Corticosteroid therapy for critically ill patients with COVID-19: A structured summary of a study protocol for a prospective meta-analysis of randomized trials

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Abstract

Objectives: Primary objective: To estimate the effect of corticosteroids compared with usual care or placebo on mortality up to 28 days after randomization. Secondary objectives: To examine whether the effect of corticosteroids compared with usual care or placebo on mortality up to 28 days after randomization varies between subgroups related to treatment characteristics, disease severity at the time of randomization, patient characteristics, or risk of bias. To examine the effect of corticosteroids compared with usual care or placebo on serious adverse events.

Study design: Prospective meta-analysis of randomized controlled trials. Both placebo-controlled and open-label trials are eligible.

Participants: Hospitalised, critically ill patients with suspected or confirmed COVID-19.

Intervention and comparator: Intervention groups will have received therapeutic doses of a steroid (dexamethasone, hydrocortisone or methylprednisolone) with IV or oral administration immediately after randomization. The comparator groups will have received standard of care or usual care or placebo.

Main outcome: All-cause mortality up to 28 days after randomization.

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Supplementary information

**Supplementary information** accompanies this paper at https://doi.org/10.1186/s13063-020-04641-3.

**Additional file 1.**

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**Authors’ contributions**

All authors contributed to drafting the protocol for the prospective meta-analysis. The author(s) read and approved the final manuscript.

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Funding for administrative and communications support was provided by the World Health Organisation. No other specific funding for the prospective meta-analysis was received. Dr Diaz contributed to the design of the study. World Health Organisation staff contacted trial investigators to request their participation in this prospective meta-analysis and that they share outcome data.

**Availability of data and materials**

All data provided by the trials, including summary outcome data overall and in the specified subgroups, will be included in supplementary material of the report of the prospective meta-analysis.

**Ethics approval and consent to participate**

All trials received ethics approval. No ethics approval was required for this secondary data analysis.

**Consent for publication**

Not applicable

**Competing interests**

Jonathan A C Sterne is partly funded by the NIHR Bristol Biomedical Research Centre. Jesus Villar received a Research grant from MAQUET (Sörna, Sweden) to perform a clinical trial on mechanical ventilation. Srinivas Murthy is a member of the REMAP-CAP International Trial Steering Committee. Arthur Slutsky is co-PI of the Dexamethasone in COVID ARDS study and is supported by grants from the Canadian Institutes of Health Research (CIHR). Anders Perner is the sponsor-investigator of the COVID STEROID trial, which is funded by the Novo Nordisk Foundation and supported by Pfizer. Peter Juni serves as unpaid member of steering groups or executive committees of trials funded by Abbott Vascular, Astra Zeneca, Biotronik, Biosensors, St. Jude Medical, Terumo and The Medicines Company, has received research grants to the institution for Apoll Therapeutics, Astra Zeneca, Biotronik, Biosensors International, Eli Lilly, The Medicines Company, and honoraria to the institution for participation in advisory boards and/or consulting from Amgen, Ava and Fresenius, but has not received personal payments by any pharmaceutical company or device manufacturer. Derek C Angus is a member of the REMAP-CAP International Trial Steering Committee and chair of the REMAP-CAP Corticosteroid Domain-specific Working Group. Djillali Annane has been involved as an investigator and in the steering committee for CAPE-COVID that was publicly funded by a grant from the French Ministry of Health; as an investigator, chief investigator for France, and member of the Steering committee for REMAP-CAP, he received a grant from the French Ministry of health to support French sites that participated to REMAP-CAP corticosteroids domain. He has not received any personal payment from any private or public entities. Luciano C P Azevedo is the PI for the corticosteroids therapy in adult patients with COVID-19 and ARDS (Steroids-SARI) trial, which was funded by a grant from the Ministry of Science and Technology; and has received donation of dexamethasone from Aché Pharmaceuticals. Bin Du is the PI for the corticosteroids therapy in adult patients with COVID-19 and ARDS (Steroids-SARI) trial, which was funded by a grant from the Ministry of Science and Technology; and has received donation of dexamethasone from Aché Pharmaceuticals. Bin Du is the PI for the corticosteroids therapy in adult patients with COVID-19 and ARDS (Steroids-SARI) trial, which was funded by a grant from the Ministry of Science and Technology; and has received donation of dexamethasone from Aché Pharmaceuticals.
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