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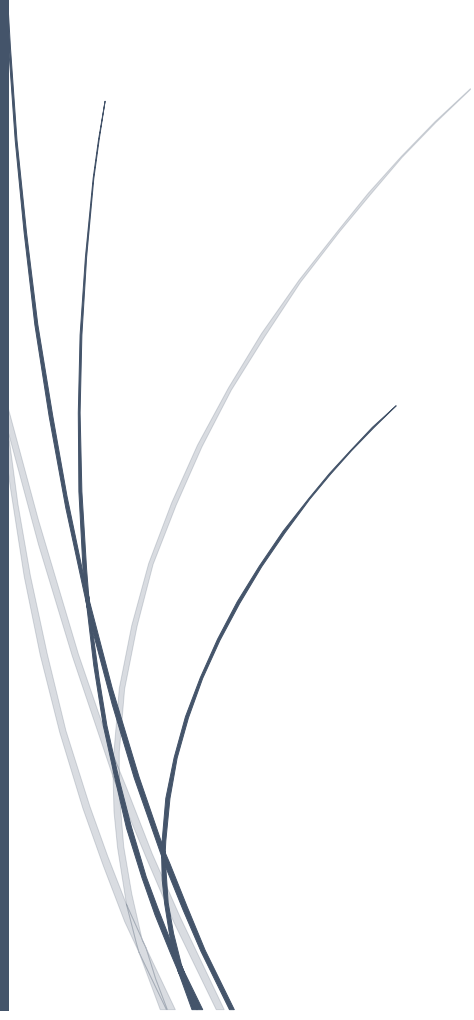
National Institute for Health and Care Research

Global Health Research Centre for Multiple Long-Term Conditions



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1. Background

Presence of two or more chronic conditions in a patient is referred to as multi-morbidity or multiple long-term conditions (MLTC)[1]. The prevalence of MLTC is high in India[2]. Yet, the health system does not address MLTC but focus on single disease conditions. Hence, there is an urgent need to develop and implement new context-specific, patient-centred, equitable, resource-sensitive, integrated management strategies with a continuum of care approach.

The public health systems of India is undergoing rapid transformation. To modernise, transform and universalise primary care, the Government of India launched the Healthy India scheme (Ayushman Bharat Yojana), under which 150,000 sub centres (per 5,000 population) and Primary Health Centres (PHCs) (per 20,000-30,000 population) are transformed to Health and Wellness Centres (HWCs)[3]. These centres are envisaged to deliver a range of services encompassing the full continuum of care from health promotion, prevention, management and rehabilitation to the rural and urban poor, who often belong to low socio-economic status. Thus, this is an opportune moment to develop, implement and evaluate the concept of responsive patient-centred MLTC care in India through large system health system transformation by establishing a Global Health Research Centre for MLTC.

2. Objectives

The proposed Centre aims to bring in a large system transformation with respect to MLTC by engaging people with MLTC, caregivers, communities, frontline health workers, health system leadership and policy makers, to co-design, implement and evaluate an integrated, technology-enabled, patient-centred, health system intervention to improve care for people living with MLTC. The objectives are divided into short-, medium- and long-term.

Short-term objectives:

1. Conduct health system assessments.
2. Assess case mix among patients visiting PHCs for treatment of various conditions.
3. Identify the challenges for people living with MLTC, caregivers, and healthcare providers.

Medium-term objectives:

4. Co-design an integrated, technology-enabled, patient-centred, health system intervention consisting of an EDSS, assisted telemedicine and patient-facing application to improve MLTC care.

5. Conduct a pilot study to assess the intervention acceptability, recruitment and retention rates, feasibility, fidelity, delivery, and costs.
6. Involve Community Champions to develop patient networks to support management of MLTC and to help new patients navigate the health system.
7. Conduct a definitive cluster randomised controlled trial (**cRCT**) to assess the effectiveness and cost-effectiveness of the co-designed health system intervention compared to usual care.

Long-term objectives:

8. Develop a fully functional Global Centre for improving MLTC related health outcomes and research, that is self-sustaining and aligned closely with the Governments of India as strategic partner.

Currently, we have completed our short- term objectives, including conduct of the case-mix and health facility assessments, alongside in-depth interviews with relevant stakeholders to identify the challenges for people living with MLTC, caregivers, and healthcare providers.

We have estimated the prevalence and clustering of MLTC through a cross-sectional survey of 600 patients aged 40 years and above attending 20 primary health centers. Health system readiness was assessed at 20 PHCs and 40 sub-centers using the Indian Public Health Standards (IPHS, 2022) framework[4-7]. Additionally, in-depth interviews with 60 patients and caregivers, 40 healthcare professionals, and 10 state and district health officials revealed critical barriers, including fragmented care pathways, lack of provider training, insufficient digital support, and gaps in continuity of care. Additionally, out of 10 we have completed 4 co-design workshops to co-develop the integrated, technology enabled, health system interventions. The current proposal is to pilot test the intervention to assess its acceptability, feasibility, fidelity and usability.

3. Methodology

Firstly, we conducted cross-sectional surveys to assess the burden and common clusters of MLTC among patients aged ≥ 40 years (n=600) visiting the primary health centre (n=20) for treatment of any condition. Further, these PHCs (n=20) and sub-centres (n=40) were assessed using the IPHS 2022 guidelines to understand the readiness of these health facilities for management of MLTC. In the formative phase, we conducted in-depth interviews among patients and caregivers (n=60), healthcare professionals (n=40) and state and district officials(n=10) to identify the challenges in management of MLTC.

As part of the co-design phase, which are part of the medium-term objectives, we have conducted 10 workshops across the two sites, with a final workshop in Delhi, which consolidated, synthesized and deliberated the findings of these workshops. The participants of the workshops were patients and their caregivers, community groups, healthcare providers, researchers, policy makers and technology developers. We conducted the workshops using a range of participatory techniques and tools (e.g., small group breakout discussions, rating and ranking exercises, card writing, sorting and consensus activities) to encourage universal contribution.

Further, we plan to conduct the pilot cluster randomized controlled trial for 6 months to assess the intervention acceptability, recruitment and retention rates, feasibility, fidelity, delivery, and costs. With the findings of the pilot cRCT, we will conduct the main cRCT for 48 months to assess the effectiveness and cost-effectiveness of the co-designed health system intervention compared to usual care.

We propose to pilot the intervention in select primary health centres of the study sites in Rajasthan and Andhra Pradesh. The objectives of the pilot are

1. To explore the acceptability of the intervention among enrolled study participants (patient-facing application) and healthcare providers (EDSS and assisted tele-medicine).

2. To assess the feasibility of implementing the intervention and determine the extent to which intervention is implemented as planned.

3. To understand challenges in using the intervention and explore potential solutions.

Trial design for main study: Cluster randomised control trial

4. Study site

The proposed study will be carried out in the Anakapalli district of Andhra Pradesh and Jodhpur in Rajasthan. The Centre investigators have more than a decade experience working in these districts implementing various projects on non-communicable diseases including hypertension, diabetes and chronic kidney disease and food systems[8-10]. The Anakapalli district has 283 sub-centres and 40 PHCs. For the co-design workshops, we have conducted workshops across the two sites in India (Anakapalli, Visakhapatnam and Jodhpur), with 8-10 participants per workshop and the findings of these workshops will be consolidated, synthesized and deliberated over in a final workshop in Delhi.

Figure 1: Study area for pilot

The pilot and full cRCT will be conducted among people living with MLTC visiting the PHCs for management of MLTC in Anakapalli, Andhra Pradesh and Jodhpur, Rajasthan. We will conduct a non-randomised pilot study to evaluate the feasibility, acceptability, usability, and fidelity of three digital health interventions in rural Primary Health Centres (PHCs). The study is designed to inform the development of a future large-scale trial.

Study setting for main cRCT: The study will be conducted across multiple geographically diverse regions to ensure representation of heterogeneous health system contexts. Implementation sites include Anakapalli district in Andhra Pradesh, Jodhpur district in Rajasthan, Sonipat district in Haryana and Lalitpur, Kathmandu, Kavre, Chitwan, Makwanpur, Nuwakot, within Bagmati Province in Nepal. These regions were selected based on existing program partnerships, variation in health system capacity, and their representativeness of rural and semi-urban primary care environments.

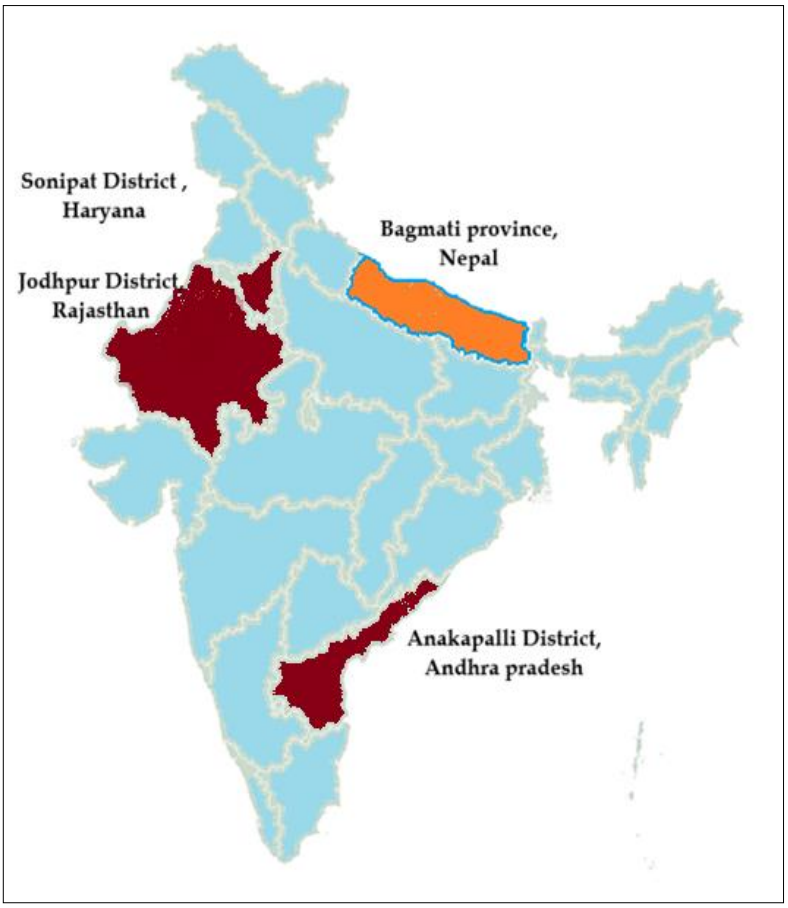

Figure 2: Study sites for main RCT

5. Clusters and randomization units for main cRCT

Primary Health Centres (PHCs) will serve as the unit of randomization, with clusters randomly allocated in a 1:1 ratio to either the intervention or control arm.

6. Eligibility criteria

Cluster eligibility: We will be using step by step approach to select primary health centres for the study to make sure they were suitable and representative. First, we map all PHCs in the study region. This included 46 PHCs in Anakapalli (Andhra Pradesh), 76 in Jodhpur (Rajasthan), 37 in Sonipat (Haryana) and 42 in selected districts of Bagmati Province (Nepal). In India, only rural PHCs were included because rural and urban facilities function differently under national health system and Indian Public Health Standards. In Nepal, both rural and urban facilities were included to reflect the decentralised health system, where primary healthcare services are delivered under nationally standardized norms defined by the Ministry of Health and Population, including uniform basic health service packages, facility readiness criteria, and routine reporting systems. From this pool, about 30 PHCs (as per sample size

calculation, explain in detail under sample size section) per site will be randomly selected by central statistics team for the final study.

7. Study participants

For the case mix assessment, we recruited patients aged 40 years and above visiting the PHCs for their treatment. For the facility assessment, we interviewed the auxiliary nurse mid wife at the sub-centre, or the medical officer at the PHC or any person designated by them. For the in-depth interviews, we conducted interviews with patients with MLTCs aged 30 years and above along with their care givers based in the same household, healthcare providers comprising of auxiliary nurse midwives, accredited social health activists, medical officers and district- and state-level department of health and family welfare officials.

For the co-design workshops, we have grouped the stakeholders consisting of patients and their caregivers, community groups, healthcare providers, researchers, policy makers, technology experts and district/state officials into three groups as follows:

Group A: Patients, their caregivers and community groups

Group B: Healthcare providers, researchers and technology experts, District and state officials

Group C: Policy makers

By considering viewpoints from these diverse stakeholders, we aim to co-create an integrated, technology-enabled health system intervention that supports all those affected by MLTC and those who are involved in MLTC care to enhance quality of life and health outcomes.

For the pilot and full cRCT, we will enrol people aged ≥40 years living with MLTC from PHCs which will be randomized into intervention and control PHCs. The intervention PHCs will receive the co-designed, integrated, technology-enabled, health system intervention consisting of electronic decision support system (EDSS), assisted telemedicine, patient facing application and community champions.

For the pilot two participant groups will be recruited

Intervention recipients: The recipients will include all individuals visiting the selected PHCs, will be screened for eligibility using a standardized screening tool. Eligible participants will include adults aged 40 years and above diagnosed with two or more of the following conditions: hypertension, diabetes mellitus, depression, anxiety, chronic obstructive pulmonary disease (COPD), asthma, vision impairment, hearing difficulties, osteoarthritis, and chronic back pain.

Intervention implementers: Medical officer (MO) and staff nurse at each PHC who will implement the EDSS and assisted telemedicine components of the intervention.

Individual eligibility for main cRCT:

Inclusion criteria: Patients attending the primary health centre (PHC) during the recruitment period who are:

1. Aged 40 years or above
2. Have been diagnosed with two or more of the following conditions such as hypertension, diabetes mellitus, depression, anxiety, chronic obstructive pulmonary disease (COPD), asthma, hearing impairment, osteoarthritis, or chronic back pain.

Exclusion:

1. Individuals below 40 years of age.
2. Individuals not residing in the selected PHC catchment area.
3. Individuals, their caregivers or household members without access to a mobile phone for communication.
4. Diagnosed with only one or none of the listed chronic conditions.
5. Pregnant or lactating women.
6. Persons with severe cognitive impairment or dementia that prevents informed consent or reliable participation.
7. Participants currently enrolled in another clinical or interventional research study that may interfere with this project's outcomes.
8. Those unable or unwilling to provide written informed consent.
9. Persons with severe communication barriers who are unable to respond to interviews or questionnaires despite assistance.

8. Recruitment and consent procedures

Patients will be recruited from primary health centres during routine outpatient visits. Trained health workers will screen adults aged ≥40 years using a standardized eligibility tool to identify individuals with MLTCs. Screening will include verification of existing diagnoses and collection of essential demographic information. Individuals meeting eligibility criteria will receive

detailed study information and will be invited to provide written informed consent prior to enrolment.

9. Intervention components:

9.1. Intervention overview

Care delivery will be supported by a codesigned integrated intervention package comprising an electronic decision support system embedded within clinical consultations, assisted telemedicine enabling specialist input and a patient-facing mobile application designed to support self-management. Healthcare providers will use the decision support platform during consultations to generate structured treatment plans, which may be modified based on clinical judgement. Telemedicine consultations will be initiated when specialist input is required, and patients will receive digital reminders and educational support through the patient-facing mobile application.

9.2. Intervention components and materials

PHC-based components include the EDSS and assisted telemedicine, which support structured clinical decision making and specialist access. The community component includes a patient-facing mobile application that provides reminders, education, and care continuity support. Together, these elements form a digitally enabled, multi-level care model.

Table 1: Intervention components and core activities

Setting	Intervention	Target/user	Core activities
PHC	Electronic Decision Support System (EDSS)	MO, staff nurse	Captures symptoms, vitals, history, and lab results through structured digital forms. Generates individualized treatment plans and determine need for up referral and follow up.
PHC	Assisted telemedicine	MO, staff nurse	Expands specialist access through structured teleconsultations
Community	Patient facing app	Enrolled participants or their care givers	Support enrolled individuals with personalized reminders, education

9.3. Procedures and delivery workflow:

Participants will enrol through a structured visit-based approach at participating primary health centres.

During wave 1, trained health workers will screen all adults aged ≥40 years using a standardized eligibility tool to identify individuals with two or more chronic conditions consistent with MLTCs. Eligibility screening will include confirmation of diagnosed conditions and basic demographic information (such as village name, phone number). Individuals meeting eligibility criteria will receive study information and will be invited to provide written informed consent.

Wave 2 will serve as the baseline assessment visit and will be conducted after obtaining written informed consent. During this visit, trained research staff will conduct comprehensive baseline evaluations using standardized interviewer administered questionnaire. Data collected will include socio-demographic characteristics, medical history, and behavioural risk factors. Objective clinical measurements will include systolic and diastolic blood pressure and anthropometry (height, weight, and body mass index). Behavioural and patient reported outcomes will be assessed using validated instruments, including diet quality, physical activity, tobacco and alcohol use, depressive symptoms (PHQ-9), anxiety (GAD-7), health-related quality of life (EQ-5D), disability (WHODAS 2.0), frailty measures, self-efficacy, and treatment burden. These baseline measurements will serve as reference values for evaluating changes in predefined clinical, behavioural, and patient-reported outcomes at follow up.

Wave 3, Fasting venous blood samples will be collected following standard operating procedures. Laboratory analyses will include glycaemic markers (fasting blood glucose and HbA1c), lipid profile, liver function tests and renal function tests, using standardised protocols to ensure comparability across sites. Participants will receive their test results within approximately 2 to 3 days of sample collection. Results will be provided as a printed report. A trained member of the study team (nurse, CCDC health worker) will explain the results to participants. Participants with abnormal findings will be counselled and referred to the nearest appropriate public health facility (e.g., PHC/CHC/District Hospital) for further evaluation and management as per standard care pathways. In cases of significantly abnormal or critical values, participants will be informed promptly and advised to seek immediate medical care, with the study team facilitating referral where feasible.

The duration of intervention up to 12 to 18 months. End line assessments will replicate baseline procedures to enable evaluation of changes over time. Follow up data will be collected using the same standardized instruments and clinical protocols, ensuring consistency across timepoints and study sites.

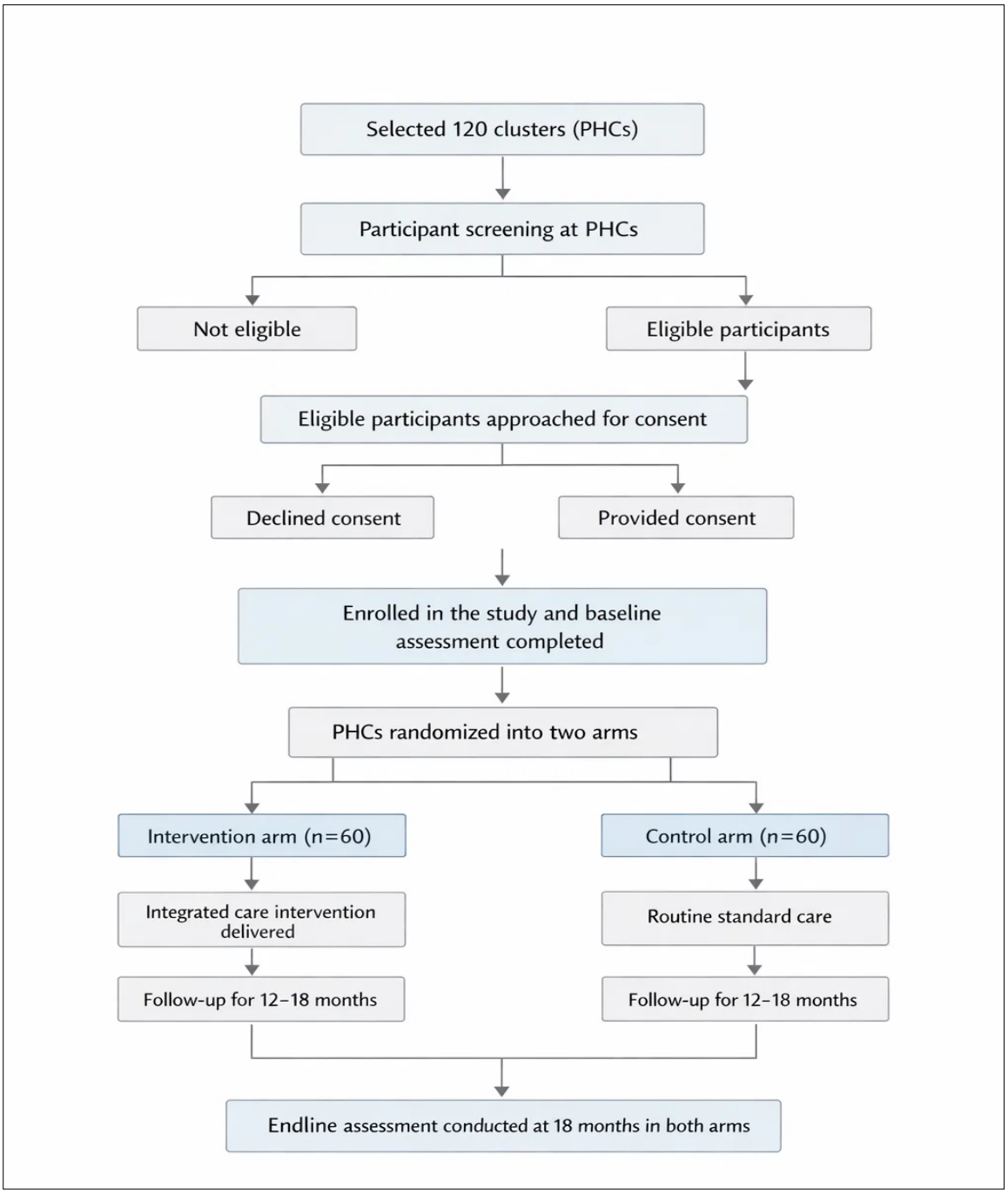

Figure 2: Workflow at the Primary health care centres during the intervention

9.4. Providers and training:

Medical officers and staff nurses of participating PHCs will undergo three days structured training on the use of the EDSS and assisted telemedicine protocols and procedures. Delivered through in person workshops the sessions will cover, standard operating procedures, system navigation, clinical workflows, patient documentation, and ethical data use. Facilitated by experts from NIHR GHRC, the training will include hands on practice, case simulations, and pre/post assessments.

9.5. Mode of delivery

The intervention will be delivered through a hybrid model combining in person clinical consultations at PHCs with digital support tools. Healthcare providers will use an electronic decision support system during routine consultations, supplemented by telemedicine enabled specialist consultations where required. Participants will additionally receive ongoing support through a patient facing mobile application. Their role will include supporting app onboarding, reinforcing follow up, addressing care barriers, and strengthening continuity of care at the household level.

9.6. Setting and Infrastructure

Intervention will be implemented within government PHCs and extended to the community to support continuity of care. Facility delivery will require basic infrastructure including electricity and internet connectivity for digital platforms. A patient facing mobile application will enable ongoing self-management support, while community level care coordination through community care coordinator reinforces follow up and linkage to primary care. The intervention is designed for integration within routine workflows in resource-constrained settings.

9.7. Dose and duration

Participants in intervention clusters will receive the integrated care package throughout the study follow-up period. The intervention will be delivered during routine clinical visits, with ongoing exposure through digital decision support during consultations and continuous engagement via the patient-facing application. The total intervention duration will correspond to the trial follow-up period (12 to 18 months).

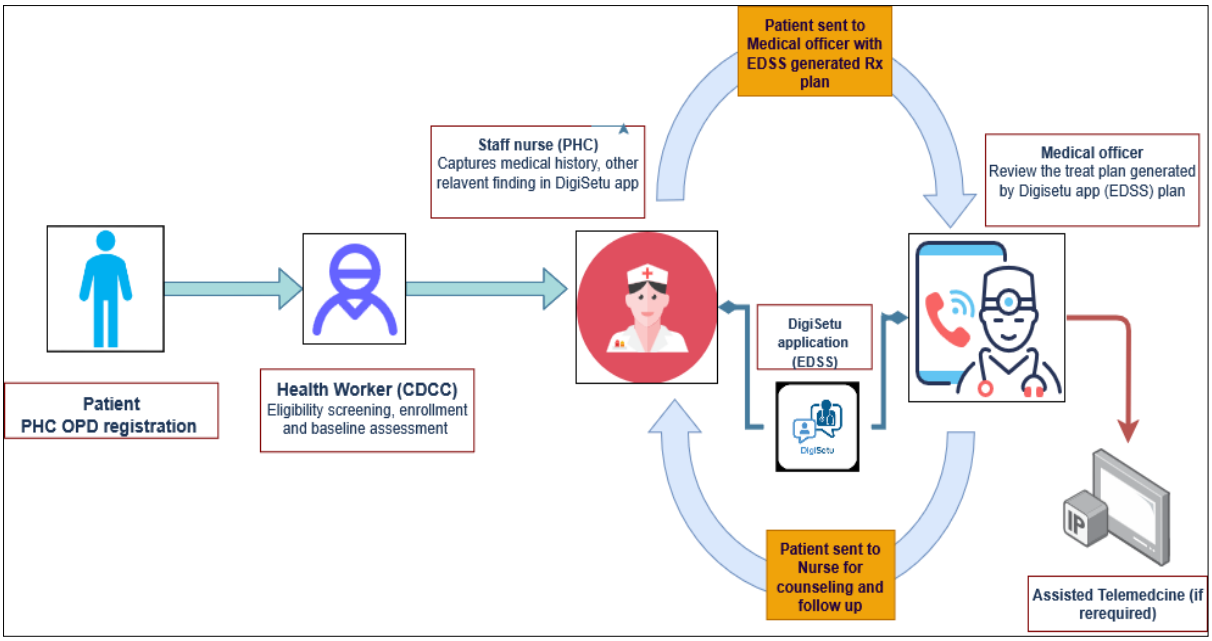

Figure 3: Workflow at the Primary health care centres during the intervention

Pilot study outcomes:

- Acceptability: Perceived relevance, satisfaction, and willingness to adopt interventions among providers and participants.
- Usability: Ease of use, navigation, and workflow integration of EDSS, telemedicine, and patient app.
- Feasibility: Practicality of implementation within PHC settings, including time, resources, and workflow fit.
- Fidelity: Delivery as intended, protocol adherence, and completeness of data entry.

10. Outcomes

Primary outcome

The primary outcome is change in health related quality of life, assessed using the EQ-5D visual analogue scale (EQ-5D VAS).

Secondary outcome:

Clinical outcomes: clinical outcomes will include cardiometabolic and anthropometric measures collected using standardized protocols.

1. Blood pressure control measured using validated digital blood pressure monitors.

2. Glycaemic control assessed using fasting blood glucose and glycated haemoglobin (HbA1c). HbA1c will be analysed from EDTA samples using NGSP-certified high-performance liquid chromatography methods.
3. Lipid profile including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides measured using standardized enzymatic assays
4. Renal function assessed using serum creatinine measured with methods traceable to isotope dilution mass spectrometry.
5. Liver function assessed using standard biochemical assays.
6. Body mass index calculated from measured height and weight.
7. Cardiovascular risk: A composite cardiovascular disease risk score will be derived using established algorithms incorporating age, blood pressure, antihypertensive medication treatment status, fasting glucose, lipid profile, and tobacco use.

Behavioural outcomes: behavioural risk factors will be assessed using validated epidemiological tools.

1. Tobacco use and alcohol consumption assessed using Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) study instruments.
2. Diet quality and physical activity assessed using PCARRS-based tools.

Psychosocial and functional outcomes will include:

1. Health related quality of life, encompassing both physical and mental health domains measured by SF-12 questionnaire
2. Depression measured using the Patient Health questionnaire (PHQ-9)
3. Anxiety measured using the Generalized Anxiety Disorder scale (GAD-7)
4. Disability and functioning assessed using the WHO Disability Assessment Schedule (WHODAS 2.0, 12-item).
5. Frailty assessed using the Fried Frailty Phenotype scale.
6. Self-efficacy assessed using the Self-Efficacy for Managing Chronic Disease (6-item scale).

Health system and economic outcomes

Health system and economic outcomes will include healthcare utilization, treatment burden, and economic burden. These will be measured using structured instruments adapted from previously validated tools and will inform cost-effectiveness analyses of the intervention.

11. Sample size:

For the case mix assessment, we will recruit all patients aged 40 years visiting the PHC for treatment over a period of one week. Since we are not testing a hypothesis, no sample size was calculated. For the health facility assessment, 20 PHCs, and two sub-centres selected randomly per PHC were included. We conducted in-depth interviews with 60 patients with MLTC along with their care givers, 40 healthcare providers and 20 district- and state-level officials. We have achieved saturation with these number of interviews14. For the co-design workshops, we have conducted 10 workshops across the two sites in India (Anakapalli, Visakhapatnam) and Jodhpur, with 8-10 participants per workshop.

For the pilot, we will enrol 120 participants living with MLTC from 4 PHCs across the two sites for a period of 6 months. Similarly, the full cRCT will be conducted for a period of 2 years among 2000 participants living with MLTC recruited from 78 PHCs across the two sites in India.

The sample size was calculated to detect a clinically meaningful difference in health-related quality of life, measured using the EQ-5D visual analogue scale (EQ-5D VAS), the primary outcome. Calculations accounted for clustering at the facility level. Assuming a two-sided alpha of 0.05 and 90% power, we estimated the required sample size using parameters derived from regional datasets and prior studies. The assumed standard deviation of EQ-5D VAS was 15.1, with a mean control group score of 74.37 and a minimum important difference of 2.5 points. An intracluster correlation coefficient (ICC) of 0.02 was used as the base-case estimate, and a 20% attrition rate was incorporated. Under these assumptions, the trial requires approximately 120 clusters with an average cluster size of 30 participants, yielding a total sample size of approximately 3,600 individuals. This design balances statistical power with operational feasibility across heterogeneous primary care settings. These analyses were performed using STATA and independently validated using PASS software, demonstrating robustness of the final design parameters.

12. Data collection methods

Case mix was assessed through a cross-sectional survey. Trained data collectors interviewed patients who provided written informed consent. The data collectors collected information on socio-demographic characteristics and the condition(s) the survey respondent has been

diagnosed with. These conditions are based on the multimorbidity assessment questionnaire for primary care (MAQ-PC)[15] and the ones recommended by an expert panel[16]. The facility assessment questionnaire was administered by a trained research fellow who has experience conducting such surveys. The questionnaire has been developed using the Indian Public Health Standards for public facilities[5-7] as well as the WHO Harmonised Health Facility Assessment Tool[17]. REDCap was used for both case mix assessment and facility assessment survey. For in-depth interviews, we used a semi-structured topic guide developed using the chronic care model. The domains of the chronic care model and topics are provided in **Table 4.** The co-design workshops were being conducted with participants by a trained moderator and research team.

Table 4: Theoretical domains utilized from the Chronic Care Model with the in-depth interview topics.

CCM Domains	**IDI Topics**
Self-management Support	Self-management of MLTCs, barriers and facilitators in self-management, socio-economic factors, health education, interpersonal relationships, family, and support
Delivery System Design	Doctor-patient relationships, system preparedness, infrastructure, and logistical issues, institutional management, capacity, skill development, specialized support
Changing the Health Care System	Potential interventions, skills training, awareness, community engagement, capacity building

The data collection for the pilot and main cRCT will be conducted by trained data collectors using semi-structured questionnaires using REDCap. The semi-structured questionnaire is being prepared. The participants will be examined and the blood pressure, BMI, and waist circumference will be checked. The blood samples will be collected to assess the various laboratory parameters including blood glucose and lipid profile. The qualitative data will be recorded and transcribed verbatim.

Data collection for main cCRT: Data will be collected using standardized electronic data capture systems across all study sites. Trained research staff will use tools and protocols to ensure consistency in data collection procedures. Baseline and follow-up data will include socio-demographic characteristics, clinical measurements, behavioural risk factors, and validated patient-reported outcomes obtained through structured study instruments through

RedCAP. In addition to research data capture, intervention delivery data will be captured through integrated digital platforms named DigiSetu. Usage data from the electronic decision support system (EDSS), assisted telemedicine platforms, and the patient facing mobile application will be automatically logged to assess intervention exposure, adherence, and engagement. Data quality will be ensured through structured training, real-time validation checks, and centralized monitoring. Built-in validation rules within electronic systems will minimize entry errors and ensure completeness, while backend analytics will enable continuous monitoring of both research and intervention data across sites.

13. Pilot study evaluation:

The EDSS and assisted telemedicine interventions will be evaluated for their acceptability, usability, and feasibility within Primary Health Centre (PHC) workflows.

Acceptability will be explored among medical officers and staff nurses using the *Theoretical Framework of Acceptability (TFA) frame work*[11]*.* This will include think-aloud sessions, where participants verbalize their thoughts while interacting with the digital tools. The evaluation will explore key TFA domains such as:

- Affective attitude – how providers feel about using the intervention
- Burden – perceived effort required to use the system
- Ethicality – alignment with professional values and norms
- Intervention coherence – understanding of how the intervention works
- Perceived effectiveness – belief in the intervention's ability to improve care
- Self-efficacy – confidence in using the system effectively

Usability will be evaluated among the same provider group using the *System Usability Scale (SUS)*[12], it's a validated 10-item questionnaire scored on a 0–100 scale, with scores ≥70 considered satisfactory and end of recruitment.

Feasibility of the interventions will be assessed by the research team through a combination of backend analytics, direct monitoring, and structured checklists. Key operational indicators will include medical officer usage logs, number of log-ins, average screening time, consultation completion rates, system stability (e.g., app crashes), and portal update frequency, teleconsultation setup duration, tele-referral success rates. All metrics will be tracked continuously throughout implementation to guide iterative improvements and inform scalability. The assisted telemedicine component will undergo a further evaluation to assess its operational feasibility and effectiveness in enhancing specialist access.

Teleconsultation logs: Researchers will analyse provider–patient teleconsultation records to generate indicators including (i) success rate of completed sessions, (ii) average consultation duration, (iii) dropout or termination rates, (iv) frequency and nature of technical issues, and (v) proportion of consultations missed due to technical problems. These data will enable estimation of the percentage of successful teleconsultations relative to scheduled sessions.

Table 2: Evaluation framework for EDSS and assisted telemedicine

Outcome	Method	Study Tool	Target Group	Time Period
Acceptability	Qualitative (Think-aloud)	TFA-based interviews & think-aloud sessions	Medical Officers, Staff Nurses	End of recruitment
Usability	Quantitative	System Usability Scale (SUS), Validated 10-item	Medical Officers, Staff Nurses	End of recruitment
Feasibility	Qualitative (backend data + monitoring checklists)	Usage logs, backend analytics, structured feasibility checklist	Researchers (observing provider use)	Continuous; summarized at (3M) & (6M)
Operational feasibility (Telemedicine)	Quantitative log analysis	Teleconsultation logs	Researchers (provider-patient sessions)	Continuous; summarized at (3M) & (6M)

The patient-facing app will be evaluated for their acceptability, usability, and feasibility with enrolled participants.

Acceptability: In-Depth Interviews (IDIs) will be conducted with enrolled partcipants and/or caregivers at endline to explore user experiences, perceived benefits, and barriers/facilitators of app engagement.

Usability: Will be quantitatively assessed using the **mHealth App Usability Questionnaire (MAUQ)**[13], a validated 18-item tool specifically designed for mobile health applications. The MAUQ covers three subscales: *Ease of Use and Satisfaction* (7 items), *System Information*

Arrangement (4 items), and *Usefulness* (7 items). Each item is scored on a **7-point Likert scale** (1 = strongly disagree to 7 = strongly agree), with higher scores indicating better usability. A mean score of **≥5.0** is considered acceptable usability.

Feasibility: Researchers will use backend data and usage logs to evaluate patient engagement patterns, including (i) number of log-ins per week, (ii) response rates to reminders, (iii) proportion of educational content accessed, and (iv) navigation patterns.

Table 3: Evaluation framework for patient facing application

Outcome	Method	Study Tool	Target Group	Time Period
Acceptability	Qualitative	In-Depth Interviews (IDIs)	Participants and/or Caregivers	End of recruitment
Usability	Quantitative	mHealth App Usability Questionnaire (MAUQ)	Participants and/or Caregivers	End of recruitment
Feasibility	Quantitative (app analytics)	Backend data and usage logs	Researchers (based on patient use)	Continuous; summarized at (3M) & (6M)

The fidelity of all interventions (EDSS, assisted telemedicine, and patient-facing app) will be evaluated using the Carroll et al. (2007) conceptual framework for implementation fidelity, with refinements by Hasson (2010). This framework emphasizes four key domains of fidelity: adherence to protocol, dose/exposure, quality of delivery, and participant responsiveness.

a. **Adherence to protocol**: Adherence refers to the extent to which intervention components are delivered as designed. For EDSS, this will include whether all required fields (symptoms, vitals, history, laboratory results) are completed and whether treatment plans are reviewed by medical officers. For telemedicine, adherence includes compliance with referral and consultation protocols. For the patient-facing app, adherence refers to consistent delivery of reminders and educational modules.

    - *Tools:* Structured fidelity checklists, backend audit trails, supervisor observations.

- *Indicators:* ≥80% of required steps completed per encounter.

b. Dose/Exposure: This domain assesses the amount of intervention actually received by participants. For EDSS, this will be the proportion of eligible participants managed using the system. For telemedicine, it includes the proportion of eligible cases successfully referred and completed. For the app, dose will be reflected in the proportion of participants actively engaging (log-ins, reminders responded to, content viewed).

- *Tools:* Usage logs, referral records, app analytics.
- *Indicators:* ≥80% of eligible participants exposed to intervention as planned.

c. Quality of delivery: Quality refers to the competence and consistency of how interventions are delivered. For EDSS, this will assess whether medical officer modifications of treatment plans are appropriate and whether rationale is documented. For telemedicine, it includes the clarity and completeness of referral documentation and the quality of specialist responses. For the app, it assesses whether educational content and reminders are delivered accurately and consistently with the protocol.

- *Tools:* Supervisor review checklists, random record audits, qualitative interviews.
- *Indicators:* ≥75% of sampled encounters rated as high-quality delivery.

d. Participant response: Responsiveness captures the engagement and receptiveness of both providers and participants. Providers will be asked about tool relevance, usability, and integration into workflow. Participants will be assessed for engagement with the app (e.g., reminder responses, navigation patterns) and satisfaction with teleconsultations.

- *Tools:* SUS, MAUQ, Acceptability of Intervention Measure (AIM), in-depth interviews, focus groups.
- *Indicators:* ≥70% of users reporting positive engagement (Likert ≥4/5)

Domain	Key Indicators
	1. % of eligible participants who received consent and were registered in EDSS by staff nurses.

Adherence to protocol	2. % of EDSS-registered participants whose treatment plans were reviewed by Medical Officers. 3. % EDSS treatment plans accepted by Medical Officers 4. % of EDSS treatment plans rejected with documented rationale 5. % of enrolled participants who returned for follow-up visits 6. % EDSS encounters with all mandatory fields completed (symptoms, vitals, labs) 7. % telemedicine referrals following protocol 8. % patient facing app users receiving scheduled reminders 9. % receipts installed patient facing app
Exposure	1. % of screened individuals found eligible for the study 2. % of eligible participants who were consented 3. % of consented participants who were initiated into EDSS workflow 4. % eligible participants managed via EDSS 5. % eligible cases referred and completed via telemedicine 6. % app users with ≥1 login and ≥1 module viewed
Quality of delivery	1. % EDSS treatment plans modified by MO 2. % tele-referrals with complete documentation and specialist response 3. % app messages delivered accurately and on time and screening time
Participant responsiveness	1. % providers rating tools as usable and relevant (SUS ≥70) 2. % receipts responding to app reminders or engaging with content

Data analysis

The quantitative data was summarized using means and proportions. For each facility, a score of one was provided for the adequacy of the following components based on Indian Public Health Standards - manpower, drugs, lab facilities and services. These scores for each component were then added to generate a summary score for that facility. Based on the median score, the facilities were divided as either high or low performing. Using the case mix survey data, we estimated the mean number of disease conditions present in a patient seeking care at primary health centre. The proportion of patients with two or more chronic conditions was estimated along with the common cluster of conditions. The in-depth interviews were digitally recorded, transcribed verbatim and to English. The data was de-identified and analysed using NVivo. A thematic analysis approach was used wherein initial codes and a codebook were developed. The codebook was to code the data and organize the issues, ideas and topics within the data. Each issue/idea/topic was then described and compared by participant type (patient/caregiver/healthcare provider) Consistency in coding was maintained by independent coding by two researchers and continually referring back to the transcripts and the codebook. The coding was reviewed by another researcher and any conflicts was resolved through discussion. The co-design workshops were recorded, transcribed verbatim and translated to English. The data is being deidentified and data extraction for each activity is done into an excel spreadsheet to prepare for content analysis. Qualitative data, including written responses, is coded and thematically analyzed using NVivo. The main output will be the co-designed health system intervention, its implementation and evaluation plan.

The quantitative data from the pilot and full cRCT will be summarized using means and proportions. After checking for normality, appropriate tests will be used to evaluate the changes in various measures, assessed before and after the intervention. Further, cost-effectiveness of the intervention will also be assessed. The digitally recorded qualitative data will be transcribed verbatim and to English. The data will be de-identified and analysed using NVivo. A thematic analysis approach will be used wherein initial codes and a codebook will be developed. The codebook will be used to code the data and organize the issues, ideas and topics within the data. Consistency in coding will be maintained by independent coding by two researchers and continually referring back to the transcripts and the codebook. The coding will be reviewed by another researcher and any conflicts will be resolved through discussion.

Quantitative Analysis for pilot:

The results of the pilot study i.e., usability, feasibility, and fidelity from provider's and patient's perspectives will be reported as number (percentages). Descriptive statistics about the baseline characteristics of the participants will also be reported as number (percentages). To assess the usability across all the three interventions, total score will be evaluated per

intervention and categorized as number(percentages). Response obtained from SUS and MAUQ will be reported as median (IQR) under Likert scales. Spearman's rank correlation will be used to measure the relationships between ordinal variables used in the respective scales, and ordinal logistic regression can help us to model the relationship between the Likert scale response and other independent variables.

Feasibility of the interventions will be assessed based on number of logins, average screening time, and estimate proportions namely for consultation completion, navigation pattern on app, response rate to reminders, and frequency to access educational content for the participants respectively. Further, feasibility of the application/patient app will be observed in terms of system stability by reporting the frequency of the participant visits to the portal, number of tele-referrals and average duration of teleconsultation. The operational feasibility will also be measured with respect to teleconsultation i.e., to measure the number of complete sessions, number of dropouts or termination due to technical issues.

Fidelity across all the interventions will be assessed in terms of adherence, response and exposure by the participants. Adherence with respect to interventions such as EDSS and telemedicine will be measured in terms of proportions of participants with completion of registration, history and advised treatment plans which will be accepted or rejected by the providers. It will also measure the percentage of enrolled participants in terms of follow-ups, referrals and frequency of reminders from application/app. The exposure under fidelity will be measured in terms of proportions of eligible participants, consented participants, under treatment via EDSS, cases referred and treatment via telemedicine.

Response of the provider will be measured in terms of usability of the tool (SUS score ≥70) and participant response will be measured with respect to response to the reminders on app as well as pattern of navigation while using app. Further, fidelity will also be assessed in terms of consistency and competence of the intervention delivered to the participants. This will be measured under quality of delivery as proportions of treatment plans modified by providers; number of tele-referrals and proportion of apps messages delivered within screening time of the participants.

Qualitative analysis for pilot:

The qualitative component of the pilot study will focus primarily on assessing the acceptability of the three intervention components i.e., Electronic Decision Support System (EDSS), assisted telemedicine (full and backpack models), and the patient-facing mobile application.

The qualitative data collected from the Think-Aloud sessions with healthcare providers (medical officers and staff nurses) as they engage with EDSS and assisted telemedicine

platforms. The participants will be encouraged to verbalize their thoughts, expectations, and decision-making processes in real time. These sessions will be audio recorded with participant consent, supplemented by researcher field notes documenting pauses, difficulties, and contextual factors. In-depth interviews (IDIs) with patients, their caregivers, and healthcare providers to explore reflective perceptions of intervention use, perceived benefits, and associated barriers/facilitators. Logbooks and process observations maintained by field researchers to record workflow integration, fidelity, user engagement, and contextual challenges documenting real-time observations during intervention delivery.

This data in from of audio recordings with participant permission and observation notes will be transcribed verbatim and translated from local language to English and imported into NVivo software for analysis. The coding will follow a framework analysis approach using TFA domains as the primary deductive coding frame, while also allowing inductive codes to capture additional emergent themes using the thematic analysis framework by *Braun & Clarke*. This will be done by applying line-by-line coding allowing multiple codes per data segment and iteratively adding inductive codes as new findings emerge, the related codes will be grouped into a single theme and be reviewed for coherence, distinctiveness, and alignment with the data set. These themes will be then mapped to the acceptability framework by TFA. These themes will be compared and triangulated across intervention components and stakeholder groups (healthcare providers, patients, caregivers) and across sites using anonymized quotes to illustrate findings. To ensure coherence in data interpretation around 20% of transcripts will be independently double coded by two researchers, with differences resolved through discussions and eventually reviewed by a third researcher. Qualitative findings will be integrated with the quantitative data to inform the acceptability outcome of the pilot study by using an explanatory approach that will guide refinement of intervention components prior to the full-scale cRCT.

Statistical analysis for main cRCT

Primary analysis: Difference in the mean quality of life score (EQ-5D VAS) score from baseline to endline (individual level) and by comparing between intervention and control clusters.

Secondary analyses: Trial data will assess differences between intervention and control groups in changes from baseline to endline across a range of clinical, behavioural, and patient reported outcomes. Continuous outcomes will include changes in systolic and diastolic blood pressure, body mass index, diet quality, physical activity levels, depressive symptoms (PHQ-9), health related quality of life, disability (WHODAS), frailty, self-efficacy (SEMCD), and treatment burden scores. In addition, differences between trial arms in the change in

prevalence of key clinical and behavioural indicators will be evaluated. These will include blood pressure control (SBP <130 mmHg and DBP <80 mmHg), glycaemic control (HbA1c <7%), lipid control (LDL-C <100 mg/dL), smoking status, alcohol use, and categorical indicators of depression and anxiety.

Main statistical model for analysis of continuous endpoints

Each continuous outcome measured at baseline and endline (SBP, HbA1c, LDL, BMI etc) will be analysed using individual level data with a linear mixed effects model. The model will include a variable for the intervention group, which will be adjusted for baseline measurement of the outcome and will have a random intercept for the site. The outcome measurements (baseline and endline) will be suitably transformed to achieve normality, and to deal with outliers depending on their distribution, and they will be centred on the mean of the baseline measure in each trial arm separately.

Such a model will effectively test if the average change in the outcome variable during the study period are different between two study arms while considering the cluster design and potential regression to the mean effect. Estimation of the parameters will be reported along with 95% confidence intervals. Further, at each study site we will study the effect of intervention and test if these effects are statistically significant from each other.

Main statistical model for analysis of categorical endpoints

Each categorical outcome measured at baseline and endline (socio demographic characteristics, smoking status, alcohol use etc) will be analysed with a logistic regression. The model will include a variable for the intervention group; it will be adjusted for baseline measurement of the outcome and will have a random intercept for the PHCs. A model with an interaction term between site and intervention group will also be used to run the estimate of the effect in each study site if there is difference of effects between sites.

Potential problem of imbalances at baseline

The statistical model described above assumes that individuals in both the arms have similar socio-demographic characteristics, which is reasonable expectation in a large trial that randomises individual patients. But as this is a trial that randomises clusters (PHCs) as there is some potential for baseline differences between individuals recruited in both the arms.

Statistical approach to handle potential baseline imbalance

A priori, we cannot tell what variables we will need to adjust until we examine the baseline data which will be doing in the cRCT. There is no statistical test for confounding to decide which variables to enter the model, so judgement will have to be made based on the actual

imbalances between arms and association of those variables with the outcomes and use analytical approach based on causal inference. There will be full transparency, and results will be presented for the models unadjusted and adjusted by baseline variables that are considered important due to their imbalances between arms.

14. Handling missing data

The primary analyses will be conducted under the principle of implementation research. Patients who withdrew consent for use of their data will not be included in any analyses. Dropouts and lost to follow-up are a concern in any trial, we will compare the baseline characteristics between those that drop out and those that stay in the trial. It is difficult to decide the best way to deal with this issue a priori before we can verify the extent of the problem in the final data set. In general, the approach for each outcome will be to perform and present both: complete case analysis and multiple imputation analysis and, if there are substantial differences in the results, we will discuss which one seems more reasonable giving the characteristics of the missing data.

15. Trial governance

This trial is conducted under the NIHR Global Health Research Centre on Multiple Long-Term Conditions (MLTC), led by the University of Leicester (UK) and Centre for Chronic Disease Control (CCDC). Implementation is supported by partner institutions in India and Nepal, including AIIMS Jodhpur, and Kathmandu Medical College, with each site led by a local Principal Investigator. The digital platforms used in the study, including the RedCAP, app and web based EDSS and assisted telemedicine system and patient facing app are developed and maintained by CCDC, which also supports data systems and implementation coordination. Training and capacity-building activities are supported by HRIDAY, including field level training and community engagement inputs. Ethical approvals have been obtained from relevant institutional ethics committees, and the study is conducted in accordance with Good Clinical Practice and NIHR governance requirements.

References

1. NIHR. NIHR Strategic Framework for Multiple Long-Term Conditions (Multimorbidity) MLTC-M Research. March 30, 2021. Accessed March 30, 2021. https://www.nihr.ac.uk/documents/nihr-strategic-framework-for-multiple-long-term-conditions-multimorbidity-mltc-m-research/24639#:~:text=The%20NIHR%20will%3A,their%20trajectories%20among%20the%

20population&text=Supports%20design%20and%20delivery%20of,term%20condition%20to%20MLTC%2DM.

2. Pati S, Swain S, Metsemakers J, Knottnerus JA, van den Akker M. Pattern and severity of multimorbidity among patients attending primary care settings in Odisha, India. Article. *PLoS One*. 2017;12(9):e0183966. doi:10.1371/journal.pone.0183966

3. National Health Systems Resource Centre. *Ayushman Bharat: Comprehensive Primary Health Care through Health and Wellness Centers*. 2018. http://nhsrcindia.org/sites/default/files/Operational%20Guidelines%20For%20Comprehensive%20Primary%20Health%20Care%20through%20Health%20and%20Wellness%20Centers.pdf

4. Ministry of Health and Family Welfare, Government of India. *Indian Public Health Standards Health & Wellness Centre - Sub Health Centre (HWC-SHC) 2022 Volume-IV*. 2022.

5. Ministry of Health and Family Welfare, Government of India. *Indian Public Health Standards Sub District Hospital and District Hospital 2022 Volume-1*. 2022.

6. Ministry of Health and Family Welfare, Government of India. *Indian Public Health Standards Health & Wellness Centre - Primary Health Centre (HWC-PHC) 2022 Volume III*. 2022.

7. Ministry of Health and Family Welfare, Government of India. *Indian Public Health Standards Community Health Centre 2022 Volume-II*. 2022

8. Ganpule A, Brown KA, Dubey M, et al. Food insecurity and its determinants among adults in North and South India. *Nutr J*. Jan 9 2023;22(1):2. doi:10.1186/s12937-022-00831-8

9. Mohan S, Jarhyan P, Ghosh S, et al. UDAY: A comprehensive diabetes and hypertension prevention and management program in India. 10.1136/bmjopen-2017-015919. *BMJ open*. Jul 10 2018;8(6):e015919. doi:10.1136/bmjopen-2017-015919

10. Srinivasapura Venkateshmurthy N, Potubariki G, Brown KA, et al. A Photovoice Study to Reveal Community Perceptions of Highly Processed Packaged Foods in India. *Ecology of food and nutrition*. Nov-Dec 2021;60(6):810-825. doi:10.1080/03670244.2021.1968853

11. Sekhon M, Cartwright M, Francis JJ. Development of a theory-informed questionnaire to assess the acceptability of healthcare interventions. BMC Health Serv Res [Internet]. 2022 Dec 1 [cited 2025 Aug 26];22(1).

12. Brooke, J. (1996). SUS—A Quick and Dirty Usability Scale. In P. W. Jordan, B. Thomas, B. A. Weerdmeester, & I. L. McClelland (Eds.), Usability Evaluation in Industry (pp. 189-194).

London Taylor & Francis. - References - Scientific Research Publishing [Internet]. [cited 2025 Aug 26].

13. Zhou L, Bao J, Setiawan IMA, Saptono A, Parmanto B. The mHealth App Usability Questionnaire (MAUQ): Development and Validation Study. JMIR Mhealth Uhealth [Internet]. 2019 [cited 2025 Aug 26];7(4).

14. Hennink M, Kaiser BN. Sample sizes for saturation in qualitative research: A systematic review of empirical tests. *Soc Sci Med*. Jan 2022;292:114523. doi:10.1016/j.socscimed.2021.114523

15. Pati S, Hussain MA, Swain S, et al. Development and Validation of a Questionnaire to Assess Multimorbidity in Primary Care: An Indian Experience. *BioMed research international*. 2016;2016:6582487. doi:10.1155/2016/6582487

16. Ho ISS, Azcoaga-Lorenzo A, Akbari A, et al. Measuring multimorbidity in research: Delphi consensus study. *BMJ Med*. 2022;1(1):e000247. doi:10.1136/bmjmed-2022-000247

17. WHO. Harmonized Health Facility Assessment (HHFA). WHO. January 2022, 2022. Accessed January 11, 2022. https://www.who.int/data/data-collection-tools/harmonized-health-facility-assessment/introduction