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**CHICAGO**  
MEDICINE

# The Changing Landscape of Noninvasive Ventilation: Introducing Helmet Ventilation

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# Conflicts of Interest

- No relevant conflicts of interest
- Funding:
  - T32 NIH/NHLBI
  - Unrestricted internal grant from the Daniel Edelman family
- Sponsor had no role in the design and conduct of the study, collection, management, analysis, and interpretation of the data or preparation, review, or approval of the manuscript

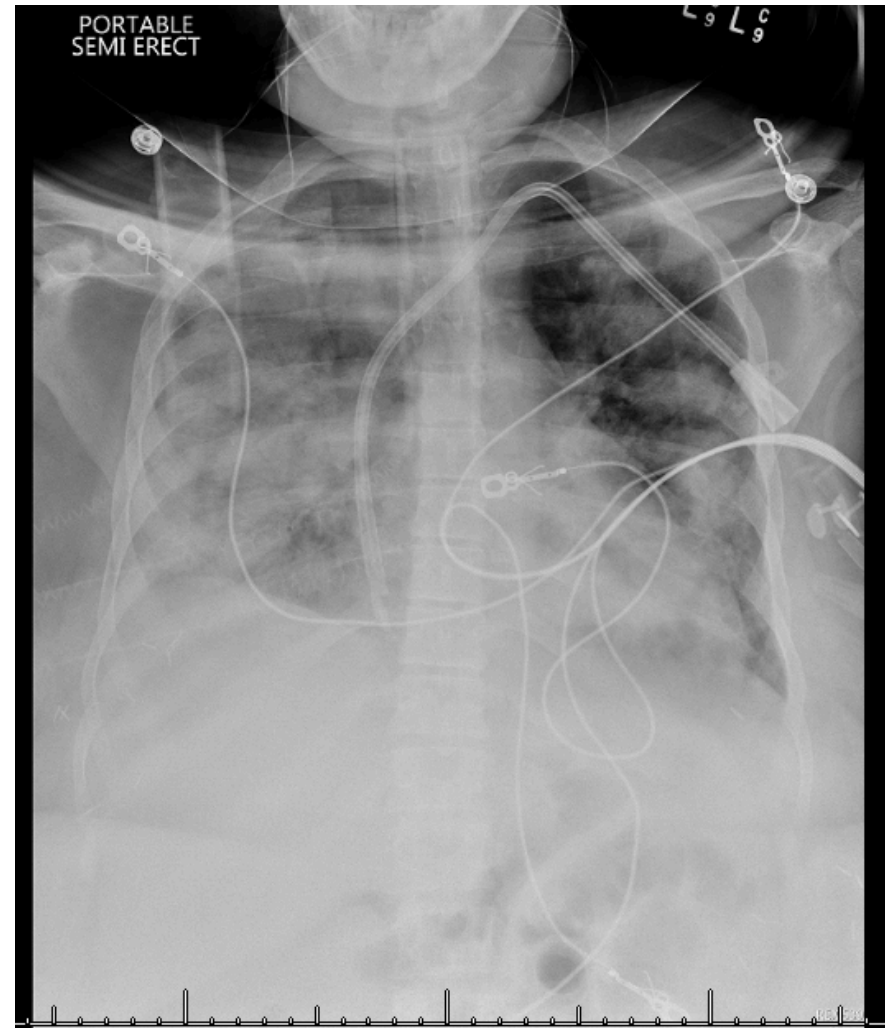
# Case

38 yo woman with hx of kidney transplant for FSGS presenting with progressive shortness of breath and productive cough x 1 week.

Despite broad spectrum abx, she developed worsening tachypnea and hypoxia and was transferred to the ICU. On admission she was afebrile, tachypneic (RR 38-42 breaths/min), and was saturating 89% on 100%NRB.

What are her treatment options?

- Immediate intubation
- High flow nasal cannula
- Noninvasive ventilation



# Noninvasive Ventilation (NIV)

- Obviates the need for endotracheal intubation
- Avoids the complications of invasive mechanical ventilation
- Benefits are compelling
  - COPD exacerbations
  - Cardiogenic pulmonary edema



# Acute Hypoxemic Respiratory Failure (AHRF)

- NIV improves outcomes in immunocompromised patients

## Noninvasive Ventilation for Treatment of Acute Respiratory Failure in Patients Undergoing Solid Organ Transplantation

A Randomized Trial

Antonelli et al. *JAMA* 2000;283:235-241

- Recent data have shown

- No benefit with face mask NIV

- *Increased* mortality

## NONINVASIVE VENTILATION IN IMMUNOSUPPRESSED PATIENTS

### NONINVASIVE VENTILATION IN IMMUNOSUPPRESSED PATIENTS WITH PULMONARY INFILTRATES, FEVER, AND ACUTE RESPIRATORY FAILURE

Gilbert et al. *NEJM* 2001; 344(7):481-7

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

### Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure A Randomized Clinical Trial

Lemiale et al. *JAMA* 2015; 314(16):1711-19.

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

JUNE 4, 2015

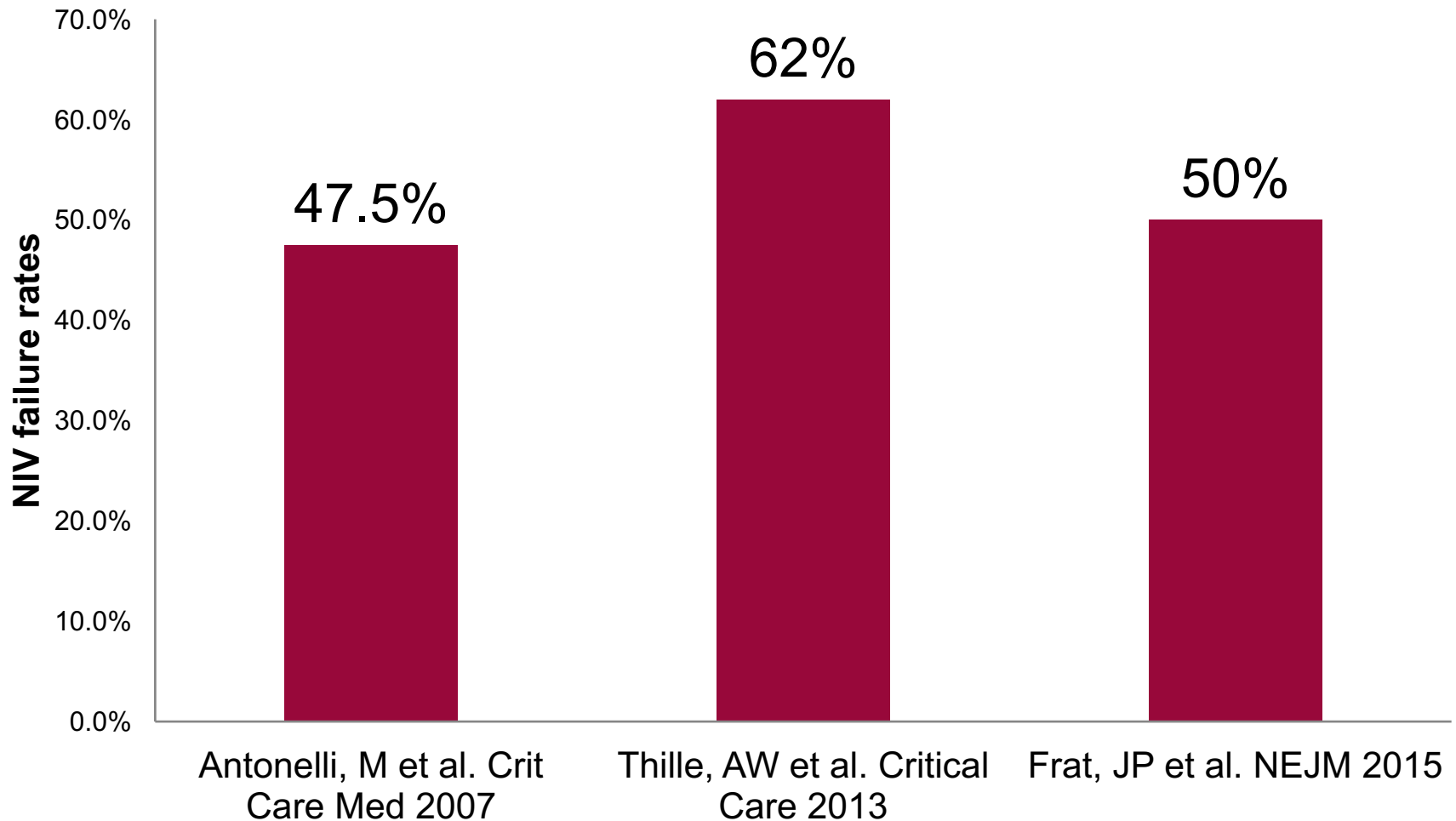
VOL. 372 NO. 23

### High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Frat et al. *NEJM* 2015;372:2185-2196



# NIV failure rates are high in patients with AHRF



# Why are NIV failure rates so high?

- High levels of PEEP are needed
- Excessive air leak
- Patient intolerance

## A possible solution...

### Continuous Positive Airway Pressure for Treatment of Postoperative Hypoxemia A Randomized Controlled Trial

- Enrolled patients with  $\text{PaO}_2/\text{FiO}_2 < 300$
- Reduced reintubation rates from 10% to 1%
- Patient intolerance was low

Squadrone et al. *JAMA*. 2005;293:589-595



# Alternative interface for NIV



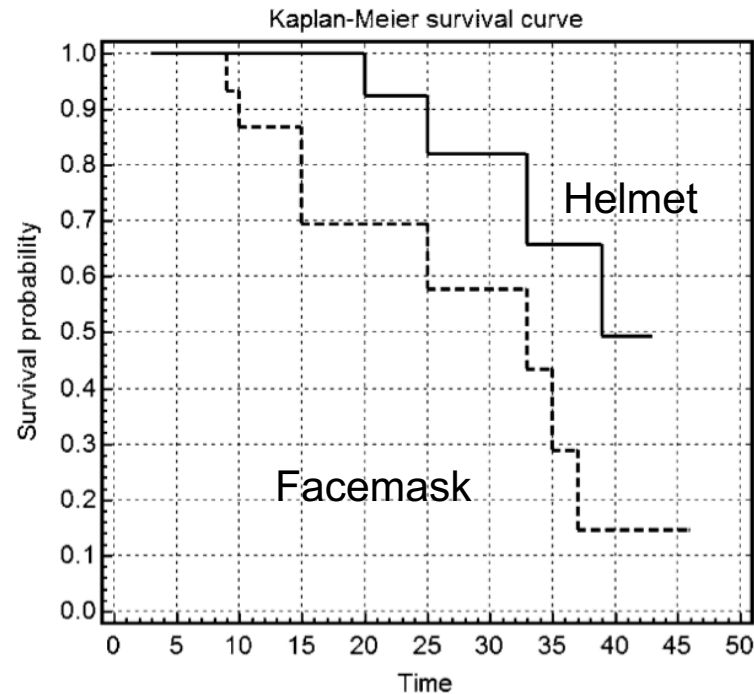
# Precedents...

- Improved tolerability
- Improved gas exchange
  
- ? Lower hospital mortality

## Noninvasive Ventilation by Helmet or Face Mask in Immunocompromised Patients\*

### A Case-Control Study

Rocco M, et al. *CHEST* 2004; 126:1508-1515



Principi T, et al. *Intensive Care Med* 2004; 30:147-50

# Study Design

- Single-center randomized clinical trial
  - Patients with ARDS requiring face mask NIV for  $\geq 8$  hours
  - ARDS defined by Berlin Criteria
- Exclusion Criteria:
  - Cardiopulmonary arrest
  - Glasgow Coma Scale  $< 8$
  - Absence of airway protective reflex
  - Elevated intracranial pressure
  - Tracheostomy
  - Upper airway obstruction
  - Pregnancy
  - Refused endotracheal intubation

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

# Study Groups

- **Intervention:** Helmet NIV
  - Switch Face Mask to Helmet



- **Control:** Face mask NIV
  - Philips Respironics



# Standard NIV titration for both groups

- PEEP titration
  - Goal:  $\text{SpO}_2 \geq 90\%$ ,  $\text{FiO}_2$  of  $\leq 60\%$
- Inspiratory pressure titration
  - Goal:  $\text{RR} < 25$  breaths/min; no accessory muscle use
- NIV weaning:
  - Reduce support progressively
  - Discontinuation criteria:
    - $\text{RR} < 30$  breaths/min
    - $\text{PaO}_2 > 75$ mm Hg with  $\text{FiO}_2 \leq 50\%$  and  $\text{PEEP} \leq 5$  cmH<sub>2</sub>O

# Pre-specified Intubation Criteria

- Neurologic deterioration
- Oxygen saturation < 88%
- Respiratory rate > 36 breaths per minute
- Intolerance of face mask or helmet
- Airway bleeding or copious respiratory secretions

# Ventilator management of intubated patients

- Low tidal volume strategy
- Daily interruption of sedation
- Awakening and breathing trials
- Early mobilization

# Study Outcomes

- **Primary outcome**: Endotracheal intubation rate
- **Secondary outcomes**:
  - 28-day invasive ventilator free days
  - Duration of ICU stay
  - Hospital length of stay
  - Hospital mortality
  - 90-day mortality
  - Adverse events



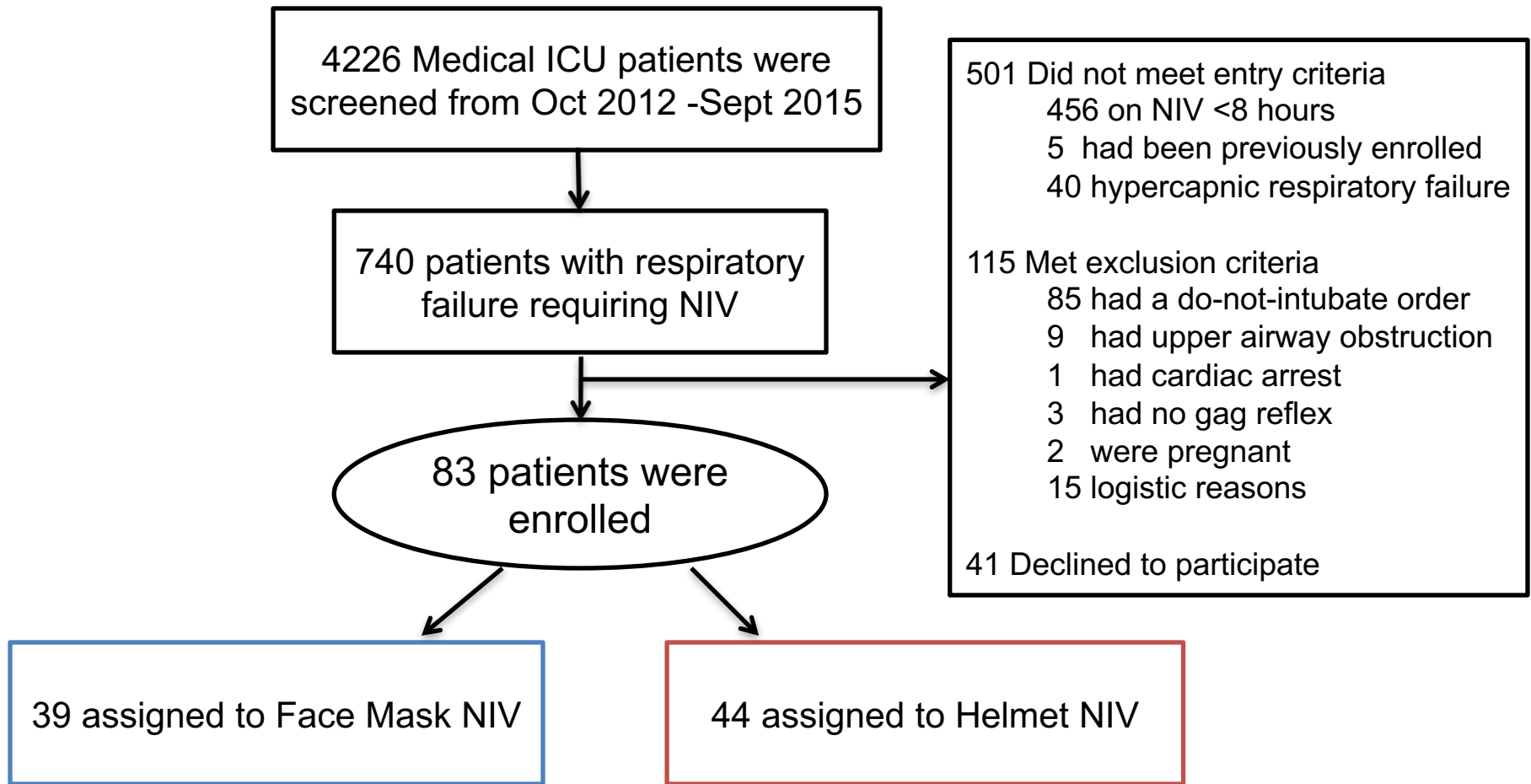
# Power Calculation

- NIV failure rate of 50% for patients with AHRF
- Target: 20% absolute reduction of the primary outcome
- Enrollment of a total of 206 patients
  - 80% power
  - Two-sided alpha level of 0.05.

# Data & Safety Monitoring Board

- The DSMB recommended early stoppage for efficacy and safety

# Consort Diagram



# Baseline Characteristics

Characteristic	Face Mask NIV (N=39)		Helmet NIV (N=44)	
	Age -- year	60.9	[56.4-71.1]	58
Female -- no. (%)	18	46%	20	45%
African American -- no. (%)	22	56%	28	64%
White, Nonhispanic – no (%)	13	33%	11	25%
White, Hispanic --no (%)	3	8%	3	7%
Asian --no (%)	1	3%	2	5%
Body Mass Index	28	[23-35]	27	[24-36]
APACHE II	26	[23-30]	25	[20-28]
<b>Past Medical History</b>				
Solid Cancer	10	26%	5	11%
Hematologic Cancer	6	15%	7	16%
Solid Organ Transplant	3	8%	5	11%
Stem Cell Transplant	1	3%	5	11%

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

## Baseline Characteristics (cont'd)

	Face Mask NIV (N=39)		Helmet NIV (N=44)	
<b>Reason for acute respiratory failure</b>				
Pneumonia	14	36%	23	52%
Aspiration	5	13%	3	7%
Extrapulmonary ARDS	6	15%	3	7%
Pneumonia due to immunosuppression	14	36%	15	34%
<b>Respiratory/hemodynamic parameters</b>				
Duration of NIV prior to randomization (hours)	13	[8-19.7]	10.3	[8.3-13.4]
Inspiratory Positive Airway Pressure	10	[10-15]	12	[10-14.5]
Expiratory Positive Airway Pressure	5	[5-8]	5	[5-8]
SpO <sub>2</sub> --(%)	95	[91-99]	97	[95-99]
FiO <sub>2</sub> --(%)	60	[50-80]	60	[40-90]
PaO <sub>2</sub> : FiO <sub>2</sub>	144	[90-223]	118	[93-170]
Shock	12	31%	9	20%

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

# Respiratory support after Randomization

	Face Mask NIV (N=39)		Helmet NIV (N=44)		p-value
Duration of NIV -- (hours)	26.4	[7.0-60.0]	19.8	[8.4-45.6]	0.68
PEEP (cm H <sub>2</sub> O) <sup>a</sup>	5.1	[5.0-8.0]	8	[5.0-10.0]	0.006
Pressure Support (cm H <sub>2</sub> O) <sup>a</sup>	11.2	[10.0-14.5]	8	[5.6-10.0]	<0.001
FiO <sub>2</sub> (%) <sup>a</sup>	60	[50.0-68.6]	50	[40.0-60.0]	0.02
SpO <sub>2</sub> (%) <sup>a</sup>	95.3	[92.3-96.7]	96.2	[94.8-98.4]	0.13

## Change in Respiratory Rate

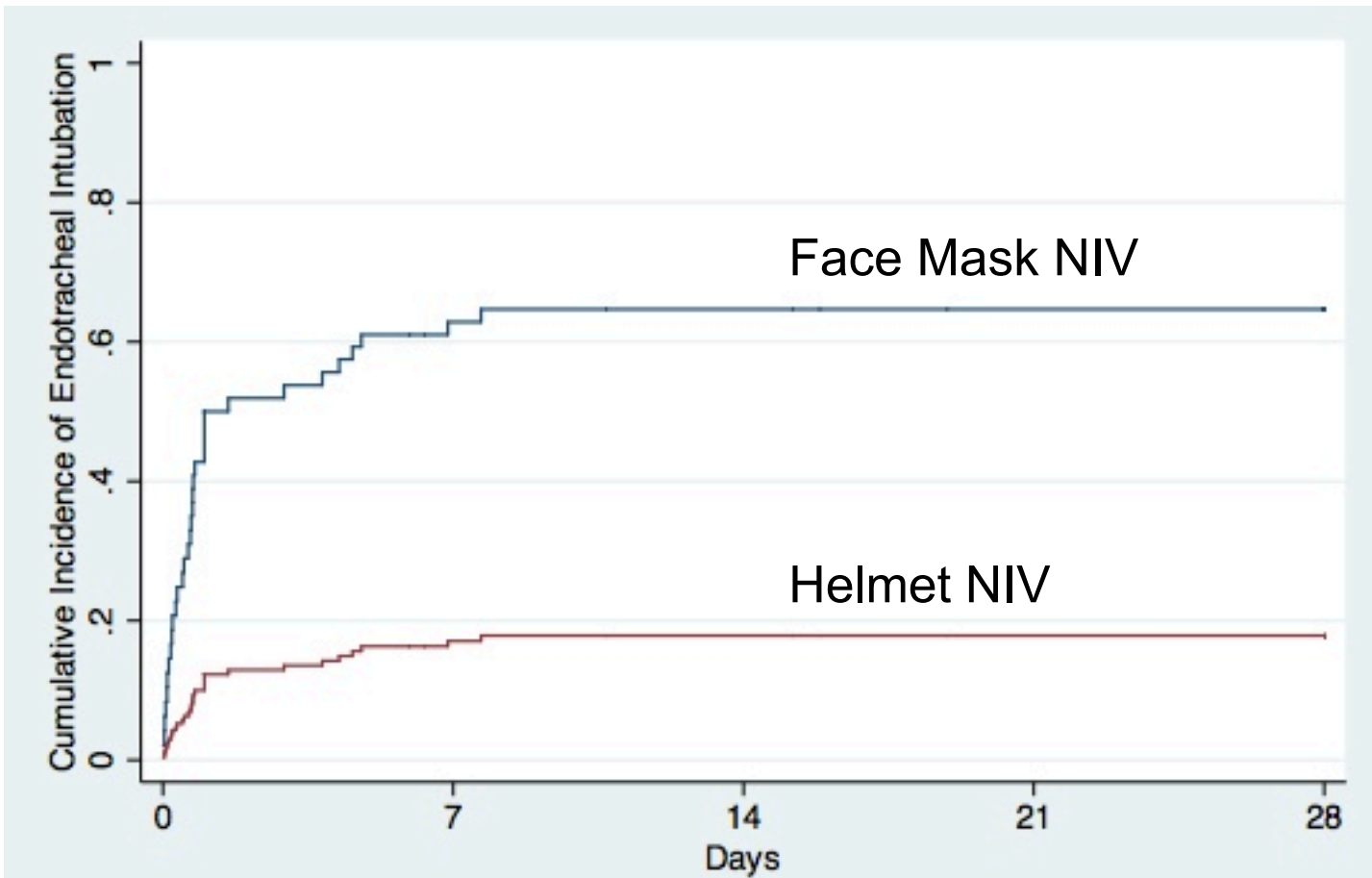
Baseline -- Breaths/min <sup>a</sup>	28.3	[22.1-34.4]	27.7	[21.5-34.6]
After Randomization -- Breaths/min <sup>a</sup>	29.1	[22.1-37.6]	24.5	[20.4-30.5]
	p=0.21		p<0.001	

<sup>a</sup>Area under the curve analysis of all vital signs and Respiratory Support

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

# Primary Outcome

	Face Mask NIV (N=39)		Helmet NIV (N=44)		p-value
Endotracheal intubation -- n (%)	24	61.5%	8	18.2%	<0.001



Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

# Reason for Endotracheal Intubation

Reason for intubation -- n (%)	Face Mask NIV (N=39)		Helmet NIV (N=44)		p-value
Respiratory Failure	20	83.3%	3	37.5%	0.01
Circulatory Failure	3	12.5%	0	0%	0.55
Neurologic Failure	1	4.2%	5	62.5%	0.001

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

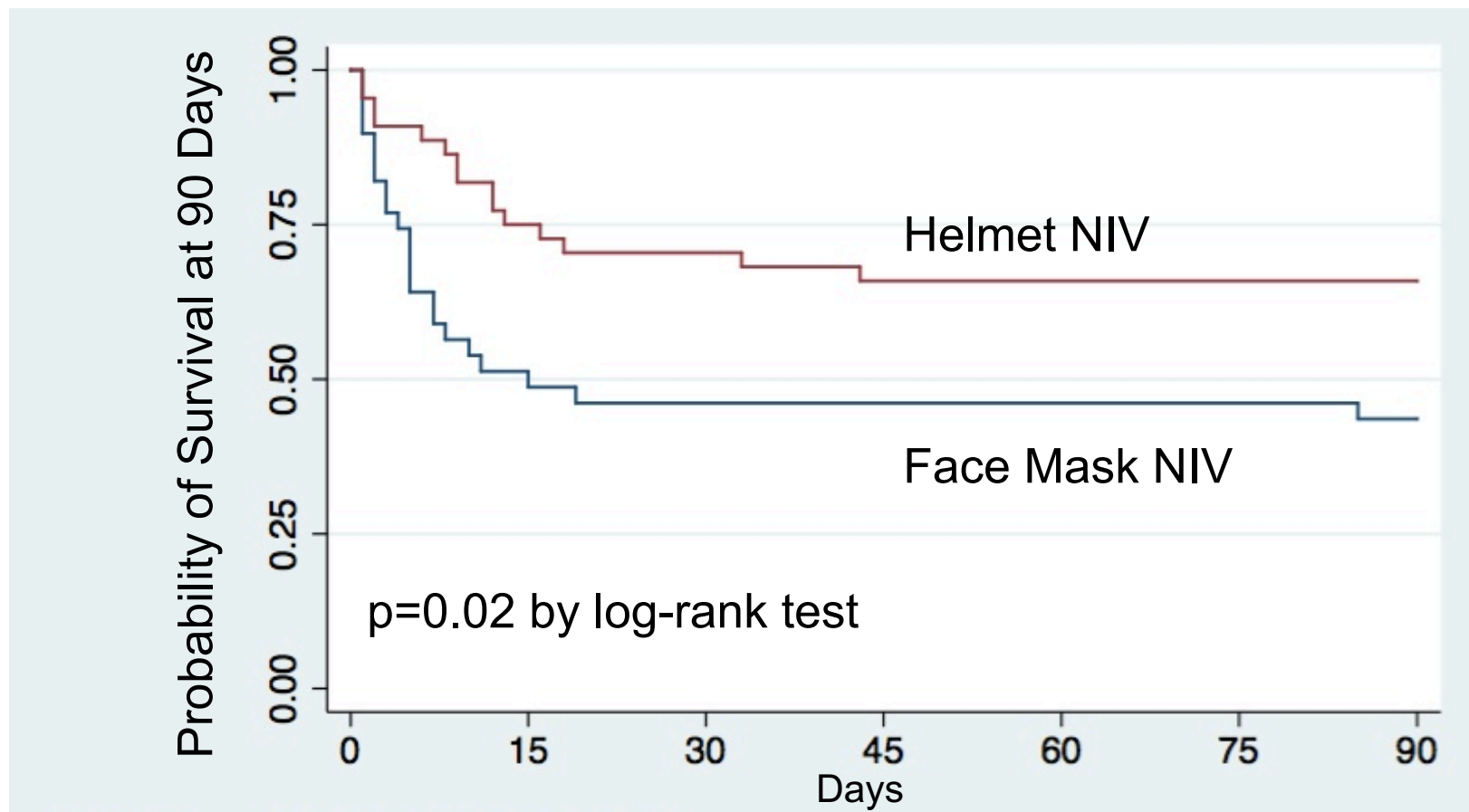


# Secondary Outcomes

	Face Mask NIV (N=39)		Helmet NIV (N=44)		p-value
28 day Ventilator Free Days	12.5	[0.5-28]	28	[13.7-28]	<0.001
ICU length of stay (days)	7.8	[3.9-13.8]	4.7	[2.5-8.7]	0.04
Hospital length of stay (days)	15.2	[7.8-19.7]	10.1	[6.5-15.9]	0.16
Hospital Mortality -- n (%)	19	48.7%	12	27.3%	0.04
<b>Adverse Events</b>					
Mask Deflation	0	0%	2	4.5%	
Skin Ulceration	3	7.6%	3	6.8%	

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

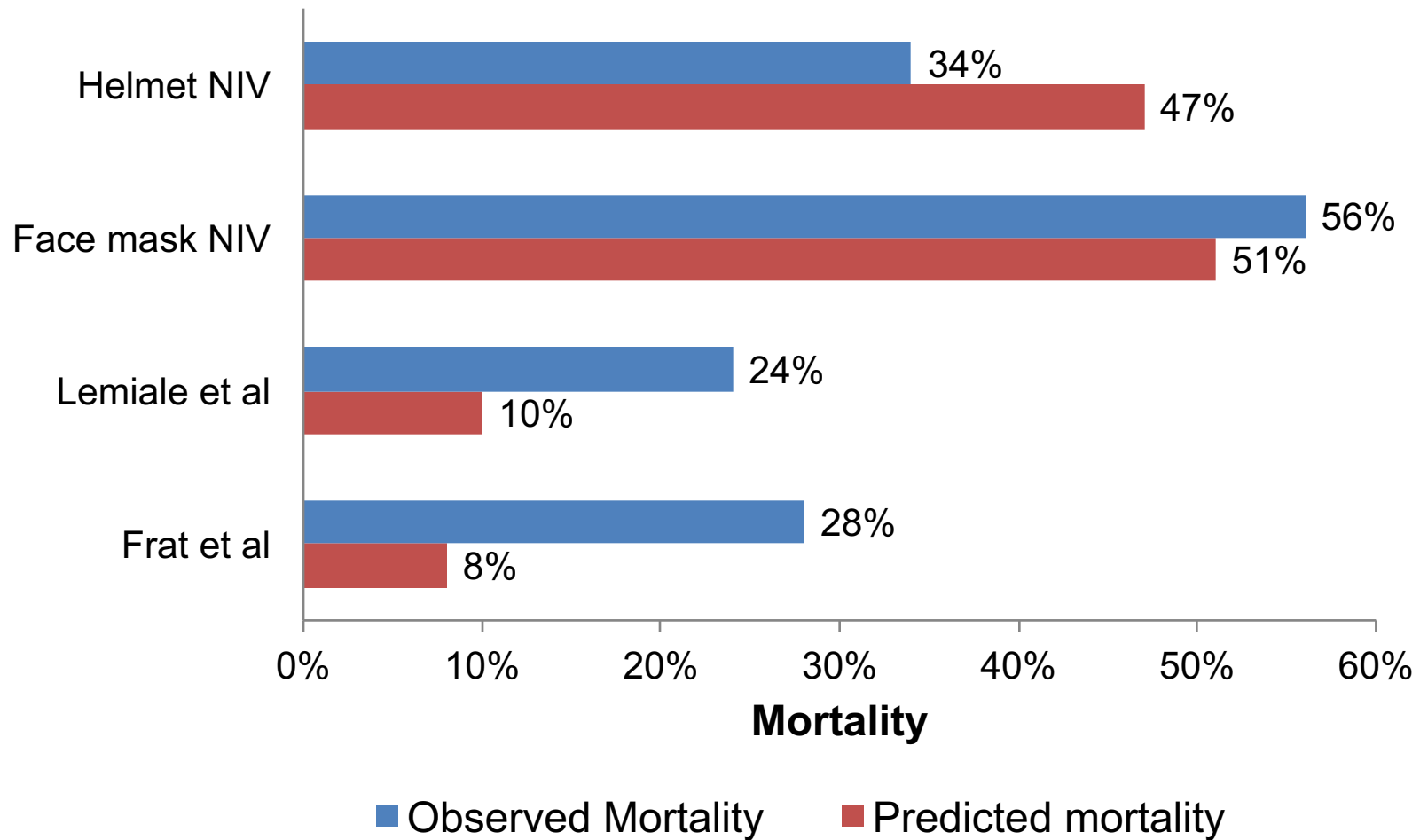
# Survival Analysis



	Face Mask NIV (n=39)		Helmet NIV (n=44)	
90 day Mortality -- n (%)	22	56.4%	15	34.1%

Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

# Comparison to Published Data



# Cautions and Limitations

1. CO<sub>2</sub> rebreathing and dyssynchrony
2. Clinician learning curve
3. Unblinded
4. Single center trial
5. Early stoppage may magnify effect size of the primary outcome



## Back to the case

- Randomized to Helmet NIV → PaO<sub>2</sub>/FiO<sub>2</sub> 108
- Titrated NIV to PEEP of 17 and weaned to fiO<sub>2</sub> of 60%
- Tachypnea improved to the mid 20s
- Tolerated helmet NIV for 43 hours and weaned to nasal cannula
- Transferred to the floor after 4 days in the ICU and later discharged home

# Conclusions

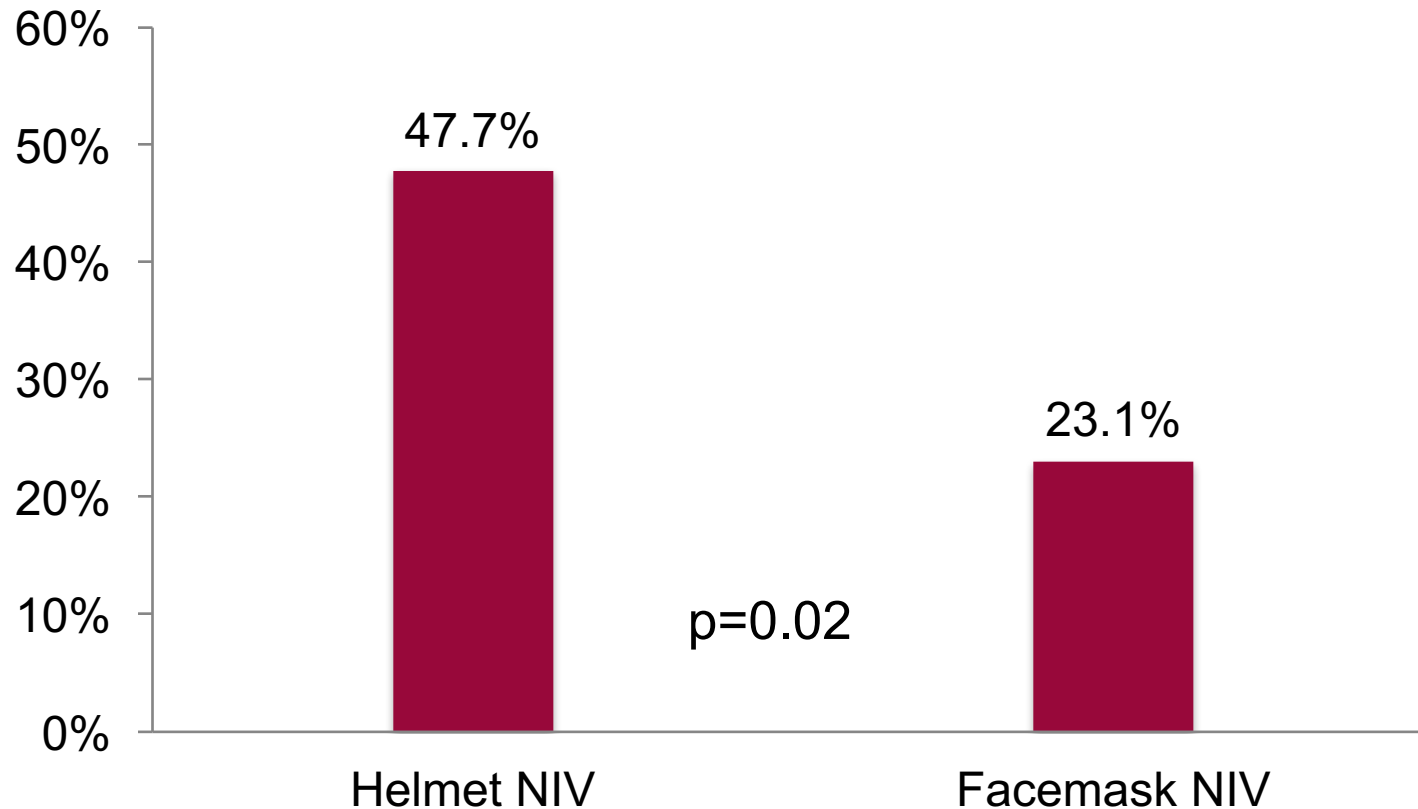
- Helmet NIV in comparison to Face Mask NIV in patients with ARDS
  - Reduced intubation rate
  - Improved ventilator free days
  - Reduced ICU length of stay
  - Improved mortality
  
- Biological Basis
  - High fresh gas flow
  - PEEP effect
  - ?High tidal volumes

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Patel BK, et al. *JAMA*. 2016;315(22):2435-2441.

# Helmet group achieved higher PEEP

## Proportion of patients on PEEP $\geq 10$



# Observed Tidal Volumes

- Expired tidal volume was significantly higher in patients who failed noninvasive ventilation as compared with those who succeeded
  - 10.6 mL/kg [9.6–12.0] vs 8.5mL/kg [7.6–10.2];  $p = 0.001$

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	<b>Face Mask NIV</b>		<b>Helmet NIV*</b>	
	<b>(n=39)</b>		<b>(n=44)</b>	
Tidal Volumes (mL)	398	[321-523]	1405	[1135-1811]
<b>Tidal Volume ml/kg</b>	6.5	[5.6-8.3]		

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\*The helmet NIV tidal volumes are unknowable as a proportion of tidal volume distends the helmet and the rest in inspired tidal volume

Carteaux G, et al. *Crit Care Med* 2016; 44: 282-290



# Next Steps

- Long term outcomes
  - Functional independence at 1 year
  - Hospitalizations after ICU discharge
- Comparison of Helmet vs High Flow Nasal Cannula
  - Predictors of failure
  - Protocol of advanced NIV support
- Translational studies
  - Animal models to understand biologic plausibility
  - Biologic samples from enrolled patients
- Physiologic studies
  - Synchrony/ CO<sub>2</sub> rebreathing
  - Tidal volume

# Acknowledgements

- Critical Care Research Group
  - John P. Kress, MD
  - Jesse B. Hall, MD
  - Anne Pohlman, MSN
  - Krysta Wolfe, MD
- Respiratory therapy
  - Rebecca Rose
  - Scott Melinauskas
  - Steve Mosakowski
- Physical/Occupational Therapy
  - Cheryl Esbrook, OT
  - Amy Pawlik, PT
  - Megan McDonald, PT
  - Erin Zeleny, OT
  - Crystal Corte, OT
  - Megan Teele, PT
- MICU Nursing Staff
- ICU Attendings/Fellows
- Medicine Housestaff