**Concept Paper Template**

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

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**P.I. Sponsor:** Andrea Danese; Terrie Moffitt
(if the proposing author is a student or colleague of an original PI)

**Today's Date:** 02/May/2018

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

## Objective of the study:

Adults reporting adverse childhood experiences (ACEs; e.g., abuse, neglect, and family dysfunction) have an elevated risk of several physical diseases and psychological problems (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 adults reporting more ACEs show worse health, including greater risk of heart disease, cancer, depression, drug abuse, and suicide attempt (Felitti et al., 1998). Regardless of whether the observed associations are causal (e.g., retrospective reports of ACEs might be affected by recall bias; Hardt and Rutter, 2004), it may be possible to assess ACEs to identify individuals at risk of health problems. As such, policy-makers and clinicians are implementing ACE screening programmes for adults and children (Finkelhor, 2017; Kuhlman et al., 2018), with the aim of providing exposed individuals with interventions to reduce their risk of health problems. For example, adults are being screened for their past exposure to 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). Children are also beginning to be screened for ACEs in some pediatric primary care clinics (Purewal et al., 2016) and family-support services (Blodgett, 2012) through parent questionnaires.

Although screening for ACEs and providing targeted interventions to exposed individuals could have 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 no being exposed, and the risk of over-referring exposed individuals who may not ever develop health problems (Finkelhor, 2017; Kuhlman et al., 2018). To assess 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 adults' reports of ACEs predict later mental and physical health problems at midlife.*

We will assess whether screening adults for ACEs could forecast mental and physical health problems several years later. Previous research describing associations between adults' reports of ACEs and health problems has largely been cross-sectional (Felitti et al., 1998; Reuben et al., 2016; Anda et al., 2006; Dube et al., 2001), and thus cannot inform expectations about the ability of ACE screening to identify individuals at risk of *future* health problems. We will therefore test whether the Dunedin participants' reports of ACEs at age 38 predict their mental and physical health outcomes at age 45 (mental health diagnoses, smoking, sleep problems, obesity, and high inflammation levels).

*Aim 2) To test whether adults' reports of ACEs predict their later mental and physical health problems beyond other readily-available risk factors.*

We will next assess whether screening adults for ACEs could forecast their later health problems above and beyond risk factors already known by professionals (e.g., sex, socioeconomic-disadvantage, and personal history of health problems). This will indicate whether ACE screening in adults could give 'added value' in identifying individuals at risk of poor health.

*Aim 3) To test whether adults' reports of 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 individuals' 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).

*Aim 4) To test whether prospective measures of ACEs in childhood predict later mental and physical health problems.*

Although the majority of ACE screening to-date has involved asking adults to retrospectively report on their experiences (Larkin, 2016), children are also being prospectively screened for ACEs in some healthcare and family support settings. However, retrospective and prospective measures of ACEs identify largely different groups of individuals (Reuben et al., 2016; Newbury et al., 2018) and therefore it is not possible to infer whether prospectively screening children for ACEs can forecast adult health from the prior analyses based on adults' retrospective ACE reports. To address this, we will conduct sensitivity analyses using a prospective measure of ACEs to predict health problems at age 45 (e.g., repeating analyses for Aims 1, 2, and 3).

Of note, we will also conduct parallel analyses in the E-Risk Study with a prospective measure of ACEs to test reproducibility.

## Data analysis methods:

*Aim 1) To test whether adults' reports of ACEs predict later mental and physical health problems at midlife.*

We will use logistic regression models to test the association between ACEs (count measure, assessed at age 38) and mental and physical health problems at age 45.

*Aim 2) To test whether adults' reports of ACEs predict their 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 heath 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 adults' reports of 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.

*Aim 4) To test whether prospective measures of ACEs in childhood predict later mental and physical health problems.*

We will repeat analyses for Aims 1, 2 and 3 using the prospective measure of ACEs as the independent variable in the place of the retrospective measure.

## Variables needed at which ages:

| Description | Phase |
|---|---|
| ***ACEs (prospective):*** | |
| Cumulative total ACE score | Childhood |
| ***ACEs (retrospective):*** | |
| Cumulative total ACE score | 38 |
| ***Health outcomes:*** | |
| Major depressive disorder | 45 |
| Generalised anxiety disorder | 45 |
| Self-harm | 45 |
| Suicide attempt | 45 |
| Alcohol dependent | 45 |
| Drug dependent | 45 |
| Smoking | 45 |
| Obesity | 45 |
| C-reactive protein | 45 |
| Sleep problems | 45 |
| ***Readily-available risk factors:*** | |
| Sex | |
| Average SES 1-15 | Childhood |
| Ever had a psychiatric disorder | Lifetime/cumulative variable including ages 11-15, 18, 21, 26, 32, and 38 (as in Schaefer et al., 2016; J. Abnorm. Psychol) |
| Any psychiatric disorder | 38 |
| Ever smoked | Lifetime/cumulative variable including ages 15, 18, 21, 26, 32, and 38 |
| Smoking (e.g., # per day) | 38 |
| Ever obese | Lifetime/cumulative variable including ages 15, 18, 21, 26, 32, and 38 |
| Obesity | 38 |
| CRP | 38 |
| Ever had sleep problems | Lifetime/cumulative variable including ages 15, 18, 21, 26, 32, and 38 |
| Sleep problems | 38 |

## 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.

## References cited:


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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**

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| Provisional Paper Title | Screening for adverse childhood experiences and prediction of health |
| Proposing Author | Jessie Baldwin |
| Today's Date | 02/05/2018 |

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Please initial your agreement

| | |
|---|---|
| X | I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent) |
| X | My project is covered by Duke or Otago 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.<br>My computer or laptop is:<br>a) encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines)<br>b) password-protected<br>c) configured to lock-out after 15 minutes of inactivity AND<br>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 Professor Moffitt or Caspi. (919-684-6758, tem11@duke.edu, ac115@duke.edu) |
| 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.<br><br>*Some journals are now requesting the data file as part of the manuscript submission process. The Dunedin Study Members have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to Terrie or Avshalom 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.<br><br>The data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses. |

**Signature: Jessie Baldwin**

**CONCEPT PAPER RESPONSE FORM**

**A**

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|---|---|
| Provisional Paper Title | Testing the clinical utility of screening for adverse childhood experiences for the prediction of health outcomes |
| Proposing Author | Jessie Baldwin |
| Other Contributors | Andrea Danese, Temi Moffitt, Avshalom Caspi, Richie Poulton, Sandhya Ramrakha |
| Potential Journals | |
| Today's Date | 02/05/2018 |
| Intended Submission Date | |

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**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:**

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