ENVIRONMENTAL-RISK (E-RISK) LONGITUDINAL TWIN STUDY
CONCEPT PAPER FORM

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Provisional Paper Title: Understanding and mitigating associations between childhood neighbourhood deprivation and adolescent mental health in two UK birth cohorts.

Date: 06 July 2022

Objective of the study and its significance:

Please note that this concept paper describes analyses using the Millennium Cohort Study, with a planned replication and extension using the E-Risk Study (see Research Questions 3 & 4 below)

Neighbourhood deprivation refers to a lack of access to opportunities and resources among residents including material/physical (e.g., food, accommodation, clothing) and social (e.g., crime, education, community services) aspects[1]. Growing up in a deprived neighbourhood has been linked with a greater risk of poor outcomes including internalising (emotional) and externalising (behavioural) problems in childhood and adolescence[2,3].

Research findings suggest that the effect of neighbourhood deprivation is typically modest in size, explaining 5-10% of the variation in child and adolescent outcomes and is robust to adjustment for family-level disadvantage[2]. The latter is important as families are not randomly selected into neighbourhoods, rather individuals with similar characteristics come to live in similar areas. Therefore, ensuring that associations between neighbourhood deprivation and poor mental health are robust to factors that influence both is critical to avoid reverse causation in observational studies.

However, there remain several important gaps in our knowledge. A review of recent studies (i.e., published since 2009) showed that the majority had been conducted in the USA, with few examining the UK context[3]. Moreover, UK studies that make use of large, representative samples have typically focused on children[4,5] with much less attention given to adolescent mental health. Adolescence and the transition to adulthood is commonly the period in which a variety of mental health problems have their onset[6,7] and for many this will signal the start of recurrent mental illness[8]. Furthermore, neighbourhood deprivation may be particularly salient for adolescent mental health as the strength of the effects may accumulate with sustained exposure across childhood. A better understanding of the relationship between neighbourhood deprivation during childhood and mental health problems in late adolescence in a contemporary UK population sample is therefore crucial. Finally, studies of neighbourhood deprivation have typically assessed mental health outcomes using parent-reported problem behaviours (e.g., Strengths and Difficulties Questionnaire[9] and the Child Behaviour Checklist[10]). It remains unclear whether similar associations are found for mental health diagnoses based on individual's own reports of their experiences, which are particularly relevant in the adolescent period.

Despite findings that neighbourhood deprivation increases the risk of emotional and behavioural problems, outcomes do vary among those exposed to socio-economic disadvantage[11]. Some individuals are described as being 'resilient' meaning that they have better than expected outcomes given their exposure to this risk[12,13]. Analyses of the UK Millennium Cohort Study (MCS) by Flouri and colleagues have highlighted factors such as self-regulation[14], cognitive ability[14], green space[15], and children's early aspirations[16] for buffering some negative effects of family-level poverty. However, there have been very few studies of neighbourhood-level deprivation that have taken a resilience approach and investigated factors that are protective for mental health. The few that have focused on protective factors for internalising and externalising problems in young children[17,18], none to our knowledge have focused on adolescents. An understanding of potential protective factors is central to improving knowledge of resilience during adolescence and may inform targets for interventions to better support young people who grow up in deprived neighbourhoods and prevent them from developing mental health disorders.

Drawing on factors that have been found to be protective of mental health in young children from deprived neighbourhoods[17,18] and among children or adolescents exposed to other forms of adversity[15,19-23] we will examine the following potential protective factors - firstly in MCS and then, where comparable constructs are available, replicated using the E-Risk Study:

Construct	MCS (measured at child age)	E-Risk (measured at child age)
Biological sex	Age 9 months	Birth
Temperament	Age 9 months	Age 5
Cognitive skills	Age 5 (British Ability Scales: naming vocab, picture similarity, & pattern construction)	Age 5 (Vocabulary test & block design) Age 5 (IQ)
Self-esteem	Ages 11 & 14	Not available
Family-level socio-economic status (SES)	Age 9 months (family income)	Age 5 (family SES; composite of income, education, occupation)
Parenting	Age 3 (Parent-child relationship) Age 14 (Parental knowledge of child going out)	Ages 5 & 10 (maternal warmth) Age 12 (Parental monitoring & control)
Green space	Ages 9 months, 3, 5, 7, & 11 averaged	Ages 5, 7, 10, 12, & 18 averaged
Social support	Age 17	Age 18

In addition, in the E-Risk Study we will also investigate the following potential protective factors (that are available only in this cohort) given previous research showing their protective role for mental health of children and adolescents exposed to adversity[19-24]:

Construct	E-Risk (measured at child age)
Sibling relationship	Ages 7 & 10 (sibling warmth)
Atmosphere at home	Ages 7, 10 & 12
Physical activity	Age 18
Positive coping strategies	Age 18
Neighbourhood social cohesion	Ages 13-14

The current study will therefore extend existing analyses of the Millennium Cohort Study to focus on (i) the association between childhood neighbourhood deprivation and *adolescent* mental health difficulties, and (ii) to explore potential protective factors at the individual-, family-, and community-level. We will then investigate whether these results replicate in the E-Risk Study, an independent UK sample born in a similar time period, and also extend to clinically relevant psychiatric diagnoses and other putative protective factors available in this sample.

Research Questions:
1. Is neighbourhood deprivation in childhood associated with age-17 internalising and externalising problems in the Millennium Cohort Study (MCS)?

2. What factors protect against age-17 internalising and externalising problems for those exposed to childhood neighbourhood deprivation in MCS?

3. Do the associations between neighbourhood deprivation and adolescent mental health problems found in MCS replicate in the E-Risk Study (using internalising and externalising symptom scores at age 18) and extend to clinically relevant psychiatric diagnoses at age 18 in this sample?

4. Do the protective factors found in MCS replicate in the E-Risk Study and are additional factors available in this cohort (i.e., sibling warmth, atmosphere at home, physical activity, positive coping strategies, and neighbourhood social cohesion) also protective against age-18 internalising and externalising symptoms and clinically relevant psychiatric diagnoses?

Statistical analyses:

** Please note that only Steps 3 and 4 below pertain to analyses using the E-Risk study however, for completeness all planned analyses (i.e., using MCS and E-Risk) are described ***

Step 1

For research question 1: Is neighbourhood deprivation in childhood associated with age 17 internalising and externalising problems in MCS?

- As MCS participants are nested within a cross-classification of neighbourhoods (i.e., lower layer super output areas, LSOAs) across childhood (ages 9 months, 3, 5, 7 and 14 years) we will account for this data structure using cross-classified multilevel models. We will examine associations between childhood IMD (Index of multiple deprivation measured at LSOA level) and (i) total SDQ problems, (ii) internalising problem score, and (iii) externalising problem score measured by self-report at age 17. We will also conduct sensitivity analyses using age-17 parent-reported SDQ.

- To test the robustness of associations, models will be adjusted for family income, maternal mental health, biological sex, ethnicity, and childhood internalising and externalising problems. In addition, we will account for the MCS sample stratification. For families with more than one child participating in MCS, one child will be randomly selected to prevent family-level clustering.

- Because measures of IMD are calculated slightly differently for England, Wales, Scotland, and Northern Ireland (and are therefore not directly comparable), we will standardise IMD ranks within country.

Step 2

For research question 2: What factors protect against age 17 internalising and externalising problems for those exposed to higher levels of childhood neighbourhood deprivation in MCS?

Focusing on the outcomes that were found to be significantly associated with neighbourhood deprivation in RQ1 we will then explore factors at the individual, family, and community level to see which are protective.

- We will identify the proportion of individuals in MCS who were exposed to high levels of neighbourhood deprivation (i.e., above the median) but did not develop mental health problems at age 17 (according to the standard cut-points for the SDQ).

- Within those exposed to high levels of neighbourhood deprivation, we will then examine whether the following factors are associated with lower levels of internalising and externalising problems at age 17 years:

  o Biological sex

  o Temperament

  o Cognitive skills

- o Self-esteem

- o Family income

- o Parenting (parent-child relationship & parental knowledge)

- o Green space

- o Social support

- For factors found to be significantly associated with lower levels of mental health problems in the previous step, we will test the statistical interaction with neighbourhood deprivation in the full MCS sample.

- To test the robustness of associations, models will be adjusted for the same covariates as in RQ1 except for family income and biological sex (as these are investigated as potential protective factors they will not be adjusted for in these models).

- We will also conduct sensitivity analyses using alternative cut-points for high neighbourhood deprivation (e.g., above the 75th and 90th centile).

Step 3

For research question 3: Do the associations between neighbourhood deprivation and adolescent mental health problems found in MCS replicate in the E-Risk Study and extend to clinically relevant psychiatric diagnoses at age 18?

- In the E-Risk Study, we will use logistic regression to examine associations between IMD (measured at LSOA level) at age 12 and (i) general psychopathology factor score, (ii) internalising symptoms factor score, (iii) externalising symptoms factor score, and then run sensitivity analyses extending to (iv) any psychiatric disorder, (v) any internalising disorder, (vi) any externalising disorder, and (vii) any thought disorder, measured by self-reported symptoms at age 18 years.

- To test the robustness of associations, models will be adjusted for family SES, family history of psychopathology, biological sex, and childhood (age 5) emotional and behavioural problems. We will also account for the non-independence of the twin data. There is no clustering of E-Risk participants at neighbourhood (LSOA) level therefore we do not need to use cross-classified models.

Step 4

For research question 4: Do the protective factors found in MCS replicate in the E-Risk Study and are additional factors available in this cohort also protective against age-18 internalising and externalising symptoms and clinically relevant psychiatric diagnoses?

- We will first identify the proportion of individuals in the E-Risk sample who were exposed to high levels of neighbourhood deprivation (i.e., above the median) but did not develop a psychiatric disorder at age 18 years.

- We will then examine within those exposed to high levels of neighbourhood deprivation whether the following factors that were examined in MCS are associated with lower levels of general psychopathology, internalising and externalising symptoms, and lower odds of having a psychiatric disorder at age 18 in the E-Risk Study:

- o Biological sex

- o Temperament

- o Cognitive skills and IQ

- o Family SES

- o Parenting (maternal warmth, parental monitoring & control)

- o Green space

- o Social support

- We will additionally examine whether the following factors that are available in the E-Risk Study (but not available in MCS) are associated with lower levels of general psychopathology, internalising and externalising symptoms, and lower odds of having a psychiatric disorder at age 18:

  - o Sibling warmth

  - o Atmosphere at home

  - o Physical activity

  - o Positive coping strategies

  - o Neighbourhood social cohesion

- For those factors that are significant, we will test a statistical interaction with neighbourhood deprivation in the full E-Risk sample.

- To test the robustness of associations, models will be adjusted for the same covariates as in RQ3 except for family SES and biological sex (as these are investigated as potential protective factors they will not be adjusted for in these models).

- We will also conduct sensitivity analyses using alternative cut-points for high neighbourhood deprivation (e.g., above the 75th and 90th centile).

Variables Needed at Which Ages (names and labels):

Study: E-Risk Study

Age 5:

General study variables:	
FAMILYID	Unique family identifier
ATWINID	Twin A ID (ex chkdig)
BTWINID	Twin B ID (ex chkdig)
RORDERP5	Random Twin Order
RISKS	Sample Groups
COHORT	Cohort
ZYGOSITY	Zygosity
SETHNIC	Ethnicity of Twins

Confounders:	
SAMPSEX	Sex of twins: In sample
SESWQ35	Social class composite
TOTEXTE5	Total Mum & Teacher Externalising Scale - Elder twin
TOTINTE5	Total Mum & Teacher Internalising Scale - Elder twin

Potential protective factors:	
IQE5	Pro-rated IQ score - Elder
VERBALE5	Twin's age adjusted vocabulary score - Elder
PERFE5	Twin's age adjusted block design score - Elder

ADJE5	Temperament – P5 – Elder – Derived by Sara Jaffee
APPE5	Approach temperament - Elder Twin (intv rating)
WARME5	Warmth towards elder twin
Green space variable (based on normalized difference vegetation index, NDVI, 1 mile radius around home) as used by Reuben et al. (2019) in Social Science & Medicine paper.	

Age 7:

Potential protective factors:	
SIBWRMM7	Sibling Warmth – derived by Sara Jaffee
ATHOME7	Atmosphere at home - Phase 7
Green space variable (based on normalized difference vegetation index, NDVI, 1 mile radius around home) as used by Reuben et al. (2019) in Social Science & Medicine paper.	

Age 10:

Potential protective factors:	
WARME10	Warmth towards elder twin
SIBWRM10	Sibling warmth (same as Bowes et al, 2010)
ATHOME10	Atmosphere at home - Phase 10
Green space variable (based on normalized difference vegetation index, NDVI, 1 mile radius around home) as used by Reuben et al. (2019) in Social Science & Medicine paper.	

Age 12:

Neighbourhood deprivation	
PH12IMDRANK_2007IWS	
If possible, please could I also request the IMD rank variable for Scottish & Welsh participants prior to these being converted into English IMD equivalents (I believe the above-listed IMD variable includes the converted Welsh & Scottish Scores). I'm requesting this so I can standardize IMD rank within country rather than using converted scores, to be consistent with my planned main analyses using Millennium Cohort Study (IMD in E-Risk will be used for a planned replication).	

Confounders	
FHANYPM12	Proportion of family members with valid data who have any disorder

Potential protective factors:	
CONTEM12	Parental Monitoring (control subscale) - P12 - Elder *** Called Monitoring in Wertz 2015 D&P paper ***
KNOWEM12	Parental Monitoring (knowledge subscale) - P12 - Elder
Green space variable (based on normalized difference vegetation index, NDVI, 1 mile radius around home) as used by Reuben et al. (2019) in Social Science & Medicine paper.	
S2COHE	Neighbourhood Social Cohesion
ATHOME12	Atmosphere at home - Phase 12 (if available, if not then the 4 variables below instead so that it can be created- thanks!!)
HOMEM12	State of the home - Mum Intv
CHSTIM12	Child Stimulation - Mum Intv
HAPPHM12	Happy home - Mum Intv
CHASOSM12	Chaos in the home - Mum Intv

Age 18:

Mental health outcomes:	

PH_E	P-factor, hierarchical, age 18
INTCF_E	Internalizing, 3-factor, age 18 elder
EXTCF_E	Externalizing: 3-Factor, E-Twin
ANYPSYDXE18	Any psychiatric disorder dx – P18 – Elder
ANYEXTDXE18	Any externalising disorder dx – P18 – Elder
ANYINTDXE18	Any internalising disorder dx – P18 Elder
PSYSYMP01E18	Psychosis Symptom Count (0,1+) - P18 - Elder

Potential protective factors:	
PHYACTE18	Physical activity (overall) - P18 – Elder
SSUPPORTE18	Social Support scale - P18 - Elder
SSFAME18	Social Support Family Subscale - P18 - Elder
SSFRNE18	Social Support Friends Subscale - P18 - Elder
SSOTHE18	Social Support Significant Other Subscale - P18 - Elder
cop1e18	Talk with other people about it
cop2e18	Talk with a therapist or counsellor
cop4e18	Exercise
cop13e18	Take steps to solve the problem
Green space variable (based on normalized difference vegetation index, NDVI, 1 mile radius around home) as used by Reuben et al. (2019) in Social Science & Medicine paper.	

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Data Security Agreement

Provisional Paper Title	Understanding and mitigating associations between childhood neighbourhood deprivation and adolescent mental health in two UK birth cohorts.
Proposing Author	Rachel Latham
Today's Date	05 July 2022

Please keep one copy for your records
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_RL_   I am familiar with the King's College London research ethics guidelines (https://www.kcl.ac.uk/innovation/research/support/ethics/about/index.aspx) and the MRC good research practice guidelines (https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/good-research-practice/).

_RL_   My project has ethical approval from my institution.

_RL_   I am familiar with the EU General Data Protection Regulation (https://mrc.ukri.org/documents/pdf/gdpr-guidance-note-3-consent-in-research-and-confidentiality/), and will use the data in a manner compliant with its requirements.

_RL_   My computer is (a) encrypted at the hard drive level, (b) password-protected, (c) configured to lock after 15 minutes of inactivity, AND (d) has an antivirus client which is updated regularly.

_RL_   I will treat all data as "restricted" and store in a secure fashion.

_RL_   I will not share the data with anyone, including students or other collaborators not specifically listed on this concept paper.

_RL_   I will not merge data from different files or sources, except where approval has been given by the PI.

_RL_   I will not post data online or submit the data file to a journal for them to post.
Some journals are now requesting the data file as part of the manuscript submission process. The E-Risk Study cannot be shared because the Study Members have not given informed consent for unrestricted open access. Speak to the study PI for strategies for dealing with data sharing requests from Journals.

_RL_   Before submitting my paper to a journal, I will submit my draft manuscript and scripts for data checking, and my draft manuscript for co-author mock review, allowing three weeks.

_RL_   I will submit analysis scripts and new variable documentation to project data manager after the manuscript gets accepted for publication.

_RL_   I will delete the data after the project is complete.

_RL_   **For projects using location data:** I will ensure geographical location information, including postcodes or geographical coordinates for the E-Risk study member's homes or schools, is never combined or stored with any other E-Risk data (family or twin-level data)

____   **For projects using genomic data:** I will only use the SNP and/or 450K data in conjunction with the phenotypes that have been approved for use in this project at the concept paper stage.

Signature: ....