Hi Flow Oxygen and Oxygen Toxicity

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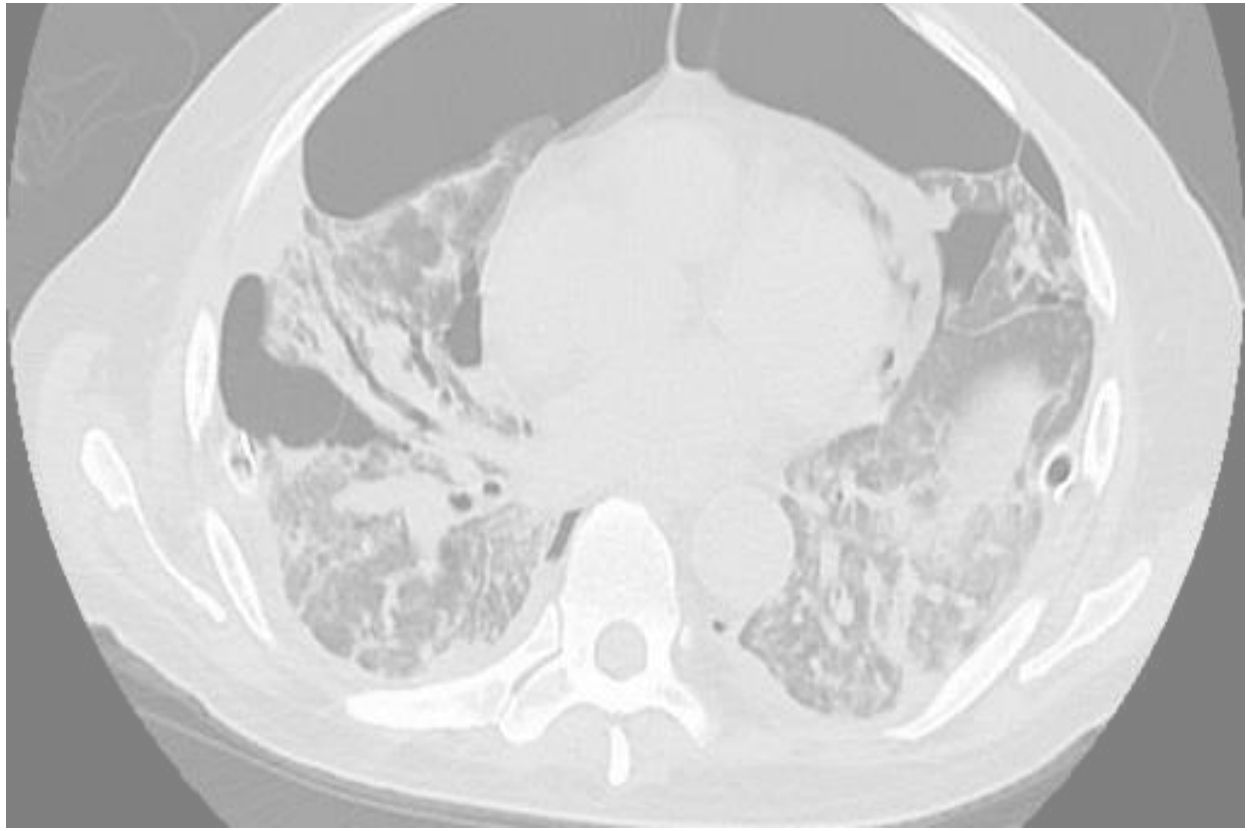

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Department of Medicine

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Disclosures

- None

Application of oxygen therapy

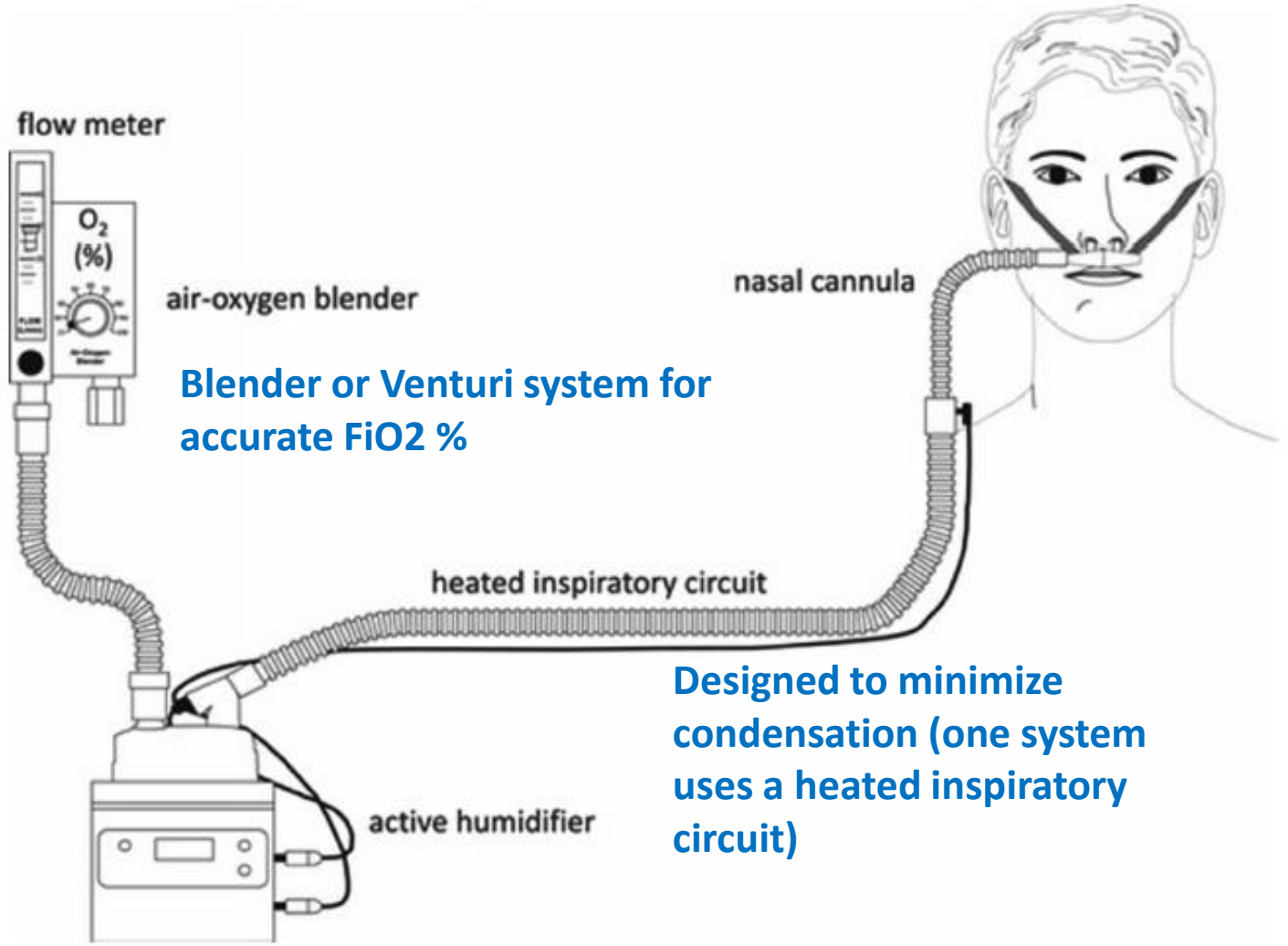
- **Nasal cannula**: limited when patients are tachypneic due to high respiratory rate (leading to increased entrainment of air) with high peak inspiratory flow rate of the patient (exceeding that of delivered oxygen). Also, lack of humidification affects mucosal dryness/patient comfort.

- **Venturi mask**: delivers higher flow rates (30-50 L/min) with FiO2 24-60%. Also limited by insufficient humidification via standard bubble humidifiers.

- **Hi Flow Nasal Oxygen**: delivers up to 60 L/min heated, humidified O2 with FiO2 range 21-100%.

Hi-Flow Nasal Cannula Oxygen (HFNC)

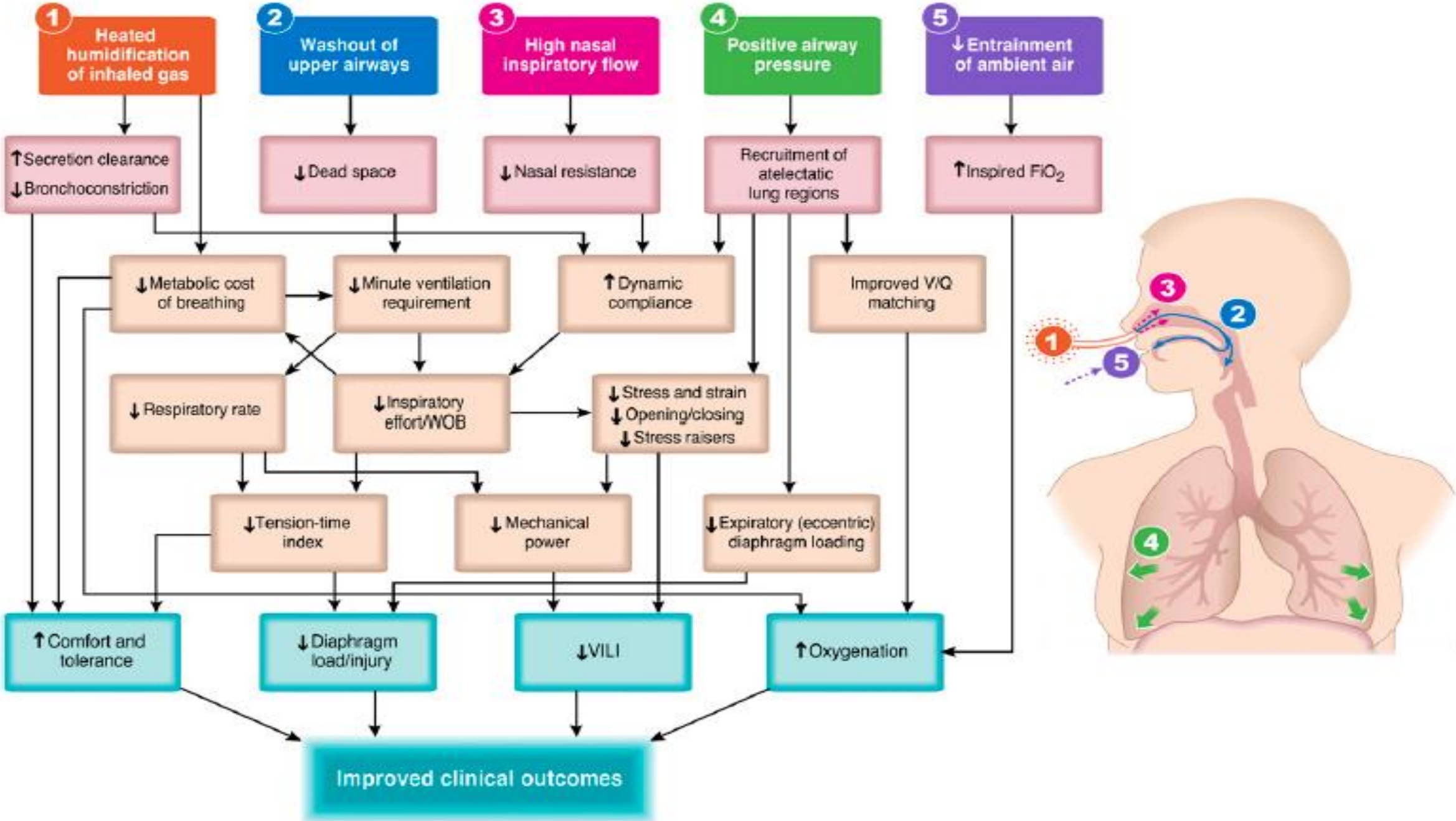
Hi pressure source of O2



Blender or Venturi system for accurate FiO2 %

Designed to minimize condensation (one system uses a heated inspiratory circuit)

Intensive Care Med 2016; 42: 1336-49



Am J Respir Crit Care Med 2017; 195: 1128-31

HFNC

Pros

- Lowers respiratory rate
- Decreases subjective dyspnea
- Increases comfort
- Improves oxygenation
- Reduces accessory muscle use
- Well tolerated, minimal claustrophobia
- Can continue to eat, drink, speak

Cons

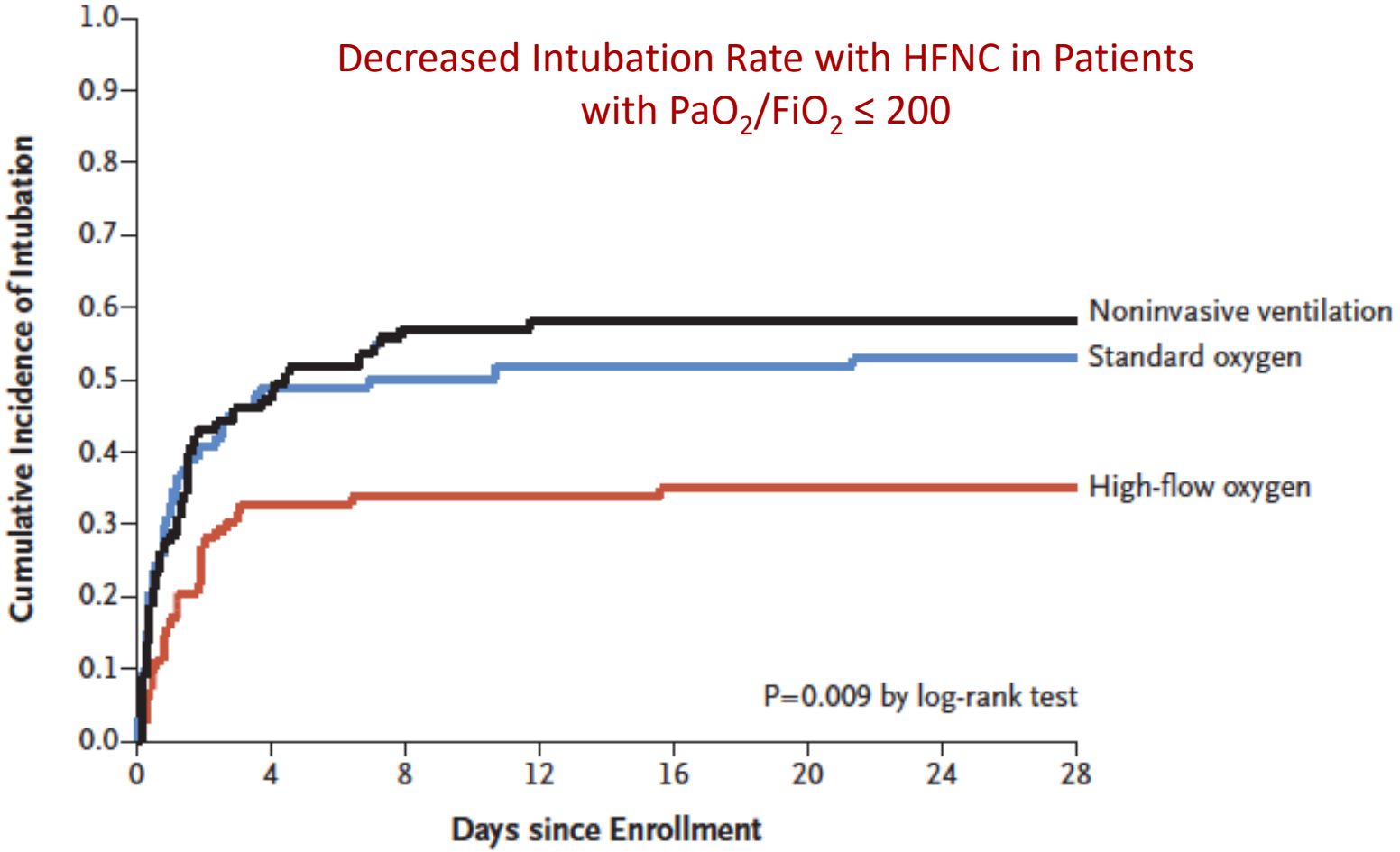
- Nasal irritation
- Runny nose
- Noisy
- Epistaxis
- Potential problem if recent nasal surgery or trauma.
- **Risk of delayed intubation**

HFNC vs. NIV vs. NRB for AHRF

- Multicenter RCT
- 310 patients ($PaO_2/FiO_2 \leq 300$, $PaCO_2 < 45$)
- 1° outcome: rate of intubation
  - Trend toward decreased intubation rate with HFNC (38% vs. 47% NRB, 50% NIV; p=0.18)
- 2° outcomes: all-cause mortality in ICU and at 90 days, number of ventilator free days, complications

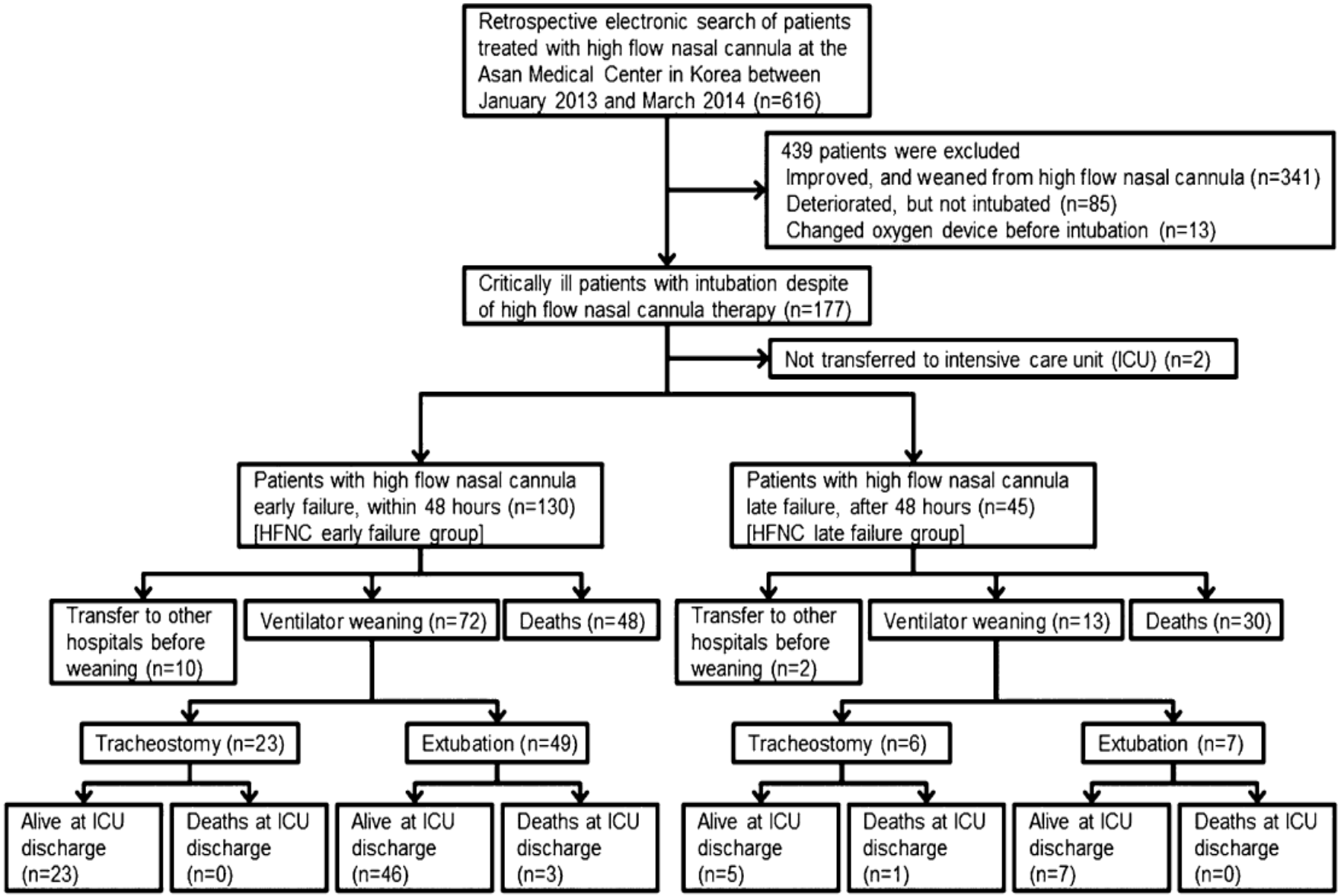
N Engl J Med 2015; 372: 2185-96

HFNC vs. NIV vs. NRB for AHRF



N Engl J Med 2015; 372: 2185-96

Failure of high-flow nasal cannula therapy may delay intubation and increase mortality



Intensive Care Med (2015) 41:623–632

Analysis of hospital outcomes for the early HFNC failure group compared with the late HFNC failure group (as reference) using the propensity score analysis

Variables	Crude		Propensity-adjusted[a]		Propensity-matched[b]	
	Odds ratio (95 % CI)	*P* value[c]	Odds ratio (95 % CI)	*P* value[c]	Odds ratio (95 % CI)	*P* value[c]
Primary outcome						
Overall ICU mortality	0.323 (0.158–0.658)	0.002	0.317 (0.143–0.700)	0.005	0.369 (0.139–0.984)	0.046
Secondary outcomes						
Extubation success	3.284 (1.361–7.923)	0.008	3.091 (1.193–8.013)	0.020	2.057 (0.746–5.672)	0.163
Ventilator-weaning	3.056 (1.470–6.351)	0.003	3.380 (1.492–7.656)	0.004	2.495 (1.039–5.991)	0.041
Ventilator-free days to day 28	0.542 (0.383–0.768)[d]	0.001[e]	0.516 (0.349–0.763)[d]	0.001[e]	0.639 (0.431–0.946)[d]	0.026[e]
14-Day mortality from HFNC application	0.949 (0.455–1.977)	0.888	0.712 (0.312–1.622)	0.418	0.608 (0.231–1.606)	0.316
14-Day mortality from intubation	0.653 (0.325–1.311)	0.231	0.482 (0.218–1.067)	0.072	0.447 (0.168–1.184)	0.105
28-Day mortality from HFNC application	0.820 (0.416–1.616)	0.566	0.680 (0.318–1.457)	0.322	0.896 (0.440–1.824)	0.763
28-Day mortality from intubation	0.571 (0.287–1.138)	0.111	0.557 (0.258–1.198)	0.134	0.802 (0.380–1.692)	0.563
Length of ICU stay	0.827 (0.586–1.169)[f]	0.282[g]	0.830 (0.552–0.800)[f]	0.372[g]	1.329 (0.598–2.952)[f]	0.485[g]

Conclusion

- HFNC failure (defined as the need for endotracheal intubation—unable to maintain SpO2 > 90%, hypercapnia with pH < 7.3, RR > 35 with distress, metabolic acidosis with hypotension, need for airway protection) after 48 hr was a predictor of mortality.
- But…
  - Single center
  - Retrospective

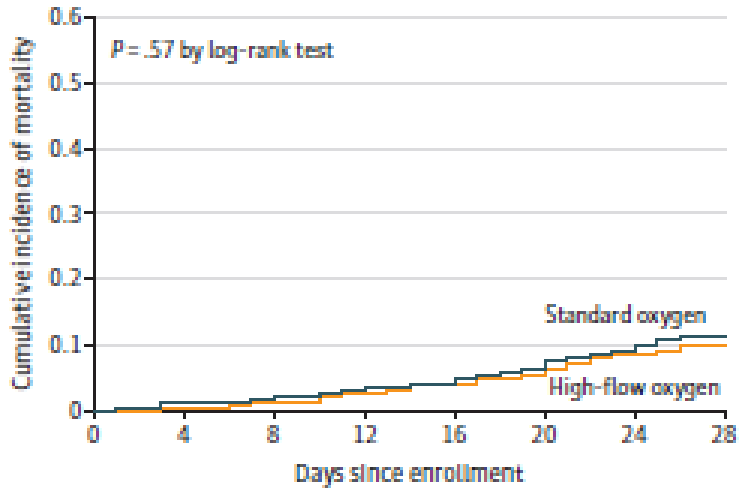
JAMA | Original Investigation

Effect of High-Flow Nasal Cannula Oxygen vs Standard Oxygen Therapy on Mortality in Patients With Respiratory Failure Due to COVID-19 The SOHO-COVID Randomized Clinical Trial

Jean-Pierre Frat, MD, PhD; Jean-Pierre Quenot, MD, PhD; Julio Badie, MD; Rémi Coudroy, MD, PhD; Christophe Guitton, MD, PhD; Stephan Ehrmann, MD, PhD; Arnaud Gacouin, MD; Hamid Merdji, MD; Johann Auchabie, MD; Cédric Daubin, MD; Anne-Florence Dureau, MD; Laure Thibault, MD; Nicholas Sedillot, MD; Jean-Philippe Rigaud, MD, PhD; Alexandre Demoule, MD, PhD; Abdelhamid Fatah, MD; Nicolas Terzi, MD, PhD; Marine Simonin, MD; William Danjou, MD; Guillaume Carteaux, MD, PhD; Charlotte Guesdon, MD; Gaël Pradel, MD; Marie-Catherine Besse, MD; Jean Reignier, MD, PhD; François Beloncle, MD, PhD; Béatrice La Combe, MD; Gwénaël Prat, MD; Mai-Anh Nay, MD; Joe de Keizer, MSc; Stéphanie Ragot, PharmD, PhD; Arnaud W. Thille, MD, PhD; for the SOHO-COVID Study Group and the REVA Network

Standard (NRB): 10L/min or more
Hi flo: 50L/min or more
SaO2 targets: 92-96%
Hi flow for at least 48 hr

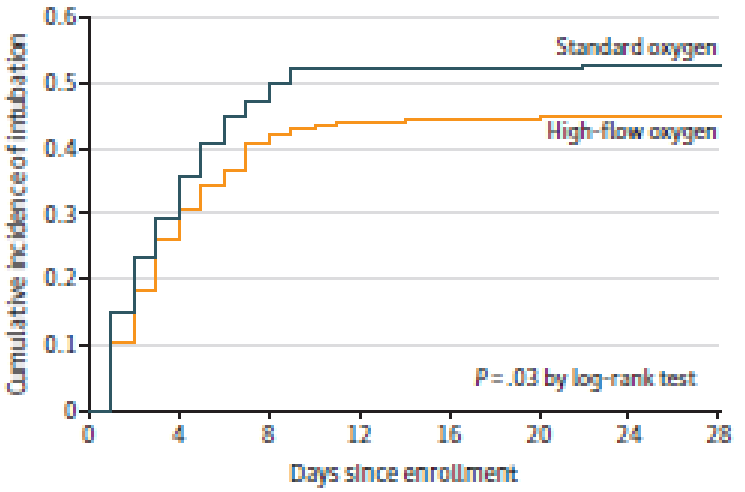
A Cumulative Incidence of mortality (primary outcome)



No. at risk

High-flow oxygen	357	355	352	348	343	337	326	321
Standard oxygen	354	349	347	342	337	328	319	311

B Cumulative Incidence of Intubation (secondary outcome)



No. at risk

High-flow oxygen	357	262	210	199	197	195	193	193
Standard oxygen	354	248	185	165	164	164	163	163

The median observation time was 28 days (IQR, 28-28) in all treatment groups.

JAMA. 2022;328(12):1212-1222. doi:10.1001/jama.2022.15613

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[Intervention Review]

High-flow nasal cannulae for respiratory support in adult intensive care patients

Sharon R Lewis[1], Philip E Baker[2], Roses Parker[3], Andrew F Smith[4]

Mortality, pneumonia, length of ICU stay

Escalation to other type of oxygen therapy

Authors' conclusions

HFNC may lead to less treatment failure when compared to standard oxygen therapy, but probably makes little or no difference to treatment failure when compared to NIV or NIPPV. For most other review outcomes, we found no evidence of a difference in effect. However, the evidence was often of low or very low certainty. We found a large number of ongoing studies; including these in future updates could increase the certainty or may alter the direction of these effects.

Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD010172.

Non-invasive ventilation

oronasal

nasal

pillows

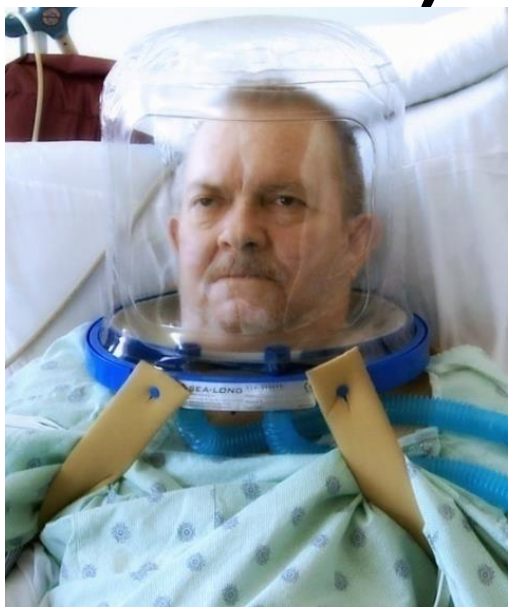
total face

hybrid

helmet

Non-invasive ventilation (CPAP and BPAP)

- **Ok to try if**:
  - Respiratory distress
  - Appropriate diagnosis (see next slide)
  - Increased work of breathing
  - Respiratory acidosis
  - No contraindications (see below)
- **Best not to try if**:
  - Unable to protect airway
  - Unable to fit interface
  - Uncooperative patient
  - Unlikely to be short term
  - Recent esophageal surgery
  - Facial trauma
  - Cardiac or respiratory arrest

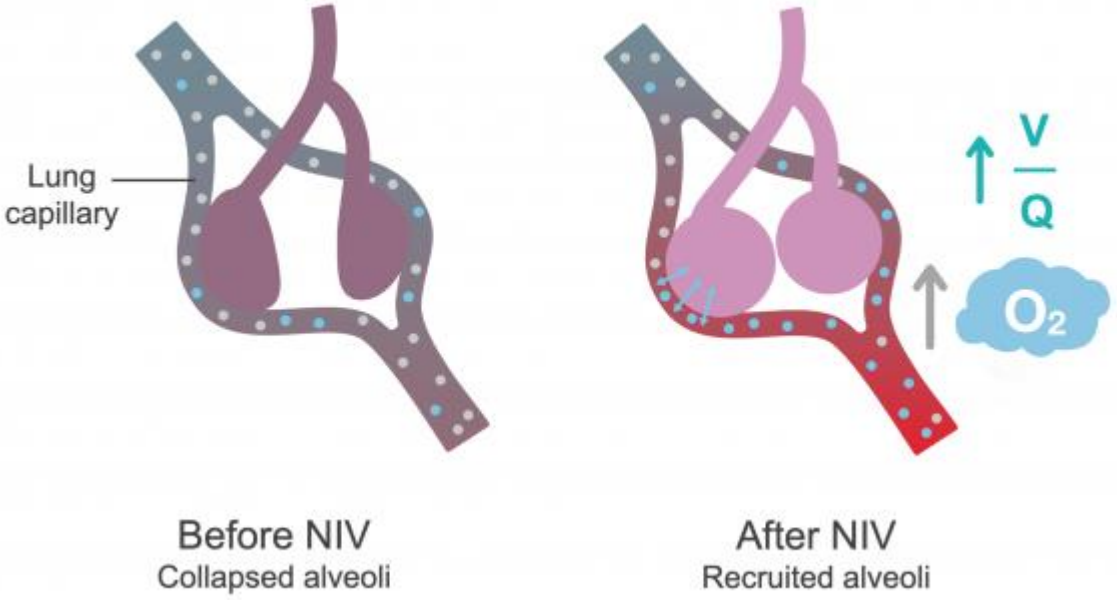


Frequent re-assessment for efficacy is critical!

- **Best to stop when**:
  - Lack of improvement within 1-2 hr
  - Patient is intolerant of the treatment

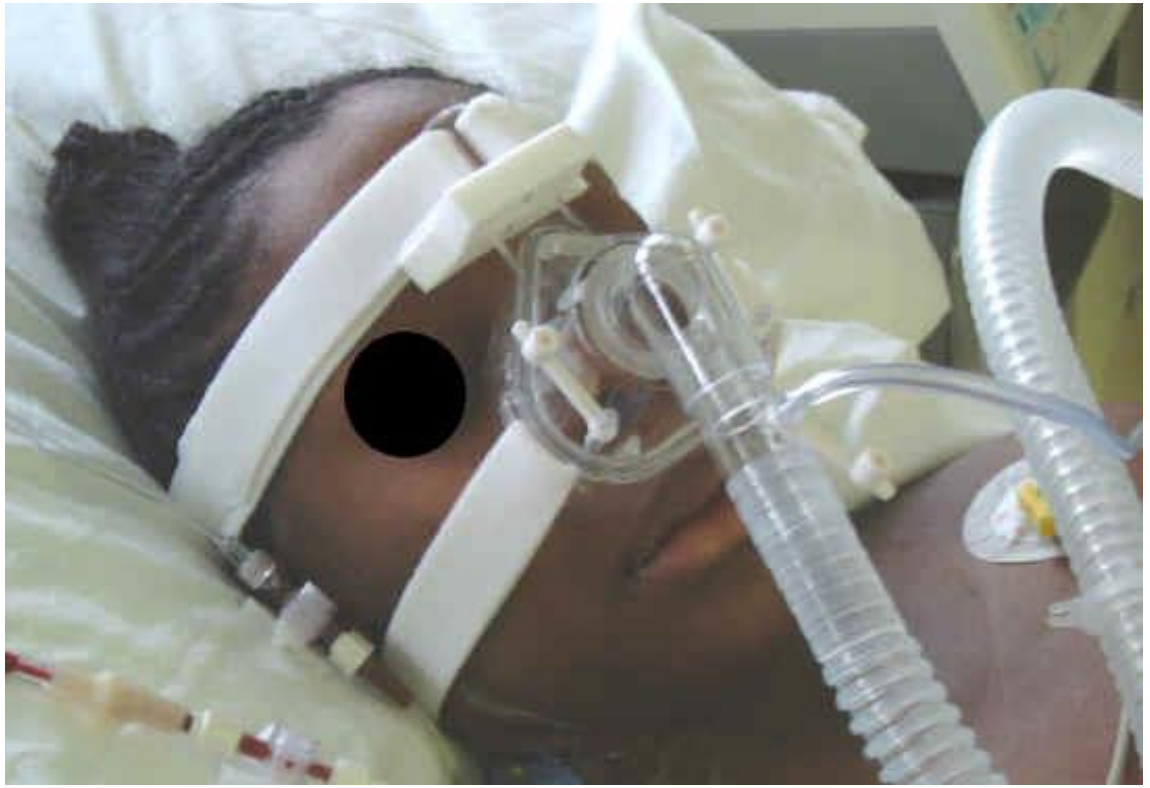
Potential benefits of NIV

- Reduce WOB
- *Improve gas exchange, decreases afterload
- Avoid complications and discomfort associated with invasive ventilation
- Reduce intubation rate
- Facilitate/accelerate extubation
- Reduce LOS
- Decrease cost
- Reduce mortality



Complications

- Leaks
- Mask discomfort, facial soreness, facial skin breakdown
- Eye irritation
- Sinus congestion
- Oronasal drying
- Gastric insufflation
- Hemodynamic compromise



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

Note: hypoxic respiratory failure is not on the list

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)

Eur Respir J 2017; 50: 1602426

TABLE 2 Recommendations for actionable PICO questions

Clinical indication#	Certainty of evidence¶	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
***De novo* respiratory failure**		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made
Post-extubation in high-risk patients (prophylaxis)	⊕⊕	Conditional recommendation for
Post-extubation respiratory failure	⊕⊕	Conditional recommendation against
Weaning in hypercapnic patients	⊕⊕⊕	Conditional recommendation for

BMJ Open Respiratory Research

Non-invasive ventilation for acute hypoxaemic respiratory failure: a propensity-matched cohort study

Dilip Jayasimhan ,[1,2] Robert Adam Martynoga,[2] Sarah M Fairweather,[1] Catherina L Chang[1]

Table 2 Study outcomes

Outcomes	NIV (n=79)	Intubation (n=79)	P value
Primary outcome			
Median VFD-28 (IQR)	23 (28)	17 (23.5)	0.013
Secondary outcomes			
Median ICU LOS (hours) (IQR)	112.5 (204.8)	117.67 (217.55)	1.000
Median hospital LOS (days) (IQR)	14 (15)	14 (15.5)	0.368
In-hospital mortality (%)	25 (31.6)	30 (37.9)	0.504
Requirement for adjunctive therapies (%)	32 (40.5)	36 (45.5)	0.630

ICU, intensive care unit; LOS, Length of Stay; NIV, non-invasive ventilation; VFD-28, ventilator-free days at day 28.

BMJ Open Resp Res 2022;**9**:e001149. doi:10.1136/bmjresp-2021-001149

Retrospective
Single-center
Propensity matched
Those trialed with NIV first vs those intubated w/o NIV
Primary outcome: ventilator free days

Conclusion: Compared with early intubation, NIV use was associated with more ventilator-free days in patients with hypoxaemic respiratory failure. However, this did not translate into a shorter length of stay or reduced mortality based on our single-centre experience.

Note: those who failed NIV trial had high mortality

JAMA | Original Investigation

Effect of Helmet Noninvasive Ventilation vs Usual Respiratory Support on Mortality Among Patients With Acute Hypoxemic Respiratory Failure Due to COVID-19
The HELMET-COVID Randomized Clinical Trial

Yaseen M. Arabi, MD; Sara Aldekhyl, MD; Saad Al Qahtani, MD; Hasan M. Al-Dorzi, MD; Sheryl Ann Abdukahil, BSN; Mohammed Khulaif Al Harbi, MD; Eman Al Qasim, MSN; Ayman Kharaba, MD; Talal Albrahim, MD; Mohammed S. Alshahrani, MD; Abdulrahman A. Al-Fares, MD; Ali Al Bshabshe, MD; Ahmed Mady, MD; Zainab Al Duhailib, MBBS; Haifa Algethamy, MD; Jesna Jose, PhD; Mohammed Al Mutairi, BS; Omar Al Zumai, BS; Hussain Al Haji, MSc; Ahmed Alaqeily, BS; Zohair Al Aseri, MD; Awad Al-Omari, MD; Abdulaziz Al-Dawood, MD; Haytham Tlayjeh, MD; for the Saudi Critical Care Trials Group

Pragmatic
Non-blinded
Helmet versus usual respiratory care (including NIV but not helmet)
Feb 8, 2021 to Nov 16, 2021
659 assessed for inclusion
322 randomized

40% either refused the helmet or, more commonly, discontinued it for intolerance within 24 hr

Primary endpoint was 28 day mortality.

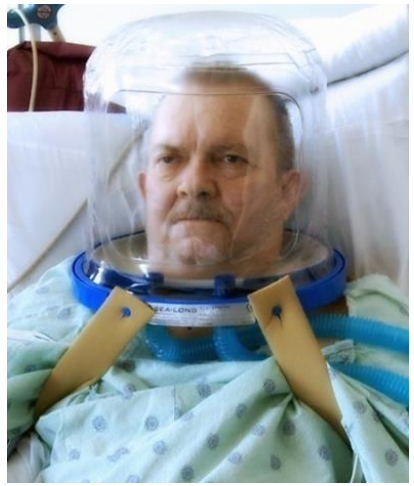
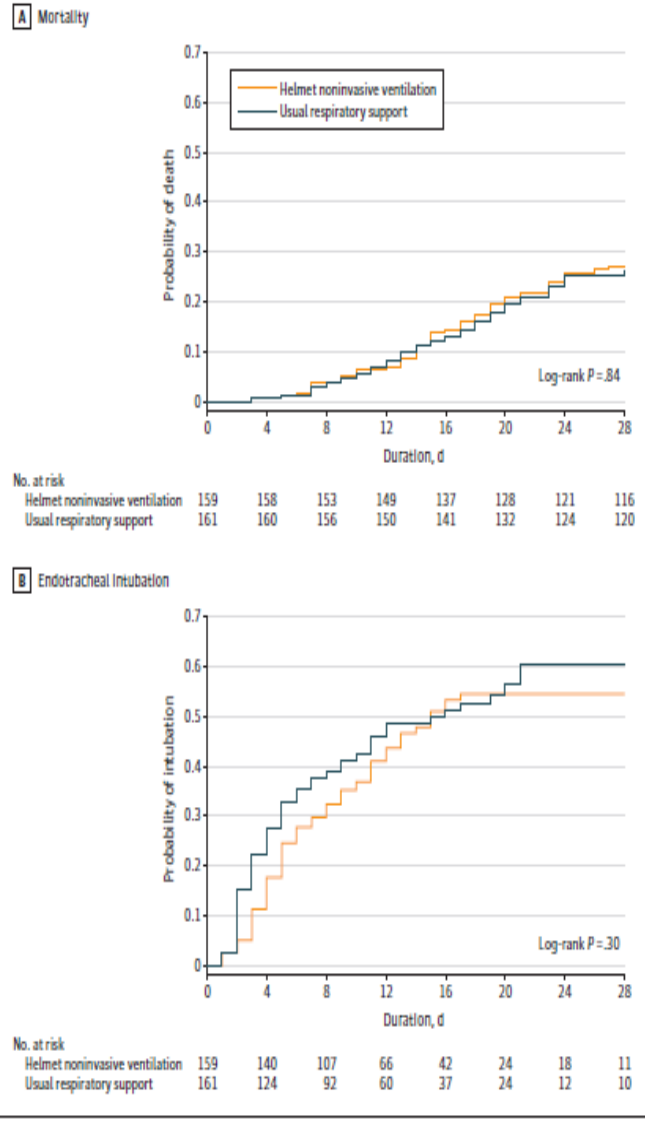


Figure 2. Kaplan-Meier Time-to-Event Curves for Mortality and Endotracheal Intubation in the Helmet Noninvasive Ventilation and Usual Respiratory Support Groups



All patients were observed to event or 28 days.

Take Home Points

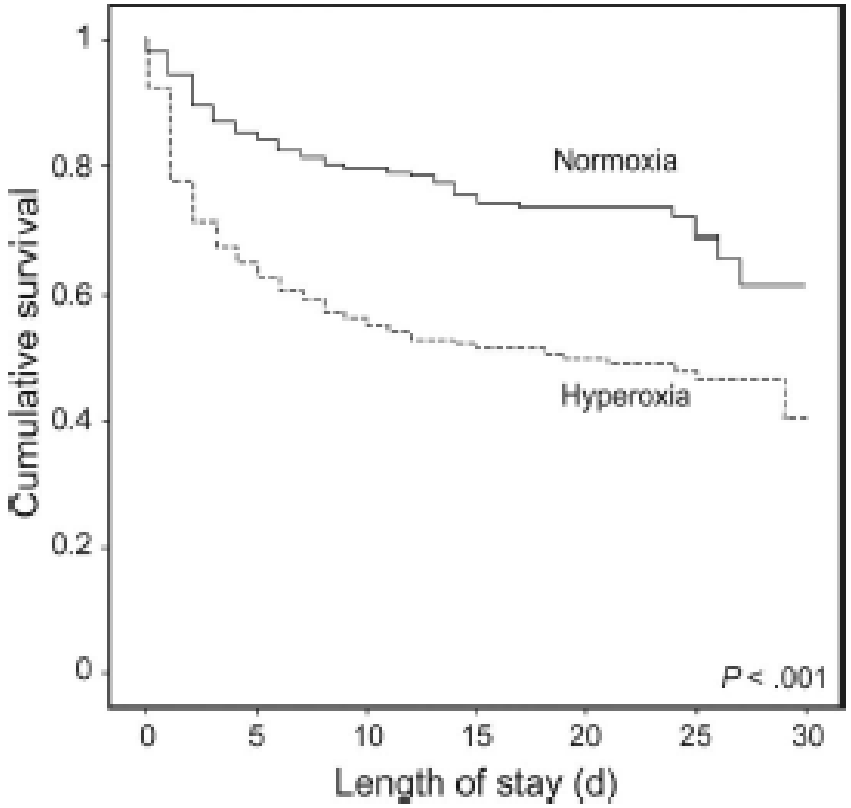
- Oxygen delivery systems each have a role in certain clinical circumstances.
- HFNC offers improved comfort over NIV, may lead to lower likelihood of intubation, and is a reasonable first step for the treatment of hypoxic respiratory failure. However….
- When trialing HFNC or NIV, it is critically important to assess and re-assess at frequent intervals. If not having the desired effect (increase pO2, decrease RR, etc) then escalation to other therapy is indicated without delay.

Oxygen therapy in the critically ill

When is it too much of a good thing?

Oxygenation of the critically ill

Which critically ill patients enjoy a mortality benefit from having higher oxygen targets as compared with lower ones?



a. Traumatic brain injury

b. Ischemic stroke

c. Post-cardiac arrest

d. All of the above

e. None of the above

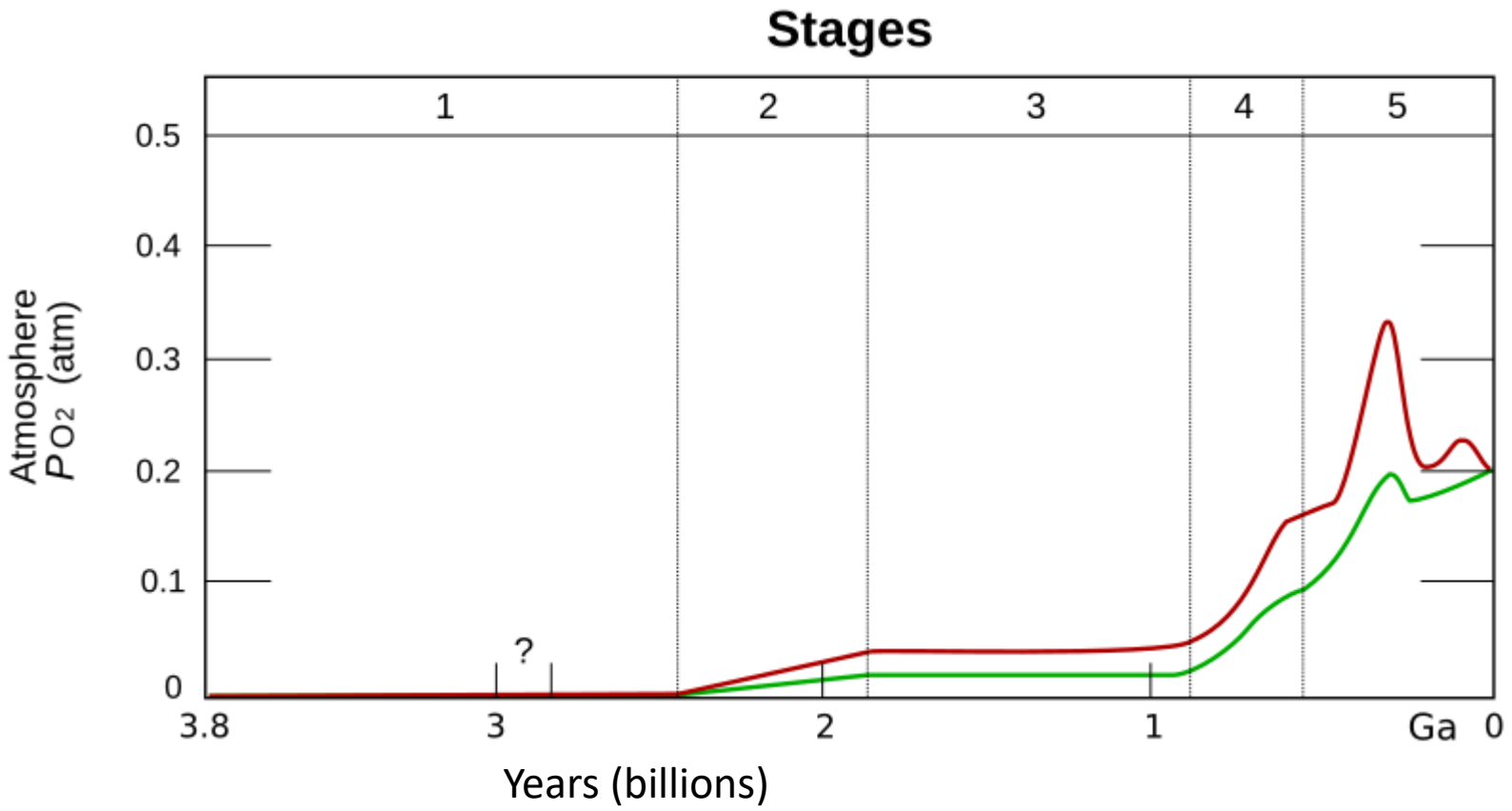
JAMA 2010;303:2165-71

- Hypoxia: sometimes bad but we can adapt within limits.

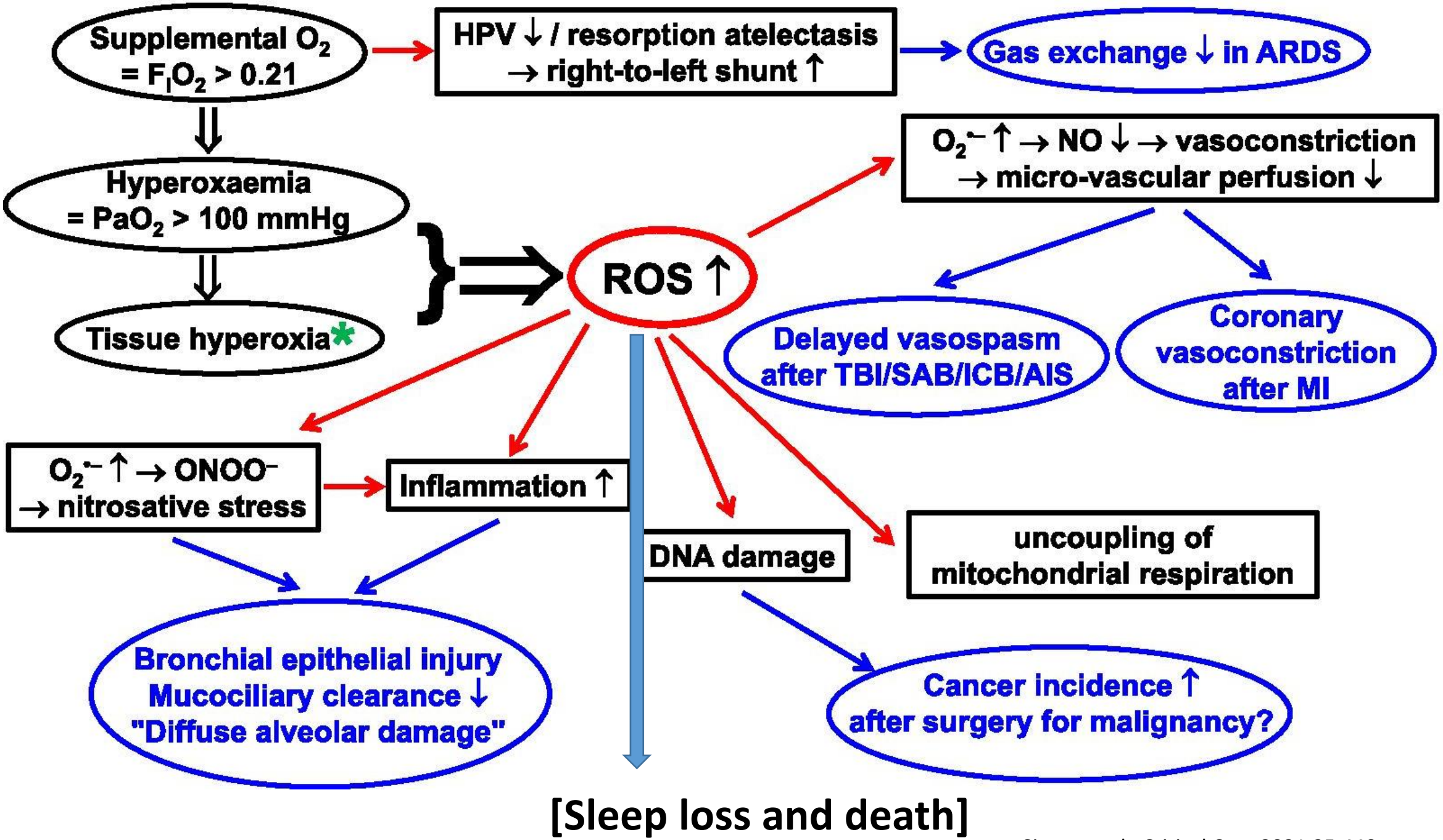
- Hyperoxia: probably bad but more so in certain circumstances

The consequences of both are probably a matter of degree and host factors

The Great Oxidative Event



It was caused by cyanobacteria doing photosynthesis. It took from about three billion years ago to about one billion years ago.



[Sleep loss and death]

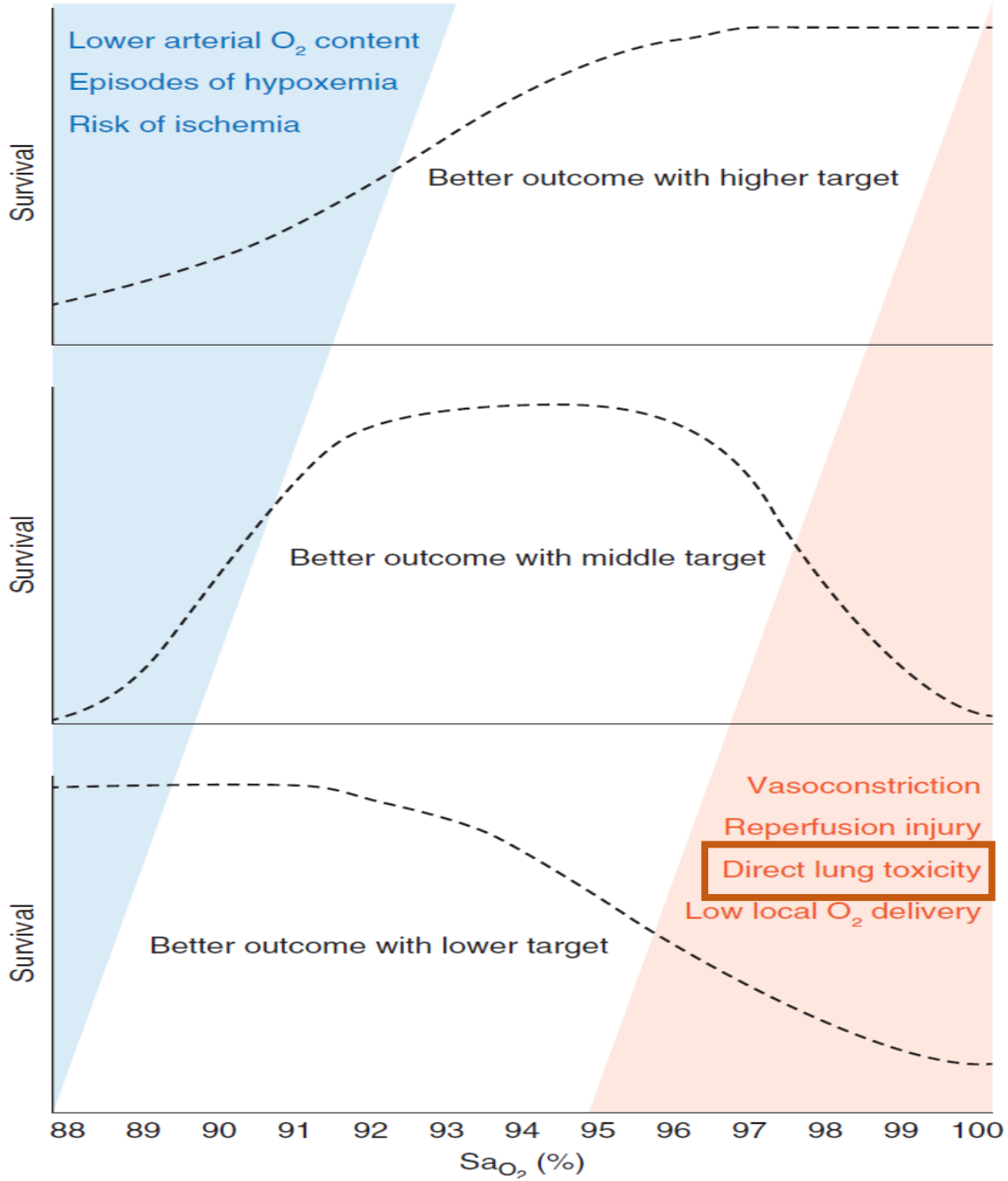
Singer et al. Critical Care 2021;25:440.

Oxygen toxicity

Everyone has heard of it but no one has seen it OR hiding in plain sight

Table 2. Randomized Trials of Conservative vs. Liberal Oxygen Targets in Critically Ill Patients

Study	Population	Sample Size	Target (Conservative vs. Liberal)	Primary Outcome	Results (Conservative vs. Liberal)
Panwar *et al.* (2016) (61)	Adult ICU patients requiring IMV	103	Sp_{O_2} of 88–92% vs. ⩾96%	Mean AUC for Sp_{O_2}, Sa_{O_2}, Pa_{O_2}, and F_{IO_2}	Feasibility study; good separation in study groups; no adverse safety signals
Girardis *et al.* (2016) (62): OX-ICU	Adult ICU admission for >72 h anticipated (IMV and no IMV)	434	Pa_{O_2} of 70–100 mm Hg (Sp_{O_2} of 94–98%) vs. Pa_{O_2} of up to 150 mm Hg and Sp_{O_2} of 97–100%	ICU mortality	Decreased mortality; ARR, 8.6% (95% CI, 1.7–15.0%)
Mackle *et al.* (2020) (64): ICU-ROX	Adult ICU patients on IMV	1,000	Sp_{O_2} >90% with alarm set at 97%, "usual-care group"; no upper-limit alarm (F_{IO_2} of <0.3 discouraged)	VFD	No differences in VFD or 90- or 180-d mortality
Barrot *et al.* (2020) (63): $LOCO_2$	Adult ARDS patients on IMV	205	Pa_{O_2} of 55–70 mm Hg/Sp_{O_2} of 88–92% vs. Pa_{O_2} of 90–105 mm Hg/Sp_{O_2} of >96% for first 7 d of MV	28-d mortality	No difference in 28-d mortality; higher 90-d mortality (absolute risk increase of 7.8% [95% CI, 0.7–27.2%]). Trial stopped early for five events of mesenteric ischemia in conservative arm
Schjørring *et al.* (2021) (65): HOT-ICU	Adults with acute hypoxemic respiratory failure (F_{IO_2} ⩾0.5 on IMV or O_2 ⩾10 L/min in open system)	2,928	Pa_{O_2} of 60 mm Hg vs. Pa_{O_2} of 90 mm Hg	90-d mortality	No difference in 90-d mortality or other secondary outcomes; no difference in serious adverse events



Am J Respir Crit Care Med Vol 204, Iss 6, pp 632–641, Sep 15, 2021

Bottom Line re oxygen use:

Take Home Points

- Too much oxygen is bad
- Too little oxygen is bad
- Finding the best oxygen target for each individual patient should probably consider the underlying problem (supply-demand mismatch versus direct lung injury for example).

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