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

Proposing Author: Jessie Baldwin

Author's affiliation, phone, and e-mail address: King's College London, +442078 480 361, jessie.baldwin@kcl.ac.uk

Sponsoring Investigator (if the proposing author is a student, a post-doc or a colleague): Andrea Danese

Proposed co-authors: Temi Moffitt, Avshalom Caspi, Louise Arseneault, Helen Fisher, Candice Odgers, Tim Matthews

Provisional Paper Title: Testing the clinical utility of screening for adverse childhood experiences for the prediction of health outcomes

Date: 02/May/2018

Objective of the study:

Adverse childhood experiences (ACEs; e.g., abuse, neglect, and family dysfunction) are associated with several physical diseases and psychological problems in later life (Felitti et al., 1998; Reuben et al., 2016; Anda et al., 2006; Dube et al., 2001; Hughes et al., 2017). These associations follow a dose-response relationship, in that exposure to more ACEs predicts worse adult health, including greater risk of heart disease, cancer, depression, drug abuse, and suicide attempt (Felitti et al., 1998). These findings have attracted attention from policy-makers interested in preventing costly adult diseases through interventions targeting ACEs. Consequently, screening programmes for ACEs are being implemented (Finkelhor, 2017; Kuhlman et al., 2018), with the aim of providing exposed individuals with interventions to reduce their risk of health problems. For example, children are being screened for ACEs in some pediatric primary care clinics (Purewal et al., 2016) and family-support services (Blodgett, 2012) through parent questionnaires. Adults are also being screened for ACEs in population-based health telephone surveys in some US states (Centers for Disease Control and Prevention, 2015) and in some healthcare settings in the UK (Larkin, 2016).

Although screening for ACEs and providing targeted interventions to exposed individuals could have potential health benefits, screening is not without costs. These costs include time, effort, and training involved in screening, distress linked to reporting ACEs, devaluation of risk in those who report not being exposed, and the risk of over-referring exposed individuals who may not ever develop health problems (Finkelhor, 2017; Kuhlman et al., 2018). To weigh up whether the costs of screening are outweighed by

the potential health benefits, it is important to evaluate the ability of ACE measures to predict later health problems. The current study will examine how well ACE screening measures predict later health problems by addressing four aims:

Aim 1) To test whether prospectively-measured ACEs predict mental and physical health problems in young adulthood.

We will begin by assessing whether prospectively assessed ACEs predict mental and physical health problems several years later. Previous research describing associations between ACEs and health problems has largely been based on adults' retrospective reports of ACEs (Felitti et al., 1998; Reuben et al., 2016; Anda et al., 2006; Dube et al., 2001; Hughes et al., 2017), but screening children for ACEs involves prospective reports, usually from the child's parent (Purewal et al., 2016; Blodgett, 2012). Because prospective and retrospective measures of ACEs identify largely different groups of individuals (Reuben et al., 2016; Newbury et al., 2018), children identified prospectively as exposed to adversity may not be at risk of the same health outcomes as adults retrospectively reporting ACEs. We will therefore test whether prospectively assessed ACEs predict mental and physical health outcomes at age 18 (mental health diagnoses, smoking, sleep problems, obesity, inflammation).

Aim 2) To test whether prospectively-measured ACEs predict later mental and physical health problems beyond other readily-available risk factors.

We will next test whether screening children for ACEs could forecast later health problems above and beyond risk factors already known by professionals (e.g., sex; socioeconomic-disadvantage; personal history of health problems). This will indicate whether ACE screening could give 'added value' in disease prediction.

Aim 3) To test whether prospectively-measured ACEs discriminate between those who do and do not develop later mental and physical health problems.

Whilst previous research has shown differences in health profiles between groups of individuals with different numbers of ACEs (Felitti et al., 1998; Reuben et al., 2016; Anda et al., 2006; Dube et al., 2001), the deterministic use of ACE scores in disease prediction is questionable because large individual differences exist in children's responses to stress (Rutter, 2012). We will therefore test how well ACE scores can discriminate between people who do and do not develop health problems at age 18. For example, we will assess the proportion of individuals with high ACE scores who develop health problems (and would thus benefit from preventative interventions) relative to those who do not develop later health problems (and would constitute over-referrals to interventions).

Of note, we will conduct parallel analyses in the Dunedin Study to test whether retrospectively screening adults for ACEs forecasts health at midlife.

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

This study will provide evidence to guide policy-makers and practitioners on the decision to screen for ACEs. For example, if ACEs predict health problems over and above readily available risk factors, and accurately discriminate between individuals who do and do not develop health problems, then ACE screening is likely to be a useful risk prediction tool. However, if the opposite is true, then there will be little value of screening for ACEs with regard to public health interventions. Although the decision to implement widespread screening for ACEs also depends on the availability of effective interventions to offer exposed individuals, the proposed analyses will provide essential quantitative evaluation to inform decision-making.

Statistical analyses:

Aim 1) To test whether prospectively-measured ACEs predict later mental and physical health problems.

We will use logistic regression models to test the association between ACEs (count measure) and mental and physical health problems at age 18.

Aim 2) To test whether prospectively-measured ACEs predict later mental and physical health problems beyond other readily-available risk factors.

We will use multivariate logistic regression models to test the associations between: (i) readily-available health risk factors (e.g., sex, socioeconomic disadvantage, personal history of health problems) and each health outcome; and (ii) ACEs and each health outcome, controlling for readily available risk factors. To assess incremental prediction by the ACE score, we will examine the independence of the prediction from the ACE score from the effects of covariates and the change in the adjusted R^2 values between these models, according to each specific health outcome.

Aim 3) To test whether prospectively-measured ACEs discriminate between those who do and do not develop later mental and physical health problems.

We will use diagnostic accuracy indicators (sensitivity, specificity, positive predictive value, negative predictive value) to test how well ACE scores can discriminate between participants who will or will not develop clinical outcomes. We will also summarise the diagnostic accuracy for prediction of each health outcome with the C-statistic.

Variables Needed at Which Ages (names and labels):

Study: E-Risk

Age 5:

sampsex	Sex
seswq35	Family SES
totemoe5	Mother + Teachers TRF Emotional Scale (Ex Somatic) - Elder
totexte5	Mother + Teachers CBCL Externalising Scale - Elder

Age 7:

totemoe7	Mother + Teachers TRF Emotional Scale (Ex Somatic) - Elder
totexte7	Mother + Teachers CBCL Externalising Scale - Elder

Age 10:

totemoe10	Mother + Teachers TRF Emotional Scale (Ex Somatic) - Elder
totexte10	Mother + Teachers CBCL Externalising Scale - Elder
se22m10	Health professional diagnosed behavioural, learning, developmental or mental health problem
pae2m10	Perceived overweight – research worker rating

Age 12:

pabsevtye12	Physical abuse
sasevtye12	Sexual abuse
eanseve12	Emotional abuse and neglect
pnseveritye12	Physical neglect
ExpV_DV510	Domestic violence
fhanypm12	Family psychopathology
fhsubpm12	Family substance abuse (proportion of family members with valid data who have problems with alcohol or drugs)
le1m12le7	Parental incarceration/criminality (mother or partner been placed in jail or prison (even for one night) when twins were aged 10-12 years)
fcevide12	Loss of /separation from parent (foster care or non-parental care through age 12)
totemoe12	Mother + Teachers TRF Emotional Scale (Ex Somatic) - Elder
totexte12	Mother + Teachers CBCL Externalising Scale - Elder
se22m12	Health professional diagnosed behavioural, learning, developmental or mental health problem
pae2c12	Perceived overweight – research worker rating
CRPeg12	CRPmgL - Germfighters

Age 18:

dxmdee18	Major depressive disorder
dxgade18	Generalised anxiety disorder
sharme18	Self-harm
suicate18	Suicide attempt
dxalcdepe18	Alcohol dependent
dxmarje18	Marijuana dependency
dxdrugme18	Drug dependent (or on methodone)
smkcure18	Smoking (daily)
bmie18	Obesity
crpe18	C-reactive protein
psqie18	Sleep

References cited:

Anda RF, Felitti VJ, Bremner JD, et al. (2006) The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience* 256: 174-186.

Blodgett C. (2012) Adopting ACEs Screening and Assessment in in Child Serving Systems. Washington: Washington State University.

Centers for Disease Control and Prevention. (2015) Behavioral Risk Factor Surveillance System Survey ACE Data, 2009-2014. Atlanta, Georgia: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

Dube SR, Anda RF, Felitti VJ, et al. (2001) Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life span: findings from the Adverse Childhood Experiences Study. *JAMA* 286: 3089-3096.

Felitti VJ, Anda RF, Nordenberg D, et al. (1998) Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *American Journal of Preventive Medicine* 14: 245-258.

Finkelhor D. (2017) Screening for adverse childhood experiences (ACEs): cautions and suggestions. *Child Abuse & Neglect*.

Hughes K, Bellis MA, Hardcastle KA, et al. (2017) The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *The Lancet Public Health* 2: e356-e366.

Kuhlman KR, Robles TF, Bower JE, et al. (2018) Screening for childhood adversity: the what and when of identifying individuals at risk for lifespan health disparities. *Journal of Behavioral Medicine*: 1-12.

Larkin W. (2016) Routine Enquiry about Adversity in Childhood. Lancashire, UK: Lancashire Care NHS Foundation Trust.

Newbury JB, Arseneault L, Moffitt TE, et al. (2018) Measuring childhood maltreatment to predict early-adult psychopathology: comparison of prospective informant-reports and retrospective self-reports. *Journal of Psychiatric Research* 96: 57-64.

Purewal SK, Bucci M, Gutiérrez Wang L, et al. (2016) Screening for adverse childhood experiences (ACEs) in an integrated pediatric care model. *Zero to Three* 37: 10-17.

Reuben A, Moffitt TE, Caspi A, et al. (2016) Lest we forget: comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry* 57: 1103-1112.

Rutter M. (2012) Resilience as a dynamic concept. *Development and Psychopathology* 24: 335-344.

Data Security Agreement

Provisional Paper Title	Screening for adverse childhood experiences and prediction of health
Proposing Author	Jessie Baldwin
Today's Date	02/May/2018

Please keep one copy for your records
(Please initial your agreement)

JB 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/)

JB My project has ethical approval from my institution.

JB 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.

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

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

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

JB 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.

JB 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.

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

____ **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: Jessie Baldwin

CONCEPT PAPER RESPONSE FORM

A. To be completed by the proposing author

Proposing Author:

JB I have read the E-Risk data-sharing policy guidelines and agree to follow them

Provisional Paper Title: Testing the clinical utility of screening for adverse childhood experiences for the prediction of health outcomes

Potential co-authors: Andrea Danese, Temi Moffitt, Avshalom Caspi, Louise Arseneault, Helen Fisher, Candice Odgers, Tim Matthews

Potential Journals:

Intended Submission Date (month/year): 12/2018

Please keep one copy for your records and return one to Louise (louise.arseneault@kcl.ac.uk)

B. To be completed by potential co-authors:

☐ Approved ☐ Not Approved ☐ Let's discuss, I have concerns

Comments:

Please check your contribution(s) for authorship:

☐ Conceptualizing and designing the longitudinal study

☐ Conceptualizing and collecting one or more variables

☐ Data collection

☐ Conceptualizing and designing this specific paper project

☐ Statistical analyses

☐ Writing

☐ Reviewing manuscript drafts

☐ Final approval before submission for publication

☐ Acknowledgment only, I will not be a co-author

Signature: .....