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A Thematic Exploration of Ethical Challenges in COVID-19 Research from the Viewpoint of South African Research Ethics Committees

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Abstract

The COVID-19 pandemic has posed substantial ethical challenges for research ethics committees (RECs), which must balance the urgent review of COVID-19 studies with careful assessment of potential risks and benefits. In Africa, these challenges are compounded by historical mistrust of research, concerns about equitable participation in COVID-19 studies, and the need to ensure fair access to treatments and vaccines. In South Africa, the prolonged absence of a National Health Research Ethics Council (NHREC) left RECs without national guidance for much of the pandemic. This study aimed to explore the experiences and perspectives of South African RECs regarding the ethical issues arising from COVID-19 research. We conducted a qualitative descriptive study using in-depth interviews with 21 REC members or chairpersons from seven major academic health institutions in South Africa that actively reviewed COVID-19 research between January and April 2021. Interviews were conducted remotely via Zoom, lasting 60–125 minutes, in English, and guided by a semi-structured interview protocol. Data collection continued until saturation was reached. Audio recordings were transcribed verbatim, supplemented with field notes, and systematically coded line by line. An inductive thematic analysis approach was employed to identify and organize key themes and sub-themes. Analysis revealed five primary themes: the rapidly shifting ethics landscape for research, heightened vulnerability of participants, distinct challenges in obtaining informed consent, difficulties in community engagement during the pandemic, and the intersection of research ethics with public health equity considerations. Each theme encompassed multiple sub-themes. South African REC members reported numerous and complex ethical challenges in reviewing COVID-19 research, with reviewer fatigue and workload pressures emerging as significant concerns. The findings underscore the importance of enhanced ethics education, particularly in informed consent, and the urgent need for national guidance for research ethics during public health emergencies. Additionally, cross-country comparative studies are warranted to enrich understanding of African RECs' experiences and ethical considerations in pandemic-related research.

Keywords: Ethical challenges, COVID-19, South African, Ethics committees

Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, has led to millions of cases and fatalities globally, with South Africa recording the highest number of infections in Africa [1]. Mortality figures in the country may, however, be underestimated, as indicated by excess death data from the South African Medical Research Council [2]. In the absence of effective therapies or vaccines early in the pandemic, South Africa implemented strict public health interventions, including lockdowns, social distancing, and contact tracing, which significantly disrupted daily life and economic activities, particularly across the African continent [3, 4]. Vulnerable populations were disproportionately affected, aggravating existing health inequities [5]. Moreover, the pandemic in South Africa was associated with rising

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mental health problems, increases in gender-based violence, substance misuse [2], and restricted access to essential healthcare services, including maternal care, HIV and TB services, and management of chronic diseases such as cancer [6].

Research is central to addressing public health emergencies. Globally, scientific efforts have concentrated on understanding COVID-19 and developing interventions such as vaccines and therapeutic drugs, resulting in numerous clinical trials [7]. While much research focused on vaccines and drug repurposing (e.g., Chloroquine, Ivermectin), the African Academy of Sciences stressed the importance of research that informs preventative and primary healthcare strategies as a core part of Africa's response to COVID-19 [8].

The urgency of finding effective treatments early in the pandemic led to proposals for adapting standard research procedures, including skipping preclinical animal studies or bypassing certain trial phases [9, 10]. Experiences from prior outbreaks highlight the challenge of balancing rapid knowledge generation with adherence to research ethics principles [11–15]. International guidance has consistently emphasized the need to uphold ethical standards and ensure robust, rapid ethics review during public health crises [16–23].

Despite these guidelines, there is limited insight into how African research ethics committees (RECs) navigated structural, social, and contextual constraints to implement them during the pandemic. In South Africa, RECs also had to address public skepticism toward research, evident in social media campaigns such as #AfricansAreNotGuineaPigs, while ensuring fair access to COVID-19 interventions [24].

The regulatory framework for research ethics in South Africa is grounded in the National Health Act 61 of 2003 (NHA), which provides authority for governance and oversight of health research [25, 26]. The NHREC, established in 2006 under Section 72 of the NHA, is responsible for setting standards, issuing guidance to RECs, and monitoring compliance [26, 27]. Section 73 mandates that all institutions conducting health research must have access to an NHREC-registered REC, and only such RECs are authorized to approve research involving human participants (NHA s 71(1)(a) and s 73(2)) [26, 27]. Currently, 46 RECs are registered with the NHREC in South Africa [28].

In South Africa, the guidelines for research ethics committees (RECs), as outlined in the National Department of Health's Ethics in Research Guidelines (2015), stress the importance of independence, diversity, and multidisciplinary membership. Committees are expected to include at least nine members representing a wide range of disciplines, sectors, and professional backgrounds relevant to the committee's mandate. Membership should reflect cultural and ethnic diversity, balance between genders, inclusion of laypersons from local communities, researchers outside human participant studies, and professionals from other relevant fields [26]. To maintain competence, REC members are required to complete formal ethics training at least every three years [26].

The COVID-19 pandemic presented additional complications for South African RECs due to the NHREC being inactive for over a year, from November 2019 to December 2020, with no official explanation for its absence [29, 30]. This left RECs to navigate the ethical review of COVID-19 research largely on their own during the early waves of the pandemic, without national guidance or oversight. How different committees interpreted and applied both national guidelines for research ethics [26] and international recommendations for COVID-19 research [24, 25] in these emergency circumstances remains largely unknown. The present study aimed to examine the experiences and viewpoints of South African RECs regarding the ethical challenges encountered while reviewing COVID-19 research.

Materials and Methods

This study used a qualitative design to investigate the ethical issues faced by South African research ethics committees (RECs) during the review of COVID-19 research. Data were gathered through in-depth interviews with REC members and chairs from major health science institutions across the country.

Participant selection

Participants were recruited using purposive sampling, focusing on individuals actively involved in reviewing COVID-19 studies of varying risk levels, including clinical trials, therapeutic interventions, preventative research, and vaccine studies. Snowball sampling was also employed to identify additional participants. Eligible individuals had to regularly attend REC meetings within the six months prior to the study and be affiliated with NHREC-registered health science institutions offering formal training in health-related disciplines. Invitations to participate were sent via email, aiming to include a diverse range of REC members and chairs from multiple institutions.

Out of 31 individuals contacted, 21 agreed to participate, representing a 67.7% response rate. These participants were affiliated with seven universities and collectively represented 10 RECs, including some linked to national governmental organizations and a charitable foundation. Together, these RECs account for roughly 21.7% of NHREC-registered committees (n = 46) and are estimated to oversee more than 75% of moderate- to high-risk COVID-19 research in South Africa during the study period (NHREC, personal communication, 29 November 2021).

To maintain confidentiality, no personally identifying information was collected, and care was taken not to disclose the specific institutions or committees involved. Among participants, 11 had formal postgraduate training in bioethics, applied ethics, or research ethics, and all had completed mandatory research ethics training within the preceding three years. Participants' professional backgrounds spanned social sciences (n = 2), laboratory and medical sciences (n = 4), clinical specialties (n = 5), other health professions (n = 6), and care-focused disciplines such as social work (n = 2). A summary of participants' characteristics is provided in **Table 1**.

Table 1. Summary of descriptive characteristics of participants (n = 21**)**

Participant Code	Role in REC	Gender	Years of REC Experience	Professional Expertise	Formal Ethics Qualification[a]
REC1	Chair	Male	>15	Clinical specialist; Regulatory affairs; Research ethics	Postgraduate Diploma
REC2	Chair	Female	10–15	Health professional; Bioethics	Master's
REC3	Member	Female	10–15	Professional care; Research ethics	Postgraduate Diploma
REC4	Chair	Female	>15	Health professional; Qualitative methods; Applied ethics	Honours
REC5	Chair	Male	>15	Medical scientist; Quantitative methods	–
REC6	Member	Female	10–15	Health professional; Research ethics	Postgraduate Diploma
REC7	Member	Female	1–5	Laboratory scientist	–
REC8	Member	Female	>15	Bioethics; Social science	Doctorate
REC9	Member	Male	6–10	Clinical specialist; Clinician researcher	–
REC10	Member	Female	1–5	Health professional	–
REC11	Member	Female	10–15	Clinical specialist; Quantitative methods	–
REC12	Member	Female	10–15	Health professional; Qualitative methods	–
REC13	Member	Female	1–5	Clinical specialist	–
REC14	Chair	Male	6–10	Laboratory scientist; Research ethics	Postgraduate Diploma
REC15	Chair	Female	>15	Clinical specialist; Research ethics; Biostatistics	Doctorate
REC16	Chair	Female	>15	Health professional; Research ethics	Postgraduate Diploma
REC17	Chair	Male	>15	Professional care	–
REC18	Chair	Female	6–10	Health professional; Research ethics	Postgraduate Diploma
REC19	Member	Female	1–5	Social scientist	–
REC20	Chair	Female	10–15	Laboratory scientist	–
REC21	Member	Female	>15	Legally qualified; Research ethics	Doctorate

Note: [a] indicates formal ethics qualification; all participants completed research ethics training within the three years prior to the study.

Data collection

In this study, interviews with REC chairs and members were conducted by TB, a clinical health professional with formal training in bioethics and qualitative research. TB's prior experience serving as chair and deputy chair of two RECs in South Africa enabled her to identify participants with substantial expertise and prominent national or international profiles in research ethics, supporting the collection of rich and relevant insights.

To reduce COVID-19 transmission risk, all interviews were conducted remotely via Zoom between January and March 2021. Each session lasted between 60 and 125 minutes. Participants selected private spaces to ensure confidentiality, and video recordings were deleted immediately after the interview to prevent retention of identifiable images. Only audio recordings were retained for analysis, and participants were reminded of these procedures before the interviews began. Interviews followed a semi-structured guide, covering topics such as REC procedures, COVID-19 review processes, inter-committee harmonization, and ethical challenges in COVID-19 research. Field notes were taken during interviews, and sessions continued until no new themes emerged (data saturation). Audio files and transcripts were securely stored in a password-protected OneDrive folder and will be retained for up to five years, after which they will be destroyed once all study findings are published.

Data analysis

Transcripts were prepared verbatim from audio recordings, and field notes were converted into analyzable documents. TB reviewed transcripts for accuracy. A codebook was initially developed by TB and a research assistant by independently coding four transcripts. All transcripts were then coded line by line, and codes were organized into themes and sub-themes. The study team (TB, SR, KM) met regularly to discuss coding decisions and ensure inter-coder consistency. The codebook was refined iteratively to incorporate new insights, and previously coded transcripts were revisited to apply novel codes. An inductive thematic analysis approach guided the interpretation of data, facilitated using Atlas.ti (Version 6.2.28, ATLAS.ti Scientific Software Development GmbH, Berlin, Germany). The full research team reviewed and discussed interpretations throughout the analysis process.

Ethics

Ethical clearance for this study was obtained from the Health Research Ethics Committee at Stellenbosch University (N20/10/062_COVID-19) and the Faculty of Health Sciences Human Research Ethics Committee at the University of Cape Town (HREC REF 045/2021), in accordance with the Declaration of Helsinki [31]. Permissions were also secured from institutional gatekeepers to access participants. Written informed consent was obtained from all participants, who were made aware of the study purpose and agreed to audio recording. Identifying information about participants and their institutions was removed prior to analysis.

Results and Discussion

Analysis of the interviews identified five main themes that captured key ethical considerations faced by RECs in reviewing COVID-19 research, with associated sub-themes summarized in **Table 2**.

Table 2. Five main themes and associated sub-themes emerging from qualitative analysis

Themes	Sub-themes
Rapidly changing research ethics environment	Ethical evaluation as a moving target in risk–benefit assessments; Considerations around placebo use in ongoing vaccine trials; Determining appropriate standards of care; Ensuring post-trial access to interventions; Assessing social value of research
Heightened vulnerability of research participants	Individual and population-level susceptibility; COVID-19-related stigma and discrimination; Misunderstanding of therapeutic intent (therapeutic misconception)
Specific challenges in obtaining informed consent	Influence of fear and isolation on participant autonomy; Practical challenges in field settings; Differing opinions on waiving consent requirements
Obstacles to community engagement during the pandemic	REC involvement in community engagement; Determining appropriate participants, timing, and methods during a public health emergency
Intersection of research ethics and public health equity	Unequal distribution of research burdens; Ensuring fairness in research priorities; Addressing disparities in access to interventions

Rapidly changing research ethics environment

Participants highlighted that a key ethical challenge in reviewing COVID-19 research was the constantly shifting research ethics environment **(Table 3)**. REC chairs and members emphasized the pace at which new COVID-19 evidence emerged and the implications this had for their decision-making. Many described the difficulty of moving from assessing whether genuine uncertainty existed (equipoise) and granting approval, to responding to emerging evidence of potential harm, which sometimes required pausing or withdrawing previously approved studies. Risk–benefit assessments were perceived as highly fluid, influenced by factors such as changing excess mortality, successive pandemic waves, rapidly accumulating scientific data, and evolving national vaccine distribution strategies, all of which added complexity to REC deliberations.

Table 3. Quotations for the theme of 'Rapidly changing research ethics environment'

Sub-themes	Quotations
Ethical evaluation as a moving target in risk–benefit assessments	What precedents can society reasonably accept moving forward? (REC3) "The rapid introduction of various vaccines—newly developed, targeted formulations, and even repurposed ones—means that the full spectrum of potential risks has not yet been fully mapped out. Their accelerated rollout required decisions to be made under uncertainty, acknowledging the possibility of still-unknown adverse reactions. Nonetheless, deploying them with strong systems for reporting, surveillance, evaluation, and incorporating lessons emerging internationally felt necessary under the circumstances." (REC1) "For many of the repurposed or newly applied treatments currently in circulation, the foundational preclinical evidence falls short of the standards we typically demand. Because of that, we feel a responsibility to carefully weigh the risks before giving approval." (REC15) "A global crisis does not justify abandoning the scientific principles and research protocols that ordinarily guide us. There can be a tendency for those standards to fade into the background when an endless stream of protocols is arriving and critically ill patients are in front of you, but disregarding them entirely is not acceptable." (REC8) "Navigating this space is difficult—there's constant pressure not to impose excessive restrictions because research urgently needs to move ahead, yet the environment remains inherently fraught." (REC19) "Justice concerns inevitably arise, but balancing fairness with possible harms and safety considerations is extremely complex. At some point, a line has to be drawn, and in most cases patient safety is likely to rank above justice in the hierarchy of priorities. Some decisions may appear inequitable, but they generally rest on defensible reasoning." (REC9)
Considerations around placebo use in ongoing vaccine trials	"…the central debate revolves around determining the appropriate moment to discontinue the use of placebos, particularly in situations where they can no longer be justified." (REC20) "A difficult ethical question is how we can justify leaving participants unvaccinated for extended follow-up in ongoing studies when we know they could have received protection, especially given that clinical trials are designed to operate with substantial resources and should, in principle, be capable of preventing this kind of avoidable exposure." (REC8) "The recent concerns around reduced vaccine efficacy against the so-called 'South African variant' raise questions about whether placebo-controlled trials might again become permissible; yet even with that possibility, significant uncertainty remains." (REC11)
Determining appropriate standards of care	"During the pandemic, decisions tended to be framed through the lens of a public health crisis rather than the purely scientific perspective that normally guides our work. The usual expectation that 'standard of care' must rest on solid evidence—typically supported by multiple phase-three trials—shifted toward assuming that whatever was being widely used must qualify as acceptable care. This raises difficult questions: how do we interpret the notion of standard care when vaccination is rolled out rapidly to high-risk groups under emergency conditions, even as clinical trials are still actively underway?" (REC7)
Ensuring post-trial access to interventions	"In the context of rapid reviews, we spent considerable time grappling with the question of post-trial access—specifically, how to safeguard participants who volunteered for research in a setting filled with uncertainty, and what obligations this creates for sponsors, particularly those overseeing clinical trials." (REC2) "We also struggled with whether participation in a vaccine trial should translate into some form of priority for the participants' families, which proved to be a contentious issue. At the same time, the debate helped

	heighten reviewers' awareness of the broader responsibilities surrounding post-trial access." (REC5)
Assessing social value of research	"When dealing with severely ill COVID-19 patients, we had to think very deliberately about the ethical implications and prepare accordingly. Even though the interventions might not offer direct benefit to the individual patient involved, we acknowledged that the work still needed to proceed because of its broader societal value." (REC4) "What was needed wasn't a binding guarantee, but at least a clear commitment that efforts would be made to secure some level of vaccine access for our population. While there was plenty of goodwill expressed, the ethical concern remained: our communities took on significant risk and played a role in advancing a vaccine that will ultimately generate substantial profit, yet no upfront assurance was provided that they would share in the benefits. I am not arguing that we will never gain from it, but there was no early agreement that our participants or our country would receive any form of priority or compensation for hosting those trials." (REC6)

The capacity of RECs to judge the strength and reliability of emerging evidence—and to determine how unreviewed datasets, preprints, and other non–peer-reviewed materials should inform assessments of risk–benefit balance and equipoise—emerged as a major ethical challenge. Participants also described persistent concerns about evaluating adaptive trial designs, defining an appropriate standard of care, determining when placebo controls were permissible in vaccine trials, and addressing obligations related to post-trial access and benefit sharing. Many additionally pointed to the need to evaluate both the anticipated societal value and the potential harms associated with COVID-19 research. Chairs and members of research ethics committees noted that their deliberations increasingly adopted a public-health-ethics perspective, signaling a shift in the traditional ethical framework. Ethical tensions embedded within implementation trials conducted during the pandemic were also emphasized.

Heightened vulnerability of research participants

Most participants underscored that individuals and communities faced profound vulnerability during the pandemic in general, and even more acutely within the context of COVID-19 research **(Table 4)**. Stigma and discriminatory attitudes were frequently identified as significant social harms. The heightened likelihood of therapeutic misconception was repeatedly noted, with several participants explaining that fear of serious illness or death—especially early on, before vaccines became available—amplified the risk that individuals would confuse research participation with guaranteed clinical benefit. Concerns were raised about whether informed consent procedures were sufficient to counteract this misconception. Some participants argued that, given the desperation and urgency at the pandemic's peak, traditional considerations of therapeutic misconception lost relevance. Others strongly disagreed, maintaining that these emotional pressures—fear, anxiety, and a sense of urgency—made a more stringent effort to prevent therapeutic misconception not less, but more necessary to ensure voluntary and informed decision-making during COVID-19 research.

Table 4. Quotations for the theme of 'Heightened vulnerability of research participants'

Sub-themes	Quotations
Individual and population-level susceptibility	"Proxy consent has become especially complicated when families are unable to enter hospitals or visit their loved ones. The emotional strain—grief layered with the heightened anxiety of COVID-19—often leaves relatives struggling to fully process or make sense of the information provided to them." (REC6) "The challenges surrounding informed consent are vast, and I sometimes question whether we are genuinely honouring participants' autonomy or merely completing administrative checklists." (REC8) "This problem extends beyond the pandemic, but it is particularly troubling now—imagine someone like Mr. Jones being presented with a stack of ten forms to sign while isolated in a hospital room, frightened,

	and without the support of his family. Under those conditions, can we really say he has a meaningful choice?" (REC11)
COVID-19-related stigma and discrimination	"Securing informed consent during a pandemic becomes extraordinarily difficult—hospitalized patients are often severely ill, their capacity to consent may fluctuate, and practical questions arise about who should obtain consent and how to manage the logistical constraints surrounding the process." (REC3) "Once again, we are caught between protecting participant autonomy and avoiding excessive demands, unnecessary repetition, and risks to the researchers themselves." (REC12)
Misunderstanding of therapeutic intent (therapeutic misconception)	"The crisis has made it extremely difficult to reach next of kin, and situations where we previously assumed independent witnesses would be readily accessible and appropriately arranged have turned out to be far more complicated." (REC21) "We also need clearer guidance on the appropriate timing for engaging with families, what information they should receive, and the most suitable ways to communicate that information to them." (REC4)

Specific challenges in obtaining informed consent

Informed consent emerged as one of the most difficult ethical issues for RECs reviewing COVID-19 research. As shown in **Table 5**, both practical and procedural complications arose when attempting to obtain consent while maintaining physical distancing. Committee chairs and members stressed the need to appreciate the actual constraints of pandemic-era clinical settings and to consider what kinds of consent procedures were realistically achievable under those conditions. They also noted that intense fear of infection, urgent hopes for a protective vaccine or treatment, and the separation of patients from their partners or families all had the potential to compromise the validity of consent. Additional challenges involved the use of delayed consent models and circumstances in which consent might be waived entirely. Participants differed considerably in their opinions on when such waivers—or postponement of consent—could be ethically justified.

Table 5. Quotations for the theme of 'Specific challenges in obtaining informed consent'

Sub-themes	Quotations
Influence of fear and isolation on participant autonomy	"Obtaining proxy consent has become particularly challenging when families are barred from visiting or accompanying patients, as grief compounded by COVID-related anxiety often prevents them from fully understanding or processing the information provided." (REC6) "There are numerous challenges surrounding informed consent, and it raises the question of whether we are truly honoring participant autonomy or merely fulfilling procedural requirements." (REC8) "This concern extends beyond the pandemic, yet it is especially pressing now—consider a patient like Mr. Jones, who must navigate ten different consent documents alone, isolated and frightened in the hospital without family support. Under these circumstances, can we genuinely say he has a meaningful choice?" (REC11)
Practical challenges in field settings	"Obtaining informed consent during a pandemic is extremely complex, particularly for hospitalized patients who may have limited capacity, raising questions about who should obtain consent and how to manage the practical challenges involved." (REC3) "This situation also requires balancing the protection of participant autonomy with the need to avoid overloading participants, creating unnecessary duplication, and maintaining the safety of researchers." (REC12)
Differing opinions on waiving consent requirements	"The pandemic created a crisis around reaching next of kin, as situations where independent witnesses were assumed to be readily available and properly arranged proved far more complicated than expected." (REC21) "We also need to clarify the appropriate timing for communicating with families, determine what

	information should be provided, and identify the most effective ways to convey it." (REC4)

Obstacles to community engagement during the pandemic

Participants notably highlighted two sub-themes concerning stakeholder engagement, as shown in **Table 6**. The first sub-theme focused on the role of RECs themselves in engaging stakeholders, with many participants linking this to the inclusion of community or lay members in REC composition, in line with the South African Department of Health's Ethics in Research Guidelines (2015). Overall, the input of lay members in REC discussions was perceived as minimal or inadequate, prompting several suggestions for enhancing community representation and involvement in REC deliberations.

Table 6. Quotations for the theme of 'Obstacles to community engagement during the pandemic'

Sub-themes	Quotations
REC involvement in community engagement	We face challenges in securing genuine layperson participation on the committee, as it's difficult for non-professionals to have a meaningful voice in a professional setting (REC20). I feel we've overlooked the importance of engaging directly with the broader community; the institution hasn't assessed public understanding of COVID-19, which could have been addressed more promptly (REC11). There's also uncertainty about who these community representatives truly speak for and how they are selected, which is especially problematic during COVID when gathering wider community input is challenging (REC18). This situation represents a missed opportunity for ethics committees to contribute to public education, particularly when communities tend to place doctors on a pedestal—so when a doctor admits that research stages were skipped, it can be profoundly concerning and counterproductive (REC3).
Determining appropriate participants, timing, and methods during a public health emergency	How should community engagement be handled during a pandemic or other emergencies? Our researchers didn't utilize established frameworks like those used in TB or HIV/AIDS studies (REC16). There's also the question of whether we're capturing genuine community perspectives, or if the voices we hear are already too familiar with research to reflect true public sentiment (REC3). In the context of COVID, it's unclear who qualifies as "the community"—with 1.4 million cases, selecting just a handful of people can't realistically represent the population (REC7). Effective community involvement requires a substantial and representative group; it can't be treated as a mere formality. To be meaningful, engagement must include extensive checks and balances and be broader in scope, especially during COVID (REC10).

The second sub-theme focused on community or stakeholder involvement in research trial processes, with participants noting that the urgent pace of ethics review and approval for COVID-19 research constrained opportunities for thorough and genuine engagement. They highlighted the difficulties in defining who truly represented the community and in determining how meaningful community participation could be achieved during the pandemic.

Intersection of research ethics and public health equity

Research ethics committee chairs and members observed that, throughout the COVID-19 pandemic, research ethics considerations often intersected with issues of public health equity **(Table 7).** A commonly cited example was the prioritization of COVID-19 studies during the national lockdown, which led to the suspension of non-COVID research—including therapeutic clinical trials and HIV and TB studies—except for essential visits that directly benefited participants.

Table 7. Quotations for the theme of 'Intersection of research ethics and public health equity'

Sub-themes	Quotations
Unequal distribution of research burdens	…if we're being honest, the majority of research has taken place in the public sector, raising ethical questions about the distribution of research burdens and what rights participants or their communities have after a trial (REC3). I've also observed opportunities where we could have acted as stronger advocates for participants throughout this process (REC14).

Ensuring fairness in research priorities	In terms of equity within the research environment, investigators linked to large organizations that could tolerate delays were able to progress and exploit opportunities to carve out niches, while smaller units—and particularly postgraduate researchers—likely faced considerable difficulties (REC1). Although we aimed to maintain fairness, we were forced to make very difficult decisions regarding the institution's research priorities (REC17).
Addressing disparities in access to interventions	From an equity perspective, even during the pandemic, significant gaps remained in research involving other vulnerable populations (REC4). It's possible that some high-risk individuals who weren't directly included in prevention studies might have benefited if they had been incorporated, but it's unclear whether this happened, and overall, equity seems to have been somewhat neglected during the pandemic (REC15).

Likewise, prioritizing clinical research with potential therapeutic benefits when research resumed during the COVID-19 pandemic sparked concerns about equity, as critical social science and educational studies were deprioritized, with many participants recognizing that this may have exacerbated health inequities and structural social harms. Participants also noted that implementation trials posed equity challenges, with research ethics committee chairs and members facing ethical dilemmas regarding vaccine access via participation in implementation studies and the increasingly blurred distinction between research and vaccine prioritization.

Public health emergencies like the COVID-19 pandemic present numerous challenges for health-related research [32], as the high morbidity and mortality rates from infection, combined with the social and economic burdens of government interventions to curb transmission, contribute to widespread disruption, distress, and uncertainty [33]. In the African context, research frequently occurs against a backdrop of historical inequities and persistent power imbalances, meaning that those who are most disadvantaged—due to poverty, marginalisation, or limited healthcare access—are often disproportionately affected [4, 32, 34].

Emmanuel *et al.* [35] outlined principles and benchmarks essential for the ethical conduct of research, designed to provide consistent guidance and reduce the risk of exploitation in multinational studies. These principles include collaborative partnership, social value, scientific validity, fair selection of study populations, favourable risk–benefit ratios, independent review, informed consent, and respect for study participants and communities [35]. In our study, RECs consistently applied these principles when addressing ethical issues in COVID-19 research, reflecting findings from other studies examining ethical challenges in pandemic or public health emergency research [36–44].

Nevertheless, our findings indicate that RECs faced significant challenges when navigating the intersections of research ethics, public health ethics, and global health ethics during the COVID-19 pandemic, particularly in emergency settings under national lockdowns. For instance, government-mandated halts on non-COVID research raised pressing public health equity concerns. This suspension affected therapeutic clinical trials as well as HIV and TB research, except for essential visits providing direct benefit to participants. South African RECs were tasked with ensuring research involving human participants remained ethical and responsible while prioritizing infection control, transmission prevention, and the protection of participants, communities, and research staff. These responsibilities were further complicated by the need to rapidly adapt to the evolving stages of the South African Government's COVID-19 Risk Adjustment Strategy and the absence of NHREC guidance from November 2019 to December 2020, leaving RECs without national-level oversight during the first and second pandemic waves [29, 30]. When non-COVID research resumed, social science and educational studies were deprioritized, and participants noted that this may have exacerbated health inequities and structural social harms.

It has been recognised that early pandemic responses, while focused on reducing mortality and infection rates, produced severe collateral effects on health and research equity [5]. Measures such as social isolation and movement restrictions not only harmed general health but also limited access to essential services [45, 46]. In South Africa, halting research further restricted participants' access to ancillary health services within clinical trials. Moreover, the diversion of limited funds and personnel to the COVID-19 response led to disproportionate neglect of other infectious diseases, such as HIV and TB [47, 48]. These inequities underscore the need for strategies that balance human rights protection, public health priorities, research ethics, and social considerations to prevent discrimination against vulnerable populations during public health emergencies [5].

RECs also faced difficulties in weighing individual participant risk–benefit ratios against the urgency of conducting public health emergency research and the broader context of global vaccine inequities. Rid *et al.* [49] highlighted that while traditional ethical principles guiding clinical research remain crucial, the accelerated development and deployment of safe and effective COVID-19 treatments and vaccines constitute a moral imperative [49]. However, ethical deliberation should not be limited to one-time REC review processes. Wright [32] emphasised that research ethics issues emerge across the research lifecycle, from setting priorities and allocating funding to translating findings into clinical practice or public health interventions, and involve multiple stakeholders whose responsibilities are shaped by context [32]. Consequently, it may be appropriate to view COVID-19 pandemic research partly through a public health ethics lens.

Willison *et al.* [50] proposed a framework to guide ethical reflection throughout the lifecycle of public health projects, from planning to knowledge dissemination, emphasizing relational autonomy (considering the individual within the community), social justice, reciprocity, respect for participants and communities, and concern for welfare (favourable risk–benefit ratio). While retaining fundamental research ethics principles—respect for persons, concern for welfare, and justice—this framework expands on them by integrating relational autonomy, community respect, the interconnection of individual and community welfare, solidarity, and the common good, with particular focus on the positive duty to promote social justice and the importance of reciprocity when participants assume risk or burdens for the benefit of others [50].

Similarly, the Nuffield Council on Bioethics introduced an ‘ethical compass’ consisting of three core values—equal respect, fairness, and reducing suffering—to guide ethical reflection in global health research both at policy and operational levels, noting that funders, institutions, governments, and journals share responsibility to ensure the research they support or publish aligns with these values [32]. This expands the accountability for ethical research conduct during the COVID-19 pandemic.

Despite the existence of international guidelines for research in public health emergencies [18, 51–54], South Africa lacked clear national guidance to operationalize key ethical considerations for COVID-19 research. For instance, the absence of guidance on mutual recognition of ethics review left RECs underprepared to prevent duplication of effort and to conduct rapid reviews of COVID-19 studies. Furthermore, variations in interpreting national guidelines regarding limits on public health emergency research and informed consent led to inconsistent ethical reviews and differing consent practices across sites [29, 55]. The absence of the NHREC during the pandemic’s peak further hindered national ethical leadership and the issuance of updated guidance.

To address this gap, South African research ethicists formed a collaborative network called Research Ethics Support in COVID-19 Pandemic (RESCOP) during the first wave. RESCOP provided a repository of ethics resources, facilitated collaboration among RECs, and developed guidance for COVID-19 ethics review, including rapid full committee review of treatment and prevention trials [29]. These guidelines complemented the National Department of Health’s Ethics in Research Guidelines (2015) [26] and complied with WHO rapid review recommendations [54], emphasizing participants’ high vulnerability while cautioning against overly restrictive approaches. Rapid review processes were successfully implemented at individual RECs, but attempts to harmonize ethics review across RECs and implement reciprocal review were less effective, highlighting the need for clear national guidance to support coordinated review and REC preparedness for future emergencies [29].

In our study, informed consent emerged as a key ethical concern for RECs evaluating COVID-19 research. Challenges included procedural and practical issues in obtaining socially distanced consent, navigating difficult clinical environments, and what was feasible under pandemic restrictions. Factors affecting voluntariness and consent validity—such as fear of infection, urgency for effective vaccines or treatments, and separation from family—were consistently noted. RECs also highlighted complexities related to delayed consent and consent waivers. These concerns align with other literature on consent challenges during the pandemic [27, 55–61]. Largent *et al.* [59] note that the pandemic has influenced how practicability of informed consent is determined and suggest ongoing guidance from bioethicists and regulators is needed to optimize consent approaches during COVID-19 [59].

Community engagement emerged as a significant ethical concern for South African RECs. National research ethics guidelines in South Africa encourage health researchers to involve stakeholders in their work [62], yet the COVID-19 pandemic complicated these efforts, as rapid decisions on lockdowns and physical distancing left little opportunity to engage local communities, particularly regarding research activities. Saxena *et al.* [63] advocate for enhanced community engagement during pre-pandemic or inter-pandemic periods, suggesting that such proactive engagement could strengthen public trust [63]. Research ethics committees play a crucial role in guiding researchers' practices and facilitating community involvement [62], which becomes especially important during public health emergencies.

The pandemic has also underscored how uncertainty and the risk of misinformation can shape community perceptions of research and contribute to vaccine hesitancy [64]. Effective community engagement is therefore vital for fostering trust and demonstrating respect toward communities [25, 34, 65], and it should include careful information management. However, practical models for authentic community engagement in COVID-19 research during the pandemic remain scarce, and further investigation is needed into how RECs can actively contribute to and operationalize meaningful engagement.

Equity and access were additional critical ethical challenges identified by RECs. These issues extended beyond standard-of-care considerations and encompassed both public and global health ethics, affecting the conduct of COVID-19 vaccine trials in South Africa. A prominent concern was the use of placebo groups in vaccine trials conducted in low- and middle-income countries (LMICs) with limited vaccine availability. The World Health Organization established conditions for when placebo groups are ethically acceptable at the start of vaccine development [66]. Some researchers have controversially argued that continuing randomized vaccine trials with placebo groups in LMICs—where vaccine access is restricted by cost or logistical constraints—could increase the total number of vaccinated individuals, even though the proportion of the population participating in trials remains very small [67, 68]. Ethical principles such as beneficence and engagement with local stakeholders are considered essential when using placebo groups in LMICs [69]. Nonetheless, given the strong efficacy results of approved vaccines and the contributions of research participants, the justification for ongoing placebo use, even in LMICs, is increasingly limited [49].

Strengths and limitations

Although we interviewed a substantial number of research ethics leaders from seven major academic institutions in South Africa, our sample represents only a small portion of REC members nationwide, and each participant was interviewed just once. Given the rapidly changing COVID-19 research ethics landscape, longitudinal data collection could have provided deeper insight into emerging issues and captured shifts in REC perceptions and experiences over time. Nevertheless, despite these limitations in generalisability, our findings offer a solid foundation for future empirical studies aimed at understanding ethical challenges in COVID-19 research and their influence on REC deliberations, and can help guide the development of ethical policies and guidance for public health emergency research in the African context.

Conclusion

This study offers valuable insights into the perspectives and experiences of RECs regarding ethical challenges in COVID-19 research in South Africa. Comparative analyses across different countries are needed to advance understanding of African RECs' approaches to COVID-19 research ethics. The wide range of ethical issues identified underscores the importance of research ethics education and training—particularly around informed consent—and highlights the urgent need for comprehensive national guidelines for research ethics during public health emergencies.

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