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

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Provisional Paper Title: Violent experiences and violent neighbourhoods during adolescence: understanding and mitigating the impact on psychiatric disorders at the transition to adulthood

Date: 23 May 2021

Objective of the study and its significance:

Violence, in all its forms, is a pervasive social and public health concern. The World Health Organisation estimates that 1.6 million people lose their lives to violence worldwide each year while many more suffer injuries and physical and mental health problems¹. These impacts are especially pronounced when violence occurs during childhood and adolescence, a crucial time for development. Indeed, research has consistently evidenced associations between violence and abuse in childhood and adolescence and a wide range of mental health problems (e.g., anxiety, depression, psychosis)^{2,3,4}. However, there remain important gaps in our knowledge including about the effects of exposure to multiple forms of violence on mental health and about the factors that prevent poor mental health outcomes.

Violence is a complex phenomenon that occurs at multiple levels. At the micro-level, violence may be experienced personally by an individual (e.g., sexual abuse, bullying) through interactions with peers, family, and others, while at the macro-level violence may be a feature of the neighbourhood in which they live (e.g., high crime rates). Multiple different forms of violence often converge, creating interconnected experiences that normalise violence with cumulative effects on mental health. However, existing research has typically focused on the different types of violence and abuse that have been experienced personally by an individual (poly-victimisation)^{4,5,6}, ignoring the wider social context of violence in which these take place. Adolescence is a key period of sensitivity during which individuals spend more time in the community, potentially exposing them to a wider range of violence and greater awareness of neighbourhood violence. Despite this, understanding violence during adolescence has received comparatively little attention. We therefore aim to examine how personal experience of violence and contextual neighbourhood violence during adolescence combine to impact mental health at the transition to adulthood (Aim 1).

The transition to adulthood is a key developmental period in which the foundations are laid for success as an adult. Unfortunately, it is also a time when mental health problems commonly emerge which may interfere with this. Moreover, those who experience mental health problems during this period are likely to experience recurrent mental ill-health in the future⁷. Understanding how experiences and contexts of violence contribute to mental health problems at the transition to adulthood is therefore critical to help these individuals prosper in this life-defining period.

Fortunately, not everyone who is exposed to violence develops mental health problems – for example, in the E-Risk cohort 40% of young people did not have a diagnosable mental health disorder at age 18 following exposure to victimisation in childhood⁸. Understanding factors that protect against poor mental health among adolescents exposed to violence (Aim 2) is essential to inform interventions at multiple levels (individual, family, community) to mitigate its effects. We propose to examine the putative protective effects of positive relationships (with family, peers, and other adults), intelligence, and higher family socio-economic status (SES). These factors were identified by young people with lived experience of violence, abuse, and mental health problems during focus group discussions about resilience and matched to measures available in the E-Risk Study⁹.

Research Questions:

- 1. How does the prevalence of mental health problems at age 18 compare between those with personal experience of violence, those who lived in neighbourhoods with high levels of violence, and those with no such violence exposure during adolescence?
- 2. Is there a cumulative effect of having both personal violence experience and living in a violent neighbourhood during adolescence on young adults' mental health?
- 3. Do supportive relationships, intelligence, and higher SES protect against the development of poor mental health following (i) personal experience of violence, (ii) living in a neighbourhood with high levels of violence, and (iii) both?

** Notes about E-Risk measures of personal experience of violence, neighbourhood violence, and mental health outcomes**

<u>Personal experience of violence and abuse during adolescence (ages 12-18):</u> At age 18 participants were interviewed about a range of victimisation experiences (including crime victimisation, peer/sibling victimisation, internet/mobile phone victimisation, sexual victimisation, family violence, and maltreatment) using the Juvenile Victimisation Questionnaire (JVQ), adapted as a clinical interview⁶. All information from this interview was compiled into a dossier for each participant which was then used to evaluate whether they had been exposed to any violence since they were aged 12. For our analyses we will focus on exposure to any violence that was rated as 'severe' based on interviewer notes contained in the dossier.

<u>Contextual neighbourhood violence:</u> A measurement of the 'dangerousness' of E-Risk participants' neighbourhoods during adolescence (ages 12 to 17) was derived from police records of crime incidents in 2011 when participants were aged 17, neighbourhood residents' ratings of how much they feared for their safety, crime related problems, and whether they had been victimsed (when children were aged 13-14), and independent raters' assessments of neighbourhood safety based on a virtual 'walk-though' using Google Street View of home addresses when children were aged 12. To index high neighbourhood dangerousness, we will dichotomise the variable at the top quartile (consistent with approaches taken in prior E-Risk papers for similar variables).

NB: We are speaking with Candice to clarify which aspects of 'neighbourhood safety' were used from the Google Street View observations to create the dangerousness variable as some items appear to capture observations of traffic/street safety rather than violence/crime-related danger that we are interested in. If the 'dangerousness' measure is not appropriate, we will instead use the following 2 measures:

- <u>Neighbourhood disorder</u>: When participants were aged 13-14 a postal questionnaire sent to closeby neighbours asked whether certain problems (e.g., assaults, muggings, deliberate damage to property) affect their neighbourhood. Item scores for each problem were averaged for each respondent. A neighbourhood score was then created by averaging the scores of respondents within the E-Risk participants' neighbourhood. To index high neighbourhood disorder, the variable is dichotomised at the top quartile.
- 2. <u>Neighbourhood crime</u>: Measured using police data for participants' postcodes at age 18. The total number of violent crimes occurring each month within a 1-mile radius of their home was tallied. To

index high neighbourhood violent crime, the variable is dichotomised at the top quartile.

<u>Mental health outcomes</u> were assessed during the age-18 interviews using the Diagnostic Interview Schedule. This provides past year-history of ten DSM-IV disorders organised into three domains – internalising, externalising, thought disorder. Binary variables were derived for each domain based on diagnostic cut-offs. Participants were classified as having 'any internalising disorder' if they met diagnostic criteria for generalised anxiety disorder, major depressive disorder, or post-traumatic stress disorder, or presented at least two of five eating disorder symptoms. Participants were classified as having 'any externalising disorder' if they met diagnostic criteria for Attention Deficit/hyperactivity disorder (ADHD), conduct disorder, alcohol dependence, cannabis dependence, or tobacco dependence. 'Any thought disorder' classification was based on the definite presence of at least one of seven psychotic symptoms. From these three domain classifications, an overall binary outcome of 'any psychiatric disorder' was also created denoting the presence of any internalising, externalising, or thought disorder, vs. the absence of all three. These outcomes have been previously utilised in the E-Risk publication by Meehan et al.⁸

References:

1. World Health Organisation (2002). World Report on Violence and Health.

- https://www.who.int/violence_injury_prevention/violence/world_report/en/abstract_en.pdf
- 2. Arseneault, L. et al. (2011). Am J Psychiatry, 168:65-72.
- 3. MacMillan, H.L. et al. (2001). Am J Psychiatry, 158:1878-1883.
- 4. Schaefer, J.D. et al. (2018). Clin Psychol Sci, 6:352-371.
- 5. Finkelhor, D. et al. (2011). J Child and Adolesc Trauma, 4:291-300.
- 6. Fisher, H.L. et al. (2015). Dev Psychopathol, 27(4pt2):1399-1416.
- 7. Caspi, A. et al. (2020). JAMA Netw Open, 3:e203221-e203221.
- 8. Meehan, A.J. et al. (2020). J Affect Disord, 262:90-98.
- 9. Latham, R.M. et al. (2020). J Ment Health. doi:10.1080/09638237.2020.1844869

Statistical analyses:

All models described below will be adjusted for the clustered nature of the twin data and the potentially confounding effects of sex, family SES, family psychiatric history, exposure to violence in childhood, and previous mental health symptoms.

Step 1

For Research Question 1 we will run a series of logistic regressions to test whether:

- a) Exposure to any severe personal violence during adolescence predicts (i) any psychiatric disorder, and then (ii) any internalising disorder, (iii) any externalising disorder, (iv) any thought disorder at age 18.
- b) Different types of severe personal experience of violence or abuse in adolescence (i.e., separately examining crime victimisation, peer/sibling victimisation, internet/mobile phone victimisation, sexual victimisation, family violence, and maltreatment) predict (i) any psychiatric disorder, and then (ii) any internalising disorder, (iii) any externalising disorder, (iv) any thought disorder at age 18.
- c) High levels of neighbourhood dangerousness predict (i) any psychiatric disorder, and then (ii) any internalising disorder, (iii) any externalising disorder, (iv) any thought disorder at age 18.

Step 2

We will use interaction contrast ratio analysis to investigate the potential cumulative and interactive effects (Research Question 2) as follows:

a) We will combine exposure to any severe personal violence and high levels of neighbourhood dangerousness to create four exposure categories that reflect neither severe personal experience or high neighbourhood dangerousness (coded 0); severe personal experience only (coded 1); high neighbourhood dangerousness only (coded 2); severe personal experience and high neighbourhood dangerousness (coded 3). We will then test if this 4-level categorical variable predicts (i) any psychiatric disorder, and then (ii) any internalising disorder, (iii) any externalising disorder, (iv) any thought disorder using logistic regression.

If all types of severe personal experience of violence and abuse are associated with the outcome in Step 1b, then Step 2 will only examine the overall measure of any exposure to violence of high severity (as per Step 2a). However, if these associations are significant only for certain types of personal experience, then we will also conduct a sensitivity analysis as follows:

Sensitivity analyses:

Repeat step 2a examining separate types of severe personal experience of violence and abuse focusing on those found to be significantly associated with mental health outcomes in Step 1b.

Step 3

To examine potential protective factors (Research Question 3) logistic regression models will test whether the 4-level categorical variable created in Step 2a interacts with:

(a) maternal warmth, (b) sibling warmth, (c) perceived social support, (d) intelligence, and (e) family SES to predict (i) any psychiatric disorder, and then (ii) any internalising disorder, (iii) any externalising disorder, (iv) any thought disorder.

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
Potential protective factors:	
SESWQ35	Social class composite
WARME5	Warmth towards elder twin
Potential confounders:	
SAMPSEX	Sex of Twins: In sample
Age 7:	
Potential protective factors:	
SIBWRMM7	Sibling Warmth – derived by Sara Jaffee
• •	
Age 10:	
Detential protective factors:	
Potential protective factors:	Mound for the last of the
	vvarmtn towards elder twin
SIBWKM10	Sibling warmth (same as Bowes et al, 2010)

Age 12:

Potential protective factors:	
IQ12E	Pro-rated IQ (INF & MR), 12E

Potential confounders:	
PABSEVTYE12	Physical abuse by 12, severity, Elder
SASEVTYE12	Sexual abuse by 12, severity, Elder
EANSEVE12	Severity of Emotional abuse/neglect of Elder twin, thru age
BULLSEVE12	Bullying victim to Age 12 - Elder
EXPV_DV510	Exposure to DV, 5 to 10, 012 (Family level)
FHANYPM12	Proportion of family members with valid data who have any
	disorder
ADHDANYE512	Any ADHD dx [incl meds] - P5-12 – Elder
ANYCDDX_EMT512	Any CD dx from 5 to 12, mum/tchr, Elder
MASCE12	Anxiety Scale – MASC – Elder
CDIE12	Depression Scale – CDI – Elder
SHARMSUICE12	Self-Harm/Suicidal Behaviour – P12 – Elder
PSYSYMP01E12	Psychosis Symptom Count - Verified Coding - 0, 1+ - Elder

Age 13-14 postal questionnaire to neighbours of E-Risk participants:

Violence:	
S2NDSRDR	SCOPIC 2 disorder
Neighbourhood disord	er as per Newbury et al., 2018 (Schizophrenia Bulletin)

Age 18:

Potential protective factors:	
SOCSUPE18	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
Violence:	
ZDANGEROUS	C-strengths "dangerous" neighborhood
VCTZDIVIOLE18	Overall violence severity 2 cat (0/1/2/3, 4/5) - P18 - Elder
VCTZDICONE18	Conventional victimisation severity 2 cat (0/1/2/3, 4/5) - P18 -
	Elder
	Maltreatment victimisation severity 2 cat $(0/1/2/3, 1/5)$ - P18 -

VCTZDIMALE18	Maltreatment victimisation severity 2 cat (0/1/2/3, 4/5) - P18 -
	Elder
VCTZDIPERE18	Peer victimisation severity 2 cat (0/1/2/3, 4/5) - P18 - Elder
VCTZDISEXE18	Sexual victimisation severity 2 cat (0/1/2/3, 4/5) - P18 - Elder
VCTZDIFAME18	Family victimisation severity 2 cat (0/1/2/3, 4/5) - P18 - Elder
VCTZDIINTE18	Internet victimisation severity 2 cat (0/1/2/3, 4/5) - P18 - Elder
VIOLENT2011	Monthly average # violent crimes in 2011
VIOLENT2011_QRTL	Monthly average # violent crimes in 2011 – quartile

Mental health outcomes:

PSYSYMP01E18	Psychosis Symptom Count (0,1+) - P18 - Elder
Any internalising disorder diagnosis (age 18) as per Meehan et al., 2020	
Any externalising disorder diagnosis (age 18) as per Meehan et al., 2020	
Any psychiatric disorder diagnosis (age 18) as per Meehan et al., 2020	

Other:	
neigbrhde1218	Home address at phases 12 and 18 - Elder

References cited:

- Herrman, H., Kieling, C., McGorry, P., Horton, R., Sargent, J., & Patel, V. (2019). Reducing the global burden of depression: A Lancet–World Psychiatric Association Commission. *The Lancet*, 393(10189), e42-e43
- 2. Thapar, A., Collishaw, S., Pine, D. S., & Thapar, A. K. (2012). Depression in adolescence. *The Lancet, 379*(9820), 1056-67.
- Rocha, T. B., Fisher, H. L., Caye, A., Anselmi, L., Arseneault, L., Barros, F.,... & Kieling, C. (2020). Identifying adolescents at risk for depression: A prediction score performance in cohorts based in three different countries. *Journal of the American Academy of Child & Adolescent Psychiatry*, doi: 10.1016/j.jaac.2019.12.004.
- 4. Howren, M. B., Lambkin, D. M., & Suls, J. (2009) Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. *Psychosomatic Medicine*, *71*, 171-186
- 5. Dantzer, R., O'Connor, J. C., Freund, G. G., Johnson, R. W., & Kelley, K. W. (2008). Froom inflammation to sickness and depression: when the inflammation system subjugates the brain. *Nature Reviews Neuroscience*, *9*, 46-56.
- Musselman, D. L., Lawson, D. H., Gumnick, J. F., Manatunga, A. K., Penna, S., Goodkin, R. S., ... & Miller, A. H. (2001). Paroxetine for the prevention of depression induced by high-dose interferon alfa. *The New England Journal of Medicine, 344*, 961-966
- 7. Rhodes, B., Fürnrohr, B. G., & Vyse, T. J. (2011). C-reactive protein in rheumatology: biology and genetics. *Nature Reviews Rheumatology, 7,* 282-289.
- 8. Hunter, C.A. & Jones, S. A. (2015). IL-6 as a keystone cytokine in health and disease. *Nature Immunology, 16,* 448-457.
- 9. Rasmussen, L.J.H., et al., (2019). Cumulative childhood risk is associated with a new measure of chronic inflammation in adulthood. *Journal of Child Psychology and Psychiatry*, *60*, 199-208

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Proposing Author	Rachel Latham
Today's Date	06 May 2021

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(Please initial your agreement)

- I am familiar with the King's College London research ethics guidelines RL (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/goodresearch-practice/).
- 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-_RL_ guidance-note-3-consent-in-research-and-confidentiality/), and will use the data in a manner compliant with its requirements.
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- I will not post data online or submit the data file to a journal for them to post. RL 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.
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- $_{RL}$ 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)

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CONCEPT PAPER RESPONSE FORM

A. To be completed by the proposing author

Proposing Author:

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

Provisional Paper Title: Violent experiences and violent neighbourhoods during adolescence: understanding and mitigating the impact on psychiatric disorders at the transition to adulthood

Potential co-authors: Louise Arseneault, Avshalom Caspi, Terrie Moffitt, Candice Odgers, Joanne Newbury, plus 4 young people with lived experience of violence and mental health difficulties who will be recruited and trained as peer researchers

Potential Journals: Intended Submission Date (month/year): February 2022

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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
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