

A scoping review of the literature of research ethics committees and ethics review framework in Pakistan: what we know and what we still need to learn

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Abstract

Objective: To map literature on research ethics committees, institutional review boards and ethics review framework in Pakistan to identify key insights during public health emergencies and normal times.

Method: The systematic scoping review was conducted in April 2022, and comprised literature search on PubMed, World Health Organisation Global Index Medicus and Summons databases for articles published between January 2005 and February 2022. Information extracted included authors' names, year of publication, title, study methodology, and key insights under the heads of challenges and solutions. Due to data heterogeneity, key themes were identified and analysed.

Results: Of the 2,190 studies initially identified, 21(0.95%) were subjected to full-text review, and, from among them, 9(45%) were analysed in detail. There were 4 key insights identified: research ethics committees and institutional review boards in Pakistan remain unregulated as they are currently not registered or accredited by a competent national-level authority; most members of such committees are not formally trained to implement the mandate; internal and external pressures hinder independent decision-making of such committees; and other issues hindering the functionality and performance of research ethics committees and institutional review boards.

Conclusion: Despite existing publications calling for urgent policy and regulatory reforms, there is a dearth of literature and minimal policy actions underlying the fact that ethics review remains a neglected area in Pakistan.

Keywords: Ethics, Pakistan, Bioethics, Ethics committees, Institutional review board

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Introduction

Pakistan, one of the low- and middle-income countries (LMICs), which underinvests in its health system, making it complex and fragmented¹. The coronavirus disease 4-2019 (COVID-19) public health emergency (PHE) adversely affected almost all facets of life globally. Similarly, it posed serious challenges for research ethics committees / institutional review boards (RECs/IRBs) in Pakistan, which are struggling to approve research projects emerging as a result of surge in research studies aimed at understanding the novel disease, at times posing major health crisis and ethical dilemmas. It has revealed the need for harmonised, efficient and comprehensive ethical review processes not only in times of a PHE, but also during normal times.

Pakistan's national ethics review system is only two decades old. The first research ethics committee in Pakistan was reportedly founded in 1987². The National Bioethics Committee (NBC) was established as the official body to oversee and uphold the ethics principle in all sectors of health research in the country in 2003-04³. Research Ethics Committee of NBC (REC-NBC) is responsible for reviewing international-level and national-level research. With the development of NBC, the number of research RECs/IRBs grew across the country. Globalisation of research and clinical trials, participation in international collaborative research, obtaining research funding, and getting published in reputable journals remain the main drivers of the trend.⁴ Soon after the ethics review system started to establish in Pakistan, the country was affected by catastrophic earthquake in the North West Frontier Province (NWFP), since renamed Khyber Pakhtunkhwa (KP), of Pakistan and large parts of Kashmir in 2005, displacing around 3.3 million people who subsequently plunged into poverty and health disaster⁵. Pakistan was confronted with the challenge of how to conduct research in times of humanitarian and health emergencies. It brought an increasing interest in the theoretical ethics framework and triggered the

discussion of ethics and regulation of research involving population and public health interventions, which was traditionally focussing on rights and protection of individuals. These 'ethical issues during emergency conditions' were deliberated in the Seventh Global Forum for Bioethics in Research (GFBR) in 2006⁶, which was organized in Pakistan with the support of several international organisations. In the same year, Pakistan's first bioethics education programmes were introduced^{7,8}. To date, NBC has been involved in providing training to REC/IRB members to help them set up ethics review processes in their institutions.

Pakistan does not have any programme to register, audit, assess or inspect RECs/IRBs at the national level⁸. RECs/IRBs are also not commonly assessed or accredited by any international programme, like the Association for the Accreditation of Human Research Protection Programme (AAHRP)⁹, as it is not mandatory, as well as it is not done by choice due to lack of resources. As a result, RECs/IRBs work in their own capacities according to their specific structures and procedures based on their institutional approaches, assumingly presenting differences in their practices. There is no organisation/association/forum or any other mechanism of formal interaction or coordination among the local RECs/IRBs, which further spans over their interaction with the REC-NBC. A comprehensive list of all RECs/IRBs is not publically available and it is not easy to collect this information. So RECs/IRBs continue to work in silos. IRBs/RECs are constrained to share capacities or experiences among each other. This impairs an effective and coordinated response during PHEs. Finally, local IRBs in Pakistan found themselves suddenly overwhelmed by the need for fast-tracked reviews of research proposals during the COVID-19 pandemic; mostly for clinical trials with insufficient data for decision-making. The COVID-19 pandemic also highlighted the lack of coordination in review of multicentre research, causing perhaps unnecessary confusion, delays and duplication of efforts by ethics review bodies as well as study teams.

During the COVID-19 pandemic, the NBC-REC developed policy guidance which primarily described how NBC-REC will carry out review of COVID-19 research⁹. This was in line with the developments witnessed internationally and also essential considering the influx of new research related to COVID-19, and then there was the need to maintain continuity in the role of the committee's review of ongoing 'normal' research. However, RECs/IRBs across the country were not incorporated in this national response.

The way the ethics review of medical research is

The Pakistan National Bioethics Committee (NBC) is the official body to oversee and uphold the ethics principles in all sectors of health service delivery and research in the country. The research ethics committee of the NBC (REC NBC) is the body that directly oversees research review and clearance in the country (3). All institutional-based research studies must secure a prior approval by Research Ethics Committees (RECs) or Institutional Review Boards (IRBs) (terms used interchangeably in the remainder of this paper). Projects with international collaborations with or without funding and National level research projects, require additional approval from Research Ethics Committee of NBC (REC NBC). Regulatory approval by the Drug Regulatory Authority of Pakistan (DRAP) is also required for clinical trials (10) following approvals by the appropriate IRBs and the NBC.

Figure-1: How ethics review of medical research is organised in Pakistan

organised in Pakistan (Figure 1) prompted interest in examining how research ethics review has been studied so far, and the level of government and academic interest in its development and progression through its journey. The current scoping review was planned to map literature on RECs/IRBs and overall ethics review framework in Pakistan to identify key insights during PHEs and normal times. To the best of our knowledge, no systematic review exists on the topic. A scoping review seems to be the most suitable methodology for the purpose of providing a broad overview of the topic, and may guide the process of development of ethics preparedness for ongoing and any future emergencies through evidence-based policymaking. The current review is part of a larger initiative.

Materials and Methods

The systematic scoping review was conducted in April 22, and comprised literature search on PubMed, World Health Organisation (WHO) Global Index Medicus and Summons databases for articles published between January 2005 and February 2022. The search was conducted using key words and Boolean operators on PubMed (Figure 2) and other search engines. The review was based on a predetermined protocol in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Review guidelines¹¹, and the protocol was registered with the Open Science Framework (OSF)¹². No restriction of language or study design was applied

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((ethics[Title/Abstract] OR ethical*[Title/Abstract] OR bio-ethic*[Title/Abstract] OR bioethic*[Title/Abstract] OR "institutional review board*" [Title/Abstract] OR IRBs[Title/Abstract] OR ("Ethics"[Mesh] OR "ethics" [Subheading])) AND ((Lahore[Title/Abstract] OR Faisalabad[Title/Abstract] OR Rawalpindi[Title/Abstract] OR Sargodha[Title/Abstract] OR Gujranwala[Title/Abstract] OR Sialkot[Title/Abstract] OR Gujrat[Title/Abstract] OR Jhelum[Title/Abstract] OR Sheikhpura[Title/Abstract] OR Nowshera[Title/Abstract] OR Mardan[Title/Abstract] OR Peshawar[Title/Abstract] OR ((pakistan*[Title/Abstract] OR islamabad[Title/Abstract] OR karachi[Title/Abstract] OR ("Pakistan"[Mesh]))))
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Figure-2: Search terms used on PubMed

during the search process. The reference lists of the included studies were examined as well. Screening of the retrieved literature was done by reviewing the titles and abstracts in terms of relevance. Full texts of all potentially eligible articles were thoroughly examined to confirm eligibility. Uncertainty regarding whether any publication met the inclusion criteria was resolved through discussion. The two-step study selection process was systematically applied by two reviewers independently. Limited publications on the topic was found as expected, and, therefore, work of key leaders was also searched instead of searching additional databases.

The selected articles were tabulated into an Excel file, where duplicates were removed and data extraction was done using a form that was developed and piloted before actual use. All findings reported in the text were recorded. Data tabulated included title, year of publication, author(s), study design and key insights. Quality of the studies was not critically appraised.

Due to heterogeneity of publications, synthesis of the findings was not possible, and, as such, key themes were generated on the basis of the findings.

Results

Of the 2,190 studies initially identified, 21(0.95%) were subjected to full-text review, and, from among them, 9(45%) were selected for detailed analysis^{4,6,8,13-18} (Figure 3; Table 1).

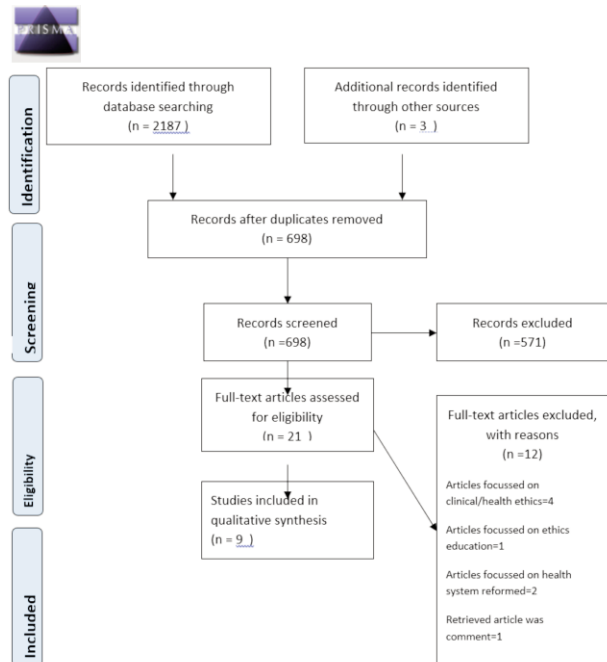


Figure-3: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram.

Table 1: Summary of the studies reviewed.

No	Authors	Title	Year	study methodology
1	Jafarey AM, 2012 ⁸	Ethical review in Pakistan: the credibility gap	2012	Workshop report
2	Abrar S, 2015 ¹³	Status Of Ethical Review Boards In Medical Colleges Of Khyber Pakhtunkhwa	2015	Cross sectional survey
3	Salim M, 2018 ¹⁴	Independent Review of Research Proposals From Ethical Point Of View In Pakistan.	2018	Questionnaire based survey
4	Sherin 2013 ¹⁵	Research Ethics Committees (Recs) And Monitoring Of Biomedical Research In Pakistan	2013	Editorial
5	Ahsin, 2017 ¹⁶	Self-evaluation of ethical review committee's functioning at Foundation University Medical College (FUMC) through structured constitution-practice-outcome (CPO) assessment model	2017	Self evaluation of single ethical review committee
6	Hyder AA, 2008 ¹⁷	Integrating ethics, health policy and health systems in lowand middle-income countries: case studies from Malaysia and Pakistan	2008	Case study
7	Moazam 2005 ⁴	Pakistan and Biomedical Ethics: Report from a Muslim Country	2005	Perspective
8	7 th Global Forum on Bioethics in Research ⁶	Bioethics In Public Health Research Seventh Global Forum on Bioethics in Research	2006	Meeting proceedings
9	Shekhani 2021 ¹⁸	Adapting the ethical review process for coronavirus disease-2019 (COVID-19) research: reviewers' perspectives from Pakistan	2021	Mixed method study

Moazam et al. (2005) is an account of the status of biomedical ethics at the time of advent of ethics in Pakistan by leading experts⁴. A report of the 7th Global Forum on Bioethics in Research, which took place at the Aga Khan University in Karachi in February 2006 was also identified⁶. The meeting focussed on ethical issues pertaining to health systems research, public health research, and health services, through presentation and discussion of case studies. Jafarey et al. (2012) reports

Table-2: Thematic framework.

Themes	Sub-themes
Bioethics development initiation in Pakistan was primarily done by medical community and Indigenizing bioethics	<p>There are no comprehensive national guidelines for conducting ethical research</p> <p>Bioethics development in Pakistan is primarily steered by members of the medical community who considered Indigenizing bioethics in line with local culture and norms.</p> <p>Approval by RECs/IRBs is still not mandatory for obtaining research funding from local sources</p> <p>IRBs started to establish in the absence of government directive, in the interest of promotion of international collaborative research, obtaining research funding and publishing in reputable journals</p> <p>The pandemic had also created different priorities for the Government, and little attention was being paid to the work of the NBC,</p>
Role of NBC	NBC is provided all-encompassing responsibilities, which presents a complex combination, a better division of labour, could lead to better results.
Lack of registration or accreditation for IRBs:	<p>NBC trains institutional officials to set up ethics committees and its members, however do not maintain any links or oversight on RECs/IRBs.</p> <p>No program exist to assess, audit, register or inspect ethics committees at national level</p>
Lack of trained personnel on IRB	<p>Majority of membership remains without any formal ethics training</p> <p>In Pakistan educational programmes and courses in bioethics are offered, however these are far and few and cannot meet the demand sufficiently</p> <p>net migration of highly trained personnel in ethics out of Pakistan</p>
Other challenges faced by IRBs	<p>Non-compliance do not meet any serious consequences</p> <p>Compromised autonomy of IRBs</p> <p>Inconsistency in the review process within an institution, and also across the institutions</p> <p>Poor methodology/science due to insufficient training of researchers</p>
Lack of HRP and research training and research integrity programs at institutes	<p>Not all research is submitted to IRB</p> <p>No legal penalty for not obtaining IRB approval or other violations</p>
Review modification during PHEs	Newly instituted Rapid Turnaround Review (RTR) system.
Call for action	Published studies have called for action for urgent regulatory reforms for better governance, and training

REC: Research ethics committee, IRB: Institutional review board, NBC: National bioethics committee, HRP: Human research protection, PHE: Public health emergency.

deliberations of members of RECs/IRBs from across Pakistan at a workshop held in November 2011 at the Centre of Biomedical Ethics and Culture (CBEC) of the Sindh Institute of Urology and Transplantation (SIUT) in Karachi⁸. The report is based on experiences reported by 24 participants from across the country.

Abrar et al. (2015) reported province-wise cross-sectional survey assessing the existence, membership and activities at 16 medical colleges registered with the Pakistan Medical and Dental Council (PMDC), and reported responses of 15 such colleges¹³. Making use of a questionnaire, with no mention of validation, it relied on responses of the representatives.

Salim et al. (2018) used a cross-sectional design to invite responses through a pretested questionnaire from all medical colleges, medical universities, dental colleges

and teaching hospitals registered with the PMDC that were filled by respective IRB members¹⁴. Sherin et al. (2013) was an editorial¹⁵. Ahsin et al. (2013) reported self-evaluation of REC's functioning at the Foundation University Medical College (FUMC) through structured constitution-practice-outcome (CPO) assessment model¹⁶. Hyder et al. (2008) presented a case study of initiatives to establish a national ethics committee in Pakistan to introduce an overview of the relationship ethics and public health, and presented an analysis¹⁷. Shekhani et al. (2021) did a cross-sectional study using 3 methods of data collection: a demographic questionnaire filled in by permanent members and co-opted reviewers; qualitative indepth interviews conducted with both groups; and document review exploring the adaptation done in the ethics review processes¹⁸.

The included studies provided little evidence, and the

quality of evidence also remained questionable with no evidence of level I. Among the included studies, three primary studies^{13,14,16} made use of cross-sectional methodology, out of which only 1 study¹⁴ mentioned the validation of its data collection tool. One study¹⁶ provided a self-evaluation of single ethics committee using a tool developed for the purpose of the study with no mention of validation.(Table-2)

There were 4 key insights identified: RECs/IRBs in Pakistan remain unregulated as they are currently not registered or accredited by a competent national-level authority; most members of such committees are not formally trained to implement the mandate; internal and external pressures hinder independent decision-making of such committees; and other issues hindering the functionality and performance of RECs/IRBs.

Initiation of Bioethics development in Pakistan traces back to the time when some members of medical community received initial training in bioethics from foreign institutes, with international funding and support^{4,8}. These medical professionals primarily steered bioethics development in Pakistan, but, realising that cultural norms as well as religious values shape bioethics in a region, put in conscious effort to present the idea of 'indigenising' bioethics instead of simply importing contemporary bioethics in Pakistan^{4,6}. Around 2004, IRBs started to get established in Pakistan, but without any government directive and comprehensive national guidelines for research conduct. Other notable trends reported at that time included the fact that no legal penalty was defined for not obtaining IRB approval or other violation following IRB approval, and IRB approval was not mandatory for obtaining local funding⁸.

In 2004, NBC Pakistan was established under the Ministry of Health with the mandate to "promote and facilitate ethical health services delivery, health research and to be an umbrella body linked with the Ethics Review Committee in various organisations/institutions"^{4,8} with the Pakistan Medical Research Council (PMRC) acting as its secretariat, working with two distinct sub-committees: the Research Ethics Committee and the Medical Ethics Committee. However, RECs/IRBs reportedly remain without any NBC oversight to date⁸. NBC has been involved in providing training to help establish RECs/IRBs in institutions.

Analysis of terms of reference of NBC demonstrated that NBC was assigned overarching responsibilities, including preparing national ethics guidelines for health research in Pakistan, reviewing research proposals for studies to be undertaken at the national level¹⁷. Arguably, a

considerate division of responsibilities and provision of sufficient resources required to perform assigned responsibilities could have led to better delivery of goals.

Lack of governance mechanisms of RECs/IRBs has been consistently identified as a fundamental factor / gap (unanimously) over a span of years. Establishment of RECs/IRBs in Pakistan started without formal government directives^{4,8} as scientific community recognised the need to be eligible for international grants, collaborations and publication process. No federal or provincial body is currently involved with registration, accreditation, and monitoring of RECs/IRBs^{8,15}. Many of the prevailing issues identified in the functioning of RECs/IRBs remain unchecked.

NBC has been involved in providing training to help establish RECs/IRBs in institutions. Ethics educational programmes are instituted in Pakistan^{4,8}, but the majority of membership remains without any formal ethics training^{8,13,14} to implement the mandate. The existing mechanisms of ethics education and training are insufficient. Net out-migration of highly trained professionals could be a contributing factor for this shortage¹⁷. In 2001, the PMDC, the certifying body for all graduating physicians and dentists, stipulated that biomedical ethics must be included in the medical curricula. However, this has not been achieved to date^{4,17}.

Other issues of RECs/IRBs could be linked to the fact that most members of RECs/IRBs lack formal training to implement the mandate. All research involving human subjects is not being submitted for ethical review⁸. In addition, no legal penalties or sanctions are defined for doing research without ethical approval or for violating the safety protocol, REC decision and recommendations¹⁵.

IRBs in Pakistan reportedly face external and internal pressures to influence deliberations. Internal pressures are from institutional leaders holding influential positions in IRBs.^{8,18}

IRBs across Pakistan work according to their own processes, and, hence, there is inconsistency in the review process^{8,15}. In multicentre research studies, the same study is subjected to different and multiple review requirements and standards.

Pakistan has confronted the challenges of limited capacity of RECs to review public health research proposals, informed consent, confidentiality, post-trial access⁶ in past emergencies confined primarily to Pakistan. During COVID-19, much-needed adaptations proposed by NBC were not among the top priorities for

the government, but NBC managed to adapt to Rapid Turnaround Review (RTR) system, in line with emerging guidance on how research must be facilitated in emergency contexts. This led to learning related to how ethics review is shaped by the science of the proposal itself, as well as structure of research ethics governance¹⁸.

All the studies reviewed consistently asked for urgent policy and regulatory reforms to address the various threats to ethics review and capacity development. Governments, NBC, institutions and RECs/IRBs should play their role in bringing credibility to the ethics review process and build professional capacity. Institutions should empower the RECs/IRBs by promoting free decision-making without any pressures from senior officials of the institutions.

Discussion

The scoping review revealed significant knowledge gaps about Pakistan's research ethics review ecosystem that have been reported earlier as well^{19,20}. Though there is no comprehensive empirical data to warrant comment on competencies of RECs/IRBs in Pakistan, existing publications have reported significant challenges, including, but not limited to, lapses in the ethics review practices of RECs/IRBs across Pakistan, lack of governance structure and shortage of trained personnel serving on RECs/IRBs. However, these gaps are not unique to Pakistan^{21,22}. In addition to reporting the threats, the studies reviewed have consistently called for action for urgent policy and regulatory reforms. However, lack of any action so far indicates that this area has faced long-standing neglect. NBC is the competent authority for training and maintaining oversight of RECs/IRBs. However, it continues to operate without sufficient patronage, funding and the required resources appropriate to the scope of services. This remained a major limiting factor in delivering its overarching objectives effectively since its establishment. It remained orphaned between 2011 and 2015 in the post-abolition of PMRC phase. These factors have led to insufficient existing capacity to provide appropriate ethical oversight of health research, and RECs/IRBs remain unregulated. Currently, NBC is housed in the Health Research Institute (HRI) within National Health Institute (NIH), which in itself is an indication of much-needed reforms in funding and ethics oversight of biomedical research. Development of comprehensive guidance for research and legal frameworks, strengthening governance structure and optimisation of training opportunities should be prioritised to address the existing well-known gaps. Many countries have national regulations enforcing some mechanisms for registration, accreditation or audits of

RECs/IRBs by national-level competent authorities which is a healthy trend. The list has representation from both high-income countries (HICs) and LMICs²³. In the United Kingdom, National Research Ethics Service (NRES) oversees a three-stage accreditation process for RECs/IRBs. In the United States, an IRB must obtain registration and federal assurance by the Office of Human Research Protection (OHRP). In South Africa and Nigeria, national regulations require RECs to register with their respective National Health Research Ethics Committees (NHRECs)²⁴. In New Zealand, RECs/IRBs are accredited with centralised Human Research Council Ethics Committee (HRCEC), and in India, with the Central Drugs Standard Control Organisation (CDSCO). Similarly, the National Health and Medical Research Council (NHMRC) in Australia is implementing a national approach for single ethics review through the Harmonisation of Multicentre Ethical Review (HoMER) initiative²⁵.

Deep-rooted inadequacies in ethics review process can only be heightened during emergencies and must be addressed in between the emergencies. Well-considered and comprehensive guidance for ethics review that are adhered to across the process can steer a national approach in Pakistan. Besides, emergencies call for open line of communication among diverse bodies involved in ethics review, which is still lacking in Pakistan. Past emergencies have clearly established the need to harmonise the ethics review process in emergency situations, proposing flexible, simultaneous, coordinated, joint review or at least proactive communication among these bodies²⁶⁻²⁹. Similarly, COVID-19 offers an opportunity to strengthen Pakistan's ethics review framework for improved preparedness and response for any future PHE. Recent developments suggest that the ethics review process should be prioritised and done collaboratively, which can involve collaboration between local and international counterparts, with at least one being well-versed in research ethics³⁰. During emergencies, defined processes for carrying out ethics review should be developed to ensure that review is done with speed and competence. It should include mechanisms for communication between diverse ethics committees, national-level competent bodies, and key national stakeholders, where appropriate. The role of WHO can be explored to support multi-country emergency ethical consultation.²⁸

Such initiatives can reduce duplication of efforts as well as promote capacity-sharing³¹. The ethics review process in Pakistan needs to consider such models to better prepare or respond to any emergency.

Pakistan needs to invest in resources to build a stronger

ethics review framework. This investment will not only enable efficient and competent ethics review, but will also significantly improve the quality of the research outputs. All stakeholders must engage in a dialogue to enhance capacity and shape a national agenda that strengthens the ethics review framework and the long-term capabilities of RECs/IRBs in Pakistan through reforms in education and governance. Research institutions also need to commit to developing human research protection programmes, research integrity programmes and researcher training programmes.

Conclusion

Despite existing publications calling for urgent policy and regulatory reforms, there is a dearth of literature and minimal policy actions underline the fact that ethics review remains a neglected area in Pakistan.

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