ISRCTN17472338 https://doi.org/10.1186/ISRCTN17472338

Advancing understanding of adolescent exposome exposure and methodology, intervention development, and translation for prevention strategies and policy

Submission date 24/02/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 07/04/2021	**Overall study status** Completed	
Last Edited 31/12/2024	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Major environmental hazards such as ambient air pollution, environmental tobacco smoke, water and food contaminants, noise, pesticides and ultraviolet light may lead to long-term health effects with large social and economic costs. As part of the previous European Commission Exposome Programme HELIX project, researchers used new tools and methods to characterise the totality of environmental exposures – known as the 'exposome' – to a wide range of hazards including both external exposures to the physical and chemical environment as well as the internal molecular signatures associated with these environmental exposures and investigated their impact on child health outcomes. This study aims to continue this research by exploring the impacts of exposure on adolescent health and co-producing interventions to reduce exposure. This is one of six birth cohort studies internationally taking part in this research.

Who can participate?
In WP1, the original HELIX cohort participants (n=231 aged 6-7 years) who are now in adolescence (aged 13-14 years) will be followed up.
In WP7, children aged 9-11 who attend two identified Bradford primary schools will be invited to participate.

What does the study involve?
In WP1, the researchers will assess a variety of measures including clinical examinations (including body composition, blood pressure, lung health, and neurodevelopment), biological samples (including blood, urine, and stool), sensor data (capturing movement and environmental exposures), as well as questionnaires capturing lifestyle behaviours and health.
In WP7, the researchers will work with two Bradford schools and 50 schoolchildren aged 10-11 to co-produce interventions to reduce exposure to pollution. School children will wear mobile sensors for up to 7 days to monitor where and when exposure to urban air pollutants occurs. The researchers will also conduct 'walking interviews' with 15 parents and their children to explore their experience of pollution on the school commute. The data collected will be used to co-

produce interventions with pupils, teachers, local decision-makers, and researchers to reduce children's exposure to pollution.

What are the possible benefits and risks of participating?
Participants will contribute to the understanding of exposure risks in early life health. Participants in WP7 will increase their understanding of urban exposures and participate in co-producing interventions to reduce child exposure to air pollutants. Potential risks include time commitments and the potential inconvenience of carrying measurement devices and blood sampling from those who consent.

Where is the study run from?
Bradford Institute for Health Research (UK)

When is the study starting and how long is it expected to run for?
January 2020 to January 2025

Who is funding the study?
European Union Horizon 2020

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
289958

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 47578, IRAS 289958

Study information

Scientific Title
Advancing Tools for Human Early Life-course Exposome Research and Translation (ATHLETE)

Acronym
ATHLETE

Study objectives
The main study hypothesis is that the exposome (all non-genetic exposures) can influence health. The researchers are seeking to characterize and examine relationships between the exposome and adolescent cardio-metabolic, respiratory, and mental health.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/12/2020, Yorkshire & The Humber - Bradford Leeds Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)2071048083; bradfordleeds.rec@hra.nhs.uk), REC ref: 20/YH/0315

Study design
Non-randomized; Both; Design type: Prevention, Psychological & Behavioural, Physical, Cohort study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Environmental hazards such as ambient air pollution, environmental tobacco smoke, water and food contaminants, noise, pesticides and ultraviolet light

Interventions
WP1 (follow up with participants):
All participants approached are part of BiB and have taken part previously in HELIX. They have given consent to be contacted in the future. Participants will be contacted by phone and by invitation letter. If interested in taking part, the researchers will have a detailed discussion with the parent and adolescent to ensure it is clear what is involved and any questions can be

answered. In view of COVID-19 this cannot happen at a home visit which would have been preferable. Given the situation, the researchers will do this over the phone and via Zoom call or similar (depending on what the participant prefers). The parent and the adolescent will complete a consent form. The adolescent will receive different devices measuring exposure over a 7-day period. These may be dropped off at the house.
- A smartphone with the ExpoApp3 installed (placed in a pouch to measure mobility)
- Carry a GENEActiv (on the wrist to measure sleeping patterns)
- Carry an Actigraph (attached to the belt to measure physical activity)
- Carry a NO_2 diffusion tube, placed on the outside of their backpack, to measure personal exposure to NO_2

During the 7-day period the researchers will also ask the adolescent to collect:
- Two urine samples every day: the first morning and the last of the day
- A faeces sample to study the adolescent's gut microbiota

The adolescent will complete a daily sleep and physical activity diary and a short questionnaire. Taking part involves ideally two visits to the study centre (due to COVID-19 all face to face data collection will be carried out at the Clinical Research Facility). One visit is for the assessment of the adolescent: measurements (height and weight, BP, bioimpedance, spirometry (depending on the COVID-19 situation), cognitive assessments and collection of a lock of hair (small enough not to affect the adolescent's appearance). Another visit will be after the 7-day measuring period for blood sampling. This will be a morning appointment to allow for fasting samples. Also, all devices will be returned. The researchers will provide transport to the Clinical Research Facility. They will also offer a reimbursement of £50 to show their appreciation for their participation.

WP7:
The researchers will be co-producing acceptable and feasible interventions to reduce the urban exposome amongst primary school-age children. There are three key parts to data collection: a) static monitoring in schools, b) personal urban exposure monitoring with primary school-age children to quantify their exposure to the urban exposome with N=50 school children recruited from two schools, and c) walk-along interviews with 15 parent and children dyads to explore their perceptions of the urban exposome on the route from school, and their perceived barriers and enablers to reducing the harmful urban exposome. The researchers will obtain informed consent from headteachers and parents, and assent from children.

These data will be used to co-produce interventions to reduce the urban exposome with children, parents, teachers and local 'healthy place decision makers' (e.g. from local authorities).

Intervention Type
Mixed

Primary outcome(s)
There is no singular outcome as WP1 will measure a host of personal and environmental exposures from personal monitoring, sensors, biosamples, and questionnaires. Similarly, there will be sensor data, questionnaires, and interviews for WP7 which will be used to describe environmental exposure.

Measures occurring at the clinical examination visit:
1. Anthropometry for height and weight is measured using SECA scales and the Leister Height Measure d=1mm; waist circumference is measured using a flexible tape measure. These are measured at one point in time and can be conducted up to 7 days before baseline (the start of the monitoring period) or 7 days after blood collection.

2. Bioimpedance is measured using the Bodystat 1500NDD device at one point in time and can be conducted up to 7 days before baseline (the start of the monitoring period) or 7 days after blood collection.
3. Blood pressure is measured using the OMRON electronic 705-CP11 device at one point in time and can be conducted up to 7 days before baseline (the start of the monitoring period) or 7 days after blood collection.
4. Spirometry is measured using the EasyOne spirometry device at one point in time and can be conducted up to 7 days before baseline (the start of the monitoring period) or 7 days after blood collection.
5. Neurodevelopment is measured using the N-back test (working memory), Roulettes task (risk-taking preferences), and Raven Standard Progressive Matrices (non-verbal general intelligence). These are computerized tasks that are conducted at one point in time and can be conducted up to 7 days before baseline (the start of the monitoring period) or 7 days after blood collection.

Biological samples:
1. Environmental exposures measured from hair (50 mg or ~1 cm^2 of scalp area) collected close to the scalp using scissors at one point in time and can be conducted at any time relative to the baseline visit.
2. Phthalates measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
3. Phenols measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
4. Organophosphate pesticides measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
5. Other pesticides (metabolites of pyrethroids, 2,4-dichlorophenoxyacid, boscalid, and imazalil) measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
6. Cotinine measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
7. Glycol ethers measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
8. Polycyclic aromatic hydrocarbon measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
9. Creatinine measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
10. Exogenous metabolomics measured from urine samples (collected using the Vitrex Vacusense 112510 kit) collected twice a day for 6 days from baseline.
11. The microbiome measured from stool samples (collected using Zymo Research 1101 collection tubes) collected once on day 7 from baseline.
12. Endogenous metabolomics measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
13. Glucose measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
14. Total and high-density lipoprotein (HDL) cholesterol measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
15. Triglycerides measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
16. Phospholipids measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
17. Glucose measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.

18. Alanine transaminase (ALT) measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
19. Aspartate aminotransferase (AST) measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
20. Gamma-glutamyl transferase (GGT) measured from fasting blood (using 6 ml silica (clot activator) vacutainer) collected once in a 3-day window starting on day 8 from baseline.
21. Exogenous metabolomics measured from fasting blood (using 5 ml silicone coated glass vacutainer 367614) collected once in a 3-day window starting on day 8 from baseline.
22. Metals and elements from fasting blood (using 6 ml K2EDTA (trace element determination) 368381) collected once in a 3-day window starting on day 8 from baseline.
23. Telomere length from fasting blood (using 6 ml K2EDTA (trace element determination) 368381) collected once in a 3-day window starting on day 8 from baseline.
24. Per- and polyfluoroalkyl substances (PFAS) from fasting blood (using 6 mL K2EDTA (trace element determination) 368381) collected once in a 3-day window starting on day 8 from baseline.
25. Endogenous metabolomics from fasting blood (using 6 mL K2EDTA (trace element determination) 368381) collected once in a 3-day window starting on day 8 from baseline.
26. Transcriptomics from fasting blood (using PAXGene 762125) collected once in a 3-day window starting on day 8 from baseline.

Sensor data:
1. Personal monitoring of sleep patterns and physical activity is collected sing the GENEActive devices for a period of 7 consecutive days from baseline.
2. Personal exposure data including to air and light pollution, sleep, physical activity, and location will be collected using the EXPOApp3 smartphone app for a period of 7 consecutive days from baseline.
3. Personal monitoring of physical activity is collected using the ActiGraph GT3X-BT for 7 consecutive days from baseline.
4. Personal exposure to NO2 is collected using Palmes passive diffusion tubes for 7 consecutive days from baseline.
5. Geocoding of home and school addresses, green spaces, and usual commuting routes is performed using the QGIS software version 3.12.3 “Bucureşti”. This is done once and can be conducted up to 7 days before baseline (the start of the monitoring period) or 7 days after blood collection.
6. Socioeconomic status is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
7. Ethnicity of the adolescent’s parents is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
8. Perceived stress of the adolescent’s parent is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
9. Adolescent’s diet is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
10. Food security is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
11. Adolescent’s physical activity is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
12. Adolescent’s asthma and allergies is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
13. COVID-19 symptoms and contact is collected using a parental questionnaire completed

flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
14. Adolescent's medication is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
15. Adolescent's sleeping patterns is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
16. Cooking and heating use is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
17. Parental medical history is collected using a parental questionnaire completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
18. Address history is collected using a parental questionnaire completed flexibly at baseline, clinical visit, over the telephone, or at home during the 7 monitoring days following the baseline visit.
19. Adolescent's schooling is collected using a parental questionnaire completed flexibly at baseline, clinical visit, over the telephone, or at home during the 7 monitoring days following the baseline visit.
20. The home environment is collected using a parental questionnaire completed flexibly at baseline, clinical visit, over the telephone, or at home during the 7 monitoring days following the baseline visit.
21. Adolescent's behavioural and emotional problems are collected using the Child Behaviour Checklist completed flexibly at baseline, clinical visit, or at home during the 7 monitoring days following the baseline visit.
22. Adolescent's dietary intake, eating habits, and food environment is collected using a Food Frequency Questionnaire (FFQ) and an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
23. Adolescent's physical activity is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
24. Adolescent's alcohol use is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
25. Adolescent's mental health is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
26. Adolescent's tobacco exposure is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
27. Adolescent's noise exposure is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
28. Adolescent's outdoor environment is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
29. Adolescent's sleeping patterns are collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
30. Adolescent's light exposure is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.
31. Adolescent's pubertal development is collected using an adolescent questionnaire completed at the clinical visit, usually 7 days before blood collection, or baseline.

Other measures collected as part of the co-produced intervention study:
1. Air pollution around schools is collected using static air quality sensors for a period of up to 18 months.
2. Personal air pollution is collected using portable air quality sensors for 1 week at baseline, 1 week pre-intervention, 1 week during the intervention period, and 1 week 6 months post-intervention.
3. Nitrogen dioxide exposure collected using NO_2 diffusion tubes for 1 week at baseline, 1 week pre-intervention, 1 week during the intervention period, and 1 week 6 months post-intervention.

4. Personal exposure data, including to air and light pollution, sleep, physical activity, and location will be collected using the EXPOApp3 smartphone app collected for 1 week at baseline, 1 week pre-intervention, 1 week during the intervention period, and 1 week 6 months post-intervention.
5. Mode of travel between home and school collected using travel diaries at 1 week at baseline, 1 week pre-intervention, 1 week during the intervention period, and 1 week 6 months post-intervention.
6. School travel modes and preferences, play and physical activity, physical and mental health collected using a survey at 1 week at baseline, 1 week pre-intervention, 1 week during the intervention period, and 1 week 6 months post-intervention.
7. Participant observations of route home from school collected using the PicVoice app at baseline.
8. Participant discussion group of PicVoice app outputs conducted using the Photovoice method within 3 months of baseline.
9. Participant experiences of taking part and perceived impact and sustainability of the intervention collected using focus groups at 6 months post-intervention.
10. Teacher interviews on experiences of taking part and perceived impact and sustainability of the intervention collected using interviews at 6 months post-intervention.

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
31/01/2025

Eligibility

Key inclusion criteria
WP 1:
All participants (parents and children) that have consented and contributed to data collection in HELIX (n=231 families)

WP7:
1. Parent with child in Year 5 or 6 (9-11 years old) attending participating school
2. Child able to follow air quality data collection protocol with support from teacher and parent
3. Parent able to give informed consent and child able to give verbal assent to the researcher

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
230

Key exclusion criteria

WP1:
1. Any participant that has consented and contributed to data collection in HELIX, but has withdrawn from the Born in Bradford cohort since or wishes to withdraw when approached for this follow-up
2. Any participant that has participated in HELIX and declines consent for Athlete

WP7:
1. Parent does not give informed consent
2. Parent does not feel that the child will be able to operate the sensor or adhere to the data collection process

Date of first enrolment
15/04/2021

Date of final enrolment
01/04/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bradford Institute for Health Research
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
Duckworth Lane
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Sponsor information

Organisation
Bradford Royal Infirmary

ROR
https://ror.org/01ck0pr88

Funder(s)

Funder type

Government

Funder Name
European Commission; Grant Codes: H2020-SC1-BHC-2018-2020

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
Contact should be made with Dan Mason (dan.mason@bthft.nhs.uk) for details on obtaining any of the data collected as part of WP1. Researchers will be required to submit an expression of interest and, if approved, sign a Collaboration Agreement. For WP7 the data are not expected to be made available because the data generated will be used to co-produce an intervention which will then be implemented and evaluated. Results for WP7 will be published.

Added 30/12/2021:
Quantitative data collected as part of WP1 will be available as part of the Born in Bradford repository. Data will be cleaned and linked to existing resources prior to availability. All data collected have been granted ethical approval and participant consent for its continued availability. Data requests are made to the BiB executive using the form available from the study website: http://www.borninbradford.nhs.uk (please click on 'Science and Research' to access the form). Guidance for researchers and collaborators, the study protocol and the data collection schedule are all available via the website. All requests are carefully considered and accepted where possible.

IPD sharing plan summary
Available on request, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 3	23/08/2021	12/12/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes