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Ethical frameworks in clinical research processes during COVID-19: a scoping review

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ABSTRACT

Objectives In response to the COVID-19 pandemic there have been significant developments in research, its conduct and the supporting ethical framework. While many protocols have been delayed, halted or modified, other research efforts have been accelerated, generating controversy. The goal of this paper is to determine the rates of references surrounding the ethical oversight of research as reported in current COVID-19-related research publications.

Design Scoping review.

Setting Population-based observational or interventional studies from December 2019 to May 2020 with sample size of two or more. Studies were searched through electronic databases including Medline, EMBASE, and Cochrane CENTRAL Register of Controlled Trials.

Participants Eligibility criteria included participants within published studies who tested positive for COVID-19.

Main outcomes and measures Data were extracted and charting methods included taking note of references to ethical frameworks, institutional review board (IRB), ethics committee (EC) or research ethics board (REB) involvement, consent processes, and other variables.

Results 11 556 articles were screened, with 656 included in the final analysis. References to ethics were present in 530 (80.8%) studies, with 491 (74.8%) involving IRB/ECs/REBs and 126 (19.2%) not referencing ethics. Consent processes were outlined in 201 (30.6%) studies, with 198 (30.2%) reporting that they obtained consent waivers, however, 257 (39.2%) did not mention consent at all. Differences ($p<0.001$) in ethics-related references were apparent when analysed by continent, publication type, sample size and IF.

Conclusions The majority of published articles pertaining to COVID-19 research made mention of ethical considerations, however, national and regional variations in research ethics review requirements introduce heterogeneity between studies and raise important questions about the conduct of scientific research during global public emergencies.

Trial registration number Open Science Framework: https://osfio/z67wb.

Strengths and limitations of this study

- ► Systematic review of existing literature for references to ethical frameworks and consent processes in the context of COVID-19 pandemic.
- ► Statistical analyses of variables relevant to ethical frameworks can potentially account for variations including region and study type.
- ► Documentation processes related to research ethical oversight vary between countries, health systems and institutions.

INTRODUCTION

The pandemic of COVID-19 has created evolving healthcare, economic and social crises. The rapid rise in worldwide incidence of COVID-19 has created an unprecedented, urgent need to learn, understand and bridge the therapeutic gap.[1 2] The international scientific community has responded swiftly by initiating hundreds of clinical trials, evidenced on clinicaltrials.gov and the WHO COVID-19 databases.[3 4] However, balancing research quality, integrity and protection of vulnerable subjects with the apparent need for speed on research processes are important facets which deserve attention. It is essential to maintain acceptable ethical standards and scientific rigour at all times, including during global pandemics, where various aspects of trial design and conduct may be modified to meet shortened development timelines. Vigorous debate continues with respect to the ethical standards appropriate to the protection of participants in times of global crisis.[5]

Despite well-established existing normative guidance from national and international bodies which set out general principles pertaining to the ethical conduct of human subjects research during emergency circumstances, ultimately, the decision to approve clinical research remains the responsibility of local or regional research review bodies.[6] In Canada, these are known as research ethics boards (REB). The USA has similarly constituted review processes provided

by committees called institutional review boards (IRB). Other countries may rely on ethics committees (EC).[7]

Recognising the high stakes associated with ongoing exceptional circumstances affecting the global community, we performed a scoping review of current literature related to COVID-19 in order to identify references to ethical frameworks and consent processes, and correlated these with various study and publication characteristics.

METHODS

We developed a protocol using the scoping review methods proposed by Arksey and O'Malley,[8] and refined by the Joanna Briggs Institute.[9] This review was registered through the Open Science Framework (https://osf.io/z67wb/). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews[10] was used to guide reporting (online supplemental file 1).

Eligibility criteria

Our eligibility criteria were defined using 'Population, Intervention, Comparison, Outcomes, Study designs, Timeframe' components. The population of interest was patients with history of active or past COVID-19 infection. Studies with a mixed population of COVID-19 infected and non-infected patients were also included. Interventions of interest included were studies referencing drugs, devices or other interventions. Studies including diagnostic laboratory or radiological procedures were also eligible. Outcomes of any measure were eligible for inclusion. Studies included were clinical trials, observational studies and case series. We excluded case reports describing a single patient; trials still in progress; studies analysing population-based database-driven, aggregate or pooled data; non-COVID-19 infected subjects; studies described only in social media; and surveys surrounding medical workforce, health services or staff attitudes. We restricted the timeframe from 1 December 2019 to 8 May 2020, at which time the literature search was performed. We excluded studies without full-text available, and due to the rapid nature of the review those not available in the English language were excluded.

Information sources and search strategy

The protocol for the comprehensive literature search was developed by an experienced information specialist (RF) in consultation with the research team and was completed by the information specialist. Due to the rapid nature of the review, the search was limited to publications in the English language from December 2019 to May 2020. A comprehensive search was conducted in Medline ALL (Medline and Epub Print Ahead of Print and In-Process and Other Non-Indexed Citations), EMBASE and Cochrane CENTRAL Register of Controlled Trials all from the OvidSP platform. Where provided, controlled vocabulary terms and text words were compromised. Grey literature was not searched as the reviewers felt it was beyond the scope of this review to analyse the ethical procedures and requirements of published sources outside of non-indexed journal databases. The search was restricted to original research involving human participant. The search strategy for MEDLINE is presented in the supplementary appendix (online supplemental file 2). Additional search strategies are available from the corresponding author on request.

Study selection

Search results were imported into EndNote V.X9 citation software, following which results were uploaded onto Covidence for duplicate removal, two-tiered screening and data extraction. Reviewers were familiarised with the review protocol and eligibility criteria prior to abstract screening and full-text review.

A series of calibration exercises prior to each stage of screening to ensure reliability across reviewers was completed. Inter-rater agreement for study inclusion was calculated using per cent agreement and when it reached >75% across the research team, we proceeded to the next stage. If the per cent agreement was <75%, the inclusion criteria were clarified, and another pilot test occurred. For abstract screening, one pilot test of 50 citations was conducted with all team members and we achieved 90% agreement. Subsequently, two reviewers (LK and AM) independently reviewed all titles and abstracts for inclusion. For full-text screening, one pilot test of 10 full-text articles was conducted, and we achieved 80% agreement. Following this calibration exercise, two reviewers (LK and AM) screened full-text articles for inclusion. All discrepancies between reviewers were resolved by a third reviewer consistently (QL).

Data collection

For each study, data were abstracted on ethical frameworks referenced (defined as any reference to any ethics, participant consent or institutional or ethics committee review), including whether an IRB, REB or EC was involved in approving the study, as well as description of consent processes (including alterations of consent processes such as waivers of the requirement to obtain consent). Other variables extracted included type of publication (brief communication vs letter vs original research vs case report); month of first availability online; countries involved; single site versus multicentre study; sample size; study population (COVID-19 positive or both positive and negative); and longitudinal nature (prospective vs retrospective vs cross-sectional). A pilot test of 12 articles was conducted with inter-rater agreement of 82%. The data abstraction form was developed and modified as required based on feedback from the team. Studies were distributed among six reviewers (LK, AM, QL, MM, LB and SLL), and data were cross-checked by two reviewers (LK and AM). Any discrepancies were resolved through consensus. The information specialist (RF) extracted impact factor (IF) for each journal.

Methodological quality appraisal

Quality appraisal and risk of bias of studies were not assessed as this was a scoping review.

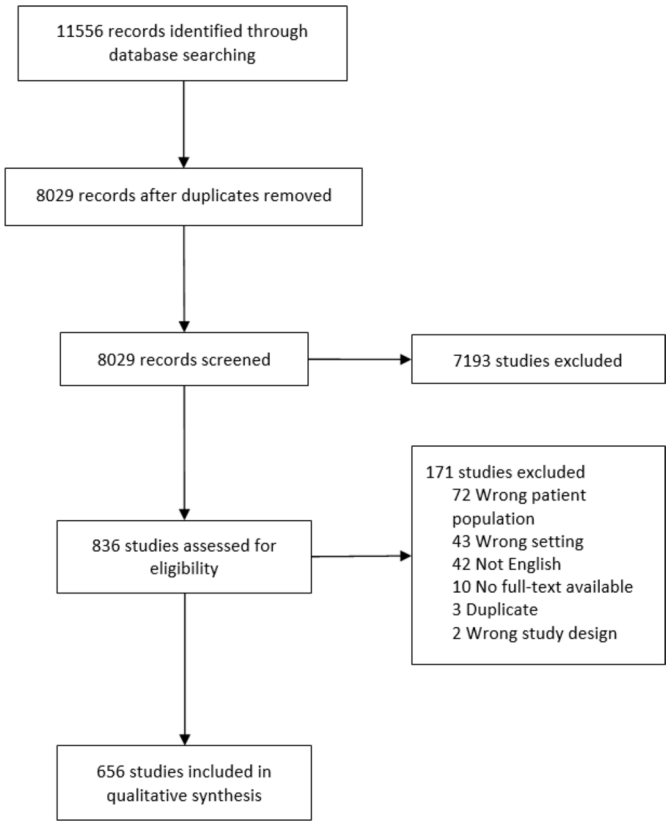

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (2009) diagram of literature search.

Data synthesis and charting

Extracted data points were compiled into an Excel spreadsheet, from which descriptive statistical analyses were generated. Due to heterogeneity, types of publication were condensed into four categories (online supplemental file 3). Study countries were condensed into continents for analysis, with subgroup analyses of countries with high frequencies. For those without ethics referenced within each continent, analyses were performed broken down by sample size and type of publication. The association between a continuous variable and a categorical variable was determined by using Wilcoxon and Kruskal-Willis tests, respectively, to compare continuous variables between two and more than three groups, whereas the χ^2 test was used to compare categorical variables, unless the underlying assumptions were not satisfied. In that case, we used a Fisher's exact test. Sample size was analysed as a continuous variable, as well as dichotomous variables with cut-offs of 3 and 10 participants. Analyses on IF were performed as continuous and dichotomous variables, focusing on those within Scientific Journal Ranking Quartile 1 (lower cut-off 2.32) in 'Medicine (miscellaneous)' compared with the remainder.[11]

RESULTS

The electronic database search obtained 11 556 results (figure 1). A total of 3527 duplicates were removed and 8029 records underwent abstract screening. A total of 836 studies were eligible for full-text review, following which 656 were included in the qualitative synthesis. The full reference list is included in online supplemental file 4.

Ethical frameworks referenced

A reference to ethics or consent was made in 530 (80.8%) studies, with 491 (74.8%) involving IRB/EC/REB. One hundred and twenty-six (19.2%) records did not reference ethics in any way. Consent processes were referenced in 201 (30.6%) studies, 198 (30.2%) described a consent waiver and 257 (39.2%) made no mention of consent.

Correlation with other variables

There were no interactions between rates of reference to ethics, REB/IRB/EC or consent processes when comparing study populations or centres (figure 2, additional data in online supplemental file 5). Most (n=595, 91%) were first available or published from March to May 2020, however further analyses were not performed.

Continent

In terms of where studies were done, the majority were from Asia (n=488, 74.4%), Europe (n=92, 14%) and North America (n=62, 9.5%), with largest contributions from China (n=438, 66.8%), USA (62, 9.5%) and Italy (n=51, 7.8%) and studies with largest sample sizes coming from the former two regions (see figure 3). Studies from Asia were more likely to reference ethical frameworks (86.3%, p<0.001) and REB/IRB/EC (81.6%, p<0.001) compared with Europe (64.1%, 53.3%) and North America (64.5%, 56.5%). The mention of consent processes was also more common among studies from Asia, with 33.2% (p<0.001) obtaining consent and 33.6% (p<0.001) obtaining a waiver of consent, compared with Europe (30.4%, 11.96% waiver) and North America (8.1%, 32.3% waiver). Subgroup analyses by continent are presented in the supplementary appendix (online supplemental figures 1 and 2).

Publication type

With respect to type of publication (figure 2A–C), the majority were original research pieces (n=485, 73.9%), followed by brief communications (n=91, 13.9%), letters (n=54, 8.2%) and case reports (n=26, 4%). Studies described as case reports had a sample size of at least two (range: 2– 191, median 3). Original research was more likely (p<0.001) to reference ethics (87%) compared with brief communications (62.6%), case reports (53.9%) or letters (68.5%). REB/IRB/EC approval/waiver was also mentioned more frequently (p<0.001) in original research (83.1%), and likewise in terms of consent processes (32%) or waivers (33.4%, p<0.001).

Study type

In terms of study design (figure 2G–I), most studies were observational (n=545, 83.1%). Only 13 (2%) were interventional drug studies and 14 (2%) were described as interventional 'other' studies. Reference to ethics was not significantly different (p=0.16) between study types

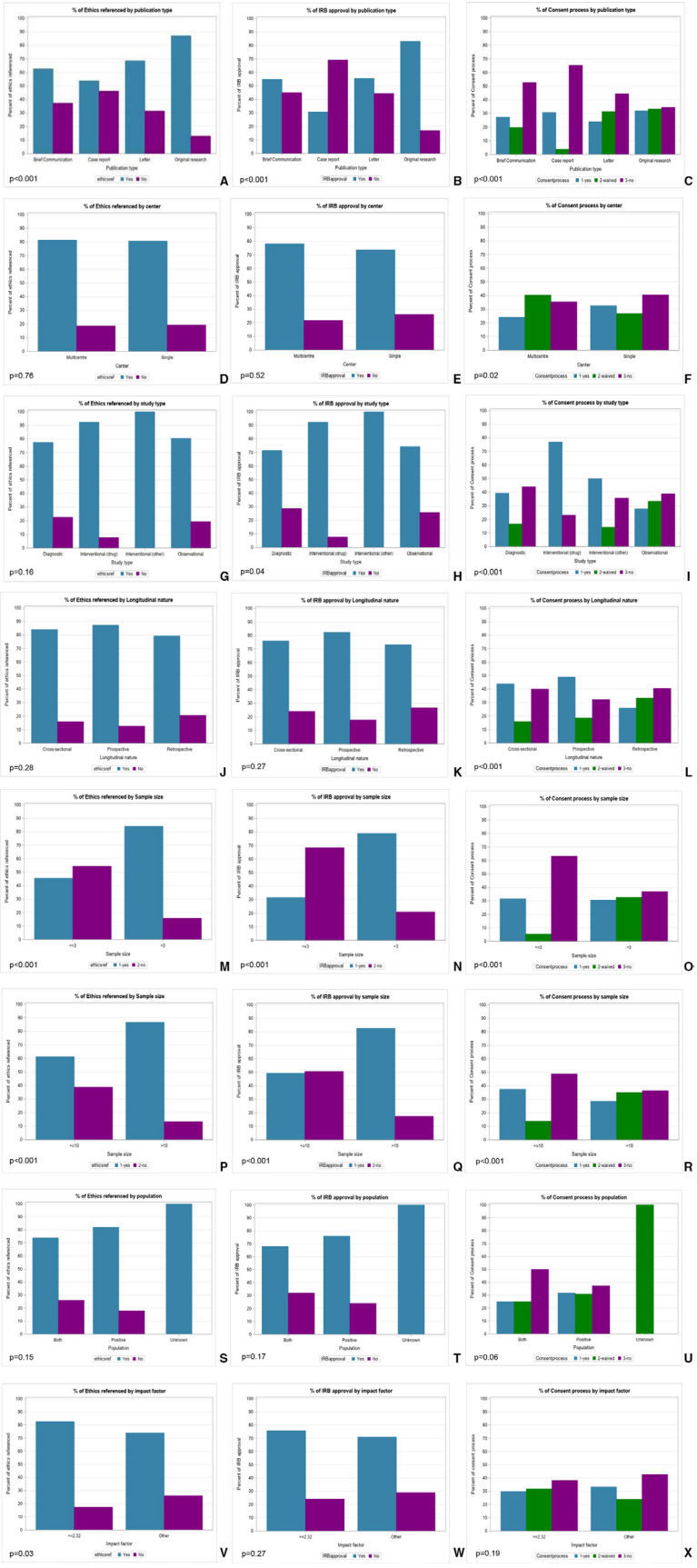

Figure 2 Ethics referenced, researchethics board/institutionalreview board/ethicscommittee involved and consent process described by publication type (A–B), centre (D–F), type of study (G–I), longitudinal nature (J–L), proportion of sample size greater than three, or three or less (M–O), proportion of sample size greater than 10, or 10 or less (P–R), study population (S–U) and impact factor (V–X). P values provided reflect statistical significance of interaction using Fisher's exact test.

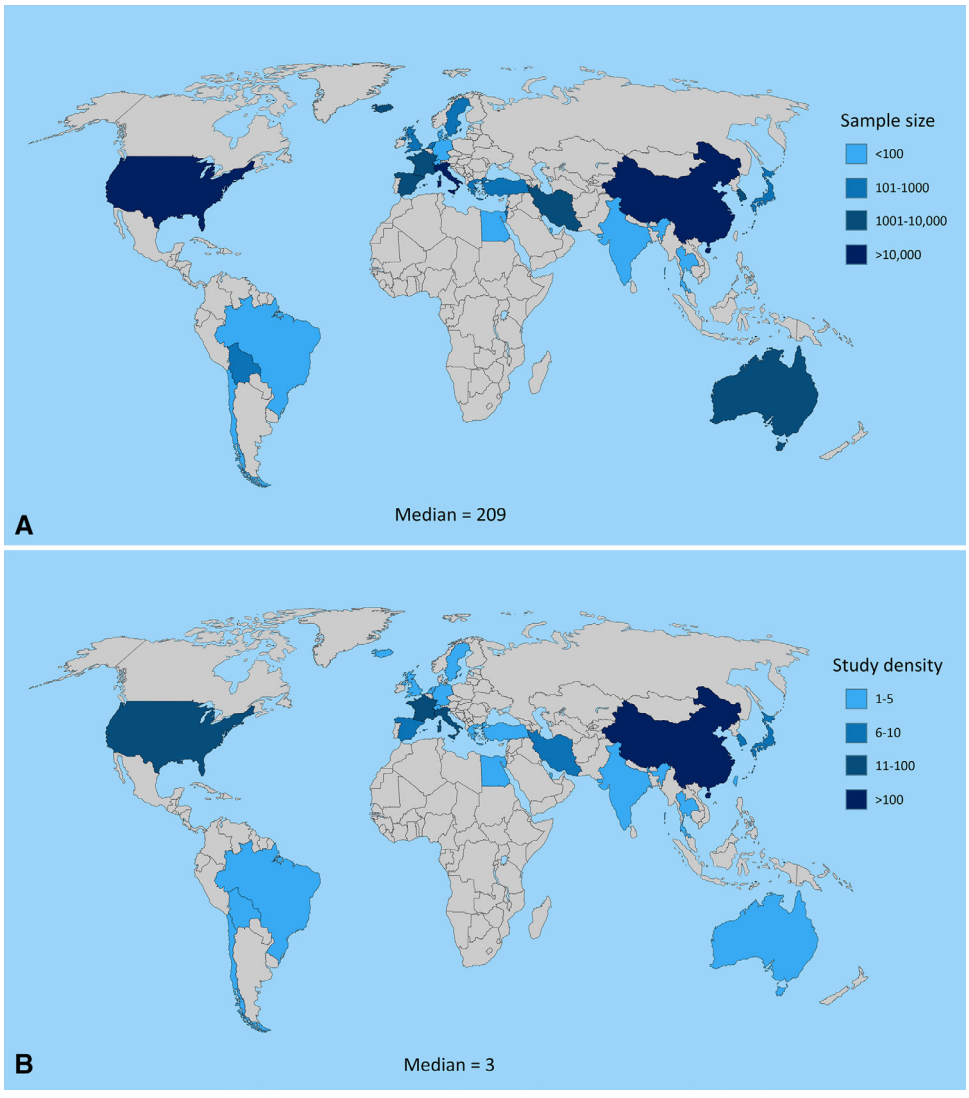

Figure 3 Graphical distribution by country of (A) sample size of included studies and (B) study density.

and REB/IRB/EC reference was borderline significant (p=0.04). Consent processes were statistically significantly different (p<0.001), with 3 (23.1%) out of 13 interventional drug studies and 5 (35.7%) out of 14 interventional 'other' studies not referencing consent. No consent processes were described in 37 (44.1%) diagnostic and 212 (38.9%) observational studies.

Longitudinal nature

In terms of longitudinal nature (figure 2J–L), the majority of studies were retrospective (n=520, 79.3%), followed by prospective (n=102, 15.5%), cross-sectional (n=25, 3.8%) and not reported (n=9, 1.4%). There were no differences in rates of references to ethics (p=0.28) or references to REB/IRB/EC (p=0.27). Consent was more often described in non-retrospective studies (p<0.001), with nearly twice the rates of waivers (n=174, 33.46%) being granted in retrospective studies compared with the rest. Consent processes were not described in 33 (32.35%) prospective studies.

Sample size

The median study sample size was 59 (range: 2–257 353). Of the 530 studies referencing ethics, the median sample size was 72 (range: 2–257 353) compared with 126 in those that did not reference ethics (range: 2–7425, p<0.001). The differences in median sample size were also significantly different when comparing rates of REB/IRB/EC (p<0.001) and consent process (p<0.001) references.

When dichotomising sample size comparisons using a cut-off of 3 (figure 2M–O) or 10 (figure 2P–R), all interactions were significantly different (p<0.001) across ethics, REB/IRB/EC references and consent processes. Of the 599 studies with sample size greater than 3, 84.1% (n=504) referenced ethics compared with 45.6% (n=26) of 57 articles with sample size of 3 or less. When the cut-off was increased to 10, 61.2% (n=93) of 152 studies with sample size of 10 or less referenced ethics as compared with 86.7% (n=437) of 504 studies with more than 10 patients. Similar trends were observed with lower rates of studies that did not mention REB/IRB/EC references

or consent processes when analysis cut-off was increased from sample size of 3 to 10.

Impact factor

IF was available for 631 (96.2%) studies, with a median of 4.62 (range: 0.86–74.7). The median IF of articles with ethics referenced (n=530) was 4.83 (range: 0.86–74.7) compared with a median of 4.16 (range: 1.11–74.7, p=0.06) in those with no ethics referenced (n=126). For Quartile 1 (median: 5.6, range: 2.327–74.699), 428 (82.6%) of 518 articles referenced ethics compared with 102 (73.9%) of 138 articles within non-Quartile 1 journals (median: 1.911, range: 0.86–2.286, p=0.03; see figure 2V–X). The interactions were not statistically significant when analysed by REB/IRB/EC reference (p=0.27) or consent process (p=0.19).

DISCUSSION

The main objective of this scoping review was to assess the prevalence of references to ethical concerns in original research involving patients with COVID-19 . We detected that 19.2% of published studies reported no mention of ethical framework or oversight process, with an additional 6% of studies not referring to review board approval or waiver.

The obligation of researchers to attend to the welfare, rights and interests of human participants is not diminished in Public Health Emergencies such as the COVID-19 pandemic. During times when public goals may be in tension with the interests of individual research participants, there is heightened need for attention to ethical principles and for oversight bodies and review mechanisms attuned to specific vulnerabilities of those who may be subject to the attention of researchers.

Historically, three main ethical codes have shaped contemporary research principles. The first well-recognised ethical code that established international research standards was the *Nuremberg Code*,[12] which was created in response to the Nuremberg trials at the end of the Second World War. In 1964, the *Declaration of Helsinki* (now in its seventh iteration) established ethical principles for medical research involving human subjects.[13] Lastly, the *Belmont Report*, written in 1978, articulated three main ethical principles applicable to the conduct of human subject's research: respect for persons, beneficence and justice.[14] Current normative standards and research regulations show variation across different countries, but most express respect for these fundamental principles (table 1).

At the institutional level, research review committees (REB/IRB/EC) assess the ethical acceptability of human research conducted within their jurisdictions. The committee model is designed to protect participants from harm by ensuring that physical and non-physical risks of study participation are not overlooked in the rush to achieve scientific breakthroughs.

Table 1 Research standard examples for human research protection

Research standards	Country	Summary
CFR Title 21	USA	50: Protection of Human Subjects https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm 56: Institutional Review Boards https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm
CFR Title 45	USA	46: Protection of human subjects. https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML
ICH GCP E6	International	International ethical and scientific quality standard https://www.fda.gov/media/93884/download
CIOMS and WHO	International	*International ethical guidelines for health-related research involving humans* https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/
TCPS 2	Canada	Ethical conduct for research involving humans http://publications.gc.ca/site/eng/381622/publication.html
ICMR	India	National ethical guidelines for biomedical and health research involving humans https://ethics.ncdirindia.org//asset/pdf/ICMR_National_Ethical_Guidelines.pdf

CFR, Code of Federal Regulations; CIOMS, Council for International Organizations of Medical Sciences; GCP, Good Clinical Practice; ICH, International Conference Harmonization; ICMR, Indian Council of Medical Research; TCPS, Tri-Council Policy Statement.

The gold standard for ethical research is the voluntary and ongoing informed consent from legally competent individuals or authorised third parties prior to the initiation of research-related procedures. Even access to identifiable patient data generally requires consent; although departures from usual consent processes may be justified if requisite institutional or other approvals are secured.[15] Under exceptional circumstances, permission to deviate from usual processes may be granted provided participants' rights are protected and appropriate institutional authorisations are obtained.[15] In this review, we detected a large proportion of studies without consent processes mentioned (39.2%), while 30.2% described a consent waiver and 30.6% obtained informed consent.

Although informed consent to research ordinarily is obtained in the form of signed documents, other means, including verbal and electronic,[16] may be appropriate when paper records may be vectors for disease transmission. In order to maintain the research quality standards and to ensure protection of vulnerable research participants, journals should request information about consent processes at the time of article submission and ensure appropriate declarations within submitted manuscripts. Additionally, where applicable, the scientific community should consider incorporating written or electronic consent process documentation as supplementary material related to all original research involving interventions, participant data or biological samples. Ethical principles and requirements should not be compromised during a pandemic, and any changes in processes must ensure the rights and safety of subjects are not emasculated.

Our review excluded single case reports. Arguably, they do not meet the definition of research as they do not constitute systematic investigations and are not undertaken with prior research intent.[17] Approaches to the review and reporting of case reports vary between institutions and jurisdictions, but frequently medical record reviews of three or fewer individuals do not require oversight by institutional review committees. However, ethical considerations should be mentioned in all studies regardless of the sample size. We detected that the median sample size in studies with ethics referenced was lower than in those without ethics referenced (72 vs 126, p<0.001).

Journal IF can sometimes positively correlate with number of citations; interestingly we detected that the manuscripts published in Quartile 1 journals were more likely to include references to ethics compared with others (82.6% vs 73.9%, p=0.03). It is worth noting that there were no significant differences in REB/IRB/EC review or consent processes between these two groups.

We also demonstrate that while the rates of REB/IRB/EC approval or waiver mentioned are similar to rates of whether ethics was referenced at all, a small proportion of studies with ethics referenced did not mention whether REBs/IRBs/ECs were involved (table 1 and figure 2). Instead, a clause on consent only, or a general statement not specifying what approval was sought was included. The disparity between these two proportions could be explained by variable journal requirements with respect to statements on ethics in studies involving human participation. Differing publication types may also explain this variation; our analysis supports the interpretation that original research articles are more likely to reference ethical approval and consent processes as compared with other types of publications. Increased emphasis and transparency is needed about how research participants and their rights were protected and this should be reinforced in published scientific research. Organisations such as the Committee on Publication Ethics (COPE),[18] which aims to promote integrity in scholarly research and publication, may view our findings with concern. The COPE Core Practices suggest that all journals should have robust, well-described and documented procedures, including policies pertaining to consent, vulnerably situated populations, research conducted on human subjects and confidential handling of data.[18] Following this guidance, reviewers might, for example request copies of study protocols or evidence of ethics review board approvals, which could assist in inhibiting the publication of ethically problematic research.

This study has several limitations. The majority of included studies were observational, contributing to lower rates of references to ethics. This was likely due to the timing of study conceptualisation and database searching, which preceded the publication of many interventional studies. While the authors attempted to identify subcategories of types of publication included for analysis, there is heterogeneity with respect to journal requirement. Furthermore, study assessment for prospective or retrospective nature was unclear for a number of records, which may reflect on publication clarity. Finally, the authors acknowledge that results generated from this review rely on studies across the globe, and documentation processes related to research ethical oversight vary between countries, health systems and institutions.

CONCLUSION

The ethical conduct of scientific research requires attention to timeliness, innovation, feasibility and quality, while preserving the safety, well-being and rights of participants. Flexibility may be required during extenuating circumstances, however, processes must retain respect for the principles of ethical research. Trying times present important opportunities to ensure oversight and processes are in place to maintain research and ethical rigour, and identify permissible variations in practice. Priority should be given to developing novel strategies which accelerate research in a safe, meaningful manner in concert with relevant ethical, regulatory and funding bodies. Adaptive trial designs represent larger-scale studies which can adhere to regulatory requirements while also permitting shorter development timelines. The current pandemic has created opportunities to rethink efficiency in clinical research conduct, but also highlights the importance of defining and maintaining ethical oversight.

This scoping review found that although the majority of research published during this time of global stress was conducted in the context of some form of ethical review, there is considerable variability and may reflect important gaps in process or reporting. An important lesson from the current outbreak is that existing ethical norms cannot be overlooked and should continuously be revisited. While it is a truism that poor science can never be ethical, poor ethics cannot be redeemed or justified by valid science or good intentions. Research participants have a right to expect their sacrifices will be honoured by devoting appropriate attention to both aspects of the scientific enterprise.

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REFERENCES

1 Bindra RS, Gibson SL, Meng A, *et al*. Hypoxia-Induced down-regulation of BRCA1 expression by E2Fs. *Cancer Res* 2005;65:11597–604.
2 Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *The Lancet* 2020;395:1225–8.
3 Tentori L, Lacal PM, Muzi A, *et al*. Poly(ADP-ribose) polymerase (PARP) inhibition or PARP-1 gene deletion reduces angiogenesis. *Eur J Cancer* 2007;43:2124–33.
4 Madariaga A, Kasherman L, Karakasis K, *et al*. Optimizing clinical research procedures in public health emergencies. *Med Res Rev* 2021;41:725–38.
5 Blumenthal-Barby J. COVID-19 current controversies. *J Med Ethics* 2020;46:419–20.
6 World Health Organization. *Guidance for managing ethical issues in infectious disease outbreaks*. Geneva: World Health Organization, 2016. https://apps.who.int/iris/handle/10665/250580
7 Emanuel EJG, Crouch Robert A, Reidar K, *et al*, eds. *The Oxford textbook of clinical research ethic*. Oxford; New York: Oxford University Press, 2008.
8 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
9 Peters MDJ, Godfrey C, McInerney P. Chapter 11: scoping reviews (2020 version). In: Aromataris E, Munn Z, eds. *JBI manual for evidence synthesis*. Adelaide, Australia: JBI, 2020. https://synthesismanual.jbi.global
10 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
11 SJR. Scimago Journal & Country Rank, 2020. Available: https://www.scimagojr.com/journalrank.php?area=2700&category=2701
12 The Nuremberg Code (1947). *BMJ* 1996;313:1448.
13 World Medical Association. World Medical association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013;310:2191–4.
14 United States. *The Belmont report: ethical principles and guidelines for the protection of human subjects of research*. Bethesda, Md.: The Commission, 1978.
15 Canadian Institutes of Health Research. Natural sciences and engineering Research Council of Canada, and social sciences and humanities Research Council of Canada, Tri-Council policy statement: ethical conduct for research involving humans, December 2018, 2020. Available: https://ethics.gc.ca/eng/documents/tcps2-2018-en-interactive-final.pdf
16 Welch BM, Marshall E, Qanungo S, *et al*. Teleconsent: a novel approach to obtain informed consent for research. *Contemp Clin Trials Commun* 2016;3:74–9.
17 University Health Network Research Ethics Board. UHN REB guidance on case reports, 2020. Available: https://www.uhnresearch.ca/documents_and_forms/send_doc/15106
18 Committee on Publication Ethics. Promoting integrity in scholarly research and its publication, 2020. Available: https://publicationethics.org/