BMJ Open

Nepal Family Cohort study: a study protocol

Om P. Kurmi ,[1,2,3] Nagendra Chaudhary ,[4] Gayathri Delanerolle,[5,6] Charlotte E Bolton ,[7,8] Puspa Raj Pant ,[3] Pramod R Regmi ,[9] Sanjivan Gautam,[3] Imran Satia ,[2] Padam Simkhada,[10] Ioannis Kyrou ,[11] Tara Kant Sigdel,[3] Vanora Hundley ,[12] Prashil Raj Dali,[3] Anders Løkke ,[13] Kin Bong Hubert Lam ,[14] Derrick Bennett,[14] Adnan Custovic,[15] Edwin van Teijlingen ,[12] Paramjit Gill ,[16] Harpal Randeva,[17,18] Paul O'Byrne ,[2] Nepal Family Cohort Collaborators

To cite: Kurmi OP, Chaudhary N, Delanerolle G, *et al*. Nepal Family Cohort study: a study protocol. *BMJ Open* 2024;**14**:e088896. doi:10.1136/bmjopen-2024-088896

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-088896).

Received 17 May 2024
Accepted 16 October 2024

For numbered affiliations see end of article.

Correspondence to
Dr Om P. Kurmi;
om.kurmi@coventry.ac.uk

ABSTRACT

Introduction The Nepal Family Cohort study uses a life course epidemiological approach to collect comprehensive data on children's and their parents' environmental, behavioural and metabolic risk factors. These factors can affect the overall development of children to adulthood and the onset of specific diseases. Among the many risk factors, exposure to air pollution and lifestyle factors during childhood may impact lung development and function, leading to the early onset of respiratory diseases. The global incidence and prevalence of respiratory diseases are rapidly increasing, with the rate of increase in Nepal being the highest. Although the cohort will primarily focus on respiratory health, other health outcomes such as cardiovascular, metabolic and mental health will be assessed to provide a comprehensive overall health assessment. All other health outcomes are self-reported following doctor diagnosis. Some of these health outcomes will be quality controlled during the follow-up by measuring disease specific markers. Our cohort study will likely provide evidence of risk factors and policy recommendations.

Methods and analysis Using a life-course epidemiology approach, we established a longitudinal study to address the determinants of lung health and other health outcomes from childhood to adulthood. The baseline data collection (personal data anonymised) was completed in April 2024, and 16 826 participants (9225 children and 7601 parents) from 5829 families were recruited in different geographical and climate areas (hills and plains) of Nepal. We plan to follow up all the participants every 2–3 years. Descriptive analysis will be used to report demographic characteristics and compare rural and semi-urban regions. A linear regression model will assess the association between air pollution, particularly household air pollution (HAP) exposure, and other lifestyle factors, with lung function adjusted for potential confounders. A two-stage linear regression model will help to evaluate lung development based on exposure to HAP.

Ethics Ethical approval was obtained from the Nepal Health Research Council, Kathmandu, Nepal, and McMaster University, Hamilton, Canada. Permissions were obtained from two municipalities where the study sites are located. Parents provided signed informed consent and children their assent.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The Nepal Family Cohort is the first family cohort carried out in two geographically diverse locations (the hilly and plain regions) of Nepal that will follow children until their mid-20s to late 30s, capturing the different transitions from children to adolescence and then adulthood (mid-20s to mid-30s).
⇒ The study has measured exposures comprehensively, which will help understand various determinants of health outcomes, particularly lung health and lung-health–associated comorbidities.
⇒ Early identification of various determinants of health outcomes will provide enriched information that will help design prevention measures in resource-poor settings.
⇒ Long-term follow-up of the study participants is planned for the next two decades, but at this stage, we cannot precisely calculate the loss to follow-up, which might reduce the sample size; therefore, specific stratified analyses might not be possible, limiting our understanding of the causation.
⇒ Carrying out a longitudinal study is resource intensive, and hence, the available resources will determine whether we can enhance additional measurements during follow-up to ensure the findings' wider applicability.

Dissemination Findings will be disseminated through traditional academic pathways, including peer-reviewed publications and conference presentations. We will also engage the study population and local media (ie, research blogs and dissemination events) and prepare research and policy briefings for stakeholders and leaders at the local, provincial and national levels.

BACKGROUND AND RATIONALE

Cross-sectional studies from Nepal have highlighted that adverse respiratory health, particularly chronic obstructive pulmonary disease, has the highest prevalence among all non-communicable diseases; however, no respiratory health-related longitudinal studies

exist in the country, neither in children nor adults.[1 2] Lung health is influenced by multiple, complex factors throughout life, starting in utero and contributing factors that change over the life cycle.

Some intergenerational cohorts, the majority from high-income countries (HICs), have suggested that parental environmental factors can also affect foetal development, including the lung.[3–5] Parental nutrition, lifestyle, and environmental and occupational exposures can significantly impact the health outcomes of their offspring. Moreover, intergenerational insults, such as exposure to environmental toxins or stressors, can also affect long-term foetal development.[6]

Studies from HICs have suggested that impaired lung growth is associated with numerous clinical outcomes, for example, an increased risk of cardiorespiratory diseases, early morbidity and premature mortality.[1 2] The effect of early insults on subsequent early morbidity and premature mortality can only be understood if the many prenatal and postnatal factors affecting lung development are considered holistically.

Early life events, including childhood and adolescence, are critically important in determining an individual's health expectancy throughout life and open new opportunities for understanding diseases, disease prevention, early treatment, therapeutic optimisation and prognosis improvement. Asthma has been less extensively studied in low and middle-income countries (LMICs); hence, our understanding of the different risk factors associated with asthma development, notably the indoor environment and lifestyle in LMICs, is limited.

Cross-sectional studies in Nepal suggest increased respiratory symptoms and reduced lung function in Nepalese adults exposed to household air pollution (HAP). By 16–25 years, lung function is reduced in smoke-exposed wood compared with liquefied petroleum gas users.[7 8] The reduced lung function in young adults may reflect impaired lung growth during early childhood because of ante/postnatal exposure to HAP.[7] In a study of 4000 newborns in Nepal, we reported that mothers who regularly used biomass fuel to cook before and during pregnancy were five times more likely to deliver small gestational age babies, indirectly suggesting a role of HAP on lung growth.[9] No previous studies in Nepal provide a holistic picture of environmental, behavioural and metabolic risk factors associated with respiratory health problems. Young children exposed to HAP have a two to three times greater risk of severe acute lower respiratory tract infection (ALRTI) than unexposed children after adjusting for potential confounders such as parental smoking.[10] Whether the rate of lung function decline during adulthood in Nepal's population is a function of reduced lung growth during childhood is unknown. Prospective family cohort studies with serial measurement of lung function; objective assessment of childhood respiratory conditions (asthma, ALRTI, etc.); and various risk factors, including lifestyle factors, are needed to identify how to prevent the growing burden of adverse respiratory health in both children and adults in Nepal and effectively manage the conditions.

The proposed Nepal Family Cohort study will address some of the questions raised by our previous cross-sectional studies that explored the relationship between air pollution from various sources and its link with respiratory health and lung function in Nepalese adolescents and adults (16+ years). *The primary aim of this Nepal Family Cohort study is to establish a longitudinal cohort of children and their parents in Nepal to understand the prevalence, incidence and determinants of lung and other health conditions from childhood to adulthood using a life course epidemiology approach.*

METHODS AND ANALYSIS

Study design and settings

The Nepal Family Cohort study is a prospective observational family cohort. We will follow this cohort's participants (children and their parents) every 2–3 years for over two decades from childhood to adulthood. Linkage to electronic health records is currently impossible for the study participants as Nepal still needs to have electronic health records (with unique identifiers) in most healthcare systems, including tertiary hospitals. The study is being conducted in two of Nepal's geographically diverse regions (hilly and plain regions) (figure 1). The altitude of the plain region is about 150 m from sea level, whereas that of the Hilly region is between 731 and 1500 m above sea level. We plan to expand this to other areas, including the mountainous Himalayan region of Nepal, which will be subject to securing additional funding during the follow-up. This will help represent the Nepali population from all geographical regions.

Recruitment and consent

Field researchers visited each household in both recruitment regions to explain the study's aims and objectives and invite them to participate. The parents provided informed consent, and the children above seven consented to participate in the baseline and subsequent follow-up studies.

Inclusion criteria

Each family from each household in the two geographical regions with children ranging from 6 to 9 years old was invited to join the study. Parents of children who provided informed written consent to be included in the baseline and consented to be contacted for follow-up studies were enrolled. Only permanent residents of the sampling locations were included in the family. Only those children with at least one of the parents also consenting to participate were included.

Exclusion criteria

Temporary residents within these areas and children with a medical condition, such as recent surgical procedures that prevent the assessment of lung function, were excluded, as were those not providing consent.

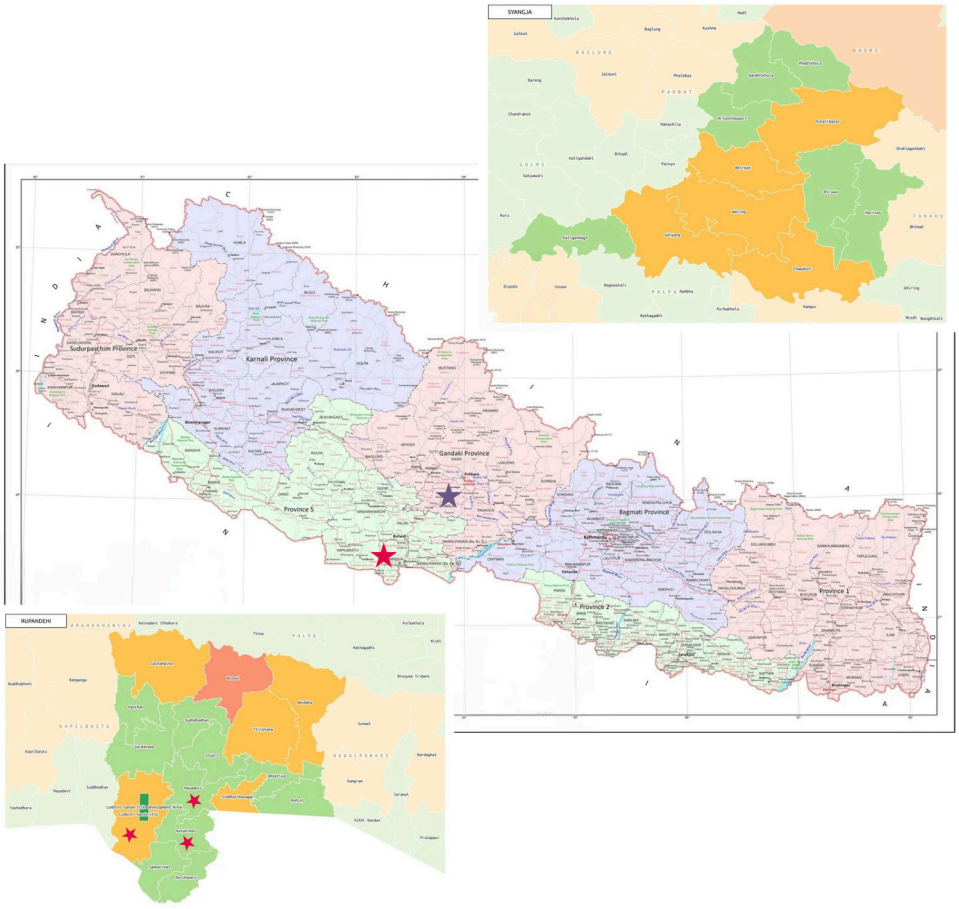

Figure 1 Sampling locations (plain region (red star) and hilly region (blue star)).

Data collection

Following 2 weeks of training for all field researchers in June 2022, a pilot study was conducted in the plain region in late June. The actual baseline data collection started in July 2022. Field researchers visited each household in the villages to explain the study and request that they participate. About 90% of those household visited and meeting the eligibility criteria participated in the study. Similarly, about 50% of the participants were from semi-urban areas and 75% from rural areas of hilly regions. Each participant in the sampling site was provided with the opportunity to participate in the study. All field data were collected and managed by Research Electronic Data Capture (REDCap)[11 12] software installed on tablets. Once the data were captured on the tablet through REDCap, they were sent and stored in a secure iCloud platform at the end of the day. Three labels of access were provided to the people involved in the research. Field researchers were provided first (primary) data entry-level and edit facilities for new participants only. The field researchers had no edit facility once the data were uploaded to iCloud. The data management team had a second level of access facility, checked the data and locked it, assuring that all data were quality controlled. Only the head of the data manager and the principal investigator (PI) had full access to all the data once the quality control was conducted. online supplemental table 1 lists major themes and questionnaires for data acquisition.

Primary outcomes

Our primary aims are to measure respiratory health and post-bronchodilator lung function[13] in participating children and their parents through spirometry at baseline and lung growth using repeat lung function measurement during follow-up visits. We will further assess the incidence and prevalence of respiratory health in children and adults, including asthma and acute lower-respiratory tract infection. Moreover, other health outcomes such as mental health, cardiovascular-related health outcomes, cancer, tuberculosis, kidney diseases and metabolic disorders were assessed in both children and parents.

Questionnaire

An investigator-delivered questionnaire collected data from the children and their parents using REDCap[14] installed on tablets. The questionnaire was designed in English and translated into Nepali, and it was back-translated to English by a qualified independent translator. The questionnaire includes demographic data, socioeconomic status (SES), domestic fuel use (for cooking, heating and light purposes), lifestyle factors (such as smoking, diet and alcohol consumption),

occupational history, breastfeeding, birth complication, general health during pregnancy, the weight of children at birth, type of delivery, premature birth, micro-nutrients intake, physical activities, health-related quality of life,[15] validated respiratory questionnaires to measure asthma (eg, International Study of Asthma and Allergies in Childhood questionnaire),[16 17] respiratory symptoms (Medical Research Council (MRC) and European Community Respiratory Health Survey (ECRHS)),[8 18–20] parental smoking, environmental tobacco smoke, ventilation and other related exposures. We collected information about income, education, types and duration of the jobs, home characteristics, fuel use and transport so that socioeconomic status can be measured comprehensively.

Anthropometry, bio-impedance and handgrip strength measurements

Both adults and children were measured for weight using a digital scale with 100 g accuracy. Standing and sitting height were measured using a stadiometer. Skinfold thickness at seven sites ((1) *tricep,* vertical fold at midpoint of the posterior side of the tricep between the shoulder and elbow with arm relaxed at side; (2) *chest*, diagonal fold half the distance between the anterior axillary line and nipple; (3) *subscapular,* diagonal fold 2 cm from the inferior angle of the scapula; (4) *midaxillary*, at midaxillary line horizontal to xiphoid process of sternum (5) *suprailiac*, diagonal fold parallel and superior to the iliac crest; (6) *abdominal*, vertical fold 2 cm right of the navel; and (7) *thigh*, midpoint of the anterior side of the upper leg between the patella and top of the thigh) was measured by Harpenden Calliper.[21] Circumferences of the head, chest, waist, hip, upper leg and mid-upper arm were recorded using a RENPHO measuring tape. The four-limb Tanita bioimpedance monitor measured fat-free mass, body water content and fat percentage in children and their parents.[22] Handgrip measurements in both arms were taken in triplicate using a Jamar dynamometer in a sitting position, and the dominant hand was recorded.[23]

Lung function, oxygen saturation, pulse rate and blood pressure measurement

Spirometry was used to measure lung function in children and their parents using hand-held spirometers (EasyOne NDD spirometer or Ganshorn Spirometer) following the European Respiratory Society/American Thoracic Society guidelines.[13 24] The spirometers were calibrated using three-litre syringes. Lung function was repeated 15 min after salbutamol was given to both children and their parents. Children were given 200 µg of salbutamol, whereas their parents were given 400 µg of salbutamol through a metered dose using a spacer.[25] A pulse oximeter measured oxygen saturation and heart rate.[26] A digital automated portable blood pressure monitor was used to measure brachial and ankle blood pressure in a sitting position.[27] For all individuals, three blood pressure measurements were carried out in the left arm and left leg following a 5-min rest before starting the first measurement.[28]

Measurement of dietary and micro-nutrient information

The dietary intake of parents and their children was measured using a 24-hour nutritional record using a validated food frequency questionnaire for the Nepalese population.[29] The questionnaire data will be compared with the Nepalese food composition table to calculate the average calories the children consume. Any vitamin and micronutrient supplements taken were recorded as well.

Urine sample

We measured eleven different parameters (urobilinogen, glucose, ketone, bilirubin, protein, nitrite, pH level, blood, specific gravity, leucocytes and ascorbic acid) in spot urine using a semiquantitative method (dipsticks).[30]

Environmental exposure assessment

Using a low-cost sensor device (Atomotube PRO), real-time area monitoring of particulate matter of different aerodynamic diameters ($PM_{1.0}$, $PM_{2.5}$, PM_{10}), volatile organic compounds, atmospheric pressure, temperature and relative humidity were measured in a population subsample to represent household and ambient air pollution in each village.

Statistical analysis plan

First, we briefly describe our plan for the primary outcome of respiratory health (respiratory symptoms and lung function measurement) and HAP exposure. Frequencies will be calculated for the baseline characteristics and compared between rural and semiurban children using a suitable test for heterogeneity.

A linear regression model will assess the association between HAP exposure (particulate matter) and lung function indices, adjusting for potential confounders. When multiple-point lung function data becomes available after follow-up, we will use linear regression methods to assess the differences in lung growth based on a study group or HAP exposure using a two-stage model. The first stage will be a linear regression of lung function variables on age by subject, generating a separate lung growth slope for each subject for each spirometric variable. In the second stage, the subject-specific growth slopes will be analysed on the study group to estimate average lung growth. Secondary exposure-response analyses using log-transformed (if asymmetrical) mean PM data from baseline to follow-up periods in both the summer and winter will be conducted to estimate the change in lung growth associated with changes in airborne pollutants exposure. We will compare the change in lung growth in the biomass with the reference group (used clean fuel only and no respiratory health problems) to see the degree of reversibility from impaired lung function. 95% CI will be estimated using a robust estimator. Sex, height at first lung function measurement, the annual change in height and parents' smoking history will be included as a priori confounding in all second-stage models. All potential

confounders will be assessed for inclusion by backward elimination, and variables with a p value <0.1 will be retained. A generalised estimating equation approach and empirical standard errors (SEs) will account for multiple episodes of ALRTI and asthma within a child. We will undertake exposure-response research with the child's airborne pollutant exposure measurements to assess how exposure misclassification might limit the ability to detect effects in the analysis and examine an additional potential contribution to causal inference.

After adjusting for potential confounders, we will use regression analysis (mixed-effect logistic regression) to assess the association between self-reported biomass use and respiratory health outcomes, followed by a sensitivity analysis.

ETHICS AND REGULATORY ASPECTS

Ethics approval

Ethical approval has been obtained from the Nepal Health Research Council (NHRC) reference: 2905 (Plus amendments 674 and 3700) and the Hamilton Integrated Ethics Review Board (Reference: 13605). The parents provided a signed consent form, and the children provided an assent form.

Dissemination

We plan to disseminate findings of major public health importance to research communities mainly through traditional routes such as scientific abstracts and publications to the general public, communities through mass media (social, newspaper articles, television) and dedicated websites, and policy-making bodies (Nepal Health Research Council, Ministry of Population and Health of Nepal) through written reports and policy briefs. We also plan to deliver webinars, prepare podcasts and organise workshops for greater outreach. A dedicated webpage (www.nepalstudy.org) has been built, but this will be reformatted and redesigned by a professional web designer with regular updates about project activities and research findings.

Unexpected findings and reporting

The field staff are well trained along Good Clinical Practice guidelines to ensure quality assurance in data acquisition and identifying specific values outside the standard/reference range. Any participants, particularly the parents with abnormal findings, are advised to consult their clinicians. In contrast, the children with abnormal findings are referred to Dr. Chaudhary, a practising paediatrician near the sampling sites, for appropriate advice. The field staff are not clinically trained and, therefore, cannot provide medical advice. The field staff are well trained to maintain confidentiality and not to discuss any personal or health issues as reported by the participants with anyone except the PI (Dr. Kurmi) and country PI (Dr. Chaudhary). All the signed consent forms and any paper containing some information about the measurement are stored in a locked storage area in the office of the coordinating centres.

Data management and oversight

The data were collected in English, but the questionnaires were read in Nepali and the local language. Any discrepancies will be addressed before the analysis. A combined database will be built for questionnaires, exposure and clinical data.

Field research workers discussed the study with parents, obtained informed consent and collected study data. Dr. Kurmi provided the overall supervision, whereas Dr. Chaudhary coordinated and supervised the team in the field. A coordinating centre has been established at the sampling sites.

Data storage and security

Our data sharing and preservation strategy will follow NHRC policy and established principles for data access. Data will be adequately curated throughout its life cycle and released with updated and relevant metadata. The data will be stored on the Coventry University server in England and backed up daily to avoid data loss.

All data collected will be stored on a secure database with limited access and password entry. Each enrolled participant will be allocated a unique study identifier, which will be used on source documents. The Good Clinical Practice code of practice and procedures will handle all personal data collected during the study.

Although a data privacy breach is unlikely because the data are anonymised, there is still a risk. If there is any privacy breach, we will follow local guidelines to contain it, evaluate the risks, notify individuals and prevent the violation by thoroughly investigating the cause.

Study governance

The principal investigator and Nepal-based country PI oversee the Nepal Family Cohort study. Based in Kathmandu, Nepal, the Nexus Institute of Research and Innovation manages staff-related issues or local guidelines. The follow-up study and any potentially new component or change to the study will be discussed in regular monthly meetings and after appropriate ethical approval.

Outputs and anticipated impact

During the baseline study, 5829 families participated. During the baseline study, 16826 participants (9225 children and 7601 parents) participated. Among the children, 4863 (52.7%) were boys, and 4362 (47.3%) were girls. Among the 16826 participants, 16043 (95.4%) provided post-bronchodilator spirometry. The 16043 participants with post-bronchodilator spirometry constitute of male parents (11.6%), female parents (33.7%), boys (28.9%) and girls (25.7%). This is the largest family cohort from any LMIC with the most extensive post-bronchodilator spirometry data.

The major strengths of this family cohort are as follows: (i) recruitment from marginalised ethnic groups with one of the highest risks of adverse health outcomes, including

lung health; (ii) sampling unit consisting of children and their parents for holistic study in understanding the major determinants of diseases; (iii) first longitudinal design in Nepal to understand the adverse health outcomes from healthy individuals to onset of health problems; (iv) it is representative of rural and peri-urban communities from two geographical regions with various environmental, climatic conditions and different lifestyles; (v) the sample consisting of objective measurement of various health outcomes, particularly lung health; (vi) inclusion of biological samples (urine) during the baseline with planned collection for blood and saliva during the follow-up; (vi) inclusion of both healthy individuals and those with existing health problems; (vii) detailed collection of intergenerational risk factors such as environmental, metabolic and occupational; and (viii) provide a unique platform for understanding determinants of various health problems and carrying out interventions for prevention and management of various diseases.

Our research aims to identify and reduce the burden of respiratory health and other non-communicable diseases in children and their parents in LMIC settings. This could increase healthy life expectancy, reduce healthcare costs and boost productivity. Our goal is to produce high-quality data that can be used to diagnose, prevent, and manage disease burdens and support future research proposals. We plan to implement our findings beyond research settings to improve healthy life expectancy in multiple regions, aligning with social care objectives. Additionally, our research will help build local capacity in Nepal.

Author affiliations
[1]Centre for Healthcare and Communities, Coventry University, Coventry, UK
[2]Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[3]Nexus Institute of Research and Innovation, Lalitpur, Nepal
[4]Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal
[5]University of Birmingham, Birmingham, UK
[6]Southern Health NHS Foundation Trust, Southampton, UK
[7]NIHR Nottingham Biomedical Research Centre, Nottingham, UK
[8]Centre for Respiratory Research, Translational Medical Sciences, School of Medicine, University of Nottingham, Nottingham, UK
[9]Faculty of Health and Social Sciences, Bournemouth University, Bournemouth, UK
[10]School of Human and Health Sciences, University of Huddersfield, Huddersfield, UK
[11]WISDEM Centre, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK
[12]Centre for Midwifery & Women's Health, Bournemouth University, Bournemouth, UK
[13]Lung Department, B, Aarhus University Hospital, Aarhus C, Denmark
[14]Nuffield Department of Population Health, University of Oxford, Oxford, UK
[15]Imperial College London, London, UK
[16]Warwick Centre for Global Health, University of Warwick, Coventry, UK
[17]Cardiology, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK
[18]University of Warwick Warwick Medical School, Coventry, UK

X Charlotte E Bolton @bolton_char, Puspa Raj Pant @Puspa_RPant, Pramod R Regmi @iresearch and Edwin van Teijlingen @EvanTeijlingen

Acknowledgements We acknowledge all the families that have participated and thank them for their time. We also thank our field staff (Ganesh Prasad Ahir, Rabindra Kumar Yadav, Santosh Kumar Yadav, Gulab Yadav, Amit Tiwari, Grijesh Kurmi, Sant Kumar Maurya, Ganesh Prajapati, Sarita Chaudhary, Srijana Chaudhary, Autari Tharu, Sabika Dhaval, Bishwas Tiwari, Padam BK, Sabita Shrestha, Tara Basnet, Tara Lamsal) for their dedication in data collection and Mr. Suraj Parajuli for assisting in the administration. We would also like to thank the village and municipality representatives for helping with the fieldwork and Dr. Nirmal Aryal for helping check the Nepali translation of the questionnaire. A special thanks to Mr. Lars Kuettel, Ganshorn Medizin Electronic GmbH, for providing Ganshorn spirometers and accessories at a subsidised rate for this research.

Collaborators Nepal Family Cohort Collaborators Group: Rajendra Pangeni, Milan Bimali, Dipak Uprety, Ashish Shetty, Peter Phiri, Jian Shi Qing, Ashesh Dhungana, John Hurst, John Balmes, Balram Gautam, Tara Ballav Adhikari, Jagat Jeevan Ghimire, Sudhir Kumar Tyagi, Satyendra Upadhyay.

Contributors OK wrote the first draft of the protocol, and all other co-authors reviewed and edited the manuscript. All authors agreed on the final submitted manuscript. OK is the guarantor.

Funding The study has received cash and in-kind support from McMaster University, Hamilton, Canada; Nepal Health Research Council, Kathmandu, Nepal; University of Huddersfield, Huddersfield, UK; America Nepal Medical Foundation, USA; and Bournemouth University, Bournemouth, UK.

Map disclaimer The inclusion of any map (including the depiction of any boundaries therein), or of any geographic or locational reference, does not imply the expression of any opinion whatsoever on the part of BMJ concerning the legal status of any country, territory, jurisdiction or area or of its authorities. Any such expression remains solely that of the relevant source and is not endorsed by BMJ. Maps are provided without any warranty of any kind, either express or implied.

Competing interests None declared except PG, who is supported by the NIHR Applied Research Collaboration West Midlands and an NIHR Senior Investigator, and CEB, who is supported by the NIHR Nottingham Biomedical Research Centre.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Om P. Kurmi http://orcid.org/0000-0002-9518-4716
Nagendra Chaudhary http://orcid.org/0000-0002-3216-8671
Charlotte E Bolton http://orcid.org/0000-0002-9578-2249
Puspa Raj Pant http://orcid.org/0000-0002-8827-0018
Pramod R Regmi http://orcid.org/0000-0003-0226-3894
Imran Satia http://orcid.org/0000-0003-4206-6000
Ioannis Kyrou http://orcid.org/0000-0002-6997-3439
Vanora Hundley http://orcid.org/0000-0003-3578-4135
Anders Løkke http://orcid.org/0000-0002-6905-4141
Kin Bong Hubert Lam http://orcid.org/0000-0003-1228-3362
Edwin van Teijlingen http://orcid.org/0000-0001-5523-8583
Paramjit Gill http://orcid.org/0000-0001-8756-6813
Paul O'Byrne http://orcid.org/0000-0003-0979-281X

REFERENCES

1 Bista B, Dhimal M, Bhattarai S, *et al*. Prevalence of non-communicable diseases risk factors and their determinants: Results from STEPS survey 2019, Nepal. *PLoS ONE* 2021;16:e0253605.

2 Dhungana RR, Karki KB, Bista B, *et al*. Prevalence, pattern and determinants of chronic disease multimorbidity in Nepal: secondary analysis of a national survey. *BMJ Open* 2021;11:e047665.
3 Eriksen KG, Radford EJ, Silver MJ, *et al*. Influence of intergenerational *in utero* parental energy and nutrient restriction on offspring growth in rural Gambia. *FASEB J* 2017;31:4928–34.
4 Townsend ML, Riepsamen A, Georgiou C, *et al*. Longitudinal Intergenerational Birth Cohort Designs: A Systematic Review of Australian and New Zealand Studies. *PLoS ONE* 2016;11:e0150491.
5 Klijs B, Angelini V, Mierau JO, *et al*. The role of life-course socioeconomic and lifestyle factors in the intergenerational transmission of the metabolic syndrome: results from the LifeLines Cohort Study. *Int J Epidemiol* 2016;45:1236–46.
6 Braun JM, Messerlian C, Hauser R. Fathers Matter: Why It's Time to Consider the Impact of Paternal Environmental Exposures on Children's Health. *Curr Epidemiol Rep* 2017;4:46–55.
7 Kurmi OP, Devereux GS, Smith WC, *et al*. Reduced lung function due to biomass smoke exposure in young adults in rural Nepal. *Eur Respir J* 2013;41:25–30.
8 Kurmi OP, Semple S, Devereux GS, *et al*. The effect of exposure to biomass smoke on respiratory symptoms in adult rural and urban Nepalese populations. *Env Health* 2014;13:92.
9 Chaudhary N, Yadav SN, Kalra SK, *et al*. Prognostic factors associated with small for gestational age babies in a tertiary care hospital of Western Nepal: A cross-sectional study. *Health Sci Rep* 2021;4:e250.
10 Ezzati M, Kammen D. Indoor air pollution from biomass combustion and acute respiratory infections in Kenya: an exposure-response study. *Lancet* 2001;358:619–24.
11 Blumenberg C, Barros AJD. Electronic data collection in epidemiological research. The use of REDCap in the Pelotas birth cohorts. *Appl Clin Inform* 2016;7:672–81.
12 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
13 Graham BL, Steenbruggen I, Miller MR, *et al*. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med* 2019;200:e70–88.
14 Agnihotri AK, Joshi HS, Agnihotri S. Air pollution problems in Nepal and its prevention. *International Journal of Medical Toxicology and Legal Medicine* 2005;8:17–9.
15 Janssen MF, Pickard AS, Golicki D, *et al*. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. *Qual Life Res* 2013;22:1717–27.
16 Yoshida K, Adachi Y, Sasaki M, *et al*. Test-retest reliability of the International Study of Asthma and Allergies in Childhood questionnaire for a web-based survey. *Ann Allergy Asthma Immunol* 2014;112:181–2.
17 Valle SOR, Kuschnir FC, Solé D, *et al*. Validity and reproducibility of the asthma core International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire obtained by telephone survey. *J Asthma* 2012;49:390–4.
18 Stenton C. The MRC breathlessness scale. *Occup Med (Lond)* 2008;58:226–7.
19 Sunyer J, Basagaña X, Burney P, *et al*. International assessment of the internal consistency of respiratory symptoms. European Community Respiratory Health Study (ECRHS). *Am J Respir Crit Care Med* 2000;162:930–5.
20 Definition and classification of chronic bronchitis for clinical and epidemiological purposes. A report to the Medical Research Council by their Committee on the Aetiology of Chronic Bronchitis. *Lancet* 1965;1:775–9.
21 Kuo F-C, Lu C-H, Wu L-W, *et al*. Comparison of 7-site skinfold measurement and dual-energy X-ray absorptiometry for estimating body fat percentage and regional adiposity in Taiwanese diabetic patients. *PLoS ONE* 2020;15:e0236323.
22 Parker H, Hunt ET, Brazendale K, *et al*. Accuracy and Precision of Opportunistic Measures of Body Composition from the Tanita DC-430U. *Child Obes* 2023;19:470–8.
23 Guerra RS, Amaral TF, Sousa AS, *et al*. Comparison of Jamar and Bodygrip Dynamometers for Handgrip Strength Measurement. *J Strength Cond Res* 2017;31:1931–40.
24 Duong M, Islam S, Rangarajan S, *et al*. Mortality and cardiovascular and respiratory morbidity in individuals with impaired FEV_1 (PURE): an international, community-based cohort study. *Lancet Glob Health* 2019;7:e613–23.
25 Bhatta L, Leivseth L, Carslake D, *et al*. Comparison of pre- and post-bronchodilator lung function as predictors of mortality: The HUNT Study. *Respirology* 2020;25:401–9.
26 Crooks CJ, West J, Morling JR, *et al*. Pulse oximeter measurement error of oxygen saturation in patients with SARS-CoV-2 infection stratified by smoking status. *Eur Respir J* 2022;60:2201190.
27 Stergiou GS, Parati G, McManus RJ, *et al*. Guidelines for blood pressure measurement: development over 30 years. *J Clin Hypertens (Greenwich)* 2018;20:1089–91.
28 Nexøe J, Damsbo B, Lund JO, *et al*. Measurement of blood pressure, ankle blood pressure and calculation of ankle brachial index in general practice. *Fam Pract* 2012;29:345–51.
29 Upreti DK, Kyle J, Simkhada PP, *et al*. Development and Validation of a Food Frequency Questionnaire for Assessment of Diet in Lower and Middle Income Countries; A study among People Living with HIV/AIDS in Nepal. *Asian J Agric Food Sci* 2015;3.
30 Berthet A, Bartolo S, Subtil D, *et al*. Spot urine protein-to-creatinine ratio as a diagnostic test in pre-eclampsia: A gold standard? *Int J Gynaecol Obstet* 2020;149:76–81.