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

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Provisional Paper Title: Clinical and functional outcomes in young adulthood of children with psychotic symptoms: a longitudinal twin cohort study.

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Objective of the study and its significance:

Individual psychotic symptoms, such as seeing or hearing things that other people do not, being suspicious, thinking one can read others' minds and vice versa, are reasonably common in the general population, with a lifetime prevalence of around 5% [1]. A previous meta-analysis suggested that psychotic symptoms are more prevalent in childhood compared to adulthood, with a median of 17% in 9- to 12-year-olds [2]. Despite longitudinal research showing a decline in the incidence of psychotic symptoms in young people followed over time [3], a reasonable proportion continue to report anomalous experiences throughout adolescence [2]. Furthermore, although only a small percentage of young people who report psychotic symptoms develop a full-blown psychotic disorder [4], recent research has highlighted the importance of these symptoms in increasing risk for a range of other mental health problems [5]. For instance, we have previously shown that individuals who report psychotic symptoms at age 11 are at elevated risk for post-traumatic stress disorder (PTSD) and suicide attempts by mid-adulthood as well as schizophrenia [6].

However, childhood psychotic symptoms may not only be linked with adverse clinical outcomes but also with functional impairment. In clinical populations, psychotic symptoms are associated with a higher rate of unemployment, increased number of hospital admissions and service costs, and these detrimental outcomes are maintained over time [7]. However, less is known about the functional outcomes of children who report psychotic symptoms. One cross-sectional study found that adolescents with psychotic experiences had poorer concurrent social and occupational functioning than those without such experiences [8]. However, the longer-term functional outcomes of children who report psychotic symptoms are largely unknown. This is particularly important to investigate in young adulthood when individuals are transitioning to independence from their families of origin to forge romantic partnerships and develop their own families, as well as typically undertaking qualifications or apprenticeships that will shape their future earning power and capacity to contribute economically to society. Indeed previous research has highlighted the long-term economic costs of psychological problems during childhood, which are largely due to loss of income through being unable to work or being employed in lower-paid jobs [9].

Therefore, this study will utilise prospectively-collected data from the Environmental Risk (E-Risk) Longitudinal Twin Study to examine the psychopathological and functional outcomes in young adulthood of children with and without psychotic symptoms at age 12. We will explore associations between childhood psychotic symptoms and a wide range of young-adult (age-18) outcomes, including mental health problems (anxiety, attention-deficit hyperactivity disorder, conduct disorder, depression, PTSD, psychotic phenomena, substance dependence), occupational functioning (educational level and NEET status), physical health (BMI, physical disorders, sleeping problems), quality of life, social functioning (social support, social isolation, loneliness), risky behaviours (e.g. self-injurious behaviours, having a child

by age 18, smoking), and offending (police records of convictions). In order to test the robustness of these associations, we will control for gender, age-5 IQ, family socioeconomic status, family psychiatric history, maternal psychosis, and other forms of childhood and adolescent psychopathology, as well as conducting analyses using twins discordant for age-12 psychotic symptoms (to take into account unmeasured familial and genetic confounders). We hypothesize that children who report psychotic symptoms at age 12 will have a higher prevalence of mental health problems, worse social and occupational functioning, undertake more risky behaviours, and have higher rates of offending in young adulthood than children without such symptoms.

Statistical analyses:

We will estimate the relative risks of age-18 mental health problems, physical health issues, social and occupational functioning, risky behaviours, and offending for Study Members who reported psychotic symptoms at age 12 compared to those who did not. We will check whether these associations are robust after controlling for gender, age-5 IQ, family socioeconomic status, family psychiatric history, maternal psychotic symptoms, and also for other forms of psychopathology at age 12, and finally for other forms of psychopathology at age 18. These analyses will be corrected for the non-independence of twin observations using the Huber-White variance estimator. Additionally, we will repeat analyses using twins discordant for age-12 psychotic symptoms to exclude the potentially confounding influence of unmeasured family and genetic factors (first MZ & DZ pairs together and then MZ pairs only, numbers permitting).

Variables Needed at Which Ages (names and labels):

Study: E-Risk

Age 5

FAMILYID	Unique family identifier
ATWINID	Twin A ID (ex chkdg)
BTWINID	Twin B ID (ex chkdg)
RORDERP5	Random Twin Order
RISKS	Sample Groups
COHORT	Cohort
SAMPSEX	Sex of Twins: In sample
ZYGOSITY	Zygosity
SESWQ35	Social Class Composite
IQE5	Childhood IQ

Age 12

PSYSYMP01E12	Psychosis Symptom Count-Verified Coding-Elder - 0, 1+ - Elder
PSYSYMP01Y12	Psychosis Symptom Count-Verified Coding-Younger - 0, 1+ - Younger
PSYSYM12	Mother Psychosis - Symptom Count
FHANYPM12	Proportion of family members with valid data who have any disorder
CDICATE12	Clinically significant depression (CDI >= 20) - P12 - Elder
MASCCATE12	Extreme anxiety (>= 95th percentile) - P12 - Elder
SHARMSUICE12	Self-Harm/Suicidal Behaviour - P12 - Elder
ADHDD3E12	ADHD diagnosis at 12 - elder
DXCD12_12E	Conduct disorder diagnosis at 12 - elder

Age 18

DXMDEE18	Major depressive episode, dsm4 - P18 - Elder
·DXGADE18	Gen Anxiety Disorder, dsm4_based - P18 - Elder
PSYSYMPO1E18	Psychosis Symptom Count (0,1+) – P18 – Elder
PSYEXPCE18	Psychotic Experiences (cat) - P18 - Elder
SUICATE18	Suicide attempted - P18 - Elder
SHARME18	Self harm - P18 - Elder

DXADHD5X_18E DSM-5 ADHD Dx (based on >=5 Symp) [incl 4 NEET & meds] - P18 - ET
DXPTSD5CUE18 PTSD Current dx, dsm5 - P18 - Elder
DXAUDE18 Alcohol use disorder, dsm5 - P18 - Elder
DXMARJ5E18 Marijuana use disorder, dsm5 - P18 - Elder
DXDRG5E18 Substance use disorder, dsm5 - P18 - Elder
CDMODE18 Moderate Conduct Disorder (>=5 count) - P18 – Elder

PREGE18 Pregnant at visit - P18 – Elder
BMICATE18 BMI (categorical) - P18 – Elder
WAISTHIPE18 Waist Hip Ratio - P18 – Elder
PSQIE18 PSQI - Global Score - P18 – Elder
LIFSATE18 Life satisfaction (average) - P18 – Elder
EDUCACHVE18 Highest educational achievement (based on QCF) - P18 - Elder
NEETE18 NEET: Not in educ, employmt or training - P18 – Elder

SOCSUPE18 Social Support scale - P18 - Elder
SOCISOE18 Social Isolation scale - P18 - Elder
LONELYE18 Loneliness scale - P18 - Elder

SMKCURE18 Smoking daily - current - P18 – Elder
SMKCNUME18 Smoking - current (number of cigarettes) - P18 – Elder
Integrate these into a variable of “no”, “light”, “moderate” and “heavy” smoker (as done in Danese et al., 2007) [10]
SMKDXFTNDE18 [D][F] Fagerstrom Dx for Nicotine Dependence - P18 - Elder

ANYCRIME18 [D][F] MoJ - any criminal offence - P18 - Elder
ANYVIOE18 [D][F] MoJ - any violent offence - P18 - Elder
NVIOSTATE18 [D][F] MoJ - non-violent/violent offence status - P18 - Elder

Physical health problems reported at 18 (elder) – is there a variable indexing any physical health disorders between 12-18 from the Your Health section of the Phase 18 booklet?

References cited:

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Data Security Agreement

Provisional Paper Title	Clinical and functional outcomes in young adulthood of children with psychotic symptoms: a longitudinal twin cohort study
Proposing Author	Dr Antonella Trotta
Today's Date	13/06/2017

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

_AT__ I am current on Human Subjects Training (CITI (www.citiprogram.org) or training in human subject protection through my post or courses.

_AT__My project is covered by Duke or King's IRB OR I have /will obtain IRB approval from my home institution.

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

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

_ AT _ 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 Terrie or Avshalom for strategies for dealing with data sharing requests from Journals.

AT_ 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.

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

AT __ I will return all data files to the Data Manager after the project is complete. Collaborators and graduates of DPPP may not take a data file away from the DPPP office. The data remains the property of the Study and cannot be used for further analyses without express, written permission.

AT __ I will ensure geographical location information, including postcodes or geographical coordinates for the E-Risk study member's homes or schools, is <u>never</u> combined or stored with any other E-Risk data (family or twin-level data)

Signature: .....Antonella Trotta.....

CONCEPT PAPER RESPONSE FORM

A. To be completed by the proposing author

Proposing Author: Dr Antonella Trotta

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

Provisional Paper Title: Clinical and functional outcomes in young adulthood of children with psychotic symptoms: a longitudinal twin cohort study

Potential co-authors: Helen Fisher, Louise Arseneault, Terrie Moffitt, Avshalom Caspi

Potential Journals:

Intended Submission Date (month/year): September 2017

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: . .....