

## Background

- 40-60% of patients with severe alcoholic hepatitis (SAH) die within a few months of diagnosis. (1)
- Since 1971, the treatment of SAH has generated much controversy, with many clinical trials and meta-analyses having inconsistent results
- We specifically reviewed if prednisolone or prednisone improves the survival of patients with SAH at four weeks

## Methodology

- This review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. (fig.1)
- PubMed, Embase, Ovid, Web of Science, and Cochrane Library were comprehensively searched from inception of these databases to June 2022
- Search string was: (severe alcoholic hepatitis) AND ((prednisolone) OR (prednisone))
- Pre-specified primary endpoint was all-cause mortality within 4 weeks of starting prednisolone or prednisone
- Using DerSimonian and Laird method, Random-effects model meta-analysis via Cochrane RevMan 5.4 statistical software was performed on extracted data. (2)
- Statistical significance level was set at 0.05 with confidence interval calculated at 95%
- Heterogeneity was assessed with Higgins I<sup>2</sup>, and funnel plot was used to assess for publication bias. (3)
- Risk of Bias -2 (RoB-2) tool was used to evaluate the biases of each included randomized controlled trial (RCT). (4)

## Results

- Out of 443 studies, 9 studies (8 RCTs and 1 retrospective study) including 920 patients were included in the meta-analysis
- Mean age of participants was 48.1 ± 9.5 years, male to female ratio was 1.55 : 1
- Oral prednisolone 40mg/day was administered for at least 2 weeks in 8 of the 9 studies
- On pooled multivariate analysis, there was no statistically significant difference in the short-term mortality rate between the steroid-treated group and placebo-treated group (OR: 0.66, 95% CI: 0.42 - 1.02, p: 0.06, I<sup>2</sup>: 21%).

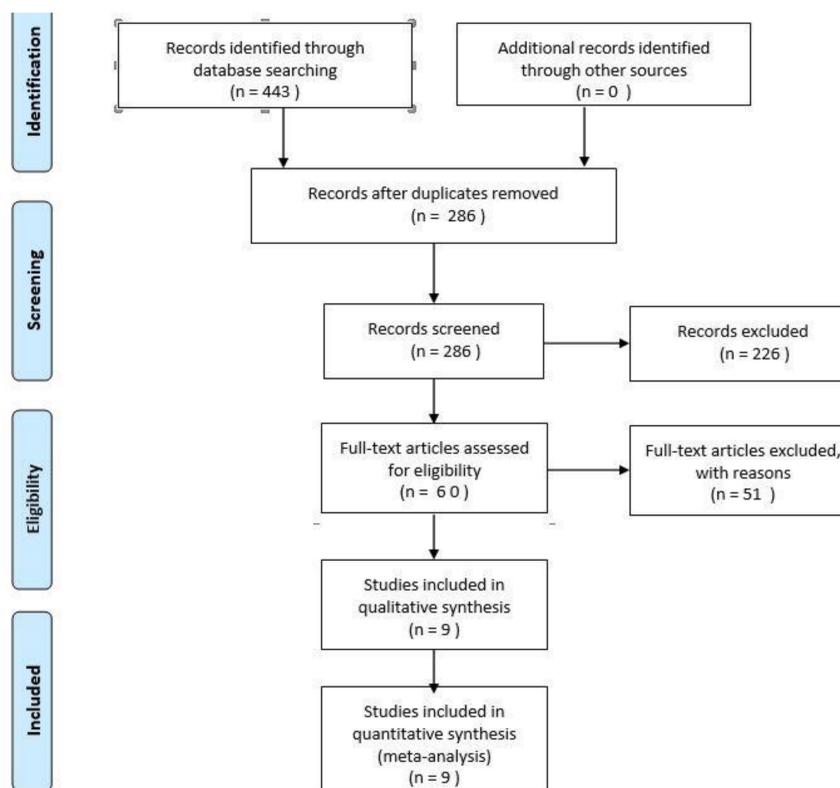
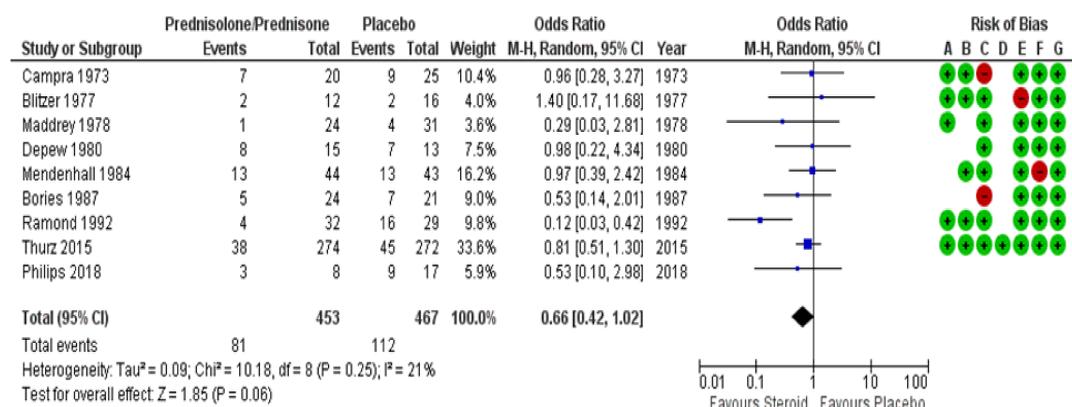


Figure 1: PRISMA flow chart for the systematic review



**Risk of bias legend**  
 (A) Random sequence generation (selection bias)  
 (B) Allocation concealment (selection bias)  
 (C) Blinding of participants and personnel (performance bias)  
 (D) Blinding of outcome assessment (detection bias)  
 (E) Incomplete outcome data (attrition bias)  
 (F) Selective reporting (reporting bias)  
 (G) Other bias

Figure 2: Pooled multivariate odds ratio of impact of prednisolone/prednisone on short-term mortality rate in Severe Acute Hepatitis

## Discussion

- Corticosteroid interventions in the included studies varied regarding dosing style and duration
- Our meta-analyses showed that corticosteroid, in comparison to placebo, did not show significant benefit in reducing all-cause mortality rate at one month in patients with SAH
- However, because the confidence interval of the effect estimate only slightly cross the statistical significance threshold, we cannot exclude the possibility of a short-term beneficial effect in some sub-group of patients
- Although current body of evidence does not show a reduction in short-term all-cause mortality rate in steroid treated group compared to placebo. Further larger scale RCTs and sub-group sensitivity analyses are still needed on this topic.

## Conclusion and Recommendation

- Prednisolone/prednisone does not improve short-term survival in patients with severe alcoholic hepatitis
- Future studies should explore sub-group sensitivity analyses

## References

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## Disclosure

- All authors declare that they have no conflicts of interest