Synopsis for EU-GEI Publication

Synopsis no.: S2.12

Preliminary title: The course of cognitive decline in schizophrenia

Contact info for the person(s) proposing the synopsis

Name: Eva Velthorst
Partner no: 8
e-mail address: eva.velthorst@mssm.edu

Publication category: 1 (publication from integrated work from several Work Packages)

Working and writing group:
Eva Velthorst, Lieuwe de Haan, Avi Reichenberg

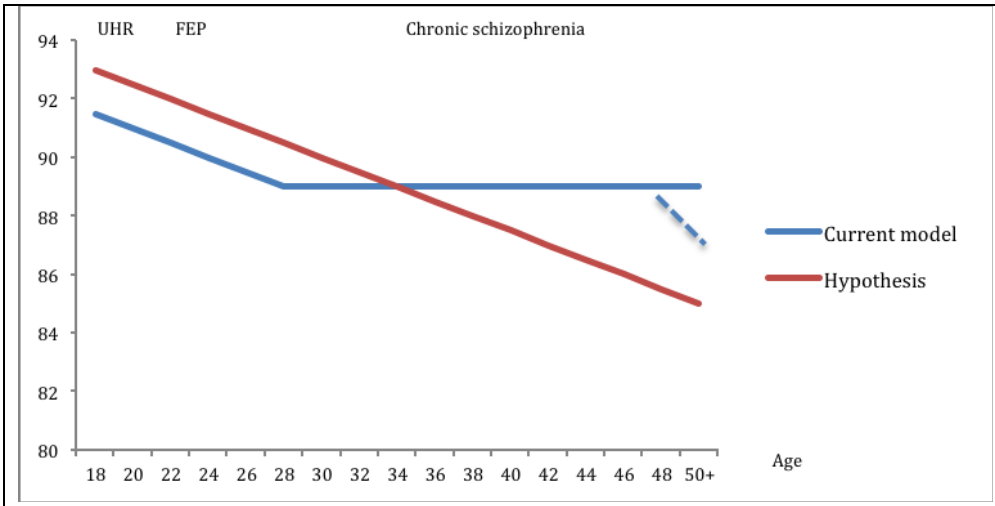
Work Packages involved:
WP2, WP5, WP6, WP7

Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated:
All centres part of WP2, WP5, WP6 and WP7

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

Scientific background
Current models of cognition in schizophrenia are mainly based on the idea that the largest cognitive decline occurs prior to- or in the first years of overt clinical psychotic symptoms (e.g. Bora & Murray, 2014; Becker et al., 2011; Maccabe et al., 2013; Kim et al., 2011; Simon et al., 2007). Some studies suggest a second 'peak' in decline during the late chronic stages (Harvey 2013, 2014), but most emphasize at least some level of stability in the later phases of the illness. However, studies examining cognition mostly do so in relation to illness- status (i.e. early onset schizophrenia, UHR, FEP, chronic schizophrenia). Surprisingly few, if any, examined the possibility that the decline of cognition is actually an age-associated slow and progressive progress that has little to do with where a patient lies on the psychosis continuum.

Hypothesis
With the present study we aim to test the hypotheses that cognitive decline starts early on but, as opposed to the common perspective, continues to deteriorate and diverge from the healthy population as patients get older, possibly accelerated by symptoms, cannabis use and urbanicity.



Including patients with an ARMS, First Episode Psychosis and patients in later stages of the illness, their siblings and a healthy control group, we will address the following hypotheses:

1. Cognitive capacity diverges from healthy controls over time (as a function of age, rather than a function of patient status)
2. This decline is accelerated by symptom severity, urbanicity and cannabis use
3. Siblings of affected patients show cognitive impairments, but there is no decline over time

Data needed for the study:

- WAIS-IV shortened version (cognition)
- OPCRIT
- CAARMS +
- Combined Social Scales (socio demographics/ urbanicity)
- Cannabis Experience questionnaire
- GAF symptoms

Plan for statistical analysis (overall strategy):

The extent to which cases (ARMS, FEP and CS) and siblings differ from healthy controls will be tested with an Analysis of Covariance, adding urbanicity, cannabis use and symptom severity (GAF symptoms) to the model as possible confounders.

To analyse the decline in cognition with age, we will employ a longitudinal growth model that permits the combined using of cross-sectional and longitudinal data, a method frequently used in examining progressive brain changes (e.g. Giedd et al., 1999; Castellanos et al., 2002). This method will allow us to combine cognitive measures across Work Packages, of which some have only assessed cognition at

baseline (e.g. WP2) while others incorporate follow-up measures as well (e.g. WP7). We will examine if there is a significant change with age, and if developmental curves differ by sex, diagnostic status, cannabis use, symptom severity and urbanicity.
Other analyses/methods: N/A
Involvement of external Parties (non EU-GEI): Icahn School of Medicine at Mount Sinai (Eva Velthorst, Avi Reichenberg)
IPR check: N/A
Timeframe: Start date: Date of completion data collection in all centers Month 2: Literature search; obtaining, merging, checking, cleaning of data Month 4: Completion of statistical analysis and first draft of manuscript Month 6: Manuscript submission
Additional comments: N/A