E-Risk Study Concept Paper template

Provisional Paper Title: Maternal expressed emotion and adolescent psychopathology: utilizing longitudinal monozygotic twin-difference analyses to approach causal inference
Proposing Author: Alice Wickersham
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Academic supervisor: Click or tap here to enter text. (if the proposing author is a student)
E-Risk Sponsor: Helen Fisher (if the proposing author is not an E-Risk co-investigator)
Today's Date: 5/15/2023
Please indicate if you will require an E-Risk independent reproducibility check: YES

Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Background & objective of the study:

Approximately one in eight children and adolescents in England have a mental health disorder (1). Poor mental health during this period is associated with poorer longitudinal outcomes across various domains, including worse school, social, economic and health outcomes (2). To effectively combat this major health challenge, research is needed to identify children at increased risk of later mental illness as early as possible, so that preventative interventions can be appropriately targeted.

Expressed emotion (EE) within families might play a particularly powerful role in child and adolescent wellbeing (3). EE refers to the type and intensity of emotions shown by parents towards their children, from negative (e.g. critical, hostile) to positive (e.g. warmth) emotions. The Five-Minute Speech Sample (FMSS) has been found to be a brief but effective way of measuring EE (4). Parents are asked to talk about their child for five minutes, and the resulting speech sample is coded for negativity, warmth, and sometimes also emotional over-involvement. These draw not just on the content of what was said, but also the tone with which it was said.

EE has been shown to be a robust predictor of poor outcomes in adult mental health literature, for example, predicting likelihood of mental health relapse (5, 6). Only relatively recently has the focus of EE research shifted towards prediction of child and adolescent mental health (7). A previous study conducted using the E-Risk cohort used a genetically-sensitive design, and suggested that EE as rated from maternal speech samples may play a causal role in the development of antisocial behavioural problems in children (8). Other studies have shown that ratings of negative emotions from parents' speech predict the onset and course of other mental health issues in children including anxiety (9), depression (10), and attention-deficit hyperactivity disorder (11). However, there has been little research exploring whether EE is associated with mental health issues during adolescence.

Given that adolescence is a key period for emergence of mental health issues and that around half of adults with mental health disorders have received a diagnosis by the time they turn 15 and almost three-quarters by 18 (12), it is important to examine whether EE in childhood is associated with mental health issues in adolescence. Therefore, the objective of this study is to investigate the association between mothers' EE towards her twin offspring measured at age 10, and the psychopathology of these twins assessed in early (age 12) and late (age 18) adolescence in the

Environmental Risk (E-Risk) Longitudinal Twin Study. It is hypothesized that higher maternal negativity and lower warmth at age 10 will be associated with higher scores on all measures of psychopathology at ages 12 and 18 years (given the multitude of mental health outcomes previously associated with EE). In order to get closer to causal inference, we will utilise monozygotic (MZ) twin-difference analyses to examine associations between differences in age-10 EE ratings between MZ twins in a pair and differences in their scores on continuous psychopathology measures at ages 12 and 18. This will enable us to control for unmeasured confounding in the shared family environment (as twins were brought up in the same households) and genetic confounding (as MZ twins share all of their genes).

Note, we have specifically chosen to use only the age 10 measures of EE in order to mirror the analyses we will be doing using automated approaches to coding EE and their associations with adolescent mental health funded by the MRC (these will be explained in a separate concept paper).

Significance of the study (for theory, research methods or clinical practice):

For academics, this project will be an informative addition to ongoing research about the association between EE and child and adolescent mental health. The findings will also inform an ongoing proof of concept project investigating automated approaches to coding EE from speech, improving the feasibility of assessing EE for future research. In the long-term, findings from both of these studies may inform clinical decision-making. If EE is found to be an important predictor of adolescent mental health, and if our related work finds that EE can be easily derived using automated approaches, then it might be feasible to use speech samples to identify families whose children are vulnerable to mental health problems, and offer preventative interventions and psychoeducation as appropriate. This in turn could mitigate onset of serious mental illness in young people, thus improving their long-term health and psychosocial outcomes.

Data analysis methods:

Main exposure

Maternal EE dimensions at age 10, as scored from the FMSS (negativity, warmth).

Main outcomes

Psychopathology scores at age 12 (continuous measures of depression, anxiety, ADHD, and conduct disorder) and age 18 (P-factor, internalising, externalising, and thought disorder dimensions).

Covariates

For analyses using the full sample, we will adjust for biological sex, family socioeconomic status, and twins' emotional and behavioural problems at age 10 (in an attempt to control for the possibility of reverse causality). For the twin-difference analyses, we will adjust for twin differences in emotional and behavioural problems at age 10 and twin differences in birth weight (as a proxy for potential neurological differences between twins in a pair that may potentially result in differential attitudes by the mother towards them as well as potentially influence differences in their mental health outcomes).

Statistical analysis

Before commencing inferential statistical analysis, descriptive statistics will be produced: means and standard deviations for all continuous variables, and frequencies and percentages for all categorical variables. We will also investigate missing data patterns, and develop an appropriate missing data strategy (e.g. inverse probability weighting, multiple imputation) if needed. All analyses will be conducted in Stata version 17.

Analysis 1: Is maternal EE associated with adolescent psychopathology? Comparing children in different families.

Linear regressions will be conducted to test associations between (i) maternal negativity and (ii) maternal warmth and each mental health outcome variable in turn, first unadjusted and then adjusted for all covariates. Family clustering will be accounted for in all of these analyses using robust standard errors with the Huber-White variance estimator.

Analysis 2: How similar or different are MZ twins in their EE ratings and their psychopathology?

Pearson intrapair correlations will be conducted between MZ twins within a pair in terms of their mothers' EE ratings at age 10, and in the psychopathology scores at ages 12 and 18.

Analysis 3: Are differences in maternal EE related to differences in psychopathology for MZ twins reared in the same family?

Linear regressions will be conducted investigating associations between MZ twin-differences in maternal EE ratings (negativity and warmth separately) and MZ twin-differences in each of the psychopathology scores at ages 12 and 18, unadjusted and then adjusted for twin differences in emotional and behavioural problems at age 10 and twin differences in birth weight.

Variables needed and at which ages:

Age 5

familyid	Unique family identifier
atwinid	Twin A ID (ex chkdg)
btwinid	Twin B ID (ex chkdg)
rorderp5	Random Twin Order
sampsex	Sex of Twins: In sample
zygosity	Zygosity
seswq35	Social class composite
bwgre5	Birth weight (gr) - Elder twin
bwgry5	Birth Weight (gr) - Younger Twin

Age 10

WARME10	Warmth towards elder twin
WARMY10	Warmth towards Younger twin
DISSE10	Dissatisfaction/Negativity towards elder twin
DISSY10	Dissatisfaction/Negativity towards younger twin
TOTEXTE10	Total Mum & Teacher Externalising Scale - Elder twin
TOTEXTY10	Total Mum & Teacher Externalising Scale - Younger twin
TOTEMOE10	Total Mum & Teacher Emotional Scale (Ex Somatic) - Elder twin
TOTEMOY10	Total Mum & Teacher Emotional Scale (Ex Somatic) - Younger twin

Age 12

CDIE12	Depression Scale - CDI - Elder
CDIY12	Depression Scale - CDI - Younger
MASCE12	Anxiety Scale - MASC – Elder
MASCY12	Anxiety Scale - MASC – Younger
TOTADDE12	Total Mum & Teacher ADHD Scale – Elder twin
TOTADDY12	Total Mum & Teacher ADHD Scale - Younger twin
CDTOTCRIT_EMT12	Tot CD criteria met p12_Mum or Tchr Elder, 2015
CDTOTCRIT_YMT12	Tot CD criteria met p12_Mum or Tchr Younger, 2015

Age 18

ph_e	P-factor, hierarchical, age 18
ph_y	P-factor, hierarchical, age 18
intcf_e	Internalizing, 3-factor, age 18
intcf_y	Internalizing, 3-factor, age 18
extcf_e	Externalizing, 3-factor, age 18
extcf_y	Externalizing, 3-factor, age 18
thdcf_e	Thought disorder, 3-factor, age 18
thdcf_y	Thought disorder, 3-factor, age 18

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DATA SECURITY AGREEMENT

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X	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
X	My project is covered by the Duke or King's ethics committee OR I have /will obtain ethical approval from my home institution.
X	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: a) encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) b) password-protected c) configured to lock-out after 15 minutes of inactivity AND d) has an antivirus client installed as well as being patched regularly.
X	I will not "sync" the data to a mobile device.
X	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact Prof Helen Fisher (helen.2.fisher@kcl.ac.uk).
X	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
X	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. Study participants have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to* Prof *Helen Fisher (helen.2.fisher@kcl.ac.uk) for strategies for achieving compliance with data-sharing policies of journals.*
X	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. This data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.
X	I have read the Data Use Guidelines and agree to follow the instructions.

Signature: Alice Wickersham