

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

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Proposed co-authors:

Provisional Paper Title:

Individual and family moderators for the link between peer victimization and inflammation

Date:

Objective of the study and its significance:

OBJECTIVE: To identify possible moderators, from both the individual (IQ, anxious/depressed disposition) and the family level (SES, family support), that explain differences in the effect of peer victimization on systemic inflammation.

SIGNIFICANCE: 1) Identifying early factors that provide insight in which children/adolescents are more at risk for the effects of peer victimization on systemic inflammation 2) identifying factors that can function as protective factors against the effects of peer victimization on systemic inflammation.

Expanded Significance: Peer victimization in childhood and adolescence can have far-reaching consequences on mental and physical health both within these developmental periods as well as many decades later in life (Taylor, 2010; Takizawa et al., 2015). One of the important factors that can explain the effects of peer victimization on adverse health outcomes is inflammation (Danese & McEwen, 2012). Systemic inflammation increases the risks for many health problems, including cardiovascular disease, diabetes, rheumatoid arthritis, and anxiety and depression (Irwin & Miller, 2007; Miller, Chen, & Parker, 2011). However not every child/adolescent is equally affected by peer victimization. And, although there is interest for investigating which youth are most at risk for such stressors, little has been done to identify specific individual differences that may be relevant to alter the effects of such social stressors on inflammation. This while identifying possible moderators (both protective and risk factors) of the relation between peer victimization and inflammation may have crucial implications for promoting children well-being and preventing risk for long-term mental and physical health problems.

Especially moderators from the individual and family domain may play a role in explaining individual differences of the effects of peer victimization on inflammation. First, at the individual level childhood disposition and IQ have been proposed as moderators between negative life events and health outcomes. Increasing evidence shows that systemic inflammation might not always arise from differences in 'absolute' levels of social stress (e.g., more experiences of victimization in childhood) but that it is the subjective perception (e.g., the feelings of exclusion in a situation) those social threats that may explain individual differences in systemic inflammation (Slavich & Cole, 2013). In particular, an interpersonal sensitive (IS) disposition has been suggested to make children more susceptible for the effects of peer victimization on inflammation (Marin & Miller 2013). Additionally, IQ has consistently been shown to function as a protective factor against the effects of negative (social) events on different health outcomes (Masten, 2001; Johnson et al., 2011). Children with a high IQ are suggested to use their cognitive resources to come up with strategies to overcome the negative effects of peer victimization (Salekin et al.,

2010). In addition to these two individual characteristics family support and family SES have been shown to be two of the more important environmental protective factors against the effects of negative (social) event in children (Jackson & Frick 1998; Chen et al., 2011; Runsten et al., 2014).

Overall, investigating both individual and family environment moderators would add to current research that discusses factors that would be able to biologically protect those who experience adversity from poor health outcomes (Chen et al., 2011; Luther & Brown, 2007).

Statistical analyses:

We propose to conduct 4 separate linear models with SuPAR as dependent variable for the 4 moderators (peer victimization by resp. IQ, IS disposition, SES and maternal warmth) adjusted for the twin clustering. For this we will create a cumulative victimization score (childhood victimization + adolescent victimization). Analysis will be adjusted for gender, BMI and smoking. To account for multiple testing we will set the significance level at $p < 0.25$.

As secondary analysis we will investigate the same models for CRP instead of SuPAR and explore if there are independent effects for childhood and adolescent peer victimization.

Variables Needed at Which Ages (names and labels):

Study: E-risk

Age 5:

Sampsex : Sex

seswq35: family SES

Iqe5: IQ

Warme5: maternal warmth elder twin

Totadepanxe5: IS disposition (anxious/depressed)

Age 12:

Bullseve12: peer victimization to age 12

Age 18:

SuPAR: as used in Rasmussen et al. 2019

crpe18: C-reactive protein (as secondary analyses)

vctzperce18: peer victimization to age 18

smkcure18: Smoking (daily)

bmie18: BMI

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Data Security Agreement

Provisional Paper Title	Individual and family moderators for the link between peer victimization and inflammation
Proposing Author	Marieke de Bruine
Today's Date	2-18-2019

Please keep one copy for your records

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_MdB 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/>).

Guest

at Duke My project has ethical approval from my institution.

MdB_ 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.

MdB_ 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.

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

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

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

MdB_ 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.

MdB_ 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.

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

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

_____ **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:



CONCEPT PAPER RESPONSE FORM

A. To be completed by the proposing author

Proposing Author:

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

Provisional Paper Title: Individual and family moderators for the link between peer victimization and inflammation

Potential co-authors: Marieke, Avshalom, Temi, Louise Arseneault, Andrea Danese, Line Rasmussen

Potential Journals:

Intended Submission Date (month/year): January 2020

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: