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Clinical Research Coordination in India: Operational Challenges in Protocol Adherence, Participant Recruitment, Informed Consent, and Clinical Data Management

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Abstract—

Background: Clinical research quality depends on site processes that protect participants, preserve protocol fidelity and generate reliable data. We assessed reported operational barriers across protocol adherence, recruitment and retention, informed consent and clinical data management at a tertiary teaching institution in India.

Methods: A descriptive cross-sectional survey was conducted at Prathima Institute of Medical Sciences, Karimnagar, from 1 August to 30 November 2024, and reported with reference to the STROBE statement. From an institutional registry of 195 research personnel (88 coordinators, 72 investigators, 35 data managers or quality auditors), stratified random sampling was used to invite 165 personnel, and 150 completed a 42-item questionnaire (response rate 90.9 percent; 95 percent confidence interval 85.5 to 94.4). Five experts assessed content validity (index 0.92) and pilot testing among 20 excluded personnel gave an overall Cronbach alpha of 0.86. Counts, percentages and Wilson 95 percent confidence intervals were calculated with item-specific denominators.

Results: The analytic sample comprised 78 clinical research coordinators (52.0 percent), 51 principal or co-investigators (34.0 percent) and 21 data managers or quality auditors (14.0 percent); stratum response rates were 91.8, 91.1 and 87.5 percent. The most frequently reported barriers were therapeutic misconception (93 of 150; 62.0 percent; 95 percent confidence interval 54.0 to 69.4), language or vernacular barriers (58.7 percent; 50.7 to 66.2), restrictive eligibility criteria (52.7 percent; 44.7 to 60.5), amendments without timely re-training (48.0 percent; 40.2 to 55.9) and electronic case report form transcription delay beyond five days (46.0 percent; 38.2 to 54.0). Among coordinators, 40 of 78 (51.3 percent; 40.4 to 62.1) managed more than four active protocols, which equals 26.7 percent of all respondents, illustrating the importance of the denominator. Consent was the domain with the highest mean item prevalence (52.2 percent).

Conclusion: Consent communication, recruitment feasibility, amendment-related training, complexity-sensitive coordinator workload assessment and timely data entry are priorities for local quality improvement. A proposed, untested framework with process indicators, workflows and a twelve-month roadmap is presented. These single-institution, self-reported findings do not establish causality, participant-level event rates or national prevalence.

Keywords—clinical research coordination; protocol adherence; recruitment and retention; informed consent; therapeutic misconception; electronic data capture; Good Clinical Practice; India.

Key points—(1) Informed-consent barriers were the most prevalent domain (mean item prevalence 52.2%). (2) Over half of CRCs (51.3%) managed more than four active protocols. (3) Reported amendment re-training gaps (48.0%) and eCRF transcription delays (46.0%) point to workflow vulnerabilities. (4) Denominators matter: the same 40 CRCs are 51.3% of CRCs but 26.7% of all respondents. (5) A proposed, untested twelve-month framework is offered for local quality improvement.

I. INTRODUCTION

A. Background

Clinical research generates the evidence on which prevention, diagnosis and treatment decisions rest, but the reliability of that evidence depends heavily on what happens at the investigational site. Site teams translate protocols into daily routines: they screen participants against eligibility criteria, obtain informed consent, schedule and conduct visits, maintain source documentation, account for investigational products, report safety information and respond to monitoring queries. A weakness in any of these steps can compromise participant welfare, protocol fidelity, endpoint ascertainment and the traceability of study records [1–3].

Within the site team, the clinical research coordinator (CRC) occupies a pivotal position. The CRC interfaces with participants, investigators, ethics committees, sponsors and data systems, often across several concurrent protocols. Protocol design has become progressively more complex, with more procedures and data points per study [4]; this complexity ultimately lands on the people who operationalise it. India has become a substantial setting for clinical research, and the conduct and oversight of trials there have attracted sustained ethical scrutiny [5]. Yet empirical descriptions of how site personnel themselves experience operational barriers remain scarce, and workload, recruitment, consent and data workflows are rarely examined together.

B. Regulatory and ethical context

Good Clinical Practice (GCP) provides the international ethical and scientific quality standard for trials involving human participants. **The study was conducted between August and November 2024, when ICH E6(R2) was the operative international GCP guideline [3].** The ICH E6(R3) Principles and Annex 1 reached Step 4 and were adopted on 6 January 2025, after data collection ended; they place greater emphasis on quality by design, proportionate risk management, participant-centred consent and fit-for-purpose computerised systems [1], consistent with the critical-to-quality approach of ICH E8(R1) [2]. E6(R3) is therefore used here only as a contemporary interpretive lens for improvement priorities and not as a standard that governed data

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collection (Fig. 1). The 2024 revision of the Declaration of Helsinki, ratified on 19 October 2024 during the survey period, provides additional ethical context [6], alongside the CIOMS international guidelines [7]. In India, trials of new drugs are regulated under the New Drugs and Clinical Trials (NDCT) Rules, 2019 [8], and biomedical research is guided by the ICMR National Ethical Guidelines [9].

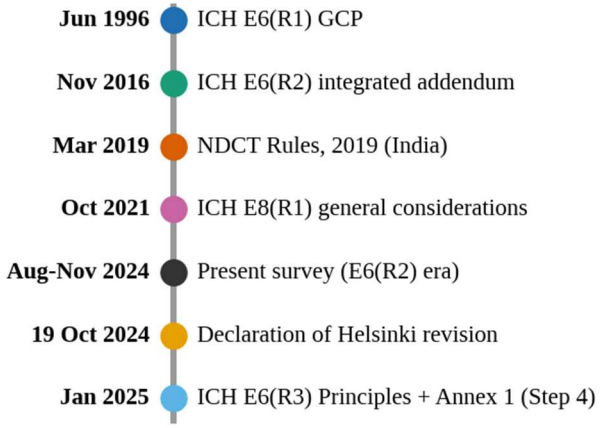


Fig. 1. Timeline of regulatory and ethical frameworks relevant to this study. The survey (August to November 2024) was conducted in the E6(R2) era and pre-dates E6(R3); later frameworks are used only as an interpretive lens.

C. Rationale and conceptual framework

Site operations can be understood as four interdependent domains: protocol adherence, recruitment and retention, informed consent, and clinical data management (Fig. 2). A coordinator who manages several complex protocols may have less protected time for amendment training, visit-window review and prompt eCRF completion. Restrictive eligibility criteria and travel costs may reduce recruitment feasibility, while communication barriers complicate consent and follow-up. These relationships are hypothesised, not tested; the framework is an organising device for a descriptive survey and for local quality improvement.

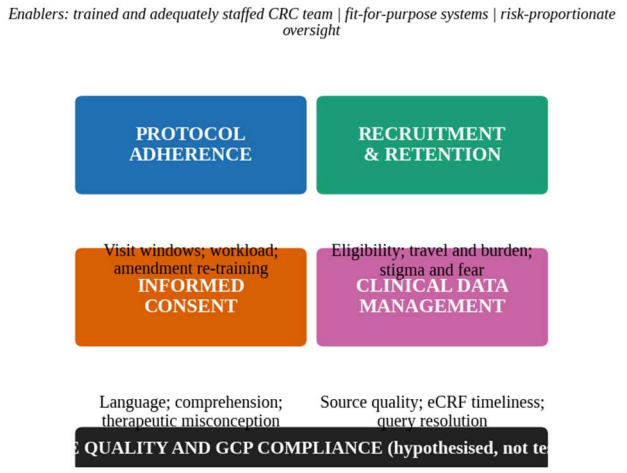


Fig. 2. Conceptual framework linking the four operational domains with site-level quality. The framework is explanatory and hypothesis-generating; causal pathways were not tested.

D. Objectives

The objectives were (1) to describe the professional profile and research experience of site personnel; (2) to estimate the reported frequency of selected operational barriers across the four domains, with appropriate denominators and interval estimates; (3) to describe CRC workload using the CRC-specific denominator; and (4) to propose a site-level quality-improvement framework grounded in the findings. The study was not designed to estimate national prevalence, identify independent predictors or test an intervention.

II. MATERIALS AND METHODS

A. Study design, setting and period

We conducted a descriptive cross-sectional survey at Prathima Institute of Medical Sciences (PIMS), Karimnagar, Telangana, India, from 1 August to 30 November 2024. The study population comprised personnel involved in Phase II–IV clinical trials and observational registry studies. The individual research professional was the unit of analysis. Reporting followed the STROBE statement for cross-sectional studies [10] (Table IV). Key terms are defined in Table I.

TABLE I. KEY CONCEPTS AND WORKING DEFINITIONS

Term	Working definition
Protocol adherence	Conduct of the study as approved, including eligibility, visit windows and procedures
Therapeutic misconception	Confusion of research purpose or design with individualised clinical care [11]
Teach-back	Participant restates key information so the explainer can check clarity of the explanation
eCRF transcription latency	Interval between a visit and entry of its data into the electronic case report form
EDC query backlog	Number of unresolved data queries pending in the electronic data capture system
Source documentation	Original records in which trial data are first recorded
CAPA	Corrective and preventive action addressing the cause of a deviation

CRC, clinical research coordinator; eCRF, electronic case report form; EDC, electronic data capture.

B. Sampling frame, sampling and participant flow

The sampling frame was the active human-research personnel registry maintained by the PIMS Institutional Ethics Committee and Clinical Trials Unit as of July 2024, comprising **N = 195** eligible professionals in three strata: CRCs (n = 88), principal and co-investigators (PIs/Co-Is; n = 72) and clinical data managers or quality auditors (CDM/QA; n = 35). Stratified random sampling was used to invite 165 personnel (84.6% of the frame; 95% CI 78.9–89.0): **85 CRCs, 56 PIs/Co-Is and 24 CDM/QA**. Invitation fractions therefore differed by stratum (96.6%, 77.8% and 68.6% of each stratum respectively), so the allocation was not proportional to stratum size.

A total of 150 personnel completed the questionnaire (response rate 90.9%; 95% CI 85.5–94.4): 78 CRCs (91.8%), 51 PIs/Co-Is (91.1%) and 21 CDM/QA (87.5%). Non-response (n = 15; 7 CRCs, 5 PIs/Co-Is, 3 CDM/QA) was attributed to scheduling conflicts (n = 9) or formal opt-out (n = 6). Twenty personnel who took part in preliminary pilot testing were separate from, and excluded from, the analytic cohort. Participant flow and stratum-level figures are shown in Fig. 3, Fig. 4 and Table II.

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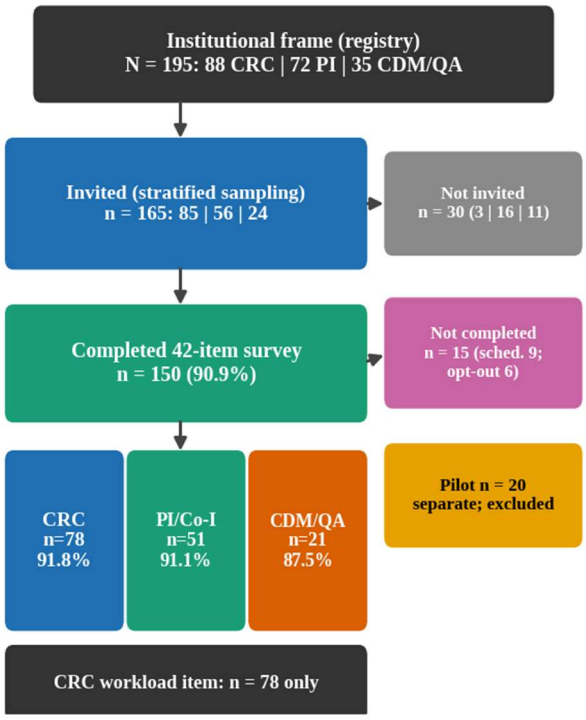


Fig. 3. STROBE participant flow from the institutional frame (N = 195) to the analytic cohort (N = 150), with stratum-specific invitation and completion counts (PIMS, Karimnagar). CDM/QA, clinical data manager or quality auditor.

TABLE II. SAMPLING FRAME, STRATUM-SPECIFIC INVITATIONS AND RESPONSE

Stratum	Frame (N)	Invited n (% of frame)	Analysed (n)	Response % (Wilson 95% CI)	Analysed / frame (%)
CRC	88	85 (96.6)	78	91.8 (84.0–96.0)	88.6
PI / Co-I	72	56 (77.8)	51	91.1 (80.7–96.1)	70.8
CDM / QA	35	24 (68.6)	21	87.5 (69.0–95.7)	60.0
Total	195	165 (84.6)	150	90.9 (85.5–94.4)	76.9

Response rate = analysed / invited within stratum. Pilot participants (n = 20) are not counted in the analysed column.

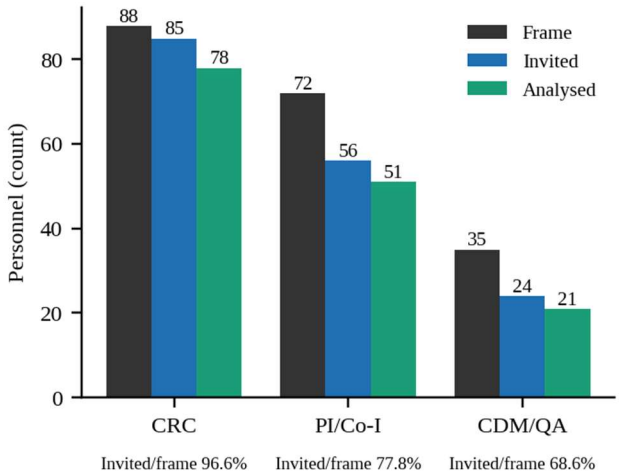


Fig. 4. Frame, invited and analysed personnel by professional stratum. Invitation coverage was highest for CRCs (96.6% of the stratum) and lowest for CDM/QA (68.6%).

Because invitation fractions differed, the unweighted pooled sample over-represents CRCs (52.0% of analysed respondents versus 45.1% of the frame) and under-represents PIs/Co-Is (34.0% versus 36.9%) and CDM/QA (14.0% versus 17.9%). Barrier data were analysed at the pooled level only, so stratum-specific or design-weighted estimates could not be produced (see Limitations).

C. Instrument development and pilot reliability

The investigators developed a structured 42-item questionnaire covering professional characteristics and four operational domains (Table III), informed by ICH GCP guidance and Central Drugs Standard Control Organisation requirements. Five clinical-trial experts reviewed the content, yielding a reported content validity index (CVI) of 0.92; the calculation method was not documented, and the CVI is conventionally interpreted with reference to the number of experts [12,13]. Pilot testing among 20 personnel gave Cronbach alpha of 0.84 (protocol adherence), 0.81 (recruitment and retention), 0.88 (informed consent), 0.85 (data management) and 0.86 overall [14,15]. These coefficients describe internal consistency in a small pilot sample; they do not establish factor structure, test–retest reliability or equivalence across professional roles.

TABLE III. STRUCTURE OF THE 42-ITEM QUESTIONNAIRE

Domain	Content assessed	Pilot α
Protocol adherence	Visit windows, workload, amendment training	0.84
Recruitment/retention	Eligibility, stigma/fear, travel and cost	0.81
Informed consent	Comprehension, language, recording	0.88
Data management	Transcription, queries, source legibility	0.85
Overall instrument	Four domains plus profile items	0.86

α, Cronbach alpha (pilot n = 20, excluded from analysis).

D. Measures and data collection

Respondents reported their professional role, research experience, time since GCP re-certification and (for CRCs) the number of concurrently active protocols. Selected barriers were captured as respondent-level endorsements; respondents could report more than one. The thresholds of more than four active protocols, more than five days for eCRF transcription and more than ten pending EDC queries are retained as questionnaire categories, not validated overload cut-offs or regulatory standards. Barrier counts indicate how many staff members reported an experience; they do not measure the proportion of participants affected or the number of verified protocol deviations.

E. Statistical analysis

Data were analysed with IBM SPSS Statistics version 28.0. Categorical variables are presented as counts and percentages with item-specific denominators: n = 78 for CRC workload and N = 150 for all other items. We computed 95% Wilson score confidence intervals from aggregate counts [16,17], because the Wilson interval has better coverage than the simple Wald interval, especially for modest sample sizes. Unweighted domain means of item prevalence were derived for description only. The intervals do not account for stratification, finite-population correction, clustering of staff within shared protocols or measurement error. No hypothesis tests or adjusted associations are reported, because only aggregate counts were available for this analysis.

F. Ethical considerations

The Institutional Ethics Committee of PIMS approved the study (IEC/PIMS/2024/CR-41; 28 July 2024). Written informed consent was obtained from all participating personnel. Participation was voluntary and responses were analysed in aggregate.

TABLE IV. STROBE REPORTING STATUS (CROSS-SECTIONAL)

Item	Status	Comment
Design and setting	Reported	Single-site cross-sectional survey, Aug–Nov 2024
Participants	Reported	Frame, stratum invitations, response and flow (Fig. 3, Table II)
Variables	Reported	Outcomes and exposures defined (Table I)
Measurement	Reported	Self-report; pilot α and CVI given
Bias	Discussed	Selection, recall, social desirability

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Item	Status	Comment
Study size	Not reported	No sample-size rationale available
Statistical methods	Reported	Descriptive; Wilson 95% CI
Missing data	Not reported	Item-level missingness unavailable
Ethics, funding	Reported	Declarations section

Items mapped to the STROBE checklist [10]; a completed checklist can be supplied on request.

III. RESULTS

A. Response and professional profile

Of 165 invited personnel, 150 completed the survey (90.9%). The analytic sample comprised 78 CRCs (52.0%), 51 PIs/Co-Is (34.0%) and 21 CDM/QA (14.0%). Nearly half had three to seven years of research experience (74/150; 49.3%), and 94 (62.7%) reported GCP re-certification within the preceding 12 months. Among CRCs, 40/78 (51.3%; 95% CI 40.4–62.1) managed more than four active protocols (Table V, Fig. 5).

TABLE V. PROFESSIONAL PROFILE OF THE ANALYTIC COHORT (N = 150)

Characteristic	n	%	95% CI
CRC	78	52.0	44.1–59.8
PI/Co-I	51	34.0	26.9–41.9
CDM/QA	21	14.0	9.3–20.5
Experience <3 years	42	28.0	21.4–35.7
Experience 3–7 years	74	49.3	41.4–57.3
Experience >7 years	34	22.7	16.7–30.0
GCP re-certified ≤12 months	94	62.7	54.7–70.0
GCP re-certified >12 months	56	37.3	30.0–45.3
CRC ≤4 protocols (of 78)	38	48.7	37.9–59.6
CRC >4 protocols (of 78)	40	51.3	40.4–62.1

CI, Wilson 95% confidence interval. CRC workload percentages use n = 78.

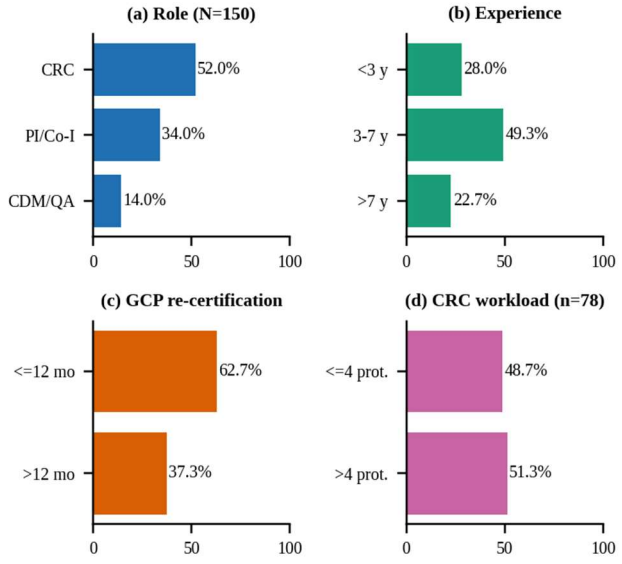


Fig. 5. Professional profile of respondents: (a) role, (b) research experience, (c) time since GCP re-certification, (d) CRC workload among 78 CRCs.

B. Instrument internal consistency

The overall pilot alpha was 0.86, with domain coefficients from 0.81 to 0.88 (Fig. 6). These values lie within the range conventionally regarded as acceptable to good [15] but derive from 20 respondents who were not part of the analytic sample.

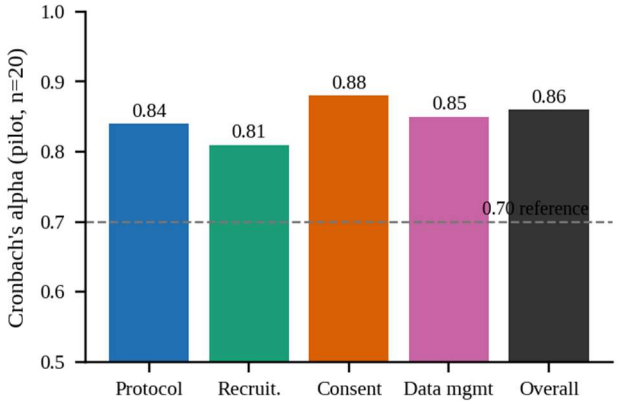


Fig. 6. Internal consistency (Cronbach alpha) from pilot testing (n = 20). The 0.70 line is a conventional reference, not a pass/fail threshold.

C. Reported operational barriers

Therapeutic misconception was the most frequently reported barrier (93/150; 62.0%; 95% CI 54.0–69.4), followed by language or vernacular barriers (88/150; 58.7%; 50.7–66.2) and restrictive eligibility criteria (79/150; 52.7%; 44.7–60.5). Amendments without timely re-training were reported by 72 respondents (48.0%). In data management, 69 (46.0%) reported eCRF transcription delays exceeding five days and 66 (44.0%) more than ten pending EDC queries. Table VI and Fig. 7 present all twelve barriers. Because intervals overlap broadly and respondents contributed to several items, the ranking is descriptive and not a tested ordering.

TABLE VI. REPORTED OPERATIONAL BARRIERS WITH WILSON 95% CIS

Domain	Barrier	n/N	%	95% CI
Protocol	CRC workload >4 protocols	40/78	51.3	40.4–62.1
Protocol	No timely amendment re-training	72/150	48.0	40.2–55.9
Protocol	Out-of-window visits	58/150	38.7	31.2–46.7
Recruit.	Restrictive eligibility	79/150	52.7	44.7–60.5
Recruit.	Stigma/fear of drug harm	71/150	47.3	39.5–55.3
Recruit.	Financial/travel constraints	63/150	42.0	34.4–50.0
Consent	Therapeutic misconception	93/150	62.0	54.0–69.4
Consent	Language/vernacular barriers	88/150	58.7	50.7–66.2
Consent	Audio-visual recording hesitation	54/150	36.0	28.8–43.9
Data	eCRF transcription >5 days	69/150	46.0	38.2–54.0
Data	EDC query backlog >10	66/150	44.0	36.3–52.0
Data	Illegible paper source records	52/150	34.7	27.5–42.6

Multiple responses permitted; percentages do not sum to 100%. CIs describe respondent proportions, not participant-level event rates.

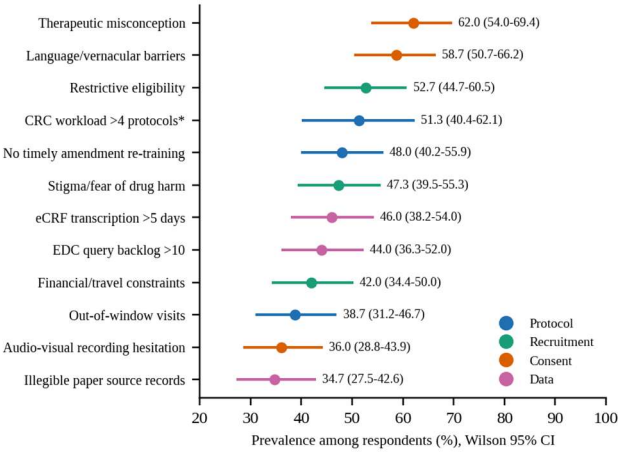


Fig. 7. Reported operational barriers with Wilson 95% confidence intervals, coloured by domain. *Denominator is 78 CRCs; all other items use 150.

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D. The importance of the denominator

The CRC workload item applies only to coordinators. Expressed among the 78 CRCs it is 51.3%, but expressed among all 150 respondents the same 40 persons yield 26.7% (95% CI 20.2–34.3), a figure that is arithmetically correct yet answers a different question (Fig. 8). Direct visual comparison of the CRC workload bar with whole-cohort items should therefore be avoided or explicitly qualified. Appendix Fig. A1 gives the decision rule applied.

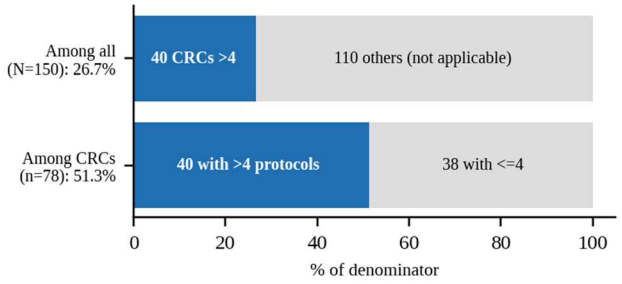


Fig. 8. Why the denominator matters: the same 40 CRCs represent 51.3% of CRCs but 26.7% of the full cohort.

E. Domain-level patterns

Averaging item-level prevalences gives a descriptive domain profile (Table VII, Fig. 9): informed consent had the highest unweighted mean (52.2%), followed by recruitment (47.3%), protocol adherence (46.0%) and data management (41.6%). The consent domain was also the most heterogeneous, from therapeutic misconception (62.0%) to audio-visual recording hesitation (36.0%). These means are not scale scores and carry no inferential weight.

TABLE VII. DOMAIN-LEVEL DESCRIPTIVE SUMMARY

Domain	Items	Range (%)	Mean (%)	Highest item
Protocol adherence	3	38.7–51.3	46.0	CRC workload (of CRCs)
Recruitment/retention	3	42.0–52.7	47.3	Restrictive eligibility
Informed consent	3	36.0–62.0	52.2	Therapeutic misconception
Data management	3	34.7–46.0	41.6	eCRF latency >5 days

Means are unweighted averages of item percentages; the protocol domain mixes denominators 78 and 150.

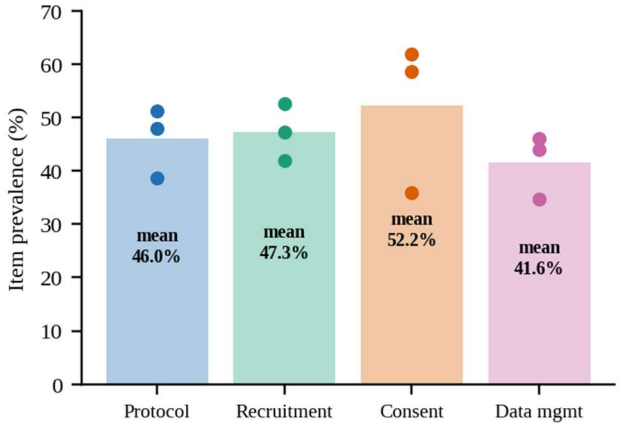


Fig. 9. Domain-level item prevalence: points are individual items; bars show the unweighted domain mean.

F. Precision of the estimates

With N = 150 the Wilson half-width is at most about 8 percentage points, whereas for the CRC subgroup (n = 78) it approaches 11 points, and for the 21 CDM/QA respondents it exceeds 19 points (Fig. 10). Role-specific estimates would therefore be imprecise even if participant-level data were available, an argument for larger multicentre samples.

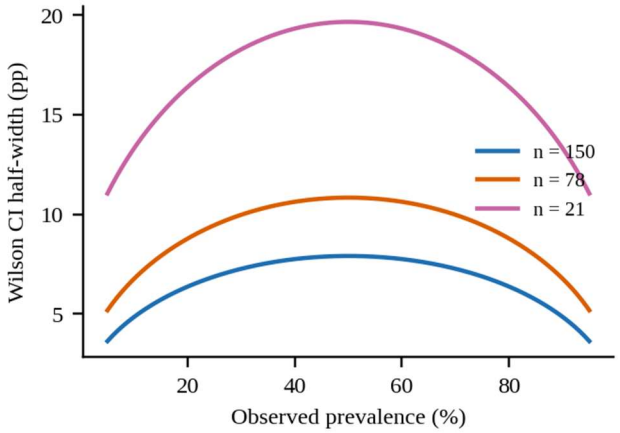


Fig. 10. Wilson 95% CI half-width by observed prevalence for sample sizes of 150, 78 and 21.

IV. DISCUSSION

A. Principal findings

In this single-institution survey, research personnel most often reported challenges around consent communication, namely therapeutic misconception (62.0%) and language barriers (58.7%), followed by restrictive eligibility criteria (52.7%), delayed amendment-related re-training (48.0%) and delays in electronic data workflows. More than half of CRCs managed more than four active protocols. These findings support a view of site quality as an integrated system, but they describe staff experience, not independently verified events. Because staff share studies, several reports may refer to the same underlying problem. Table VIII summarises how these results should and should not be read.

B. Consent communication and therapeutic misconception

Therapeutic misconception arises when participants conflate research with individualised care or assume that study procedures are selected for their personal benefit [11]. That 62.0% of staff reported it is a signal to review consent communication; it does not mean that 62.0% of participants held the misconception, because understanding was not measured. A signed form documents a process, not comprehension. A meta-analysis found that the proportion of participants understanding different consent components varied from 52.1% to 75.8% [18], indicating that incomplete understanding is a global problem and not a uniquely local one. Consent quality has long been a concern [19,20], and a recent systematic review noted wide variation in the tools used to measure understanding [21].

Evidence on remedies is encouraging but conditional. A systematic review found that improved understanding was most consistently associated with interactive discussion between participant and study team member [22], and a review of 54 randomised interventions suggested that understanding can improve with added discussion or feedback, although effects vary [23]. Language barriers (58.7%) point to practical needs: ethics-approved translations, identification of preferred language before the encounter, trained interpreters or qualified bilingual staff, and documentation of the version used. Teach-back should be framed as a check on the explainer's clarity, not an examination of the participant. Hesitation about audio-visual recording (36.0%) should be read against Indian regulatory requirements for trials of new drugs [8,9]; where recording is required, staff should explain the process and protect privacy through controlled access and secure storage.

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C. Recruitment and retention

Restrictive eligibility, fear of experimental harm and travel or financial constraints were each reported by over 40% of respondents, suggesting that recruitment difficulty arises from protocol design and from the circumstances of potential participants. Eligibility criteria should be scientifically justified and no narrower than needed to protect participants and answer the research question; any change must go through sponsor and ethics channels. The most recent Cochrane review identified 65 recruitment strategies but only five supported by high-certainty evidence [24], and retention strategies show similar variability in evidence quality [25]. Local audits should therefore record reasons for screen failure, non-enrolment and discontinuation separately, since the survey gave no actual withdrawal or retention rates.

D. Protocol adherence and coordinator capacity

That 51.3% of CRCs managed more than four active protocols identifies a workload pattern worthy of assessment; it does not show that these coordinators were overloaded or that workload caused deviations. Protocol count is a crude proxy: phase, participant volume, visit frequency, investigational-product accountability, safety reporting and monitoring intensity differ widely [4]. A complexity-sensitive capacity assessment is therefore preferable to a fixed ratio. The 48.0% reporting amendments without timely re-training suggests examining version control and task-specific competency checks; recent GCP re-certification does not establish that staff were trained on a given amendment. Risk-proportionate oversight of critical processes is consistent with regulatory thinking [1,26].

E. Data workflows and digital systems

Transcription delays (46.0%), query backlogs (44.0%) and illegible paper records (34.7%) point to the whole source-to-database pathway. Electronic source data can improve traceability when systems are validated, access-controlled and audit-trailed [27–29], but digitisation alone does not secure quality: roles, training, change control, backup and downtime procedures remain necessary. The ALCOA+ attributes (attributable, legible, contemporaneous, original, accurate, complete, consistent, enduring, available) offer a practical lens for source records [30]. Sites should monitor queries by both count and age, because many new queries differ operationally from a few long-standing critical ones. International guidance informs system design but does not by itself establish Indian legal requirements.

TABLE VIII. INTERPRETATION GUIDE FOR READERS

Tempting reading	Appropriate reading
62% of participants had therapeutic misconception	62% of staff reported it as a barrier; understanding was not measured
51.3% of all staff are overloaded	51.3% of CRCs reported >4 active protocols; this is not a validated overload cut-off
Barrier ranking is statistically tested	Ranks are descriptive; CIs overlap and respondents are shared
Results apply to India	Single teaching institution; no national estimate
Workload causes deviations	Cross-sectional; no temporal or causal inference
Results represent all personnel equally	Invitation fractions differed by stratum; pooled results are unweighted

Guide to avoiding over-interpretation of aggregate, self-reported data.

F. Positioning within the wider literature

Three aspects of the present findings align with the broader evidence. First, the proportion of staff reporting therapeutic misconception is consistent with the long-recognised difficulty of separating research from care [11,19] and with the incomplete understanding documented across three decades of consent studies [18]. Second, the prominence of eligibility and access barriers mirrors the observation that recruitment problems are common and that few strategies have robust evidence [24]. Third, the data-workflow findings echo regulatory emphasis on traceable, contemporaneous records and controlled computerised systems [28–30]. The study adds a site-personnel perspective across four domains simultaneously, with transparent denominators and interval estimates. It does not allow comparison with other Indian or international sites, because comparable surveys using the same definitions are not available. Replication with a common instrument would permit benchmarking and the study of between-site variation.

G. Role-specific implications

The findings carry different messages for different stakeholders (Table IX). Because the barriers span participant-facing and data-facing work, improvement is unlikely to succeed if assigned to the CRC alone; it needs investigator leadership, data-management ownership and ethics-committee engagement.

TABLE IX. ROLE-SPECIFIC IMPLICATIONS AND FIRST ACTIONS

Role	Implication	First action
CRC	Workload and consent communication are daily pressure points	Log active protocols and visit burden; use teach-back
PI/Co-I	Responsible for delegation, training and oversight	Verify training before delegating amended tasks
Data manager/QA	Latency and query backlog affect timeliness	Set query-age views; triage by criticality
Ethics committee	Consent material and language versions need review	Check approved translations and recording procedures
Institution	Systems and staffing shape feasibility	Support validated eSource/EDC and capacity audits

Actions are proposals requiring local approval and governance.

H. Ethical and equity considerations

Quality-improvement measures aimed at consent, recruitment and data speed must not create pressure that undermines participant protection. Targets for enrolment or rapid data entry should never shorten the consent discussion, discourage questions or favour participants who are easier to reach. Language access and travel or cost support are equity measures as well as feasibility measures: when only literate, urban or majority-language participants can be enrolled, the evidence generated is less generalisable and the burden of research is distributed unfairly [7,9]. Teach-back and comprehension checks should be applied supportively and documented without stigmatising participants. Staff wellbeing is also an ethical and quality issue: if more than half of CRCs manage more than four protocols, sustained overload may affect attention to detail, turnover and the quality of participant contact. Workload review should therefore be framed as support for staff and participants alike, not as a performance audit of individuals.

I. Strengths and limitations

Strengths include representation of three professional groups drawn from a documented institutional frame, a 90.9% completion rate with stratum-specific response rates, expert content review, a pilot internal-consistency assessment, explicit denominators and Wilson intervals. The single teaching institution limits transferability. Self-report may be affected by recall and social-desirability bias, and neither staff reports nor documentation quality were verified against trial records. Invitation fractions differed across strata (96.6%, 77.8%, 68.6%) and pooled estimates are unweighted, so they over-represent CRCs relative to the frame; stratum-specific barrier estimates were unavailable. The within-stratum random-selection mechanism, non-respondent characteristics, recall period and item-level missingness were not documented, so selection bias cannot be fully evaluated. The full questionnaire was not available for publication, and the small pilot limits confidence in psychometric stability. Staff reports may be correlated within shared protocols, which the unweighted intervals ignore. Finally, the proposed framework was not evaluated, and neither participant comprehension nor actual recruitment and retention was measured. Principal sources of bias and mitigation strategies are summarised in Table X.

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TABLE X. PRINCIPAL SOURCES OF BIAS AND MITIGATION

Source	Issue	Mitigation in future work
Selection	Non-proportional invitation; non-response 9.1%	Proportional or weighted allocation; compare non-responders
Information	Self-reported barriers	Verify against logs, EDC timestamps, training records
Social desirability	Under-reporting of problems	Anonymous administration
Measurement	Thresholds not validated	Validate; test–retest; role equivalence
Clustering	Shared protocols	Cluster-aware methods; protocol-level data
Confounding	Study complexity not measured	Collect complexity and volume

V. IMPLICATIONS FOR PRACTICE AND SITE-LEVEL QUALITY IMPROVEMENT

The proposals below translate the survey findings into local actions. They are recommendations informed by GCP principles and the cited literature; they were not implemented or evaluated in this study. Baseline process indicators should be measured before numerical targets are set, and targets must reflect protocol risk, resources and applicable approvals.

A. From barriers to actions

Fig. 11 maps each reported barrier to a proposed action and a measurable process indicator, and Table XI consolidates the framework with review frequencies.

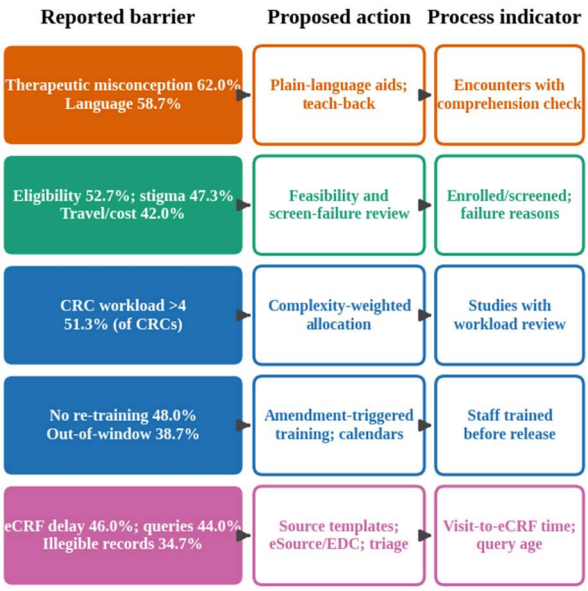


Fig. 11. Evidence-to-action map linking reported barriers (with prevalence) to proposed actions and process indicators.

TABLE XI. PROPOSED SITE-LEVEL QUALITY-IMPROVEMENT FRAMEWORK

Priority	Proposed action	Process indicator	Review
Workload	Complexity and capacity audit; complexity-weighted allocation	Active studies with documented workload review	Quarterly
Training	Role-based refreshers; amendment briefings before affected tasks; competency checks	Staff trained for assigned tasks / staff assigned	Monthly; per amendment
Consent	Approved plain-language aids; preferred-language support; teach-back	Encounters with documented comprehension check	Monthly
Recruitment	Review eligibility burden, screen failures, access barriers	Enrolled/screened; screen-failure reasons	Monthly
Data quality	Source templates; validated systems; query triage	Median visit-to-eCRF interval; query age	Weekly/ monthly
Governance	Risk-based monitoring; deviation review; CAPA	Repeat deviations; overdue CAPA	Quarterly

CAPA, corrective and preventive action.

B. Participant-centred consent workflow

A robust consent process begins before the participant enters the consultation room (Fig. 12). Staff should identify language and literacy needs, have the current approved document available, provide privacy and sufficient time, explain without therapeutic overstatement, invite questions and use teach-back to detect misunderstanding. If comprehension is inadequate, the explanation is repeated or adapted, and the decision remains voluntary with no penalty for refusal or withdrawal [6,7]. Any new consent material or procedure requires ethics approval before use.

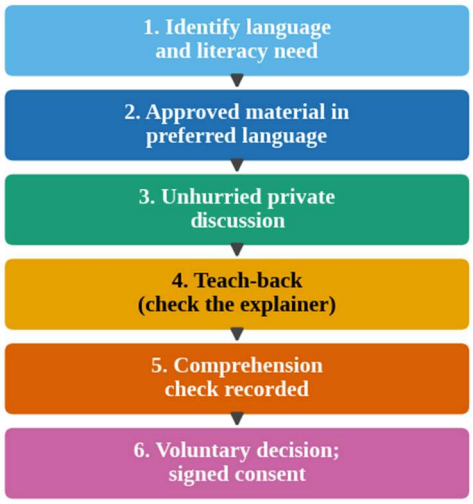


Fig. 12. Proposed participant-centred consent workflow with a re-explanation loop when comprehension is inadequate.

C. Clinical data pathway and control points

Fig. 13 and Table XII set out the proposed data pathway from source creation to audit readiness. Each stage has a minimum control and an evidence record, consistent with expectations for computerised systems and electronic records [28,29]. A query dashboard should show open-query count, median and oldest age, critical-query count, owner and overdue proportion; triage should prioritise participant safety, eligibility, primary endpoints and serious adverse events, avoiding indiscriminate queries for non-critical discrepancies.

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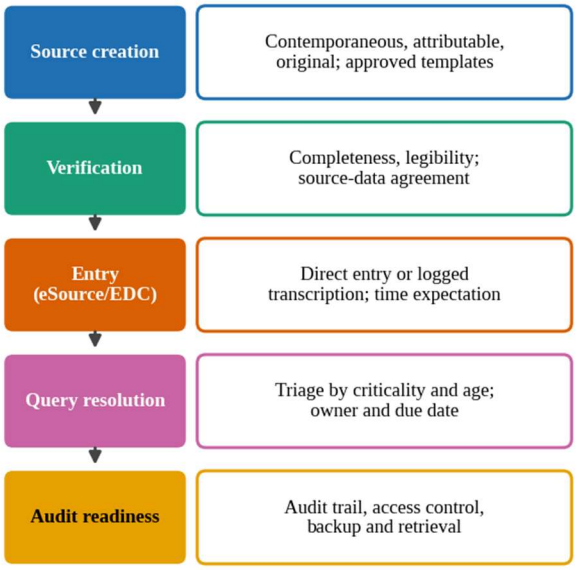


Fig. 13. Proposed clinical data pathway with control points from source creation to audit readiness, supported by validation, change control, backup and training.

TABLE XII. CONTROL POINTS ALONG THE DATA PATHWAY

Stage	Minimum control	Evidence/record
Source creation	Attributable, legible, contemporaneous, original, accurate	Author/date/time; approved template
Verification	Completeness, legibility, authorised originator	Review checklist
Entry	Direct entry or logged transcription; time expectation	eCRF timestamp; entry log
Query resolution	Triage by criticality and age; owner and due date	Query log; escalation record
Audit readiness	Access control, audit-trail review, backup, retrieval	Access review; backup test

Controls should be proportionate to system risk and documented before reliance for trial-critical data.

D. Plan–Do–Check–Act cycle and twelve-month roadmap

Implementation is best organised as an explicit improvement cycle (Fig. 14) with a baseline audit, named owners, a pilot phase, monthly dashboard review and CAPA before scale-up. Fig. 15 gives an illustrative twelve-month schedule across five workstreams; timing is indicative and changes to consent materials, study procedures or computerised systems require appropriate approval and governance.

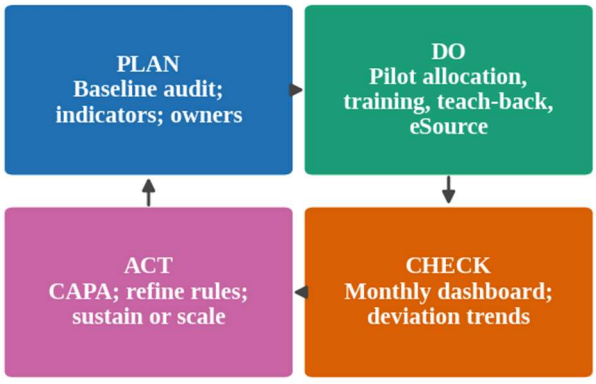


Fig. 14. Plan–Do–Check–Act cycle for the site improvement programme.

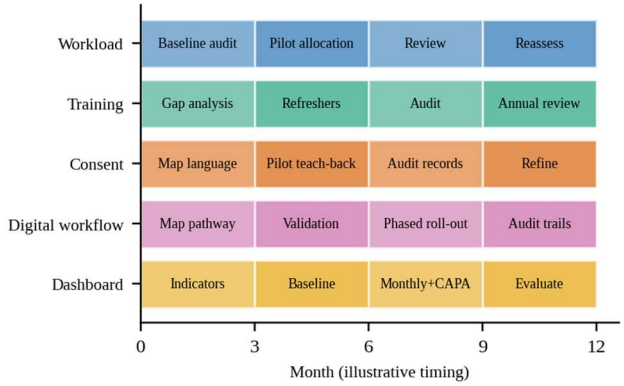


Fig. 15. Illustrative twelve-month implementation roadmap (proposed, not evaluated).

E. Operational tools for the highest-priority barriers

Amendment control. Because 48.0% reported amendments without timely re-training, release should be tied to training and authorisation (Fig. 16, Table XIII): approval status is confirmed, affected roles and documents are identified, training is delivered and logged before implementation, and superseded versions are withdrawn.

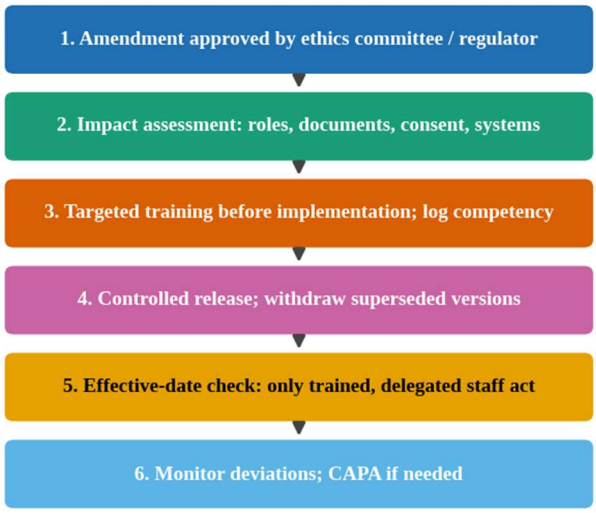


Fig. 16. Proposed amendment-triggered training and controlled-release process.

TABLE XIII. AMENDMENT RELEASE CHECKLIST

Step	Check	Evidence
Approval	Current approval and version confirmed	Approval letter; version log
Impact	Eligibility, procedures, safety, consent, data fields reviewed	Impact assessment
Training	Affected roles trained before go-live	Training log; competency note
Documents	Superseded versions withdrawn; new aids issued	Document control record
Go-live	Only trained, delegated staff perform changed tasks	Delegation log

Changes to consent material or procedures require ethics approval before use.

Query triage. Where 44.0% reported more than ten pending queries, triage by criticality and age avoids treating all discrepancies alike (Fig. 17). Safety, eligibility, primary-endpoint and serious-adverse-event queries are resolved first and traceably [26,29]; recurring themes are fed back into training and source templates.

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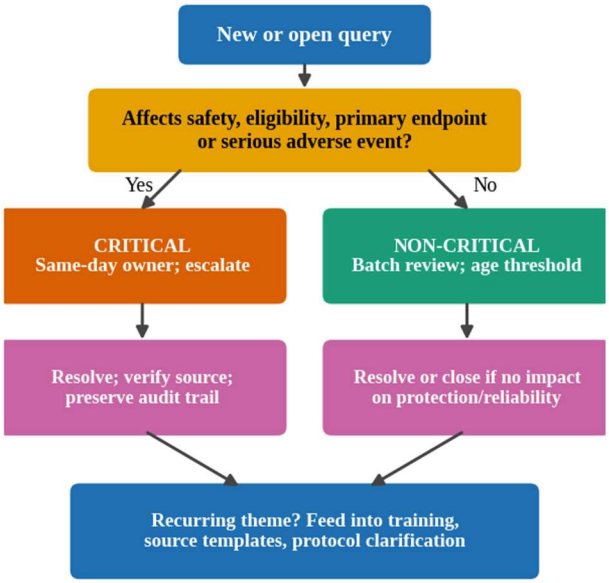


Fig. 17. Proposed query triage logic prioritising critical data and participant protection.

Complexity-weighted workload. Because 51.3% of CRCs reported more than four active protocols, a simple protocol count should be replaced by a composite workload score reflecting the factors in Fig. 18 and Table XIV. No weights are proposed here; they should be developed locally and validated against objective measures such as overtime, visit-window deviations and data-entry lag.

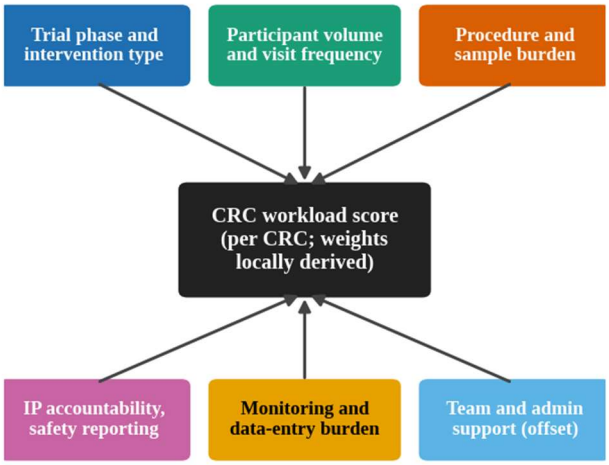


Fig. 18. Components of a proposed complexity-weighted CRC workload score (weights to be locally derived).

TABLE XIV. CANDIDATE WORKLOAD-SCORE COMPONENTS

Component	Example measure	Source
Phase/intervention	Phase II–IV; drug, device, observational	Protocol
Participants and visits	Active participants; visits per month	Visit schedule
Procedures	Samples, imaging, questionnaires per visit	Schedule of assessments
Accountability/safety	IP reconciliation; SAE reports	IP log; safety log
Monitoring/data	Monitoring visits; eCRF forms per visit	Monitoring plan; EDC
Support (offset)	Administrative or data-entry support hours	Rota

SAE, serious adverse event; IP, investigational product.

F. Indicators and self-assessment

Each indicator needs a written numerator, denominator, data source, owner, frequency and escalation threshold (Table XV). Sites can use Table XVI for a rapid self-assessment before starting a baseline audit.

TABLE XV. PROPOSED KEY PERFORMANCE INDICATORS

Indicator	Numerator / denominator	Source	Freq.
Workload coverage	Studies with workload review / active studies	Study register	Qtrly
Training currency	Staff trained before go-live / affected staff	Training log	Per amendment
Comprehension check	Consent encounters with check / reviewed	Consent audit	Monthly
Screen-to-enrolment	Enrolled / screened	Screening log	Monthly
Data timeliness	Median days visit to eCRF	EDC report	Weekly
Query ageing	Queries over site threshold / open queries	Query log	Weekly
CAPA effectiveness	CAPAs with effectiveness check / closed	CAPA log	Qtrly

Targets should be set only after baseline measurement and risk assessment.

TABLE XVI. SITE SELF-ASSESSMENT CHECKLIST

Question	Yes/No
Is complexity-based CRC workload reviewed for each active protocol?	
Is staff training verified before each amendment goes live?	
Are approved consent materials available in each language used?	
Is teach-back or an equivalent comprehension check documented?	
Are eligibility criteria and screen failures reviewed regularly?	
Are source templates in use and legible records ensured?	
Is median visit-to-eCRF time monitored?	
Are open queries tracked by age and criticality?	
Are CAPAs checked for effectiveness?	

A "No" response indicates an area for baseline audit.

G. Regulatory-to-operational mapping

Table XVII links recurring GCP and ethics themes to concrete site practices that correspond to the barriers observed. The table is a practical translation, not a legal interpretation; Indian sites remain bound by national rules and by their ethics committee and sponsor requirements.

TABLE XVII. FROM GUIDELINE THEMES TO SITE PRACTICE

Theme	Site practice	Ref.
Quality by design; critical-to-quality factors	Identify protocol steps critical to participant safety and data reliability and focus oversight on them	[1,2]
Participant-centred consent	Approved language versions; unhurried private discussion; comprehension check	[6,7,9]
Regulated trials in India	Follow NDCT Rules provisions on consent, ethics review and records	[8]
Risk-proportionate monitoring	Concentrate oversight on critical data and processes	[1,26]
Computerised systems	Validation, access control, audit trail, backup, change control	[28,29]
Data integrity	ALCOA+ source records and traceable corrections	[27,30]

All entries summarise general guideline themes; consult the source documents for exact requirements.

H. Visit-window management

Because 38.7% reported out-of-window follow-up visits, a visit-window routine (Fig. 19) can be added to the quality programme. The aim is not to eliminate every deviation, since some are unavoidable, but to detect them early, document reasons, assess safety and data impact, and prevent recurrence.

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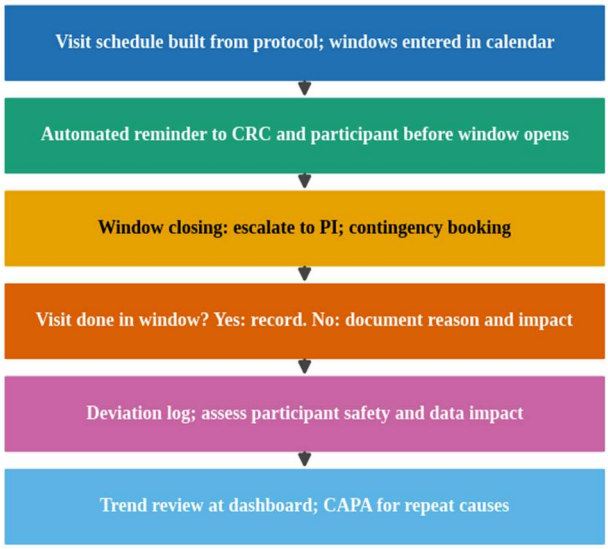


Fig. 19. Proposed visit-window management routine from calendar set-up to trend review.

I. Roles and accountability

Improvement efforts fail when responsibility is diffuse. Fig. 20 illustrates a responsibility matrix for the five main activities. The allocation is an example to be adapted to local delegation logs and standard operating procedures; accountability for each activity should rest with one named role, and its owner should appear on the dashboard.

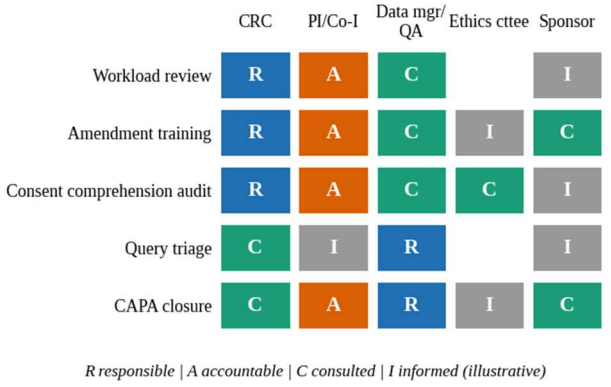


Fig. 20. Illustrative responsibility matrix (R, A, C, I) for the main improvement activities.

J. Research agenda

- Multicentre replication using a standardised, validated instrument, documented sampling frames and proportional or design-weighted allocation [17].
- Objective process measures (EDC timestamps, deviation logs, training records) alongside staff perceptions.
- Direct assessment of participant understanding using validated measures [21].
- Evaluation of the improvement package using controlled before–after or stepped-wedge designs, with cluster-aware analysis.

VI. CONCLUSION

In this single-institution survey, research personnel most often reported therapeutic misconception and language barriers, followed by restrictive eligibility criteria, delayed amendment-related training, substantial concurrent protocol allocation among CRCs and delays in electronic data workflows. These findings identify local priorities for consent communication, feasibility review, complexity-sensitive workload assessment, training and data-quality monitoring. They remain descriptive staff reports and should not be read as causal associations, verified participant-level event rates or estimates for India as a whole. Multicentre studies with objective measures are needed to assess wider applicability.

VII. DECLARATIONS

Ethics approval: Institutional Ethics Committee, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India (IEC/PIMS/2024/CR-41; 28 July 2024).

Consent to participate: Written informed consent was obtained from all participating research personnel.

Funding: Self-funded; no external grant support.

Competing interests: The authors declare no competing financial or non-financial interests.

Author contributions: A. G. Agrawal: conceptualisation, instrument development and validation, supervision, drafting. A. Agrawal: literature review, data curation, figure preparation, critical revision. Both authors approved the final manuscript.

Data availability: De-identified survey data are available from the corresponding author on reasonable academic request, subject to institutional and ethics committee permissions.

Acknowledgements: The authors thank the clinical research coordinators, investigators and research personnel at PIMS, Karimnagar.

TABLE XVIII. ABBREVIATIONS

Term	Meaning
ALCOA+	Attributable, legible, contemporaneous, original, accurate (plus complete, consistent, enduring, available)
CAPA	Corrective and preventive action
CDM/QA	Clinical data manager / quality auditor
CI	Confidence interval
CRC	Clinical research coordinator
CVI	Content validity index
eCRF	Electronic case report form
EDC	Electronic data capture
GCP	Good Clinical Practice
ICH	International Council for Harmonisation
NDCT	New Drugs and Clinical Trials (Rules)
PI/Co-I	Principal/co-investigator

APPENDICES

Appendix A. Barrier categories and denominators

TABLE XIX. REPORTED BARRIER CATEGORIES AND DEFINITIONS USED IN ANALYSIS

Barrier (domain)	Category definition	Denom.
CRC workload (Protocol)	>4 concurrently active protocols	78 CRCs
Amendments (Protocol)	Amendment implemented without timely re-training	150
Out-of-window visits (Protocol)	Follow-up visit outside protocol window	150
Eligibility (Recruit.)	Restrictive eligibility criteria	150
Stigma/fear (Recruit.)	Fear of experimental drug harm	150
Travel/cost (Recruit.)	Financial or travel constraints	150
Misconception (Consent)	Therapeutic misconception in participants/families	150
Language (Consent)	Language/vernacular barriers	150
Recording (Consent)	Hesitation about audio-visual recording	150
eCRF delay (Data)	Transcription >5 days	150
Query backlog (Data)	>10 pending EDC queries	150
Illegible source (Data)	Illegible paper source documentation	150

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Thresholds are questionnaire categories, not validated cut-offs or regulatory standards.

Appendix B. Wilson interval: worked example and sensitivity check

TABLE XX. WILSON 95% CI FOR THERAPEUTIC MISCONCEPTION (93/150)

Step	Calculation	Value
Observed proportion	93 / 150	0.6200
Adjusted denominator	$1 + z^2/n$, z = 1.96	1.0256
Adjusted centre	$(p + z^2/2n)$ / den	0.6170
Half-width	$z \cdot \sqrt{(p(1-p)/n + z^2/4n^2)}$ / den	0.0768
95% CI	centre ± half-width	54.0–69.4%

Method follows Wilson [16]; coverage advantages are reviewed by Brown et al. [17].

TABLE XXI. WILSON VERSUS WALD INTERVALS (SENSITIVITY CHECK)

Item	%	Wilson	Wald
Therapeutic misconception	62.0	54.0–69.4	54.2–69.8
Language/vernacular barriers	58.7	50.7–66.2	50.8–66.5
Restrictive eligibility	52.7	44.7–60.5	44.7–60.7
CRC workload >4 protocols	51.3	40.4–62.1	40.2–62.4
No timely amendment re-training	48.0	40.2–55.9	40.0–56.0
Stigma/fear of drug harm	47.3	39.5–55.3	39.3–55.3
eCRF transcription >5 days	46.0	38.2–54.0	38.0–54.0
EDC query backlog >10	44.0	36.3–52.0	36.1–51.9
Financial/travel constraints	42.0	34.4–50.0	34.1–49.9
Out-of-window visits	38.7	31.2–46.7	30.9–46.5
Audio-visual recording hesitation	36.0	28.8–43.9	28.3–43.7
Illegible paper source records	34.7	27.5–42.6	27.1–42.3

The two methods agree to within about one percentage point at these sample sizes and proportions.

Appendix C. Consent encounter audit form

TABLE XXII. CONSENT ENCOUNTER AUDIT ITEMS

Audit item	Met?
Current ethics-approved version used	
Preferred language identified and recorded	
Approved translation or interpreter used	
Private setting and adequate time provided	
Research purpose distinguished from routine care	
Randomisation, uncertainty and alternatives explained (where relevant)	
Teach-back or comprehension check documented	
Questions invited and answered	
Voluntariness and right to withdraw stated	
Audio-visual recording handled per applicable requirements	

For internal audit use; adapt to the study and ethics committee conditions.

Appendix D. Denominator decision flow

Mixed denominators are a common source of misreporting. Fig. A1 summarises the rule applied in this study and can be reused in similar surveys.

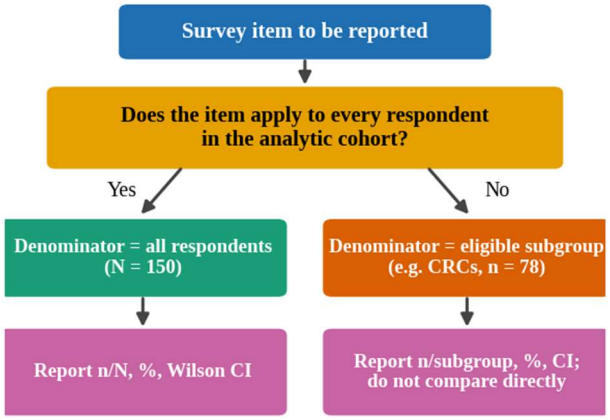


Fig. A1. Decision flow for selecting and reporting item denominators in a mixed-role survey.

Appendix E. Glossary for postgraduate readers

TABLE XXIII. GLOSSARY OF METHODOLOGICAL TERMS

Term	Plain-language meaning
Cross-sectional survey	Measures exposures or experiences at one point in time; cannot show cause and effect
Denominator	The group in which the percentage is calculated
Wilson 95% CI	Range of plausible population proportions given the sample; better behaved than the simple Wald interval
Cronbach alpha	Index of how consistently items vary together; not proof of validity
Content validity index	Proportion of experts rating items as relevant
Social-desirability bias	Tendency to give answers that appear favourable
Therapeutic misconception	Mistaking research for personalised treatment
Teach-back	Asking people to explain information in their own words to check the explanation
CAPA	Action to correct a problem and prevent recurrence

Appendix F. Graphical abstract

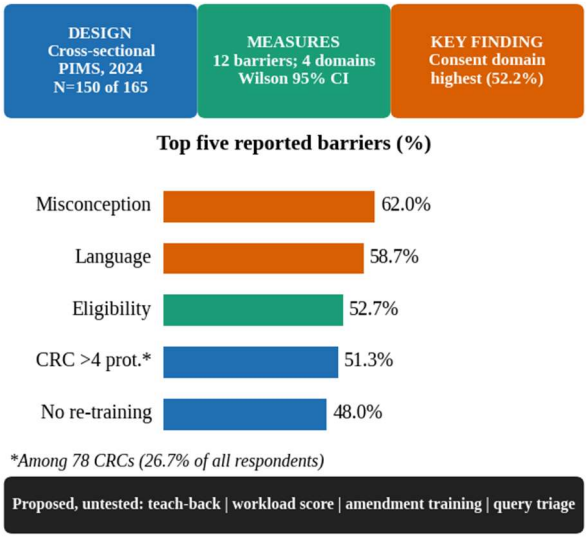


Fig. A2. Graphical abstract summarising design, principal findings and the proposed improvement package.

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