STUDY PROTOCOL
Protocol for systematic review of ethical declarations made in clinical publications concerning COVID-19 [version 1; peer review: awaiting peer review]

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Abstract
COVID-19 is a respiratory disease caused by a coronavirus, designated SARS-CoV-2, which is responsible for a global pandemic in 2020. Public interest in this disease has led to the publication of thousands of articles in the medical literature in a very short timeframe. It is imperative that medical research into COVID-19 is conducted quickly and safely, and that due reference is given to the ethical considerations enshrined in the ICH GCP guidelines, according to the Declaration of Helsinki. In order to review the reporting of ethical considerations in these papers, we hereby propose a protocol for a systematic review of COVID-19 papers up to April 14th 2020. The search criteria proposed for the review are based upon what would be a reasonable search conducted by a lay member of the public with access to PubMed.gov. It is proposed to publish the findings of the review with a summary of the institutional Research Ethics Committee response to the challenges of reviewing and approving clinical research proposals in the time of a pandemic.

Keywords
COVID-19, pandemic, research ethics, clinical trials, case studies

This article is included in the HRB-TMRN collection.

This article is included in the Coronavirus (COVID-19) collection.
Introduction

In December 2019 the first reports of a novel coronavirus, now designated SARS-CoV-2, emerged from China. Since then SARS-CoV-2 has spread across the globe and is the agent responsible for a viral pneumonitis called COVID-19. Its virulence, the rapidity of its spread and the lack of either a vaccine or a treatment have led to the adoption of unprecedented public health measures worldwide; and to high levels of interest and anxiety in the general population.

The international medical and scientific research community has responded to the COVID-19 pandemic by generating a huge amount of literature to which the general public has access. The COVID-19 related publications range from commentary and case reports to epidemiological studies and clinical trials. It is the policy of many journals during the pandemic to offer rapid review in order to make reports and research on COVID-19 available quickly. The authors have observed considerable variability in the reported ethical review of the studies published and seek to conduct a systematic review of this question – what is the nature of ethical disclosure reported in the COVID-19 literature?

Protocol

Protocol design and registration

The protocol is designed in line with the PRISMA-P checklist for systematic review. The protocol is not eligible for registration on the PROSPERO database, as the question of interest relates to reporting and methodology rather than to a clinical outcome for participants.

The ethical standards of interest are adopted from the paper by Yank and Rennie, which was an assessment of the standards agreed by the International Committee of Medical Journal Editors following the Declaration of Helsinki; this focuses on the report of consent obtained for the study and the report of ethical review of the study.

The search parameters are: Pubmed search of the term “COVID-19” with the filters of Free full text and English language publication – the rationale for this search is that it would be reasonable for a lay member of the public to conduct such a search. No start date is applied and the finish date of the search is April 14th, 2020.

Search record and outcome management

The bibliography of the search will be saved and the assessors will use an Excel spreadsheet to record excluded and included studies, using the reference number from the search bibliography. Papers may be included if they are defined by an assessor as a case report, case series, observational study or clinical trial. Papers will be excluded if they are classified as a commentary, editorial, review, guideline, non-clinical report, cell-based study, animal study, epidemiologic study or report of a mathematical model. Two reviewers will conduct the initial assessment (half of the papers each, identified by the initial search). The reviewers will confer where there is any uncertainty.

Two independent reviewers will conduct a bias assessment. Each independent reviewer will assess 10 studies each for each initial assessor, identified randomly from the search bibliography (20 papers in total by each independent assessor). A threshold of 20% discrepancy between initial and independent assessors has been set to determine whether a further methodological revision is required. A further five records each will be reviewed following this initial method assessment.

For case studies and case series, the assessor will record: the first three authors; journal; study title; whether written consent reported; if not written consent whether oral consent reported or whether not available (i.e., patient deceased); whether written consent to publish provided to journal; the wording of consent; the nature of identifiers reported; whether the article included a statement of compliance with International Conference on Harmonisation (ICH) good clinical practice (GCP)/Declaration of Helsinki standards.

For observational studies and clinical trials, the assessor will record: the first three authors; journal; study title; whether written consent reported; if not written consent whether oral consent reported; review by research ethics committee; whether that committee is identifiable on line; whether the article included a statement of compliance with ICH GCP/Declaration of Helsinki standards and in the case of a clinical trial, whether the trial was registered.

Analysis

The outcome is the proportion of papers where informed consent to publish (in case studies and series) and for inclusion in a clinical study as well as publication (observational studies and clinical trials) was recorded. A qualitative assessment of the role of ethics committees will be included; specifically, whether ethics committee approval was sought and whether requirement for consent was waived by said committee and whether there is a geographical or publication pattern associated with the reported role of the ethics committee.

This is a methodologic review; therefore, bias in interpretation of results is not relevant to this study. The proposed assessment of the ethics reporting standard categorized by journal may identify a publication bias.

A quantitative summary of numbers of studies identified, and their classification by assessor, will be provided. A further summary of consent reported and the nature of that consent will be prepared. The proportion of studies reporting ethical review and including a statement of compliance with ethical guidelines for conduct of clinical studies, will be included. A qualitative description of the measures to preserve anonymity of the participants will be made.

Ethical review and lay opinion

This study will not be clinical in nature and does not meet the requirement for a research ethics committee review. In view of the nature of the study and the impact of ethical conduct of research on public confidence in research, it is proposed to share...
the final draft of the study manuscript with two lay volunteers for lay perspective prior to submission for publication. The protocol will be made available for the public on the UCD COVID-19 website.

Future dissemination and availability of data
The search bibliography and finalized Excel spreadsheets will be included as supplementary documents with the final publication. As a publication relating to COVID-19, it is anticipated that this will be open access. Should this not be the case, the authors will make these files available on request to the corresponding author.

Conclusions
The purpose of conducting this review is to describe the existing publication status for ethical standards in COVID-19 clinical trials and the potential impact on public trust in clinical research. It is proposed to include the findings with a description of how ethical assessment can be expedited safely in a time of pandemic; in order to maintain ethical standards, maximize public access to participation in clinical trials and research, and maintain public confidence in future research studies and their findings.

Data availability
Underlying data
No data are associated with this article.

Reporting guidelines

The completed PRISMA-P checklist is available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Author contributions
All authors contributed to the protocol design. LOS and RC drafted the manuscript which was approved by all authors. Funding was acquired by PD.

References

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