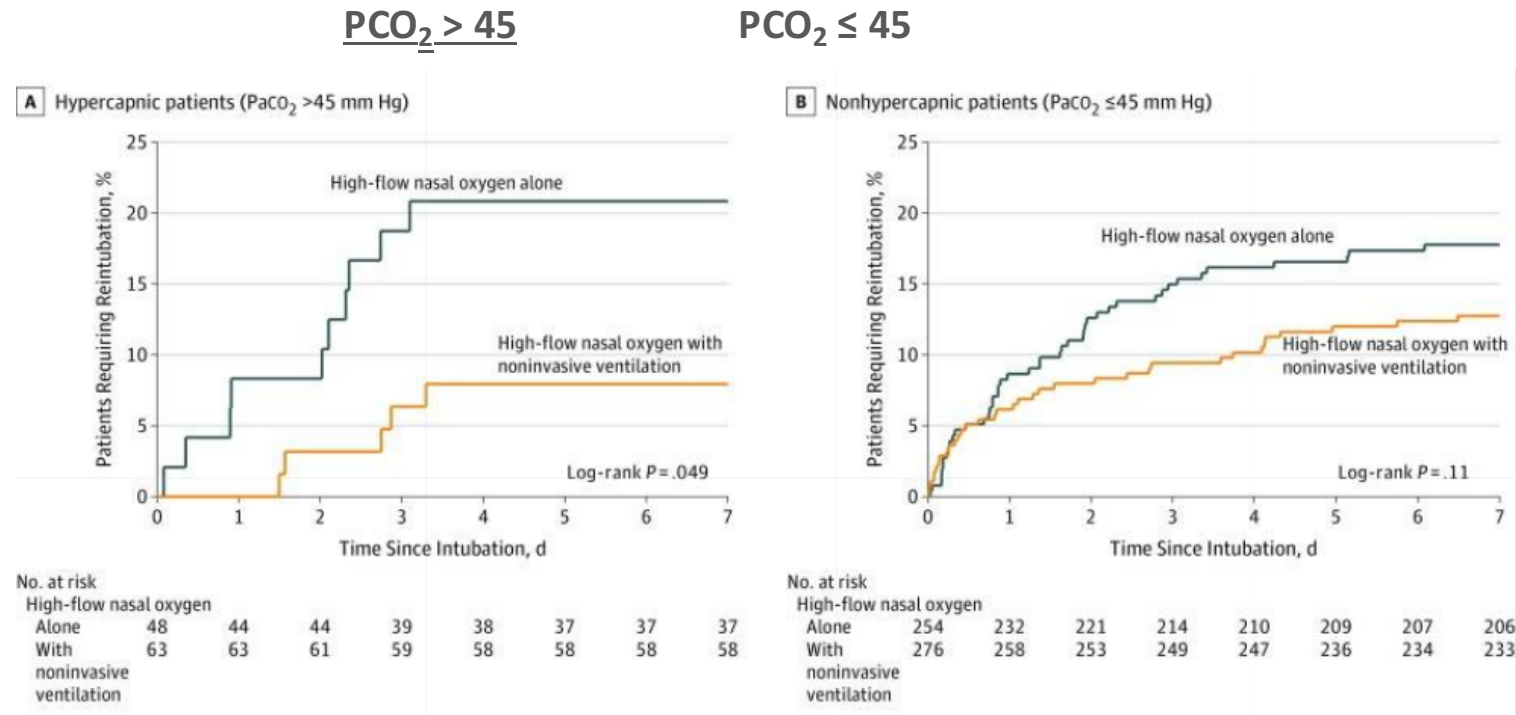
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## ORIGINAL ARTICLE

# Protocolized Postextubation Respiratory Support to Prevent Reintubation

## A Randomized Clinical Trial

Jonathan D. Casey<sup>1</sup>, Erin M. Vaughan<sup>1</sup>, Bradley D. Lloyd<sup>2</sup>, Peter A. Billas<sup>3</sup>, Karen E. Jackson<sup>1</sup>, Eric J. Hall<sup>4</sup>, Alexandra H. Toporek<sup>4</sup>, Kevin G. Buell<sup>4</sup>, Ryan M. Brown<sup>1</sup>, Roger K. Richardson<sup>2</sup>, J. Craig Rooks<sup>2</sup>, Reagan B. Buie<sup>5</sup>, Li Wang<sup>6</sup>, Christopher J. Lindsell<sup>6</sup>, E. Wesley Ely<sup>1,7,8</sup>, Wesley H. Self<sup>9</sup>, Gordon R. Bernard<sup>1</sup>, Todd W. Rice<sup>1</sup>, and Matthew W. Semler<sup>1</sup>; for the Vanderbilt Learning Healthcare System and the Pragmatic Critical Care Research Group

- The PROPER trial was a prospective, unblinded, pragmatic, cluster–crossover trial
- October 1, 2017, and March 31, 2019, in the medical ICU of Vanderbilt University Medical Center in Nashville, Tennessee
- All adults (age >18 yr) undergoing extubation from invasive mechanical ventilation in the study ICU immediately..

### Intervention:

#### ➤ NIV for

- AECOPD
- chronic hypercapnic respiratory failure
- obesity hypoventilation syndrome
- PCO<sub>2</sub> > 45 mm Hg on an ABG during a spontaneous breathing trial

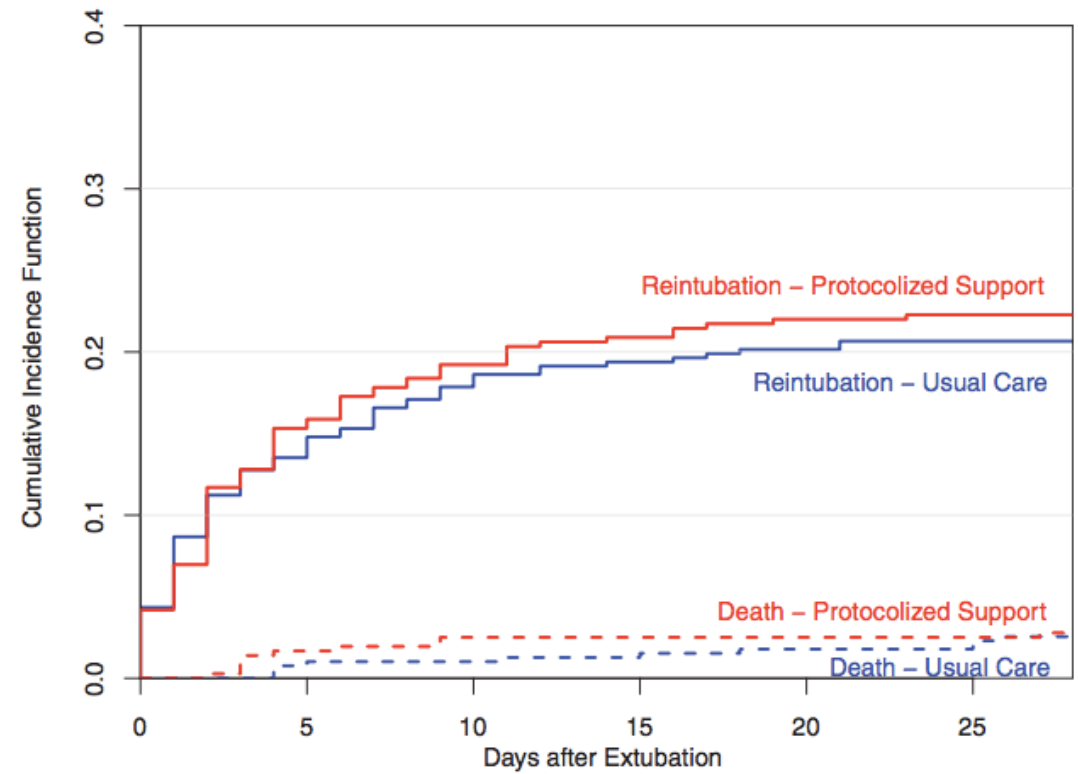
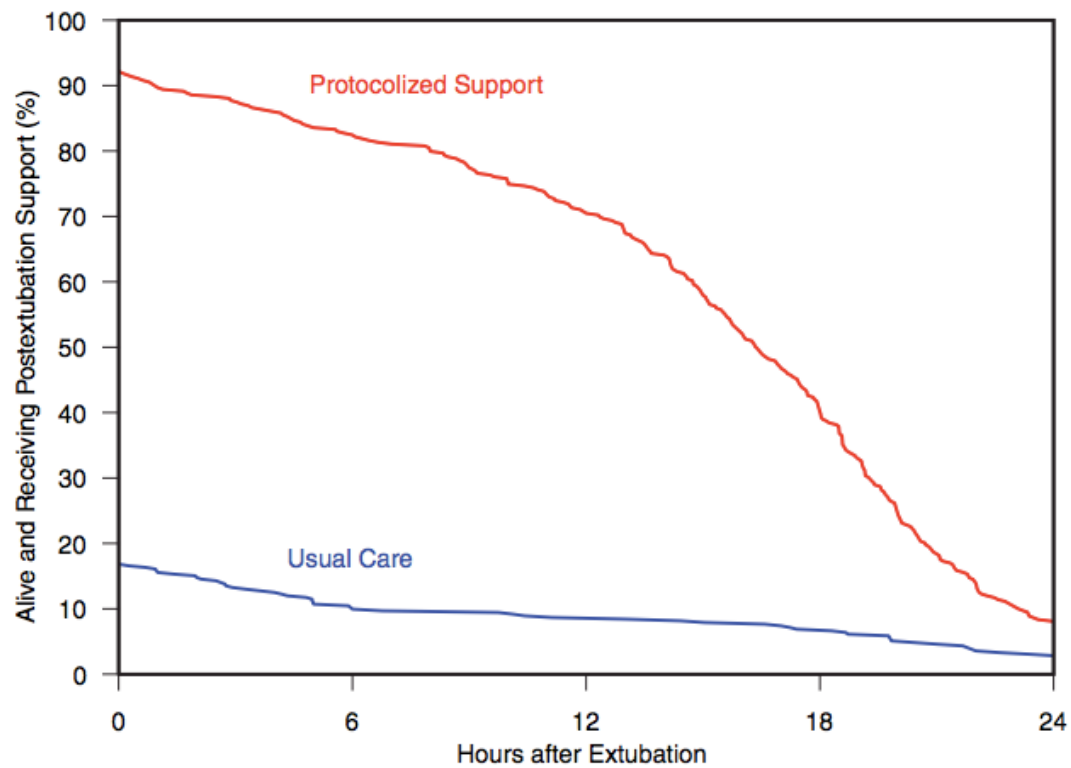
#### ➤ HFNO :

- All others

- Control group: usual care determined by treating clinicians



# PROPER Trial results







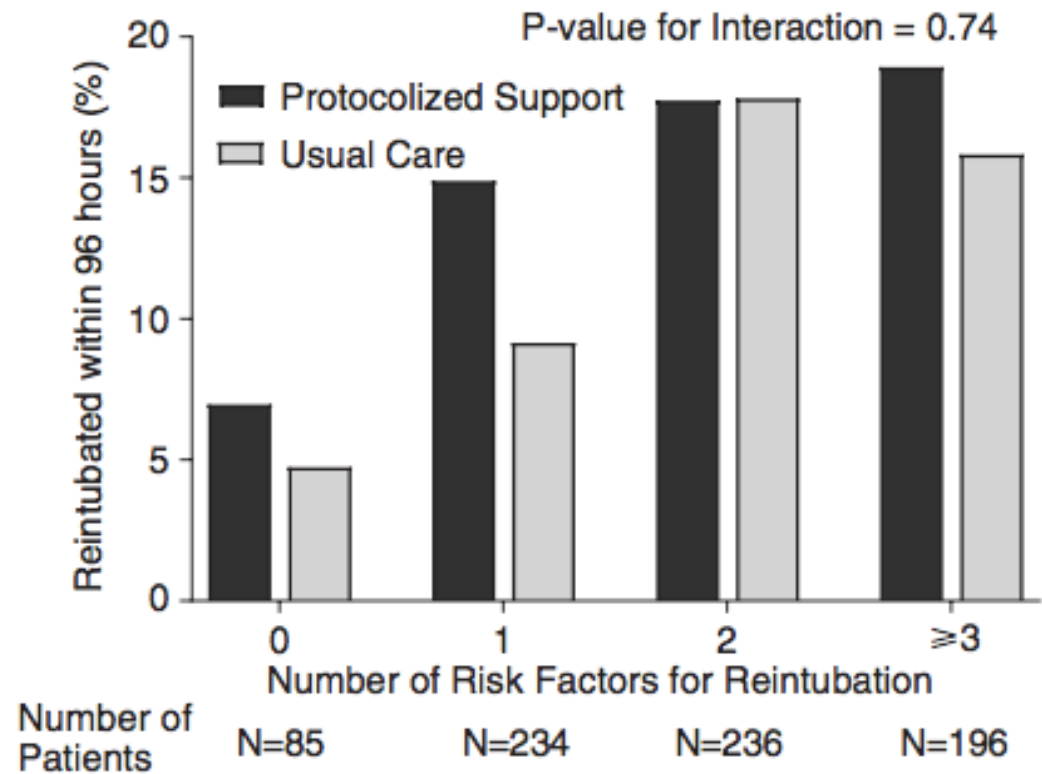
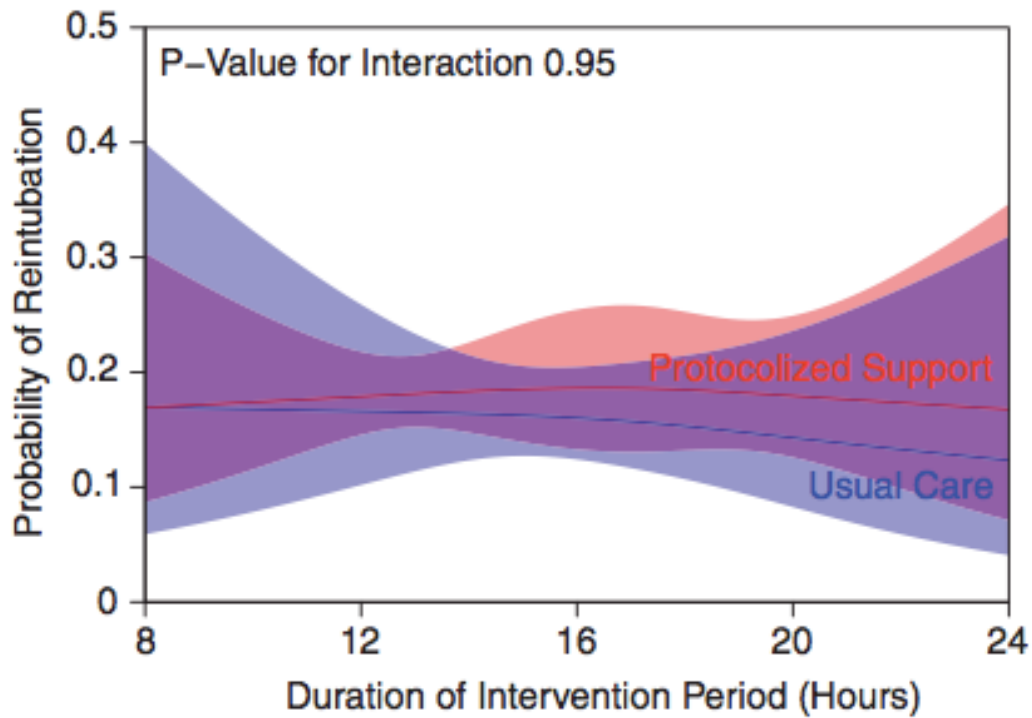
| Patient Characteristic   | Protocolized Support<br>( <i>n</i> = 359) | Usual Care<br>( <i>n</i> = 392) |
|--|---|---------------------------------|
| Age, median (IQR), yr  | 56 (43–66)                                | 57 (42–66)                      |
| Sex, M, <i>n</i> (%)   | 204 (56.8)                                | 205 (52.3)                      |
| White race*, <i>n</i> (%)  | 287 (81.3)                                | 317 (81.7)                      |
| Body mass index†, median (IQR), kg/m <sup>2</sup>                              | 26.6 (23.0–31.7)                          | 28.0 (23.2–33.8)                |
| Chronic respiratory comorbidity‡, <i>n</i> (%)                                 | 138 (38.4)                                | 163 (41.6)                      |
| Chronic obstructive pulmonary disease  | 58 (16.2)                                 | 87 (22.2)                       |
| Asthma   | 21 (5.8)                                  | 18 (4.6)                        |
| Obstructive sleep apnea  | 39 (10.9)                                 | 47 (12.0)                       |
| Pulmonary malignancy   | 14 (3.9)                                  | 16 (4.1)                        |
| Indications for intubation‡, <i>n</i> (%)                                      |   |                                 |
| Airway protection for decreased level of consciousness                         | 180 (50.1)                                | 168 (42.9)                      |
| Hypoxemic respiratory failure  | 141 (39.3)                                | 175 (44.6)                      |
| Hypercarbic respiratory failure  | 42 (11.7)                                 | 65 (16.6)                       |
| Preprocedural  | 45 (12.5)                                 | 36 (9.2)                        |
| Duration of invasive mechanical ventilation before extubation, d, median (IQR) | 3.0 (2.0–5.0)                             | 3.0 (2.0–4.0)                   |
| Unplanned extubation   | 17 (4.7%)                                 | 27 (6.9%)                       |
| APACHE II score at ICU admission§, median (IQR)                                | 19 (12–24)                                | 18 (13–24)                      |
| APACHE II score at extubation§, median (IQR)                                   | 17 (13–22)                                | 17 (12–22)                      |
| Active medical conditions‡, <i>n</i> (%)                                       |   |                                 |
| Sepsis or septic shock   | 136 (37.9)                                | 146 (37.2)                      |
| Pneumonia  | 135 (37.6)                                | 135 (34.4)                      |
| Acute respiratory distress syndrome  | 23 (6.4)                                  | 21 (5.4)                        |
| Aspiration   | 44 (12.3)                                 | 57 (14.5)                       |
| Gastrointestinal bleeding  | 45 (12.5)                                 | 42 (10.7)                       |
| Altered mental status  | 190 (52.9)                                | 204 (52.0)                      |
| Vasopressors in the 6 h before extubation, <i>n</i> (%)                        | 47 (13.1)                                 | 48 (12.2)                       |
| Failed one or more spontaneous breathing trial, <i>n</i> (%)                   | 83 (23.1)                                 | 80 (20.4)                       |
| Highest respiratory rate on a spontaneous breathing trial¶                     | 22 (17–28)                                | 22 (18–28)                      |
| At least one risk factor for reintubation¶                                     | 316 (88.0)                                | 350 (89.3)                      |



| Outcomes   | Protocolized Support<br>(n = 359) | Usual Care<br>(n = 392) | Odds Ratio<br>(95% Confidence Intervals) |
|--|-----------------------------------|-------------------------|--|
| Primary outcome*   |                                   |                         |  |
| Reintubation in the 96 h after extubation, n (%)   | 57 (15.9)                         | 52 (13.3)               | 1.23 (0.82–1.84)                         |
| Indication for reintubation <sup>†</sup> , n (%)   |                                   |                         |  |
| Hypoxemic respiratory failure  | 25 (43.9)                         | 24 (46.2)               | —  |
| Hypercapnic respiratory failure  | 5 (8.8)                           | 2 (3.8)                 | —  |
| Hypercapnic, hypoxemic respiratory failure   | 5 (8.8)                           | 7 (13.5)                | —  |
| Altered mental status  | 6 (10.5)                          | 5 (9.6)                 | —  |
| Procedure  | 7 (12.3)                          | 8 (15.4)                | —  |
| Other  | 3 (5.3)                           | 6 (11.5)                | —  |
| Death without reintubation   | 6 (10.5)                          | 0 (0.0)                 | —  |
| Secondary outcome  |                                   |                         |  |
| ICU-free days, median (IQR)  | 26 (23–26)                        | 26 (22–26)              | 0.96 (0.81–1.13)                         |
| Exploratory outcomes <sup>‡</sup>  |                                   |                         |  |
| Highest respiratory rate within 6 h after extubation <sup>§</sup> , median (IQR), breaths per minute | 23 (20–28)                        | 24 (21–28)              | 0.77 (0.60–0.98)                         |
| Lowest SaO <sub>2</sub> within 6 h after extubation <sup>  </sup> , median (IQR), %                  | 94 (91–97)                        | 93 (90–95)              | 1.85 (1.44–2.39)                         |
| Highest FIO <sub>2</sub> within 6 h after extubation <sup>  </sup> , median (IQR)                    | 0.40 (0.36–0.45)                  | 0.33 (0.27–0.41)        | 2.61 (1.67–4.07)                         |
| Reintubation within 28 d <sup>  </sup> , n (%)   | 80 (22.3)                         | 82 (20.9)               | 1.07 (0.79–1.45)                         |
| Time from extubation to reintubation, median (IQR), h  | 56 (21–147)                       | 47 (18–163)             | —  |
| Ventilator-free days, median (IQR)   | 28 (28–28)                        | 28 (28–28)              | 1.21 (0.91–1.62)                         |
| Died before hospital discharge, n (%)  | 29 (8.1)                          | 41 (10.5)               | 0.76 (0.53–1.08)                         |



# PROPER Trial results



# نتیجه گیری

آ) استفاده از NIV بعد از اکستوباسیون ممکن است (*may*) عواقب و نتایج بالینی را در گروه مشخصی از بیماران (*selected*) بهتر کند.

ب) استفاده از NIV باید بلافاصله بعد از اکستوباسیون (*immediately*) بکار گرفته شود و نیاز به مراقبت از نزدیک دارد.

پ) آموزش مداوم پرسنل آیسو و تجربه بیشتر استفاده از NIV در نتیجه گیری نهایی تاثیرگذار است.

ت) همه بیماران از این مداخله سود نمی برند.





با تشکر از توجه شما.  
سلامت باشید.