E-Risk Study Concept Paper Form

Response was completed on 06-09-2025 18:27.

Record ID	59

1. Collaborating researchers

Please note:

Once approved, a formal data use agreement will be required between King's College London and the university or research organisation that employs any collaborator having access to the data if they are not a member of staff, a student or affiliate of King's College London. This needs to be signed by both universities/organisations before data access can be granted.

For projects carried out by a student (e.g., MSc/MA, MPhil/PhD, clinical doctorate), the lead applicant should be the student's supervisor at the same university, and the student should be named as the student collaborator requiring access to the data.

If you have additional collaborators, please name them below and indicate whether they need to have access to the data. It would be common, for instance, for other researchers to see summary results of analyses and act as co-authors on your paper without having access to the data. You will not be permitted to share the dataset except with those indicated in the table as requiring access.

Applicable?	**Category**	**Name**	**Email address**	**University/organisation**	**Needs access to data for analysis?**
	Applicant **(lead researcher)**	Dr Anne-Kathrin Fett	anne-kathrin.fett@city.ac.uk	City St George's, University of London	(•) Yes ( ) No
(•) Applicable ( ) Not applicable	**Student collaborator** ***(if data is for their dissertation/thesis)***	Akke Ganse-Dumrath	akke.ganse-dumrath@city.ac.uk	City St George's, University of London	(•) Yes ( ) No
(•) Applicable ( ) Not applicable	**E-Risk Sponsor** ***(if applicant is not an E-Risk investigator)***	Prof Helen Fisher	helen.2.fisher@kcl.ac.uk	King's College London	( ) Yes (•) No

Are there additional collaborators to add?	(•) Yes ( ) No
If yes, how many additional collaborators would you like to add?	1

Category	Name	Email address	University/organisation	Needs access to data for analysis?
Other collaborator #1	Prof Corinna Haenschel	corinna.haenschel.1@city.ac.uk	City St George's, University of London	(•) Yes ( ) No

Applicants: If you would like to continue your application later, please press the "Save and return later" button below. Please copy or write down the Return code provided.

To return later, you may click on "Returning?" on the top right of the screen in the E-Risk Concept Paper Form link, which is the same link that was used to access this form: https://redcap.link/ERiskConceptPaperForm

2. The project proposal

Note: *Please provide sufficient detail to enable the committee to review your proposal. Please be as specific as possible about the project aims and analysis methods as once approved this concept paper will be posted publicly and thus will act as a form of pre-registration of your project. Expand boxes as required.*

Title of project	Vision, social cognition, and functional outcomes in adolescents with psychotic-like experiences: A longitudinal cohort study
Background and rationale for project ***(approx. 300 - 1000 words)***	Research increasingly suggests that schizophrenia reflects the end point of a neurodevelopmental sequence beginning early in life, rather than a disorder that emerges abruptly in adulthood (Fusar-Poli et al., 2013). In this framework, subtle disruptions in basic sensory and cognitive functions have been proposed as possible endophenotypes - measurable traits reflecting genetic liability that may presage clinical symptoms (Gottesman & Gould, 2003; Ramsay et al., 2020). Studies in clinical and high-risk populations have shown that individuals who later develop psychosis often have difficulties in basic visual tasks, including visual acuity, contrast sensitivity, motion detection, and perceptual organisation (Butler et al., 2008; Silverstein & Keane, 2011; Shoham et al., 2021, 2023). These difficulties appear to emerge before clear symptom onset and correlate with milder, subclinical psychotic-like experiences (PLEs) in community samples. For instance, Schubert et al. (2005) reported that reduced visual acuity at age four, but not impairments in other sensory domains, predicted a later schizophrenia diagnosis, with no comparable associations for other psychiatric disorders. At the same time, visual deficits have been linked to functional difficulties in individuals with psychotic disorders, including in academic, occupational, and interpersonal domains (Bowie & Harvey, 2006; Tandon et al., 2009). For example, de Waal et al. (2018) reported moderate correlations between both basic and complex visual-perceptual skills assessed around age 12 and concurrent academic achievement, while Herrera et al. (2021) found that reduced contrast sensitivity was associated with a lower likelihood of independent living. Similarly, both social cognition (the ability to infer others' mental states, recognise emotions, and attribute intent) and non-social cognition (e.g., attention, memory, executive control) have been robustly linked to functional outcomes in schizophrenia and its prodrome (Nuechterlein et al., 2004; Green et al., 2015). For instance, Holthausen et al. (2007) found that deficits in non-social cognitive domains were associated with poorer work performance regardless of the specific cognitive domain impaired, and Ludwig et al. (2017) reported that impairments in social cognition were linked to poorer functioning across domains. However, most existing studies are cross-sectional and conducted in adults, so the

	temporal ordering among visual deficits, cognitive dysfunction, and functional decline remains uncertain. Visual, social, and non-social cognitive impairments could each independently predict poorer functional outcomes. Alternatively, visual deficits may impair later social and non-social cognition, which then affect functional outcomes. A small number of clinical studies are consistent with the latter mediational hypothesis, suggesting that degraded visual input can impair the accurate interpretation of facial expressions and body language and thereby contribute to social withdrawal and vocational decline (Sergi et al., 2006; Green et al., 2015). However, these pathways have not been tested longitudinally from childhood through adolescence in population cohorts, and it remains unclear whether similar mechanisms operate in individuals who do not develop psychosis or whether PLEs amplify these links. The E-Risk cohort - with repeated assessments from early childhood through late adolescence, detailed cognitive and clinical measures, and high retention - provides an opportunity to address these gaps. Using longitudinal modelling that adjusts for key confounders (e.g., sex, socioeconomic status) and a series of sensitivity checks, we will examine temporal ordering, prospective associations, and mediation pathways to clarify developmental pathways and identify perceptual and cognitive markers that merit further mechanistic and intervention research.
Project aims / objectives	The main aim of this project is to clarify the developmental pathways linking visual deficits to social and non-social cognitive performance and functional outcomes in adolescents with PLEs. Specifically, we aim to: 1. Test the cross-sectional and longitudinal relationships between visual acuity (age 10), social cognition (age 10), non-social cognition (age 12), PLEs (age 18), and functional outcomes (age 18). And, if conditions for mediation are met: 2. Assess whether social cognition (age 10) and non-social cognition (age 12) mediate the observed associations between visual acuity (age 10) and functional outcomes (age 18), and whether these associations are moderated by PLEs (age 18).
Brief statement of your hypothesis	1. All variables of interest will be significantly associated with each other: 1a. Poorer visual acuity (age 10) will be cross-sectionally and longitudinally related to poorer social-cognitive (age 10) and non-social cognitive (age 12) performance, poorer functional outcomes (age 18), and higher levels of PLEs (age 18). 1b. Poorer social-cognitive performance (age 10) will be cross-sectionally and longitudinally related to poorer non-social cognitive performance (age 12), poorer functional outcomes (age 18), and higher levels of PLEs (age 18). 1c. Poorer non-social cognitive performance (age 12) will be cross-sectionally and longitudinally related to poorer functional outcomes (age 18) and higher levels of PLEs (age 18). 1d. Higher levels of PLEs (age 18) will be cross-sectionally related to poorer functional outcomes (age 18). 2. Social-cognitive (age 10) and non-social cognitive (age 12) performance will partially mediate the association between visual acuity (age 10) and functional outcomes (age 18). We expect an indirect effect via social and non-social cognition, with a residual direct effect of visual acuity remaining. This mediational association will be stronger among participants with higher levels of PLEs (age 18).

Data analysis methods to be used ***(approx. 100 - 500 words)***	Visual acuity will be proxied by corrective-lens use at age 10 (spectacles: yes/no); as a sensitivity check we will also use low reading ability at age 10 (standard reading/SWE scores). Social cognition will be indexed by emotion-recognition performance at age 10. Non-social cognition will be represented by prorated IQ at age 12. Functional outcomes at age 18 will be grouped into domains: academic attainment (highest qualification), employment (NEET: not in education, employment, or training), social functioning (subjective social status, social support, social isolation, loneliness), and overall life satisfaction. PLEs will be defined from the age-18 psychotic-experience measure, with clinician-verified psychotic symptoms at ages 12 and 18 used for sensitivity analyses. Where appropriate we will standardise scores and test alternative variable definitions to check robustness. To test associations among all variables of interest, we will fit models appropriate to each outcome (linear regression for continuous scales, logistic regression for binary outcomes, and ordinal logistic regression for ordered categories). All models will control for sex, socioeconomic status, and the non-independence of twin observations. If the conditions for mediation are met (i.e., significant associations between all variables of interest), we will fit a model in which visual acuity (age 10) predicts functional outcomes (age 18) both directly and indirectly through their effect on social (age 10) and non-social cognition (age 12). To test whether these associations depend on the extent of PLEs (age 18), we will also conduct moderation analysis.
Significance for theory, research methods, or clinical practice	This project will advance our theoretical understanding of how perceptual and social-cognitive processes unfold over development in relation to emerging psychotic symptoms. By mapping the sequence from early visual deficits to later social-cognitive performance and functioning, the findings will offer a more nuanced model of risk pathways that can guide future research into targeted prevention strategies.
References cited	Bowie, C. R., & Harvey, P. D. (2006). Cognitive deficits and functional outcome in schizophrenia. Neuropsychiatric Disease and Treatment, 2(4), 531-536. Butler, P. D., Silverstein, S. M., & Dakin, S. C. (2008). Visual Perception and Its Impairment in Schizophrenia. Biological Psychiatry, 64(1), 40-47. https://doi.org/10.1016/j.biopsych.2008.03.023 De Waal, E., Pienaar, A. E., & Coetzee, D. (2018). Influence of Different Visual Perceptual Constructs on Academic Achievement Among Learners in the NW-CHILD Study. Perceptual and Motor Skills, 125(5), 966-988. https://doi.org/10.1177/0031512518786806 Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., Keshavan, M., Wood, S., Ruhrmann, S., Seidman, L. J., Valmaggia, L., Cannon, T., Velthorst, E., De Haan, L., Cornblatt, B., Bonoldi, I., Birchwood, M., McGlashan, T., Carpenter, W., ... Yung, A. (2013). The Psychosis High-Risk State: A Comprehensive State-of-the-Art Review. JAMA Psychiatry, 70(1), 107. https://doi.org/10.1001/jamapsychiatry.2013.269 Gottesman, I. I., & Gould, T. D. (2003). The Endophenotype Concept in Psychiatry: Etymology and Strategic Intentions. American Journal of Psychiatry, 160(4), 636-645. https://doi.org/10.1176/appi.ajp.160.4.636 Green, M. F., Horan, W. P., & Lee, J. (2015). Social cognition in schizophrenia. Nature Reviews. Neuroscience, 16(10), 620-631. https://doi.org/10.1038/nrn4005 Herrera, S. N., Zemon, V., Revheim, N., Silipo, G., Gordon, J., & Butler, P. D. (2021). Cognitive function mediates the relationship between visual contrast sensitivity and functional outcome in schizophrenia. Journal of Psychiatric Research, 144, 138-145. https://doi.org/10.1016/j.jpsychires.2021.09.055 Holthausen, E. A. E., Wiersma, D., Cahn, W., Kahn, R. S., Dingemans, P. M., Schene, A. H., & Van Den Bosch, R. J. (2007). Predictive value of cognition for different domains of outcome in recent-onset schizophrenia. Psychiatry Research, 149(1-3), 71-80. https://doi.org/10.1016/j.psychres.2005.07.037 Ludwig, K. A., Pinkham, A. E., Harvey, P. D., Kelsven, S., & Penn, D. L. (2017). Social cognition psychometric evaluation (SCOPE) in people with early psychosis: A preliminary study. Schizophrenia Research, 190, 136-143. https://doi.org/10.1016/j.schres.2017.03.001 Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F., & Heaton, R. K.

(2004). Identification of separable cognitive factors in schizophrenia. Schizophrenia Research, 72(1), 29-39. https://doi.org/10.1016/j.schres.2004.09.007
Ramsay, I. S., Schallmo, M.-P., Biagianti, B., Fisher, M., Vinogradov, S., & Sponheim, S. R. (2020). Deficits in Auditory and Visual Sensory Discrimination Reflect a Genetic Liability for Psychosis and Predict Disruptions in Global Cognitive Functioning. Frontiers in Psychiatry, 11, 638. https://doi.org/10.3389/fpsyt.2020.00638
Schubert, E. W., Henriksson, K. M., & McNeil, T. F. (2005). A prospective study of offspring of women with psychosis: Visual dysfunction in early childhood predicts schizophrenia-spectrum disorders in adulthood. Acta Psychiatrica Scandinavica, 112(5), 385-393. https://doi.org/10.1111/j.1600-0447.2005.00584.x
Sergi, M. J., Rassovsky, Y., Nuechterlein, K. H., & Green, M. F. (2006). Social Perception as a Mediator of the Influence of Early Visual Processing on Functional Status in Schizophrenia. American Journal of Psychiatry, 163(3), 448-454. https://doi.org/10.1176/appi.ajp.163.3.448
Shoham, N., Eskinazi, M., Hayes, J. F., Lewis, G., Theodorsson, M., & Cooper, C. (2021). Associations between psychosis and visual acuity impairment: A systematic review and meta-analysis. Acta Psychiatrica Scandinavica, 144(1), 6-27. https://doi.org/10.1111/acps.13330
Shoham, N., Lewis, G., Hayes, J. F., Silverstein, S. M., & Cooper, C. (2023). Association between visual impairment and psychosis: A longitudinal study and nested case-control study of adults. Schizophrenia Research, 254, 81-89. https://doi.org/10.1016/j.schres.2023.02.017
Silverstein, S. M., & Keane, B. P. (2011). Vision Science and Schizophrenia Research: Toward a Re-view of the Disorder Editors' Introduction to Special Section. Schizophrenia Bulletin, 37(4), 681-689. https://doi.org/10.1093/schbul/sbr053
Tandon, R., Nasrallah, H. A., & Keshavan, M. S. (2009). Schizophrenia, "just the facts" 4. Clinical features and conceptualization. Schizophrenia Research, 110(1-3), 1-23. https://doi.org/10.1016/j.schres.2009.03.005

Are there any files you would like to upload to support your concept paper?	○ Yes ◉ No

Applicants: If you would like to continue your application later, please press the "Save and return later" button below. Please copy or write down the Return code provided.

To return later, you may click on "Returning?" on the top right of the screen in the E-Risk Concept Paper Form link, which is the same link that was used to access this form: https://redcap.link/ERiskConceptPaperForm

3. Expected project outcomes

Please note:

The stated end date must be within 24 months of the date when this form is submitted. This end date will form part of the formal data use agreement and on this date you should delete the dataset. Therefore, it must be a realistic date for completion of the project including all analysis, writing a manuscript, review of the manuscript by all collaborators, submission, revisions, and acceptance of a paper for publication.

If you require an extension to the end date of the project, then you should contact Prof Fisher (helen.2.fisher@kcl.ac.uk) to discuss this. If you have signed a formal data use agreement, you will need to complete a form to request a licence extension. In some cases, we may also ask you to complete a new concept paper form if there have been substantial changes to the project or a long period of time has elapsed (e.g., greater than a year since the end date of the original project).

If the objective of the project is not a journal publication, please suggest an end date within 12 months instead of 24 months, and state a measurable, concrete outcome. If the objective of the project is a student dissertation, then the expected end date should be the deadline for submission of the dissertation; dissertation projects will only be accepted on agreement that they are strictly not for publication.

Date form submitted	05-09-2025 *DD-MM-YYYY*
End date for the project	05-09-2027 D-M-Y *DD-MM-YYYY*

Do you expect to publish your results in a journal?	◉ Yes ○ No

If yes, please provide a provisional list of author names	**Akke Ganse-Dumrath, Corinna Haenschel, Helen Fisher, Anne-Kathrin Fett, + other interested E-Risk investigators**
If yes, please provide a provisional list of journals	**Schizophrenia Bulletin, Psychological Medicine**

Applicants: If you would like to continue your application later, please press the "Save and return later" button below. Please copy or write down the Return code provided.

To return later, you may click on "Returning?" on the top right of the screen in the E-Risk Concept Paper Form link, which is the same link that was used to access this form: https://redcap.link/ERiskConceptPaperForm

4. List of variables required

Please note:

When specifying variables, please be unambiguous. For each variable, specify the name of the measure, twin age, informant, and if you want specific subscales/derived categories (e.g., Depression from interview with twin at age 18; both number of symptoms and DSM-IV diagnosis). Alternatively, for maximum clarity, give actual variable names (e.g., MDESXE18 - MDE Symptom scale - P18 - Elder; DXMDEE18 - Major depressive episode, dsm4 - P18 - Elder).

By default, the dataset will usually include twin and family IDs, the "random" and "true" twin order variables, the cohort the twin is from (1994 or 1995), twin sex, ethnicity and zygosity variables, and family socioeconomic status at age 5. These routine background variables are listed in the table below. If you require further background variables, please specify them in your list.

Access to some parts of the dataset are restricted, namely identifiable data (e.g., postcodes, video recordings, individual-level genotypic and epigenetic data) which will not be shared outside King's College London, and linked administrative data which is only accessible via the UK Longitudinal Linkage Collaboration's Trusted Research Environment (this requires a separate formal data access agreement).

Background variables that will be included by default:

Variable name	Description
FAMILYID	**Unique family identifier**
ATWINID	**Twin A ID (ex chkdg)**
BTWINID	**Twin B ID (ex chkdg)**
RORDERP5	**Random Twin Order**
TORDER	**True Twin Order**
RISKS	**Sample Groups**
COHORT	**Cohort**
SAMPSEX	**Sex of Twins**

ZYGOSITY	**Zygosity**
SETHNIC	**Ethnicity of Twins**
SESWQ35	**Social Class Composite**

Please select the variables that will be requested	☐ Age 5 variables ☐ Age 7 variables ☑ Age 10 variables ☑ Age 12 variables ☑ Age 18 variables ☐ Age 26 variables ☐ Age 30* variables
Age 10 variables	**STRWEM10 - Standard Reading Scores - Real Words - Elder Twin** **STRWGEM10 - Grouped Standard Reading Scores - Real Words - Elder Twin** **PAE6M10 - Spectacles - Elder Twin** **AVANGE10 - Lowest Morph of Correct Detection of Anger - Elder Twin** **AVFEARE10 - Lowest Morph of Correct Detection of Fear - Elder Twin** **AVHAPE10 - Lowest Morph of Correct Detection of Happy - Elder Twin** **AVSADE10 - Lowest Morph of Correct Detection of Sad - Elder Twin**
Age 12 variables	**FSIQ12E_STD - Pro-rated IQ Score - Elder Twin** **PSYSYMP01E12 - Psychosis Symptom Count (0, 1+) - Elder Twin**
Age 18 variables	**PSYSYMP01E18 - Psychosis Symptom Count (0, 1+) - P18 - Elder Twin** **PSYEXPCE18 - Psychotic Experiences (cat) - P18 - Elder Twin** **EDUCACHVE18 - Highest Educational Achievement (based on QCF) - P18 - Elder Twin** **NEETE18 - NEET: Not in Education, Employment, or Training - P18 - Elder Twin** **SICOUNTRYE18 - Subjective Social Status Ladder Task - Elder Twin** **SOCSUPE18 - Social Support Scale - P18 - Elder Twin** **SOCISOE18 - Social Isolation Scale - P18 - Elder Twin** **LONELYE18 - Loneliness Scale - P18 - Elder Twin** **TOTLIFSATE18 - Total Life Satisfaction Score - P18 - Elder Twin**
Are you requesting access to identifiable or linked data?	○ Yes ◉ No