How COVID-19 Randomized Controlled Trials Reported on Demographic and Clinical Characteristics

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Overview

- Mortality in COVID-19 patients varies by sex, age, race/ethnicity, and concomitant comorbid conditions
- As a result, treatments to prevent or treat COVID-19 are likely to have heterogenous effects, making RCT external validity especially important
- This study assesses the reporting of key patient-level demographic and clinical characteristics among COVID-19 related RCTs
- Findings highlight the need for more robust reporting on the clinical and demographic profiles of COVID-19 related RCT populations due to limited reporting on race and other markers of socioeconomic status

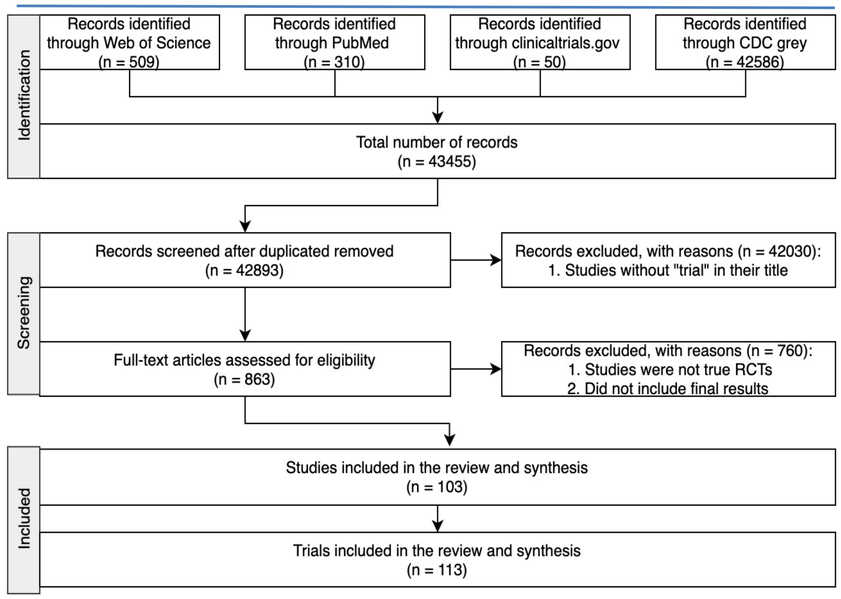
Background

- **Randomized controlled trials (RCTs)** are often considered the gold standard for assessing treatment efficacy.[1]
- Enrolling in RCTs related to pandemics like COVID-19 is difficult[2,3] as those at the highest risk of complications from the disease may be unwilling to be randomized when active treatments are available[5,6]
- Effect estimates from RCTs may not reflect benefits and harms in real-world populations given that case fatality rates from COVID-19 vary markedly based on sex, age, race/ethnicity, and respiratory and cardiovascular comorbidities[7]
- As a result, it is **important to understand likely patterns of enrollment and participation** when it comes to trials attempting to treat COVID-19 patients or prevent the spread of COVID-19 within and across communities
- We conducted a **large-scale systematic review** of COVID-19 related clinical trials to assess **the extent to which trials reported on key demographic and clinical risk factors**

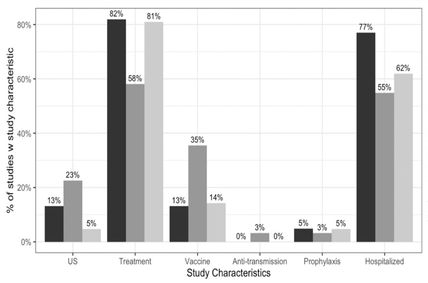
Study Design

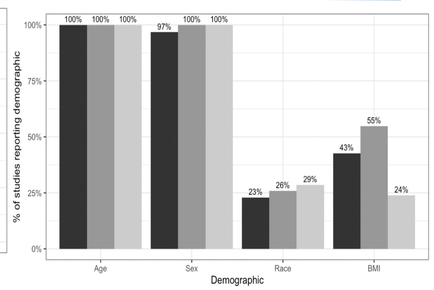
- Identified studies with a search of electronic English-language databases, including PubMed, Web of Science, the searchable CDC library of gray literature, and clinicaltrials.gov
- Searched within the title, keywords, and abstract of the article for MESH terms: ‘coronavirus’, ‘covid’, ‘clinical trial’ and ‘randomized controlled trial’
- Articles were pulled three times: 10/31/20, 1/31/21, 3/31/21
- For each RCT, we collected basic publication information, study characteristics (title, region/country of research, study type, inclusion of pregnant women, etc.), key demographics (age, sex, race) and clinical risk factors (hypertension, diabetes, etc.)
- Summarized and synthesized basic study characteristics, including demographic and clinical characteristics, using summary statistics
- Repeated analysis stratified by pull, study type, and country (studies including US vs studies not including US)

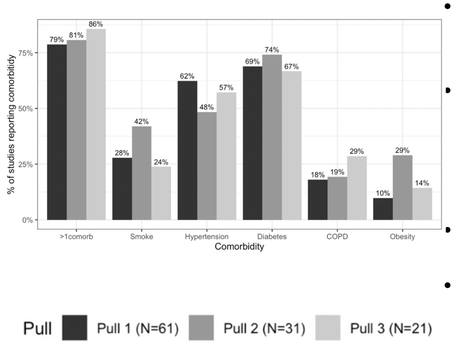
Data Collection Flowchart



Results







- **Study types:** 85 treatment, 22 vaccine, 5 prophylaxis strategies, and 1 anti-transmission
- **Demographics**: 113 reported on age, 111 on sex, 91 on the prevalence of at least one health condition and 28 on race (17% of studies with US patients)
- **Comorbid risk factors:** 79 reported DM, 65 HTN, 27 asthma, 23 COPD
- 73% and 80% of treatment-related studies published data on HTN and DM, respectively
- Pregnant women were explicitly excluded from 91 of the trials

Discussion

- Simple demographic statistics (age, sex) and comorbidities (hypertension, diabetes) were frequently collected and reported on
- While the number of studies reporting on race was low, the proportion of studies with US participants reporting race was high (88%)
- More complex comorbidities (immunosuppression, COPD) were not commonly reported on, even in treatment-related studies of hospitalized patients
- There is a need for robust reporting on complex demographics and risk factors to estimate effects in high-risk populations

Limitations

- Due to lag time of trial reporting and publication, some key emerging factors (like COVID-19 variants) were not collected and reported
- Some trials may have collected more detailed data that was not reported in their published results
- Only searched English-language databases

Conclusion

- COVID-19 related trials always or nearly always report simple, easy to gather demographic and clinical risk factors
- Lack of reporting on more complex risk factors makes it difficult to understand treatment effect variability based on those factors
- This may make it more difficult to assess the similarity of effect estimates in trials and observational studies

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