

INTRODUCTION

BACKGROUND

- Delirium** is a frequent and severe complication, **exacerbated by inflammation** and common among patients with acute respiratory distress syndrome (ARDS) [Brummel NE et al. Intensive Care Med. 2024]
- Recently, two **ARDS phenotypes**, **hypoinflammatory** and **hyperinflammatory**, have been described based on distinct biomarker profiles [Redaelli S et al. Intensive Care Med. 2023]
- We investigated how these inflammatory phenotypes are linked to delirium and through which clinical pathways

METHODS

SETTING AND STUDY DESIGN

- We performed a retrospective cohort study of ARDS patients who underwent extubation in an intensive care unit at Beth Israel Deaconess Medical Center in Boston, Massachusetts (2011–2024)
- Primary exposure:** Phenotype assigned by validated open-access AI Clinical Classifier (<https://bostonmontpelliercare.shinyapps.io/AIClarity>) at ARDS onset
- Primary Outcome:** Delirium after extubation, assessed every 12 hours until ICU discharge, reintubation or death using CAM-ICU

STATISTICAL APPROACH

- Multivariable logistic regression** estimated adjusted effects and **Fine–Gray models** accounted for competing risks of death, reintubation, and ICU discharge
- Multi-block mediation** quantified indirect effects.
- Effect modification** by corticosteroids, statins, and acetaminophen

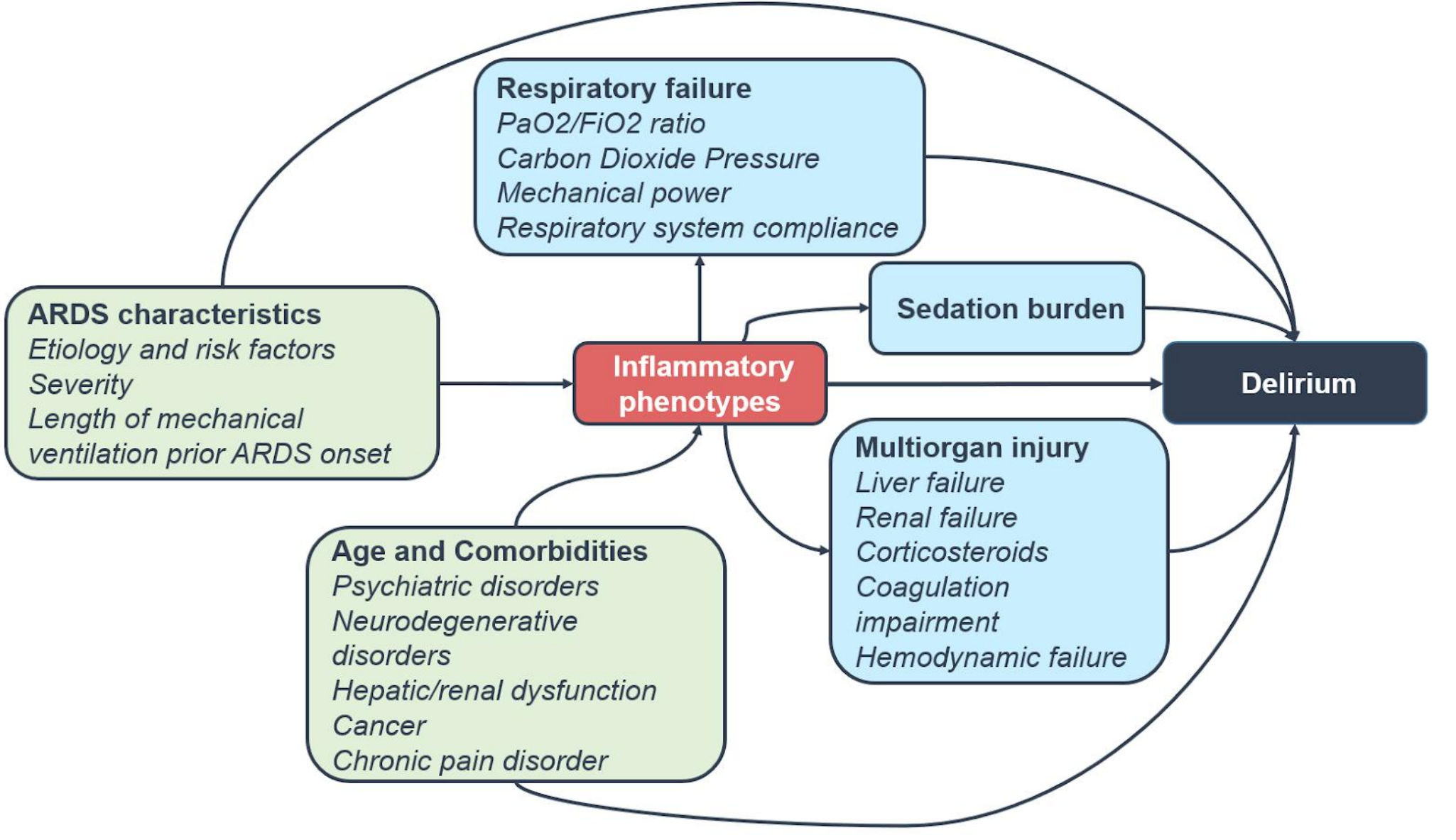


Figure 1: Directed acyclic graph depicting the analysis structure including factors assessed as confounders and mediators. Green boxes include potential confounders and light blue boxes include potential mediators of the relation between inflammatory phenotype and delirium.

QR Code: Link to the validated open-access AI Clinical Classifier for inflammatory phenotypes in ARDS



RESULTS

STUDY POPULATION

- Among **2,904 extubated ARDS patients** 1,924 (**66%**) were classified as **hypoinflammatory** and 980 (**34%**) as **hyperinflammatory** at ARDS onset. **Delirium** occurred in **55%** (1,058/1,924) of **hypoinflammatory** and **68%** (668/980) of **hyperinflammatory** patients following extubation

PRIMARY ANALYSIS

- The **hyperinflammatory phenotype** was associated with **post-extubation delirium** (adjusted absolute risk difference = 11.3%, 95% confidence interval (95%CI) [7.4–14.9]; adjusted odds ratio (OR_{adj}) = 1.62, 95%CI [1.37–1.91], $P < 0.001$)
- Findings were robust in competing-risk analysis (subdistribution hazard ratio = 1.19, 95%CI [1.05–1.33])

MEDIATION ANALYSIS

- Multiorgan injury** (35.2%, $P < 0.001$) and higher degrees of **sedation** (21.2%, $P < 0.001$) **mediated the association** between the hyperinflammatory phenotype and delirium, while **respiratory failure did not** ($P = 0.46$) (Figure 2)
- Delirium** was equally **associated with increased ICU mortality** across both phenotypes ($OR_{adj} = 2.58$, 95%CI [1.83–3.64]) and mediated the relation between the hyperinflammatory phenotype and higher risk of mortality (13.6%, $P < 0.001$)

EFFECT-MODIFICATION ANALYSIS

- Exploratory effect-modification analysis for potential delirium-protective medications suggested a **higher delirium risk with corticosteroids in hypoinflammatory ARDS**, **lower risk with statins in hyperinflammatory ARDS**, and no interaction with acetaminophen (Figure 3)

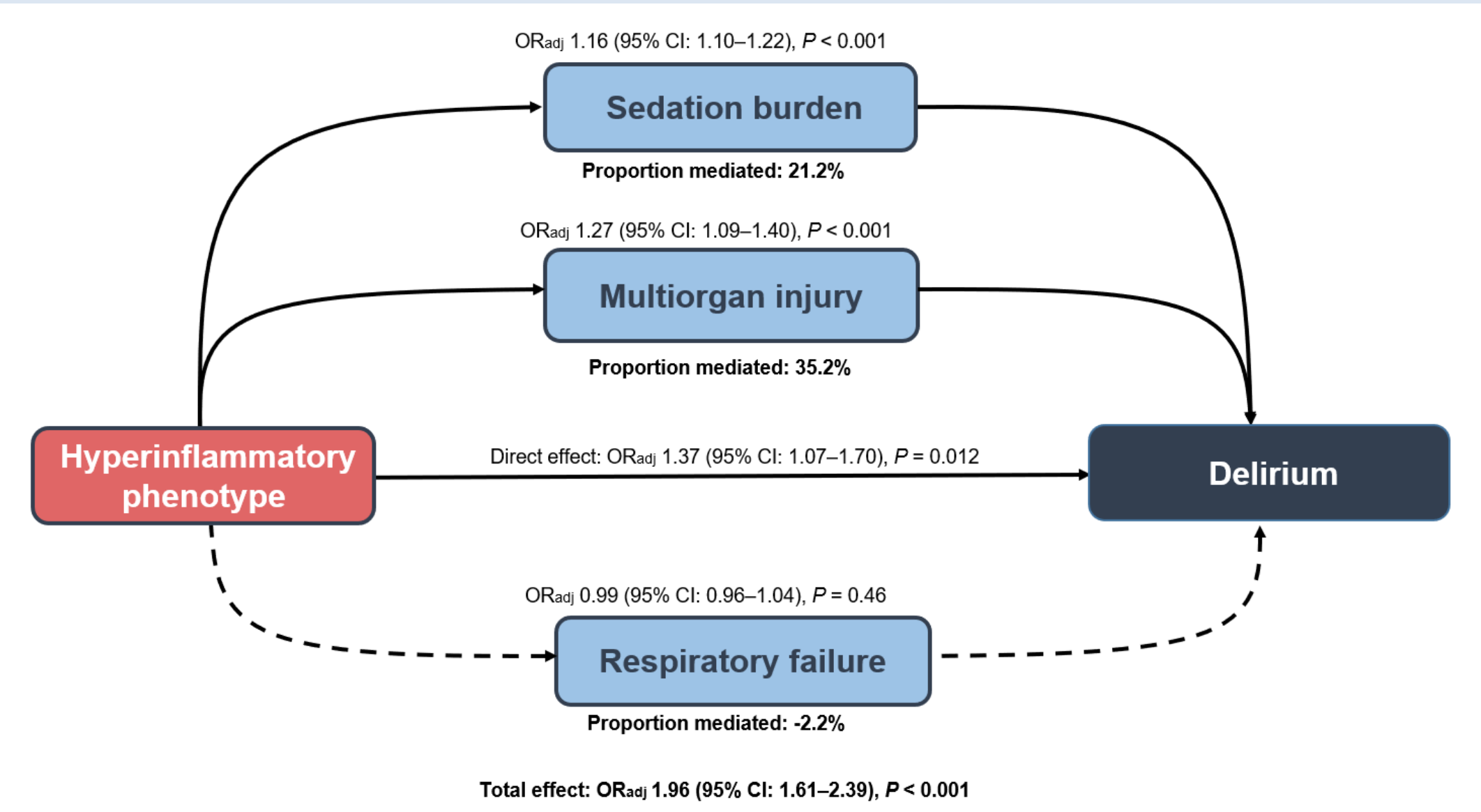


Figure 2: Mediation pathways between hyperinflammatory phenotype and delirium

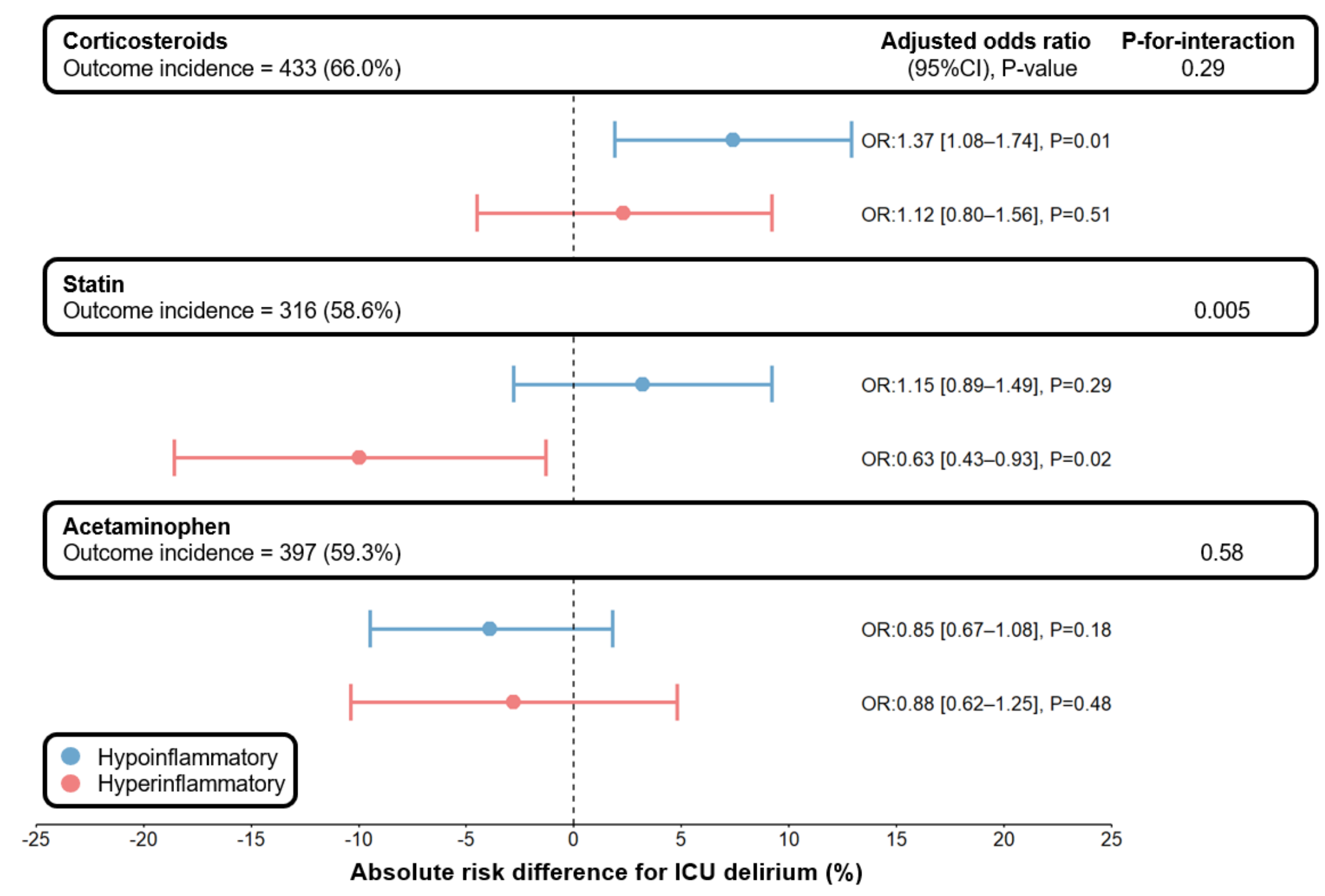


Figure 3: Effect modification of the risk of ICU delirium by corticosteroids, statins and acetaminophen

CONCLUSION

The **hyperinflammatory ARDS phenotype** carries a **higher risk of post-extubation ICU delirium** than the hypoinflammatory phenotype, driven by **greater sedation burden, multiorgan injury, and inflammatory neurologic effects**. **Phenotyping** may help guide **personalized neuroprotective strategies** to reduce delirium risk after ARDS.

CONNECT WITH US

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