What empirical research has been undertaken on the ethics of clinical research in India? A systematic scoping review and narrative synthesis

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ABSTRACT

Introduction The post-2005 rise in clinical trials and clinical research conducted in India was accompanied by frequent reports of unethical practices, leading to a series of regulatory changes. We conducted a systematic scoping review to obtain an overview of empirical research pertaining to the ethics of clinical trials/research in India.

Methods Our search strategy combined terms related to ethics/bioethics, informed consent, clinical trials/research and India, across nine databases, up to November 2019. Peer-reviewed research exploring ethical aspects of clinical trials/research in India with any stakeholder groups was included. We developed an evidence map, undertook a narrative synthesis and identified research gaps. A consultation exercise with stakeholders in India helped contextualise the review and identify additional research priorities.

Results Titles/Abstracts of 9699 articles were screened, full text of 282 obtained and 80 were included. Research on the ethics of clinical trials/research covered a wide range of topics, often conducted with little to no funding. Studies predominantly examined what lay (patients/public) and professional participants (eg, healthcare staff/students/faculty) know about topics such as research ethics or understand from the information given to obtain their consent for research participation. Easily accessible groups, namely ethics committee members and healthcare students were frequently researched. Research gaps included developing a better understanding of the recruitment-informed consent process, including the doctor-patient interaction, in multiple contexts and exploring issues of equity and justice in clinical trials/research.

Conclusion The review demonstrates that while a wide range of topics have been studied in India, the focus is largely on assessing knowledge levels across different population groups. This is a useful starting point, but fundamental questions remain unanswered about informed consent processes and broader issues of equity that pervade the clinical trials/research landscape. A priority-setting exercise and appropriate funding mechanisms to support researchers in India would help improve the clinical trials/research ecosystem.

Key questions

What is already known?

► The increase in the number of clinical trials and clinical research conducted in India after 2005 was accompanied by many reports of ethical misconduct, with bioethics reports and health activism prompting a series of regulatory changes by the government.

► While there was a corresponding increase in empirical research on various ethical aspects of clinical trials/research in India, little was known about the scope of this research or what areas of research required further attention to improve the clinical trials/research ecosystem.

What are the new findings?

► Research on ethical aspects of clinical trials/research in India was often carried out with limited to no funding, covered a wide range of topics but with a focus on knowledge assessments of lay and professional groups on topics such as research ethics, and leaned on easily accessible groups such as ethics committee members and healthcare students for study populations.

► A range of research gaps were identified, facilitated by a consultation exercise with key stakeholders from India, and included developing a better understanding of the different components of the recruitment and informed consent process, such as the doctor-patient interaction, developing models of informed consent specific to the Indian context and exploring issues such as equity and justice within the context of clinical trials/research.

INTRODUCTION

International clinical trials recruit participants from low-income and middle-income countries (LMICs) for economic, pragmatic and scientific reasons. Post-2005, when the World Trade Organisation-Trade Related Intellectual Property Rights agreement
began fully binding for India, the number of clinical trials approved by the Indian government’s regulatory authority, Central Drugs Standard Control Organisation, began to increase, peaking in 2010 followed by a sharp decline to 2013 (online supplemental file 1). An identical pattern of growth and contraction was observed in India’s clinical trial sector’s growth rate, in research using clinicaltrials.gov data.

The downward trend is attributed to the chain of events that began with unacceptable ethical practices, such as failure to obtain participants’ informed consent for trial participation, being reported nationally and internationally. In 2013, the Supreme Court of India intervened and briefly halted approvals for new clinical trials in response to concerns for participant autonomy and safety, and public interest litigations from non-governmental organisations. New regulations were introduced in 2013 as amendments to Schedule Y of the Drugs and Cosmetics Rules 1945, mandating measures such as registration of ethics committees and audio-visual (AV) recordings of the informed consent discussion, the latter being a requirement that is unique to India (see Gogtay et al for an overview of regulatory changes/requirements in India from 2005 to 2016). Also specific to India is that the term ‘clinical trial’ is limited to the study of ‘new drugs’ only, with Biomedical and Health Research (BMHR) referring to all other basic, applied, operational and clinical research (in contrast to broader definitions of ‘clinical trial’, which include medical, surgical and behavioural interventional research). The most recent regulatory changes outlined in the New Drugs and Clinical Trial (NDCT) Rules of 2019 bring non-drug-related research (ie, BMHR) within the regulatory ambit for the first time (previously, regulatory mechanisms in India were principally focused on ‘new drug’ research). The NDCT Rules also separate the ethics and governance processes for clinical trials and bioavailability/bioequivalence studies from those for BMHR studies. For instance, two different types of ethics committees, each with separate authorities responsible for their registration and monitoring, will approve the two groups of studies. It is also now mandatory for BMHR ethics committees and academic clinical trials to adhere to the Indian Council for Medical Research’s National Ethical Guidelines for Biomedical and Health Research Involving Human Participants.

Given this backdrop, there is a large body of theoretical bioethics literature and commentary by researchers, advocacy groups and bioethicists, covering topics such as lessons learnt from conducting clinical trials, ‘standard care’ in clinical trials, structure of the clinical trial industry, informed consent placed within the wider socioeconomic context, role of ethics committees and ensuring appropriate compensation mechanisms. There has also been a corresponding increase in empirical research on the ethics of clinical trials specifically and clinical research more broadly (henceforth clinical trials/research) in India, which has not been comprehensively reviewed. We therefore sought to summarise this body of research evidence through a systematic scoping review and narrative synthesis to help identify research gaps.

### Methods

We undertook a systematic scoping review following the established six-step framework by Arksey and O’Malley, drawing from recommendations to enhance the methodology and adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for scoping reviews (online supplemental file 2).

An initial systematic review of clinical trial informed consent interventions in India (PROSPERO registration: CRD42017068966) was amended to a systematic ‘scoping’ review (not within PROSPERO’s remit, hence withdrawn) of research on the ethics of clinical trials/research in India, as the latter method is particularly useful when the aim is to map the evidence base in a broad but complex unreviewed area.

#### Identifying the research question

We sought to obtain an overview of the empirical evidence in relation to the ethics of conducting clinical trials/research in India. More specifically, we aimed:

a. to map the empirical research undertaken on any ethical aspect of conducting clinical trials/research in India;

b. to synthesise the key themes from this evidence base, with a focus on informed consent;

c. to identify gaps to inform future research priorities.

#### Identifying relevant studies

**Inclusion criteria**

The research questions were assessed in relation to the setting, population, phenomenon of interest and the study design of articles (online supplemental file 3). We included articles that reported (a) on original research in a peer-reviewed journal, (b) on India as a country for data collection (if study involved many countries, included if India-specific findings could be differentiated), (c) on ethical issues in relation to clinical trials/research and (d) with any key stakeholder groups—lay (public; clinical trials/research participants; patients/guardians), professional (healthcare/research faculty, students or practitioners; ethics committee members;
regulatory/governmental agencies) or documents (informed consent forms; ethics applications).

Exclusion criteria
We excluded commentaries, ‘lessons learnt’ articles, abstracts, letters, audits (eg, Clinical Trials Registry-India audits, except when linked to an ethical issue), and studies from countries other than India (eg, studies exploring views of researchers from high-income countries undertaking research in LMICs). We excluded studies on the following topics:
a. Willingness to participate (WTP) in clinical trials/research and recruitment-focussed studies, except when they considered ethical issues (there are other systematic reviews on WTP14–46; WTP components of included studies were not considered in this review).
b. Informed consent/ethical issues in relation to procedures/treatment outside of clinical trials/research (eg, in routine surgery).47 48
c. Pharmacovigilance (PV) studies (there are systematic reviews on PV49; PV components of included studies were not considered in this review).
d. Other: studies on medical/healthcare/clinical ethics (ie, not in relation to clinical trials/research or research ethics) and research skills/capacity with professional groups (eg, healthcare students).50 51

No restrictions were applied based on language, age (children/adult), study design or quality of research.

Search strategy
We searched the following nine electronic bibliographic databases with no start date and up to 5 September 2017 and this was updated using the technique by Bramer and Bain to 12 November 2019: MEDLINE, Cochrane Library, Web of Science, Scopus, Embase, PsycINFO, Cumulative Index of Nursing and Allied Health Literature, International Bibliography of Social Sciences and Online Resource for Recruitment research in Clinical Trials.52 Search terms relating to three domains were combined: (a) ethics, bioethics, informed consent; (b) clinical trials/research and (c) India. A comprehensive search strategy first developed on MEDLINE (SP) drew from systematic reviews on related topics,54 55 was refined by an information specialist (ARi) and adapted to the other databases (online supplemental file 4—MEDLINE search strategy). Searches included other South Asian countries to gather contextual information, but the review focused on India. We used a combination of Medical Subject Headings, text word searches and search strings using proximity indicators. We searched the reference lists of eligible research articles and ineligible key opinion/commentary pieces, and contacted authors of published conference abstracts to trace studies.

Study selection
All articles identified from the databases and other sources were downloaded to EndNote-X956 and duplicates removed. Following the original search in September 2017, one reviewer (SP) screened the titles and abstracts of all articles with a 20% random sample screened independently by a second reviewer (PD). There was a high level of agreement across the two reviewers (disagreement in 3 of 1292 articles), with discrepancies discussed and resolved. Full text of all relevant articles were obtained and screened independently by at least two authors (SP with NM, JW, LR). Discordance was again resolved through group discussion among all four reviewers. Where it was unclear if an article or a particular topic should be included (eg, biobanking, data sharing), a decision was made by meeting with two content experts (ethicists JI and RH) and reviewing the articles together. For the search and screening update in November 2019, SP carried out all steps.

Charting the data: data extraction and quality assessment
A data extraction form was developed (SP) and independently applied by two reviewers (SP and ARe) on a sample of articles (n=10). The form was refined after discussion and captured the following information (SP, ARe, JPR, SS): authors, year of publication and data collection, location, study aim, topic area, population, study design/methods, participants and findings. Subsequently, further information was captured on (SP): (a) whether studies were conducted within the context of a real or hypothetical study/scenario and (b) whether they explored broad (eg, clinical trials/research, research ethics) or specific topics (eg, data sharing, compensation).

Two review authors (SP with LR, JW, PD, JPR, SS) independently assessed the quality57 of the majority of studies using the following tools: Critical Appraisal Skills Programme (CASP) checklist58 for qualitative studies; Appraisal tool for Cross-Sectional Studies (AXIS; adapted to have 14 items instead of 20)59 for quantitative studies and AXIS, CASP and a section of the Mixed Methods Appraisal Tool60 for mixed methods studies. Quality assessments were discussed to resolve discrepancies and used to summarise relevant methodological issues in the narrative synthesis.

Collating, synthesising and reporting the results
We first quantified the data in relation to the study characteristics. Next, we created an evidence map to visualise the volume of studies by topic, population group and methods. Finally, we synthesised the quantitative and qualitative findings reported in included studies, using EndNote-X960 for data management and MaxQDA-1261 for coding articles, and used narrative and thematic description to write detailed descriptive accounts. The synthesis broadly followed the categorisations in the evidence map, but looked across all included articles to provide a comprehensive account of research on a given topic.
Consultation

The consultation phase, considered optional in scoping reviews, took place after the synthesis, with the aim of informing the review and ensuring local priorities and context were accounted for. We approached colleagues in India who were researchers, ethicists and representatives from advocacy groups, through prior networks or because they had authored seminal empirical and/or conceptual papers (online supplemental file 5—consultation members). Consultation was carried out via virtual conferencing, email and telephone. Findings and research gaps identified through the review were discussed. Key recommendations made by stakeholders were grouped by topic and incorporated in the manuscript, tables or supplements.

Patient and public involvement

No patients or members of the public were involved in this review.

RESULTS

Description of included studies

A total of 9699 unique records were identified (original, updated and manual searches), of which 282 full-text articles were assessed against the inclusion/exclusion criteria and 80 included (figure 1). Key study characteristics are summarised in table 1 (individual study details are in online supplemental file 6).

Most studies were conducted in urban settings (47/80), in the western (24/80) and southern (21/80) parts of India. Studies were mainly quantitative (60/80), questionnaire surveys (36/60), conducted with professional groups (34/80) and appeared in journals published in India (49/80), primarily the Indian Journal of Medical Ethics and Perspectives in Clinical Research (n=15 and 16, respectively).

There were no research studies published on the ethical issues around conducting clinical trials/research until 2008, with a large proportion published a few years before and after the landmark regulatory changes of 2013 (53/80 were published 2011–2016; online supplemental file 1). Many studies did not mention the year of data collection (27/80) and of those that did, only a few were carried out in/after 2013 (17/53).

Corresponding authors of most studies were based within academic institutions (69/80; 15 outside India and 54 within India), primarily within Departments of Pharmacology of various Indian institutions (24/54). Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai had the most number of corresponding authors (12/54), followed by Christian Medical College, Vellore (5/54). Two-thirds of studies (55/80) did not provide information on their funding source (26/55) or stated they did not receive any funding (27/33); of the remaining, 21 were funded/supported by international grants, 4 by intramural grants and 2 by pharmaceutical companies. There was no statement on conflicts of interest in 28 studies.

Evidence map: research on ethical aspects of conducting clinical trials/research in India

We developed an evidence map that charts the total articles included (n=80) by the main focus of the topics and population covered in the studies, alongside the methods used (table 2).

Primary research (n=58): more than half (32/58) were studies exploring knowledge (with or without attitude and practice components) of participants on topics such as information provided to obtain informed consent (primarily with lay participants), clinical trials/research, research ethics and ethics committees (primarily with professional participants), and were mainly quantitative (27/32). Studies that assessed comprehension of the informed consent form or verbal information provision (n=10) were carried out in real (8/10) and hypothetical (2/10) randomised controlled trials (RCTs), clinical trials and cohort studies.

Another large group of primary research studies (26/38) focused on perceptions, experiences and practices/processes on topics such as the extent of patient participation in informed consent discussions, AV recording of consent processes, ethics committees, research governance (eg, data sharing) and the larger clinical trials landscape in India (such as outsourcing, contract research organisations and civil society organisations). Studies employed a wider range of methods (11 quantitative, 13 qualitative studies, 2 mixed methods) and some (9/26) were conducted in the context of a real and/or hypothetical study.

Secondary research (n=22): these studies were all quantitative and were centred around documentary reviews of the quality of application forms submitted to ethics committees, compliance of informed consent documents to guidelines/regulations, and Indian journal articles’ reporting practices on informed consent and ethical approval.

Narrative synthesis: key findings and research gaps

The findings from included studies were synthesised based on population groups (lay/professional) and key topic areas, with summaries of methodological issues where relevant. Sections A1–A6 and B1 indicated below correspond to those in table 3, which highlights the key findings from the synthesis alongside identified gaps (see online supplemental file 7 for full report of synthesis).

Primary research was synthesised in six key areas (A1–A6). The first four (A1–A4) covered studies that involved comprehension of the informed consent form and knowledge of clinical trials/research, research ethics and ethics committees (where attitudes and/or practices were reported, these were synthesised). Research on informed consent processes (A5) and broader cross-cutting themes that provided a more holistic understanding of the clinical trials industry (A6) were also synthesised. Secondary
**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-analysis flow diagram.160 *One study was identified through the consultation exercise. †This includes articles that reported on different aspects of the results derived from the same dataset3 92 93 107 108 or on different datasets obtained through the same grant.113 114 120 126 127 160

Research (B1) was synthesised based on the type of documents scrutinised (eg, ethics application forms, informed consent documents, journal articles) and the area under investigation (eg, completeness, errors, quality; reporting practices). The number of articles tagged to a given topic includes studies where that topic was the main focus as well as those where the topic was briefly explored. Salient findings from the synthesis are presented below narratively.

**Primary research**

The synthesis (table 3) established that, despite the focus on knowledge-based studies evident in the evidence map (table 2), it was difficult to build a coherent picture of lay and professional participants’ understanding of the topics explored (written/verbal information provision, clinical trials/research, research ethics, ethics committees), primarily due to the methodological (eg, validity of survey instruments) and reporting limitations in studies...
### Table 1 Key characteristics of included studies

#### 1. Location

| Type               | N   | %   |
|--------------------|-----|-----|
| Urban              | 47  | 58.8|
| Rural              | 3   | 3.8 |
| Mixed              | 3   | 3.8 |
| Not available* / Not applicable† | 27  | 33.8|

#### 2. Methods

**a. Quantitative**
- Surveys (inferential) | 21  |
- Surveys (descriptive) | 15  |
- Documents (descriptive) | 13  |
- Documents (inferential) | 4   |
- Other (documents, data, observation, RCT, websites) | 7   |

**b. Qualitative**
- Interviews | 10  |
- Interviews and focus groups | 3   |
- Interviews and observations | 2   |
- Interviews, observations, focus groups | 1   |

**c. Mixed methods**
- Survey (descriptive) and interviews | 2   |
- Survey (descriptive) and focus groups | 1   |
- Survey (inferential) and focus groups | 1   |

#### 3. Population

**a. Professional**
- Ethics committee members | 8   |
- Researchers (two with CT investigators; two with clinical research professionals; one with CRO staff) | 5   |
- Healthcare students (five with medical students; one each with nursing and pharmacy students) | 7   |
- Healthcare faculty (two with dental faculty; one with medical faculty) | 3   |
- Healthcare students and faculty (two with dental students and faculty; one with medical students and faculty) | 3   |
- Healthcare service providers (one with healthcare faculty) | 3   |
- Mixed professional groups | 5   |

#### 4. Journal

**a. Published in India** | 49  |
**b. Published in a high-income country** | 29  |
**c. Unknown/not clear** | 2   |

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*When information is not reported.
†When data collected is documents.
‡Includes surveys, documents, journal articles, websites that were not specific to one region.

CRO, contract research organisation; CT, clinical trial; RCT, randomised controlled trial.

(A1–A4). Methodological research aimed at developing locally validated tools to assess knowledge will help improve the quality of future studies and facilitate meta-analysis.

Ethics committees (A4) were among the most studied topics (18 studies) and also the source of data in a large volume of studies (16 studies, 8 each with committee members and documents submitted to/produced by committees). Studies highlighted a number of challenges faced by ethics committees (eg, conflicts of interest, onerous workload, impact of frequent regulatory changes without support for implementation), which would benefit from the development of interventions to support the optimal functioning of ethics committees.

Healthcare students were the next most researched group (10 studies).

Research on interventions to optimise comprehension of written/verbal information provision for informed consent (A1) were particularly lacking (except one RCT that compared group and individual counselling and found no difference in comprehension). While there is some evidence of the difficulties of communicating research terminology (around terms such as research, trial, randomisation) particularly in local languages, research is required on interventions to overcome these barriers (A2). There was overwhelming support for education and training on clinical trials/research and research ethics in the curriculum for key stakeholder groups, including healthcare students, but we do not know what, if any, aspects of these topics are currently covered in healthcare students’ curriculums so that deficiencies can be identified and addressed (A3).
### Table 2  Evidence map of the number of primary and secondary research articles by topic and population group (studies explored multiple areas and have been categorised by main topic area studied)

| Population | Topic | Lay (a) | Professional (b) | Mixed (a and b) | Total |
|------------|-------|---------|------------------|----------------|-------|
| A. Primary research: Knowledge (or awareness/comprehension), attitudes (or perceptions), practice (or behaviour)* |
| **Comprehension of the informed consent form and/or verbal information provision in:** |
| Real | Randomised Controlled Trial | 2 | 115 | 2 | 117 |
| | Clinical Trial | 3 | 62 | 3 | 65 |
| | Cohort Study | 3 | 67 | 3 | 66 |
| Hypothetical | Randomised Controlled Trial | 1 | 90 | 1 | 91 |
| | Clinical Trial | 1 | 91 | 1 | 91 |
| **Knowledge, Attitudes, Practices in relation to:** |
| **Broad topics:** |
| Clinical Trials | Compensation for clinical trial related injury | 1 | 157 | 1 | 158 |
| Clinical Research | Ethical guidelines | 1 | 101 | 1 | 101 |
| | Informed consent | 1 | 130 | 1 | 130 |
| | Ethics committees’ composition and/or functioning (incl. ethical review) | 1 | 114 | 1 | 114 |
| **Specific topics within:** |
| Clinical Trials | 13 | 18 | 1 | 32 |
| Clinical Research Ethics | 2 | 18 | 1 | 19 |
| **Subtotal** | 15 | 18 | 1 | 32 |
| A. Primary research: Perceptions, experiences, practices/processes¶ in relation to: |
| Real | Randomised Controlled Trial | Feasibility of informed consent procedure | 1 | 120 | 1 |
| | Clinical Trial | Patient participation in / content of informed consent discussion | 1 | 111 | 1 |
| | Clinical Research | Audio-visual recording of informed consent process (description and views) | 1 | 128 | 1 |
| | Clinical Research Ethics | Recruitment experience/process and informed consent in bioavailability/bioequivalence studies | 1 | 140 | 1 |
| Hypothetical | Clinical Trial | Audio-visual recording of informed consent process (acceptability) | 1 | 122 | 1 |
| | Clinical Trial and Biobanking Research | Meaning of consent, benefit sharing, incentives | 1 | 117 | 1 |
| | Biobanking Research (results sharing, benefits sharing, data ownership) | 1 | 128 | 1 |
| Real and hypothetical | Clinical Research | Coercion in research participation | 1 | 126 | 1 |

Continued
## Table 2  Continued

### Population Topic

| Broad topics: | Clinical Research Ethics and/or Ethics Committees | Lay(a) | Professional(b) | Mixed(a and b) | Total |
|---------------|---------------------------------------------------|-------|-----------------|---------------|-------|
| Specific topics within: | Clinical Research Ethics | | | | |
| Ethics Committees (composition, functioning, ethical review process) | | | | | |
| Data sharing | | | | | |
| Outsourcing, Clinical Research Organisations and Civil Society Organisations | | | | | |
| Community stakeholder engagement | | | | | |
| Informed consent documents and processes | | | | | |
| Impact of regulatory changes†* | | | | | |
| **Subtotal** | | | | | |
| **Primary Research Total** | | | | | |

### B. Secondary Research

| Population Reviews of: | EC documents | Informed consent documents | Study data / documents | Websites | Journal articles | Total |
|-----------------------|--------------|---------------------------|------------------------|----------|-----------------|-------|
| Completeness, errors, quality | 396 118 120 | 110 | | | | 4 |
| Payment / compensation for: | | | | | | 2 |
| Participation | 190 | | | | | |
| Injury | | | | | | |
| Compliance / adherence with: | | | | | | 4 |
| Regulations | | | | | | |
| Guidelines | 1107 | | | | | |
| Protocol | 1107 | | | | | |
| Readability | | | | | | 1 |
| Ethics committee: | | | | | | 2 |
| Registration / accreditation | | | | | | |
| Changes in composition/ structure after regulatory changes | | | | | | |
| Reasons for uninitiated studies | | | | | | 1 |
| Registered clinical trials and disease burden | | | | | | 2 |

Continued
### Table 2  Continued

#### B. Secondary Research

| Population Reviews of: | EC documents | Informed consent documents | Study data / documents | Websites | Journal articles | Total |
|------------------------|--------------|----------------------------|------------------------|---------|-----------------|-------|
| Reporting practices on: |              |                            |                        |         |                 |       |
| Ethical clearance and/or obtaining informed consent/assent |              |                            |                        |         |                 |       |
| Funding sources and conflicts of interest |              |                            |                        |         |                 |       |
| Ethical issues/methods of RCTs; journal editorial policies |              |                            |                        |         |                 |       |
| Secondary Research Total |              |                            |                        |         |                 | 22    |

Some studies were with parents of children.\textsuperscript{3} 111 116\textsuperscript{117} Studies where India is one of the countries among others, but where some findings specific to India were reported have been included.\textsuperscript{30} 93 94 121

\*Studies that explored knowledge/comprehension were included here, even when Attitude and Practice components were not studied; some studies not included here that minimally explored or mentioned knowledge/awareness have been included elsewhere.\textsuperscript{30 105 127}

†There is only one RCT\textsuperscript{116} in the dataset.

‡This study comprised no lay people, but was categorised as ‘Mixed’ because the population comprised Professionals and Documents.

§Pharmacovigilance studies were excluded in general; this study was included as it was in relation to clinical trials in particular and included views on EC functioning.

\*\*Studies that explored perceptions (or attitudes) or experiences or practices, or a combination of these, were included here.

\*\*\*Five other studies also address the impact of regulatory changes.\textsuperscript{90 78 79 106}

††Governance related documents included meeting minutes, project registers/files, standard operating procedures, site visit monitoring reports, study approval letters.

‡‡One other study\textsuperscript{126} also included readability of informed consent form.

\(\text{§§Study data included journal articles and website (Clinical Trials Registry-India); could also be categorised within compliance/adherence with guidelines (includes journal editorial policy compliance with international guidelines).}\)

EC, ethics committee; RCT, randomised controlled trial.
A1. Studies were questionnaire surveys that varied in methodological quality, with most deficiencies being in relation to survey instruments and reporting practices.

A2. Studies were overall generally positive (eg, some support for fabricating data to improve research outcomes if it did not harm patients and ethical aspects reviewed and guidelines followed) and the dilemmas faced in being expected to align with international standards for ethical review and the increasing pharmaceuticalisation of society, while also protecting national interests and preventing the perpetuation of existing health and social inequities.121

A3. Despite a large proportion of studies focusing on knowledge (or awareness/comprehension) research (with or without attitudes/perceptions and practice/behaviour (or process) components), some studies reported poor or limited knowledge (eg, some support for fabricating data to improve research outcomes if it did not harm patients and ethical aspects reviewed and guidelines followed) and the dilemmas faced in being expected to align with international standards for ethical review and the increasing pharmaceuticalisation of society, while also protecting national interests and preventing the perpetuation of existing health and social inequities.121

A4. Despite a large proportion of studies focusing on knowledge (or awareness/comprehension) research (with or without attitudes/perceptions and practice/behaviour (or process) components), some studies reported poor or limited knowledge (eg, some support for fabricating data to improve research outcomes if it did not harm patients and ethical aspects reviewed and guidelines followed) and the dilemmas faced in being expected to align with international standards for ethical review and the increasing pharmaceuticalisation of society, while also protecting national interests and preventing the perpetuation of existing health and social inequities.121
### Table 3 Continued

| Topic | Summary of synthesised findings | Research gaps |
|-------|---------------------------------|---------------|
| **A. Primary research: perceptions, experiences, practices/processes** | ![Insert Table Content](continued) | ![Insert Table Content](continued) |
| **A6. Informed consent processes: lay (and some professional) participants** | ![Insert Table Content](continued) | ![Insert Table Content](continued) |
| Number of studies tagged to topic-13 (of which only 5 were focused on topic) | ![Insert Table Content](continued) | ![Insert Table Content](continued) |
| **A6. Bigger picture: professional (and some lay) participants** | ![Insert Table Content](continued) | ![Insert Table Content](continued) |
| Number of studies tagged to topic-20 (of which only 7 were focused on topic) | ![Insert Table Content](continued) | ![Insert Table Content](continued) |
There is some evidence in relation to the ‘reported’ practice of informed consent (eg, not conducting informed consent in local languages or indication of coercion among student research participants), but limited information on the ‘actual’ practice of gaining informed consent, what research participants consider important to know or models of informed consent that are tailored to the local context (A3, A5). Where ‘actual’ practice was examined, it was illuminating—for instance, in healthy volunteer studies, informed consent appeared to be a formality and discussions were centred around payment for participation rather than risks to volunteers’ health. Future research on informed consent processes should include an in-depth exploration of the recruitment interaction with potential research participants that delves beyond the questions participants ask, towards the identification and dissemination of good practice, across multiple contexts (eg, consent/assent in trials with children; student-informed consent processes should include an exploration of the recruitment interaction with potential research participants, especially members of ethics committees and civil society organisations. Imbalances of concern included the paternalistic doctor-hierarchy between medical and non-medical experts—exploited due to their lower socioeconomic status) and contract research organisations (with whom the volunteers have bargaining power), capacity building that does not foster local innovation and the hierarchy between medical and non-medical experts in ethics committees. Some of these concerns would benefit from empirical investigation—for instance, studying the doctor-patient interaction in tri-
communication that contribute to therapeutic misconception. Similarly, research, particularly qualitative, that further explores issues of equity and justice in relation to clinical trial recruitment processes is warranted. Research on patient and public involvement in clinical trials is conspicuous by its absence and should be prioritised to redress some of the power inequities.

iv. A small group of studies provided nuanced insights into organisations that appear to be at opposite ends of the ethical debates on clinical trials in India—contract research organisations (CROs) and civil society organisations (CSOs). Although critical of ethical malpractice in general, CRO staff were less inclined to acknowledge instances of the same in their own CROs. CSO representatatives were supportive of clinical trials, felt the need to move away from pitting Indian and/or public sector clinical trials against foreign and/or private sector clinical trials as good versus bad and emphasised the need to focus on wider ethical issues that delive beyond simplistic procedure-based agendas.

Secondary research
The synthesis of documentary research (B1) corroborated findings from the synthesis of primary research and reported: inadequacies in informed consent documentation, increased workload for ethics committees particularly after the 2013 regulatory changes, mismatch between clinical trials and India’s disease burden, lack of uniformity in compensation mechanisms and suboptimal clinical trial reporting practices in Indian journals. The use of Western readability tests for written information provided in India needs addressing with the development of readability tests in Indian languages. Similarly, while studies on journal reporting practices have focused on the reporting of ethical approval and informed consent, future studies could investigate reporting practices in relation to questionnaire surveys (given their frequent use and methodological/reporting limitations as indicated earlier).

Consultation exercise
Nine of the 10 individuals approached agreed to participate in the consultation exercise (virtual conferencing group: n=7, one meeting, 1 hour 30 min; telephone: n=1; email: n=1). The consultation group’s recommendations and actions taken were grouped into five key areas as summarised in table 4 (detailed in online supplemental file 5).

DISCUSSION
We carried out a scoping review and narrative synthesis of the empirical literature on ethical issues in relation to clinical trials/research in India. We developed an evidence map of 80 studies and synthesised the findings narratively, revealing a wide range of topics investigated and the gaps that exist, with key insights from the consultation group. We found that some topics and populations were more favoured than others—the literature was heavily focused on ‘knowledge’ assessments of participants from lay/professional groups on various topics; ethics committees were examined from multiple angles while also being the source of data in many studies and healthcare students were often research participants. On the other hand, studies that investigated the recruitment-informed consent process, models of informed consent tailored to the Indian context and issues such as equity and justice in the context of clinical trials/research were far fewer in number or absent.

To our knowledge, this is the first systematic scoping review that focuses on empirical research on the ethical aspects of clinical trials/research in one country. Systematic reviews on related aspects (eg, willingness to participate) have tended to combine LMICs together or included people living in India with those of Indian origin living in other countries.

Our findings indicated that the volume of literature on a given topic was not associated with whether or not it allowed the development of a cohesive synthesis on the topic. We found it challenging to develop a lucid picture of some frequently researched areas such as knowledge on clinical trials/research and research ethics. Given the diversity and scale of the population in India, this could be a reflection of reality, but the numerous methodological limitations and reporting variations, particularly among questionnaire surveys, made it difficult to identify commonalities that may exist. By contrast, although only a small number of studies focused on the wider ethical issues, they provided valuable insights into the workings of the clinical trials/research industry. This may also be because the former group of studies, primarily questionnaire surveys, were likely aiming for breadth but were often compromised methodologically, while the explorations of wider ethical issues were more amenable to qualitative research and successfully provided the depth that was warranted in intense and nuanced debates.

Research gaps were identified on topics that need to be researched (when limited or missing from current literature) as well as topics that need to be ‘better’ researched (when present in literature but requiring methodological/reporting improvements). Given that questionnaire surveys (particularly those exploring knowledge) were the predominant method used, methodological research on developing and validating culturally relevant survey tools and minimum journal reporting standards for surveys would be crucial, drawing from existing guidelines. Small-scale, single-centre surveys may be useful to inform local practice, but consistent use of validated measures and standardised reporting practices are needed to contribute to national policy and practice. Calls to ensure inclusion of research ethics and clinical trials education in the curriculum of healthcare students would be bolstered if research can establish and evaluate the content of aspects that are already covered.
Table 4  Recommendations from the consultation group and actions taken

| Area | Recommendations | Action |
|------|----------------|--------|
| 1. Improving the manuscript | ▶ Change title to better reflect the scope of the review.  
▶ Ensure better acknowledgement of the rich bioethics literature and lack of grey literature in the review.  
▶ Incorporate a reflexive section on the authors.  
▶ Emphasise the value of qualitative research in addressing key research gaps. | Reflexive note in online supplemental file 5; others incorporated in manuscript. |
| 2. Additional analysis and missed literature | ▶ Consider impact of the 2013 regulatory changes.  
▶ Consider impact of studies’ funder/sponsor on the research landscape.  
▶ Examine four missed articles for inclusion. | ▶ Additional analysis undertaken (data extracted for year of data collection and funder).  
▶ One article met inclusion criteria and was included; others, where relevant, have been mentioned in methods/discussion. |
| 3. Research gaps | There is insufficient empirical information on:  
▶ Informed consent/assent processes for children in clinical trials/research.  
▶ Models of informed consent to suit multiple contexts.  
▶ Issues of equity and social justice in relation to clinical trials.  
▶ Doctor-recruiter dual role and the arising conflicts of interest.  
▶ Regulatory processes.  
▶ Academic trials conducted in medical institutions and vaccine trials.  
▶ Therapeutic misconception.  
▶ Questionnaire validation processes. | These gaps have either been highlighted separately within the review or incorporated within existing gaps. |
| 4. Reasons for paucity of research | ▶ Lack of funding initiatives to carry out nested studies within clinical trials and related methodological work is a major obstacle for researchers in India.  
▶ Not all ethical issues are 'researchable' and are sometimes better captured through bioethics literature. | Incorporated in discussion. |
| 5. Concerns | Most concerns expressed were in relation to ethics committees:  
▶ Lack of awareness of principles underpinning clinical research and good clinical practice guidelines among committee members.  
▶ Non-trial study designs encouraged by committees to avoid institutional liability for serious adverse events in clinical trials.  
▶ Excessive workloads and undeclared roles and conflicts of interests among members. | Noted here as this is a reflection of the large proportion of studies on ethics committees. |

The direct impact of the 2013 regulatory changes on the research landscape are unclear in this review. A few studies investigated professionals’ perceptions of regulatory changes,\textsuperscript{56,80} acceptability and impact of new measures such as the AV recording of consent\textsuperscript{72,78,79} and the impact of changes on ethics committees\textsuperscript{66,106} (latter is examined in-depth in an excluded literature review\textsuperscript{147}). It would have been useful to further examine the review findings through the prism of the landmark 2013 regulatory changes, but with a third of the studies not reporting the year of data collection, this was not feasible. It is also important to interpret the findings in light of the continually evolving regulatory landscape in India, with the most recent changes introduced in March 2019 (NDCT Rules).\textsuperscript{19} For instance, some studies raised concerns in relation to the conflicts of interest that compromise the independence of ethics committee members and the hierarchy between medical and non-medical (lay) members of ethics committees, stemming partly from issues such as lack of adequate training for lay members.\textsuperscript{92,108,133} With the NDCT Rules now requiring 50% of members to not be affiliated to the institution in which the committee is based and necessitating mandatory training for ethics committee members,\textsuperscript{148} future studies can investigate if this has redressed some of the concerns around the independence of ethics committees and the power imbalances within. Similarly, Indian regulations on compensation for trial-related injuries are acknowledged as comprehensive and having unique features (eg, the compensation for injuries not related to research),\textsuperscript{149} but it would be crucial to study the challenges in the implementation of these national laws on compensation.
The views expressed by some participants (and authors) of studies in this review that there was an excessive focus on the proceduralism of informed consent is conceivably true in practice and appears well documented, yet the informed consent process was grossly underresearched. Given the breaches of good practice reported in the past and the routine AV recording of the informed consent interaction, it is notable that only one study was conducted using this resource. It is unclear if the challenges in undertaking, storing and retrieving AV recordings has a role in their underutilisation for research purposes or if this is due to regulatory restrictions. Opening the black box of the informed consent process in future qualitative research can help optimise comprehension of participants, communication of complex trial-related terminology in local languages and identify aspects of the doctor-patient interaction that contribute towards therapeutic misconception.

Given the lack of established benchmarks for what constitutes optimal information provision for potential clinical trial participants in India or in the West, researchers could also establish core information sets (information of core importance to convey to patients, drawing from empirical evidence and consensus building approaches). Patient and public involvement would need to be a central component in such efforts. Interventions to identify informed consent models that are suited to the Indian context (community-family based and/or Western-individual autonomy based) and to specific situations (eg, industry-led and investigator-led trials) are warranted.

It would also be useful to critically consider the topics, populations and methods that we, as researchers, choose to investigate and employ in future studies—for instance, (a) whether the ease of access to healthcare students and ethics committee members and/or its documentation justifies them being frequently researched, especially when they are so unrepresentative of participants in trials or (b) whether assessing comprehension of informed consent information is meaningful without assessing the quality of written and/or verbal information provision that preceeded it. Future research could also address the lack of readability tests in Indian languages, develop interventions to improve ethics committee functioning by overcoming some of the identified barriers and curtail the excessive focus on ‘knowledge’ to redirect efforts on the larger ethical issues to tackle the inequities and imbalances in the clinical trial industry. However, if knowledge assessments were to be undertaken, it would be prudent to consider what constitutes optimal understanding among research participants and whether the outcome of any knowledge assessments can be used to improve the informed consent process or the comprehension of participants locally. The suitability of interventions employed in high-income countries to improve participant understanding in informed consent for research needs to be carefully assessed for India. Qualitative research methods, underused in the range of topics covered in this review, are best suited to investigate the larger issues that require depth of understanding rather than breadth.

The consultation exercise with key stakeholders in India was instrumental in contextualising this scoping review and identifying missed research priorities. A key structural constraint identified in the consultation exercise and evident in the dataset was that most studies were conducted with no to limited external funding. Calling for high-quality studies that span a range of topics to fill the identified gaps would be misguided without appropriate funding mechanisms. Initiatives such as the Medical Research Council’s trials methodology hubs across the UK have been instrumental in improving clinical trial design, conduct and reporting (eg, see final report of trials methodology research carried out over 4 years, 2014–2018, in one of the hubs), with subsequent provisions for initiating trials methodology projects in LMICs. It is time for international/national funding agencies to consider establishing similar methodology hubs led by researchers in India, with a focus on the ethical conduct of clinical trials. It would be important, however, to ensure that in our pursuit of empirical evidence, we do not downplay the vital role played by other forms of evidence and catalysts for change, given that not all ethical issues are amenable to being researched.

**Limitations**

Despite our best efforts, we may have missed some relevant journal articles and studies included in books. However, if missed articles reflected the patterns of published research included in this review, it is likely that they would not substantially alter our synthesis and conclusions. A decision to only include peer-reviewed research also meant we did not seek out grey/unpublished literature (although condensed publications from them, if any, are included). Some of the topics we excluded may have helped contextualise our findings. For instance, we included studies on research ethics but excluded those on medical/clinical ethics—an associated topic of interest that requires a separate review. While the review has helped underline the gaps in the existing literature, it is not exhaustive and cannot claim to have identified all gaps. It also cannot prioritise the identified gaps in a meaningful way and is limited in identifying key topics that are completely absent or of importance to key stakeholders. Designing and conducting the review with the input of researchers in India from conception stages may have resulted in a different focus and outcome. Our intention was that the critical input of key stakeholders at the consultation phase helped focus the review and overcome some of the shortcomings. A locally led priority-setting exercise, informed by this review, to determine pressing concerns that warrant empirical investigation would be an ideal next step.

**CONCLUSION**

This systematic scoping review is the first attempt at summarising peer-reviewed empirical research on topics related to the ethics of clinical trials/research in India.
The review demonstrates that while a wide range of topics have been studied in India, the focus is largely on assessing knowledge levels across different population groups. This is a useful starting point, but fundamental questions remain unanswered about the recruitment and informed consent process, such as the doctor-patient interaction, and the larger issues of equity and justice that dominate the clinical trials/research landscape.

The evidence map and narrative synthesis are meant to be a starting point for discussions on future research directions, to be used in ways that benefit the research community and patient population and contribute towards the ongoing efforts within India to improve the clinical trials/research landscape. A priority-setting exercise that could be informed by this review, led by researchers in India, would be an ideal next step, alongside funding mechanisms that support researchers based in India to undertake research in priority areas in clinical trials/research methodology and ethics.

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REFERENCES
1 Lang T, Sribaddana S. Clinical trials have gone global: is this a good thing? PLoS Med 2012;9:e1001228.
2 Singh S. Clinical trials: new horizon – India. CDsCO/DCGI presentation at the who, International Conference of drug regulatory authorities. Available: http://www.pharmexcil.com/data/uploads/ci/trialstrails.dr.su.rinder.ppt [Accessed 26 Nov 2020].
3 Chawan VS, Gawand KD, Phatak AM. Impact of new regulations on clinical trials in India. Int J Clin Trials 2015;2:56.
4 Burt T, Sharma P, Dhillon S, et al. Clinical research environment in India: challenges and proposed solutions. J Clin Res Bioeth 2014;5:1–8.
5 Nadimpally S, Srinivasan S, Madhavi Y, et al. The HPV vaccine: science, ethics and regulation 2010.
6 Politzer M, Krishnan V. The dark underbelly of India’s clinical trials business. Livemint 2012.
7 Sharma K. The other half: unformed consent. The Hindu 2010.
8 Sinha K. 49 babies die during clinical trials at AIIMS. Times of India 2008.
9 Buncombe A, Lakhani N. Without consent: how drugs companies exploit Indian ‘guinea pigs’. Independent 2011.
10 Lloyd-Roberts S. Have India’s poor become human guinea pigs? BBC News 2012.
11 Yee A. Regulation failing to keep up with India’s trial boom. The Lancet 2012.
12 Bagchi S. Indian Supreme Court halts approval of new clinical trials until regulatory framework is set up. BMJ 2013;347:f5996.
13 Barnes M, Flaherty J, Caron M. The evolving regulatory landscape for clinical trials in India. Food and Drug Law Journal 2018;73:601–23.
14 Roy Chaudhury R, Mehta D. Regulatory developments in the conduct of clinical trials in India. Glob Health Epidemiol Genom 2016;1:e4.
15 Ministry of Health and Family Welfare. The drugs and cosmetics act, 1940 and the drugs and cosmetics rules, 1945. New Delhi: Department of Health, Government of India, 2016.
16 Ministry of Health and Family Welfare. Amendment to the Drugs & Cosmetics Rules-1945, Gazette Notification [GSR 72 (E)]. New Delhi: Department of Health, Government of India, 2013.
17 Ministry of Health and Family Welfare. File no: GCT/20/SC/ Clin.2013 DGCI: Audio–Video Recording of Informed Consent Process of All New Subjects in Clinical Trials-Administrative Orders Monitoring of Clinical Trials - regarding. New Delhi: Department of Health, Government of India, 2013.
18 Gogoi NY, Ravi R, Thatte UM. Regulatory requirements for clinical trials in India: what academicians need to know. Indian J Anaesth 2017;61:192–9.
Ministry of Health and Family Welfare. Notification-The Gazette of India: extraordinary, part II, section 3, subsection (l); new drugs and clinical trials rules. New Delhi: Government of India, 2019.

National Institute of Health-National Institute on Aging. What are clinical trials and studies? 2020. Available: https://www.nia.nih.gov/health/what-are-clinical-trials-and-studies [Accessed 17 Jan 2021].

World Health Organization. Clinical trials: overview, 2021. Available: https://www.who.int/health-topics/clinical-trials#tab=tab_1 [Accessed 17 Jan 2021].

Singh N, Madakkar NJ, Gokhale PM, et al. New drugs and clinical trials rules 2019: changes in responsibilities of the ethics Committee. Perspect Clin Res 2020;11:37–43.

Jesani A, Srinivasan S. New drugs and clinical trials rules, 2019: the market trumps ethics and participant rights. Indian J Med Ethics 2019;4:89–91.

Mathur R, Thakur K, Hazam RK. Highlights of Indian Council of medical research national ethical guidelines for biomedical and health research involving human participants. Indian J Pharmacol 2019;51:214.

Indian Council for Medical Research. National ethical guidelines for biomedical and health research involving human participants. In: Indian Council for Medical Research, 2017.

Mahapatra T, Mahapatra S, Pal D. Trials and tribulations of conducting interventional studies in urban slums of a developing country: experiences from Kolkata, India. Hum Vaccin Immunother 2016;12:182–6.

Mohindra KS, Narayana D, Haddad SH. Towards ethically sound participatory research with marginalised populations: experiences from India. Development in practice 2015;21:1189–75.

Sahay S, Kumar M, Srikrishnan AK, et al. Experiences in recruiting volunteers through community based initiatives in phase-1 vaccine trials in India. Hum Vaccin Immunother 2014;10:485–91.

Pramesh CS, Shastri S, Mittra I, et al. Ethics of “standard care” in randomised trials of screening for cervical cancer should not ignore scientific evidence and ground realities. Indian J Med Ethics 2013;10:250–1.

Srinivasan S. Ethics of “standard care” in randomised controlled trials of screening for cervical cancer. Indian J Med Ethics 2013;10:147–5.

Jeffrey R, Porter G, Jesani A, et al. Structure, organization and knowledge production of the Indian clinical trials industry. In: Jesani A, Prasad P, eds. Equity and Access: Health Care Studies in India. Noida, India: OUP India, 2018: 178–201.

Bhan A. Clinical trial ethics in India: one step forward, two steps back. J Pharmacol Pharmacother 2012;3:95–7.

Jesani A. Ethics in ethics committees: time to share experiences, discuss challenges and do a better job. Indian J Med Ethics 2008;6:62–3.

Kang G. Putting patients first: draft guidelines for compensation for research-related injury in clinical trials in India. Indian J Med Ethics 2012;9:77–9.

Arksy H, O’Malley L. Scoping studies: towards a methodology. Int J Soc Res Methodol 2009;6:19–32.

Levac D, Colquhoun H, O’Brian K, O’Brian K. Scoping studies: advancing the methodology. Implement Sci 2010;5:69.

Munn Z, Peters MDJ, Stern C, et al. Systematic review or scoping review? guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 2018;18.

Peters MDJ, Godfrey CM, Khatt H, et al. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc 2015;13:141–6.

Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018;169:667–73.

Chavan VS, Badwane SV, Gawand KV, et al. An analysis of clinical trials registered with CTRI in India from 2007 to 2015. Int J Clin Trials 2016;3:155.

Bharmarapu Pilli Johan A, Saberwal G. An analysis of deficiencies in the data of interventional drug trials registered with Clinical Trials Registry - India. Trials 2019;20:535.

Hyder AA, Wali SA. Informed consent and Collaborative research: perspectives from the developing world. Dev World Bioeth 2006;6:33–40.

Newton SK, Appiah-Poku J. The perspectives of researchers on obtaining informed consent in developing countries. Dev World Bioeth 2007;7:19–24.

Browne JL, Rees CO, Delden JM, et al. The willingness to participate in biomedical research involving human beings in low- and middle-income countries: a systematic review. Trop Med Int Health 2019;24:264–79.

Shah J, Phadare A, Rajgor D. What leads Indians to participate in clinical trials? A meta-analysis of qualitative studies. PloS one 2010;5:e10730.

Zammar G, Meister H, Shah J, et al. So different, yet so similar: meta-analysis and policy modeling of willingness to participate in clinical trials among Brazilians and Indians. PloS one 2010;5:e14368.

Karan A, Somasundaram P, Michael H, et al. The effect of multimedia interventions on the informed consent process for cataract surgery in rural South India. Indian J Ophthalmol 2014;62:171–5.

Kumar S, Mohanraj R, Rose A, et al. How ‘informed’ is informed consent? Findings from a study in South India. Indian J Med Ethics 2012.

Bhagavathula AS, Elnour AA, Jamshed SQ, et al. Health professionals’ knowledge, attitudes and practices about pharmacovigilance in India: a systematic review and meta-analysis. PLoS One 2016;11:e0152221.

Dsoouza MA, Balakrishnan T, Vora M, et al. The Attitude of Undergraduate Medical Students towards Research: A Case Study from Two Medical Colleges in Maharashtra, India. Curr Sci 2017;113:1129–34.

Giri PA, Bangal VB, Phalke DB. Knowledge, attitude and practices towards medical research amongst the Postgraduate students of Pravara Institute of medical sciences University of Central India. J Family Med Prim Care 2014;3:533–42.

Symnot A, Lowe D. Audio-Visual presentation of information for informed consent for participation in clinical trials: evidence Bulletin 2016.

Tam NT, Huy NT, Thoa LT. Participants’ understanding of informed consent in clinical trials over three decades: systematic review and meta-analysis. Bull World Health Organ 2015;93:186–98.

Endnote X9 [computer program]. Version Endnote X9. Philadelphia, PA: Clarivate Analytics 2013.

Daudt HML, van Mossel C, Scott SJ. Enhancing the scope of clinical research: making informed consent form more accessible. J Med Ethics 2016;1:210–4.

Dowmies M, Brennan M, Williams H, et al. Development of a critical appraisal tool to assess the quality of cross-sectional studies (axis). BMJ Open 2016;6:e014158.

Hong QN, Fabbregues S, Bartlett G, et al. The mixed methods appraisal tool (MMAT) version 2018 for information professionals and researchers. Education for Information 2018;34:285–91.

MAXQDA 12 [computer program]. Version MAXQDA 12. Berlin, Germany: VERBI Software, 2015.

Arora A, Rajagopalan S, Shafiq N, et al. Development of tool for the assessment of comprehension of informed consent form in healthy volunteers participating in first-in-human studies. Contemp Clin Trials 2011;32:814–7.

Bavedkar SB, Gogtay NJ, Wagh S. Reporting ethical processes in two Indian journals. Indian J Med Sci 2008;62:134–40.

Bavedkar SB. Informed consent documents submitted for initial review: what do they state about compensation for injured research participants? Indian J Med Sci 2009;63:455–60.

Bhansali S, Shafiq N, Malhotra S, et al. Evaluation of the ability of clinical research participants to comprehend informed consent form. Contemp Clin Trials 2009;30:427–30.

Bhide SS, Jalgaonkar SV, Katkar JV, et al. Impact of recent regulatory notifications on an institutional ethics Committee. Indian J Med Ethics 2016;1:210–4.

Bindra S, Kochhar P. Survey on perceptions of Indian Investigators on research ethics. Perspect Clin Res 2010;1:94–7.

Brahme R, Mehendale S. Profile and role of the members of ethics committees in hospitals and research organisations in Pune, India. Indian J Med Ethics 2009;6:78–84.

Burt T, Dhillon S, Sharma P, et al. PARTAKE survey of public knowledge and perceptions of clinical research in India. PLoS One 2013;8:e68866.

Chatterjee S, Kieselsbach B, Naik S, et al. Customising informed consent procedures for people with schizophrenia in India. Soc Psychiatry Psychiatr Epidemiol 2015;50:1527–36.
Chaturvedi SK, Somashekar BS. Reporting ethical aspects in published research articles in the Indian Journal of psychiatry. *Indian J Psychiatry* 2009;51:34–7.

Chauhan RC, Purty AJ, Singh N. Consent for audio-video recording of informed consent process in rural South India. *Perspect Clin Res* 2015;6:159–62.

Chenneville T, Menezes L, Kosambiya J, et al. A case-study of the resources and functioning of two research ethics committees in Western India. *J Empir Res Hum Res Ethics* 2016;11:387–96.

Chin LJ, Rifa'i-Bashjwih H, Kleint J, et al. HIV/AIDS research conducted in the developing world and sponsored by the developed world: reporting of research ethics Committee review in two countries. *J Empir Res Hum Res Ethics* 2011;6:83–91.

Choudhury S, Pradhan R, Dubey L. Knowledge and perceptions regarding clinical trials among doctors of government medical colleges: a questionnaire-based study. *Perspect Clin Res* 2016;7:94–9.

Davis S, Sule P. Bughedwala M, et al. Ethics committees and the changed clinical research environment in India in 2016: a perspective. *Perspect Clin Res* 2017;8:17–21.

Deoisa SG, Prasad K, Chhabra KG, et al. An insight into research ethics among dental professionals in a dental Institute, India- a pilot study. *J Clin Diagn Res* 2014;8:ZC11–14.

Figer BH, Chaturvedi M, Thaker SJ, et al. A comparative study of the informed consent process with and without audiovisual recording. *Natt Med J India* 2017;30:262–5.

Ganguly B. Newer practice of informed consent process of clinical trials in India. *Asian Bioeth Rev* 2016;8:327–36.

George DE, Dolakia S, Tharayan P. Assessing decisional capacity for research participation in psychiatric patients and their relatives. *Indian J Med Ethics* 2018;8:125–33.

Gopinath NM, John J, Senthilkumar E, et al. A study of awareness and attitude about research ethics among dental faculties in India. *Indian Journal of Medical Ethics* 2018;3:125–33.

Gupta M, Tripathy JP, Verma S. Audiovisual informed consent process in vaccine trials: experience from North India. *Indian J Med Ethics* 2018;3:179–85.

Hate K, Meherally S, Shah More N, et al. Sweat, skepticism, and Uncharted Territory: a qualitative study of opinions on data sharing among public health researchers and research participants in Mumbai, India. *J Empir Res Hum Res Ethics* 2015;10:239–250.

Jadhav A, Jadhav S, Padwal S. Completeness of institutional ethics application forms submitted to the ethics committee in a rural tertiary teaching hospital. *National Journal of Medical Research* 2015;5:1.

Jhawar VG, Bhisnoi RJ. Comprehensibility of translated informed consent documents used in clinical research in psychiatry. *Indian J Psychiatry* 2010;52:7–12.

Joglekar NS, Deshpande SS, Sahay S, et al. Correlates of lower comprehension of informed consent among participants enrolled in a cohort study in Pune, India. *Int Health* 2013;5:64–71.

Joshi V, Kulkami AA. Public awareness of clinical trials: a qualitative pilot study in Pune. *Perspectives in Clinical Research* 2012;3:125–32.

Kadam R, Borde S, Madas S, et al. Opinions and perceptions regarding the impact of new regulatory guidelines: a survey in Indian clinical trial Investigators. *Perspectives in Clinical Research* 2016;7:81–7.

Kamat VR. Fast, cheap, and out of control? speculations and ethical concerns in the conduct of Ou$tourced clinical trials in India. *Social Science & Medicine* 2014;104:48–55.

Kamath A, Up R, Shenoy KA. Willingness to participate in a clinical trial and understanding of informed consent information among medical students. *Indian Journal of medical ethics* 2014;11:16–18.

Kandhari R. Justice in jeopardy: a qualitative study of institutional ethics committees in New Delhi. *Indian Journal of medical ethics* 2013;10:176–83.

Klitzman R, Chin LJ, Rifa'i-Bashjwih H, et al. Disclosures of funding sources and conflicts of interest in published HIV/AIDS research conducted in developing countries. *Journal of Medical Ethics* 2010;36:505–10.

Klitzman RL, Kleint J, Rifa'i-Bashjwih H, et al. The reporting of IRB review in Journal articles presenting HIV research conducted in the developing world. *Developing World Bioethics* 2011;1:1161–9.

Kundapura SV, Dubey LR, Ghooli RB. The big Cs of the informed consent form: compliance and comprehension. *Indian Journal of medical ethics* 2013;10:232–7.
119 Shetty VC, Marathe P, Kamat S, et al. Continuing oversight through site monitoring: experiences of an institutional ethics committee in an Indian tertiary-care Hospital. Indian J Med Ethics 2012;9:22–6.

120 Shetty VC, Marathe PA, Billa GV, et al. A study to assess completeness of project application forms submitted to institutional ethics committees (IEC) of a tertiary care hospital. Perspect Clin Res 2012;3:133–8.

121 Simpson B, Khatri R, Ravindran D, et al. Pharmaceuticalisation and ethical review in South Asia: issues of scope and authority for practitioners and policy makers. Soc Sci Med 2015;131:247–54.

122 Sridharan K, Mehta M, Sivaramakrishnan G. Awareness and attitude of general public about clinical trials in a developing country. American Journal of Experimental and Clinical Research 2016;33:146–6.

123 Taur SR, Balwant SB, Thatte UM. Survey of ethics Committee protocol approval letters: compliance with schedule Y/ICMR guidelines 2006. Indian J Med Ethics 2011;8:214–6.

124 Tharyan P, George AT, Kirubakaran R, et al. Reporting of methods was better in the clinical trials Registry-India than in Indian Journal publications. J Clin Epidemiol 2013;66:10–22.

125 Thatte UM, Kulkarni-Munshi R, Kalekar SA. Review of policies for injuries to research participants in India. J Med Ethics 2009;35:133–9.

126 Vaidya P, Kamat S, Shetty Y, et al. Is coercion involved in the decision-making of medical students participating in research? A cross-sectional study. Asian Bioethics Review 2015;8:20–36.

127 Vaz M, Vaz M, Srinivasan K. Listening to the voices of the general public in India on biomedical research—an exploratory study. Indian J Med Ethics 2014;11:68–77.

128 Vaz M, Vaz M, K S. The views of ethics Committee members and medical researchers on the return of individual research results and incidental findings, ownership issues and benefit sharing in biobanking research in a South Indian City, Dev World Bioeth 2018;18:231–5.

129 Vittalrao AM, Kumari KM, V. Bhat S, et al. A questionnaire survey on awareness of clinical trials among medical students. Biomedical and Pharmacology Journal 2018;11:2005–9.

130 Bhowmick S, Banerjee K, Sikdar S, et al. An evaluation of knowledge, attitude, and practice of institutional ethics Committee members from eastern India regarding ethics Committee functioning and pharmacovigilance activities conducted during clinical trials: a pilot study. Perspect Clin Res 2014;5:115–20.

131 Dholi D, Thakkur K, Billa G, et al. Knowledge, attitude and practices of medical students and teachers towards clinical research in a tertiary care hospital in Mumbai and #8211; cross sectional survey. J Contemp Med Educ 2013;1:238.

132 Hussain A, Ningude AS, Kotian H. Knowledge, attitude and practice of informed consent process in biomedical research among postgraduate medical students. Int J Community Med Public Health 2019;6:1–4.

133 Jadhav M, Bhatt A. Ethics in clinical research in India: a survey of clinical research professionals’ perceptions. Perspect Clin Res 2013;4:4–8.

134 Joshi VD, Oka GA, Kulkarni AA, et al. Public awareness and perception of clinical trials: quantitative study in Pune. Perspect Clin Res 2013;4:169–74.

135 Mohammad M, Ahmad F, et al. Knowledge, attitudes and practices of bioethics among doctors in a tertiary care government teaching hospital in India. J Clin Res Bioeth 2011:02.

136 Parikh RM, Pandia K, Goyal M, et al. Perception of various stakeholders regarding clinical drug trial industry in India. Perspect Clin Res 2011;2:86–9.

137 Reddy RSudhakara, Jyothirmai K, Kiran CHSai, et al. Knowledge, awareness and attitudes about research ethics among dental professionals in a dental institution of South India. Journal of Education and Ethics in Dentistry 2013;3:34.

138 Vyas N, Jadhav P, Sane R. Knowledge, attitude, and practices regarding informed consent for research purposes among postgraduate resident doctors. Natl J Physiol Pharm Pharmacol 2019;10:1.

139 Chaturvedi M, Gogtay NJ, Thatte UM. Do clinical trials conducted in India match its healthcare needs? an audit of the clinical trials registry of India. Perspect Clin Res 2017;8:172–5.

140 Krishna S, Prasad NP. Ethical issues in recruitment of “healthy volunteers”: a study of a clinical research organisation in Hyderabad. Indian J Med Ethics 2014;11:228–32.

141 Selvarajan S, George M, Kumar SS, et al. Clinical trials in India: where do we stand globally? Perspect Clin Res 2013;4:160–4.

142 Indian Journal of Medical Ethics. Indian Journal of medical ethics. forum for medical ethics Society. Available: www.ijme.in [Accessed 26 Nov 2020].

143 Perspectives in Clinical Research. Perspectives in Clinical Research. Indian Society for Clinical Research and Wolters Kluwer - Medknow. Available: www.picronline.org [Accessed 26 Nov 2020].

144 Kelley K, Clark B, Brown V, et al. Good practice in the conduct and reporting of survey research. Int J Qual Health Care 2003;15:261–6.

145 Draugalis JR, Coons SJ, Plaza CM. Best practices for survey research reports: a synopsis for authors and reviewers. Am J Pharm Educ 2008;72:11.

146 Bennett C, Khangura S, Brehaut JC, et al. Reporting guidelines for survey research: an analysis of published guidance and reporting practices. PLoS Med 2010;8:e1001069.

147 Thatte UM, Marathe PA. Ethics committees in India: past, present and future. Perspect Clin Res 2017;8:22–30.

148 G S, lb P. New drugs and clinical trial rules 2019, what is new? our views from ethical perspective. J Assoc Physicians India 2019;67:75.

149 Chingarande GR, Moodley K. Disparate compensation policies for research related injury in an era of multinational trials: a case study of Brazil, Russia, India, China and South Africa. BMC Med Ethics 2016;17:6.

150 Shetty PA, Maurya MR, Figer BH, et al. Audiovisual recording of the consenting process in clinical research: experiences from a tertiary referral center. Perspect Clin Res 2018;9:44–7.

151 Kulkarni NG, Dalal JJ, Kulkarni TN. Audio-video recording of informed consent process: boon or bane. Perspect Clin Res 2014;5:6–10.

152 Wendler D, Grady C. What should research participants understand to understand they are participants in research? Bioethics 2008;22:203–8.

153 Main BG, McNair AGK, Huxtable R, et al. Core information sets for informed consent to surgical interventions: baseline information of importance to patients and clinicians. BMC Med Ethics 2017;18:29.

154 J, Emel E. Interventions to improve research participants’ understanding in informed consent for research: a systematic review. JAMA 2004;292:1593–601.

155 Cass NE, Taylor HA, Ali J, et al. A pilot study of simple interventions to improve informed consent in clinical research: feasibility, approach, and results. Clin Trials 2015;12:54–66.

156 Mrc ConDuCT-II hub for trials methodology research. final report. Bristol: University of Bristol 2018.

157 Medical Research Council and National Institute for Health Research. Improving Health by Improving Trials - Trials Methodology Research Partnership and Hubs for Trials Methodology, Medical Research Council, 2015. Available: http://www.network-hubs.org.uk/about/ [Accessed 26 Nov 2020].

158 SAMA. Compensation in clinical trials: a comparative analysis of seven countries. SAMA, New Delhi: Sama-Resource Group for Women and Health, 2016.

159 SAMA. Trials and Travails: perceptions and experiences of clinical trial participants in India. in. New Delhi 2013.

160 Moher D, Liberati A, et al, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.