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Low-dose corticosteroids and septic shock resolution: implications for randomized trial design?

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Dear Editor,

We read with interest Rygard and colleague's¹ "Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis". While the authors discuss the potential clinical ramifications of their findings, the evidence that corticosteroids reduce the duration of shock and mechanical ventilation also likely has important ramifications for the design of current and future randomized trials evaluating interventions for the treatment of septic shock. A number of randomized clinical trials are underway in which low-dose corticosteroids and adjunctive therapies (i.e., vitamin C) are compared to placebo, with a primary outcome of time to shock resolution or change in SOFA score. Can the authors comment on how their findings regarding shock reversal might inform the design of ongoing septic shock trials, especially where the primary outcome is time to shock resolution or the related outcome of change in SOFA score? If these trials combining corticosteroids and adjunctive therapies demonstrate a significant difference in vasopressor free days or time to shock reversal, there is limited additional knowledge gained outside of confirming that steroids do indeed reduce time on vasopressors. In light of the authors' findings, should ongoing trials change their control arm to low dose corticosteroids rather than placebo?

References

1. Rygard SL, Butler E, Granholm A, et al. Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med* 2018.