INPLASY PROTOCOL

To cite: Gupta et al. Coronavirus disease 2019 (COVID-19) and Medical/ Pharmacological Therapies (CoMeT): A Network Meta-Analysis Protocol. Inplasy protocol 202070057. doi: 10.37766/inplasy2020.7.0057

Received: 15 July 2020

Published: 15 July 2020

Corresponding author:
Tejpal Gupta

tejpalgupta@rediffmail.com

Author Affiliation:
ACTREC, Tata Memorial Centre

Support: **None.**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Coronavirus disease 2019 (COVID-19) and Medical/ Pharmacological Therapies (CoMeT): A Network Meta-Analysis Protocol

Gupta, T[1]; Kannan, S[2]; Kalra, B[3]; Parikh, P[4].

Review question / Objective: **Which is the best medical/ pharmacological therapy for patients of COVID-19 stratified by the severity of disease.**
Condition being studied: **Coronavirus disease 2019 or COVID-19 caused by a novel coronavirus (SARS Cov-2) which has become a global pandemic and infected millions of people worldwide.**
Information sources: **Details provided in the study protocol (PubMed, Lit-COVID, medRxiv, bioRxiv)**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 July 2020 and was last updated on 15 July 2020 (registration number INPLASY202070057).

INTRODUCTION

Review question / Objective: **Which is the best medical/pharmacological therapy for patients of COVID-19 stratified by the severity of disease.**

Rationale: **There is no known cure for COVID-19 and a large number of experimental medical/pharmacological therapies are being tested worldwide. This network meta-analysis would compare all such investigational therapies and rank them to identify the best treatment for COVID-19 based on severity of disease.**

Condition being studied: **Coronavirus disease 2019 or COVID-19 caused by a novel coronavirus (SARS Cov-2) which has**

become a global pandemic and infected millions of people worldwide.

METHODS

Search strategy: Detailed search strategy is provided in the protocol appendix.

Participant or population: Patients proven to have Covid-19 disease.

Intervention: Any medical/pharmacological treatment.

Comparator: Standard of care plus/minus placebo.

Study designs to be included: Only randomized controlled trials.

Eligibility criteria: Trials with relevant extractable data.

Information sources: Details provided in the study protocol (PubMed, Lit-COVID, medRxiv, bioRxiv).

Main outcome(s): Mild/moderate COVID-19: Clinical Improvement. Moderate to severe/ critical COVID-19: All cause mortality.

Additional outcome(s): Time to RT-PCR negativity, Oxygen requirement, ICU admission, Invasive/mechanical ventilation.

Data management: The Clinical Research Secretariat at ACTREC, Tata Memorial Centre would be responsible for the data management.

Quality assessment / Risk of bias analysis: Cochrane risk of bias tool will be used for risk of bias.

Strategy of data synthesis: For each direct comparison with at least two studies providing data, results will be synthesized in a random-effects model to compute summary point estimates with 95% confidence intervals (CIs). Odds ratio (OR) or relative risk (RR) will be used as outcome measures for dichotomous data, while mean difference or standardized mean difference (SMD) will be used for continuous outcomes. A random-effects NMA will be performed to compare different medical/pharmacological interventions or combination of interventions with results being presented as summary effect sizes with 95%CI in league tables. The restricted maximum likelihood method will be used to estimate heterogeneity, assuming a common variance estimate across different comparisons for each single outcome considered. Frequentist or Bayesian approach as appropriate will be used in the network to compare available treatment strategies within a single analytical framework. Potential publication bias will be evaluated through a funnel plot. NMA will performed with Stata 14.0 (StataCorp, College Station, TX, USA) using the 'network' command and routines. The relative ranking probability of each treatment and rankograms will be used to estimate the hierarchy of each intervention. The mean rank values and the surface under the cumulative ranking (SUCRA) curves will also be calculated.

Subgroup analysis: Mild to moderate cases subgroup. Moderate to severe/critical case subgroup.

Sensibility analysis: The network will also be checked for inconsistency to assess when the direct comparison of one treatment versus another one, derived from one or more studies included in NMA, conflicts with evidence drawn via the indirect comparison estimated through the NMA. The restricted maximum likelihood method will be used to estimate heterogeneity, assuming a common variance estimate across different comparisons for each single outcome considered. Frequentist or Bayesian approach as appropriate will be used in the network to compare available treatment strategies within a single analytical framework. Potential publication bias will be evaluated through a funnel plot. NMA will performed with Stata 14.0 (StataCorp, College Station, TX, USA) using the 'network' command.

Language: English.

Country(ies) involved: India.

Other relevant information: None.

Keywords: COVID-19; therapy; randomized; network; meta-analysis.

Dissemination plans: Presentation and publication.

Contributions of each author:
Author 1 - Tejpal Gupta - Concept, study design, drafting the protocol. Will be responsible for interpretation and reporting as well.
Author 2 - Sadhana Kannan - Bio-statistician involved with the framing of the literature search strategy, statistical analysis and data synthesis. Will be responsible for the analysis.
Author 3 - Babusha Kalra - Responsible for retrieval and extraction of data independently for synthesis of results. Will be responsible for drafting the results after analysis.
Author 4 - Prafulla Parikh - Responsible for retrieval and extraction of data independently for synthesis of results. Will be responsible for editing the manuscript after analysis.