

Serveur Académique Lausannois SERVAL [serval.unil.ch](http://serval.unil.ch)

## Author Manuscript

Faculty of Biology and Medicine Publication

This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Published in final edited form as:

**Title:** Influence of polygenic risk scores on lipid levels and dyslipidemia in a psychiatric population receiving weight gain-inducing psychotropic drugs - SUPPLEMENTARY DATA

**Authors:** Delacrétaz A, Lagares Santos P, Saigi Morgui N, Vandenberghe F, Glatard A, Gholam-Rezaee M, von Gunten A, Conus P, Eap CB

**Journal:** Pharmacogenetics and genomics

**Year:** 2017 Dec

**Issue:** 27

**Volume:** 12

**Pages:** 464-472

**DOI:** [10.1097/FPC.0000000000000313](https://doi.org/10.1097/FPC.0000000000000313)

In the absence of a copyright statement, users should assume that standard copyright protection applies, unless the article contains an explicit statement to the contrary. In case of doubt, contact the journal publisher to verify the copyright status of an article.

## **SUPPLEMENTARY DATA**

### **Material and methods**

#### **Psychiatric samples**

Anthropometric measurements (weight and height), demographic variables (sex and age), history of treatments (treatment duration and psychotropic treatment), co-medications and lipid variables (i.e. HDL, LDL, TC and TG) were collected at baseline (i.e. before psychotropic treatment) and 1, 3 and 12 months after initiating a treatment with weight gain – inducing psychotropic drug. Patients having switched to such medication (i.e. non treatment-naive patients) were also included. Most blood samples were drawn in the morning in fasting conditions. Non-fasting blood samples (i.e. within six hours following last meal) were excluded for triglyceride analysis [1] and not for total, HDL- and LDL-cholesterol [1]. Most clinical chemistry assays were conducted by the clinical laboratory, Department of Biomedicine, Lausanne University Hospital, which is ISO 15189:2012 certified. LDL-cholesterol was calculated using the Friedewald formula only if triglyceride levels were lower than 4.6 mmol/l [2].

#### **Quantification of drug concentration**

Plasma drug concentrations were quantified at one, three and twelve months in trough conditions (i.e. in the morning before the next drug intake). Liquid chromatography/mass spectrometry methods were used for measuring aripiprazole, amisulpride, clozapine, haloperidol, olanzapine, risperidone, OH-risperidone (paliperidone), quetiapine or plasma levels as previously described [3-5] and/or as recommended in our unit (Eap et al., unpublished data, available on request). Mirtazapine was measured by gas-

chromatography-nitrogen detector (Eap et al., unpublished data, available on request), valproate by fluorescence polarization immunoassay (Cobas integra 400 plus Roche®, Roche Diagnostic, Rotkreuz, Switzerland) and lithium by ion selective electrode (EasyLyte Na/K/Cl/Li, Medica®, Chatel St-Denis, Switzerland). All methods are used on a routine basis in our accredited laboratory (ISO 15189 and 17025). Patients were considered compliant when drug plasma concentrations were higher than 10% of the lower value of the recommended therapeutic range [6]. Of note, the sum of plasma concentrations risperidone and of its metabolite OH-risperidone was used.

### **DNA extraction, SNP selection and genotyping**

DNA was extracted from blood samples as described by the manufacturer protocols using Flexigene DNA kit and QIAamp DNA Blood Mini QIAcube Kit (Qiagen AG, Switzerland).

In the meta-analysis from Willer et al., variants for which the minor allele was observed <7 times were excluded. In the meta-analysis from Surakka et al, SNPs with MAF <1%, with call rate <95% (or 99% if the SNP had MAF <5%) or that failed the Hardy-Weinberg equilibrium exact test (precise threshold depending on study) and sex-chromosome SNPs were also excluded. In the present study, the selection of SNPs was made according to the following criteria: firstly, to avoid overrepresentation of a particular gene in the PRS calculation, only one SNP per gene was considered. This also avoided indirect correlation between variants for SNPs with high linkage disequilibrium (LD) [7]. As a result, minor allele frequencies (MAF),  $\beta$ -coefficients, p-values and LD were taken into account as described in **S1 Figure** with a systematic approach to choose between

SNPs located in the same gene. All variants reached genome-wide significance for at least one lipid trait, as mentioned in the meta-analyses [8,9]. Hardy-Weinberg equilibrium (HWE) testing was determined for all SNPs by performing a chi-square test [10].

The iSelect genotyping array was designed to test DNA variations of 200'000 SNPs from regions associated with metabolic and cardiovascular characteristics [11]. All genotyped SNPs underwent quality control tests: when sex was inconsistent with genetic data from X-linked markers and genotype call rate was  $< 0.8$ , samples were excluded from the analyses. The results were extracted using the software GenomeStudio Data Analysis.

From the reviewed variants, SNPs (or proxies with  $r^2 \geq 0.8$  and a  $MAF \geq 5\%$ ) that were not available in the CardioMetaboChip in the psychiatric sample were genotyped by the KBioscience Institute in the United Kingdom using the novel fluorescence-based competitive allele-specific PCR technology (KASP™) as described by the manufacturer. Genotyping of one SNP (rs1047891) with missing values for a subset of patients was performed using TaqMan SNP Genotyping Assays on ViiA™ 7 Real-Time PCR System as described by the manufacturer's instructions.

Ethnicity was assessed by patient's reported ethnicity and confirmed by genotyping using principal component analysis with the EIGENSTRAT algorithm implemented in GCTA software [12]. The majority of the variance was explained by the two first vectors, and Caucasian ethnicity was arbitrarily selected when  $pca1 < 0.0025$  and  $pca2 > -0.0125$ , values which gave the highest concordance with the patient's reported ethnicity.

## **Construction of the PRSs**

Among the different PRS model approaches (e.g. simple count or odds ratio weighted PRS), a weighted PRS (wPRS) is a more adequate option than unweighted PRS since allele effects ( $\beta$ -coefficients) vary among SNPs [13]. In the present study, PRS were constructed as a weighted sum of all SNPs. Each patient received for each SNP the coding value of 0, 1 or 2 according to the number of risk alleles. For instance, for a given SNP, a score of 1 was assigned for a carrier of one risk allele, whereas a value of 0 was attributed to non-carriers of this risk allele. Weighted PRS were subsequently obtained by the summation of the lipid-associated risk alleles multiplied by their effect size reported for each SNP in corresponding meta-analyses, assuming that each SNP contributes to the PRS in an additive way [14,15]. In order to facilitate interpretation of the results, wPRS were then rescaled according to a calculation described elsewhere [13]. Of note, increasing the wPRS by one unit indicates one additional lipid-association risk allele [16].

### **Construction of categorical PRS**

The influence of categorical PRS (wPRS\_cat) on the evolution of lipid levels during the treatment was assessed. Firstly, wPRS were categorised into two groups with values higher and lower than the median of wPRS (i.e. high-risk wPRS\_group versus low-risk wPRS\_group, respectively). Other categorisations of wPRS were also constructed, considering only extreme values of the wPRS: percentile 25 versus percentile 75 and percentile 10 versus percentile 90. Then, GAMM and linear mixed models (LMM) were fitted to compare the change in lipid variables during psychotropic treatment according

to wPRS\_cat. Models were implemented using the mgcv and nlme packages in R (settings were fixed at package defaults) [17].

### **Construction and interpretation of AUC**

ROC graphs are two-dimensional graphs in which sensibility (true positive rate) is plotted on the y-axis and 1-specificity (false positive rate) on the x-axis. The area under the curve (AUC) represents the probability that the model correctly classifies a patient as a positive or a negative case (i.e. a patient with abnormal lipid levels or not). AUC of the models were compared using a bootstrap test as published previously [18]. An AUC of 0.5 would indicate a random test with 50% chance of positive response, whereas an AUC of 1 suggests an ideal test where all patients are correctly classified [19]. Tests having an AUC of 0.75 or higher are considered informative and useful [20].

## **Results**

### **Influence of GAMM covariates on the evolution of lipid levels during psychotropic treatment**

The evolution of lipid levels during psychotropic treatment according to covariates taken into account in GAMM analyses is presented in **S2-S6 Figures**. Because of their known influence on psychotropic-drug induced metabolic abnormalities [21], these variables were included in mixed models. Of note, although no study has been conducted yet to determine an influence of psychotropic drug class on the deterioration of lipid profile, this variable was also considered in mixed models. The difference of lipid levels between patients whose BMI was above or below the BMI median was statistically significant for HDL, LDL, TC and TG levels ( $p=0.03$ ,  $0.0005$ ,  $0.003$  and  $0.001$ ,

respectively, **S2 Figure**). In addition, the difference of HDL, LDL and TC levels between patients younger or older than the median age was statistically significant ( $p=0.007$ ,  $0.01$ ,  $0.001$ , respectively, **S3 Figure**), but not for TG levels ( $p=0.82$ ). Women had significantly higher levels of HDL, LDL and TC ( $p<0.0001$ ,  $p=0.005$ ,  $p<0.0001$ ) but not of TG levels ( $p=0.32$ , **S4 Figure**). No difference of HDL, LDL and TC levels was observed between psychotropic drug classes. However, patients receiving mood stabilizers had significantly higher TG levels compared to those receiving antipsychotics (**S5 Figure**). Finally, although smoking status was not associated with lipid levels ( $p>0.05$ , **S6 Figure**), this variable was considered in GAMM because non smokers were observed to have a more favourable lipid profile compared to smokers in a recent systematic review and meta-analysis [22].

### **Influence of polygenic risk scores on lipid phenotype worsening during psychotropic treatment**

The evolution of lipid levels during psychotropic treatment according to high- and low-wPRS groups is presented in **S7-S8 Figures**. The more extreme the groups were, the higher the differences of each lipid level were measured between the groups. Overall, HDL was the only lipid trait that did not significantly change along the psychotropic treatment ( $p=0.62$ ), whereas LDL, TC and TG levels significantly increased over time ( $p=0.01$ ,  $0.001$  and  $0.03$  respectively, **S9 Figure**). The difference of lipid levels between high- and low- risk wPRS were statistically significant for HDL and TG levels ( $p=0.002$ ), but not for LDL and TC levels ( $p=0.25$  and  $0.31$ , respectively; **S9 Figure**). **S10 Figure** represents the evolution of dyslipidemia prevalence according to the two groups of p50-classified wPRS. The same patterns of evolution were observed as described

previously (i.e. influence of p50-classified wPRS groups on HDL and TG levels, but no clear effect on LDL and TC levels). Comparison of extreme wPRS percentiles (i.e. p25-p75 and p10-p90) in **S11 and S12 Figures**, respectively, allowed to better illustrate the evolution of lipid variables in function of the wPRS.

To date, many publications showed that the influence of genetic susceptibilities is greater among young patients [23-26]. For exploratory purposes, and despite the fact that there was no significant interaction between age and wPRS on lipid levels in the present study, GAMMs were performed by stratifying the combined psychiatric sample according to the median of age (**S15 Table**). In young patients, weighted PRSs were significantly associated with each lipid trait ( $p \leq 0.006$ ) apart from LDL ( $p = 0.08$ ), whereas they were significant for all lipid traits in old patients ( $p \leq 0.03$ ). Among statistical analyses not adjusted for covariates, in young patients (**S13 and S14 Figures**), a significant influence of low- and high- risk wPRS groups was observed on HDL ( $p = 0.02$ ) and a similar trend was observed for TG ( $p = 0.07$ ). In patients older than the median of age, low- and high- risk wPRSs were also significantly associated with HDL and TG (**S15 and S16 Figures**;  $p = 0.002$  and  $0.009$  respectively), but along the treatment, HDL and TG levels of the two wPRS groups tended to converge. Interestingly, it seemed that low-risk wPRS patients tended to reach the same lipid levels than high-risk wPRS patients for HDL and TG after several months of psychotropic treatment.

#### *Interaction between polygenic risk scores and covariates on lipid phenotypes*

**S17 Table** displays results of interaction between wPRSs and age, sex and BMI on the four lipid phenotypes. A significant interaction was observed between wPRSs and BMI



on LDL ( $p=0.02$ ), and between wPRS and sex on TC ( $p=0.04$ ). These results suggest that the influence of wPRS on LDL may be tested in BMI-stratified subsamples, and that the influence of wPRS on TC may be tested in men and women separately. GAMM performed in BMI-stratified samples showed a significant association between p50-classified wPRS groups and LDL only in patients having a BMI higher than the median value (**S18 Table**;  $0.46$  mmol/l;  $p<0.0001$ ). In analyses not adjusted for covariates, no influence of wPRS on LDL within both BMI subgroups was observed (**S18 Figure**). Moreover, AUC of the model including genetics compared to the model with only clinical data was not significantly increased in both BMI subgroups (**S19 Figure**), possibly because of a poor statistical power. With regard to analyses of association between p50-classified wPRS groups and TC levels performed in men and women separately, significant influences were observed in both sexes (**S18 Table**;  $p\leq 0.01$ ). **S20 Figure** shows that the prevalence of hypercholesterolemia seemed higher in women than in men, and that the influence of p50-classified wPRS groups on total hypercholesterolemia was greater in the former group compared to the latter ( $p=0.009$  for women and  $p=0.98$  for men). ROC curves suggest a higher increase of AUC with the model incorporating genetic data compared to the model with clinical data only, in women (AUC =  $0.74$  versus  $0.67$ ;  $p=0.11$ ), compared to men (AUC =  $0.78$  versus  $0.77$ ;  $p=0.43$ ), although none reached statistical significance in both gender.

S1 Table. Characteristics of psychiatric Caucasian samples: discovery, replication and combined samples

Characteristics	n Discovery sample		n Replication sample		p-value <sup>7</sup>	n Combined sample	
	n	%	n	%		n	%
Male, n (%)	332	142 (42.8)	140	65 (46.4)	0.46	472	207 (43.8)
Age, median (IQ range), years	332	48 (29-73)	140	49.5 (33-68)	0.87	472	48 (30-71)
<b>BMI</b>							
Initial BMI, median (IQ range), kg/m <sup>2</sup> <sup>1</sup>	332	23.3 (20.6-26.9)	140	24.9 (21.4-28.2)	0.06	472	23.7 (20.9-27.5)
Initial BMI ≤25 kg/m <sup>2</sup> , n (%) <sup>1,2</sup>		211 (63.5)		75 (53.6)			286 (60.6)
Initial BMI 25-30 kg/m <sup>2</sup> , n (%) <sup>1,2</sup>		69 (20.8)		42 (30.0)	0.07		111 (23.5)
Initial BMI ≥30 kg/m <sup>2</sup> , n (%) <sup>1,2</sup>		52 (15.7)		23 (16.4)			75 (15.9)
Current BMI, median (IQ range), kg/m <sup>2</sup> <sup>3</sup>	332	24.4 (21.7-28.1)	140	25.1 (21.6-29.5)	0.31	472	24.5 (21.7-28.4)
Current BMI ≤25 kg/m <sup>2</sup> , n (%) <sup>2,3</sup>		184 (55.4)		70 (50.0)			254 (53.8)
Current BMI 25-30 kg/m <sup>2</sup> , n (%) <sup>2,3</sup>		90 (27.1)		38 (27.1)	0.36		128 (27.1)
Current BMI ≥30 kg/m <sup>2</sup> , n (%) <sup>2,3</sup>		58 (17.5)		32 (22.9)			90 (19.1)
<b>Lipids levels</b>							
<b>Lipids levels at baseline <sup>4</sup></b>							
Total cholesterol, median (IQ range), mmol/l	331	4.7 (3.9-5.6)	140	5.2 (4.3-5.9)	<b>0.002</b>	471	4.8 (4-5.7)
Total cholesterol < 5 mmol/l, n (%) <sup>5</sup>		189 (57.1)		62 (44.3)	<b>0.01</b>		251 (53.3)
Total cholesterol ≥ 5 mmol/l, n (%) <sup>5</sup>		142 (42.9)		78 (55.7)			220 (46.7)
Total cholesterol < 5 mmol/l, n (%) <sup>5</sup> without hypolipemiant		167 (50.5)		55 (39.3)	<b>0.02</b>		222 (47.3)
Total cholesterol ≥ 5 mmol/l, n (%) <sup>5</sup> or treated dyslipidemia		164 (49.6)		85 (60.7)			249 (52.7)
HDL, median (IQ range), mmol/l	325	1.4 (1.1-1.6)	139	1.4 (1.1-1.7)	0.41	464	1.4 (1.1-1.7)
HDL > 1 mmol/l, n (%) <sup>5</sup>		272 (83.7)		111 (79.9)	0.32		383 (82.5)
HDL ≤ 1 mmol/l, n (%) <sup>5</sup>		53 (16.3)		28 (20.1)			81 (17.5)
HDL > 1 mmol/l, n (%) <sup>5</sup> without hypolipemiant		251 (77.2)		104 (74.8)	0.57		355 (76.5)
HDL ≤ 1 mmol/l, n (%) <sup>5</sup> or treated dyslipidemia		74 (22.8)		35 (25.2)			109 (23.5)
LDL, median (IQ range), mmol/l	314	2.6 (2.1-3.5)	133	3.0 (2.4-3.6)	<b>0.005</b>	447	2.7 (2.1-3.5)
LDL < 3 mmol/l, n (%) <sup>5</sup>		187 (59.6)		66 (49.6)	<b>0.05</b>		253 (56.6)
LDL ≥ 3 mmol/l, n (%) <sup>5</sup>		127 (40.5)		67 (50.4)			194 (43.4)
LDL < 3 mmol/l, n (%) <sup>5</sup> without hypolipemiant		164 (52.2)		60 (45.1)	0.15		224 (50.1)
LDL ≥ 3 mmol/l, n (%) <sup>5</sup> or treated dyslipidemia		150 (47.7)		73 (54.9)			223 (49.9)
Triglycerides, median (IQ range), mmol/l	168	1.0 (0.8-1.3)	59	1.1 (0.8-1.6)	0.5	227	1.0 (0.8-1.4)
Triglycerides < 2 mmol/l, n (%) <sup>5,8</sup>		153 (91.1)		48 (81.4)	0.54		201 (88.6)
Triglycerides ≥ 2 mmol/l, n (%) <sup>5,8</sup>		15 (8.9)		11 (18.6)			26 (11.5)
Triglycerides < 2 mmol/l, n (%) <sup>5,8</sup> without hypolipemiant		142 (84.5)		46 (77.9)	0.97		188 (82.8)
Triglycerides ≥ 2 mmol/l, n (%) <sup>5,8</sup> or treated dyslipidemia		26 (15.5)		13 (22.1)			39 (17.2)
Treatment with hypolipemiant, n (%)	332	28 (8.4)	140	9 (6.4)	0.29	472	37 (7.8)
<b>Lipids levels at current state <sup>6</sup></b>							
Total cholesterol, median (IQ range), mmol/l	328	5.0 (4.1-5.8)	140	5.2 (4.4-5.8)	0.06	468	5.0 (4.2-5.8)
Total cholesterol < 5 mmol/l, n (%) <sup>5</sup>		164 (50.0)		59 (42.1)			223 (47.6)
Total cholesterol ≥ 5 mmol/l, n (%) <sup>5</sup>		164 (50.0)		81 (57.9)			245 (52.3)
Total cholesterol < 5 mmol/l, n (%) <sup>5</sup> without hypolipemiant		134 (40.9)		50 (35.7)	0.30		181 (38.7)
Total cholesterol ≥ 5 mmol/l, n (%) <sup>5</sup> or treated dyslipidemia		194 (59.2)		90 (64.3)			287 (61.3)
HDL, median (IQ range), mmol/l	325	1.3 (1.1-1.6)	139	1.4 (1.1-1.7)	0.23	464	1.3 (1.1-1.6)
HDL > 1 mmol/l, n (%) <sup>5</sup>		256 (78.8)		110 (79.1)	0.93		366 (78.9)
HDL ≤ 1 mmol/l, n (%) <sup>5</sup>		69 (21.2)		29 (20.9)			98 (21.1)
HDL > 1 mmol/l, n (%) <sup>5</sup> without hypolipemiant		228 (70.2)		100 (71.9)	0.69		327 (70.5)
HDL ≤ 1 mmol/l, n (%) <sup>5</sup> or treated dyslipidemia		97 (29.9)		39 (28.1)			137 (29.5)
LDL, median (IQ range), mmol/l	305	2.8 (2.2-3.5)	131	3.1 (2.4-3.7)	0.13	436	2.9 (2.3-3.5)
LDL < 3 mmol/l, n (%) <sup>5</sup>		174 (57.1)		60 (45.8)	<b>0.03</b>		234 (53.7)
LDL ≥ 3 mmol/l, n (%) <sup>5</sup>		131 (43.0)		71 (54.2)			202 (46.3)
LDL < 3 mmol/l, n (%) <sup>5</sup> without hypolipemiant		143 (46.9)		52 (39.7)	0.16		193 (44.3)
LDL ≥ 3 mmol/l, n (%) <sup>5</sup> or treated dyslipidemia		162 (53.1)		79 (60.3)			243 (55.7)

Characteristics	n Discovery sample		n Replication sample		p-value <sup>7</sup>	n Combined sample	
Male, n (%)	332	142 (42.8)	140	65 (46.4)	0.46	472	207 (43.8)
Age, median (IQ range), years	332	48 (29-73)	140	49.5 (33-68)	0.87	472	48 (30-71)
Lipids levels at current state <sup>6</sup>							
Triglycerides, median (IQ range), mmol/l	241	1.2 (0.8-1.6)	96	1.3 (0.6-1.9)	0.06	337	1.2 (0.9-1.7)
Triglycerides < 2 mmol/l, n (%) <sup>5,8</sup>		198 (82.2)		74 (77.1)	0.38		272 (80.7)
Triglycerides ≥ 2 mmol/l, n (%) <sup>5,8</sup>		43 (17.8)		22 (22.9)			65 (19.3)
Triglycerides < 2 mmol/l, n (%) <sup>5,8</sup> without hypolipemiant		176 (73.0)		67 (69.8)	0.65		243 (72.1)
Triglycerides ≥ 2 mmol/l, n (%) <sup>5,8</sup> or treated dyslipidemia		65 (27.0)		29 (30.2)			94 (27.9)
Treatment with hypolipemiant, n (%)	332	38 (11.4)	140	13 (9.3)	0.44	472	51 (10.8)
Medication, n (%)							
Amisulpride	331	27 (8.2)	140	10 (7.1)	0.15	471	37 (7.9)
Aripiprazole		24 (7.3)		15 (10.7)			39 (8.3)
Clozapine		25 (7.6)		9 (6.4)			34 (7.2)
Lithium		23 (7.0)		13 (9.3)			36 (7.6)
Mirtazapine		13 (3.9)		9 (6.4)			22 (4.7)
Olanzapine		43 (13.0)		8 (5.7)			51 (10.8)
Paliperidone		1 (0.3)		3 (2.1)			4 (0.8)
Quetiapine		109 (32.9)		49 (35.0)			158 (33.5)
Risperidone		50 (15.1)		17 (12.1)			67 (14.2)
Valproate		16 (4.8)		7 (5.0)			23 (4.9)
Main diagnosis, n (%)							
Organic mental disorders	276	30 (10.9)	94	11 (11.7)	0.49	370	41 (11.1)
Psychotic disorders		90 (32.6)		31 (32.9)			121 (32.7)
Schizoaffective disorders		22 (7.9)		13 (13.8)			35 (9.5)
Bipolar disorders		66 (23.9)		20 (21.3)			86 (23.2)
Depressive disorder		68 (24.6)		19 (20.2)			87 (23.5)
Smoker, n (%)	332	108 (32.5)	140	57 (40.7)	0.51	472	165 (34.9)
Treatment duration, median (IQ range), days	332	146.5 (67-370)	140	110 (51-372)	0.12	472	134 (59-370)

<sup>1</sup> Initial BMI represents BMI before the current psychotropic treatment.

<sup>2</sup> BMI from >25 to <30 kg/m<sup>2</sup> refers to overweight, BMI ≥ 30 kg/m<sup>2</sup> refers to obesity.

<sup>3</sup> Current BMI represents BMI at the end of the follow-up.

<sup>4</sup> Lipid levels at baseline represent lipid values before the current psychotropic treatment.

<sup>5</sup> Lipid level thresholds were defined according to ESH/ESC guidelines [27].

<sup>6</sup> Lipid levels at current state represent lipid values at the end of the follow-up.

<sup>7</sup> P-values were calculated using Wilcoxon-Mann-Whitney tests for Chi<sup>2</sup> tests between the two psychiatric samples.

Values in bold are significant.

<sup>8</sup> Triglyceride levels were collected in fasting conditions.

**S2 Table. List of SNPs from the Global Lipids Genetics Consortium meta-analysis with their  $\beta$ -effect on HDL and HWE p-value**

Number	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAf	$\beta$ -effect (effect/other)	GWAS p-value	HWE p-value
1	rs1883025	ABCA1	rs1883025		C/T	0.75	0.070	2E-65	0.463
2	rs4148008	ABCA8	rs4148005	1.000	C/G	0.67	0.028	1E-12	0.546
3	rs13076253	ACAD11	rs13076253		G/T	0.86	0.028	5E-09	0.060
4	rs2602836	ADH5	rs2602836		A/G	0.44	0.019	5E-08	0.129
5	rs2923084	AMPD3	rs2923084		A/G	0.82	0.026	5E-08	0.062
6	rs7255436	ANGPTL4	rs2278236	0.965	A/C	0.53	0.032	2E-08	0.788
7	rs737337	ANGPTL8	rs737337		T/C	0.89	0.056	5E-17	0.511
8	rs964184	APOA1	rs964184		C/G	0.84	0.106	6E-48	0.482
9	rs6450176	ARL15	rs6450176		G/A	0.74	0.025	7E-10	0.287
10	rs2606736	ATG7	rs2606736		C/T	0.39	0.025	5E-08	0.734
11	rs10019888	C4orf52	rs10019888		A/G	0.82	0.027	5E-08	0.461
12	rs3764261	CETP	rs3764261		A/C	0.32	0.241	1E-769	0.432
13	rs605066	CITED2	rs651837	1.000	T/C	0.58	0.028	3E-08	0.756
14	rs2925979	CMIP	rs2925979		C/T	0.69	0.035	1E-19	0.479
15	rs12328675	COBLL1	rs12328675		C/T	0.13	0.045	2E-15	0.542
16	rs1047891	CPS1	rs1047891		C/A	0.67	0.027	9E-10	0.737
17	rs702485	DAGLB	rs702485		G/A	0.45	0.024	6E-12	0.905
18	rs174546	FADS1-2-3	rs174546		C/T	0.64	0.039	8E-28	0.450
19	rs3822072	FAM13A	rs3822072		G/A	0.54	0.025	4E-12	0.237
20	rs1121980	FTO	rs1121980		G/A	0.57	0.020	7E-09	0.812
21	rs4846914	GALNT2	rs4846914		A/G	0.59	0.048	4E-41	0.441
22	rs6805251	GSK3B	rs6805251		T/C	0.39	0.020	1E-08	0.593
23	rs17695224	HAS1	rs17695224		G/A	0.74	0.029	2E-13	0.916
24	rs12145743	HDGF-PMVK	rs12145743		G/T	0.34	0.020	2E-08	0.946
25	rs1800961	HNF4A	rs1800961		C/T	0.95	0.127	2E-34	0.647
26	rs4917014	IKZF1	rs4917014		G/T	0.32	0.022	1E-08	0.201
27	rs2972146	IRS1	rs1515100	0.891	G/T	0.37	0.032	2E-17	0.082
28	rs4731702	KLF14	rs4731702		T/C	0.49	0.029	5E-17	0.965
29	rs2652834	LACTB	rs2652834		G/A	0.79	0.028	4E-11	0.346
30	rs16942887	LCAT	rs16942887		A/G	0.14	0.083	8E-54	0.117
31	rs386000	LILRA3	rs386000		C/G	0.26	0.048	3E-23	0.818
32	rs1532085	LIPC	rs1532085		A/G	0.40	0.107	1E-188	0.688
33	rs7241918	LIPG	rs10438978	1.000	T/G	0.81	0.090	1E-44	0.064
34	rs12678919	LPL	rs12678919		G/A	0.13	0.155	1E-149	0.411
35	rs11613352	LRP1	rs11613352		T/C	0.26	0.028	2E-13	0.165
36	rs3136441	LRP4	rs3136441		C/T	0.18	0.054	7E-29	0.380
37	rs970548	MARCH8-ALOX5	rs970548		C/A	0.26	0.026	2E-10	0.787
38	rs12967135	MC4R	rs523288	1.000	G/A	0.75	0.026	4E-08	0.327
39	rs499974	MOGAT2-DGAT2	rs499974		C/A	0.81	0.026	1E-08	0.472
40	rs7134594	MVK	rs7134594		T/C	0.52	0.035	2E-13	0.128

Number	SNP	Nearest gene	CardiometaboChip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	GWAS p-value	HWE p-value
41	rs11246602	OR4C46	rs11246602		C/T	0.15	0.034	2E-10	0.140
42	rs4660293	PABPC4	rs4660293		A/G	0.76	0.035	3E-18	0.201
43	rs7134375	PDE3A	rs7134375		A/C	0.43	0.021	1E-08	0.526
44	rs731839	PEPD	rs731839		A/G	0.65	0.022	3E-09	0.109
45	rs4129767	PGS1	rs4129767		A/G	0.52	0.024	2E-11	0.359
46	rs12748152	PIGV-NROB2	rs12748152		C/T	0.91	0.051	1E-15	0.672
47	rs6065906	PLTP	rs6065906		T/C	0.81	0.059	5E-40	0.093
48	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.082	2E-41	0.352
49	rs2013208	RBM5	rs2013208		T/C	0.50	0.025	9E-12	0.374
50	rs1936800	RSPO3	rs1936800		C/T	0.49	0.020	3E-10	0.858
51	rs4759375	SBNO1	rs4759377	1.000	T/C	0.08	0.056	3E-08	0.380
52	rs838880	SCARB1	rs838880		C/T	0.34	0.048	6E-32	0.645
53	rs13107325	SLC39A8	rs13107325		C/T	0.92	0.071	1E-15	0.345
54	rs4142995	SNX13	rs4142995		G/T	0.62	0.026	9E-12	0.869
55	rs13326165	STAB1	rs13326165		A/G	0.21	0.029	9E-11	0.099
56	rs11869286	STARD3	chr17:35067382		C/G	0.65	0.032	3E-17	0.142
57	rs17173637	TMEM176A	rs17173637		T/C	0.88	0.036	2E-08	0.830
58	rs2954029	TRIB1	rs2954029		T/A	0.47	0.040	3E-29	0.592
59	rs581080	TTC39B	chr9:15295378		C/G	0.79	0.042	1E-19	0.156
60	rs7941030	UBASH3B	rs7941030		C/T	0.39	0.027	1E-14	0.349
61	rs181362	UBE2L3	rs181362		C/T	0.77	0.038	4E-18	0.514
62	rs998584	VEGFA	rs1358980	0.837	C/A	0.51	0.026	2E-11	0.786
63	rs4983559	ZBTB42-AKT1	rs4983559		G/A	0.40	0.020	1E-08	0.297
64	rs1689800	ZNF648	rs1689800		A/G	0.65	0.034	5E-20	0.757
65	rs4765127	ZNF664	rs11057408	1.000	T/G	0.35	0.032	8E-10	0.834

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S3 Table. List of the selected SNPs from the Engage Consortium meta-analysis with their  $\beta$ -effect on HDL and HWE p-value**

Number	SNP	Nearest gene	CardiometaboChip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	rs1883025	ABCA1	rs1883025		C/T	0.76	0.085	0.007	6.9E-31	0.463
2	rs4148008	ABCA6/8	rs4148005	1.000	C/G	0.68	0.020	0.007	3.0E-03	0.546
3	rs2602836	ADH5	rs2602836		A/G	0.44	0.023	0.006	2.9E-04	0.129
4	rs7255436	ANGPTL4	rs2278236	0.965	A/C	0.55	0.027	0.006	1.1E-05	0.788
5	rs2678379	APOB	rs1042034	1.000	A/G	0.24	0.065	0.007	7.2E-21	0.192
6	rs964184	APO-cluster	rs964184		C/G	0.87	0.102	0.009	9.7E-29	0.482
7	rs2606736	ATG7	rs2606736		C/T	0.38	0.034	0.006	3.7E-08	0.734
8	rs6657811	CELSR2-SORT1	rs6657811		T/A	0.12	0.057	0.009	1.9E-09	0.637
9	rs17231506	CETP	rs3764261	1.000	T/C	0.31	0.243	0.006	6.9E-316	0.432
10	rs605066	CITED2	rs651837	1.000	T/C	0.56	0.026	0.006	1.3E-05	0.756
11	rs56823429	CMIP	rs2925979	0.885	A/C	0.71	0.037	0.007	1.7E-08	0.479
12	rs174601	FADS1-2-3	rs174546	0.895	C/T	0.60	0.036	0.006	1.1E-08	0.450
13	rs4846914	GALNT2	rs4846914		A/G	0.59	0.048	0.006	3.3E-14	0.441
14	rs77147124	GPAM	rs1129555	1.000	A/G	0.28	0.039	0.007	7.4E-09	0.418
15	rs116569761	HLA-area	rs9275052		A/G	0.53	0.036	0.006	3.5E-08	0.182
16	rs1800961	HNF4A	rs1800961		C/T	0.96	0.149	0.016	5.1E-20	0.647
17	rs2713536	IRS1	rs1515100	1.000	C/T	0.38	0.038	0.006	3.4E-10	0.082
18	rs13241165	KLF14	rs4731702	1.000	T/A	0.51	0.037	0.006	8.4E-10	0.965
19	rs386000	LILRA3/5	rs386000		C/G	0.26	0.043	0.007	5.6E-09	0.818
20	rs1532085	LIPC	rs1532085		A/G	0.40	0.121	0.006	4.2E-86	0.688
21	rs10438978	LIPG	rs10438978		C/T	0.81	0.095	0.008	7.7E-36	0.064
22	rs12678919	LPL	rs12678919		G/A	0.09	0.167	0.011	5.7E-54	0.411
23	rs3741414	LRP1	rs11613352	0.959	T/C	0.27	0.028	0.007	9.4E-05	0.165
24	rs4660293	MACF1, PABPC4	rs4660293		A/G	0.77	0.039	0.007	2.2E-08	0.201
25	rs10838692	MADD	rs10838692		C/T	0.36	0.060	0.006	8.2E-21	0.704
26	rs970548	MARCH8	rs970548		C/A	0.25	0.028	0.007	3.8E-05	0.787
27	rs7134594	MMAB-MVK	rs7134594		T/C	0.52	0.036	0.006	1.7E-09	0.128
28	rs483465	MSL2L1	rs1279840	1.000	A/G	0.21	0.045	0.007	3.7E-10	0.226
29	rs12948394	PGS1	rs4129767	0.904	C/T	0.55	0.034	0.006	3.9E-08	0.359
30	rs12748152	PIGV-NROB2	rs12748152		C/T	0.91	0.050	0.010	1.3E-06	0.672
31	rs6073972	PLTP	rs6065906	1.000	C/G	0.81	0.065	0.008	9.2E-18	0.093
32	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.094	0.010	5.7E-20	0.352
33	rs78058190	PRKAG3	rs78058190		G/A	0.95	0.141	0.020	5.7E-12	0.811
34	rs73591976	RANBP10, LCAT	rs16942887	1.000	A/C	0.12	0.096	0.009	8.6E-26	0.117
35	rs7188861	RMI2	rs2867936	0.813	A/C	0.20	0.044	0.008	6.9E-09	0.734
36	rs1936800	RSP03	rs1936800		C/T	0.47	0.021	0.006	4.8E-04	0.858
37	rs838880	SCARB1	rs838880		C/T	0.36	0.056	0.006	3.7E-18	0.645
38	rs13107325	SLC39A8	rs13107325		C/T	0.97	0.120	0.018	9.6E-12	0.345
39	rs2814944	SNRPC	rs2814944		G/A	0.84	0.048	0.008	1.7E-08	0.085
40	rs10808546	TRIB1	rs2954029	1.000	T/C	0.46	0.037	0.006	3.7E-09	0.592
41	rs540885	TTC39B	rs643531	1.000	A/G	0.87	0.055	0.009	5.2E-10	0.733
42	rs7115089	UBASH3B	rs7941030	0.871	G/C	0.39	0.019	0.006	2.2E-03	0.349
43	rs5754344	UBE2L3	rs181362	1.000	A/G	0.78	0.045	0.007	2.2E-10	0.514
44	rs998584	VEGFA	rs1358980	0.837	C/A	0.51	0.018	0.006	4.9E-03	0.786
45	rs4983559	ZBTB42-AKT1	rs4983559		G/A	0.38	0.039	0.007	1.9E-08	0.297
46	rs1689800	ZNF648	rs1689800		A/G	0.67	0.033	0.006	1.6E-07	0.757

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S4 Table. List of the selected SNPs from combined meta-analyses with their  $\beta$ -effect on HDL and HWE p-value**

Number	Article	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	I	rs1883025	ABCA1	rs1883025		C/T	0.76	0.085	0.007	6.9E-31	0.463
2	D	rs4148008	ABCA8	rs4148005	1.000	C/G	0.67	0.028		1E-12	0.546
3	D	rs13076253	ACAD11	rs13076253		G/T	0.86	0.028		5E-09	0.060
4	D	rs2602836	ADH5	rs2602836		A/G	0.44	0.019		5E-08	0.129
5	D	rs2923084	AMPD3	rs2923084		A/G	0.82	0.026		5E-08	0.062
6	D	rs7255436	ANGPTL4	rs2278236	0.965	A/C	0.53	0.032		2E-08	0.788
7	D	rs737337	ANGPTL8	rs737337		T/C	0.89	0.056		5E-17	0.511
8	I	rs964184	APO-cluster	rs964184		C/G	0.87	0.102	0.009	9.7E-29	0.482
9	I	rs2678379	APOB	rs1042034	1.000	A/G	0.24	0.065	0.007	7.2E-21	0.192
10	D	rs6450176	ARL15	rs6450176		G/A	0.74	0.025		7E-10	0.287
11	I	rs2606736	ATG7	rs2606736		C/T	0.38	0.034	0.006	3.7E-08	0.734
12	D	rs10019888	C4orf52	rs10019888		A/G	0.82	0.027		5E-08	0.461
13	I	rs6657811	CELSR2-SORT1	rs6657811		T/A	0.12	0.057	0.009	1.9E-09	0.637
14	I	rs17231506	CETP	rs3764261	1.000	T/C	0.31	0.243	0.006	6.9E-316	0.432
15	D	rs605066	CITED2	rs651837	1.000	T/C	0.58	0.028		3E-08	0.756
16	D	rs2925979	CMIP	rs2925979		C/T	0.69	0.035		1E-19	0.479
17	D	rs12328675	COBLL1	rs12328675		C/T	0.13	0.045		2E-15	0.542
18	D	rs1047891	CPS1	rs1047891		C/A	0.67	0.027		9E-10	0.737
19	D	rs702485	DAGLB	rs702485		G/A	0.45	0.024		6E-12	0.905
20	D	rs174546	FADS1-2-3	rs174546		C/T	0.64	0.039		8E-28	0.450
21	D	rs3822072	FAM13A	rs3822072		G/A	0.54	0.025		4E-12	0.237
22	D	rs1121980	FTO	rs1121980		G/A	0.57	0.020		7E-09	0.812
23	I	rs4846914	GALNT2	rs4846914		A/G	0.59	0.048	0.006	3.3E-14	0.441
24	I	rs77147124	GPAM	rs1129555	1.000	A/G	0.28	0.039	0.007	7.4E-09	0.418
25	D	rs6805251	GSK3B	rs6805251		T/C	0.39	0.020		1E-08	0.593
26	D	rs17695224	HAS1	rs17695224		G/A	0.74	0.029		2E-13	0.916
27	D	rs12145743	HDGF-PMVK	rs12145743		G/T	0.34	0.020		2E-08	0.946
28	I	rs116569761	HLA-area	rs9275052		A/G	0.53	0.036	0.006	3.5E-08	0.182
29	I	rs1800961	HNF4A	rs1800961		C/T	0.96	0.149	0.016	5.1E-20	0.647
30	D	rs4917014	IKZF1	rs4917014		G/T	0.32	0.022		1E-08	0.201
31	I	rs2713536	IRS1	rs1515100	1.000	C/T	0.38	0.038	0.006	3.4E-10	0.082
32	I	rs13241165	KLF14	rs4731702	1.000	T/A	0.51	0.037	0.006	8.4E-10	0.965
33	D	rs2652834	LACTB	rs2652834		G/A	0.79	0.028		4E-11	0.346
34	I	rs386000	LILRA3/5	rs386000		C/G	0.26	0.043	0.007	5.6E-09	0.818
35	I	rs1532085	LIPC	rs1532085		A/G	0.40	0.121	0.006	4.2E-86	0.688
36	I	rs10438978	LIPG	rs10438978		C/T	0.81	0.095	0.008	7.7E-36	0.064
37	I	rs12678919	LPL	rs12678919		G/A	0.09	0.167	0.011	5.7E-54	0.411
38	D	rs11613352	LRP1	rs11613352		T/C	0.26	0.028		2E-13	0.165
39	I	rs4660293	MACF1, PABPC4	rs4660293		A/G	0.77	0.039	0.007	2.2E-08	0.201
40	I	rs10838692	MADD	rs10838692		C/T	0.36	0.060	0.006	8.2E-21	0.704

Number	Article	SNP	Nearest gene	Cardiometabochip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	SE	GWAS p-value	HWE p-value
41	D	rs970548	MARCH8-ALOX5	rs970548		C/A	0.26	0.026		2E-10	0.787
42	D	rs12967135	MC4R	rs523288	1.000	G/A	0.75	0.026		4E-08	0.327
43	D	rs499974	MOGAT2-DGAT2	rs499974		C/A	0.81	0.026		1E-08	0.472
44	I	rs7134594	MMAB-MVK	rs7134594		T/C	0.52	0.036	0.006	1.7E-09	0.128
45	I	rs483465	MSL2L1	rs1279840	1.000	A/G	0.21	0.045	0.007	3.7E-10	0.226
46	D	rs11246602	OR4C46	rs11246602		C/T	0.15	0.034		2E-10	0.140
47	D	rs7134375	PDE3A	rs7134375		A/C	0.43	0.021		1E-08	0.526
48	D	rs731839	PEPD	rs731839		A/G	0.65	0.022		3E-09	0.109
49	I	rs12948394	PGS1	rs4129767	0.904	C/T	0.55	0.034	0.006	3.9E-08	0.359
50	D	rs12748152	PIGV-NROB2	rs12748152		C/T	0.91	0.051		1E-15	0.672
51	I	rs6073972	PLTP	rs6065906	1.000	C/G	0.81	0.065	0.008	9.2E-18	0.093
52	I	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.094	0.010	5.7E-20	0.352
53	I	rs78058190	PRKAG3	rs78058190		G/A	0.95	0.141	0.020	5.7E-12	0.811
54	I	rs73591976	RANBP10, LCAT	rs16942887	1.000	A/C	0.12	0.096	0.009	8.6E-26	0.117
55	D	rs2013208	RBM5	rs2013208		T/C	0.50	0.025		9E-12	0.374
56	I	rs7188861	RM12	rs2867936	0.813	A/C	0.20	0.044	0.008	6.9E-09	0.734
57	D	rs1936800	RSPO3	rs1936800		C/T	0.49	0.020		3E-10	0.858
58	D	rs4759375	SBNO1	rs4759377	1.000	T/C	0.08	0.056		3E-08	0.380
59	I	rs838880	SCARB1	rs838880		C/T	0.36	0.056	0.006	3.7E-18	0.645
60	I	rs13107325	SLC39A8	rs13107325		C/T	0.97	0.120	0.018	9.6E-12	0.345
61	I	rs2814944	SNRPC	rs2814944		G/A	0.84	0.048	0.008	1.7E-08	0.085
62	D	rs4142995	SNX13	rs4142995		G/T	0.62	0.026		9E-12	0.869
63	D	rs13326165	STAB1	rs13326165		A/G	0.21	0.029		9E-11	0.099
64	D	rs11869286	STARD3	chr17:35067382		C/G	0.65	0.032		3E-17	0.142
65	D	rs17173637	TMEM176A	rs17173637		T/C	0.88	0.036		2E-08	0.830
66	I	rs10808546	TRIB1	rs2954029	1.000	T/C	0.46	0.037	0.006	3.7E-09	0.592
67	I	rs540885	TTC39B	rs643531	1.000	A/G	0.87	0.055	0.009	5.2E-10	0.733
68	D	rs7941030	UBASH3B	rs7941030		C/T	0.39	0.027		1E-14	0.349
69	I	rs5754344	UBE2L3	rs181362	1.000	A/G	0.78	0.045	0.007	2.2E-10	0.514
70	D	rs998584	VEGFA	rs1358980	0.837	C/A	0.51	0.026		2E-11	0.786
71	I	rs4983559	ZBTB42-AKT1	rs4983559		G/A	0.38	0.039	0.007	1.9E-08	0.297
72	D	rs1689800	ZNF648	rs1689800		A/G	0.65	0.034		5E-20	0.757
73	D	rs4765127	ZNF664	rs11057408	1.000	T/G	0.35	0.032		8E-10	0.834

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error, I: meta-analysis from Engage Consortium (from Surakka and al.), D: meta-analysis from the Global Lipids Genetics Consortium (from Willer and al.). CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.



**S5 Table. List of SNPs from the Global Lipids Genetics Consortium meta-analysis with their  $\beta$ -effect on LDL and HWE p-value**

Number	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	GWAS p-value	HWE p-value
1	rs4299376	ABCG5/8	rs4299376		G/T	0.31	0.081	4E-72	0.598
2	rs9411489	ABO	rs507666		T/C	0.21	0.077	2E-41	0.934
3	rs17404153	ACAD11	rs17404153		G/T	0.86	0.034	2E-09	0.198
4	rs2131925	ANGPTL3	rs3850634	0.965	T/G	0.66	0.049	3E-32	0.937
5	rs267733	ANXA9-CERS2	rs267733		A/G	0.84	0.033	5E-09	0.761
6	rs964184	APOA1	rs964184		G/C	0.16	0.086	2E-26	0.482
7	rs1367117	APOB	rs1367117		A/G	0.32	0.119	1E-182	0.053
8	rs1801689	APOH-PRXCA	rs1801689		C/A	0.04	0.103	1E-11	0.403
9	rs11065987	BRAP	rs11065987		A/G	0.59	0.027	1E-11	0.509
10	rs4942486	BRCA2	rs4942486		T/C	0.48	0.024	2E-11	0.474
11	rs3764261	CETP	rs3764261		C/A	0.68	0.053	2E-34	0.432
12	rs10401969	CILP2	rs10401969		T/C	0.91	0.118	3E-54	0.595
13	rs7640978	CMTM6	rs7640978		C/T	0.91	0.039	1E-08	0.297
14	rs4530754	CSNK1G3	rs4530754		A/G	0.54	0.028	4E-12	0.121
15	rs2081687	CYP7A1	rs1030431	0.845	T/C	0.36	0.031	1E-07	0.084
16	rs314253	DLG4	rs314253		T/C	0.63	0.024	3E-10	0.412
17	rs12670798	DNAH11	rs12670798		C/T	0.25	0.034	5E-14	0.168
18	rs2710642	EHBP1	rs2710642		A/G	0.65	0.024	6E-09	0.368
19	rs174546	FADS1-2-3	rs174546		C/T	0.64	0.051	2E-39	0.450
20	rs1250229	FN1	rs1250229		C/T	0.73	0.024	3E-08	0.093
21	rs9488822	FRK	rs3798236	1.000	T/A	0.36	0.031	2E-07	0.593
22	rs2255141	GPAM	rs2255141		A/G	0.30	0.030	1E-13	0.380
23	rs1800562	HFE	rs1800562		G/A	0.93	0.062	8E-14	0.778
24	rs3177928	HLA	rs3177928		A/G	0.17	0.045	3E-17	0.786
25	rs12916	HMGCR	rs12916		C/T	0.40	0.073	8E-78	0.900
26	rs1169288	HNF1A	rs1169288		C/A	0.34	0.038	6E-21	0.639
27	rs2000999	HPR	rs2000999		A/G	0.20	0.065	4E-41	0.716
28	rs10490626	INSIG2	rs10490626		G/A	0.92	0.051	2E-12	0.291
29	rs514230	IRF2BP2	rs514230		T/A	0.52	0.036	9E-12	0.167
30	rs6511720	LDLR	rs6511720		G/T	0.88	0.221	4E-262	0.346
31	rs12027135	LDLRAP1	rs12027135		T/A	0.54	0.030	2E-14	0.721
32	rs2030746	LOC84931	rs2030746		T/C	0.40	0.021	9E-09	0.393
33	rs1564348	LPA	rs1564348		C/T	0.18	0.048	3E-21	0.133
34	rs6818397	LRPAP1	rs6818397		G/A	0.42	0.022	2E-08	0.783
35	rs4722551	MIR148A	rs4722551		C/T	0.20	0.039	4E-14	0.633
36	rs2642442	MOSC1	rs2642442		T/C	0.67	0.036	5E-11	0.555
37	rs5763662	MTMR3	rs5763662		T/C	0.04	0.077	1E-08	0.664
38	rs3757354	MYLIP	rs3757354		C/T	0.76	0.038	2E-17	0.142
39	rs2072183	NPC1L1	rs2072183		C/G	0.29	0.039	7E-16	0.100
40	rs8017377	NYNRIN	rs8017377		A/G	0.46	0.030	3E-15	0.497

Number	SNP	Nearest gene	CardiometaboChip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	GWAS p-value	HWE p-value
41	rs7206971	OSBPL7	rs6504872	0.935	A/G	0.49	0.029	3E-07	0.328
42	rs2479409	PCSK9	rs2479409		G/A	0.32	0.064	3E-50	0.597
43	rs12748152	PIGV-NROB2	rs12748152		T/C	0.09	0.050	3E-12	0.672
44	rs11136341	PLEC1	rs11785060	1.000	G/A	0.40	0.045	7E-12	0.231
45	rs4253776	PPARA	rs4253776		T/C	0.11	0.031	3E-08	0.319
46	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.071	9E-24	0.352
47	rs2328223	SNX5	rs2328223		C/A	0.21	0.030	6E-09	0.559
48	rs629301	SORT1	rs646776	1.000	T/G	0.76	0.167	5E-241	0.568
49	rs10102164	SOX17	rs10102164		A/G	0.21	0.032	4E-11	0.666
50	rs364585	SPTLC3	rs364585		G/A	0.62	0.025	4E-10	0.730
51	rs11220462	ST3GAL4	rs11220462		A/G	0.14	0.059	7E-21	0.642
52	rs6882076	TMD4	rs6882076		C/T	0.64	0.046	3E-31	0.199
53	rs6029526	TOP1	rs6072249	1.000	A/T	0.47	0.044	5E-18	0.999
54	rs2954029	TRIB1	rs2954029		A/T	0.53	0.056	2E-50	0.592
55	rs3780181	VLDLR	rs3780181		A/G	0.92	0.044	2E-09	0.371

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S6 Table. List of the selected SNPs from the Engage Consortium meta-analysis with their  $\beta$ -effect on LDL and HWE p-value**

Number	SNP	Nearest gene	Cardiometabochip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	rs4299376	ABCG8	rs4299376		G/T	0.27	0.074	0.007	8.3E-28	0.598
2	rs649129	ABO	rs507666	0.955	T/C	0.20	0.064	0.008	1.3E-17	0.934
3	rs3850634	ANGPTL3, DOCK7	rs3850634		T/G	0.68	0.042	0.006	4.7E-11	0.937
4	rs1367117	APOB	rs1367117		A/G	0.32	0.108	0.007	7.1E-58	0.053
5	rs964184	APO-cluster	rs964184		G/C	0.13	0.080	0.009	3.6E-18	0.482
6	rs1065853	APOE	rs1065853		G/T	0.93	0.603	0.013	<5E-324	0.515
7	rs646776	CELSR2-SORT1	rs646776		T/C	0.22	0.146	0.007	2.0E-91	0.568
8	rs247617	CETP	rs3764261	1.000	C/A	0.69	0.069	0.007	1.7E-24	0.432
9	rs10401969	CILP2	rs10401969		T/C	0.92	0.111	0.012	1.0E-21	0.595
10	rs1030431	CYP7A1	rs1030431		A/G	0.31	0.037	0.007	2.5E-08	0.084
11	rs314253	DLG4	rs314253		T/C	0.63	0.040	0.007	1.6E-09	0.412
12	rs12670798	DNAH11	rs12670798		C/T	0.24	0.050	0.007	7.3E-12	0.168
13	rs174583	FADS1-2-3	rs174546	1.000	C/T	0.62	0.063	0.006	1.1E-22	0.450
14	rs79588679	GATA6	rs79588679		C/T	0.83	0.049	0.009	3.6E-08	0.454
15	rs1129555	GPAM	rs2255141	0.959	A/G	0.27	0.035	0.007	5.4E-07	0.380
16	rs11136341	GRINA, PLECI	rs11785060	1.000	G/A	0.34	0.038	0.007	9.8E-09	0.231
17	rs3177928	HLA-area	rs3177928		A/G	0.17	0.050	0.009	1.3E-08	0.786
18	rs12916	HMGCR	rs12916		C/T	0.41	0.089	0.006	7.0E-45	0.900
19	rs1169314	HNF1A	rs2464196	1.000	G/A	0.30	0.037	0.007	2.3E-08	0.411
20	rs11648003	HP-HPR-DHX38	chr16:70609849		G/A	0.22	0.067	0.007	2.0E-20	0.976
21	rs514230	IRF2BP2	rs514230		T/A	0.54	0.041	0.006	1.1E-11	0.167
22	rs112374545	LDLR	chr19:11049899		C/T	0.89	0.250	0.010	7.2E-142	0.369
23	rs12027135	LDLRAP1	rs12027135		T/A	0.54	0.032	0.006	6.9E-08	0.721
24	rs2297374	LPA	rs9295125	0.865	C/T	0.64	0.029	0.006	4.7E-06	0.056
25	rs6818397	LRPAP1	rs6818397		T/G	0.36	0.025	0.007	1.4E-04	0.783
26	rs2902941	MAFB	rs2902941		A/G	0.66	0.022	0.006	6.0E-04	0.223
27	rs3757354	MYLIP	rs3757354		C/T	0.75	0.043	0.007	2.0E-09	0.142
28	rs41279633	NPC1L1	chr7:44547401		T/G	0.18	0.054	0.008	1.0E-10	0.432
29	rs11621792	NYNRIN, CBLN3	rs6573778	0.934	T/C	0.42	0.037	0.007	1.7E-08	0.806
30	rs7206971	OSBPL7	rs6504872	0.935	A/G	0.51	0.038	0.006	3.5E-10	0.328
31	rs2479409	PCSK9	rs2479409		G/A	0.31	0.071	0.007	3.5E-23	0.597
32	rs12748152	PIGV-NROB2	rs12748152		T/C	0.09	0.047	0.010	5.2E-06	0.672
33	rs2920503	PPARG	rs2920502	0.959	T/C	0.30	0.041	0.007	2.9E-10	0.280
34	rs2126259	PPP1R3B	rs9987289	0.803	C/T	0.89	0.078	0.010	3.8E-15	0.352
35	rs2618568	SNX5	rs2618568		C/A	0.37	0.049	0.006	6.9E-15	0.613
36	rs11220462	ST3GAL4	rs11220462		A/G	0.14	0.053	0.009	3.0E-09	0.642
37	rs6882076	TIMD4-HAVCR1	rs6882076		C/T	0.65	0.042	0.006	1.7E-11	0.199
38	rs2954022	TRIB1	rs2954029	0.966	C/A	0.52	0.054	0.006	2.8E-19	0.592
39	rs117492019	ZNF274	rs117492019		G/T	0.81	0.047	0.008	1.2E-08	0.072

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S7 Table. List of the selected SNPs from combined meta-analyses with their  $\beta$ -effect on LDL and HWE p-value**

Number	Article	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	I	rs4299376	ABCG8	rs4299376		G/T	0.27	0.074	0.007	8.3E-28	0.598
2	I	rs649129	ABO	rs507666	0.955	T/C	0.20	0.064	0.008	1.3E-17	0.934
3	D	rs17404153	ACAD11	rs17404153		G/T	0.86	0.034		2.0E-09	0.198
4	I	rs3850634	ANGPTL3, DOCK7	rs3850634		T/G	0.68	0.042	0.006	4.7E-11	0.937
5	D	rs267733	ANXA9-CERS2	rs267733		A/G	0.84	0.033		5.0E-09	0.761
6	I	rs964184	APO-cluster	rs964184		G/C	0.13	0.080	0.009	3.6E-18	0.482
7	I	rs1367117	APOB	rs1367117		A/G	0.32	0.108	0.007	7.1E-58	0.053
8	I	rs1065853	APOE	rs1065853		G/T	0.93	0.603	0.013	<5E-324	0.515
9	D	rs1801689	APOH-PRXCA	rs1801689		C/A	0.04	0.103		1.0E-11	0.403
10	D	rs11065987	BRAP	rs11065987		A/G	0.59	0.027		1.0E-11	0.509
11	D	rs4942486	BRCA2	rs4942486		T/C	0.48	0.024		2.0E-11	0.474
12	I	rs646776	CELSR2-SORT1	rs646776		T/C	0.22	0.146	0.007	2.0E-91	0.568
13	I	rs247617	CETP	rs3764261	1.000	C/A	0.69	0.069	0.007	1.7E-24	0.432
14	I	rs10401969	CILP2	rs10401969		T/C	0.92	0.111	0.012	1.0E-21	0.595
15	D	rs7640978	CMTM6	rs7640978		C/T	0.91	0.039		1.0E-08	0.297
16	D	rs4530754	CSNK1G3	rs4530754		A/G	0.54	0.028		4.0E-12	0.121
17	I	rs1030431	CYP7A1	rs1030431		A/G	0.31	0.037	0.007	2.5E-08	0.084
18	I	rs314253	DLG4	rs314253		T/C	0.63	0.040	0.007	1.6E-09	0.412
19	I	rs12670798	DNAH11	rs12670798		C/T	0.24	0.050	0.007	7.3E-12	0.168
20	D	rs2710642	EHBP1	rs2710642		A/G	0.65	0.024		6.0E-09	0.368
21	I	rs174583	FADS1-2-3	rs174546	1.000	C/T	0.62	0.063	0.006	1.1E-22	0.450
22	D	rs1250229	FN1	rs1250229		C/T	0.73	0.024		3.0E-08	0.093
23	D	rs9488822	FRK	rs3798236	1.000	T/A	0.36	0.031		2.0E-07	0.593
24	I	rs79588679	GATA6	rs79588679		C/T	0.83	0.049	0.009	3.6E-08	0.454
25	D	rs2255141	GPAM	rs2255141		A/G	0.30	0.030		1.0E-13	0.380
26	I	rs11136341	GRINA, PLECI	rs11785060	1.000	G/A	0.34	0.038	0.007	9.8E-09	0.231
27	D	rs1800562	HFE	rs1800562		G/A	0.93	0.062		8.0E-14	0.778
28	I	rs3177928	HLA-area	rs3177928		A/G	0.17	0.050	0.009	1.3E-08	0.786
29	I	rs12916	HMGCR	rs12916		C/T	0.41	0.089	0.006	7.0E-45	0.900
30	I	rs1169314	HNF1A	rs2464196	1.000	G/A	0.30	0.037	0.007	2.3E-08	0.411
31	I	rs11648003	HP-HPR-DHX38	chr16:70609849		G/A	0.22	0.067	0.007	2.0E-20	0.976
32	D	rs10490626	INSIG2	rs10490626		G/A	0.92	0.051		2.0E-12	0.291
33	I	rs514230	IRF2BP2	rs514230		T/A	0.54	0.041	0.006	1.1E-11	0.167
34	I	rs112374545	LDLR	chr19:11049899		C/T	0.89	0.250	0.010	7.2E-142	0.369
35	D	rs12027135	LDLRAP1	rs12027135		T/A	0.54	0.030		2.0E-14	0.721
36	D	rs2030746	LOC84931	rs2030746		T/C	0.40	0.021		9.0E-09	0.393
37	D	rs1564348	LPA	rs1564348		C/T	0.18	0.048		3.0E-21	0.133
38	D	rs6818397	LRPAP1	rs6818397		G/A	0.42	0.022		2.0E-08	0.783
39	I	rs2902941	MAFB	rs2902941		A/G	0.66	0.022	0.006	6.0E-04	0.223
40	D	rs4722551	MIR148A	rs4722551		C/T	0.20	0.039		4.0E-14	0.633

Number	Article	SNP	Nearest gene	CardiometaboChip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	SE	GWAS p-value	HWE p-value
41	D	rs2642442	MOSC1	rs2642442		T/C	0.67	0.036		5.0E-11	0.555
42	D	rs5763662	MTMR3	rs5763662		T/C	0.04	0.077		1.0E-08	0.664
43	I	rs3757354	MYLIP	rs3757354		C/T	0.75	0.043	0.007	2.0E-09	0.142
44	I	rs41279633	NPC1L1	chr7:44547401		T/G	0.18	0.054	0.008	1.0E-10	0.432
45	D	rs8017377	NYNRIN	rs8017377		A/G	0.46	0.030		3.0E-15	0.497
46	I	rs7206971	OSBPL7	rs6504872	0.935	A/G	0.51	0.038	0.006	3.5E-10	0.328
47	I	rs2479409	PCSK9	rs2479409		G/A	0.31	0.071	0.007	3.5E-23	0.597
48	D	rs12748152	PIGV-NROB2	rs12748152		T/C	0.09	0.050		3.0E-12	0.672
49	D	rs4253776	PPARA	rs4253776		T/C	0.11	0.031		3.0E-08	0.319
50	I	rs2920503	PPARG	rs2920502	0.959	T/C	0.30	0.041	0.007	2.9E-10	0.280
51	D	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.071		9.0E-24	0.352
52	I	rs2618568	SNX5	rs2618568		C/A	0.37	0.049	0.006	6.9E-15	0.613
53	D	rs10102164	SOX17	rs10102164		A/G	0.21	0.032		4.0E-11	0.666
54	D	rs364585	SPTLC3	rs364585		G/A	0.62	0.025		4.0E-10	0.730
55	I	rs11220462	ST3GAL4	rs11220462		A/G	0.14	0.053	0.009	3.0E-09	0.642
56	I	rs6882076	TIMD4-HAVCR1	rs6882076		C/T	0.65	0.042	0.006	1.7E-11	0.199
57	D	rs6029526	TOP1	rs6072249	1.000	A/T	0.47	0.044		5.0E-18	0.999
58	I	rs2954022	TRIB1	rs2954029	0.966	C/A	0.52	0.054	0.006	2.8E-19	0.592
59	D	rs3780181	VLDLR	rs3780181		A/G	0.92	0.044		2.0E-09	0.371
60	I	rs117492019	ZNF274	rs117492019		G/T	0.81	0.047	0.008	1.2E-08	0.072

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error, I: meta-analysis from Engage Consortium (from Surakka and al.), D: meta-analysis from the Global Lipids Genetics Consortium (from Willer and al.). CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S8 Table. List of SNPs from the Global Lipids Genetics Consortium meta-analysis with their  $\beta$ -effect on TC and HWE p-value**

Number	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	GWAS p-value	HWE p-value
1	rs1883025	ABCA1	rs1883025		C/T	0.75	0.067	6.E-53	0.463
2	rs2287623	ABCB11	rs2287623		G/A	0.41	0.027	4.E-12	0.319
3	rs4299376	ABCG5/8	rs4299376		G/T	0.31	0.079	3.E-73	0.598
4	rs9411489	ABO	rs507666	0.955	T/C	0.21	0.069	3.E-35	0.934
5	rs2131925	ANGPTL3	rs3850634	0.965	T/G	0.66	0.075	4.E-80	0.937
6	rs964184	APOA1	rs964184		G/C	0.16	0.121	3.0.E-55	0.482
7	rs1367117	APOB	rs1367117		A/G	0.32	0.100	3.E-139	0.053
8	rs1077514	ASAP3	rs1077514		T/C	0.85	0.030	6.E-09	0.718
9	rs11065987	BRAP	rs11065987		A/G	0.59	0.031	2.E-16	0.509
10	rs2814982	C6orf106	rs2814982		C/T	0.88	0.044	4.E-15	0.589
11	rs3764261	CETP	rs3764261		A/C	0.32	0.050	4.E-31	0.432
12	rs10401969	CILP2	rs10401969		T/C	0.91	0.137	4.E-77	0.595
13	rs7640978	CMTM6	rs7640978		C/T	0.91	0.038	2.E-08	0.297
14	rs4530754	CSNK1G3	rs4530754		A/G	0.54	0.023	2.E-09	0.121
15	rs2081687	CYP7A1	rs1030431	0.845	T/C	0.36	0.038	9.E-12	0.084
16	rs314253	DLG4	rs314253		T/C	0.63	0.023	3.E-10	0.412
17	rs12670798	DNAH11	rs12670798		C/T	0.25	0.036	1.E-16	0.168
18	rs2277862	ERGIC3	rs2277862		C/T	0.85	0.035	5.E-11	0.287
19	rs7515577	EVI5	rs6603981	1.000	A/C	0.77	0.037	2.E-08	0.704
20	rs174546	FADS1-2-3	rs174546		C/T	0.64	0.048	3.E-37	0.450
21	rs11694172	FAM117B	rs11694172		G/A	0.25	0.028	2.E-09	0.136
22	rs492602	FLJ36070	rs492602		G/A	0.47	0.031	1.E-16	0.125
23	rs9488822	FRK	rs3798236	1.000	T/A	0.36	0.034	1.E-09	0.593
24	rs1260326	GCKR	rs1260326		T/C	0.39	0.051	3.E-42	0.633
25	rs2255141	GPAM	rs2255141		A/G	0.3	0.031	7.E-16	0.380
26	rs1997243	GPR146	rs1997243		G/A	0.16	0.033	3.E-10	0.596
27	rs1800562	HFE	rs1800562		G/A	0.93	0.056	2.E-12	0.778
28	rs3177928	HLA	rs3177928		A/G	0.17	0.048	1.E-21	0.786
29	rs12916	HMGCR	rs12916		C/T	0.4	0.068	5.E-74	0.900
30	rs1169288	HNF1A	rs1169288		C/A	0.34	0.032	4.E-17	0.639
31	rs1800961	HNF4A	rs1800961		C/T	0.95	0.106	1.E-24	0.647
32	rs2000999	HPR	rs2000999		A/G	0.2	0.062	7.E-41	0.716
33	rs17526895	INSIG2	rs17526895		G/A	0.92	0.042	6.E-09	0.212
34	rs514230	IRF2BP2	rs514230		T/A	0.52	0.039	5.E-14	0.167
35	rs2758886	KCNK17	rs2758886		A/G	0.3	0.023	3.E-08	0.707
36	rs6511720	LDLR	rs6511720		G/T	0.88	0.185	5.E-202	0.346
37	rs12027135	LDLRAP1	rs12027135		T/A	0.54	0.027	5.E-12	0.721
38	rs1532085	LIPC	rs1532085		A/G	0.4	0.054	7.E-47	0.688
39	rs7241918	LIPG	rs10438978	1.000	T/G	0.81	0.058	4.E-18	0.064
40	rs2030746	LOC84931	rs2030746		T/C	0.4	0.020	4.E-08	0.393

Number	SNP	Nearest gene	Cardiometabochip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	GWAS p-value	HWE p-value
41	rs1564348	LPA	rs1564348		C/T	0.18	0.049	3.E-23	0.133
42	rs6818397	LRPAP1	rs6818397		G/A	0.42	0.025	1.E-10	0.783
43	rs970548	MARCH8-ALOX5	rs970548		C/A	0.26	0.025	8.E-09	0.787
44	rs4722551	MIR148A	rs4722551		C/T	0.2	0.029	7.E-09	0.633
45	rs2642442	MOSC1	rs2642442		T/C	0.67	0.035	3.E-11	0.555
46	rs3757354	MYLIP	rs3757354		C/T	0.76	0.035	2.E-15	0.142
47	rs1495741	NAT2	rs1495741		G/A	0.26	0.032	3.E-08	0.835
48	rs2072183	NPC1L1	rs2072183		C/G	0.29	0.036	4.E-15	0.100
49	rs7206971	OSBPL7	rs6504872	0.935	A/G	0.49	0.030	1.E-07	0.328
50	rs2479409	PCSK9	rs2479409		G/A	0.32	0.054	2.E-39	0.597
51	rs4883201	PHC1-A2ML1	rs4883201		A/G	0.88	0.035	2.E-09	0.581
52	rs11603023	PHLDB1	rs11603023		T/C	0.42	0.022	1.E-08	0.418
53	rs11136341	PLEC1	rs11785060	1.000	G/A	0.4	0.038	6.E-09	0.231
54	rs4253772	PPARA	rs4253772		T/C	0.11	0.032	1.E-08	0.833
55	rs9987289	PPP1R3B	rs9987289		G/A	0.9	0.084	2.E-36	0.352
56	rs13315871	PXK	rs13315871		G/A	0.9	0.036	4.E-08	0.213
57	rs7570971	RAB3GAP1	rs7570971		A/C	0.35	0.030	1.E-13	0.334
58	rs629301	SORT1	rs646776	1.000	T/G	0.76	0.134	2.E-170	0.568
59	rs10102164	SOX17	rs10102164		A/G	0.21	0.030	5.E-11	0.666
60	rs10128711	SPTY2D1	rs10128711		C/T	0.7	0.031	1.E-11	0.844
61	rs11220462	ST3GAL4	rs11220462		A/G	0.14	0.047	6.E-15	0.642
62	rs6882076	TIMD4	rs6882076		C/T	0.64	0.051	5.E-41	0.199
63	rs138777	TOM1	rs138777		A/G	0.36	0.021	5.E-08	0.072
64	rs6029526	TOP1	rs6072249	1.000	A/T	0.47	0.040	1.E-16	0.999
65	rs2954029	TRIB1	rs2954029		A/T	0.53	0.062	2.E-65	0.592
66	rs581080	TTC39B	chr9:15295378		C/G	0.79	0.038	1.E-13	0.156
67	rs7941030	UBASH3B	rs7941030		C/T	0.39	0.028	2.E-14	0.349
68	rs10904908	VIM-CUBN	rs10904908		G/A	0.43	0.025	3.E-11	0.869
69	rs3780181	VLDLR	rs3780181		A/G	0.92	0.044	7.E-10	0.371

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S9 Table. List of the selected SNPs from the Engage Consortium meta-analysis with their  $\beta$ -effect on TC and HWE p-value**

Number	SNP	Nearest gene	Cardiometabochi p position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	rs1883025	ABCA1	rs1883025		C/T	0.76	0.068	0.007	6.0E-21	0.463
2	rs4299376	ABCG8	rs4299376		G/T	0.27	0.069	0.007	1.5E-25	0.598
3	rs507666	ABO	rs507666		A/G	0.18	0.067	0.008	2.0E-18	0.934
4	rs3850634	ANGPTL3, DOCK7	rs3850634		T/G	0.68	0.076	0.006	3.8E-34	0.937
5	rs1041968	APOB	rs952275	1.000	A/G	0.48	0.095	0.006	4.6E-54	0.123
6	rs964184	APO-cluster	rs964184		G/C	0.13	0.118	0.009	3.7E-39	0.482
7	rs7412	APOE	chr19:50103919		C/T	0.93	0.413	0.013	7.5E-239	0.964
8	rs646776	CELSR2-SORT1	rs646776		T/C	0.22	0.120	0.007	1.9E-64	0.568
9	rs10401969	CILP2	rs10401969		T/C	0.92	0.123	0.011	1.7E-27	0.595
10	rs1030431	CYP7A1	rs1030431		A/G	0.31	0.035	0.007	9.4E-08	0.084
11	rs314253	DLG4	rs314253		T/C	0.63	0.037	0.007	2.5E-08	0.412
12	rs55649657	DNAH11	rs12670798	0.853	G/C	0.21	0.052	0.007	4.1E-13	0.168
13	rs2277862	ERGIC3	rs2277862		C/T	0.89	0.052	0.009	2.7E-08	0.287
14	rs174554	FADS1-2-3	rs174546	1.000	A/G	0.63	0.062	0.006	5.1E-24	0.450
15	rs115400054	FAM117B	rs6705330	1.000	C/T	0.88	0.054	0.009	5.4E-09	0.055
16	rs1260326	GCKR	rs1260326		T/C	0.36	0.045	0.006	2.5E-13	0.633
17	rs2255141	GPAM	rs2255141		A/G	0.27	0.036	0.007	3.5E-08	0.380
18	rs7515577	GVI1-EVI5	rs6603981	1.000	A/C	0.80	0.042	0.007	4.2E-09	0.704
19	rs3177928	HLA-area	rs3177928		A/G	0.16	0.055	0.008	6.7E-11	0.786
20	rs12916	HMGCR	rs12916		C/T	0.40	0.082	0.006	2.9E-40	0.900
21	rs1169288	HNF1A	rs1169288		C/A	0.33	0.037	0.007	2.1E-08	0.639
22	rs11648003	HP-HPR-DHX38	chr16:70609849		G/A	0.22	0.070	0.007	2.8E-23	0.976
23	rs514230	IRF2BP2	rs514230		T/A	0.54	0.048	0.006	1.1E-15	0.167
24	rs112374545	LDLR	chr19:11049899		C/T	0.89	0.217	0.010	1.5E-113	0.369
25	rs12027135	LDLRAP1	rs12027135		T/A	0.54	0.032	0.006	7.1E-08	0.721
26	rs1532085	LIPC	rs1532085		A/G	0.40	0.049	0.006	4.6E-16	0.688
27	rs7239867	LIPG	rs7239867		G/A	0.82	0.047	0.008	2.3E-09	0.118
28	rs12208357	LPA	chr6:160463138		T/C	0.06	0.092	0.012	8.5E-14	0.567
29	rs6818397	LRPAP1	rs6818397		T/G	0.36	0.028	0.007	2.0E-05	0.783
30	rs970548	MARCH8	rs970548		C/A	0.25	0.035	0.007	1.5E-07	0.787
31	rs2807834	MOSC1	rs2642442	0.962	G/T	0.71	0.037	0.007	1.7E-08	0.555
32	rs2072183	NPC1L1	rs2072183		C/G	0.27	0.041	0.007	3.2E-08	0.100
33	rs7206971	OSBPL7	rs6504872	0.935	A/G	0.51	0.043	0.006	3.7E-13	0.328
34	rs2479409	PCSK9	rs2479409		G/A	0.31	0.066	0.007	4.9E-21	0.597
35	rs1699337	PPARG	rs1151996	1.000	G/A	0.65	0.043	0.006	9.3E-12	0.523
36	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.097	0.010	1.4E-21	0.352
37	rs6759321	RAB3GAP1	rs6759321		T/G	0.28	0.036	0.007	7.7E-07	0.073
38	rs2814982	SNRPC	rs2814982		C/T	0.88	0.027	0.009	3.8E-03	0.589
39	rs2618568	SNX5	rs2618568		C/A	0.37	0.044	0.006	1.8E-12	0.613



Number	SNP	Nearest gene	CardiometaboChip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	SE	GWAS p-value	HWE p-value
41	rs6882076	TIMD4-HAVCR1	rs6882076		C/T	0.65	0.051	0.006	6.0E-17	0.199
42	rs2954022	TRIB1	rs2954029	0.966	C/A	0.52	0.063	0.006	2.0E-27	0.592
43	rs581080	TTC39B	chr9:15295378		C/G	0.83	0.027	0.008	7.6E-04	0.156
44	rs7128198	UBASH3B	rs7941030	0.934	T/C	0.38	0.036	0.006	4.0E-09	0.349

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S10 Table. List of the selected SNPs from combined meta-analyses with their  $\beta$ -effect on TC and HWE p-value**

Number	Article	SNP	Nearest gene	Cardiometabochi P position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	I	rs1883025	ABCA1	rs1883025		C/T	0.76	0.068	0.007	6.0.E-21	0.463
2	D	rs2287623	ABCB11	rs2287623		G/A	0.41	0.027		4.0.E-12	0.319
3	I	rs4299376	ABCG8	rs4299376		G/T	0.27	0.069	0.007	1.5.E-25	0.598
4	I	rs507666	ABO	rs507666		A/G	0.18	0.067	0.008	2.0.E-18	0.934
5	I	rs3850634	ANGPTL3, DOCK7	rs3850634		T/G	0.68	0.076	0.006	3.8.E-34	0.937
6	I	rs964184	APO-cluster	rs964184		G/C	0.13	0.118	0.009	3.7.E-39	0.482
7	I	rs1041968	APOB	rs952275	1.000	A/G	0.48	0.095	0.006	4.6.E-54	0.123
8	I	rs7412	APOE	chr19:50103919		C/T	0.93	0.413	0.013	7.5.E-239	0.964
9	D	rs1077514	ASAP3	rs1077514		T/C	0.85	0.030		6.0.E-09	0.718
10	D	rs11065987	BRAP	rs11065987		A/G	0.59	0.031		2.0.E-16	0.509
11	D	rs2814982	C6orf106	rs2814982		C/T	0.88	0.044		4.0.E-15	0.589
12	I	rs646776	CELSR2-SORT1	rs646776		T/C	0.22	0.120	0.007	1.9.E-64	0.568
13	D	rs3764261	CETP	rs3764261		A/C	0.32	0.050		4.0.E-31	0.432
14	I	rs10401969	CILP2	rs10401969		T/C	0.92	0.123	0.011	1.7.E-27	0.595
15	D	rs7640978	CMTM6	rs7640978		C/T	0.91	0.038		2.0.E-08	0.297
16	D	rs4530754	CSNK1G3	rs4530754		A/G	0.54	0.023		2.0.E-09	0.121
17	I	rs4738684	CYP7A1	rs1030431	0.885	A/G	0.34	0.041	0.006	2.8.E-11	0.084
18	I	rs314253	DLG4	rs314253		T/C	0.63	0.037	0.007	2.5.E-08	0.412
19	D	rs12670798	DNAH11	rs12670798		C/T	0.25	0.036		1.0.E-16	0.168
20	I	rs2277862	ERGIC3	rs2277862		C/T	0.89	0.052	0.009	2.7.E-08	0.287
21	I	rs174554	FADS1-2-3	rs174546	1.000	A/G	0.63	0.062	0.006	5.1.E-24	0.450
22	I	rs115400054	FAM117B	rs6705330	1.000	C/T	0.88	0.054	0.009	5.4.E-09	0.055
23	D	rs492602	FLJ36070	rs492602		G/A	0.47	0.031		1.0.E-16	0.125
24	D	rs9488822	FRK	rs3798236	1.000	T/A	0.36	0.034		1.0.E-09	0.593
25	I	rs1260326	GCKR	rs1260326		T/C	0.36	0.045	0.006	2.5.E-13	0.633
26	I	rs2255141	GPAM	rs2255141		A/G	0.27	0.036	0.007	3.5.E-08	0.380
27	D	rs1997243	GPR146	rs1997243		G/A	0.16	0.033		3.0.E-10	0.596
28	I	rs7515577	GVI1-EVI5	rs6603981	1.000	A/C	0.80	0.042	0.007	4.2.E-09	0.704
29	D	rs1800562	HFE	rs1800562		G/A	0.93	0.056		2.0.E-12	0.778
30	I	rs3177928	HLA-area	rs3177928		A/G	0.16	0.055	0.008	6.7.E-11	0.786
31	I	rs12916	HMGCR	rs12916		C/T	0.40	0.082	0.006	2.9.E-40	0.900
32	I	rs1169288	HNF1A	rs1169288		C/A	0.33	0.037	0.007	2.1.E-08	0.639
33	D	rs1800961	HNF4A	rs1800961		C/T	0.95	0.106		1.0.E-24	0.647
34	I	rs11648003	HP-HPR-DHX38	chr16:70609849		G/A	0.22	0.070	0.007	2.8.E-23	0.976
35	D	rs17526895	INSIG2	rs17526895		G/A	0.92	0.042		6.0.E-09	0.212
36	I	rs514230	IRF2BP2	rs514230		T/A	0.54	0.048	0.006	1.1.E-15	0.167
37	D	rs2758886	KCNK17	rs2758886		A/G	0.30	0.023		3.0.E-08	0.707
38	I	rs112374545	LDLR	chr19:11049899		C/T	0.89	0.217	0.010	1.5.E-113	0.369
39	D	rs12027135	LDLRAP1	rs12027135		T/A	0.54	0.027		5.0.E-12	0.721
40	I	rs1532085	LIPC	rs1532085		A/G	0.40	0.049	0.006	4.6.E-16	0.688

Number	Article	SNP	Nearest gene	Cardiometabochip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	SE	GWAS p-value	HWE p-value
41	I	rs7239867	LIPG	rs7239867		G/A	0.82	0.047	0.008	2.3 E-09	0.118
42	D	rs2030746	LOC84931	rs2030746		T/C	0.40	0.020		4.0 E-08	0.393
43	I	rs12208357	LPA	chr6:160463138		T/C	0.06	0.092	0.012	8.5 E-14	0.567
44	D	rs6818397	LRPAP1	rs6818397		G/A	0.42	0.025		1.0 E-10	0.783
45	D	rs970548	MARCH8-ALOX5	rs970548		C/A	0.26	0.025		8.0 E-09	0.787
46	D	rs4722551	MIR148A	rs4722551		C/T	0.20	0.029		7.0 E-09	0.633
47	D	rs2642442	MOSC1	rs2642442		T/C	0.67	0.035		3.0 E-11	0.555
48	D	rs3757354	MYLIP	rs3757354		C/T	0.76	0.035		2.0 E-15	0.142
49	D	rs1495741	NAT2	rs1495741		G/A	0.26	0.032		3.0 E-08	0.835
50	I	rs2072183	NPC1L1	rs2072183		C/G	0.27	0.041	0.007	3.2 E-08	0.100
51	I	rs7206971	OSBPL7	rs6504872	0.935	A/G	0.51	0.043	0.006	3.7 E-13	0.328
52	I	rs2479409	PCSK9	rs2479409		G/A	0.31	0.066	0.007	4.9 E-21	0.597
53	D	rs4883201	PHC1-A2ML1	rs4883201		A/G	0.88	0.035		2.0 E-09	0.581
54	D	rs11603023	PHLDB1	rs11603023		T/C	0.42	0.022		1.0 E-08	0.418
55	D	rs11136341	PLEC1	rs11785060	1.000	G/A	0.40	0.038		6.0 E-09	0.231
56	D	rs4253772	PPARA	rs4253772		T/C	0.11	0.032		1.0 E-08	0.833
57	I	rs1699337	PPARG	rs1151996	1.000	G/A	0.65	0.043	0.006	9.3 E-12	0.523
58	I	rs9987289	PPP1R3B	rs9987289		G/A	0.90	0.097	0.010	1.4 E-21	0.352
59	D	rs13315871	PXK	rs13315871		G/A	0.90	0.036		4.0 E-08	0.213
60	D	rs7570971	RAB3GAP1	rs7570971		A/C	0.35	0.030		1.0 E-13	0.334
61	I	rs2618568	SNX5	rs2618568		C/A	0.37	0.044	0.006	1.8 E-12	0.613
62	D	rs10102164	SOX17	rs10102164		A/G	0.21	0.030		5.0 E-11	0.666
63	D	rs10128711	SPTY2D1	rs10128711		C/T	0.70	0.031		1.0 E-11	0.844
64	D	rs11220462	ST3GAL4	rs11220462		A/G	0.14	0.047		6.0 E-15	0.642
65	I	rs6882076	TIMD4-HAVCR1	rs6882076		C/T	0.65	0.051	0.006	6.0 E-17	0.199
66	D	rs138777	TOM1	rs138777		A/G	0.36	0.021		5.0 E-08	0.072
67	D	rs6029526	TOP1	rs6072249	1.000	A/T	0.47	0.040		1.0 E-16	0.999
68	I	rs2954022	TRIB1	rs2954029	0.966	C/A	0.52	0.063	0.006	2.0 E-27	0.592
69	D	rs581080	TTC39B	chr9:15295378		C/G	0.79	0.038		1.0 E-13	0.156
70	I	rs7128198	UBASH3B	rs7941030	0.934	T/C	0.38	0.036	0.006	4.0 E-09	0.349
71	D	rs10904908	VIM-CUBN	rs10904908		G/A	0.43	0.025		3.0 E-11	0.869
72	D	rs3780181	VLDLR	rs3780181		A/G	0.92	0.044		7.0 E-10	0.371

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error, I: meta-analysis from Engage Consortium (from Surakka and al.), D: meta-analysis from the Global Lipids Genetics Consortium (from Willer and al.). CardioMetabochip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S11 Table. List of SNPs from the Global Lipids Genetics Consortium meta-analysis with their  $\beta$ -effect on TG and HWE p-value**

Number	SNP	Nearest gene	CardiometaboChip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	GWAS p-value	HWE p-value
1	rs1832007	AKR1C4	rs1832007		A/G	0.82	0.033	2E-12	0.385
2	rs2131925	ANGPTL3	rs3850634	0.965	T/G	0.66	0.066	3E-74	0.937
3	rs964184	APOA1	rs964184		G/C	0.16	0.234	7E-224	0.482
4	rs2412710	CAPN3	rs2412710		A/G	0.04	0.099	2E-11	0.647
5	rs3764261	CETP	rs3764261		C/A	0.68	0.040	2E-25	0.432
6	rs10401969	CILP2	rs10401969		T/C	0.91	0.121	1E-69	0.595
7	rs11649653	CTF1	rs11649653		C/G	0.60	0.027	2E-07	0.874
8	rs2068888	CYP26A1	rs2068888		G/A	0.55	0.024	2E-11	0.340
9	rs174546	FADS1-2-3	rs174546		T/C	0.36	0.045	7E-38	0.450
10	rs2929282	FRMD5	rs2929282		T/A	0.07	0.072	2E-09	0.600
11	rs9930333	FTO	rs1121980	1.000	A/G	0.43	0.021	3E-08	0.812
12	rs4846914	GALNT2	rs4846914		G/A	0.41	0.040	7E-31	0.441
13	rs1260326	GCKR	rs1260326		T/C	0.39	0.115	2E-239	0.633
14	rs7248104	INSR	rs7248104		G/A	0.58	0.022	5E-10	0.386
15	rs2972146	IRS1	rs1515100	0.891	T/G	0.63	0.028	3E-15	0.082
16	rs10761731	JMJD1C	rs10761739	1.000	A/T	0.56	0.031	8E-12	0.218
17	rs442177	KLHL8	rs442177		T/G	0.58	0.031	1E-18	0.835
18	rs1532085	LIPC	rs1532085		A/G	0.40	0.031	2E-18	0.688
19	rs12678919	LPL	rs12678919		A/G	0.87	0.170	2E-199	0.411
20	rs11613352	LRP1	rs11613352		C/T	0.74	0.028	9E-14	0.165
21	rs6831256	LRPAP1	rs6831256		G/A	0.42	0.026	2E-12	0.082
22	rs9686661	MAP3K1	rs9686661		T/C	0.20	0.038	3E-16	0.432
23	rs38855	MET	rs38855		A/G	0.53	0.019	2E-08	0.749
24	rs4719841	MIR148A	rs4719841		C/T	0.20	0.023	9E-11	0.938
25	rs8077889	MPP3	rs8077889		C/A	0.22	0.025	1E-08	0.212
26	rs645040	MSL2L1	rs645040		T/G	0.77	0.029	2E-12	0.124
27	rs1495741	NAT2	rs1495741		G/A	0.26	0.040	3E-12	0.835
28	rs3198697	PDXDC1	rs3198697		C/T	0.57	0.020	2E-08	0.411
29	rs731839	PEPD	rs731839		G/A	0.35	0.022	3E-09	0.109
30	rs12748152	PIGV-NROB2	rs12748152		T/C	0.09	0.037	1E-09	0.672
31	rs11776767	PINX1	rs2271357	1.000	C/G	0.37	0.022	3E-11	0.291
32	rs5756931	PLA2G6	rs5756931		T/C	0.60	0.020	3E-08	0.872
33	rs6065906	PLTP	rs6065906		C/T	0.19	0.053	2E-34	0.093
34	rs719726	RSPO3	chr6:127456494		T/C	0.51	0.020	3E-08	0.138
35	rs6882076	TIMD4	rs6882076		C/T	0.64	0.029	2E-15	0.199
36	rs2954029	TRIB1	rs2954029		A/T	0.53	0.076	1E-107	0.592
37	rs998584	VEGFA	rs1358980	0.837	A/C	0.49	0.029	3E-15	0.786
38	rs4765127	ZNF664	rs11057408	1.000	G/T	0.65	0.029	2E-08	0.834

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S12 Table. List of the selected SNPs from the Engage Consortium meta-analysis with their  $\beta$ -effect on TG and HWE p-value**

Number	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	rs2035403	AFF1-KLHL8	chr4:88238015		G/A	0.39	0.039	0.006	1.8E-10	0.654
2	rs2131925	ANGPTL3, DOCK7	rs3850634	0.965	T/G	0.68	0.074	0.006	5.1E-32	0.937
3	rs4665710	APOB	rs1042034	1.000	C/A	0.76	0.082	0.007	1.1E-31	0.192
4	rs964184	APO-cluster	rs964184		G/C	0.13	0.244	0.009	1.7E-157	0.482
5	rs439401	APOE	rs439401		C/T	0.65	0.073	0.007	1.5E-26	0.547
6	rs2540948	CEP68	rs2540950	0.929	T/C	0.65	0.036	0.006	6.6E-09	0.617
7	rs7205804	CETP	rs7205804		G/A	0.56	0.034	0.006	6.0E-08	0.288
8	rs10401969	CILP2	rs10401969		T/C	0.92	0.120	0.012	2.0E-25	0.595
9	rs17585887	CITED2	rs668459	1.000	T/C	0.44	0.039	0.006	7.1E-11	0.722
10	rs174546	FADS1-2-3	rs174546		T/C	0.38	0.053	0.006	3.2E-18	0.450
11	rs2929282	FRMD5	rs2929282		T/A	0.04	0.046	0.014	1.5E-03	0.600
12	rs10864728	GALNT2	rs4846914	0.965	A/G	0.39	0.052	0.006	4.5E-16	0.441
13	rs1260326	GCKR	rs1260326		T/C	0.36	0.123	0.006	4.8E-88	0.633
14	rs2255811	GPR85	rs2255811		G/A	0.25	0.041	0.007	2.3E-08	0.697
15	rs419132	HLA-area	rs419132		G/A	0.20	0.056	0.008	4.7E-12	0.267
16	rs2943645	IRS1	rs2943645		T/C	0.63	0.029	0.006	3.2E-06	0.162
17	rs10761731	JMJD1C	rs10761739	1.000	A/T	0.58	0.034	0.006	1.9E-08	0.218
18	rs1077835	LIPC	rs1077834	1.000	G/A	0.22	0.059	0.008	1.9E-14	0.243
19	rs7759633	LPA	rs5014650	0.800	G/A	0.87	0.051	0.009	8.6E-09	0.508
20	rs12678919	LPL	rs12678919		A/G	0.91	0.194	0.011	1.0E-71	0.411
21	rs61352607	LRP1	rs11613352	1.000	G/T	0.73	0.038	0.007	1.2E-08	0.165
22	rs6831256	LRPAP1	rs6831256		G/A	0.41	0.037	0.006	1.5E-09	0.082
23	rs9638182	MLXIPL	rs11974409	1.000	T/G	0.81	0.100	0.008	1.2E-40	0.058
24	rs645040	MSL2L1	rs645040		T/G	0.80	0.040	0.007	6.8E-08	0.124
25	rs12748152	PIGV-NROB2	rs12748152		T/C	0.09	0.038	0.010	2.8E-04	0.672
26	rs4810479	PLTP	rs4810479		C/T	0.27	0.052	0.007	1.9E-13	0.750
27	rs340839	PROX1	rs340839		A/G	0.47	0.039	0.006	4.4E-10	0.700
28	rs72959041	RSPO3	chr6:127496586		A/G	0.06	0.075	0.014	4.8E-08	0.602
29	rs8077889	SOST-DUSP3	rs8077889		C/A	0.19	0.011	0.008	1.3E-01	0.212
30	rs1553318	TIMD4-HAVCR1	rs6882076	0.883	C/G	0.65	0.042	0.006	2.2E-11	0.199
31	rs2954029	TRIB1	rs2954029		A/T	0.52	0.082	0.006	4.4E-44	0.592
32	rs2412710	UBR1, CAPN3	rs2412710		A/G	0.02	0.086	0.024	2.9E-04	0.647
33	rs1358980	VEGFA	rs1358980		T/C	0.47	0.039	0.007	3.3E-09	0.786

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error. CardioMetabochip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S13 Table. List of the selected SNPs from combined meta-analyses with their  $\beta$ -effect on TG and HWE p-value**

Number	Article	SNP	Nearest gene	Cardiometabochip position	LD ( $R^2$ )	Allele (effect/other)	EAF	$\beta$ -effect (effect/other)	SE	GWAS p-value	HWE p-value
1	I	rs2035403	AFF1-KLHL8	chr4:88238015		G/A	0.39	0.039	0.006	1.8E-10	0.654
2	D	rs1832007	AKR1C4	rs1832007		A/G	0.82	0.033		2.0E-12	0.385
3	I	rs2131925	ANGPTL3, DOCK7	rs3850634	0.965	T/G	0.68	0.074	0.006	5.1E-32	0.937
4	I	rs964184	APO-cluster	rs964184		G/C	0.13	0.244	0.009	1.7E-157	0.482
5	I	rs4665710	APOB	rs1042034	1.000	C/A	0.76	0.082	0.007	1.1E-31	0.192
6	I	rs439401	APOE	rs439401		C/T	0.65	0.073	0.007	1.5E-26	0.547
7	I	rs2540948	CEP68	rs2540950	0.929	T/C	0.65	0.036	0.006	6.6E-09	0.617
8	D	rs3764261	CETP	rs3764261		C/A	0.68	0.040		2.0E-25	0.432
9	I	rs10401969	CILP2	rs10401969		T/C	0.92	0.120	0.012	2.0E-25	0.595
10	I	rs17585887	CITED2	rs668459	1.000	T/C	0.44	0.039	0.006	7.1E-11	0.722
11	D	rs11649653	CTF1	rs11649653		C/G	0.60	0.027		2.0E-07	0.874
12	D	rs2068888	CYP26A1	rs2068888		G/A	0.55	0.024		2.0E-11	0.340
13	I	rs174546	FADS1-2-3	rs174546		T/C	0.38	0.053	0.006	3.2E-18	0.450
14	D	rs2929282	FRMD5	rs2929282		T/A	0.07	0.072		2.0E-09	0.600
15	D	rs9930333	FTO	rs1121980	1.000	A/G	0.43	0.021		3.0E-08	0.812
16	I	rs10864728	GALNT2	rs4846914	0.965	A/G	0.39	0.052	0.006	4.5E-16	0.441
17	I	rs1260326	GCKR	rs1260326		T/C	0.36	0.123	0.006	4.8E-88	0.633
18	I	rs2255811	GPR85	rs2255811		G/A	0.25	0.041	0.007	2.3E-08	0.697
19	I	rs419132	HLA-area	rs419132		G/A	0.20	0.056	0.008	4.7E-12	0.267
20	D	rs7248104	INSR	rs7248104		G/A	0.58	0.022		5.0E-10	0.386
21	D	rs2972146	IRS1	rs1515100	0.891	T/G	0.63	0.028		3.0E-15	0.082
22	I	rs10761731	JMJD1C	rs10761739	1.000	A/T	0.58	0.034	0.006	1.9E-08	0.218
23	I	rs1077835	LIPC	rs1077834	1.000	G/A	0.22	0.059	0.008	1.9E-14	0.243
24	I	rs7759633	LPA	rs5014650	0.800	G/A	0.87	0.051	0.009	8.6E-09	0.508
25	I	rs12678919	LPL	rs12678919		A/G	0.91	0.194	0.011	1.0E-71	0.411
26	I	rs61352607	LRP1	rs11613352	1.000	G/T	0.73	0.038	0.007	1.2E-08	0.165
27	I	rs6831256	LRPAP1	rs6831256		G/A	0.41	0.037	0.006	1.5E-09	0.082
28	D	rs9686661	MAP3K1	rs9686661		T/C	0.20	0.038		3.0E-16	0.432
29	D	rs38855	MET	rs38855		A/G	0.53	0.019		2.0E-08	0.749
30	D	rs4719841	MIR148A	rs4719841		C/T	0.20	0.023		9.0E-11	0.938
31	I	rs9638182	MLXIPL	rs11974409	1.000	T/G	0.81	0.100	0.008	1.2E-40	0.058
32	D	rs645040	MSL2L1	rs645040		T/G	0.77	0.029		2.0E-12	0.124
33	D	rs1495741	NAT2	rs1495741		G/A	0.26	0.040		3.0E-12	0.835
34	D	rs3198697	PDXDC1	rs3198697		C/T	0.57	0.020		2.0E-08	0.411
35	D	rs731839	PEPD	rs731839		G/A	0.35	0.022		3.0E-09	0.109
36	D	rs12748152	PIGV-NROB2	rs12748152		T/C	0.09	0.037		1.0E-09	0.672
37	D	rs11776767	PINX1	rs2271357	1.000	C/G	0.37	0.022		3.0E-11	0.291
38	D	rs5756931	PLA2G6	rs5756931		T/C	0.60	0.020		3.0E-08	0.872
39	I	rs4810479	PLTP	rs4810479		C/T	0.27	0.052	0.007	1.9E-13	0.750
40	I	rs340839	PROX1	rs340839		A/G	0.47	0.039	0.006	4.4E-10	0.700

Number	Article	SNP	Nearest gene	CardiometaboChip position	LD (R <sup>2</sup> )	Allele (effect/other)	EAF	β-effect (effect/other)	SE	GWAS p-value	HWE p-value
41	I	rs72959041	RSPO3	chr6:127496586		A/G	0.06	0.075	0.014	4.8E-08	0.602
42	D	rs8077889	MPP3	rs8077889		C/A	0.22	0.025		1.0E-08	0.212
43	D	rs6882076	TIMD4	rs6882076		C/T	0.64	0.029		2.0E-15	0.199
44	I	rs2954029	TRIB1	rs2954029		A/T	0.52	0.082	0.006	4.4E-44	0.592
45	D	rs2412710	CAPN3	rs2412710		A/G	0.04	0.099		2.0E-11	0.647
46	I	rs1358980	VEGFA	rs1358980		T/C	0.47	0.039	0.007	3.3E-09	0.786
47	D	rs4765127	ZNF664	rs11057408	1.000	G/T	0.65	0.029		2.0E-08	0.834

EAF: effect allele frequency, LD: linkage disequilibrium, SE: standard error, I: meta-analysis from Engage Consortium (from Surakka and al.), D: meta-analysis from the Global Lipids Genetics Consortium (from Willer and al.). CardioMetaboChip position = SNP identification used to extract genotyping data from psychiatric cohort. HWE p-value = p-value calculated with genotyping data from psychiatric cohort.

**S14 Table. Association of rescaled PRS (SNPs selected from each meta-analysis) with lipid traits in GAMM adjusted for age, sex, BMI, medications and smoking status.**

	number of SNPs	n	Estimates [95% CI]	Explained variability [%]	Explained variability by GRS [%]	p-value
wPRS_HDL_ds_dMA	65	242	0.01 [0.01 - 0.02]	19.24	4.11	<0.01
wPRS_LDL_ds_dMA	55	232	0.02 [0.00 - 0.03]	13.28	0.75	0.02
wPRS_TC_ds_dMA	69	239	0.03 [0.02 - 0.05]	15.82	1.85	<0.01
wPRS_TG_ds_dMA	38	216	0.06 [0.04 - 0.08]	26.16	6.32	<0.01
wPRS_HDL_ds_iMA	46	233	0.02 [0.01 - 0.03]	18.33	3.45	<0.01
wPRS_LDL_ds_iMA	39	214	0.03 [0.01 - 0.05]	15.29	1.48	<0.01
wPRS_TC_ds_iMA	44	234	0.04 [0.03 - 0.07]	15.99	2.35	<0.01
wPRS_TG_ds_iMA	33	213	0.06 [0.03 - 0.07]	24.06	4.23	<0.01
wPRS_HDL_rs_dMA	65	105	0.02 [0.01 - 0.03]	36.64	5.29	<0.01
wPRS_LDL_rs_dMA	55	102	0.03 [0.01 - 0.06]	8.24	3.24	<0.01
wPRS_TC_rs_dMA	69	106	0.05 [0.02 - 0.07]	14.13	3.44	0.01
wPRS_TG_rs_dMA	38	90	0.03 [0.00 - 0.05]	26.47	2.62	0.03
wPRS_HDL_rs_iMA	46	98	0.03 [0.01 - 0.04]	41.37	6.65	<0.01
wPRS_LDL_rs_iMA	39	93	0.05 [0.03 - 0.08]	14.14	8.13	<0.01
wPRS_TC_rs_iMA	44	102	0.07 [0.03 - 0.10]	17.04	6.14	<0.01
wPRS_TG_rs_iMA	33	87	0.04 [0.01 - 0.06]	27.74	4.77	<0.01
wPRS_HDL_ts_dMA	65	347	0.02 [0.01 - 0.02]	22.25	4.32	<0.01
wPRS_LDL_ts_dMA	55	334	0.02 [0.01 - 0.04]	10.83	1.13	<0.01
wPRS_TC_ts_dMA	69	345	0.03 [0.02 - 0.05]	14.8	2.09	<0.01
wPRS_TG_ts_dMA	38	306	0.05 [0.03 - 0.06]	25.38	5.08	<0.01
wPRS_HDL_ts_iMA	46	331	0.02 [0.01 - 0.03]	22.87	4.41	<0.01
wPRS_LDL_ts_iMA	39	307	0.04 [0.02 - 0.06]	13.33	2.91	<0.01
wPRS_TC_ts_iMA	44	336	0.05 [0.04 - 0.07]	15.72	3.06	<0.01
wPRS_TG_ts_iMA	33	300	0.05 [0.04 - 0.06]	24.52	4.39	<0.01

ds: discovery sample, rs: replication sample, ts: total sample, dMA: Willer meta-analysis, iMA: Surakka meta-analysis, MA\_: not corrected for psychotropic medication categories, n: number of patients, CI: confidence interval. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



**S15 Table. Association of rescaled PRS (SNPs selected from each meta-analysis) with lipid traits in GAMM adjusted for age, sex, BMI, medications and smoking status, with PRS treated as a categorical variable in age-stratified samples.**

	number of SNPs	n	Estimates [95% CI]	p-value
wPRS_median_HDL_ts_cMA_	73	331	0.13 [0.07 - 0.19]	<0.0001
wPRS_p25_HDL_ts_cMA_	73	167	0.28 [0.19 - 0.36]	<0.0001
wPRS_p10_HDL_ts_cMA_	73	68	0.35 [0.22 - 0.49]	<0.0001
<hr/>				
wPRS_median_LDL_ts_cMA_	60	303	0.20 [0.04 - 0.36]	0.004
wPRS_p25_LDL_ts_cMA_	60	158	0.31 [0.11 - 0.53]	0.003
wPRS_p10_LDL_ts_cMA_	60	68	0.63 [0.27 - 1.00]	0.0004
<hr/>				
wPRS_median_TC_ts_cMA_	72	336	0.32 [0.15 - 0.49]	<0.0001
wPRS_p25_TC_ts_cMA_	72	171	0.50 [0.28 - 0.74]	<0.0001
wPRS_p10_TC_ts_cMA_	72	76	0.66 [0.30 - 1.07]	0.0002
<hr/>				
wPRS_median_TG_ts_cMA_	47	299	0.26 [0.13 - 0.38]	<0.0001
wPRS_p25_TG_ts_cMA_	47	146	0.47 [0.30 - 0.64]	<0.0001
wPRS_p10_TG_ts_cMA_	47	56	0.60 [0.19 - 0.91]	0.002

ts: total sample, cMA: combined meta-analyses, MA\_: not corrected for psychotropic medication categories, n: number of patients, CI: confidence interval. wPRS\_median = GAMM performed with PRS as a categorical variable with two groups: one with PRS lower than the median value and the other with PRS higher than the median value. Young = patients whose age is younger than the median age of patients. Old = patients whose age is older than the median age of patients. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

**S16 Table. Predictive statistics in the combined sample**

Dependent variable	Logistic model	Sensitivity % (95%CI)	Specificity % (95%CI)	Accuracy % (95%CI)	AUC (95%CI)	P-value <sup>3</sup>
<b>TC hypercholesterolemia</b>	Clin <sup>1</sup>	72.2 (60.4-84.4)	63.3 (52.2-73.3)	70.0 (61.9-78.1)	0.70 (0.63-0.77)	0.08
	Clin + Gen <sup>2</sup>	73.3 (67.4-80.7)	67.7 (57.7-76.6)	71.9 (66.9-77.5)	0.73 (0.67-0.80)	
<b>LDL hypercholesterolemia</b>	Clin <sup>1</sup>	70.5 (57.7-78.4)	60.9 (51.4-72.4)	67.2 (59.9-72.9)	0.66 (0.59-0.73)	0.41
	Clin + Gen <sup>2</sup>	65.6 (55.5-80.2)	62.9 (50.5-73.3)	65.1 (58.7-72.9)	0.68 (0.61-0.74)	
<b>HDL hypocholesterolemia</b>	Clin <sup>1</sup>	71.2 (62.6-79.1)	67.6 (60.7-75.3)	69.3 (64.3-73.7)	0.73 (0.74-0.78)	<b>0.03</b>
	Clin + Gen <sup>2</sup>	70.5 (62.6-79.1)	73.1 (64.4-80.8)	72.4 (67.3-76.8)	0.76 (0.71-0.81)	
<b>Hypertriglyceridemia</b>	Clin <sup>1</sup>	70.0 (60.0-79.1)	71.3 (61.6-80.5)	70.4 (64.9-75.9)	0.74 (0.68-0.80)	0.57
	Clin + Gen <sup>2</sup>	70.9 (56.4-80.9)	67.1 (57.9-82.3)	68.9 (63.5-74.8)	0.75 (0.69-0.80)	

AUC: area under the curve.

<sup>1</sup> Logistic model including only clinical variables.

<sup>2</sup> Logistic model including clinical and genetic variables.

<sup>3</sup> P-values of difference between the AUC of the model containing clinical data and the model containing clinical and genetic data. 2000 bootstraps were used for the analysis.

**S17 Table. Interaction tests between rescaled PRS and age, sex and BMI in GAMM on lipid traits for SNPs selected from combined meta-analyses in the combined sample**

	p-value
HDL_age*wPRS_ts_cMA	0.25
HDL_sexe*wPRS_ts_cMA	0.19
HDL_BMI*wPRS_ts_cMA	0.31
LDL_age*wPRS_ts_cMA	0.32
LDL_sexe*wPRS_ts_cMA	0.19
LDL_BMI*wPRS_ts_cMA	0.02
TC_age*wPRS_ts_cMA	0.3
TC_sexe*wPRS_ts_cMA	0.04
TC_BMI*wPRS_ts_cMA	0.47
TG_age*wPRS_ts_cMA	0.14
TG_sexe*wPRS_ts_cMA	0.25
TG_BMI*wPRS_ts_cMA	0.20

ds: discovery sample, rs: replication sample, ts: total sample, cMA: combined meta-analyses, MA\_: not corrected for psychotropic medication categories. Age\*wPRS = interaction between age and genetic risk score, sexe\*wPRS = interaction between sex and genetic risk score, BMI\*wPRS = interaction between BMI and genetic risk score. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

**S18 Table. Association of rescaled PRS (SNPs selected from each meta-analysis) with lipid traits in GAMM adjusted with age, sex, BMI, medications and smoking status with PRS treated as a categorical variable in stratified samples.**

	number of SNPs	n	Estimates [95% CI] (mmol/l)	p-value
wPRS_median LDL_BMI_low_ts_cMA_	60	179	0.03 [-0.19 - 0.17]	0.42
wPRS_median LDL_BMI_high_ts_cMA_	60	155	0.46 [0.23 - 0.72]	<0.0001
wPRS_median TC_female_ts_cMA_	72	199	0.40 [0.18 - 0.62]	<0.0001
wPRS_median TC_male_ts_cMA_	72	137	0.27 [0.04 - 0.58]	0.01

ts: total sample, cMA: combined meta-analyses, MA\_: not corrected for psychotropic medication categories, n: number of patients, CI: confidence interval. wPRS\_median = GAMM performed with PRS as a categorical variable with two groups: one with PRS lower than the median value and the other with PRS higher than the median value. BMI\_low = patients whose BMI is smaller than the median value. BMI\_high = patients whose BMI is higher than the median value. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

S19 Table. Explained variability of each covariates using GAMM with SNP selected from combined meta-analyses in the combined sample

Total sample Combined meta-analyses	Explained variability [%]	Variability explained without variable [%]	Variability explained by variable [%]
wGRS_HDL	22.79	18.46	<b>4.33</b>
BMI_HDL	22.79	16.20	<b>6.59</b>
Age_HDL	22.79	21.39	1.40
Gender_HDL	22.79	16.64	<b>6.15</b>
Smoker_HDL	22.79	22.52	0.27
Medication_HDL	22.79	22.51	0.28
wGRS_LDL	13.61	10.21	<b>3.40</b>
BMI_LDL	13.61	10.44	<b>3.17</b>
Age_LDL	13.61	10.94	<b>2.67</b>
Gender_LDL	13.61	12.77	0.84
Smoker_LDL	13.61	12.01	1.60
Medication_LDL	13.61	13.54	0.07
wGRS_TC	15.91	12.66	<b>3.25</b>
BMI_TC	15.91	13.22	<b>2.69</b>
Age_TC	15.91	12.65	<b>3.26</b>
Gender_TC	15.91	13.80	<b>2.11</b>
Smoker_TC	15.91	15.19	0.72
Medication_TC	15.91	15.70	0.21
wGRS_TG	24.97	20.14	<b>4.83</b>
BMI_TG	24.97	10.42	<b>14.55</b>
Age_TG	24.97	24.63	0.34
Gender_TG	24.97	23.02	1.95
Smoker_TG	24.97	24.34	0.63
Medication_TG	24.97	23.63	1.34

Explained variability = variability explained by the clinical and genetic data. Variability explained without variable = variability explained by the whole model without the considered variable. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

**S20 Table. Explained variability of each SNP groups using GAMM with SNPs selected from combined meta-analyses in the combined sample**

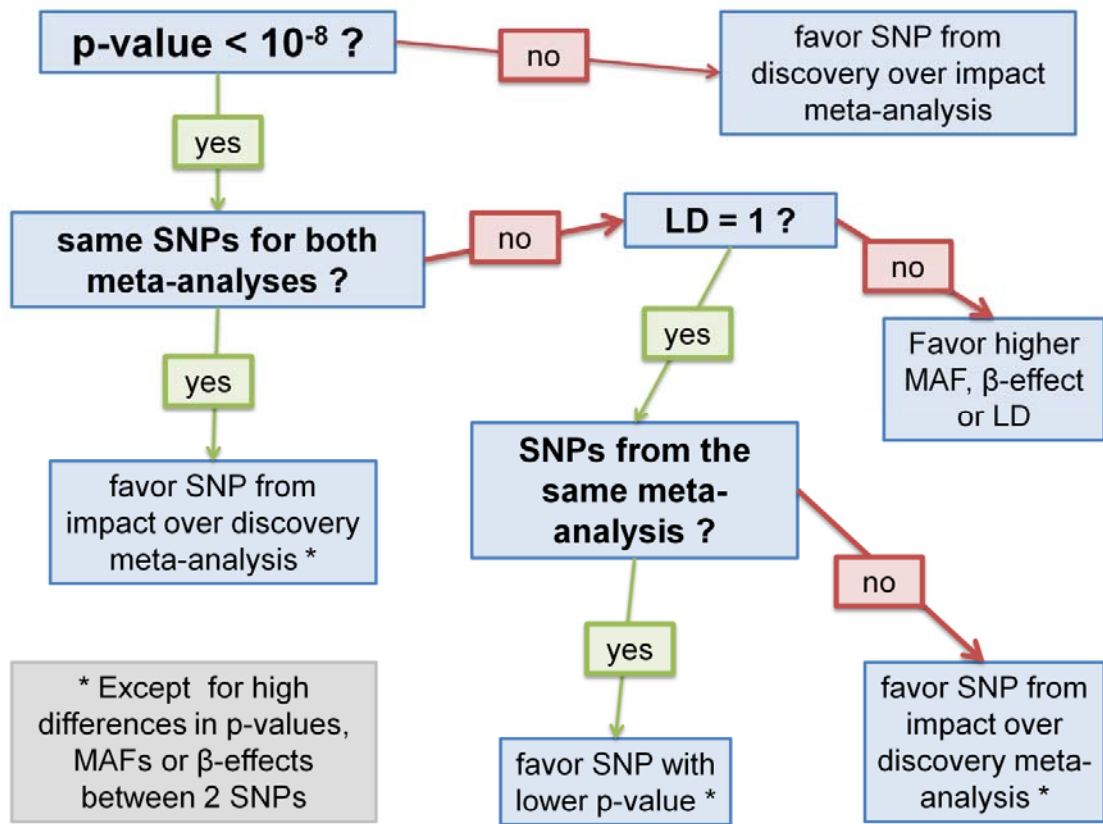
	Total sample Combined meta-analyses	n SNPs	n obs	Explained variability [%]	Variability explained without genetics [%]	Variability explained by genetics [%]
<b>ALL SNPs</b>	<b>wPRS_HDL</b>	<b>73</b>	<b>331</b>	<b>22.79</b>	<b>18.46</b>	<b>4.33</b>
<b>ALL SNPs <math>\beta=1</math></b>	wPRS_HDL	73	331	20.04	18.46	1.58
<b><math>\leq\beta</math> p50 SNPs</b>	wPRS_HDL	36	361	18.04	17.77	0.27
<b><math>&gt;\beta</math> p50 SNPs</b>	wPRS_HDL	37	331	22.54	18.46	4.08
<b><math>&gt;\beta</math> p95 SNPs</b>	wPRS_HDL	4	358	21.71	18.16	3.55
<b>ALL SNPs</b>	<b>wPRS_LDL</b>	<b>60</b>	<b>303</b>	<b>13.61</b>	<b>10.21</b>	<b>3.40</b>
<b>ALL SNPs <math>\beta=1</math></b>	wPRS_LDL	60	303	10.25	10.21	0.04
<b><math>\leq\beta</math> p50 SNPs</b>	wPRS_LDL	30	346	9.79	9.64	0.15
<b><math>&gt;\beta</math> p50 SNPs</b>	wPRS_LDL	30	307	15.03	10.42	4.61
<b><math>&gt;\beta</math> p95 SNPs</b>	wPRS_LDL	3	346	12.5	9.41	3.09
<b>ALL SNPs</b>	<b>wPRS_TC</b>	<b>72</b>	<b>336</b>	<b>15.91</b>	<b>12.66</b>	<b>3.25</b>
<b>ALL SNPs <math>\beta=1</math></b>	wPRS_TC	72	336	13.81	12.66	1.15
<b><math>\leq\beta</math> p50 SNPs</b>	wPRS_TC	36	361	12.66	12.66	0.00
<b><math>&gt;\beta</math> p50 SNPs</b>	wPRS_TC	36	339	16.69	12.85	3.84
<b><math>&gt;\beta</math> p95 SNPs</b>	wPRS_TC	4	363	15.57	13.01	2.56
<b>ALL SNPs</b>	<b>wPRS_TG</b>	<b>47</b>	<b>299</b>	<b>24.97</b>	<b>20.11</b>	<b>4.86</b>
<b>ALL SNPs <math>\beta=1</math></b>	wPRS_TG	47	299	22.72	20.11	2.61
<b><math>\leq\beta</math> p50 SNPs</b>	wPRS_TG	26	317	19.77	19.24	0.53
<b><math>&gt;\beta</math> p50 SNPs</b>	wPRS_TG	21	300	23.73	20.13	3.6
<b><math>&gt;\beta</math> p95 SNPs</b>	wPRS_TG	3	308	23.52	20.19	3.33

Explained variability = variability explained by the clinical and genetic data. Variability explained without genetics = variability explained by the whole model without considering genetics. ALL SNPs = wPRS constructed with the total number of SNPs. ALL SNPs  $\beta=1$  = non-weighted PRS, i.e. PRS constructed with the total number of SNPs without considering specific  $\beta$ -effects (all  $\beta$ -effects=1).  $\leq\beta$  p50 SNPs = wPRS constructed with SNPs whose  $\beta$ -effects are lower or equal to the median of all  $\beta$ -effects.  $>\beta$  p50 SNPs = wPRS constructed with SNPs whose  $\beta$ -effects are higher than the median of all  $\beta$ -effects.  $>\beta$  p95 SNPs = wPRS constructed with SNPs whose  $\beta$ -effects are higher than the percentile 95 of all  $\beta$ -effects. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

S21 Table. SNPs most involved in genetic explained variability of lipid phenotypes

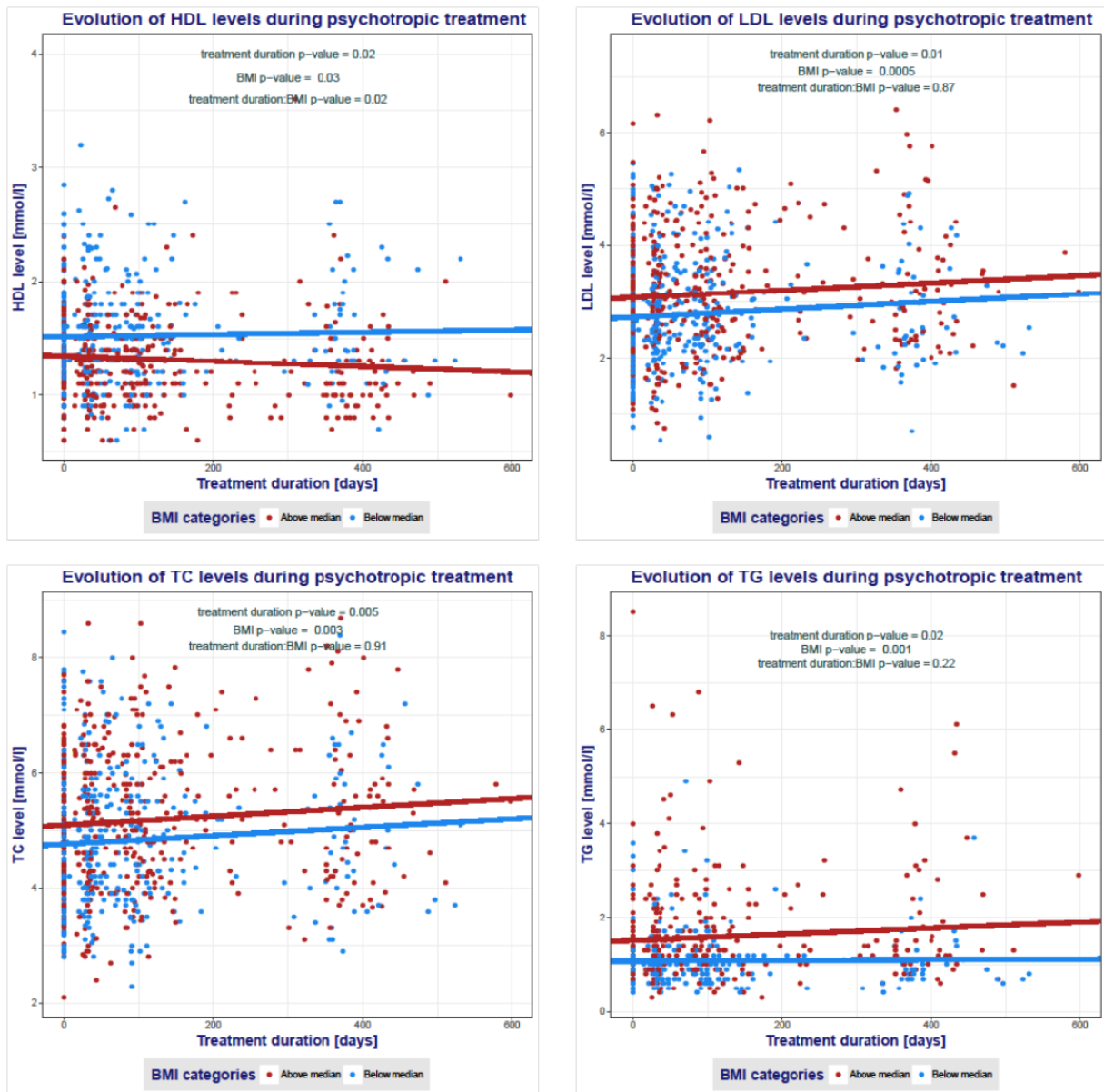
a.				
<b>HDL</b>	rs3764261	<b>rs12678919</b>	rs1800961	rs78058190
<b>LDL</b>	rs1065853	<b>rs112374545</b>	<b>rs646776</b>	
<b>TC</b>	rs7412	<b>rs112374545</b>	rs10401969	<b>rs646776</b>
<b>TG</b>	rs964184	<b>rs12678919</b>	rs1260326	
b.				
SNP	Gene	Gene name	Remarks	Phenotypes <sup>1</sup>
rs3764261	CETP	Cholesteryl Ester Transfer Protein		HDL, LDL, TC, TG
<b>rs12678919</b>	<b>LPL</b>	<b>Lipoprotein lipase</b>		HDL, TG
rs1800961	HNF4A	Hepatocyte Nuclear Factor 4 Alpha	missense SNP	HDL, TC
rs78058190	PRKAG3	Protein Kinase AMP-Activated Non-Catalytic Subunit Gamma 3		HDL
rs1065853	APOE	Apolipoprotein E		LDL
<b>rs112374545</b>	<b>LDLR</b>	<b>Low density lipoprotein receptor</b>		LDL, TC
<b>rs646776</b>	<b>CELSR2</b>	<b>Cadherin EGF LAG Seven-Pass G-Type Receptor 2</b>		LDL, TC
rs7412	APOE	Apolipoprotein E	missense SNP	TC
rs10401969	CILP2	Cartilage Intermediate Layer Protein 2		LDL, TC, TG
rs964184	APOA1	Apolipoprotein A1		HDL, LDL, TC, TG
rs1260326	GCKR	Glucokinase (Hexokinase 4) Regulator	missense SNP	TC, TG

a. SNPs whose  $\beta$ -effects are higher than the percentile 95 of all  $\beta$ -effects (i.e. p95 SNPs) for HDL, LDL, TC and TG are shown, in decreasing order. P95 SNPs shared between two or more phenotypes are in bold. b. Characteristics of each p95 SNPs of a. <sup>1</sup>: other phenotypes significantly associated with corresponding SNP in the combined meta-analysis.

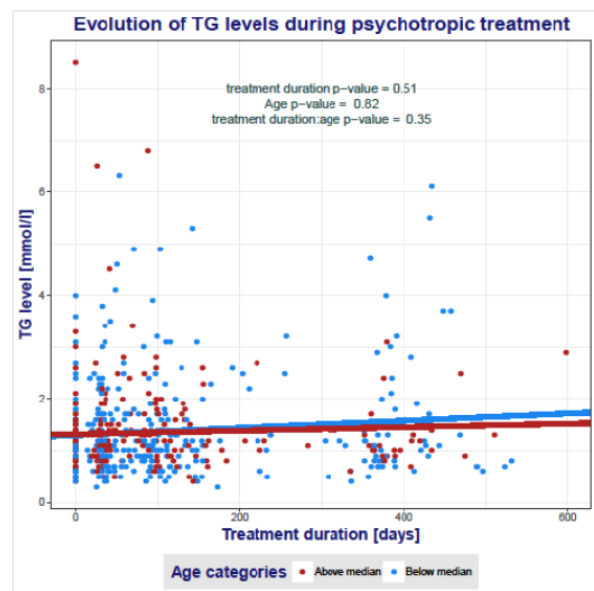
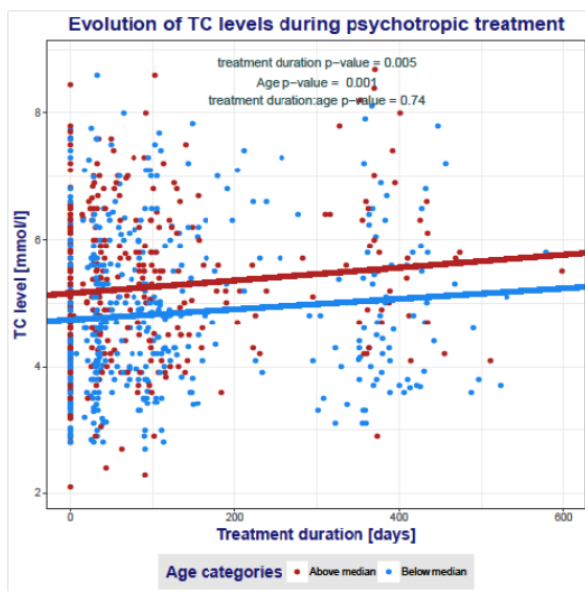
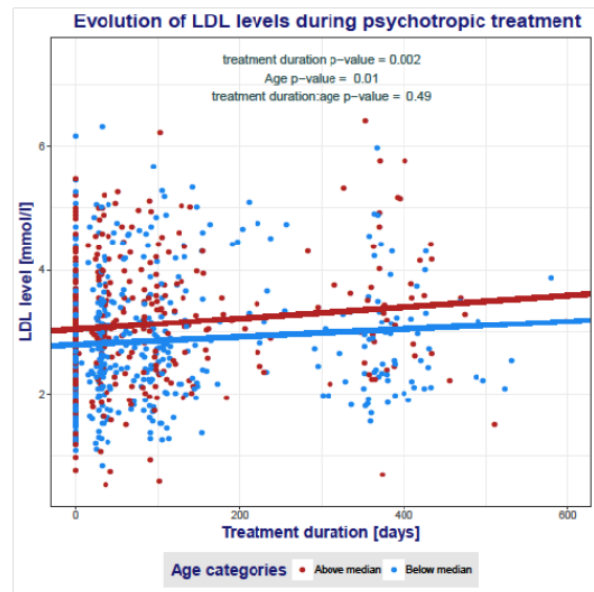
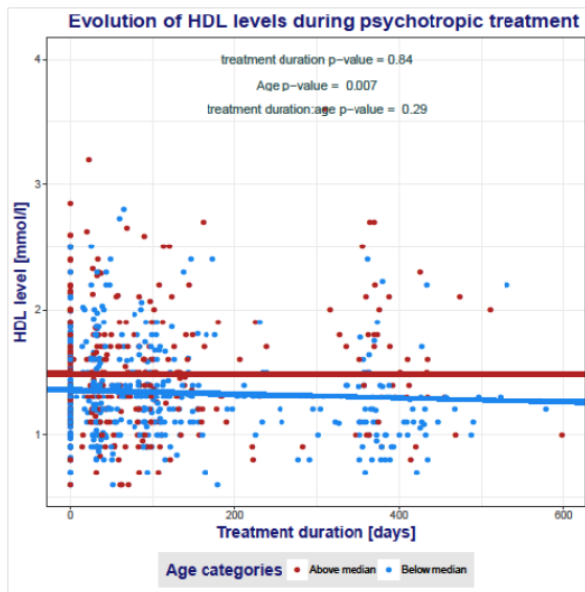


**S1 Figure. Decision tree for the selection between two SNPs located in the same gene.** LD: linkage disequilibrium, MAF: minor allele frequency. P-value of  $10^{-8}$  = p-value considered as being GWAS significant. Impact: meta-analysis from Engage Consortium (from Surakka and al.). Discovery: meta-analysis from the Global Lipids Genetics Consortium (from Willer and al.).

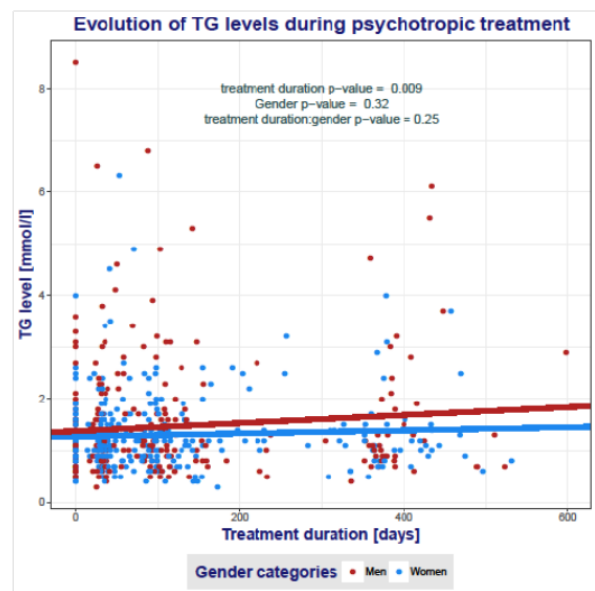
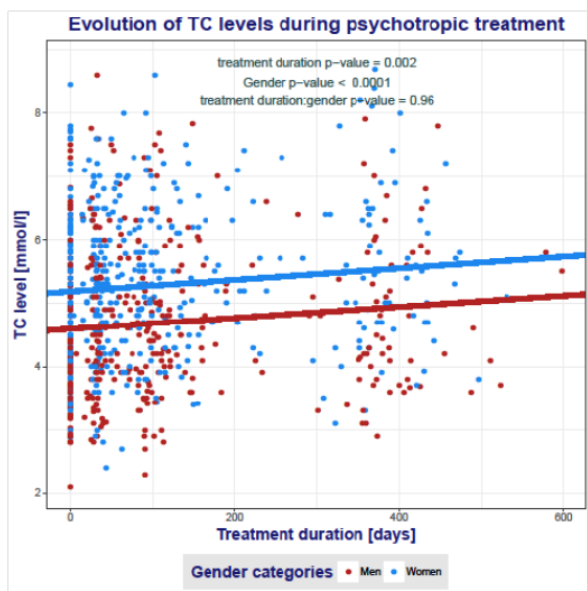
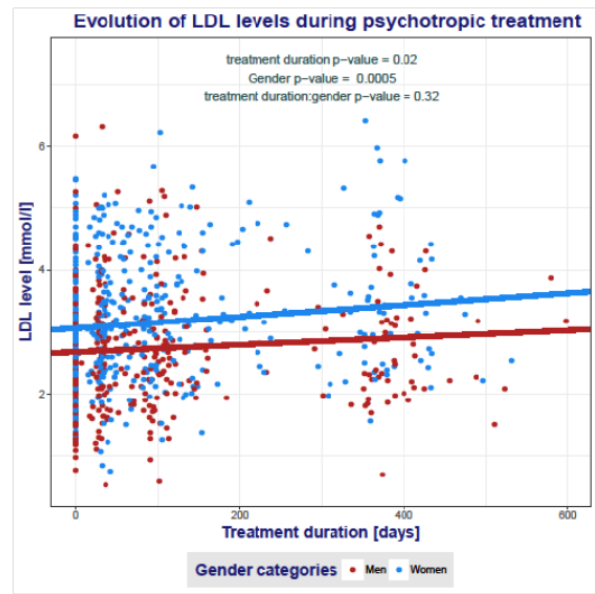
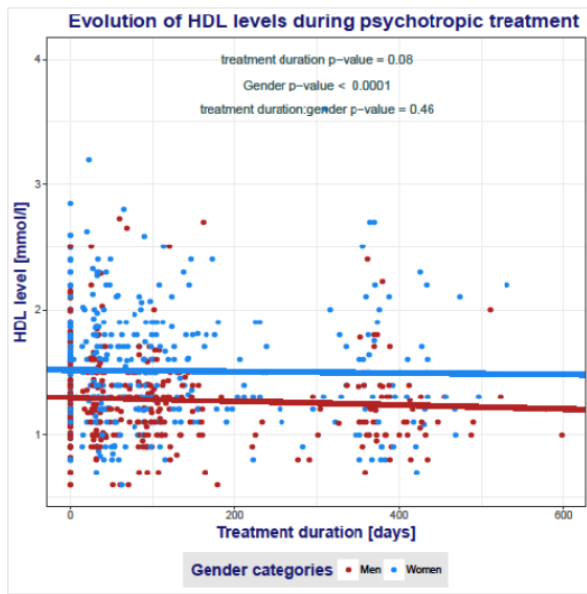




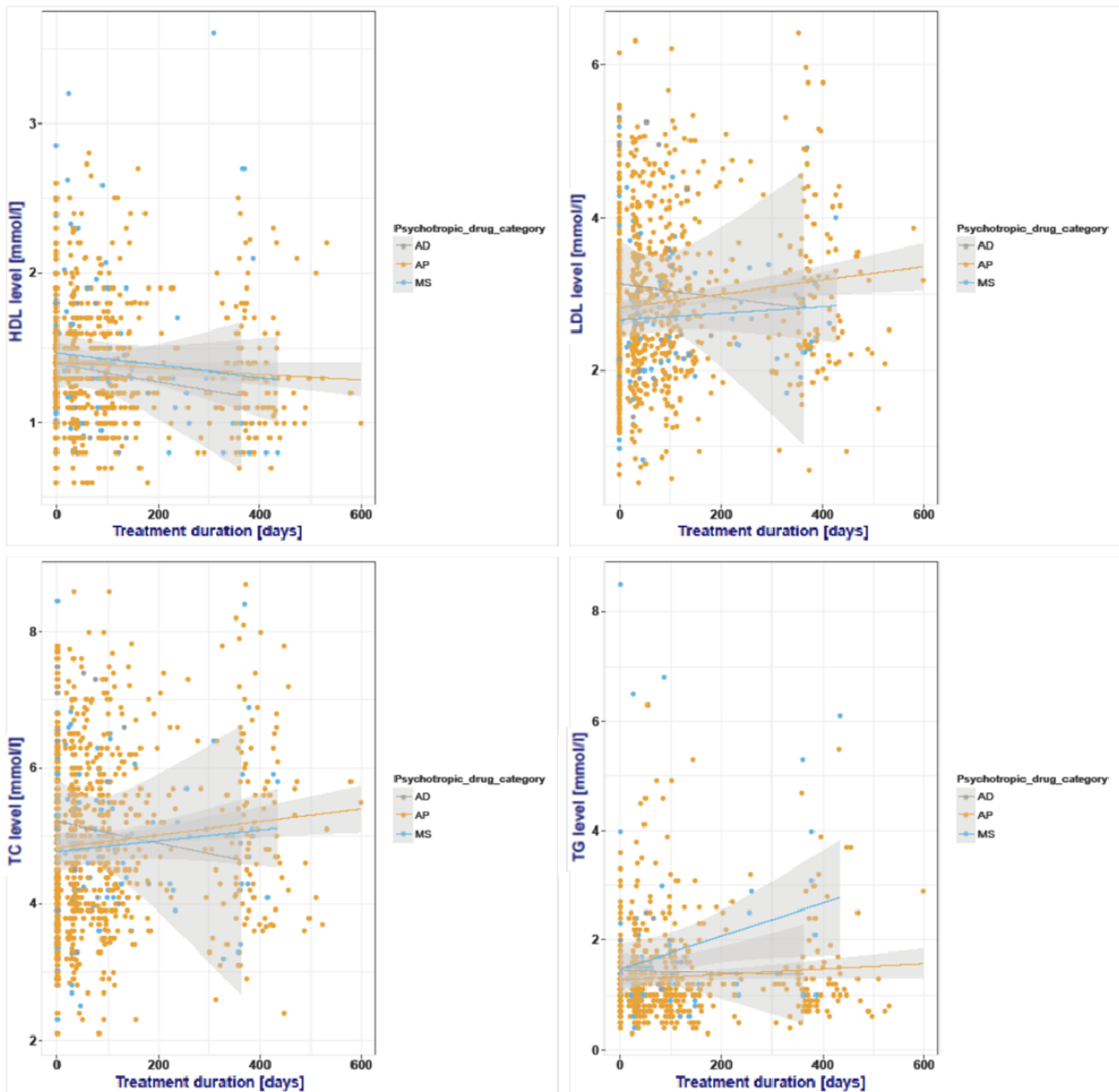
**S2 Figure. Evolution of lipid levels during psychotropic treatment according to BMI: model including patients from the discovery sample.** Blue dots represent patients whose BMI was lower or equal to the median ( $23.3 \text{ kg/m}^2$ ). Red dots represent patients whose BMI was higher than the median ( $23.3 \text{ kg/m}^2$ ). Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



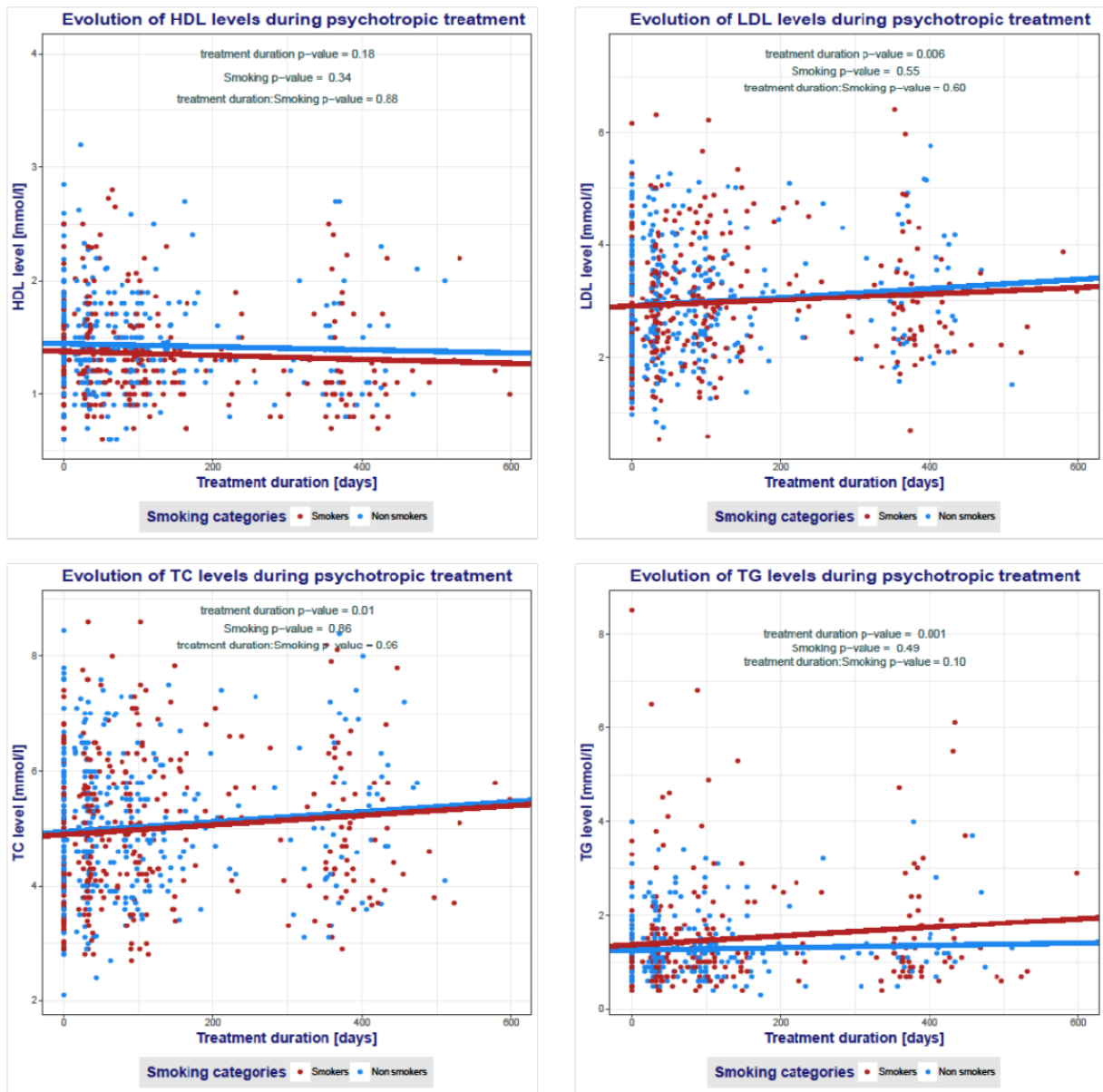
**S3 Figure. Evolution of lipid levels during psychotropic treatment according to age: model including patients from the discovery sample.** Blue dots represent patients younger or equal to the median value (48 years old). Red dots represent patients older than the median value (48 years old). Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



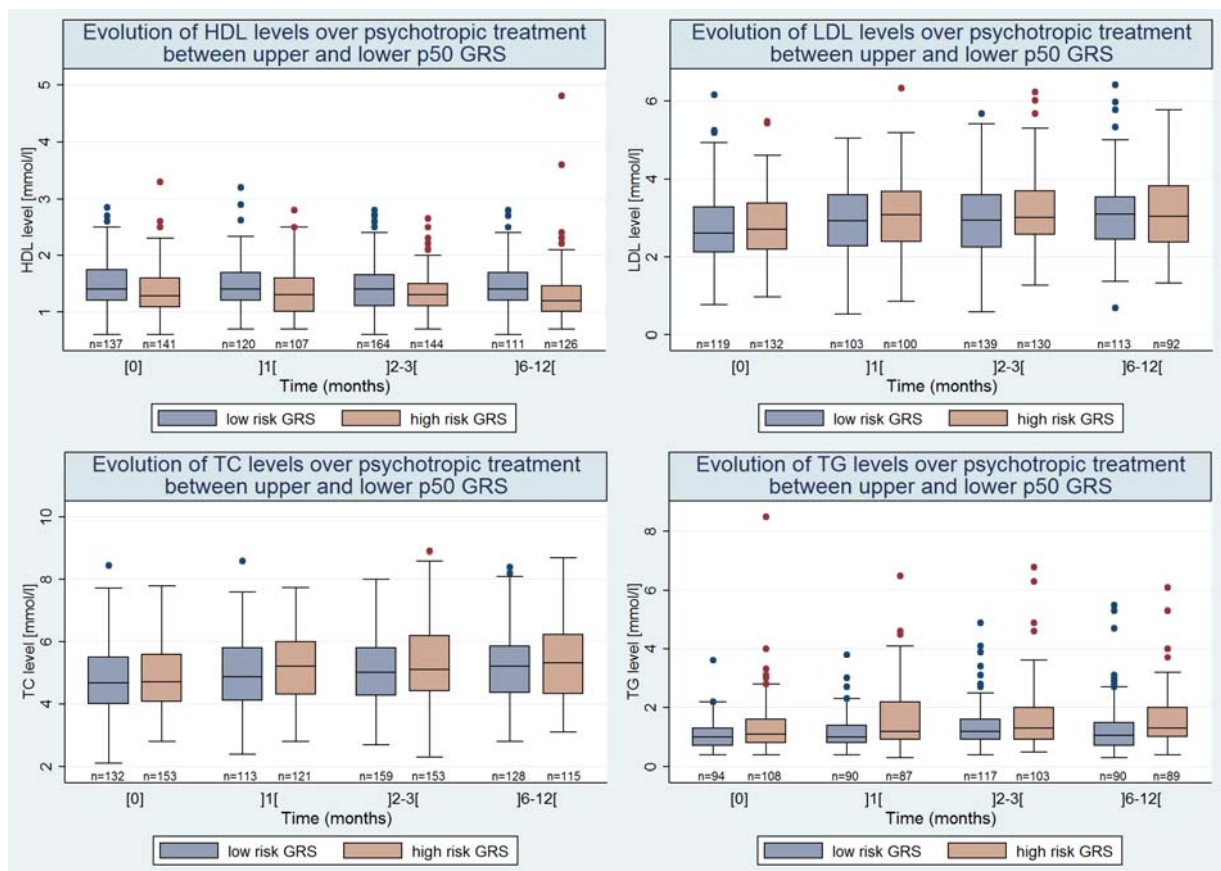
S4 Figure. Evolution of lipid levels during psychotropic treatment according to gender: model including patients from the discovery sample. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



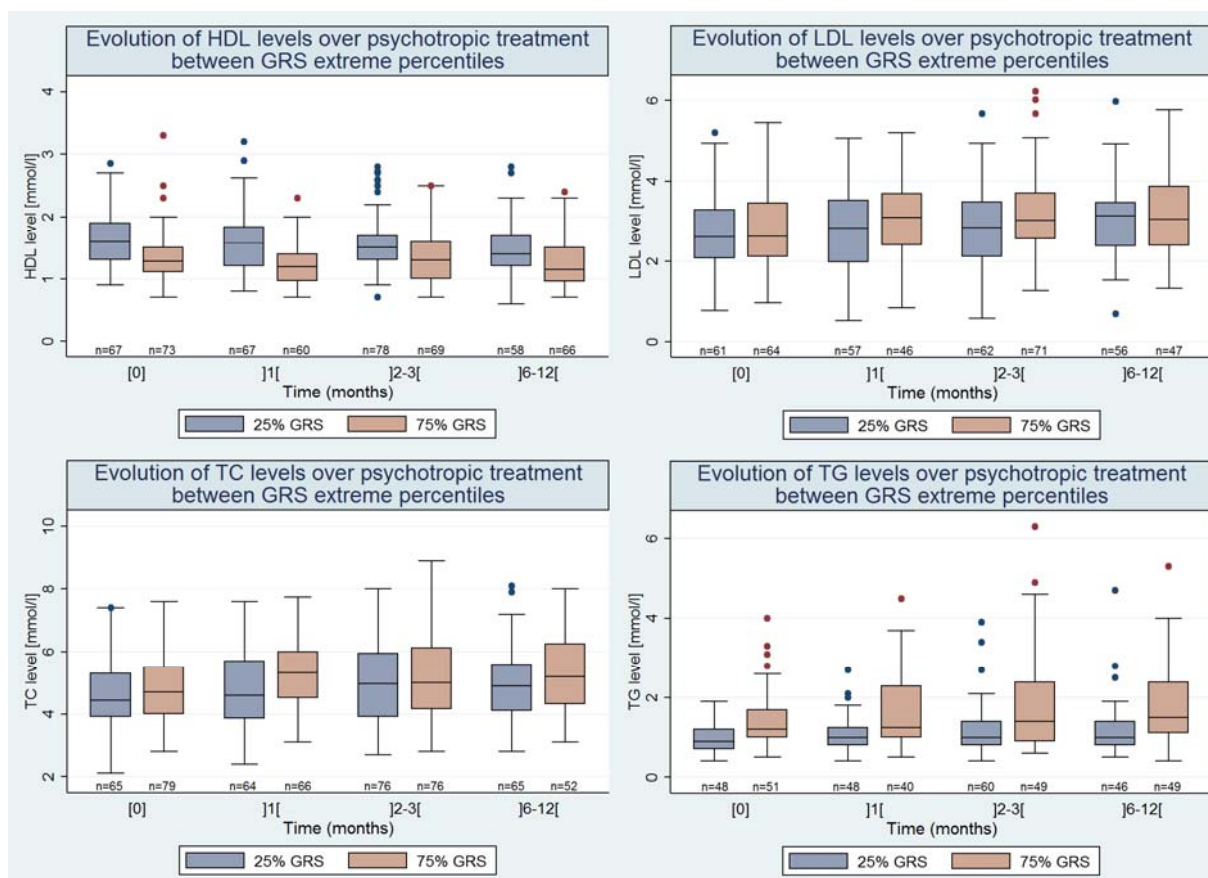
**S5 Figure. Evolution of lipid levels during psychotropic treatment according to medication classes in the discovery sample.** Patients receiving antipsychotics, mood stabilizers and antidepressants are represented in yellow, blue and grey dots, respectively. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



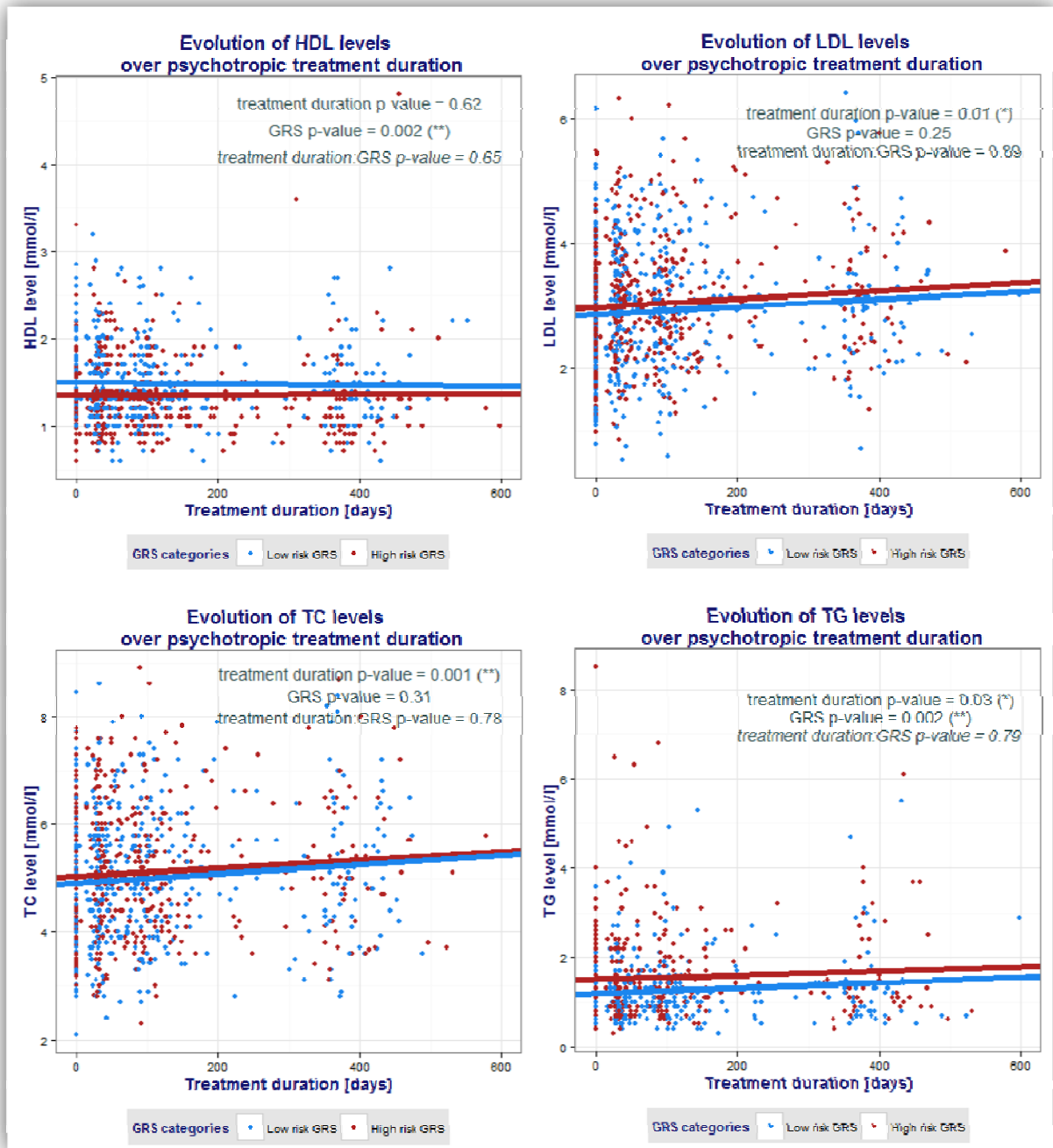
**S6 Figure. Evolution of lipid levels during psychotropic treatment according to the smoking status: model including patients from the discovery sample.** Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



**S7 Figure. Evolution of lipid variables during psychotropic treatment: boxplots including all patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Median, interquartiles and number of observations are indicated for each box. Months were defined as: month [0]: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

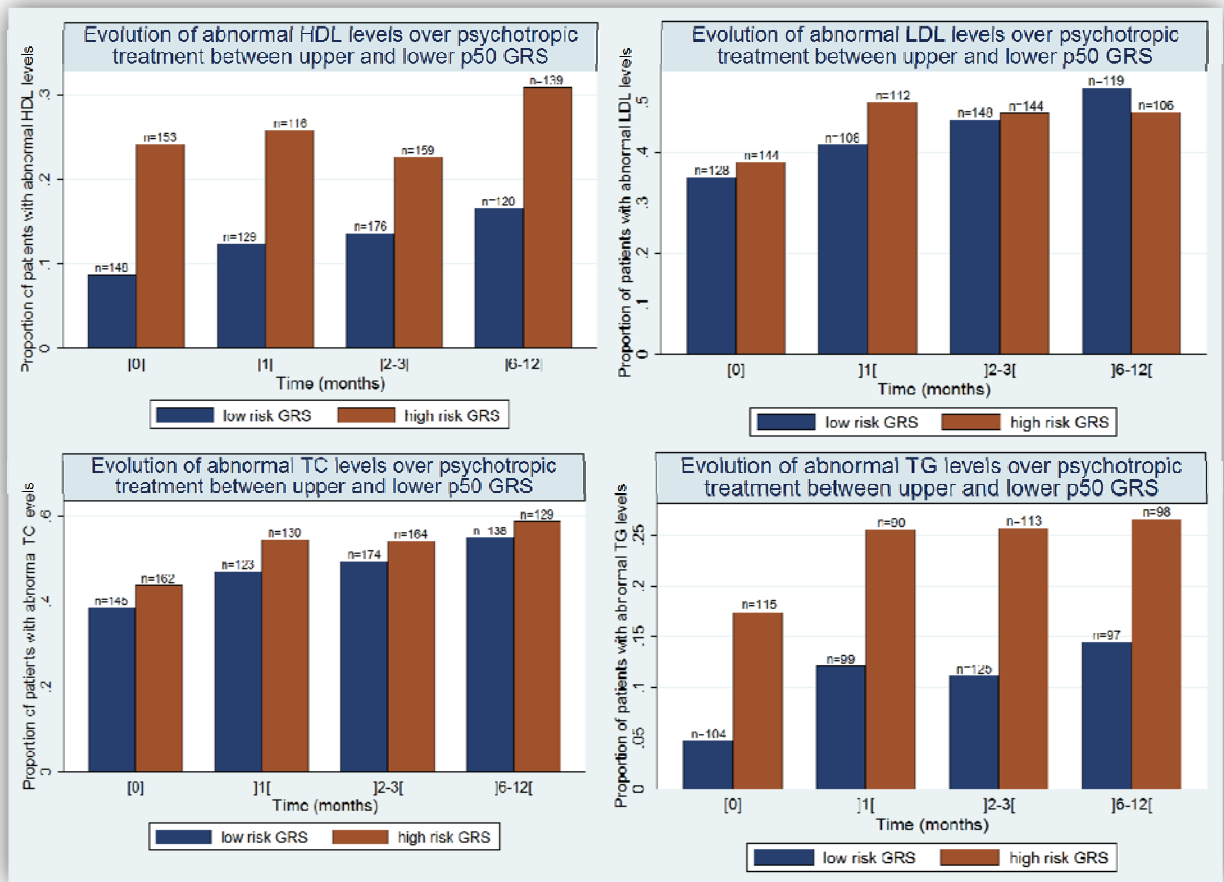


**S8 Figure. Lipid variables evolution during psychotropic treatment: boxplots including only 50% of patients having extreme PRS values.** 25% PRS = PRS lower than the 25th percentile. 75% PRS = PRS higher than the 75th percentile. Median, interquartiles and number of observations are indicated for each box. Months were defined as: month [0]: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

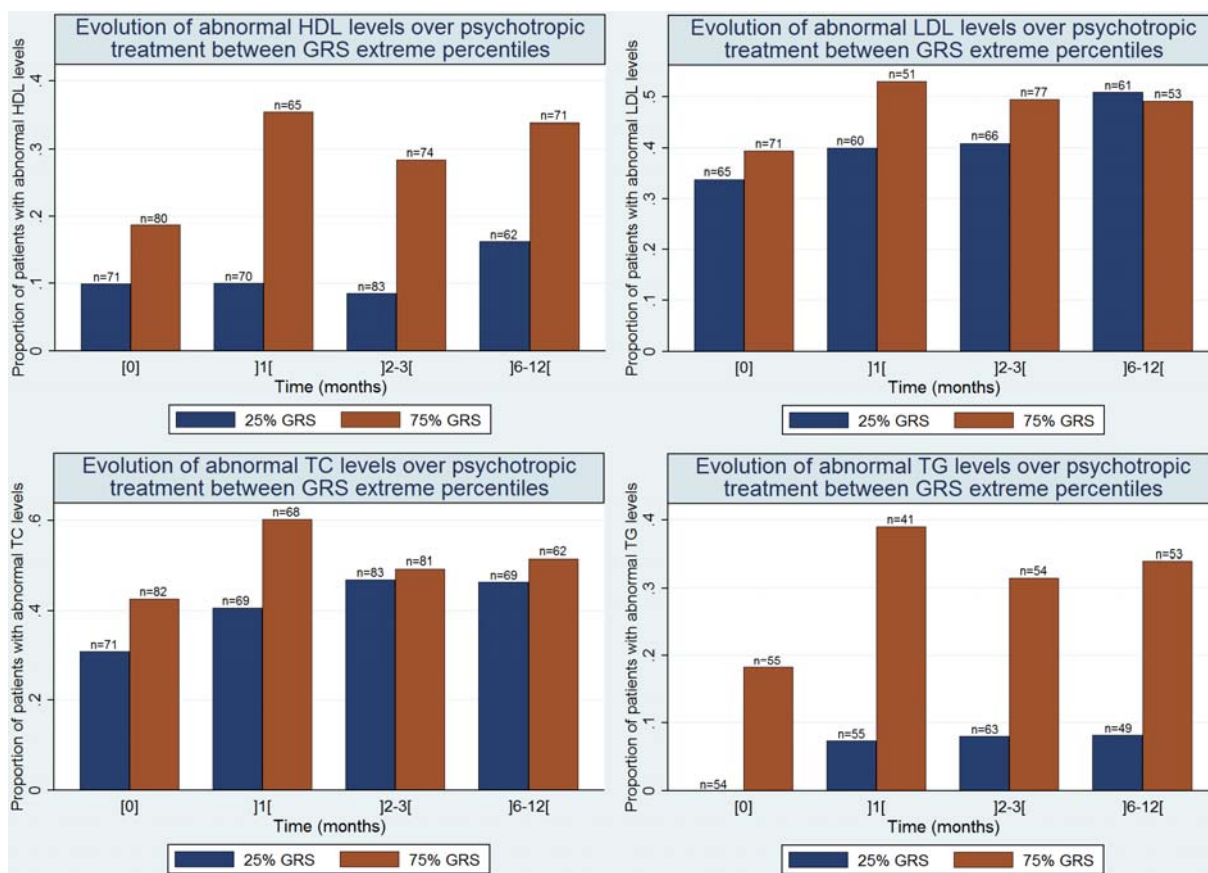


**S9 Figure. Evolution of lipid levels during psychotropic treatment with linear mixed regression: model including all patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

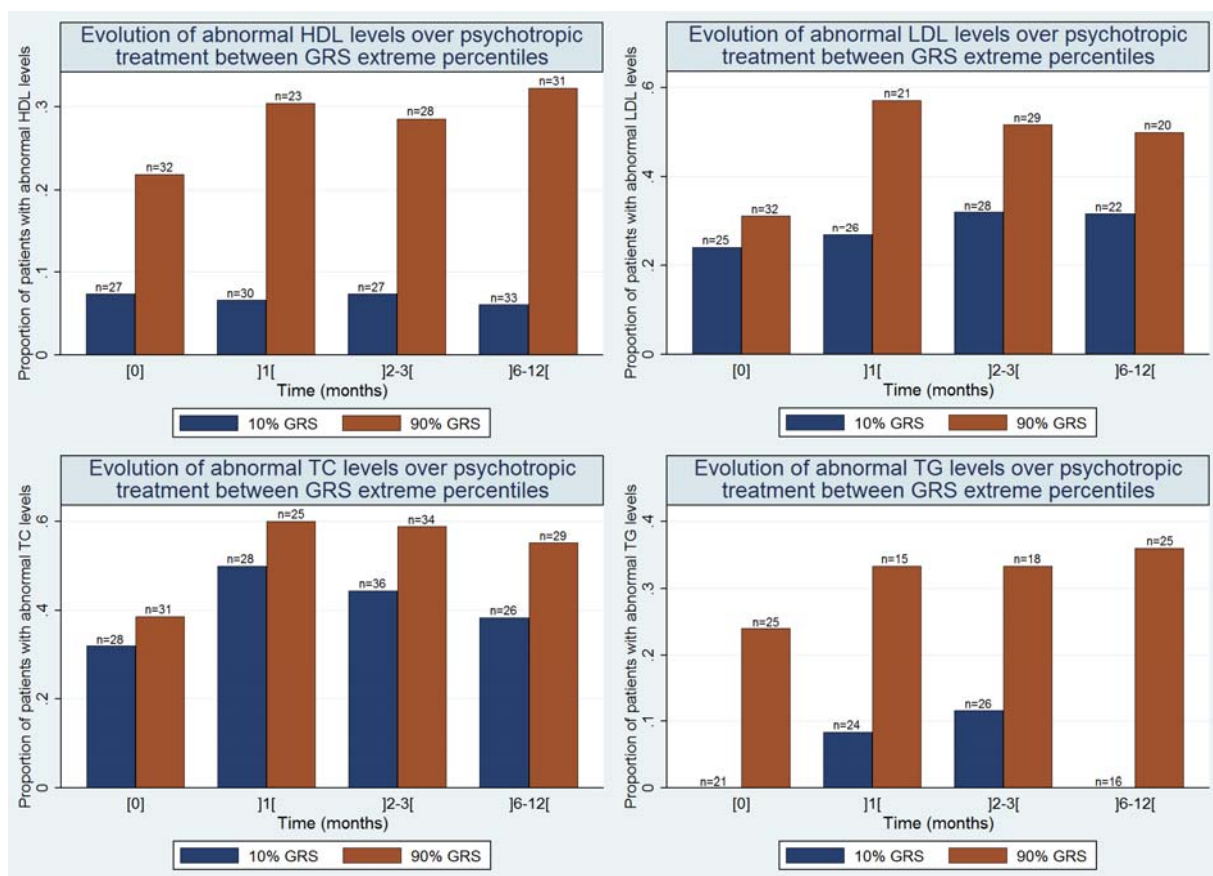




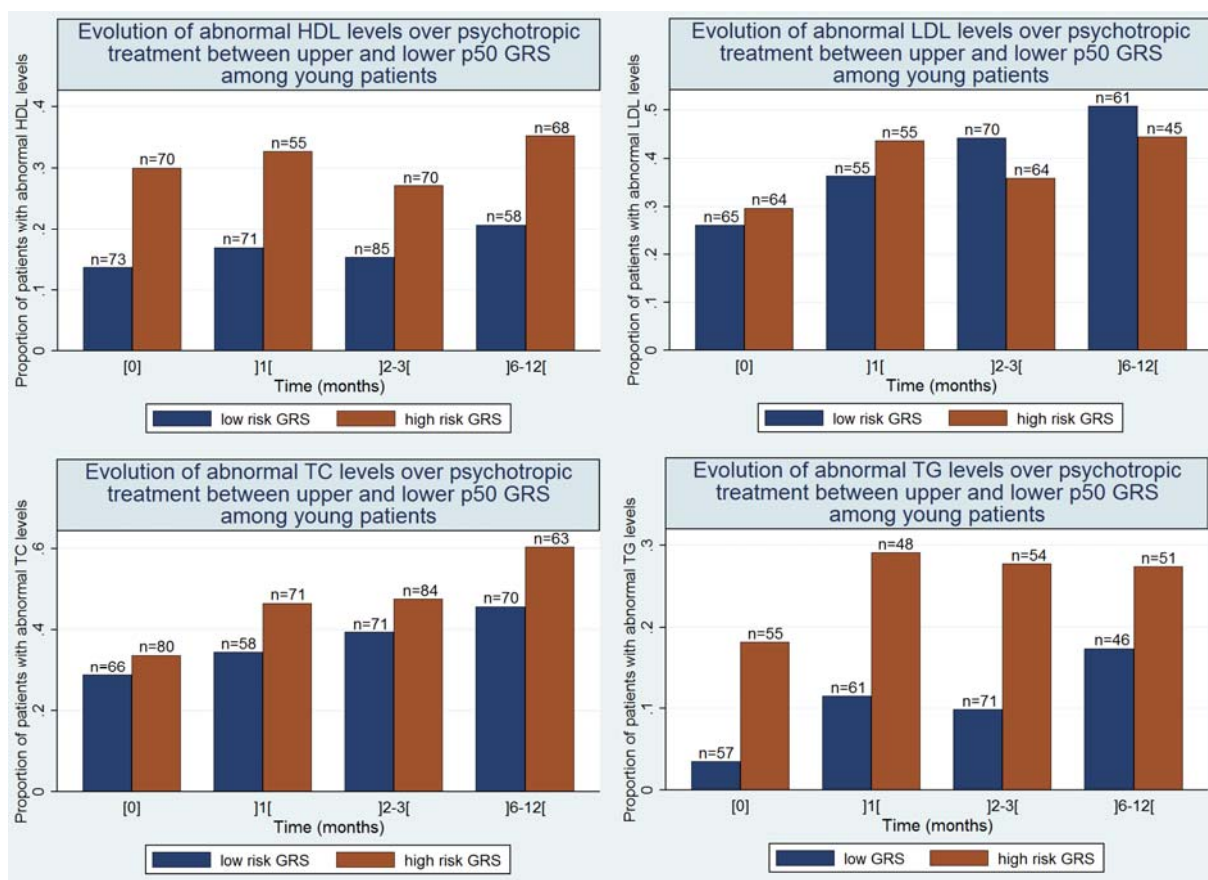
**S10 Figure: Evolution of dyslipidemia prevalence for each lipid trait during psychotropic treatment: plots including all patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Numbers of observations are indicated for each barplot. Months were defined as: month [0]: day 0, month [1]:  $\geq 10$  &  $< 45$  days, month [2-3]:  $\geq 45$  &  $< 135$  days, month [6-12]:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



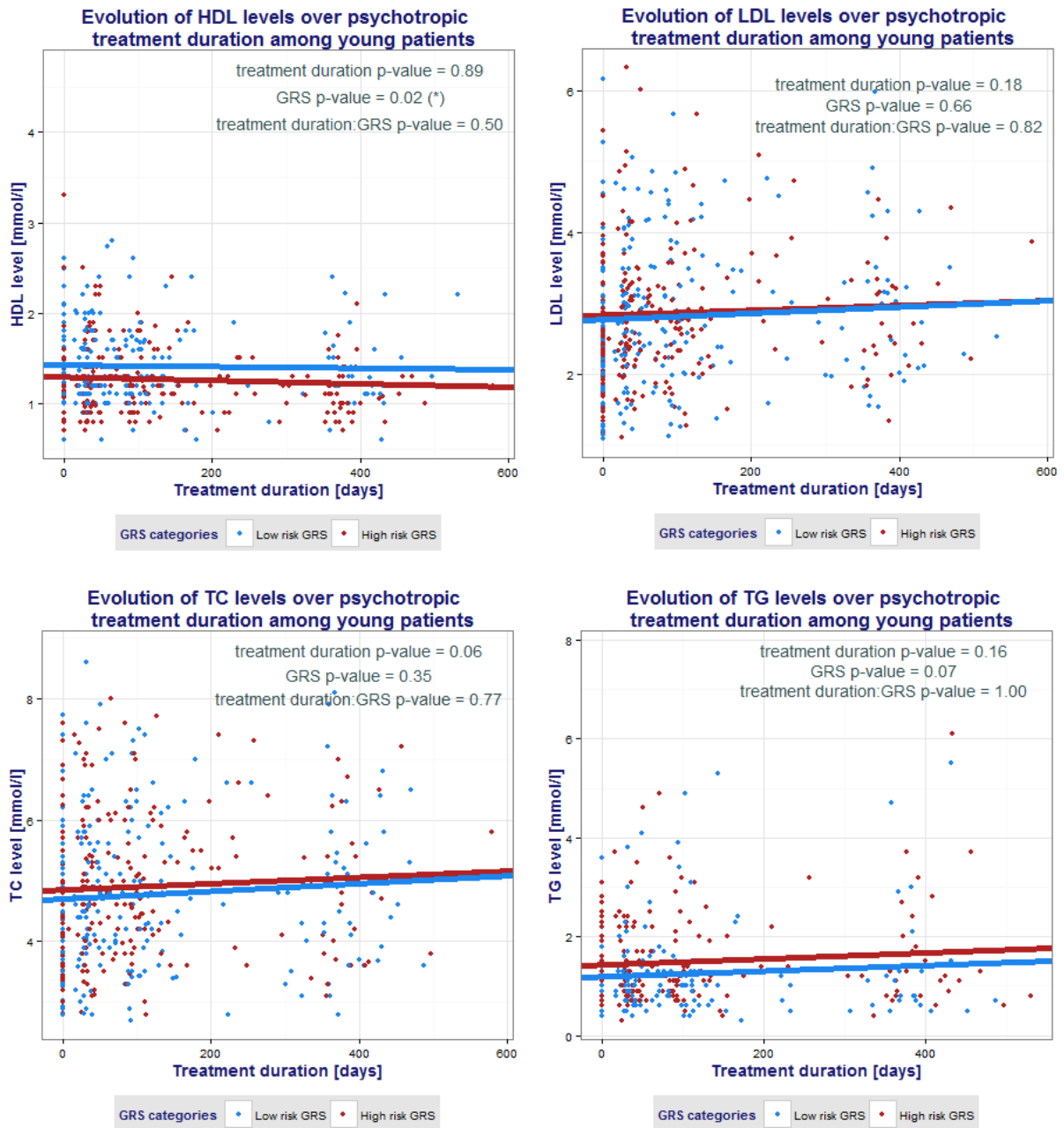
**S11 Figure. Evolution of dyslipidemia prevalence for each lipid trait during psychotropic treatment: plots including only 50% of patients having extreme PRS values.** 25% PRS = PRS lower than the 25th percentile. 75% PRS = PRS higher than the 75th percentile. Numbers of observations are indicated for each barplot. Months were defined as: month [0]: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



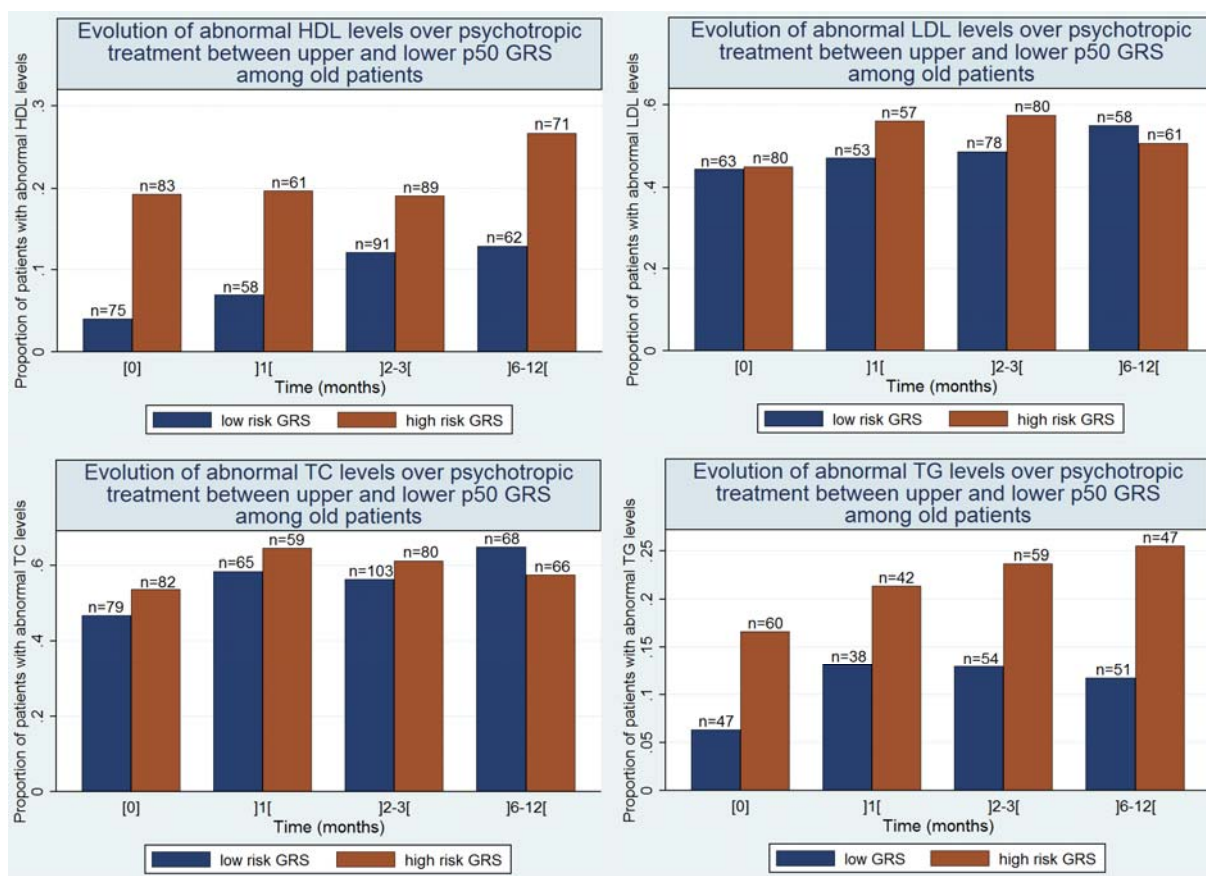
**S12 Figure. Evolution of dyslipidemia prevalence for each lipid trait during psychotropic treatment: plots including only 20% of patients having extreme PRS values.** 10% PRS = PRS lower than the 10th percentile. 90% PRS = PRS higher than the 90th percentile. Numbers of observations are indicated for each barplot. Months were defined as: month [0]: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



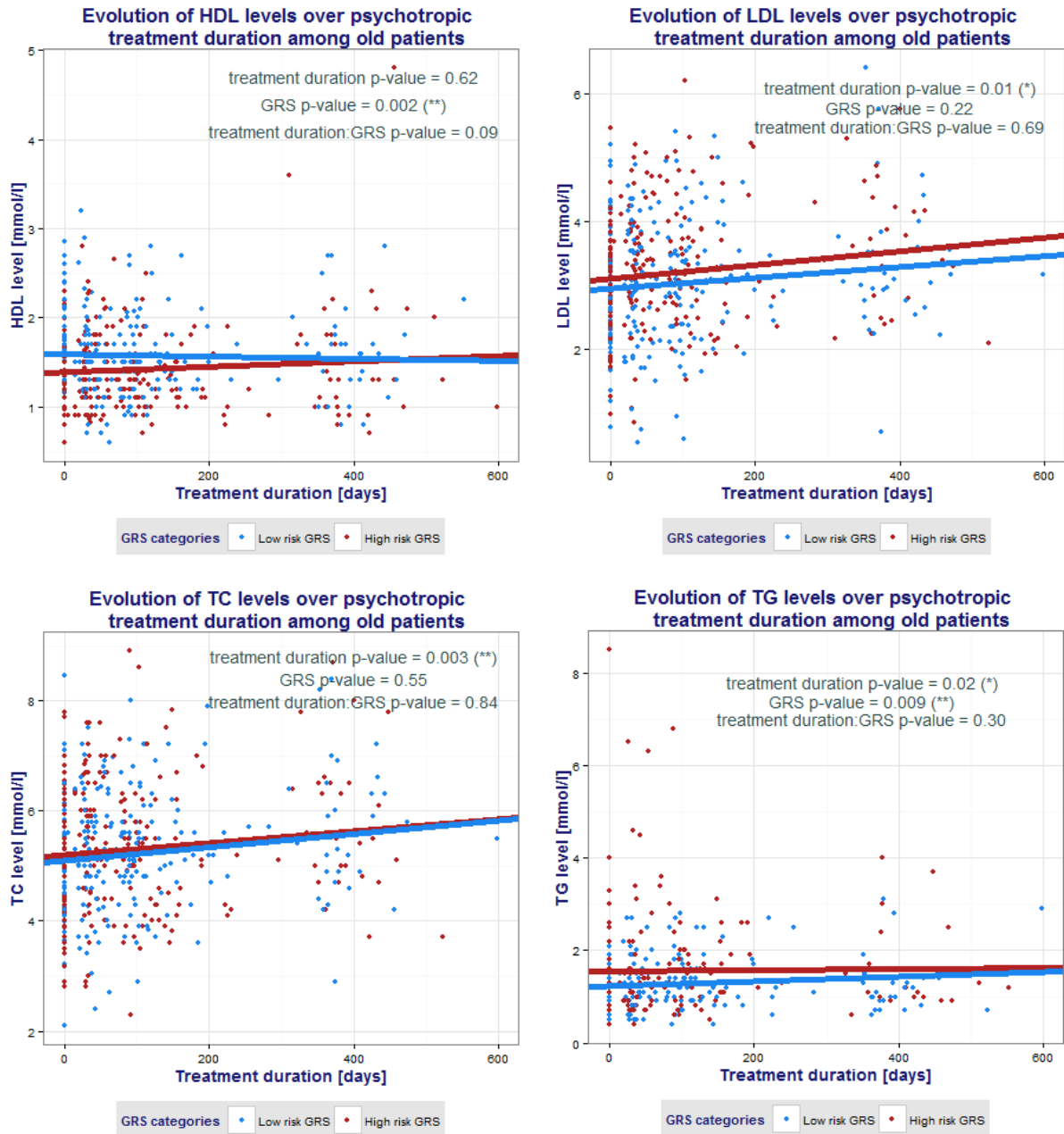
**S13 Figure. Evolution of dyslipidemia prevalence for each lipid trait during psychotropic treatment: plots including only patients younger than the median age of patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Young = patients whose age is younger than the median age of patients. Numbers of observations are indicated for each barplot. Months were defined as: month [0]: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



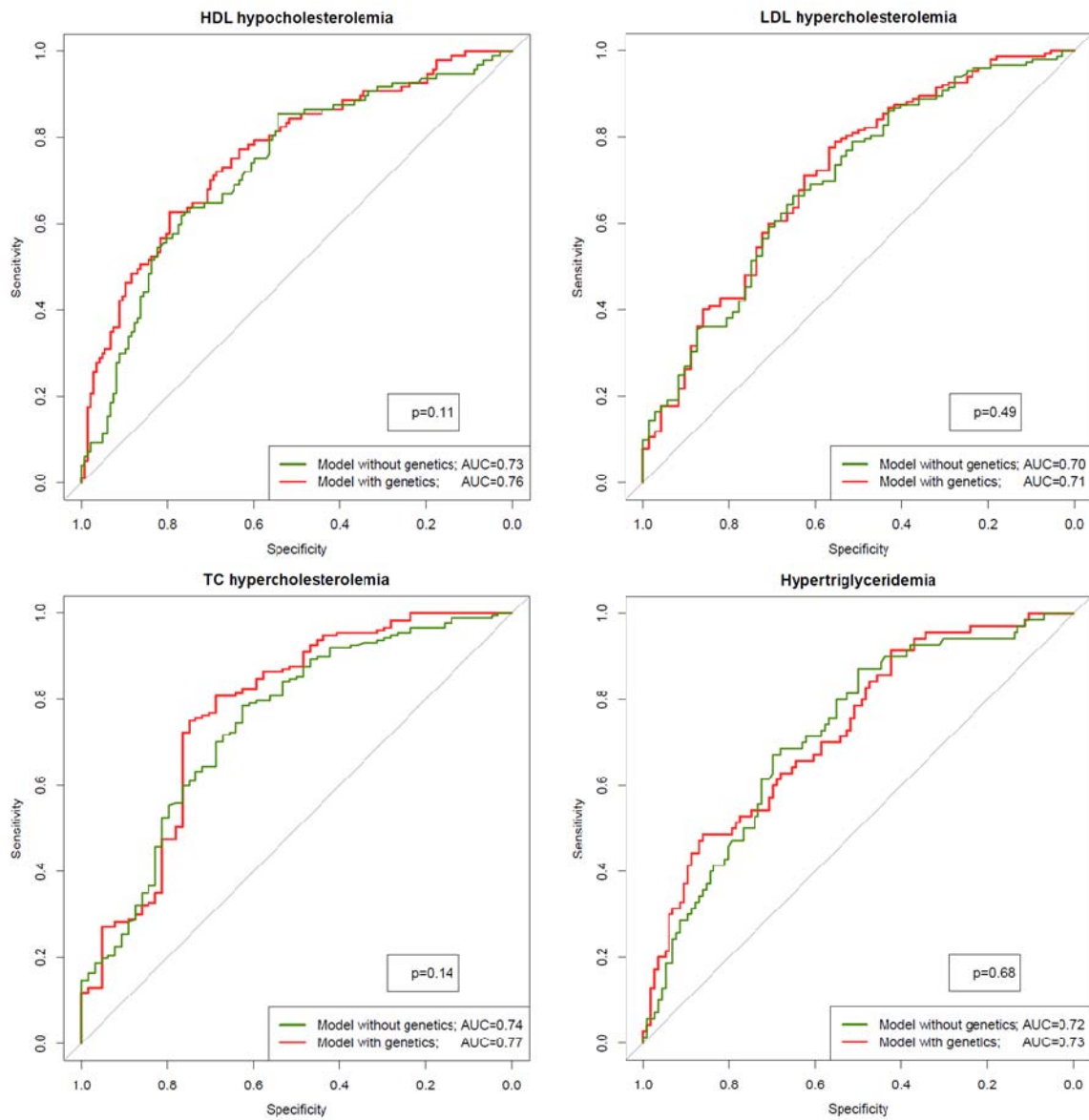
**S14 Figure. Evolution of lipid levels during psychotropic treatment with linear mixed regression: model including only patients younger than the median age of patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Young = patients whose age is younger than the median age of patients. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.



**S15 Figure. Evolution of dyslipidemia prevalence for each lipid trait during psychotropic treatment: plots including only patients older than the median age of patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Old = patients whose age is older than the median age of patients. Numbers of observations are indicated for each barplot. Months were defined as: month [0]: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

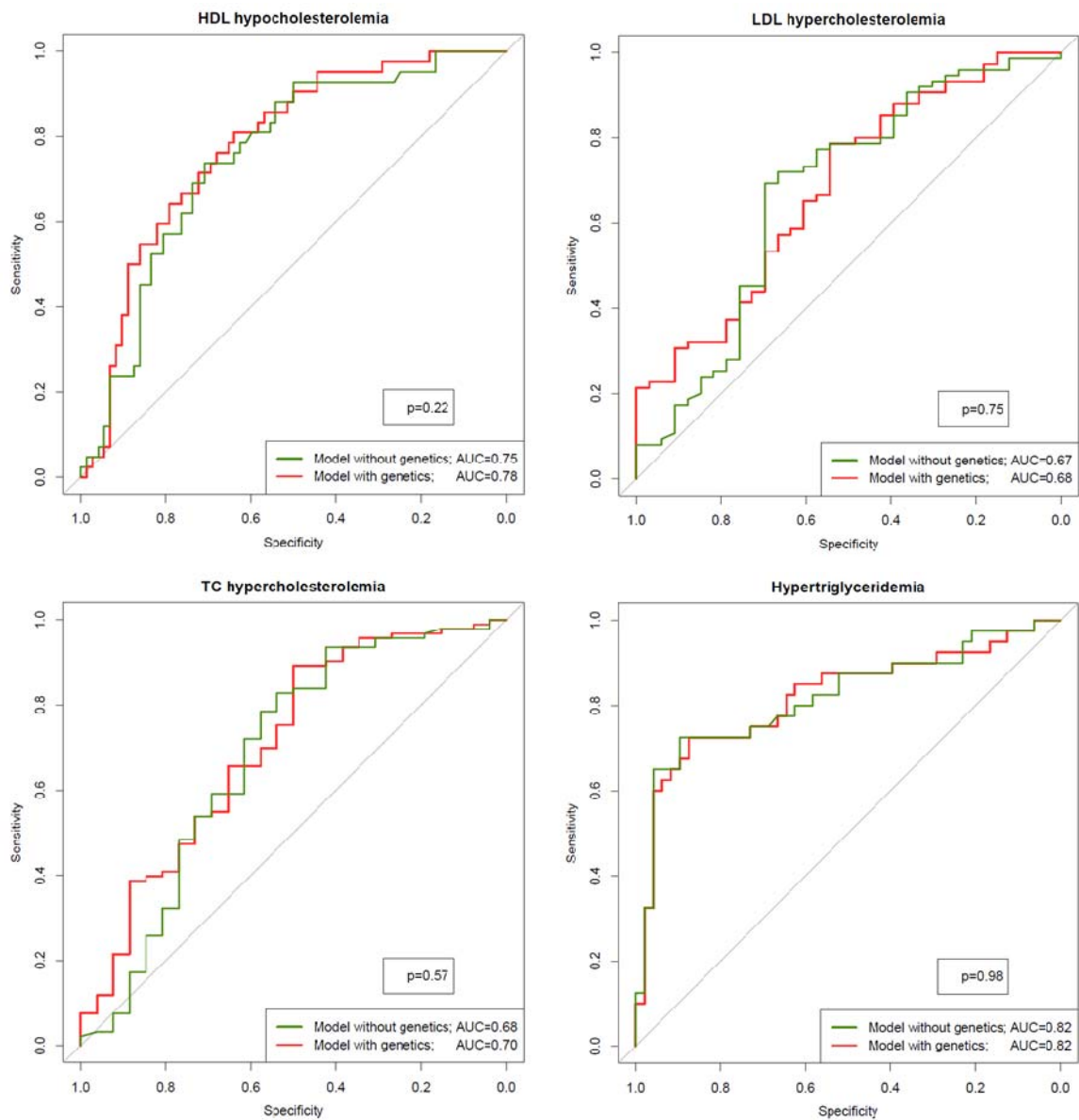


**S16 Figure. Evolution of lipid levels during psychotropic treatment with linear mixed regression: model including only patients older than the median age of patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Old = patients whose age is older than the median age of patients. Patients taking lipid-lowering medication were excluded. Only fasting patients were included for TG analyses.

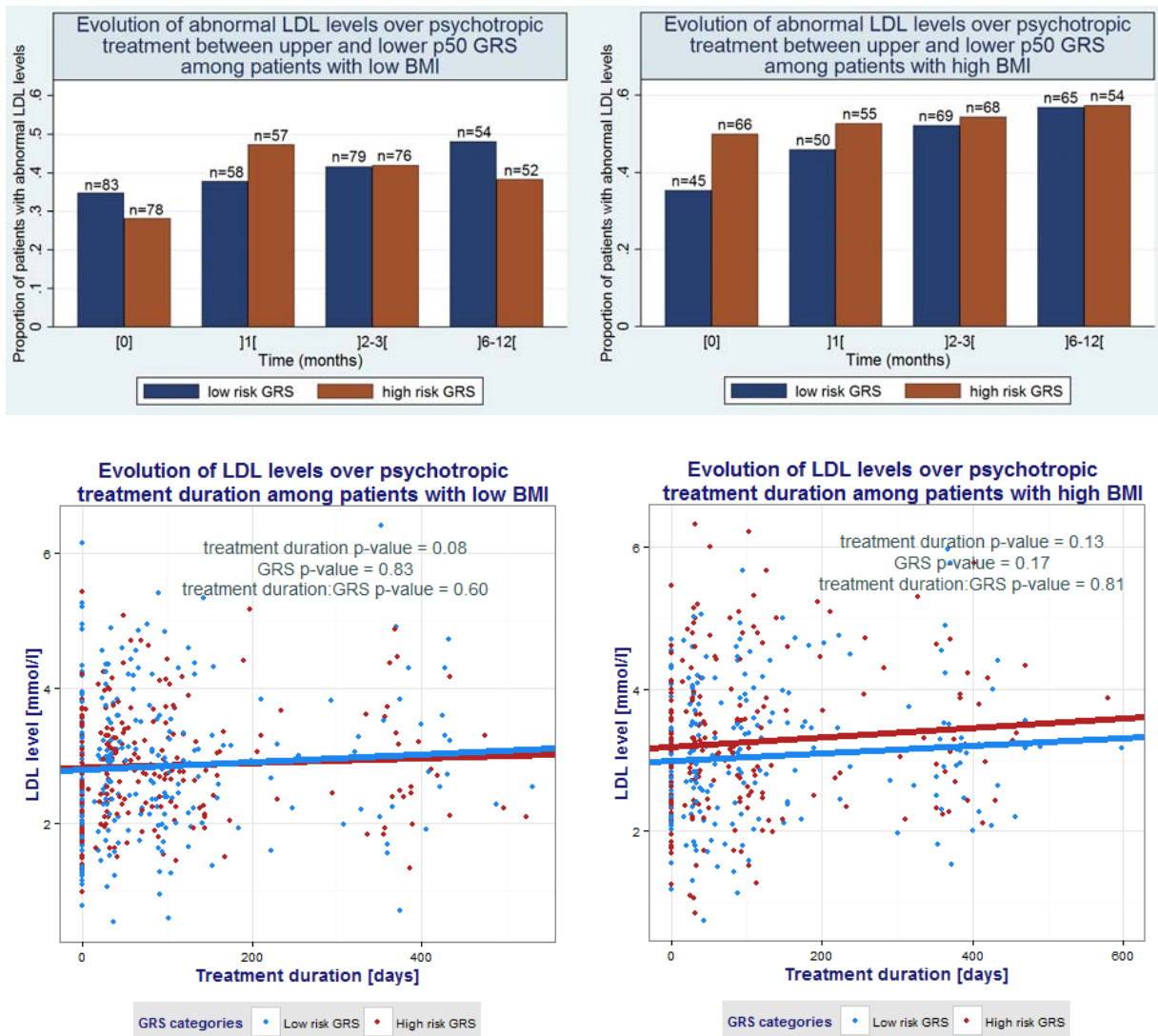


**S17 Figure a. ROC curves for HDL hypocholesterolemia, LDL hypercholesterolemia, total hypercholesterolemia and hypertriglyceridemia in the discovery sample.** The red curves correspond to the model including clinical and genetics components, whereas the green curves include only clinical values. Only fasting patients were included for TG analyses.

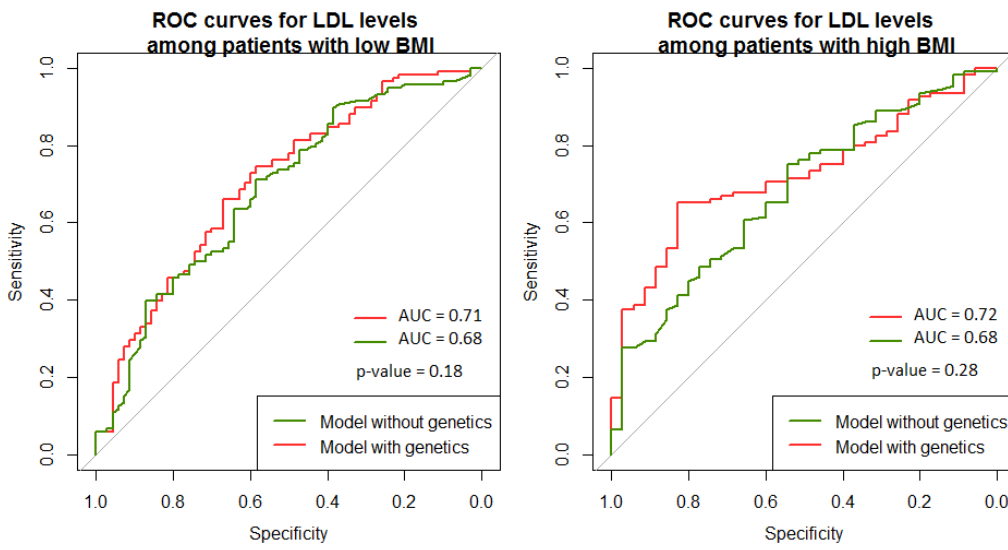




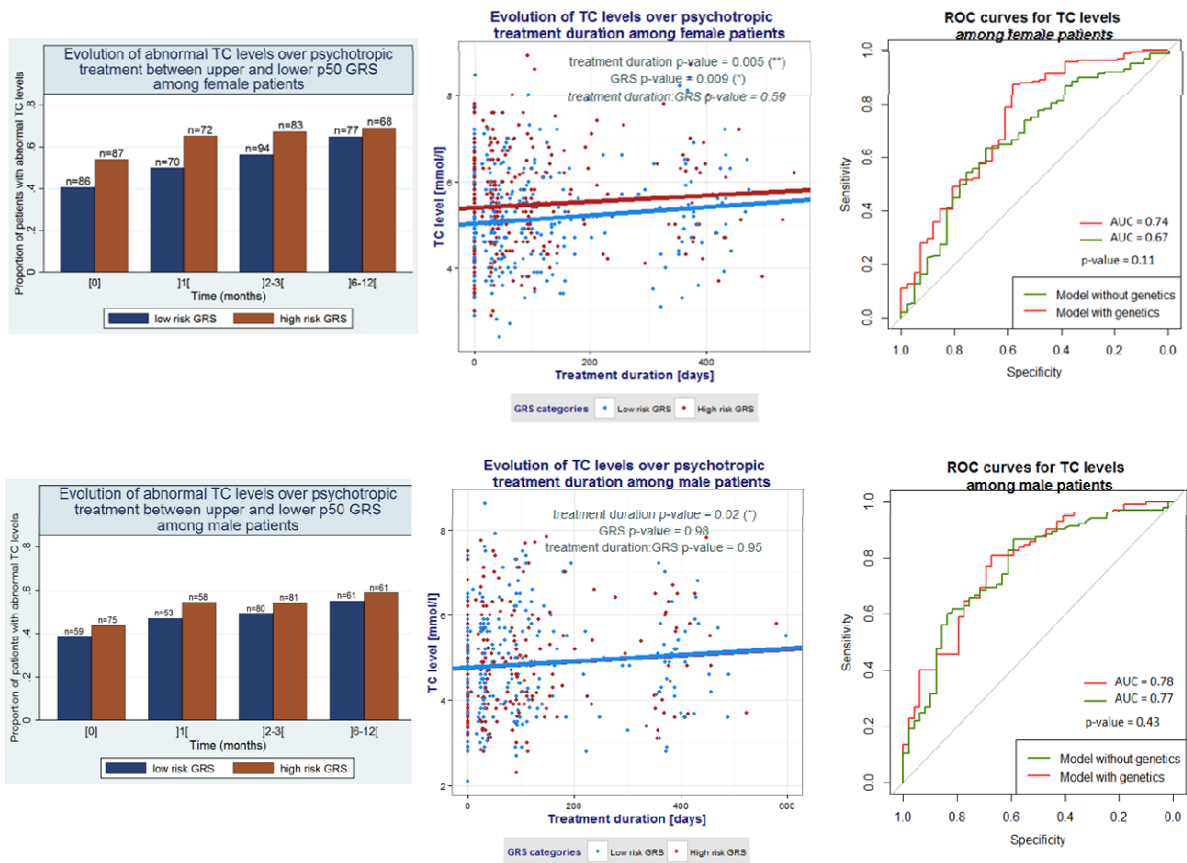
**S17 Figure b.** ROC curves for HDL hypocholesterolemia, LDL hypercholesterolemia, total hypercholesterolemia and hypertriglyceridemia in the replication sample. The red curves correspond to the model including clinical and genetics components, whereas the green curves include only clinical values. Only fasting patients were included for TG analyses.



**S18 Figure. Evolution of dyslipidemia prevalence and lipid levels for LDL during psychotropic treatment: plots including all patients (low BMI patients on the left and high BMI patients on the right). Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Numbers of observations are indicated for each barplot. Months were defined as: month [0]: day 0, month ]1[: ≥10 & <45 days, month ]2-3[: ≥45 & <135 days, month ]6-12[: ≥135 & <535 days. Patients taking lipid-lowering medication were excluded.**



**S19 Figure. LDL ROC curves for combined samples (discovery + replication) among low BMI (left) and high BMI (right) patients.** The red curves correspond to the model including clinical and genetics components, whereas the green curves include only clinical values.



**S20 Figure. Evolution of dyslipidemia prevalence, evolution of TC levels during psychotropic treatment, and ROC curves for abnormal TC levels in female (top) and male (bottom) patients.** Low risk PRS = PRS lower than the median value. High risk PRS = PRS higher than the median value. Numbers of observations are indicated for each barplot. Months were defined as: month ]0[: day 0, month ]1[:  $\geq 10$  &  $< 45$  days, month ]2-3[:  $\geq 45$  &  $< 135$  days, month ]6-12[:  $\geq 135$  &  $< 535$  days. Patients taking lipid-lowering medication were excluded.

## References

1. Doran B, Guo Y, Xu J, Weintraub H, Mora S, Maron DJ, *et al.* Prognostic value of fasting versus nonfasting low-density lipoprotein cholesterol levels on long-term mortality: insight from the National Health and Nutrition Examination Survey III (NHANES-III). *Circulation*. 2014; 130 (7):546-553.
2. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002; 106 (25):3143-3421.
3. Ansermot N, Brawand-Amey M, Kottelat A, Eap CB. Fast quantification of ten psychotropic drugs and metabolites in human plasma by ultra-high performance liquid chromatography tandem mass spectrometry for therapeutic drug monitoring. *Journal of chromatography A*. 2013; 1292:160-172.
4. Choong E, Rudaz S, Kottelat A, Guillarme D, Veuthey JL, Eap CB. Therapeutic drug monitoring of seven psychotropic drugs and four metabolites in human plasma by HPLC-MS. *Journal of pharmaceutical and biomedical analysis*. 2009; 50 (5):1000-1008.
5. Gradinaru J, Vullioud A, Eap CB, Ansermot N. Quantification of typical antipsychotics in human plasma by ultra-high performance liquid chromatography tandem mass spectrometry for therapeutic drug monitoring. *Journal of pharmaceutical and biomedical analysis*. 2014; 88:36-44.
6. Hiemke C, Baumann P, Bergemann N, Conca A, Dietmaier O, Egberts K, *et al.* AGNP Consensus Guidelines for Therapeutic Drug Monitoring in Psychiatry: Update 2011. *Pharmacopsychiatry*. 2011; 44 (6):195-235.
7. Winham SJ, Colby CL, Freimuth RR, Wang X, de Andrade M, Huebner M, *et al.* SNP interaction detection with Random Forests in high-dimensional genetic data. *BMC bioinformatics*. 2012; 13:164.
8. Global Lipids Genetics C, Willer CJ, Schmidt EM, Sengupta S, Peloso GM, Gustafsson S, *et al.* Discovery and refinement of loci associated with lipid levels. *Nature genetics*. 2013; 45 (11):1274-1283.
9. Surakka I, Horikoshi M, Magi R, Sarin AP, Mahajan A, Lagou V, *et al.* The impact of low-frequency and rare variants on lipid levels. *Nature genetics*. 2015; 47 (6):589-597.
10. Ryckman K, Williams SM. Calculation and use of the Hardy-Weinberg model in association studies. *Current protocols in human genetics / editorial board, Jonathan L Haines [et al.]*. 2008; Chapter 1:Unit 1.18.
11. Voight BF, Kang HM, Ding J, Palmer CD, Sidore C, Chines PS, *et al.* The metabochip, a custom genotyping array for genetic studies of metabolic, cardiovascular, and anthropometric traits. *PLoS genetics*. 2012; 8 (8):e1002793.
12. Yang J, Lee SH, Goddard ME, Visscher PM. Genome-wide complex trait analysis (GCTA): methods, data analyses, and interpretations. *Methods in molecular biology (Clifton, NJ)*. 2013; 1019:215-236.
13. Che R, Motsinger-Reif AA. A new explained-variance based genetic risk score for predictive modeling of disease risk. *Statistical applications in genetics and molecular biology*. 2012; 11 (4):Article 15.
14. Belsky DW, Moffitt TE, Sugden K, Williams B, Houts R, McCarthy J, *et al.* Development and evaluation of a genetic risk score for obesity. *Biodemography and social biology*. 2013; 59 (1):85-100.
15. Hung CF, Breen G, Czamara D, Corre T, Wolf C, Kloiber S, *et al.* A genetic risk score combining 32 SNPs is associated with body mass index and improves obesity prediction in people with major depressive disorder. *BMC medicine*. 2015; 13:86.

16. Rukh G, Ahmad S, Ericson U, Hindy G, Stocks T, Renstrom F, *et al.* Inverse relationship between a genetic risk score of 31 BMI loci and weight change before and after reaching middle age. *International journal of obesity* (2005). 2016; 40 (2):252-259.
17. R Development Core Team. R: A language and environment for statistical computing Vienna, Austria: R Foundation for Statistical Computing 2013.
18. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology*. 1983; 148 (3):839-843.
19. Hajian-Tilaki K. Receiver Operating Characteristic (ROC) Curve Analysis for Medical Diagnostic Test Evaluation. *Caspian journal of internal medicine*. 2013; 4 (2):627-635.
20. Janssens AC, Moonesinghe R, Yang Q, Steyerberg EW, van Duijn CM, Khoury MJ. The impact of genotype frequencies on the clinical validity of genomic profiling for predicting common chronic diseases. *Genetics in medicine : official journal of the American College of Medical Genetics*. 2007; 9 (8):528-535.
21. De Hert M, Detraux J, van Winkel R, Yu W, Correll CU. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. *Nature reviews Endocrinology*. 2012; 8 (2):114-126.
22. Kar D, Gillies C, Zaccardi F, Webb D, Seidu S, Tesfaye S, *et al.* Relationship of cardiometabolic parameters in non-smokers, current smokers, and quitters in diabetes: a systematic review and meta-analysis. *Cardiovascular diabetology*. 2016; 15 (1):158.
23. Tada H, Melander O, Louie JZ, Catanese JJ, Rowland CM, Devlin JJ, *et al.* Risk prediction by genetic risk scores for coronary heart disease is independent of self-reported family history. *European heart journal*. 2016; 37 (6):561-567.
24. Delacretaz A, Preisig M, Vandenberghe F, Saigi Morgui N, Quteineh L, Choong E, *et al.* Influence of MCHR2 and MCHR2-AS1 Genetic Polymorphisms on Body Mass Index in Psychiatric Patients and In Population-Based Subjects with Present or Past Atypical Depression. *PloS one*. 2015; 10 (10):e0139155.
25. Choong E, Quteineh L, Cardinaux JR, Gholam-Rezaee M, Vandenberghe F, Dobrinas M, *et al.* Influence of CRT1 polymorphisms on body mass index and fat mass in psychiatric patients and the general adult population. *JAMA psychiatry*. 2013; 70 (10):1011-1019.
26. Buscot MJ, Magnussen CG, Juonala M, Pitkanen N, Lehtimaki T, Viikari JS, *et al.* The Combined Effect of Common Genetic Risk Variants on Circulating Lipoproteins Is Evident in Childhood: A Longitudinal Analysis of the Cardiovascular Risk in Young Finns Study. *PloS one*. 2016; 11 (1):e0146081.
27. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, *et al.* 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Journal of hypertension*. 2013; 31 (7):1281-1357.