**Supplementary material**

**Validating the PGRS method**

SZ PGRS predicted case-control status for SZ and BD spectrums with an explained variance (Nagelkerke r2) of about 0.12 and 0.05 for SZ and BD, respectively, at the P-value threshold of 0.05 (Fig S2 Suppl Mat).

In the ANOVA with Tukey post hoc pairwise tests, SZ PGRS was significantly associated with both SZ and BD spectrums. The following *P* values were adjusted with the Tukey method. SZ PGRS was associated with the SZ spectrum at *P*=2.9 x 10-17and with the BD spectrum at *P*=4.5 x 10-6, with a significant difference between SZ and BP (*P*=0.03). When separated into diagnostic subcategories, the PGRS2 was significantly associated with SZ (*P=*2.9 x 10-12), SZA (*P*=0.004), PNOS (*P*=7.1 x 10--6), and BD1 (P= 5.9 x 10 -6). A significant difference between SZ and BP2 was observed (*P*=0.04), otherwise no significant differences between any of the subcategories and PGRS2 were observed.

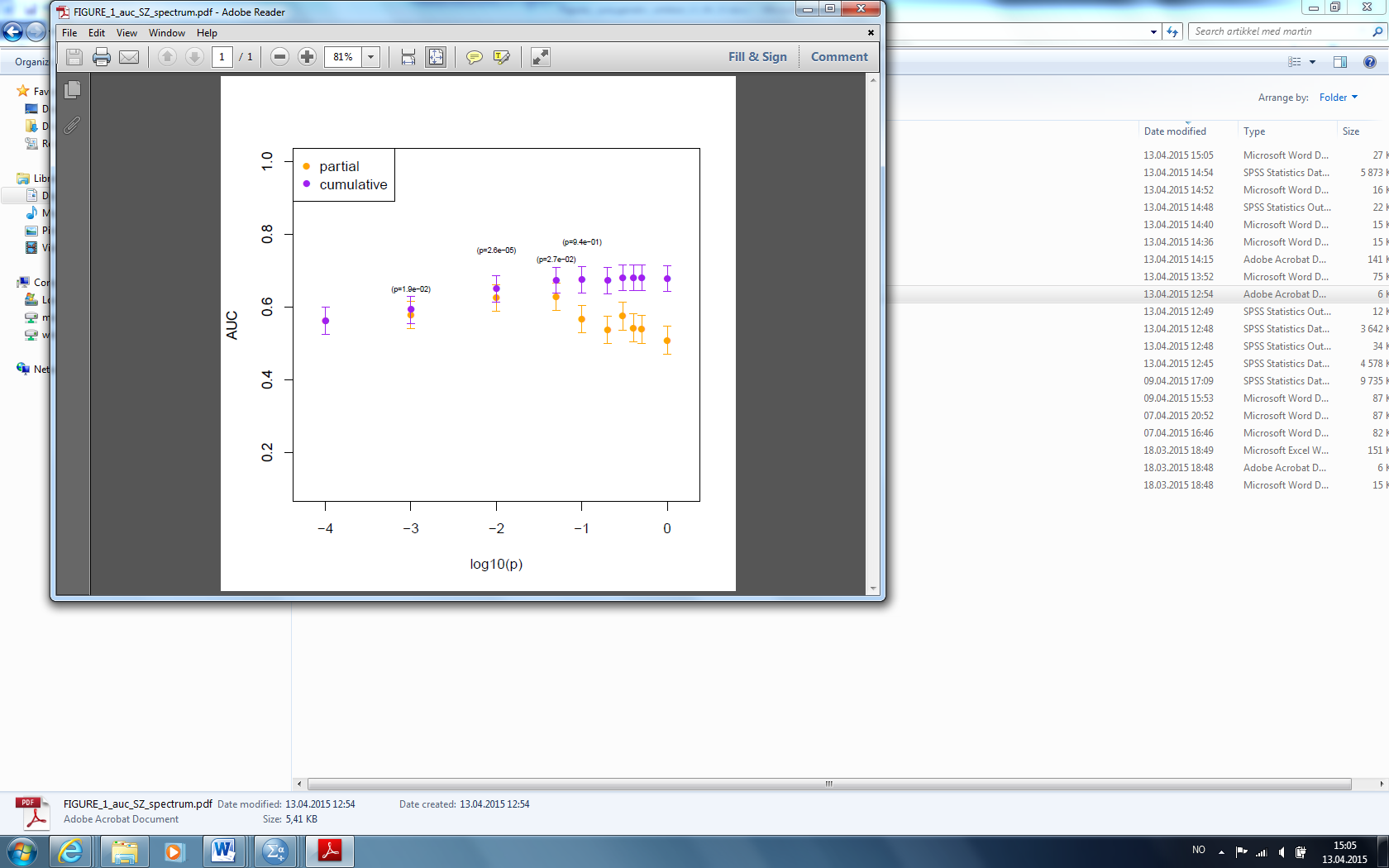
**Figure S1:** Area under the ROC curve for polygenic risk score-based prediction of a SZ diagnosis.

Fig.S1. The area under the ROC curve (AUC) for case-control status prediction is reported for PGC2 schizophrenia polygenetic risk scores (PGRS2) based on different P-value thresholds for SNP inclusion. X-axis: log10 of the P valuethreshold for SNP inclusion. Y-axis: AUC for partial log10(P) bins and cumulative log10(P) bins,with regard to SZ diagnosis.

**Figure S2:** Mean SZ polygenetic risk score in diagnostic spectrum and healthy controls

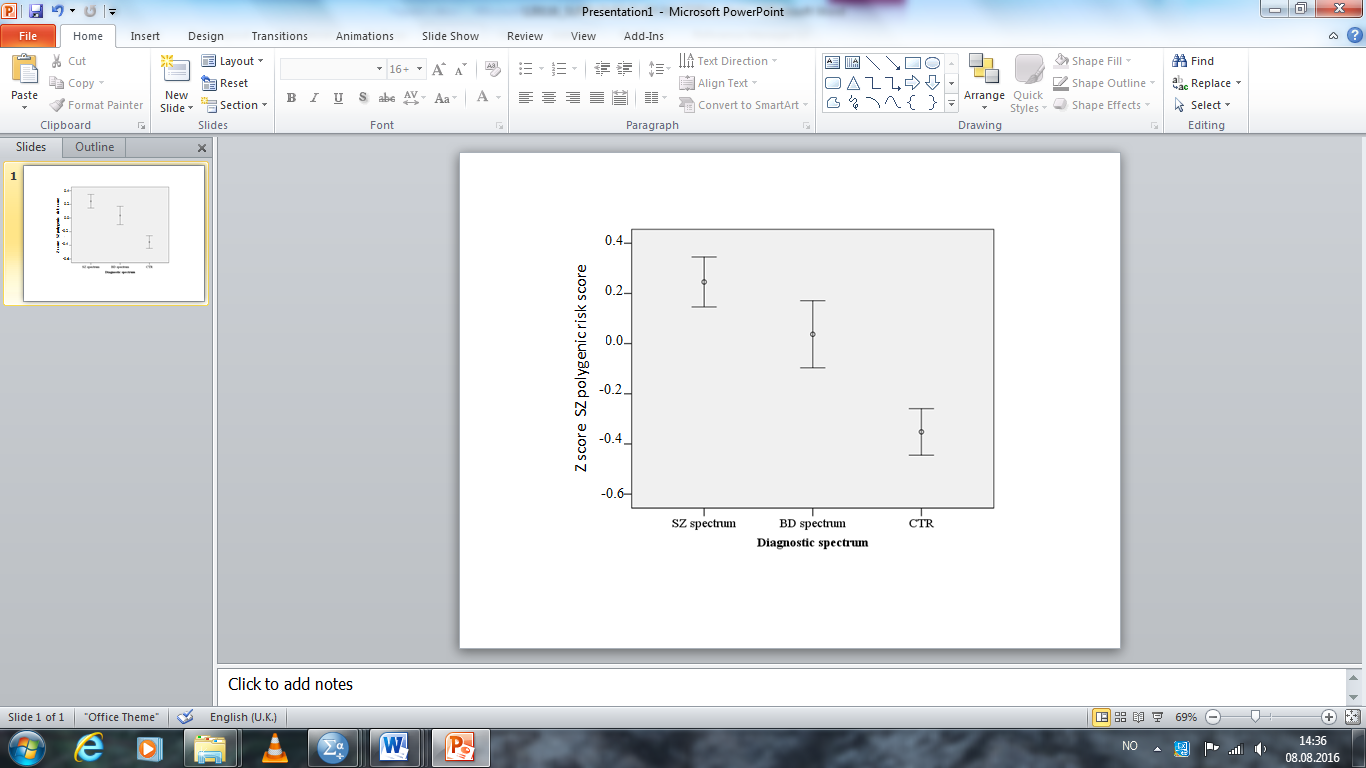


Fig.S2. Mean SZ polygenetic risk score in diagnostic spectrum and healthy controls. Error bars depict standard error of the mean.

**Figure S3:** Mean SZ polygenetic risk score in diagnostic subcategories and healthy controls

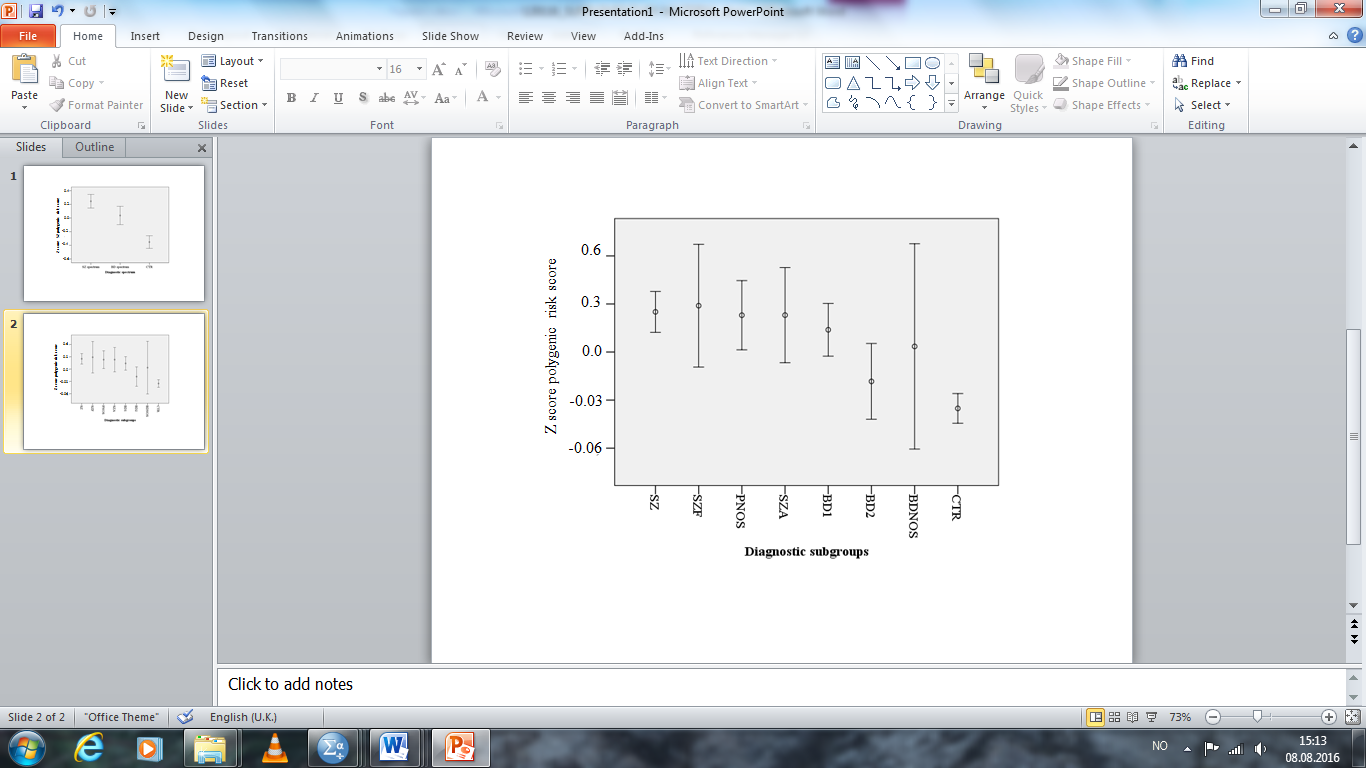


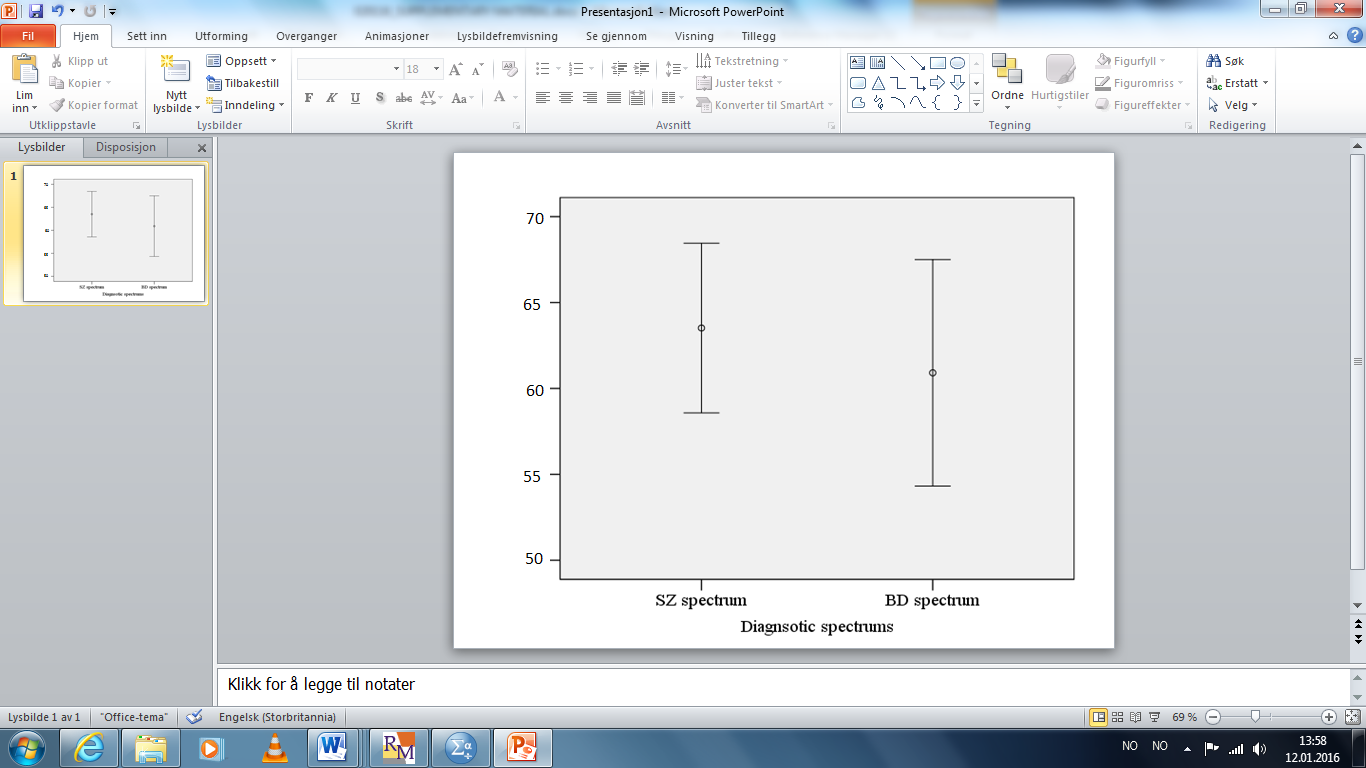
Fig.S3. Mean SZ polygenic risk score in diagnostic subcategories and healthy controls. Error bars depict standard error of the mean. BD2, bipolar disorder type 2; BDNOS, bipolar disorder not otherwise specified; SZ, schizophrenia; SZF, schizophreniform disorder; PNOS, psychosis not otherwise specified; SZA, schizoaffective disorder.

**Table S1:** Results of pairwise comparisons of mean polygenic risk score across diagnostic spectrums

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Diff | lwr | upr | P adj |
| SZ PGRS2  z score |  |  |  |  |
| CTR vs. SZ | -.5974699 | -.7614626 | -.4334772 | 2.9 x 10-17 |
| CTR vs. BP | -.3890072 | -.5817624 | -.1962521 | 4.5 x 10-6 |
| SZ vs. BP | .2084626 | .0127504 | .4041748 | 0.03 |

CTR, healthy controls; BD, bipolar disorders; SZ, schizophrenia, PGRS2, polygenetic risk score2; diff, mean difference between groups; lwr, lower bound for 95% confidence interval; upr, upper bound for 95% confidence interval. Analyses are performed with ANOVA pairwise comparisons and adjusted with the Tukey method for multiple testing correction.

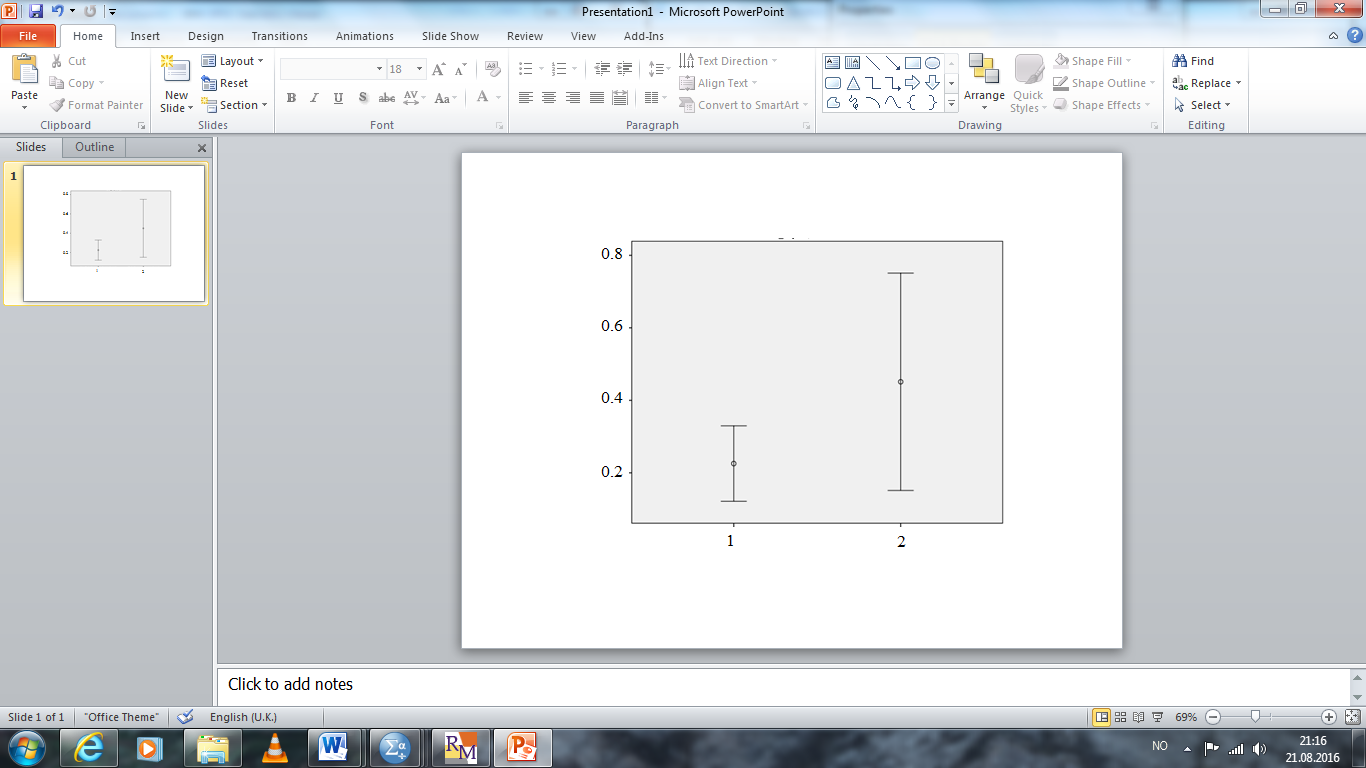
**Figure S4:** Lifetime cannabis use and diagnostic spectrums



% Reports of lifetime cannabis use

Fig.S4. Error bars depict standard error of the mean. SZ spectrum disorder; BD spectrum disorder, No significant difference in lifetime cannabis use was observed between SZ and BD (*X2*=0.41, df=1, *P*=0.53).

Figure S5A: A non-significant trend for higher SZ-PGRS in SZ spectrum with lifetime cannabis use



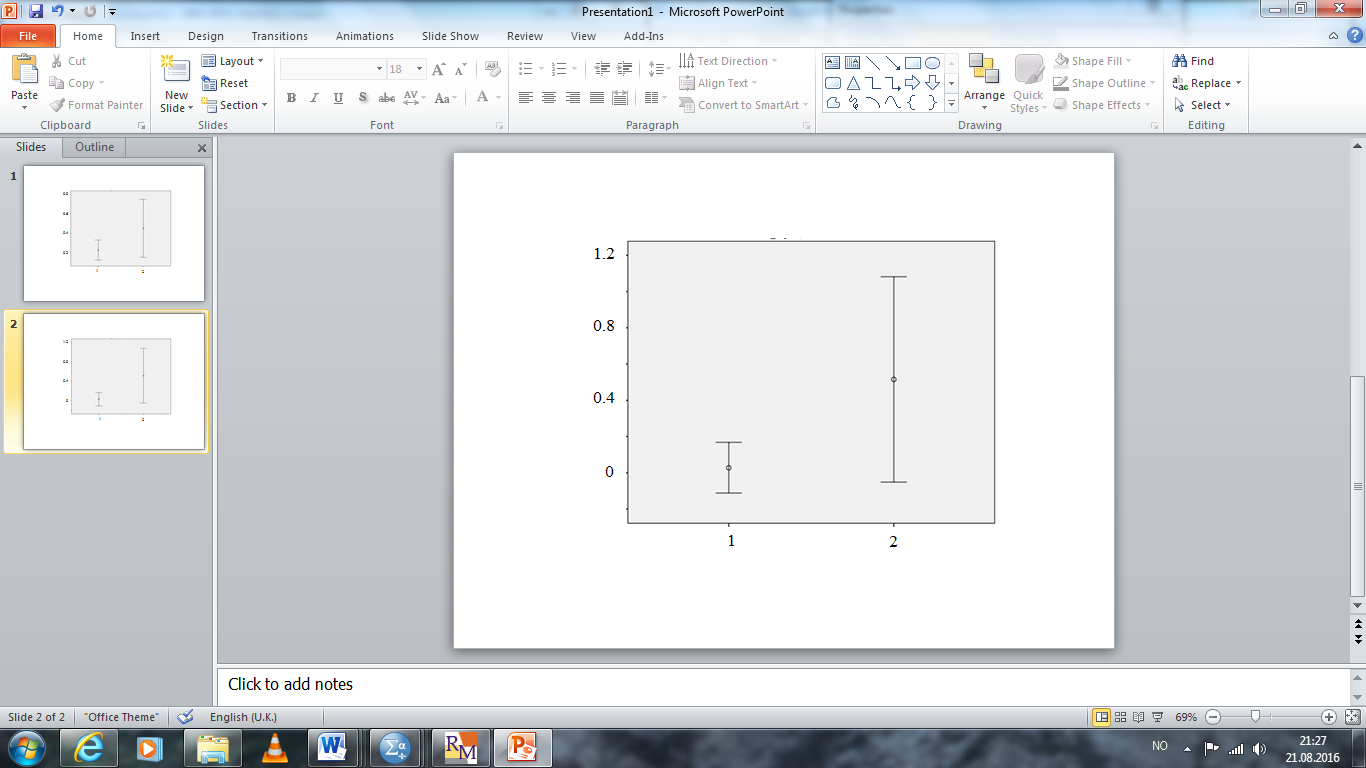
Z score SZ polygenic risk score

Fig.S5A. Error bars depict standard error of the mean

1= « No frequent cannabis use before illness onset », N=322;

2= « Frequent cannabis use before illness onset», N=55. *T*=-1.61, *P*=0.11.

Figure S5B: A non-significant trend for higher SZ-PGRS in BD spectrum with lifetime cannabis use



Z score SZ polygenic risk score

Fig.S5B. Error bars depict standard error of the mean

1= « No frequent cannabis use before illness onset », N=200;

2= « Frequent cannabis use before illness onset », N=11. *T*=-1.58, *P*=0.12.