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Interventions in early life and through the lifecourse to prevent non-communicable diseases in later life in India

Submission date
30/11/2020

Recruitment status
Recruiting

Registration date
17/12/2020

Overall study status
Ongoing

Last Edited
01/08/2025

Condition category
Other

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Non-communicable diseases (NCDs) including heart disease and diabetes are major causes of death and disability in low- and middle-income countries (LMICs) including India. This is accompanied by a growing recognition of the rising burden of mental health disorders. These diseases have significant economic implications; the treatment and related costs amount to INR 19914 (US$398) and INR 43285 ($865) per person per year for diabetes and dementia, respectively. Recent research suggests that adversity during early life influences adult NCD risk. It is now well established that low birth weight, poor infant nutrition, and rapid childhood weight gain and obesity are risk factors for poor health trajectories and development of NCDs in later life. It is therefore possible that interventions early in life may prevent NCDs in future generations.
Our overarching aim is to establish whether an integrated intervention package starting before pregnancy and continuing through pregnancy, infancy and early childhood reduces risk factors for NCDs in the children and improves their overall development, health and well-being.

Who can participate?
Women living in selected villages in the HD Kote Taluk area in Mysore district who are married, over 18 years of age, have no children or one child, and intend to have a child can participate.

What does the study involve?
Participants will be in one of three programme groups. The three programmes are different and all women in one village will be allocated to the same programme. This allocation will be done randomly (by chance) at village level and participants will not be able to choose. All three programmes will be different as we are trying to understand what works best in improving mother and child health in the longer term. All programmes will ensure that the current government recommendations are followed. We will also collect measurements on participants before pregnancy, and during pregnancy (if women become pregnant during the study). If women do not become pregnant, we will collect a set of measurements around 18-24 months

after the start of the study. We will collect further measurements on the women and on the children born during the study until 5 years of age. These measurements will include height, weight, blood pressure, blood and other samples, and information collected via questionnaires.

What are the possible benefits and risks of participating?
Participation will help to increase knowledge about healthy behaviours for themselves and for the healthy growth of their child. The study may contribute to a better understanding of maternal and child health practices that promote healthy pregnancy and childhood growth and development, and prevent diseases such as diabetes in later life. Participation will contribute to the advancement of scientific knowledge and help future generations.
There are no major health risks to participants or their child by participating in this study. Blood will be collected by trained health professionals. Some questions in the questionnaires are of a personal nature; if anyone feels uncomfortable answering them, they will have the option of not answering such questions. Only authorised research staff members will have access to the information.

Where is the study run from?
The study is run locally from the CSI Holdsworth Memorial Hospital, Mysore, and Vivekananda Memorial Hospital, Saragur, in collaboration with the University of Toronto in Canada.

When is the study starting and how long is it expected to run for?
The study is planned as a ten-year study including a period of formative work (now completed). Recruitment for the main study is expected to start in January 2021 and data collection will take place for another 8 years.

Who is funding the study?
The study is being funded national funding agencies in India and Canada: Department of Biotechnology, Government of India and the Canadian Institutes of Health Research.

Who is the main contact?
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Study website
https://helti.org

Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CSIHMH/ERU2019/1

Study information

Scientific Title
Early INterventions to Support Trajectories for healthy lifE in INdia (EINSTEIN) - a cluster randomized trial evaluating a multi-faceted intervention starting preconceptionally. A Healthy Life Trajectories Initiative (HeLTI) Study

Acronym
EINSTEIN

Study objectives
An integrated longitudinal intervention starting pre-conceptionally and continuing at appropriate points across the lifecourse (pregnancy, infancy and childhood) will reduce childhood adiposity and the risk for non-communicable diseases (NCDs) as well as improve measures of child neurodevelopment.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 14/12/2020, Institutional Review Board (Health) Swami Vivekananda Youth Movement (Vivekananda Memorial Hospital, Hanchipura road, Saragur, Mysuru district, Karnataka, 571121, India; +91 08228-265877; secretaryec@svym.org.in), ref: IRB004/2020-21

2. Approved 18/11/2019, CSI Holdsworth Memorial Hospital Ethics Committee (CSI Holdsworth Memorial Hospital, Mandi Mohalla, Mysore , 570001, India; +91 (0)821 4266371; csihmh@hotmail.com), ref: CSIHMH/ERU2019/1

3. Approved 25/03/2023, CSI Holdsworth Memorial Hospital Institutional Ethics Committee (CSI Holdsworth Memorial Hospital, Mandi Mohalla, Mysore, 570001, India; +91-821-2521651; directorcsihmh@gmail.com), ref: CSIHMH/ERU/2019/1

Study design
Community-based cluster-randomized intervention with three arms

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)

Community

Study type(s)
Prevention

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Prevention of non-communicable diseases in the next generation

Interventions
The study is a community-based, cluster-randomised intervention with three arms (preconception, pregnancy and control), with individual villages forming the basis for the cluster. Women in all three arms will be recruited together, pre-conceptionally for baseline measurements. The longitudinal multi-faceted intervention will be delivered by trained community health workers (CHWs), which will allow future scalability.

Randomisation will be undertaken through a standard computer-generated randomisation programme. The total duration of intervention and follow-up for all arms is a maximum of two years pre-conceptionally, 9 months of pregnancy and five years post-natally – a maximum of 7 years 9 months in total. However, if women become pregnant within two years (as many will based on our formative work), the duration of the pre-conceptional intervention phase will be reduced accordingly.

All participants will receive iron and folic acid tablets during pregnancy as per Indian guidelines. Calcium is routinely prescribed in pregnancy by many obstetricians. The researchers will not interfere with routine care provided by the women's obstetricians. They will liaise with local doctors to ensure that they are aware of the study and the supplements their patients are taking, so that the women do not receive 'excess' micronutrients. All women will also receive menstrual hygiene advice and will be provided with a supply of menstrual pads to promote appropriate hygiene practices.

Intervention details
Group 1 (preconception arm):
Micronutrient supplementation:
Women will receive daily micronutrient supplement tablets from recruitment preconceptionally, throughout pregnancy and during breastfeeding. Given the high likelihood of multiple deficiencies, the composition will be based on the WHO/UNICEF/UNU international multiple micronutrient preparation (UNIMMAP).

Lifestyle behavior change support:
Women will receive support from CHWs trained in Healthy Conversation Skills (HCS) in group settings. HCS is a communication technique developed at the University of Southampton by our wider team for use by health workers to support behaviour change in socio-economically disadvantaged women. This technique has been translated to LMIC settings; in a recent feasibility study involving our group in South Africa, community health workers have been successfully trained in HCS to support young women to improve their diets and lifestyles. The group work emphasises the role of increasing self-efficacy in promoting behaviour change. It is based on the understanding that providing participants with knowledge alone is not sufficient to change their behaviour unless they are also motivated and empowered to change. The aim will

be to promote a diverse diet, achieve a normal body weight, and achieve an adequate intake of micronutrients before and during pregnancy, and while breastfeeding. CHWs will provide support postnatally to encourage exclusive breastfeeding for the first 6 months and the timely introduction of diverse and nutritious infant weaning foods. Women will be educated about the importance of using safe water for feeding their infants after 6 months, and advised to use boiled and cooled water. They will receive support to ensure that their infants are fully vaccinated and that they adopt appropriate hygiene measures, particularly handwashing after using the toilet, changing 'nappies', and before preparing food, eating and feeding their infants. During the pre-conception stage, the group work will be held at approximately monthly intervals. There will be six modules, with the first module serving as an introductory and general health module. This will be delivered first to all women in the arm. The other five modules will be delivered cyclically and address diet, physical activity and sleep, environmental exposure and hygiene, mental health, and preparing for pregnancy.

Group parenting and cognitive behaviour intervention (Learning Through Play Plus {LTP Plus}):
LTP Plus is a group parenting programme, integrated with a cognitive behaviour therapy intervention (Thinking Healthy Programme) designed to address perinatal depression and improve child development in LMIC settings. It is a manual assisted, low-literacy, potentially sustainable programme whose activities enhance children's development. It simultaneously promotes attachment security through building parents' ability to be sensitive to their children's cues, and be actively involved in their children's development. These sessions will be delivered in phases which will not only match the woman's pace, but also the gestational period antenatally and the infant's developmental stages postnatally. This two-pronged psychosocial participatory group intervention will help mothers to cope with stress, reduce depression and provide information and strategies that they need to nurture their children's health and development. This will consist of a total of ten sessions, three during pregnancy and seven postnatally. LTP Plus uses a standardized manual and the material will be delivered by CHWs.

Avoiding environmental pollution:
The researchers will provide advice and information on avoidance of environmental pollutants particularly indoor smoke (cooking and smoking). They will facilitate LPG (liquefied petroleum gas) connections actively through a recently introduced government scheme which provides subsidized stoves and fuel. They will also address exposure to, and safe handling of pesticides.

Group 2 (pregnancy arm):
Women in this group will receive the same package of interventions described above, but starting only after they become pregnant, which, in practice, will mean late in the first trimester. Last menstrual period dates will be monitored monthly and women will be offered a urine pregnancy test when they report missing two consecutive periods.

Group 3 (control arm):
Women in this group will receive an enhanced standard of care. In addition to encouraging vaccinations (two doses of tetanus toxoid) during pregnancy, provision of 100 tablets of iron and folate, and promoting institutional delivery, they will have a similar number of contact sessions with CHWs untrained in our behaviour change and parenting interventions. They will receive standard advice on healthy lifestyle during pregnancy and postnatally, supported by information leaflets (mainly pictorial and using simple language); these will include advice on breastfeeding, immunizations, and infant weaning foods.

Intervention Type
Mixed

Primary outcome measure
Adiposity measured by fat mass index (fat mass/height²) using dual x-ray absorptiometry (DXA) at age 5 years in the children across all HeLTI cohorts

Secondary outcome measures
Measured in the children at age 5 years:
1. Overweight and obesity (OWO) assessed by BMI and indicators of body composition and distribution (waist circumference, skinfold thickness)
2. Glucose metabolism measured by fasting venous plasma glucose concentration
3. Resting systolic blood pressure measured using an automated blood pressure monitor
4. Child development assessed using modified Kaufman battery, validated for Indian settings

Overall study start date
01/10/2015

Completion date
31/12/2031

Eligibility

Key inclusion criteria
1. Women of childbearing age
2. Over the age of 18
3. Married
4. No children or one child
5. Planning to have a child within the next 2 years

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
105 clusters; initial recruitment of approximately 6000 women (55-60 women in each cluster); additional recruitment after a year if number of pregnancies are lower than estimated.

Key exclusion criteria
Those with two or more children

Date of first enrolment
15/03/2021

Date of final enrolment

31/12/2025

Locations

Countries of recruitment
India

Study participating centre
CSI Holdsworth Memorial Hospital
Mandi Mohalla
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Study participating centre
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Sponsor information

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Sponsor type
Hospital/treatment centre

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https://ror.org/05gfebp73

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Sponsor type
Hospital/treatment centre

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http://svym.org/programs/view/Vivekananda_Memorial_Hospital_Saragur

ROR
https://ror.org/00c44w836

Organisation
University of Toronto

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Sponsor type
University/education

Website
http://www.utoronto.ca/

ROR
https://ror.org/03dbr7087

Funder(s)

Funder type
Government

Funder Name
Department of Biotechnology, Ministry of Science and Technology, India

Alternative Name(s)
Dept. of Biotechnology, Govt of India, , , Department of Biotechnology, Department of Biotechnology, Ministry of Science & Technology, India, Department of Biotechnology, GOI, Dept. of Biotechnology, Govt. of India, Department of Biotechnology, Ministry of Sc & Tech, Govt of India, DBT

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
India

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 01/08/2025:
1. Six papers in various stages of submission and review.
2. Dissemination through local radio station, newsletters and briefs.

Previous publication and dissemination plan as of 09/04/2024:
1. Protocol paper published
2. Planned publications in peer-reviewed journals

Previous publication and dissemination plan:
1. Protocol paper under review at BMJ Open
2. Planned publications in peer-reviewed journals

Intention to publish date
31/12/2032

Individual participant data (IPD) sharing plan
The Healthy Life Trajectories Initiative (HeLTI) was launched as a joint initiative between the Canadian Institute of Health Research, the Department of Biotechnology of India, the South African Medical Research Council, the National Science Foundation of China and the World Health Organisation. Data sharing and access arrangements are included in the overall HeLTI governance document. The HeLTI consortium is in the process of establishing a Data Access Portal though which investigators can view and request access to data/biospecimens within individual HeLTI country or multiple country datasets. Data access will follow country-specific guidelines and is expected to require submission of a detailed research plan (including study rationale, hypothesis, analytic methodologies and funding support to complete the study /analyses). Once the study is completed the researchers will be required to submit all analytical and derived data with metadata to be integrated into the HeLTI country datasets, so that it is available to other researchers.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			17/12/2020	No	Yes
Other publications	Governance model for the HeLTI Consortium	16/05/2023	17/05/2023	Yes	No
Protocol article		16/02/2021	09/04/2024	Yes	No
Other files	Changes and progress update	01/08/2025	01/08/2025	No	No
Results article		01/03/2023	01/08/2025	Yes	No
Statistical Analysis Plan	version 2		01/08/2025	No	No