Challenges in setting up a large population-based prospective cohort study in India – learnings from the LoCARPoN cohort

Kamal Gulati,[a] Sada Nand Dwivedi,[b] Shashi Kant,[c] Deepti Vibha,[d] Awadh Kishor Pandit,[d] Achal Kumar Srivastava,[d] M. Arfan Ikram,[e] Henning Tiemeier,[f] and Kameshwar Prasad[g,*]

[a]Department of Centralized Core Research Facility, All India Institute of Medical Sciences, New Delhi, India
[b]Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India
[c]Centre for Community Medicine, All India Institute of Medical Sciences, New Delhi, India
[d]Department of Neurology, All India Institute of Medical Sciences, New Delhi, India
[e]Department of Epidemiology, Erasmus MC University Medical Center, Rotterdam, the Netherlands
[f]Professor of Social and Behavioral Science and The Sumner and Esther Feldberg Chair of Maternal and Child Health, Harvard T.H. Chan School of Public Health, USA
[g]Department of Neurology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

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Summary

Population-based prospective cohort studies can yield vital new evidence. However, they are difficult to setup especially in non-western contexts such as India. We describe our experience in establishing the Longitudinal Cognition and Aging Research on Population of the National Capital Region (LoCARPoN) cohort, which was the first-of-its-kind public-funded study with target sample size of 15,000, 3 sites, and funds of approx. US$ five million for eight years (2014–2022). LoCARPoN aimed to study incident stroke and dementia in adults aged ≥50 years in urban and rural populations of north India. Among the numerous challenges encountered, important were inadequate funding, lack of adequate space for medical and field sites, difficulty in hiring manpower, lack of IT infrastructure, non-availability of storage facility for biological samples, and absence of dedicated MRI machines. Meticulous planning, adequate funding, trained personnel, institutional and community support are critical for establishing such cohorts in the non-western contexts.

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Introduction

With a population of about 1.35 billion, India, a low- and middle-income country, is rapidly evolving with rising literacy, decreasing sex ratios, immense urban and rural growth, high population density and an increasing proportion of aging individuals.[1] In India, life expectancy at birth rose from 54 years in 1980 to about 70 years in 2020.[2] The elderly population i.e. those aged 60 years or older was estimated at 100 million in 2001 and is expected to cross 200 million by 2030.[3] As a result, the mortality rate and the burden of chronic diseases among elderly have also increased significantly. More than six out of 10 individuals die from non-communicable diseases (NCDs) in India.[4] Premature deaths from stroke and heart disease rose by 59% between 1990 and 2010.[5–7] Hence, population-based prospective cohort studies to identify risk factors causing deaths, and disabilities due to NCDs are important in the Indian context.

Informal discussions with many Indian peers revealed that most of them recognized the importance of setting up of a population-based prospective cohort study site. However, the potential challenges deterred them in actually embarking on this enterprise. Here we share our experience of establishing a public-funded community-based cohort. The specific objectives of the article are to document the problems encountered, and the outcomes of the remedial measures while establishing a population-based cohort in an urban and rural areas of north India.

This cohort study was a collaborative effort between All India Institute of Medical Sciences (AIIMS), New Delhi and the Erasmus University Medical Center, Rotterdam, The Netherlands.[8] The study period was

*Corresponding author. Rajendra Institute of Medical Sciences, Ranchi, 834009, Jharkhand, India.
E-mail address: drkameshwarprasad@gmail.com (K. Prasad).

eight years (2014–2022). The sample target was 15,000 participants; 7500 each from urban and rural area.

The participants of this study had to meet all of the following inclusion criteria:[9]

1. Residing in the selected geographical area;
2. Being aged 50 years or older; and
3. Consenting to participate

The study protocol was approved by the Institutional Ethics Committee of AIIMS, New Delhi (reference number: IEC/NP-53/2014 RP-12/2014, dated 15 May 2014). Written informed consent was obtained from both the community leaders and as well as the study participants. Appropriate measures were taken to maintain the confidentiality of the study participants.

Team

The cohort study included 26 investigators (24 Indian and 2 Dutch) and 74 project staff.

Administrative structure

We constituted three committees viz.

(i) *Management committee* – It was chaired by the Indian Principal Investigator (PI). Other members of the committee were in-charge of data management, in-charges of urban and rural sites, and the project consultant.
(ii) *Events committees* – *Neurological*: PI and three more investigators from neurology; *Cardiac*: Two investigators from cardiology and one from neurology; and *Mortality*: PI and three other investigators from neurology.
(iii) *International advisory committee* – Indian and Dutch PIs of the cohort study, PIs of Framingham Heart Study, Study of Health in Pomerania, and Austrian Stroke Prevention Study and Austrian Family Study.

Management committee meetings were held once a week while Events committee meetings were generally held quarterly. International Advisory Committee meetings were normally held biannually.

Knowledge mobilization and capacity building

Between August 2014 and March 2019, the Indian investigators made eight visits to the Rotterdam cohort study in Erasmus University to gain first-hand experience in implementing similar project in India. Two Indian investigators completed master-level course in clinical epidemiology at Erasmus University between 2017 and 2019.

Preparatory phase (Year 2012–2014)

The idea of initiating the cohort study was agreed upon during a workshop held in November 2012 that was attended by Indian researchers and researchers from Erasmus MC University Medical Center, The Netherlands. Department of Biotechnology (DBT), Government of India, granted approximately US$ five million for the study duration of eight years on 14 February 2014. The questionnaires on various aspects of the cohort study were finalized through modifying existing ones in view of the local needs and/or developing newer ones using standard steps.[9]

Challenges Pre-COVID period (2014–2019)

i. ***Funding***: Fund for the urban site was released in April 2014. DBT had not allocated any money for MRI machine, Information Technology requirements and genome wide association studies (GWAS). We secured, from Department of Health Research, a grant of approximately US$ 400,000 for GWAS.
ii. ***Space***: Some of the common challenges, for both urban and rural sites, were securing space for field offices in the community, medical assessment site (MAS) at the hospital, bio-bank storage facility for biological specimens, storage of participants' and records.
   a) *Urban site*: We had envisaged setting up the MAS in the first year of the study (2014–15). However, MAS could be made ready only in October 2016. We had to make a temporary arrangement for the intervening period where we could process only four instead of 12 participants per day that we had originally planned.

Though we had estimated the space requirement of 6000 square feet for the urban site MAS, only 1800 square feet was actually allocated. This space constraint, therefore, forced us to carry out multiple assessments in a single room either on sharing or rotation basis slowing down the medical assessment process considerably.

We had not anticipated the necessity of a field office in the community. Hence, no fund was available to rent a field office. After considerable efforts, we could persuade the Ministry of Labour and Employment to allot us some space in their dispensary that was located near the study area, to be used as field office. They allotted one room for a period of one year. However, this space was too small to facilitate the fieldwork efficiently. The Ministry demanded that the allotted room be returned after the expiry of one-year period. We, thereafter, requested the funding agency for re-appropriation of already sanctioned budget for rental of space to be used as field office. The request was not acceded to and thus severely reduced the efficiency of the field activities.

   b) *Rural site*: Unlike the urban site, we had not earmarked the first year of the rural site for setting up the MAS. This was possibly a major

flaw in the planning of the project. We started our recruitment as per plan in 2016. Initial two years were utilized for manpower recruitment and training, equipment procurement and development of necessary instruments. During early stages, medical examination had to be carried out at a make-shift place. However, in August 2019, the MAS was shifted to a permanent location. The new location of MAS was on the first floor of a building that had no elevator (lift).

iii. ***Procurement of machinery and equipment:*** Only a one-time budget of approx. US$ 120,000 for urban, approx. US$ 106,000 for rural, and approx. US$ 13,000 for image analysis was budgeted. Despite the activities for the urban and rural sites being the same, the rural site received 10% less funds. Therefore, we were forced not only to compromise on quality and type of the machines, but it also meant that certain important items, such as dental chair could not be purchased for the rural site. All purchases had to conform to the strict government guidelines, which included national level tendering or procurement through Government e-Marketplace (GEM) portal. Due to the complex procurement procedures often, the tenders had to be repeated, which significantly delayed the procurement.

iv. ***Manpower hiring***: We faced the following problems:
   a. Inadequate number and type of posts sanctioned: The funding agency, in order to limit the project cost, had reduced/eliminated some of the key staff positions such as data entry operator, physiotherapist, medical social worker, and laboratory technician. This resulted in increased burden for the hired employees, who were required to multi-task.
   b. Non-availability of qualified staff: Hiring qualified project staff e.g. medical doctors, clinical psychologists, data scientists, and IT personnel to work on temporary positions with low salary and limited promotional avenues was a major challenge. The salary of a specialist doctor was low (US$ 800 per month) compared to the market rate, which was almost four times higher. We could never fill up all the posts of doctors despite multiple attempts. Same was true for clinical psychologist, IT personnel and data scientist.
   c. Unwillingness of the potential staff to work in community settings, especially in rural areas: This was particularly true for female staff hired for rural site. The common reason(s) cited were distance from main city, poor transport and accommodation, and security concerns. Staff attrition rate and absenteeism were substantially higher at the rural site.

   We tried to address the manpower challenges by providing in-house training and certification so as to equip them with required skills. For example, a dentist was trained to perform echocardiography after training and certification at urban site. Our approach, however, was often resented.

v. ***Unavailability of MRI machine:*** We did not have a dedicated MRI machine. Hence, for urban participants we had planned to use hospital's patient service 1.5 T MRI machine on a time-sharing basis after routine working hours. The time slot provided to us was from 8 PM to 11 PM on weekdays, 2 PM–11 PM on Saturdays, and 8 AM to 11 PM on Sundays and holidays. The participants were provided free of cost pick-up and drop transport facility for MRI. Majority of the participants were elderly, who found it inconvenient to go for MRI in the late evening/night. During the winter season this problem became even more pronounced. Most of MRI based cohort studies worldwide were using 3-T MRI machine. Therefore, we were not only constrained by lower numbers of MRIs per week but also the quality was sub-optimal. Due to the low salary, we could not recruit a full-time neuro-radiologist. Therefore, the MRI reports were often inordinately delayed, sometimes for as long as one year. Due to this unacceptable delay, we explored alternative arrangement of either hiring a neuro-radiologist or paying for MRI reporting by a private radiologist. The institutional recruitment rules did not permit hiring of a part-time neuro-radiologist. Eventually, 156 MRI scans were outsourced for reporting.

vi. ***IT component***: We had planned to collect the data on paper to be entered into desktop computers by the data entry operators. We had, therefore, not budgeted for IT component. By the third year of the project, it became necessary to create an online data collection tool, a website, and physical servers. For setting up a good IT system, we sought support from several government entities. However, our attempts were unsuccessful. Therefore, we submitted a request to the funding agency for re-appropriation of already sanctioned budget. The funding agency took about 18 months to sanction the re-appropriation of funds.

vii. ***Regulatory approvals:*** The Preconception and Pre-Natal Diagnostic Techniques (PNDT) Act required registration of all ultrasound sonography (USG) machine with the designated district health authority. For the rural site to complete this process took more than a year due to various administrative reasons.

viii. ***Managing people:*** It was challenging to keep all investigators, most of whom were clinicians with no formal training in epidemiology, engaged and

motivated in an epidemiological study. The clinicians often insisted on a more detailed clinical work-up than was necessary for the scope of this epidemiological study. This possibly was the reason for waning of interest of the investigators over period of time.

ix. ***Managing expectations:*** Majority of the urban participants had government-funded free medical insurance. Non-altruistic participants did not find any additional personal benefit of attending the MAS. Persuading such persons to visit MAS was difficult. Participants often sought detailed reports of their medical assessments. They also demanded facilitation for consultation in various specialty departments of AIIMS, New Delhi on a priority basis. To keep the participants engaged and motivated, more than 3000 such consultations were arranged.

Challenges during COVID-19 pandemic (February 2020–February 2022)

i. ***Follow up visit:*** In July 2019, the urban site completed its phase-1 recruitment goal of 7500 participants. The International Advisory Committee and the PI decided to initiate the first follow up visits of urban site participants from February 2020. However, the first case of COVID-19 was reported in India in January 2020, prompting the Government of India to issue various containment measures. Hence, physical contact with the participants and their visit to MAS could not take place. During this period, follow up data was collected telephonically. Even when restrictions were withdrawn, participants were reluctant to visit MAS at AIIMS, New Delhi, fearing contracting COVID-19 infection. However, participants were agreeable for medical assessment if the MAS was relocated within the study area. We requested for an additional grant of approx. US$ 16,000 to set up such a facility within the community. Our request was refused.

ii. ***Discontinuation of non-emergency MRIs:*** The patient-serving MRI facility at AIIMS, New Delhi, suspended non-emergency MRIs due to the COVID-19 pandemic. As a result, MRIs for cohort were also stopped.

Conclusion

We share our experience of establishing and operationalizing a public-funded cohort study in the premier medical institute of India. Under-funding was the most important challenge that we faced. Refusal of the funding agency to allow reappropriation of the sanctioned budget was another impediment. We suggest that equipments that are critical for the research work e.g. MRI machine, should be procured for exclusive use. Large-scale research projects must provision sufficient budget for information technology support. The pay package offered to highly qualified/skilled personnel should be reasonable and reflect current market norms. Procurement, especially of high-value equipments, is a time-consuming activity and therefore sufficient time should be factored-in for the same. Some steps though relatively inexpensive (e.g. hiring of field office space) may cause great inconvenience if not anticipated. We believe that meticulous planning, adequate and timely funding, recruitment of qualified manpower, use of web-based technologies and support from all stakeholders such as funders, organization, and community are critical to implement such large cohort studies in the Indian context.

Contributors

KG conceptualized and prepared the first draft of the manuscript; SND and SK supervised the field activities and designed the analytic strategy; DV, AKP, and AKS helped conduct the literature review; HT, AI and KP directed its implementation and final review. KP and SND have accessed and verified data for this article. All authors had full access to all the data in the study and accept responsibility to submit for publication. All authors approved the final version of the manuscript.

Declaration of interests

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The authors declare no competing interests.

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