Feasibility of an adapted QuinteT Recruitment Intervention to optimise informed consent in clinical trials in India: OrION-I study

25th November 2024

Dr Sangeetha Paramasivan

Senior Research Fellow

Population Health Sciences, Bristol Medical School, University of Bristol

On behalf of the study team

Sangeetha Paramasivan, Jeffrey Pradeep Raj, Urmila M Thatte,

Saee Hinglaspurkar, Prachi Bhoir, Nikita Sawant, Jenny Donovan, Nithya J Gogtay

Background

In India, increasing focus on:

- Strengthening the clinical trials ecosystem through regulatory reforms
- Streamlining research processes
- Reinforcing ethical / methodological rigour of trials

Systematic scoping review

- **Aim:** To obtain an overview of empirical research pertaining to the ethics of clinical research in India

Original research

BMJ Global Health

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

Sangeetha Paramasivan ,[1,2] Philippa Davies,[1,3] Alison Richards,[1,3] Julia Wade,[1] Leila Rooshenas,[1,2] Nicola Mills,[1,2] Alba Realpe,[1,2] Jeffrey Pradeep Raj,[4] Supriya Subramani,[5] Jonathan Ives,[6] Richard Huxtable,[6] Jane M Blazeby,[2,7] Jenny L Donovan[1,2]

Paramasivan S, *et al. BMJ Global Health* 2021;**6**:e004729. doi:10.1136/bmjgh-2020-004729

Systematic scoping review

- **Aim:** To obtain an overview of empirical research pertaining to the ethics of clinical research in India
- **Methods**
  - 9 databases; until Nov 2019; all peer-reviewed research with any stakeholder groups
  - Evidence map, narrative synthesis, research gaps, consultation exercise
- **Key findings**
  - 9699 screened, 282 full texts obtained, 80 included
  - Wide range of topics covered; studies often conducted with little to no funding
  - Studies predominantly examined knowledge of lay and professional participants on topics such as research ethics or their understanding of information given to obtain consent for research participation
  - Easily accessible groups, namely ethics committee members and healthcare students, were frequently researched
  - A range of research gaps identified, including the need to better understand the recruitment-informed consent process

Viewpoint

Trials Methodology Research: what is it and why should India invest in it?

Sangeetha Paramasivan,[a,*] *Anant Bhan,*[b,c] *Rashmi Rodrigues,*[d] *and Usha Menon*[e]

[a]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom
[b]Bhopal Hub, Sangath, India
[c]Centre for Ethics, Yenepoya (Deemed to be University), Mangaluru, Karnataka, India
[d]Community Health, St. John's Medical College, St. John's National Academy of Health Sciences, Bengaluru, Karnataka, India
[e]MRC Clinical Trials Unit, University College London, Institute of Clinical Trials and Methodology, London, United Kingdom

The Lancet Regional Health - Southeast Asia 2024;22: 100360

What is the QuinteT Recruitment Intervention (QRI)?

To understand and optimise recruitment and informed consent

Donovan *et al. Trials* (2016) 17:283
DOI 10.1186/s13063-016-1391-4

Trials

RESEARCH Open Access

Optimising recruitment and informed consent in randomised controlled trials: the development and implementation of the Quintet Recruitment Intervention (QRI)

Jenny L. Donovan[1,2*], Leila Rooshenas[1], Marcus Jepson[1], Daisy Elliott[1], Julia Wade[1], Kerry Avery[1], Nicola Mills[1], Caroline Wilson[1], Sangeetha Paramasivan[1] and Jane M. Blazeby[1]

Intensive Triangulation of Qualitative Research and Quantitative Data to Improve Recruitment to Randomized Trials: The QuinteT Approach

Qualitative Health Research
1–8

DOI: 10.1177/1049732319828693
journals.sagepub.com/home/qhr
SAGE

Leila Rooshenas[1], Sangeetha Paramasivan[1], Marcus Jepson[1], and Jenny L. Donovan[1], on behalf of the QuinteT Research Group

MRC Hubs for Trials Methodology Research
ConDuCT-II Hub

QuinteT
Qualitative research Integrated within Trials

Comparing preparation for responsive management with preparation for renal dialysis

- Began in 1999 with the ProtecT trial
- Integrated in about 70+ RCTs
- Before-after evaluation

The Sunflower Study

The ROMIO Study

QuinteT Recruitment Intervention: methods

Phase I: Understanding recruitment and informed consent challenges

- Mapping recruitment pathways, assessing screening and eligibility procedures
- Interviews with trial staff and patients
- Audio-recordings of 'recruitment consultations'
- Document analysis (protocol, patient information, screening logs)
- Observations of investigators meetings

'Real time'

Findings discussed with CI/TMG and 'Plan of action' agreed

Phase II: Addressing recruitment obstacles

- Feedback/training
- Written guidance and information
- Changes to trial literature to improve clarity
- Adjustments to trial pathways and processes

RESEARCH METHODS AND REPORTING

Adapting interventions to new contexts—the ADAPT guidance

Graham Moore,[1] Mhairi Campbell,[2] Lauren Copeland,[1] Peter Craig,[2] Ani Movsisyan,[3,4] Pat Hoddinott,[5] Hannah Littlecott,[1] Alicia O'Cathain,[6] Lisa Pfadenhauer,[3,4] Eva Rehfuess,[3,4] Jeremy Segrott,[7] Penelope Hawe,[8,9] Frank Kee,[10] Danielle Couturiaux,[1] Britt Hallingberg,[1,11] Rhiannon Evans[1]

thebmj | *BMJ* 2021;374:n1679 | doi: 10.1136/bmj.n1679

Implementing interventions with a previous evidence base in new contexts might be more efficient than developing new interventions for each context. Although some interventions transfer well, effectiveness and implementation often depend on the context. Achieving a good fit between intervention and context then requires careful and systematic adaptation.

Aims

- Investigating the feasibility of audio-recording trial consultations
- Acceptability of using them to provide HCP feedback in India
- Facilitate scale up in a larger study

Site: King Edward Memorial (KEM) Hospital, Mumbai

- Department of Clinical Pharmacology

Methods

All approvals obtained (Health Ministry Screening Committee and Ethics Committee)

→

Informed consent from healthcare professionals (HCPs) and patients

Audio-recorded informed consent discussions (n=15)

Interviews with HCPs (n=5)

Interview with patients (n=5)

Two clinical studies

- Perceptions of audio-recording process (feasibility /acceptability)
- If feedback acceptable to HCPs
- Suggestions for QRI adaptation to India

Audio-recorded data transcribed and translated into English
Thematic analysis using techniques of constant comparison
Data triangulation across datasets

Developed data management/sharing mechanisms and guidelines

Findings

- High rate of acceptance to audio-recordings of consent discussions (15/17)
- Recordings integrated within usual clinical and research practice (prior experience)
- Patients and HCPs viewed audio-recordings as acceptable for research purposes

HCP: This we can do!

HCP: These audio recordings can be analysed and the further process of having the informed consent during the trial can be much more beneficial, if there are any faults, like that can be improved further.

Patient: The environment was pretty comfortable. It was for research purposes, that is one thing she mentioned clearly.

Patient: I feel recording part is right.

Findings

Advantages of audio-recording the trial consultation

Documentation and evidence purposes

HCP: Audio recording can be properly accessed by DCGI or IEC person, can come and audit it properly (…) they can verify it in much better way than in written or verbal consent.

Patient: The recording, it didn't really affect the conversation but it may affect further work. I think that is point. Usually, we need evidence for everything (…) Suppose it wasn't recorded and the person might claim (…) they forced me to (agree.) We will have an evidence that no it wasn't forced.

Patient: It helps to analyse information for the future.

Patient: It is where you come to know the truth.

Less conscious than audio-visual recording

HCP: Since there is no visual the patient is less conscious as compared to audio-visual, but advantage of audio-visual is we can have the facial expression as well.

Demonstrates voluntariness of participation

HCP: We can doubt the voluntariness of the participant in written consent but in audio recording the patient is already there with us so voluntariness cannot be… (…)

Patient: If the recording is happening it's fine or if it's not happening also I'm fine.

Findings

Concerns or disadvantages

- **Patients and HCPs had concerns around confidentiality and recording of personal/health data (drawing from previous experience of audio-visual recording)**

HCP: They would sometimes get anxious and scared. That we are agreeing to participate, we are assuring that we would follow your instructions but still why do you want to audio-video record? Are you going to show it to someone?

HCP: Storage (of audio-recordings) should be done in a coded manner, confidentiality needs to maintained.

Patient: For research purpose I think recording it is fine but in normal conversation it I think it shouldn't really always be the case that it should be recorded. I should also be able to consult a doctor without being recorded. People find that there are some diseases, which a person may find awkward talking to a doctor, finding it being recorded is a little bit concerning

Findings

Providing feedback to HCPs: HCP perspectives

Some HCPs indicated that they anticipated being anxious about receiving feedback

- **BUT were also keen to improve how they communicated with patients through feedback**

HCP: I can think that yes, it will be better for me because I am getting trained.

HCP: Some discomfort for me, my seniors or my auditor might hear (…) And whether it is correctly I am giving the information or not. (Interviewer: So that doesn't make you worried?) No. I am concerned about it but I'm not worried. It can be training procedure (…) I will become more confident in the future.

HCP: Not worried, no, but anxious, yeah, little bit (…) not a challenge but at back of my mind it will be there that I will receive the feedback.

Findings

Providing feedback to HCPs: Patient perspective

Patient: They can improve on them, that is the point, and they can make themselves more clear about what exactly they want to say. Suppose a patient was just quiet and sitting over there, they wouldn't really get was he understanding or not, but after the feedback they would actually understand - okay, so he wasn't understanding, so I should have been more casual or more comfortable trying to see if he actually understood or not.

Patient: The doctor may have made it clear from his point of view and the patient may have not understood it, so at times doctor may have thought like it may not be exactly my wrong position that he may not have understood it. Sometimes the changes might be concerned to only one patient, so if he changes because of only one person then it may cause problem for the other patients who feel comfortable with his normal style of speaking.

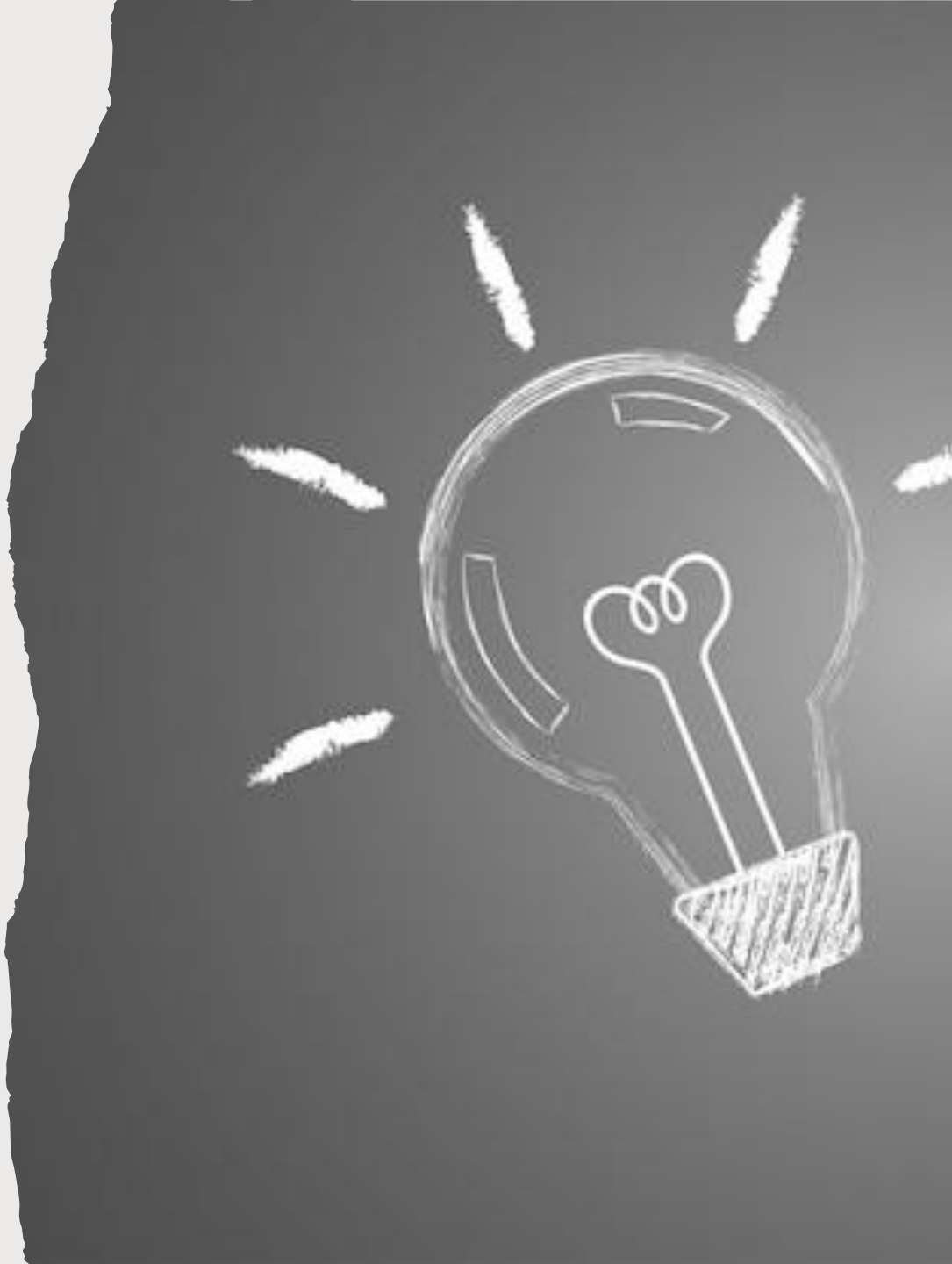
Findings

Suggestions for HCP feedback mentioned by patients and HCPs

- Use of peer feedback
- Self-appraisals by HCPs
- Feedback soon after consent appointments for real-time improvements
- Use of a structured format for feedback where feasible
- Start from what the HCP has done well

Conclusion

- Audio-recordings of consent discussions operationalised without major challenges
- HCP and patient interviews indicate that audio-recordings and feedback to HCPs are feasible and acceptable in India
- A number of adaptations that can be made to the QRI based on these findings
- Next steps… future large-scale adaptations of the QRI in India



Acknowledgements

Funding: MRC-NIHR's (Medical Research Council-National Institute of Health and Care Research) Trials Methodology Research Partnership (TMRP) global health pump-priming grant

Co-applicants:
1. Dr. Nithya Gogtay, Head of Clinical Pharmacology, KEM, Mumbai, India
2. Professor Urmila Thatte, Previous Head of Clinical Pharmacology, KEM, Mumbai, India
3. Dr. Jeffrey Raj, Clinical Pharmacology, KEM, Mumbai, India
4. Professor Jenny Donovan, Bristol Medical School, QRI founder/pioneer, UoB, Bristol, India

Collaborators:
1. Professor AS Ramakrishnan, Surgical Oncologist, Head of Research, Cancer Institute, Chennai, India
2. Dr. Abhijit Nadkarni, Founder and Co-Director of Addictions Research Group, Sangath, Goa, India and LSHTM, UK
3. Dr Anant Bhan, Adjunct Professor, Centre for Ethics, Yenepoya University, Mangalore; President, International Association of Bioethics; Lead, Sangath Bhopal hub
4. Dr. Jennifer Van Ilo Nuil, Medical Anthropologist, Research Fellow, Oxford, University Clinical Research Unit, (OUCRU), Ho Chi Minh, Vietnam
5. Dr. Nguyen Than Ha Quyen, Ethics, Team Leader, Senior Clinical Research Associate, OUCRU, Ho Chi Minh, Vietnam
6. Ms Nguyen Thi Hong Yen, Anthropologist, Social Science Research Assistant, OUCRU, Ho Chi Minh, Vietnam

Advisory panel:
1. Dr Roli Mathur: Head of Bioethics Unit, Indian Council of Medical Research, Bangalore, India
2. Ms Sarojini Nadimpally: Executive Director, SAMA Resource group for women and health, New Delhi, India
3. Dr Amar Jesani: Founder/Editor Indian Journal of Medical Ethics; Faculty member, Centre for Ethics, Yenepoya University, Mangalore
4. Ms. Evelyne Kestelyn: Head of Clinical Trials Unit, OUCRU, Vietnam
5. Dr Susan Bull: Senior Researcher, Ethics of Genomics and Global Health, Ethox Centre, University of Oxford
6. Dr Jonathan Ives: Professor of Empirical Bioethics, UoB
7. Professor Usha Menon: ProfessorGynaecological Cancer, University College London, UK
8. Professor Mike Clarke: Director of MRC Methodology Hub, Queen's University, Belfast

References

- Paramasivan S, Davies P, Richards A, Wade J, Rooshenas L, Mills N, Realpe A, Raj JP, Subramani S, Ives J, Huxtable R, Blazeby JM, Donovan JL. What empirical research has been undertaken on the ethics of clinical research in India? A systematic scoping review and narrative synthesis. *BMJ Glob Health* 2021;6(5).
- Paramasivan S, Bhan A, Rodrigues R, & Menon U. Trials Methodology Research: what is it and why should India invest in it? *The Lancet Regional Health - Southeast Asia* 2024; *22*, Article 100360.
- Donovan JL, Rooshenas L, Jepson M. Elliott D, Wade J, Avery K, Mills N, Wilson C, Paramasivan S, Blazeby JM. Optimising recruitment and informed consent in randomised controlled trials: the development and implementation of the Quintet Recruitment Intervention (QRI). *Trials* 2016;17;283.
- Rooshenas L, Paramasivan S, Jepson M, Donovan JL. Intensive Triangulation of Qualitative Research and Quantitative Data to Improve Recruitment to Randomized Trials: The QuinteT Approach. *Qualitative Health Research* 2019;29(5).
- Moore G, Campbell M, Copeland L, Craig P, Movsisyan A, Hoddinott P et al. Adapting interventions to new contexts—the ADAPT guidance. *BMJ* 2021; 374 :n1679.
- MRC-NIHR TMRP Global Health Pump Priming Awards 2020. https://www.methodologyhubs.mrc.ac.uk/about/tmrp-global-health-pump-priming-funding/

Thank You!

sangeetha.paramasivan@bristol.ac.uk
nithyagogtay@kem.edu