Acute Care Challenges in the Management of Severe COVID-19

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Subjects to cover

- 1. COVID-19 and ECMO
- 2. COVID-19 and steroids

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What is ECMO?

- The therapy of **“last resort”** in cases of cardiac and/or respiratory failure refractory, including ARDS, to other conventional therapies.
- Following **H1N1 pandemic** in 2009, experience in the use of ECMO as a supportive treatment in ARDS greatly increased.
- The **World Health Organization** and the **Society of Critical Care Medicine** have both recommended the administration of ECMO to treat severe intractable respiratory failure in patients with COVID-19

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What is ECMO?

- What can be concluded about the **added value of ECMO** in patients with severe respiratory failure from COVID-19?

- Is mortality a good marker for ECMO utilization?

- Is ECMO best used early or late?

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ECMO and COVID-19

- Raasveld et al, **“Extracorporeal Membrane Oxygenation in Patients with COVID-19: An international Multicenter Cohort Study”** March 12, 2021, *Journal of Intensive Care Medicine*

    - *Found an acceptable survival rate in ECMO patients with COVID-19, not different than non COVID19 patients with ARDS.*

Mechanical ventilation settings prior to initiation ECMO		
Type of mechanical ventilation, No. (%)		
Pressure supported ventilation	4	(6)
Volume controlled mechanical ventilation	31	(44)
Pressure controlled mechanical ventilation	31	(44)
Other	1	(1)
Missing	4	(6)
FiO_2, median (IQR), %	100	(80-100)
Peak pressure, median (IQR), cm H_2O	34	(31-39)
PEEP, median (IQR), cm H_2O	12	(8-16)
Rescue therapies applied prior to initiation ECMO, No. (%)		
Prone positioning	56	(79)
Muscle paralysis	55	(77)

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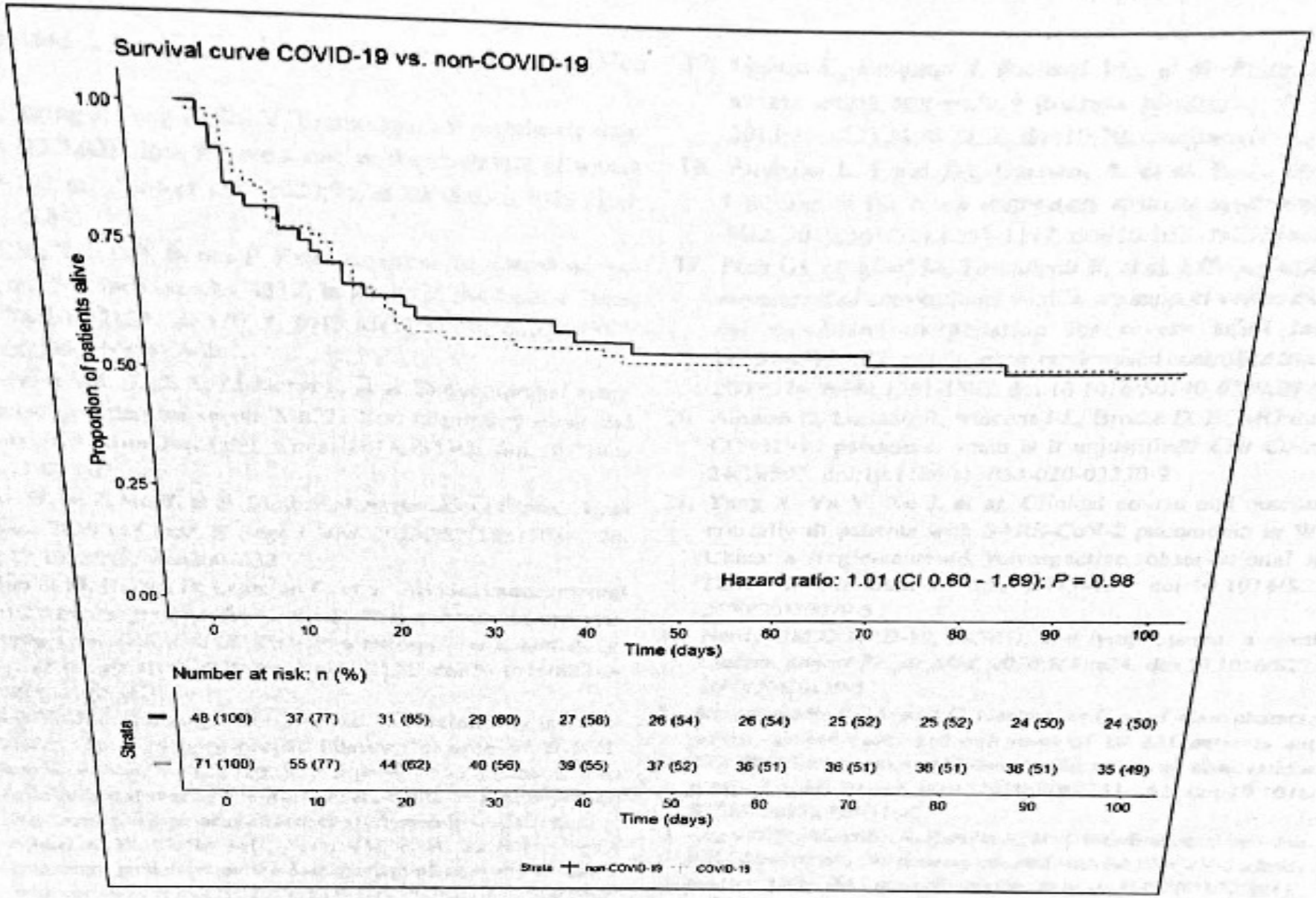

Figure 1. Kaplan-Meier estimates for patients with COVID-19 on ECMO and patients with ARDS not due to COVID-19 on ECMO. Unadjusted hazard ratio and 95% confidence interval calculated from a Cox proportional hazard model is presented.

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ECMO and COVID-19

- Lebreton et al, **“Extracorporeal membrane oxygenation network organization and clinical outcomes during the COVID-19 pandemic in Greater Paris, France: a multicentre cohort study”** April 19, 2021, *The Lancet*

    - *90 day survival among ECMO-assisted patients with COVID-19 was strongly associated with a center’s experience in venovenous ECMO during the previous year*

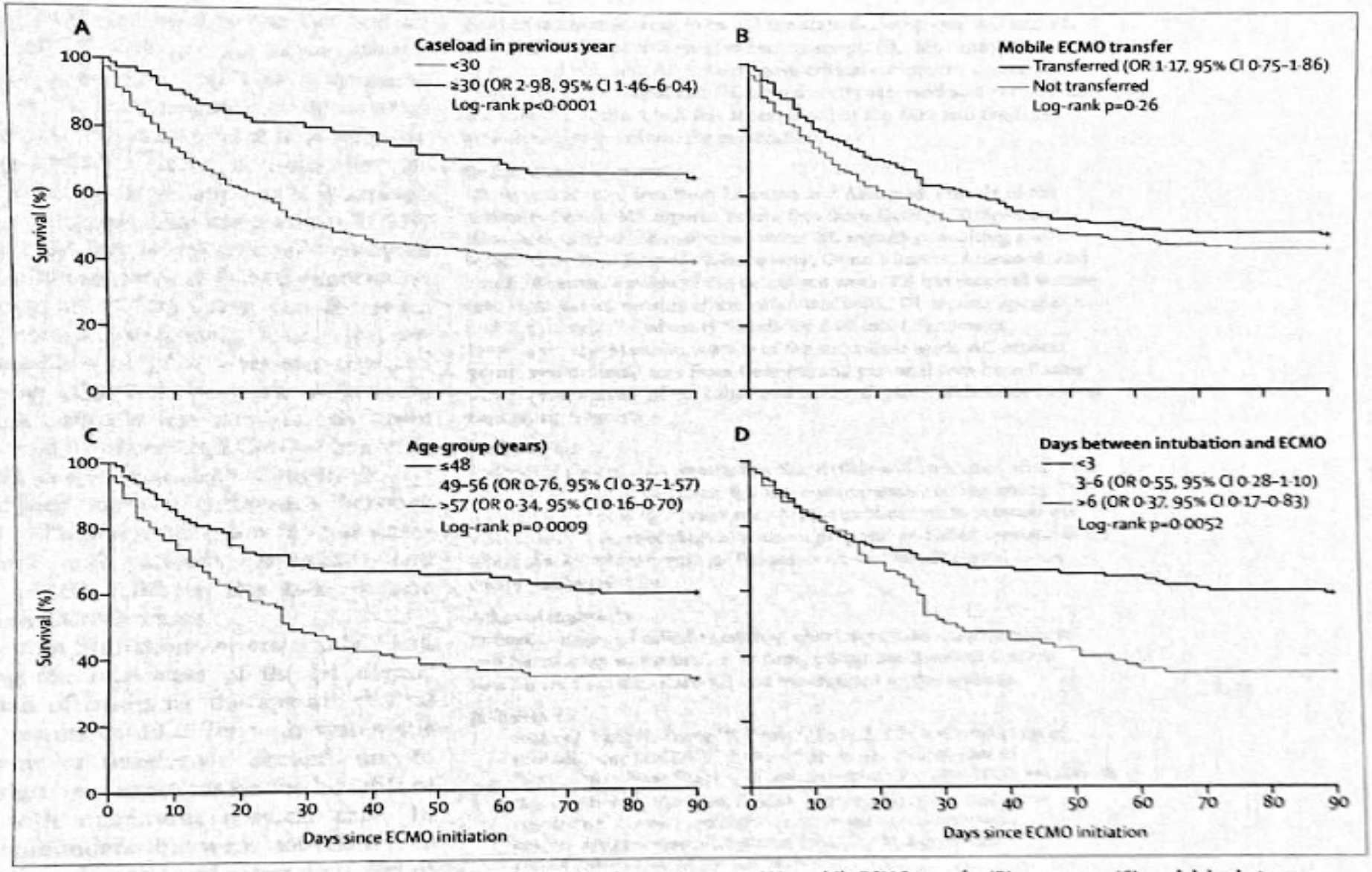

Figure 3: **90-day survival according to venovenous ECMO caseload in the previous year (A), mobile ECMO transfer (B), age group (C), and delay between orotracheal intubation and ECMO implantation (D)**

ECMO=extracorporeal membrane oxygenation. OR=odds ratio.

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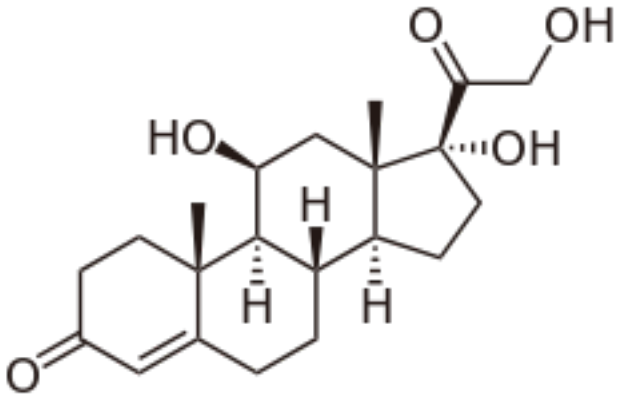
What are steroids?

- A steroid is any of a large class of organic biologically active compounds with a characteristic molecular structure containing four rings of carbon atoms (three six-membered and one five).

- They include many hormones, alkaloids, and vitamins.



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What are steroids?

- Glucocorticoids:
  - The anti-inflammatory action of glucocorticoid hormones was described by Hench and colleagues in 1949.
  - Hench and his co-workers found that small doses of cortisone dramatically improved the symptoms of patients with rheumatoid arthritis.

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What are steroids?

- Glucocorticoids:
  - Glucocorticoids combine with a cytoplasmic receptor that alters gene expression in two ways.
  - One way is dependent on the receptor's binding directly to DNA and acting (positively or negatively) as a transcription factor.
  - The other is dependent on its binding to and interfering with other transcription factors.
  - Both mechanisms could underlie suppression of inflammation.

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Steroids and ARDS

- Lin et al "**Decreased mortality in acute respiratory distress syndrome patients treated with corticosteroids: an updated meta-analysis of randomized clinical trials with trial sequential analysis"** *Crit Care* (2021) 25:122
  - *9 studies with 1371 participants, used dexamethasone, hydrocortisone and methylprednisolone*
  - *Glucocorticoid use was associated with lower mortality, increased ventilator free days, not associated with increased infection or hyperglycemia* ***(we don't know the optimal dose or duration of steroids)***

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Immunotherapy and COVID-19

- Buzon-Martin et al **"Benefits of early aggressive immunomodulatory therapy (tocilizumab and methylprednisolone) in COVID-19: Single center cohort study of 685 patients"** *Journal of Translational Autoimmunity* 4 (2021)
  - *In a large retrospective COVID-19 in-hospital cohort, lopinavir/ritinovir and interferon showed no significant impact on on survival*
  - *Extensive use of corticosteroids and tocilizumab resulted in good overall outcome and acceptable complication rates*

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Dexamethasone and COVID-19

- The RECOVERY Collaborative Group **"Dexamethasone in Hospitalized Patients with COVID-19"** *N Eng J Med* 384;8 February 25, 2021

    - *In hospitalized patients with COVID-19, the use of dexamethasone resulted in lower 28 day mortality among patients that were receiving mechanical ventilation or supplemental oxygen but not in patients that were receiving no respiratory support.*

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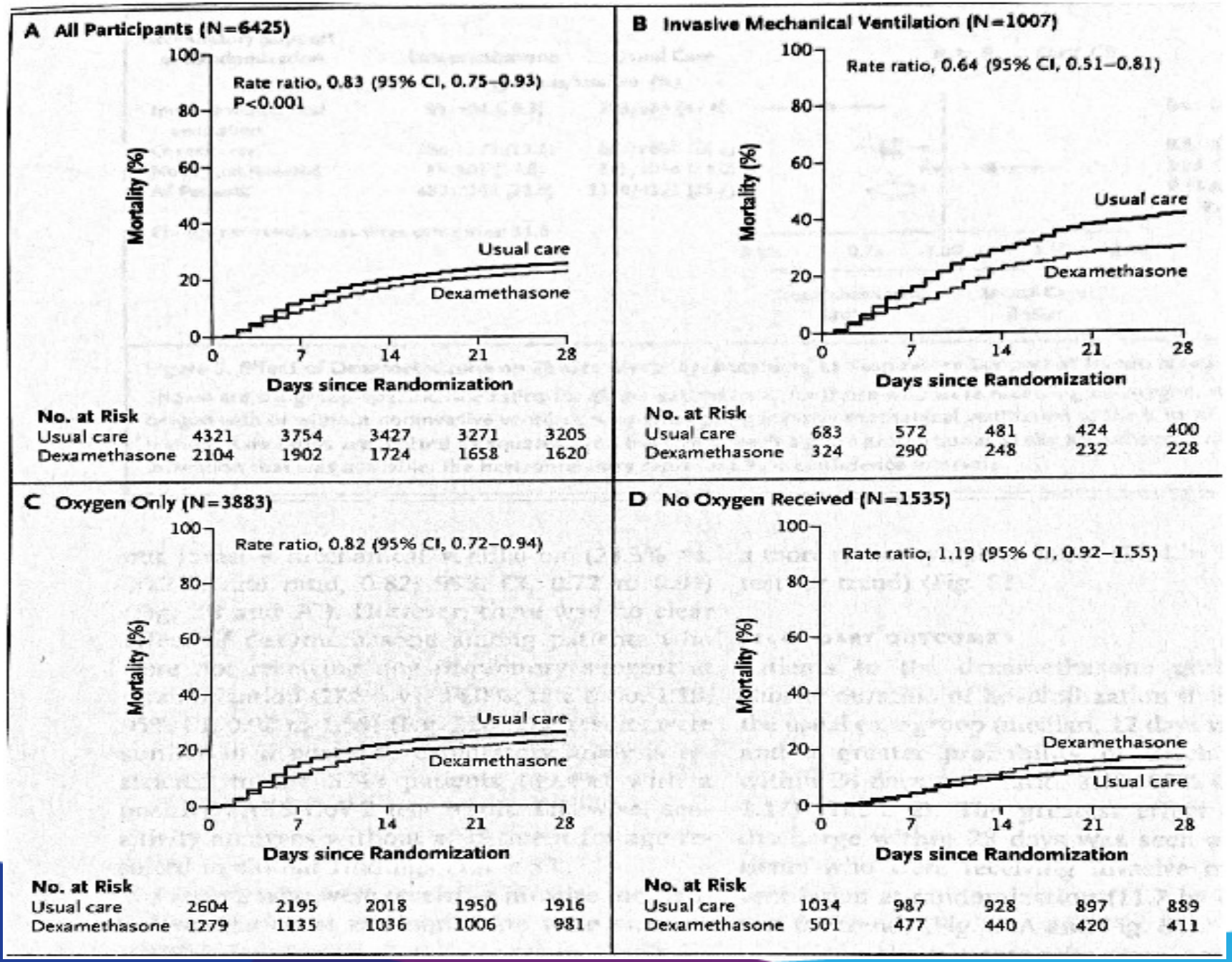

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Conclusion:

- COVID and ECMO
  - Sure
- COVID and steroids
  - Probably?