**Synopsis no.:** *S2.57*

**Preliminary title:**

**Age at migration and odds of psychosis: potential confounding, moderating and mediating effects**

**Contact info for the person(s) proposing the synopsis**

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**Publication category: 2**

**Working and writing group:** James Kirkbride, Humma Andleeb, Hannah Jongsma, Ilaria Tarricone, Craig Morgan, Els van der Ven, Jean-Paul Selten, Fabian Termorshuizen, Giuseppe D'Andrea, Charlotte Gayer-Anderson + any others from WP2 who wish to be involved.

**Work Packages involved: WP2**

**Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated:**

**Objectives (scientific background, hypothesis, methods, and expected results):**

1. **Scientific Background/ objectives**

It is well known that many migrants and their descendants experience higher rates of psychosis compared with both the majority non-migrant population and their counterparts who do not migrate. The cause of this inequality remains unknown. The findings of a recent systematic review [1] suggested that immigration at younger ages (childhood and adolescence) increased psychosis risk to a greater extent than migration at adult age, but it is unclear if this is because of exposure to migration as a disruptive event during sensitive socio-developmental periods, or because of selection effects for people who migrate in adulthood (i.e. a healthy migrant effect associated with migration in adulthood).

Using data from the 17-site, six country, European Union Gene-Environment interaction (EU-GEI) study, we aim to better understand these mechanisms by analysing the association between age-at-migration and psychosis risk. If there is an association between age-at migration and psychosis risk, we want to investigate whether there is a peak age-of-migration associated with psychosis risk.

We will examine (i) the association between age-at-migration and psychosis risk, (ii) determine whether this is confounded by ethnicity or pre-migratory social disadvantage, which has been recently associated with psychosis risk in the EU-GEI study (Tarricone et al [2]), (iii) examine whether the putative association between age-at-migration and psychosis risk has the same impact across all major ethnic groups, and (iv)

examine whether any association between age-at-migration and psychosis risk is mediated by post-migratory social disadvantage.

We want to use this data to explore these issues as part of a first-year PhD project. We expect this to deliver a single main publication for the working & writing group and approved EU-GEI WP2 authorship group.

**2. Research questions and hypotheses**

1. What is the association between age-at-migration and the odds of psychotic disorder?

   We hypothesise that those who migrate during key periods of social development (i.e. as school-aged children or during adolescence) will have
   greater odds of psychotic disorder compared with those who migrate as adults or during infancy.

2. Is this association confounded by pre-migratory social determinants of psychosis or ethnicity?

   We hypothesise that after adjusting for pre-migratory social determinants and ethnicity, the effect of age-at-migration on psychosis risk will remain present.

3. Does this association vary by ethnicity?

   We hypothesise that the association between childhood and adolescent age-at-migration and psychosis will be more pronounced in migrants from Black and South Asian minority ethnicities than migrants from White ethnic minority groups

4. Is the association between age-at-migration and psychosis mediated by social determinants that occur after migration?

   We hypothesise that social determinants that occur post-migration will mediate the association between age-at-migration and odds of psychosis. These will include experiences of racism and discrimination and any socioeconomic measures that can be reliably measured between exposure and outcome in all participants.

**3. Methods**

We will use multivariable logistic regression and multiple imputation techniques to handle missing data.

We will use several confounders to explore our hypothesis including gender, ethnicity, country of origin, country migrated to, social class, discrimination, language fluency, pre/post migration social disadvantage and family history of psychosis and length of time (months/years) since arrival. Auxiliary variables for multiple imputation as required.

Inclusion criteria

- Participants included in the WP2 case-control sample
- Participants identified as either from the majority population (i.e. majority white or non-migrant population) as reference, or migrants born overseas

Exclusion criteria

- Ethnic minority or second-generation case-control participants without a direct migration history

**References**


1. Anderson KK, Edwards J (2020) Age at migration and the risk of psychotic disorders: a systematic review and meta-analysis. Acta Psychiatr Scand 141:410–420. https://doi.org/10.1111/acps.13147
2. Tarricone I, D'Andrea G, Jongsma HE, et al (2021) Migration history and risk of psychosis: results

from the multinational EU-GEI study. Psychol Med 1–13. https://doi.org/10.1017/s003329172000495x

**Data needed for the study:**

Case-control data from WP2 to include the following variables:

- Case-control status
- OPCRIT diagnosis
- Age at first contact
- Sex
- Ethnic group
- Country of origin
- Centre/country at participation
- SES variables, as available (income (if available), education, social class)
- Migration status (first vs. later generation)
- Age at migration
- Migration history data, as per Tarricone et al 2021
- Social disadvantage index
- Language Fluency

**Plan for statistical analysis (overall strategy):**

We will account for weights in control sample versus case sample. We will use binary logistic regression models to look at associations between ethnicity, age at migration and social determinants as confounding factors using adjusted and unadjusted models. We will use multiple imputation methods to handle missing data, and use appropriate mediation methods such as causal mediation analysis to investigate mediation.

**Other analyses/methods:**

**Involvement of external Parties (non EU-GEI):**

**IPR check:**

**????**

**Timeframe:**

Analyses and write up of results will take place over the next 12 months and conclude by September 2022, or following publication in a peer-reviewed journal.

**Additional comments:**