



Transdiagnostic symptom dimensions and genetic risk scores at first episode psychosis

Diego Quattrone, MD

Research Associate, Part-time PhD student

Social, Genetic, and Developmental Psychiatry Centre

Institute of Psychiatry, King's College London

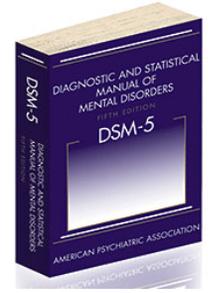
National Psychosis Service

South London and Maudsley NHS Foundation Trust

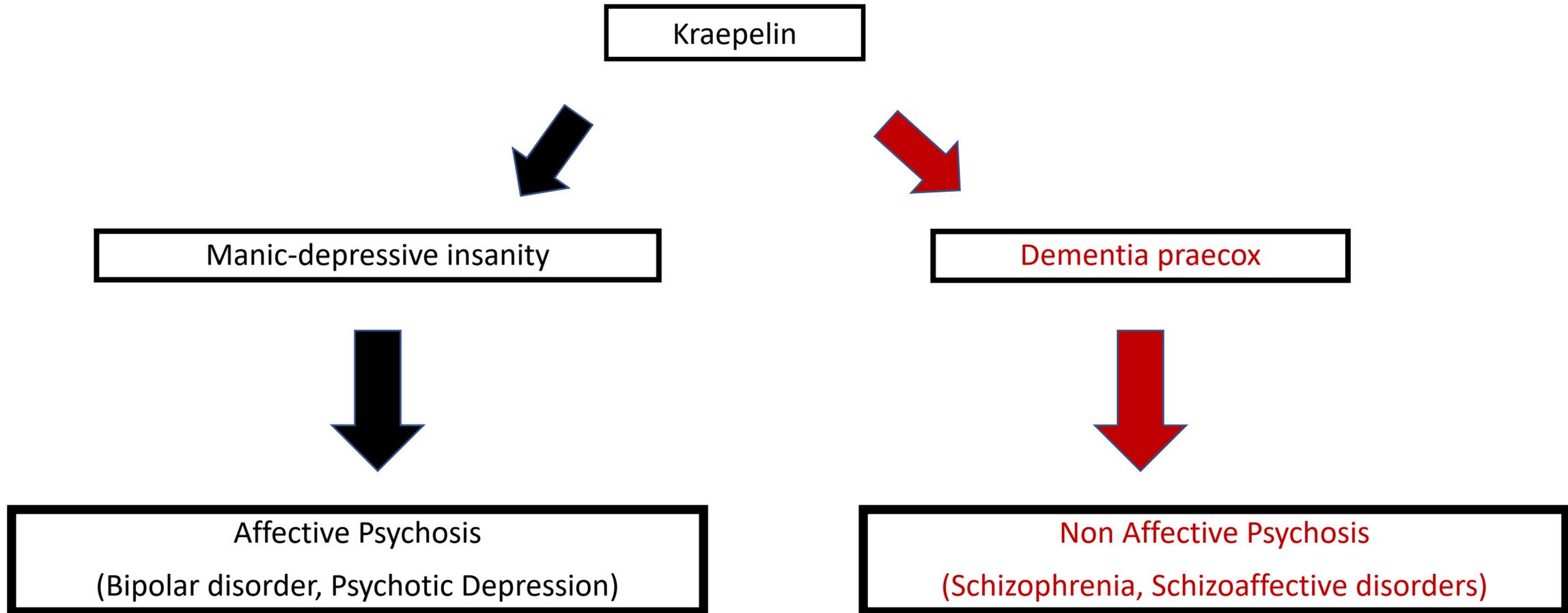


Background

The hot question in psychiatric nosology



- Categorical diagnostic classification may not reflect clear biological entities

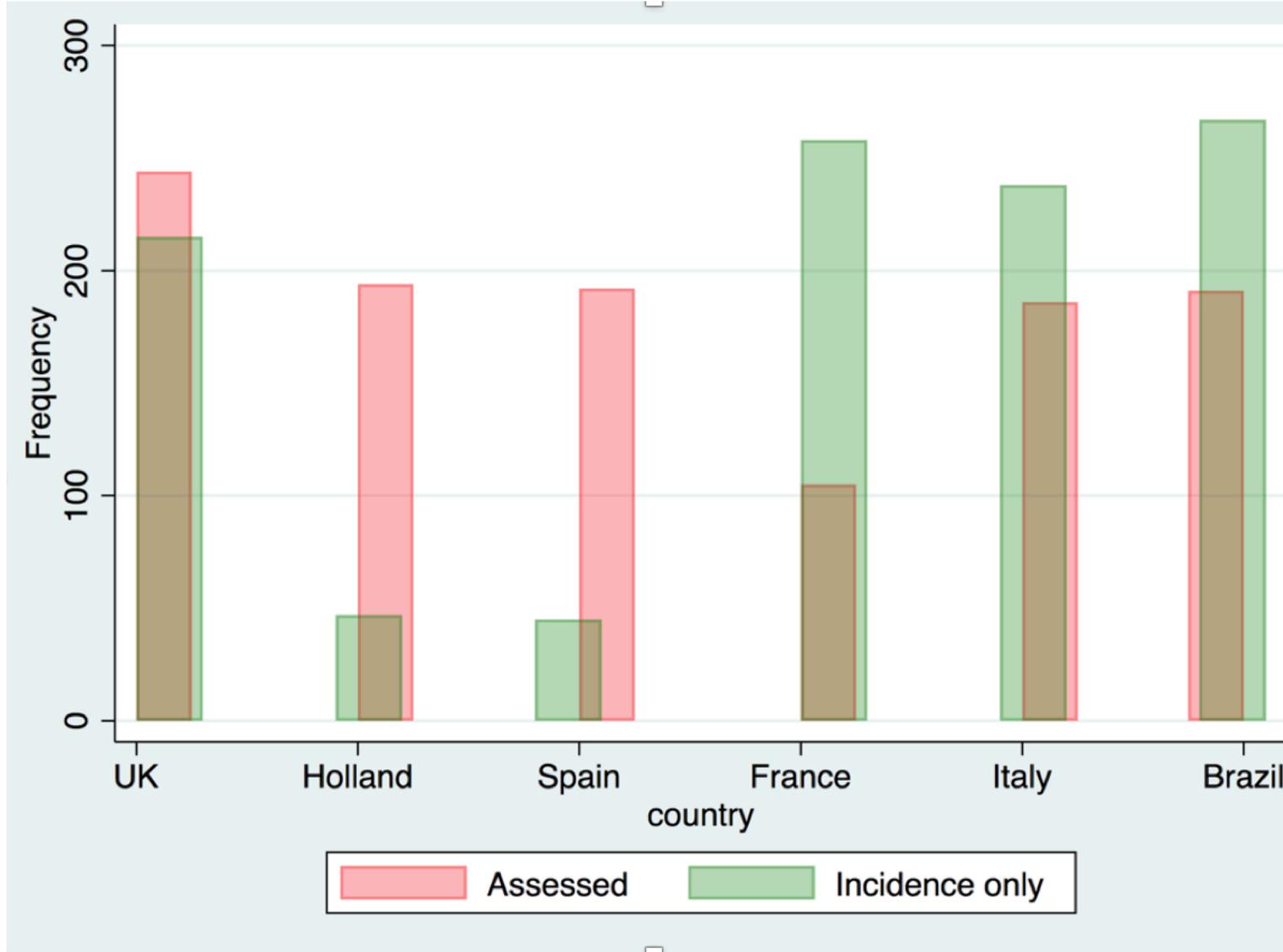


Aims and hypotheses



1. Examining the dimensional structure of psychopathology in the EUGEI study
2. Examining how cannabis use shapes psychopathology at illness onset
3. Examining the effects of common genetic variants associated with Major Mental Disorders, on general and specific psychotic symptom dimensions

First Episode Psychosis (FEP) sample



Final sample size:
2182 FEP cases
with available
psychopathology
information

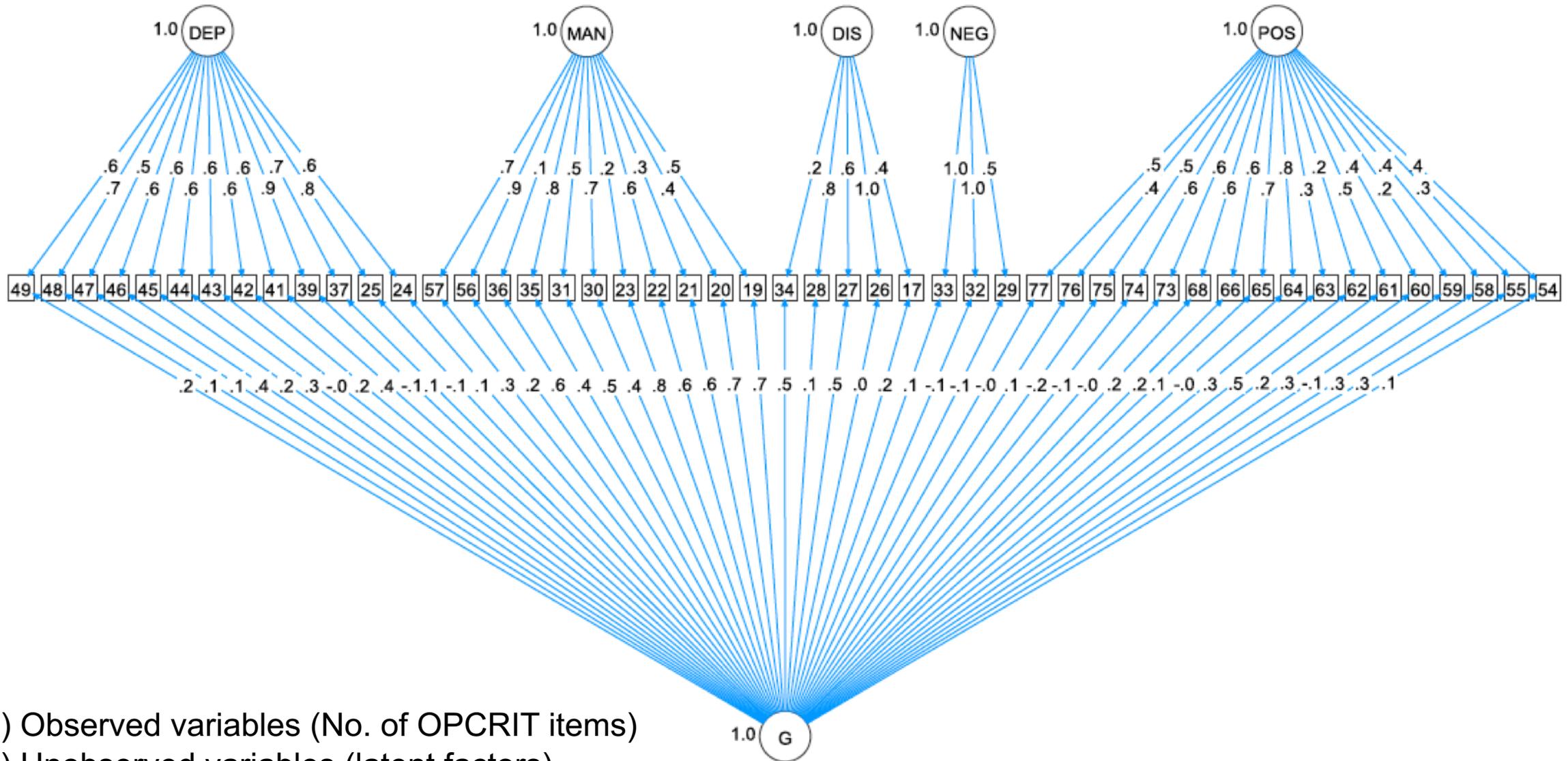
Measurements

- Medical Research Council (MRC) Sociodemographic Schedule was used for **sociodemographics** (Mallett, 1997)
- The OPERational CRITeria (OPCRIT) system was used to assess all the different aspects of **psychopathology** (McGuffin *et al.*, 1991)
- The Schedule for Deficit Syndrome (SDS) was used to assess **negative symptoms** (Kirkpatrick *et al.*, 1989)
- The Cannabis Experience Questionnaire – modified version (CEQ_{EU-GEI}) was used to collect extensive information on **cannabis** use (Di Forti *et al.*)
- Samples were **genotyped** using Illumina HumanCoreExome-24 BeadChip array

Aims and hypotheses

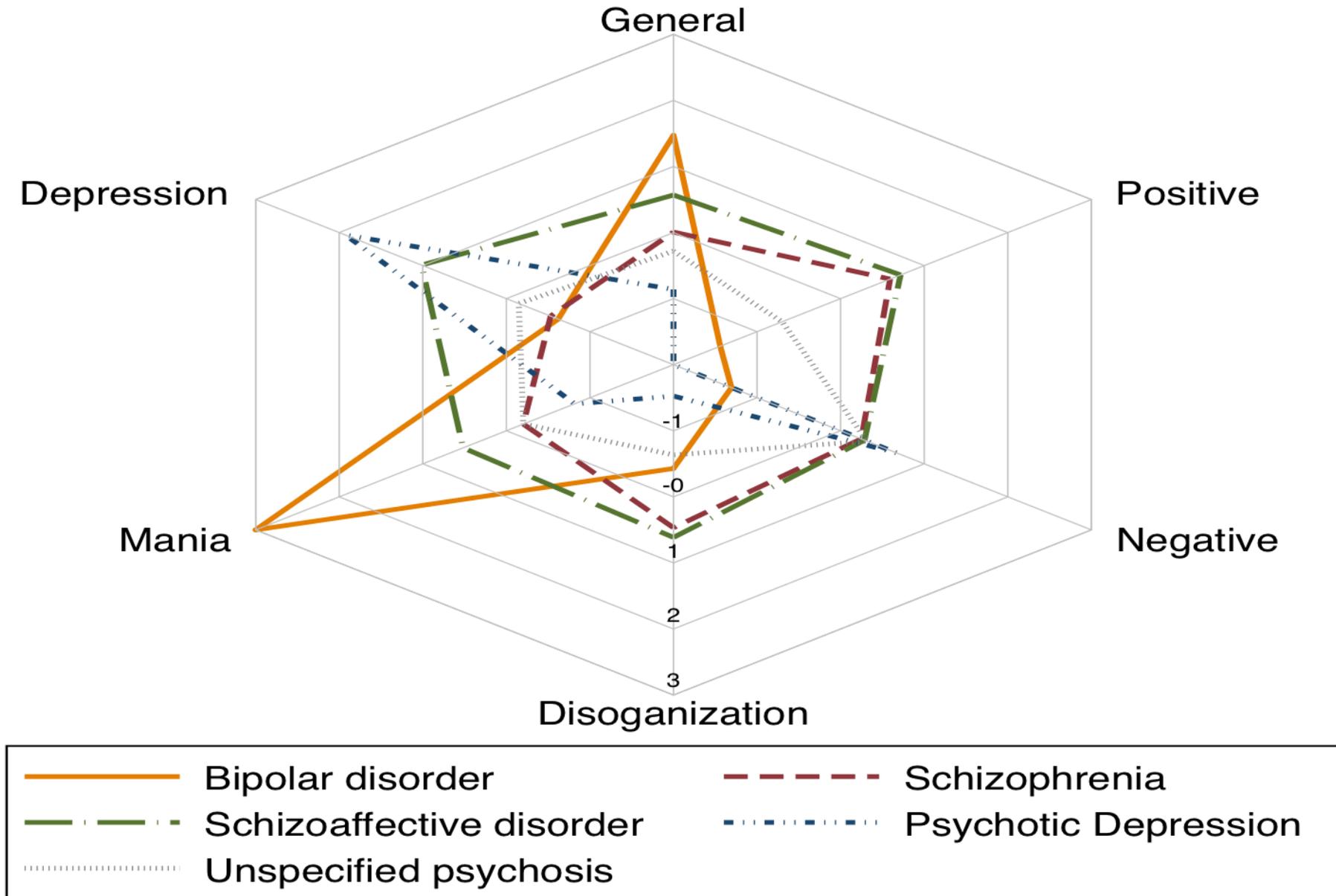
- 1. Examine the dimensional structure of psychopathology in the EUGEI study**
 - i. Does a general factor of psychopathology encompass affective and non-affective psychosis?**

Bi-factor conceptualization of psychosis



- (□) Observed variables (No. of OPCRIT items)
- (○) Unobserved variables (latent factors)
- (→) standardized item loading onto latent factors

Symptom dimensions by diagnostic category



Aims and hypotheses

1. **Examine how cannabis use shapes psychopathology at illness onset**
 - i. **Is psychopathology at FEP different in those using cannabis?**



Donald Trump said he never smoked cannabis



Boris Johnson admitted having used cannabis as a student

Positive Dimension & Cannabis Use

Frequency

Less than everyday: 

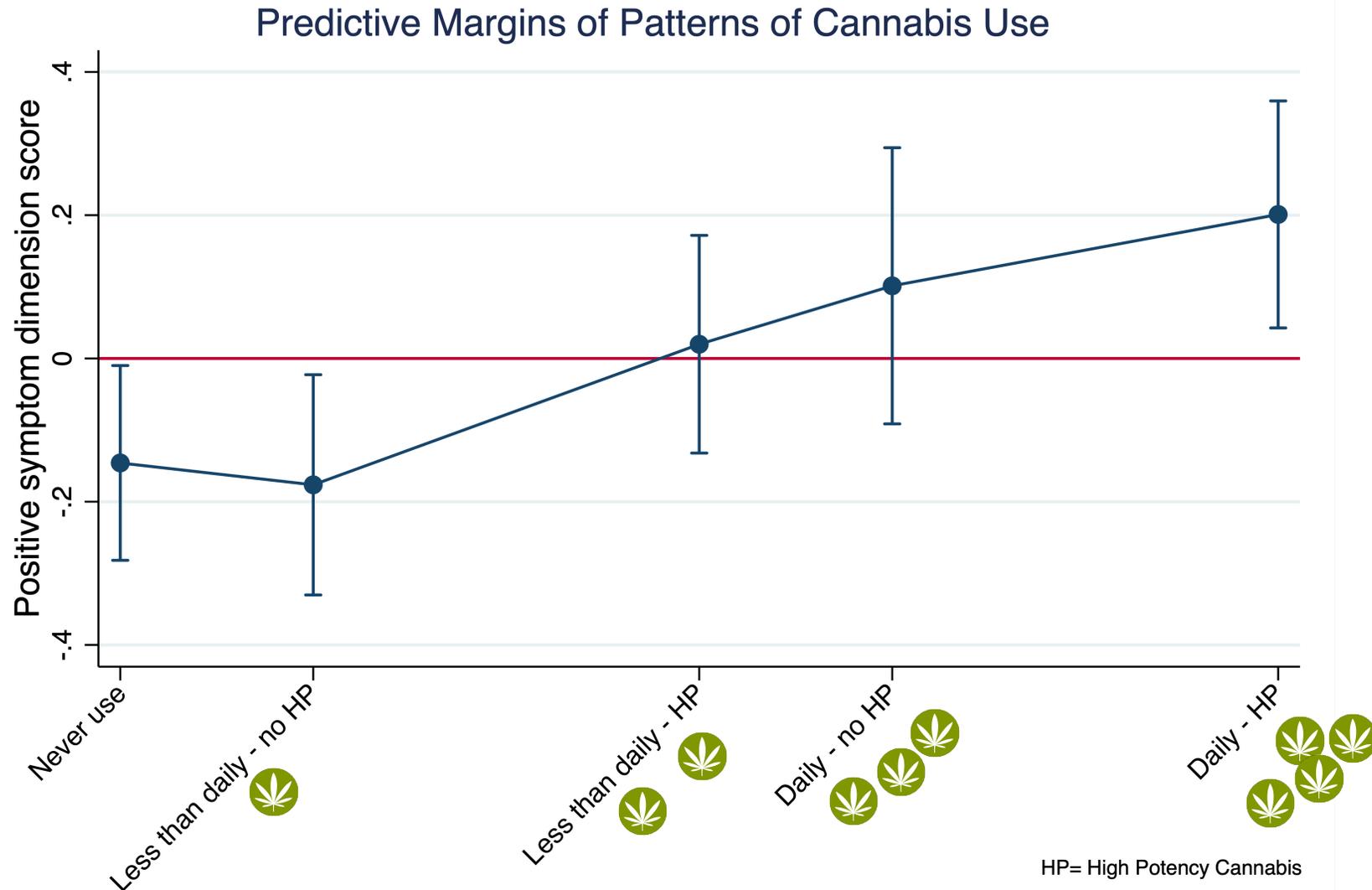
Everyday:  

Potency:

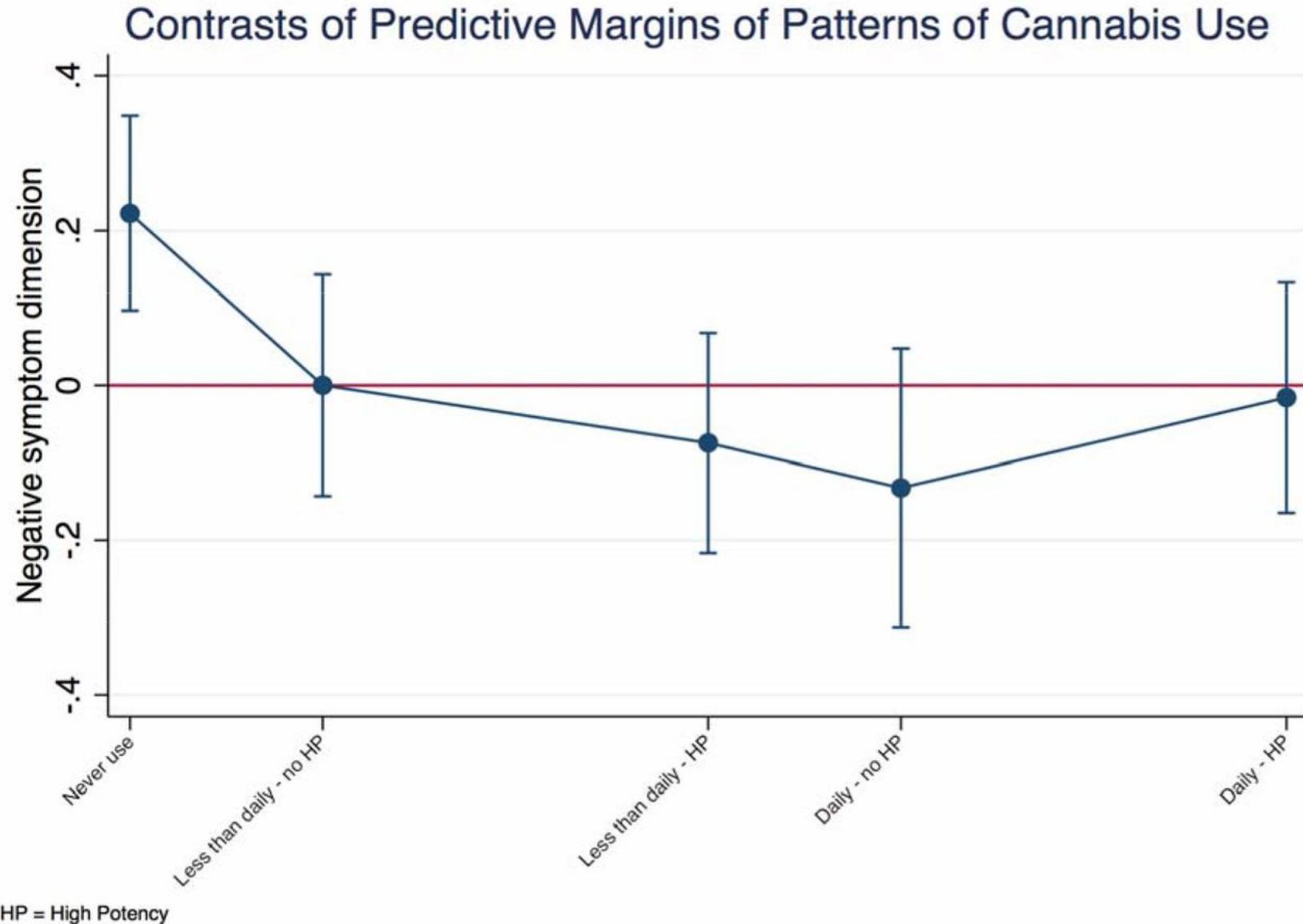
More than 10% THC: 

HP=High Potency

Variance explained, $R^2=0.16$



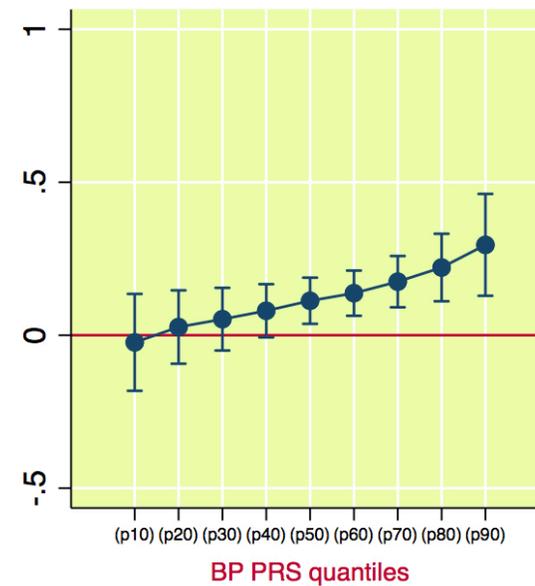
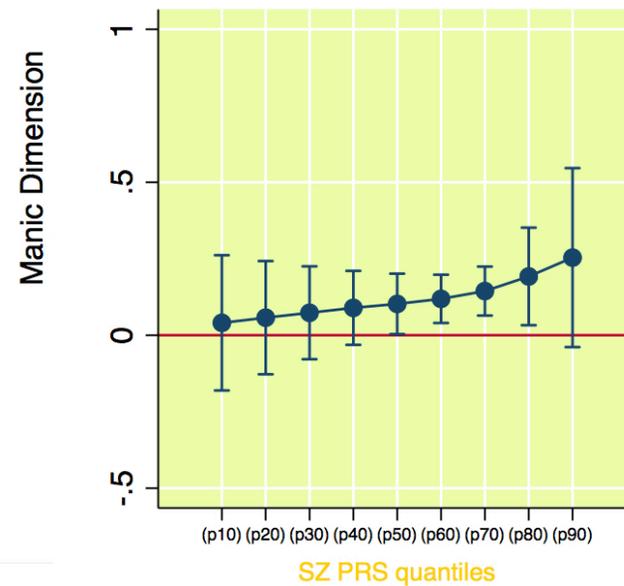
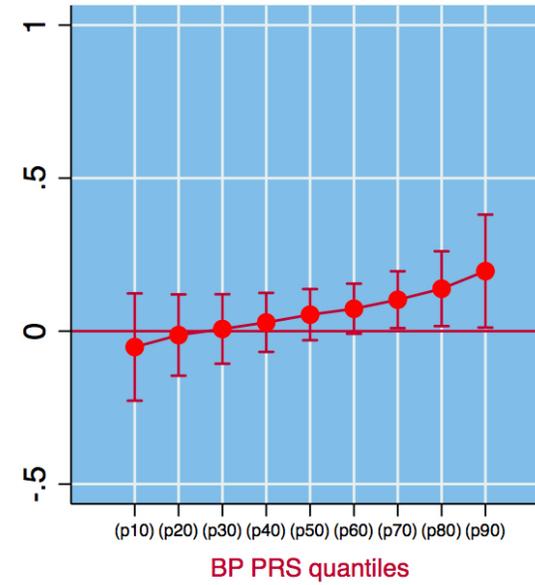
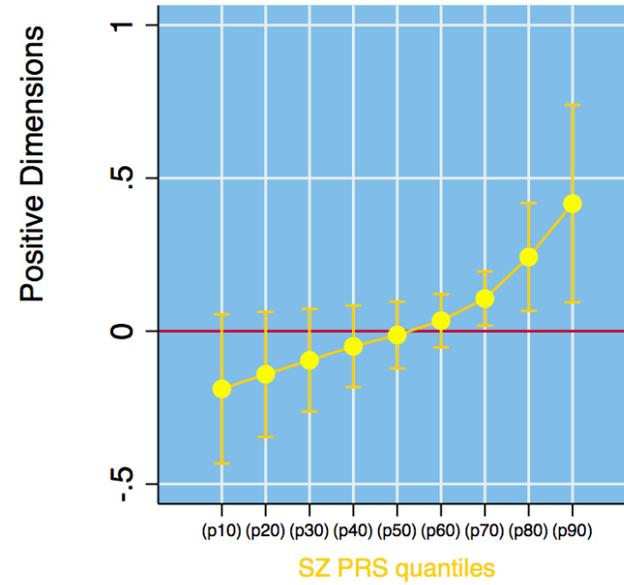
Negative Dimension & Cannabis Use



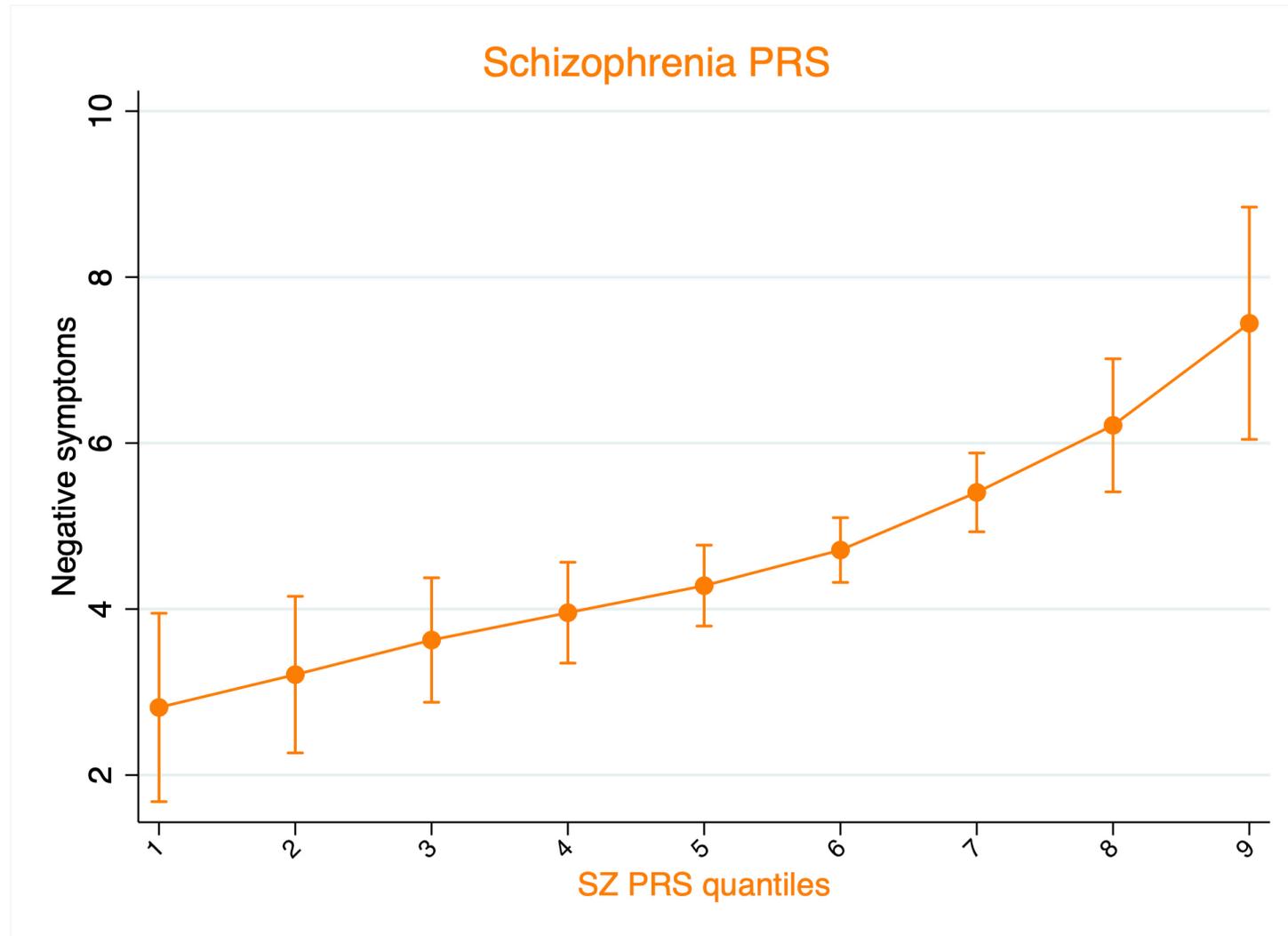
Aims and hypotheses

1. **Examine effects of common genetic variants associated with Major Mental Disorders on general and specific psychosis dimensions**
 - i. We expect that **schizophrenia PRS** would be associated with more **positive / negative symptoms**; **bipolar PRS** with **manic symptoms**

Positive and Manic Dimensions & SZ - BIP PRS



Negative Symptoms & SZ PRS



What do we know about positive symptoms in the EUGEI so far

1. Does cannabis use impact on positive symptoms?

Yes, it has a moderate effect consistently with some previous report (Ringen et al, 2016; Seddon et al., 2016)

2. Does SZ PRS impact on positive and negative symptoms?

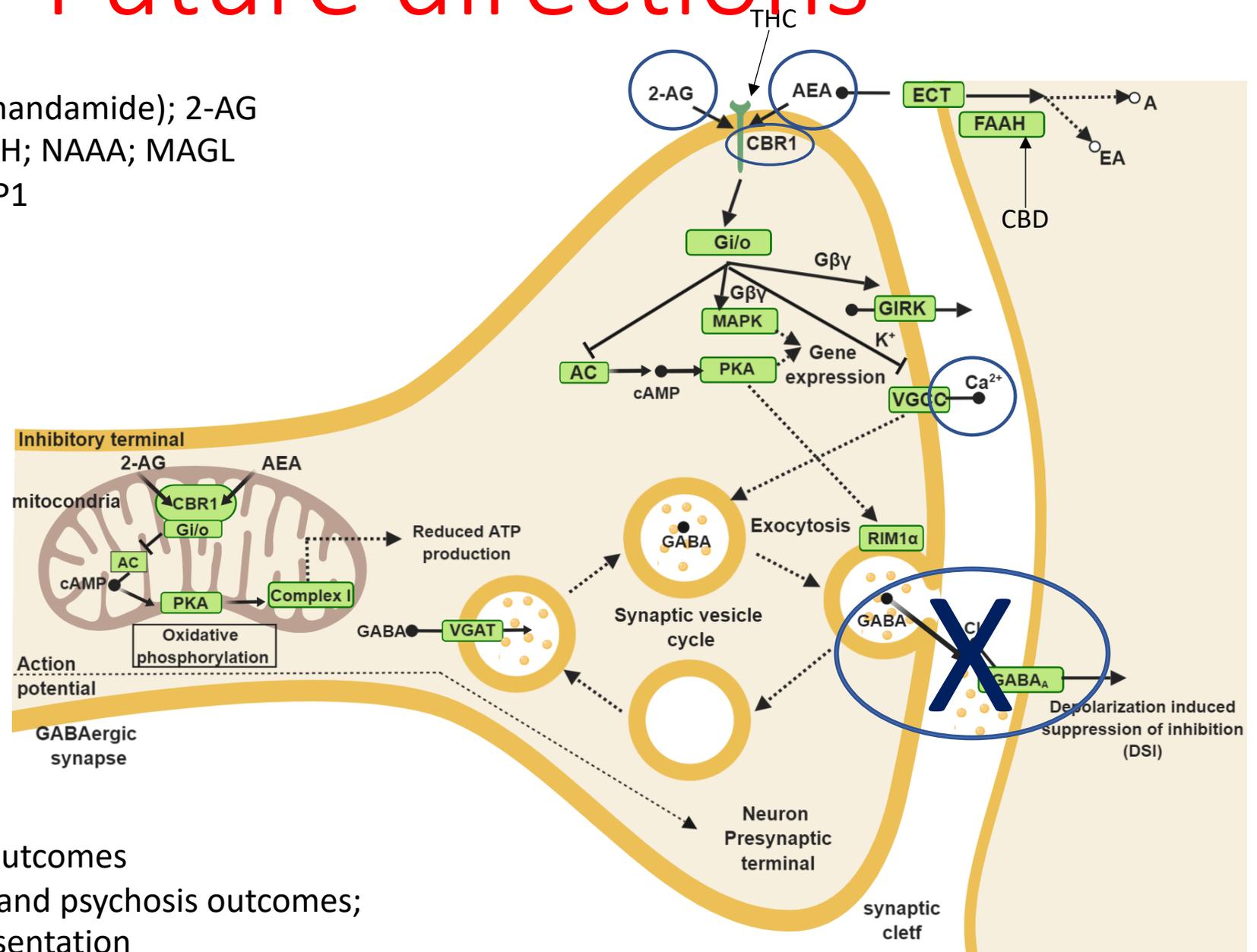
Yes, however the effect is small

3. Does cannabis use interact with SZ PRS in predicting positive symptoms?

No, the effects are independent with each other

Future directions

Endocannabinoids (eCB) - AEA (anandamide); 2-AG
 Metabolizing enzymes - e.g., FAAH; NAAA; MAGL
 Receptors - e.g. CB1R; CB2R; TRVP1



Research questions

To examine:

- 1) eCB risk alleles and psychosis outcomes
- 2) eCB risk alleles X cannabis use and psychosis outcomes;
- 3) eCB risk alleles and clinical presentation

Conclusions

- The psychosis structure at FEP can be conceptualized as being composed of one general psychosis factor and five specific symptom dimensions
- FEP patients using cannabis, especially daily users of high potency types, expressed more psychopathology, in particular positive symptoms
- There was a small effect for SZ PRS on positive and negative symptoms, and for BIP PRS on manic symptoms
- Further research will examine the impact of endocannabinoid signaling and transdiagnostic symptom dimension