HRS Documentation Report

HRS Polygenic Scores – Release 4.3
2006-2012 Genetic Data

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I. Introduction

This guide describes the construction of polygenic scores (PGSs) for a variety of phenotypes for HRS respondents who provided salivary DNA between 2006 and 2012. These scores serve as an attempt to harmonize research across studies and facilitate use among HRS data users by making these scores available publicly. PGSs for each phenotype are based on a single, replicated genome-wide association study (GWAS). These scores will be updated as sufficiently large GWAS are published for new phenotypes or as meta-analyses for existing phenotypes are updated. This document describes the general method of construction with details on each phenotype included as appendices.

A. Rationale

Complex health outcomes or behaviors of interest to the research community are often highly polygenic, or reflect the aggregate effect of many different genes so the use of single genetic variants or candidate genes may not capture the dynamic nature of more complex phenotypes. A PGS aggregates thousands to millions of individual loci across the human genome and weights them by effect sizes derived from a GWAS as an estimate of the strength of their association to produce a single quantitative measure of genetic risk and to increase power in genetic analyses.

B. Sample Selection for the Enhanced Face-to-Face Interview

In 2006, HRS initiated what is referred to as an Enhanced Face-to-Face Interview (EFTF). In addition to the core interview, the EFTF interview includes a set of physical performance tests, anthropometric measurements, blood and saliva samples, and self-administered questionnaire on psychosocial topics. Approximately fifty percent of households with at least one living respondent were selected for the EFTF interview across all primary sampling units (PSUs). A random one half of the 2006 sample was preselected to the EFTF interview. The other half was selected in 2008. Similarly, new cohort households for 2010 were randomly assigned into one of these two groups with EFTF data collection beginning in 2010 or 2012. The sample was selected at the household-level to ensure that the same request was made to both members of a household. New spouses of respondents flagged to complete an EFTF interview were also asked to do so. Thus, in coupled households, both members of the couple were selected. Some respondents who were selected for the enhanced face-to-face sample were not asked to complete the physical measures or biomarkers. This group included respondents who a) needed to be interviewed by proxy, b) resided in a nursing home, or c) declined a face-to-face interview but agreed to be interviewed by telephone. The preload variable that identifies the EFTF sample is KX090_R for 2006, LX090_R for 2008, MX090_R for 2010, and NX090_R for 2012 (located in the respondent preload file for each wave), for which a value of 3 indicates that the respondent was assigned to the EFTF sample for that wave. The variable EFTFASSIGN in the Cross-wave Tracker file indicates the respondents' permanent assignment for enhanced face-to-face rotation for 2006 and beyond.

C. Consent and Administration Procedures

Prior to administering the saliva collection, a consent form was administered by the interviewer. Respondents were asked to read and sign the form. Respondents who did not sign the consent form were not asked to complete the collection. Respondents were instructed not to eat, drink, smoke, chew gum or brush their teeth during this component of the interview (at least 30 mins prior to saliva collection). In 2006, saliva was collected using a mouthwash collection method. In 2008 and beyond, the data collection method switched to the Oragene DNA Collection Kit (OG-250). [1]

[1] More information on the saliva collection protocol can be found here:

Crimmins EM, Faul JD, Kim JK, et al. *Documentation of Biomarkers in the 2006 and 2008 Health and Retirement Study*. Ann Arbor, Michigan: Institute for Social Research, University of Michigan; 2013.
Crimmins EM, Faul JD, Kim JK, Weir DR. *Documentation of Biomarkers in the 2010 and 2012 Health and Retirement Study*. Ann Arbor, Michigan: Survey Research Center, University of Michigan; 2015.

II. HRS Genomic Data

Genotyping was conducted by the Center for Inherited Disease Research (CIDR) in 2011, 2012, and 2015 (RC2 AG0336495 and RC4 AG039029). Genotype data on over 19,000 HRS participants was obtained using the Illumina HumanOmni2.5 BeadChips (HumanOmni2.5-4v1, HumanOmni2.5-8v1, HumanOmni2.5-8v1.1), which measures ~2.4 million SNPs. Individuals with missing call rates >2%, SNPs with call rates <98%, HWE p-value < 0.0001, chromosomal anomalies, and first degree relatives in the HRS were removed. For more information on the genotype data and quality control process see the QC Report.

Imputation to the 1000 Genomes Project cosmopolitan reference panel phase 3 version 5 (initial release on May 2013, haplotypes released Oct 2014) was performed by the University of Michigan using Minimac3 (http://genome.sph.umich.edu/wiki/Minimac3), with phasing performed using SHAPEIT2. Overall, ~21 million SNPs were imputed from the original 1,905,968 SNPs that were genotyped and passed quality control. Masking of genotyped SNPs to assess the accuracy of imputation was performed to estimate the median concordance between actual and imputed genotypes (median concordance>0.995), and additional quality control metrics indicate high quality imputation.

Principal component (PC) analysis was performed to identify population group outliers and to provide sample eigenvectors as covariates in the statistical model used for association testing to adjust for possible population stratification. SNPs used for PC analysis were selected by linkage disequilibrium (LD) pruning from an initial pool consisting of all autosomal SNPs with a missing call rate < 5% and minor allele frequency (MAF) > 5%, and excluding any SNPs with a discordance between HapMap controls genotyped along with the study samples and those in the external HapMap data set. In addition, the 2q21 (LCT), HLA, 8p23, and 17q21.31 regions were excluded from the initial pool. Genetic ancestry in HRS was identified through PC analysis on genome-wide SNPs calculated across all participants using the aforementioned filtering criteria.

The final European American sample includes all self-reported non-Hispanic whites that had PC loadings within ± one standard deviations of the mean for eigenvectors 1 and 2 in the PC analysis of all unrelated study subjects. The final African American sample includes all self-reported African Americans within two standard deviations of the mean of all self-identified African Americans for eigenvector 1 and ± one standard deviation of the mean for eigenvector 2 in the PC analysis of all unrelated study subjects. Once ancestry-specific analysis samples were identified (n=3,100 non-Hispanic Black, n=12,090 non-Hispanic White), PCA was run again within each sample to create sample eigenvectors for covariates in the statistical model used for association testing to adjust for possible population stratification. These are referred to as “ancestry-specific PCs”.

A. PGS Construction

While conceptually simple, there are numerous ways to estimate PGSs, not all achieving the same end goals. We systematically investigated the impact of four key decisions in the building of PGSs from published genome-wide association meta-analysis results: 1) whether to use single nucleotide polymorphisms (SNPs) assessed by imputation, 2) criteria for selecting which SNPs to include in the score, 3) whether to account for linkage disequilibrium (LD), and 4) if accounting for LD, which type of method best captures the correlation structure among SNPs (i.e. clumping vs. pruning). Using the Health and Retirement Study (HRS) we examined the predictive ability as well as the variability and co-variability in PGSs arising from these different estimation approaches.[2]

Overall, results from these analyses concluded that including all available SNPs in a PGS (i.e. not accounting for any LD or p-value thresholding) either demonstrated the largest predictive power (incremental R^2) of the score or produced a score that did not differ significantly from scores with similar predictive power that employed

[2] For additional information on this analysis, see:
Ware EB, Schmitz LL, Faul JD, Gard AM, Smith JA, Mitchell CM, Weir DR, Kardia SLR. (2017) *Method of Construction Affects Polygenic Score Prediction of Common Human Traits*. BiorXiv. 2017 doi: https://doi.org/10.1101/106062

some degree of LD trimming or p-value thresholding. Thus, the HRS has chosen to provide scores that include all available SNPs in the PGS that overlap between the GWAS meta-analysis and the HRS genetic data.

Weighted sums were chosen to calculate the PGSs. Weights were defined by the odds ratio or beta estimate from the GWAS meta-analysis files corresponding to the phenotype of interest. If the beta value from the GWAS meta-analysis was negative (or the odds ratio (OR) < 1), the beta/OR measures were converted to positive values (OR > 1) and the reference allele flipped to represent phenotype-increasing PGSs. PGSs are calculated using the following formula:

$$PGS_i = \sum_{j=1}^{J} W_j G_{ij}$$

where *i* is individual *i* (i=1 to N), *j* is SNP *j* (j=1 to J), *W* is the meta-analysis effect size for SNP *j* and *G* is the genotype, or the number of reference alleles (zero, one, or two), for individual *i* at SNP *j*. Due to the long-range linkage disequilibrium in this region, making linkage equilibrium difficult to obtain, the MHC region on chromosome 6 (26-33Mb) was omitted from all PGSs. Missing data was imputed within ancestry using the expected genotyped given the allele frequency. Scores were similar when not employing the missing data imputation default. PGSs were calculated using PRSIce and PLINK.

B. Sources for SNP weights

To incorporate externally valid SNP weights from replicated GWAS, we performed a search of the literature to identify large GWAS meta-analysis studies related to the selected phenotype. Where possible, meta-analyses that did not include the HRS in the discovery analysis were selected to be independent of our data. SNP weights were downloaded from consortium webpages, requested from consortium authors, obtained from dbGap, or taken from published supplemental material. If the HRS was included in the analyses, we requested that the consortia repeat the analysis with the HRS removed. All base SNP files from GWAS meta-analyses were converted to NCBI build 37 annotation for compatibility with HRS SNP data.

C. Notes about the use of PGSs

PGSs are released for both the European ancestry and African ancestry groups, separately. **However, it should be noted that the majority of GWAS used to inform the SNP weights come from GWAS on European ancestry groups and, as a result, PGSs for other ancestry groups may not have the same predictive capacity (Martin et al. 2017; Ware et al. 2017).**

Ancestry specific PCs 1-10 are included for each group. PCs 1-5 and PCs 6-10 are randomly labeled within each PC set to help reduce identifiability. To control for confounding from population stratification, or to account for any ancestry differences in genetic structures within populations that could bias estimates, **we highly recommend that users perform analyses separately by ancestral group and, at the very least, adjust for PCs 1-5**. The PCs control for any genetic aspects of common ancestry that could be spuriously correlated with the PGS and the outcome of interest (Price et al., 2006).

References

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Martin, A. R., Gignoux, C. R., Walters, R. K., Wojcik, G. L., Neale, B. M., Gravel, S., ... & Kenny, E. E. (2017). Human demographic history impacts genetic risk prediction across diverse populations. *The American Journal of Human Genetics*, *100*(4), 635-649.

Price, A. L., Patterson, N. J., Plenge, R. M., Weinblatt, M. E., Shadick, N. A., & Reich, D. (2006). Principal components analysis corrects for stratification in genome-wide association studies. *Nature genetics, 38*(8), 904-909.

Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M. A., Bender, D., . . . Daly, M. J. (2007). PLINK: a tool set for whole-genome association and population-based linkage analyses. *The American Journal of*

Human Genetics, 81(3), 559-575. Ware EB, Schmitz LL, Faul JD, Gard AM, Smith JA, Mitchell CM, Weir DR, Kardia SLR. (2017) Method of Construction Affects Polygenic Score Prediction of Common Human Traits. BiorXiv. 2017 doi: https://doi.org/10.1101/106062

Ware EB, Schmitz LL, Faul JD, Gard AM, Smith JA, Mitchell CM, Weir DR, Kardia SLR. (2017). Method of Construction Affects Polygenic Score Prediction of Common Human Traits. BiorXiv. 2017 doi: https://doi.org/10.1101/106062

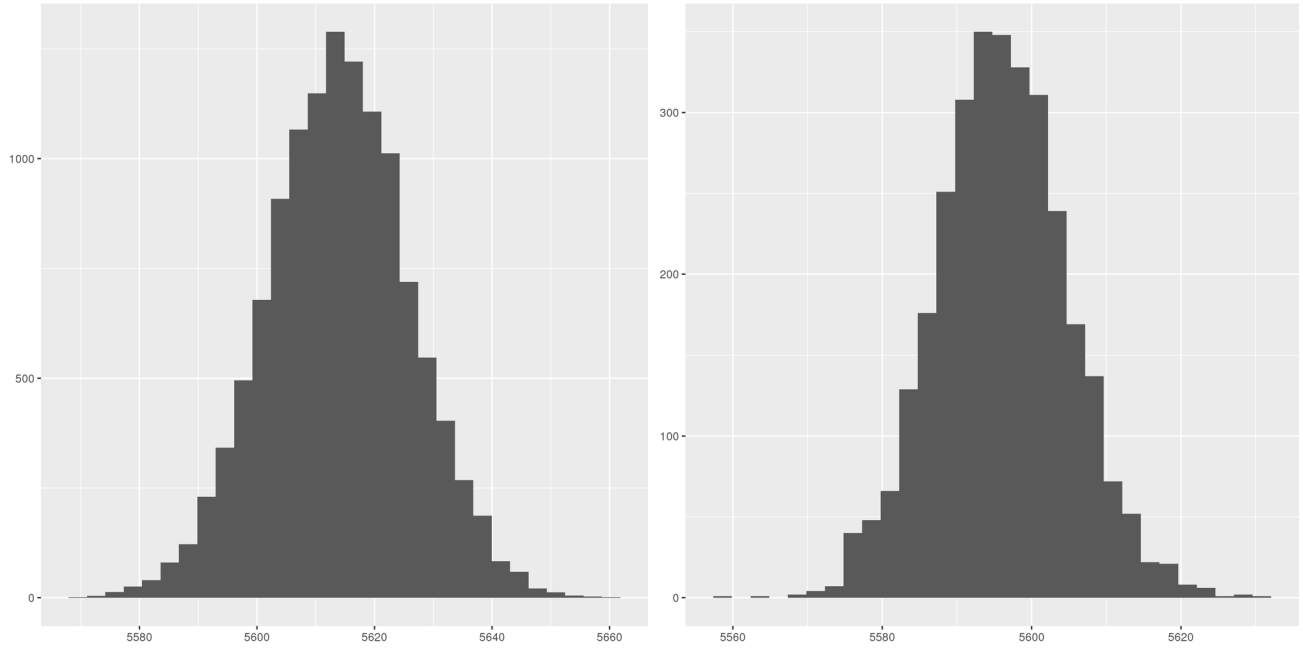
D. Educational Attainment 2 – Social Science Genetic Association Consortium 2016

OUTDATED – INCLUDED FOR POSTERITY: The educational attainment PGSs were created using results from a 2016 study by the Social Science Genetic Association Consortium (SSGAC). The meta-analysis included 293,723 individuals in the discovery sample and 111,349 in replication. Genome-wide significant SNPs were identified in 74 loci (**Supplementary Information section 1.6.1** [1]). Approximately 9.3 million SNPs were included in the analyses, with all cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G). The original GWAS included the HRS. To compute the PGSs for HRS respondents, the SSGAC provided SNP weights with the HRS and 23andMe results removed (due to data use agreements, combined discovery + replication sample size without HRS: N=395,109). Study-specific GWASs controlled for the first ten principal components of the genotypic data, a third-order polynomial in age, an indicator for being female, interactions between age and female, and study-specific controls, including dummy variables for major events such as wars or policy changes that may have affected access to education in their specific sample.

The European ancestry PGSs contain 1,309,267 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,304,335 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication. Included SNPs and weights are avaialable upon request.
Please note that the SSGAC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).
Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	5569.26	5660.05	90.79	5613.99	5613.92	0.11
African ancestry	3100	5559.34	5631.53	72.19	5596.04	5596.06	0.16



European ancestry: Dist. of E4_EDU2_SSGAC16 African ancestry: Dist. of A4_EDU2_SSGAC16

References

Okbay, A., Beauchamp, J. P., Fontana, M. A., Lee, J. J., Pers, T. H., Rietveld, C. A., ... & Oskarsson, S. (2016). Genome-wide association study identifies 74 loci associated with educational attainment. *Nature*, *533*(7604), 539.

E. Height – Genetic Investigation of ANthropometric Traits 2014

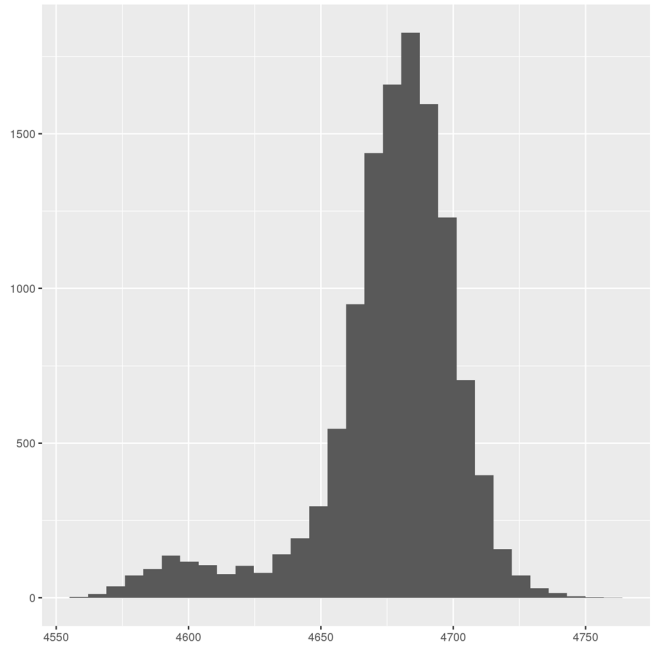
OUTDATED – INCLUDED FOR POSTERITY: PGSs for height were created using results from a 2014 study conducted by the Genetic Investigation of ANthropometric Traits (GIANT) consortium. The GWAS meta-analysis files are publicly available on their data download page: https://www.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium_data_files (GIANT HEIGHT Wood et al 2014 publicrelease HapMapCeuFreq.txt.gz). The GIANT height meta-analysis included 253,288 individuals from 79 studies imputed to HapMap II with a total of 2,550,858 SNPs. Replication was performed in a sample of 80,067 individuals. Height was measured as sex standardized height and participating studies adjusted for age and genetic principal components in their GWASs. There were 697 genome-wide significant SNPs reported (**Supplementary Table 1**).

The European ancestry PGSs contain 800,528 SNPs SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 781,900 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

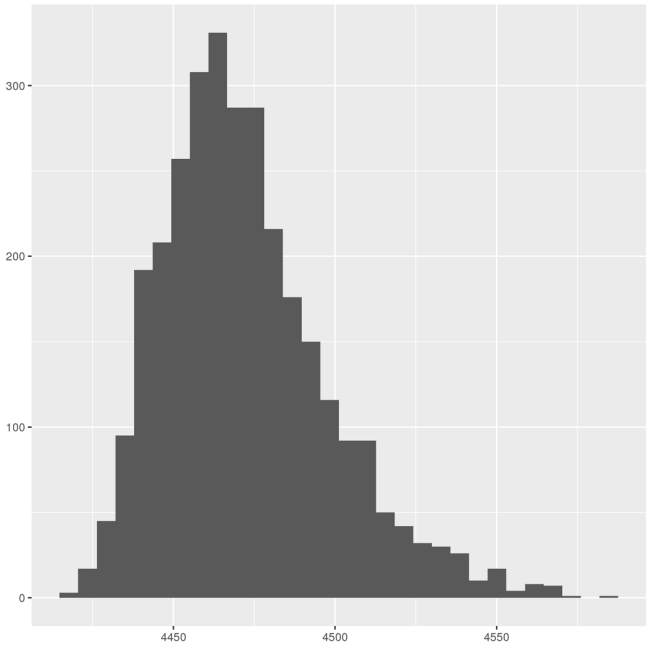
N.B.: **Please note that the GIANT results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	4555.47	4757.30	201.83	4680.30	4675.93	0.24
African ancestry	3100	4415.84	4582.87	167.03	4468.41	4472.29	0.46



European ancestry: Dist. of E4_Height_GIANT14



African ancestry: Dist. of A4_Height_GIANT14

References

Wood, A. R., Esko, T., Yang, J., Vedantam, S., Pers, T. H., Gustafsson, S., ... & Amin, N. (2014). Defining the role of common variation in the genomic and biological architecture of adult human height. *Nature Genetics*, *46*(11), 1173-1186.

F. Body Mass Index (BMI) – Genetic Investigation of ANthropometric Traits 2015

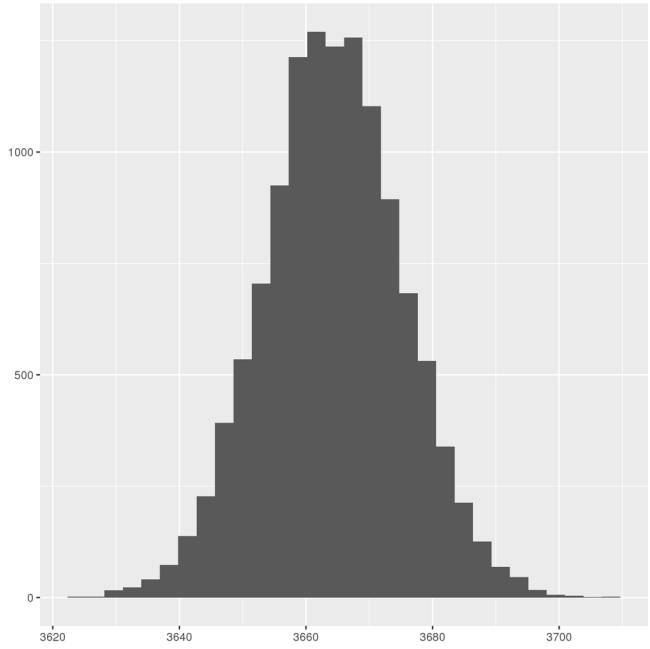
OUTDATED – INCLUDED FOR POSTERITY: PGSs for BMI were created using results from a 2015 GWAS conducted by the Genetic Investigation of ANthropometric Traits (GIANT) consortium. The GWAS meta-analysis files are publicly available on their data download page: https://www.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium_data_files (Download BMI EUR Ancestry GZIP: SNP gwas mc merge nogc.tbl.uniq.gz). GWAS meta-analysis was performed on a sample of 234,069 individuals from 80 studies across 2,550,021 SNPs, and separately in a Metabochip (MC) meta-analysis on a sample of 88,137 individuals from 34 studies across 156,997 SNPs. A joint GWAS and MC meta-analysis was then conducted on 332,154 individuals across 2,554,623 SNPs. Adjustment covariates within each contributing cohort GWAS included age, age^2, sex, and genetic principal components. A total of 97 SNPs were reported as genome-wide significant (**Table 1 and 2 and Extended Data Table 2**).

The European ancestry PGSs contain 761,985 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 766,424 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

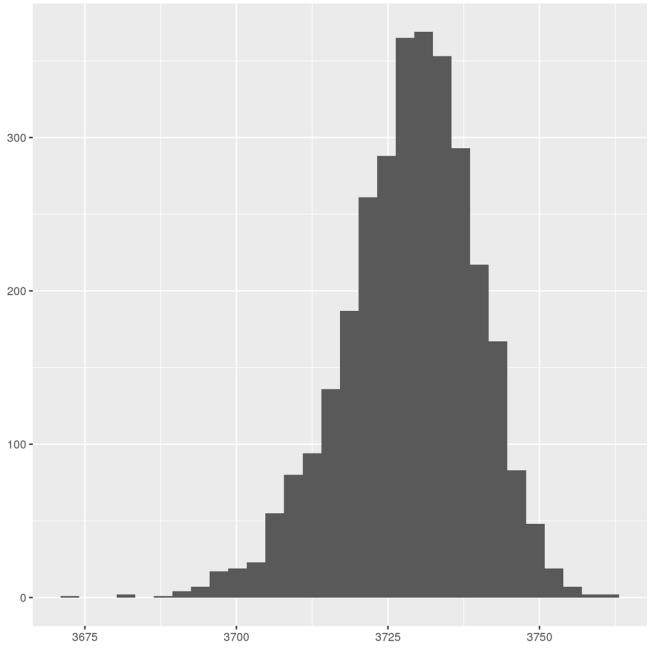
N.B.: These weights are from the joint analysis of GWAS and MC meta-analysis conducted on 332,154 individuals. HRS is included in this sample but comprises <3% of the total sample.
Please note that the GIANT results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	3624.50	3708.91	84.41	3664.22	3664.29	0.10
African ancestry	3100	3672.69	3761.74	89.05	3729.47	3728.62	0.20



European ancestry: Dist. of E4_BMI_GIANT15



African ancestry: Dist. of A4_BMI_GIANT15

References

Locke, A. E., Kahali, B., Berndt, S. I., Justice, A. E., Pers, T. H., Day, F. R., ... & Croteau-chonka, D. C. (2015). Genetic studies of body mass index yield new insights for obesity biology. *Nature*, *518*(7538), 197-206.

G. Waist Circumference and Waist-to-Hip Ratio – Genetic Investigation of ANthropometric Traits 2015

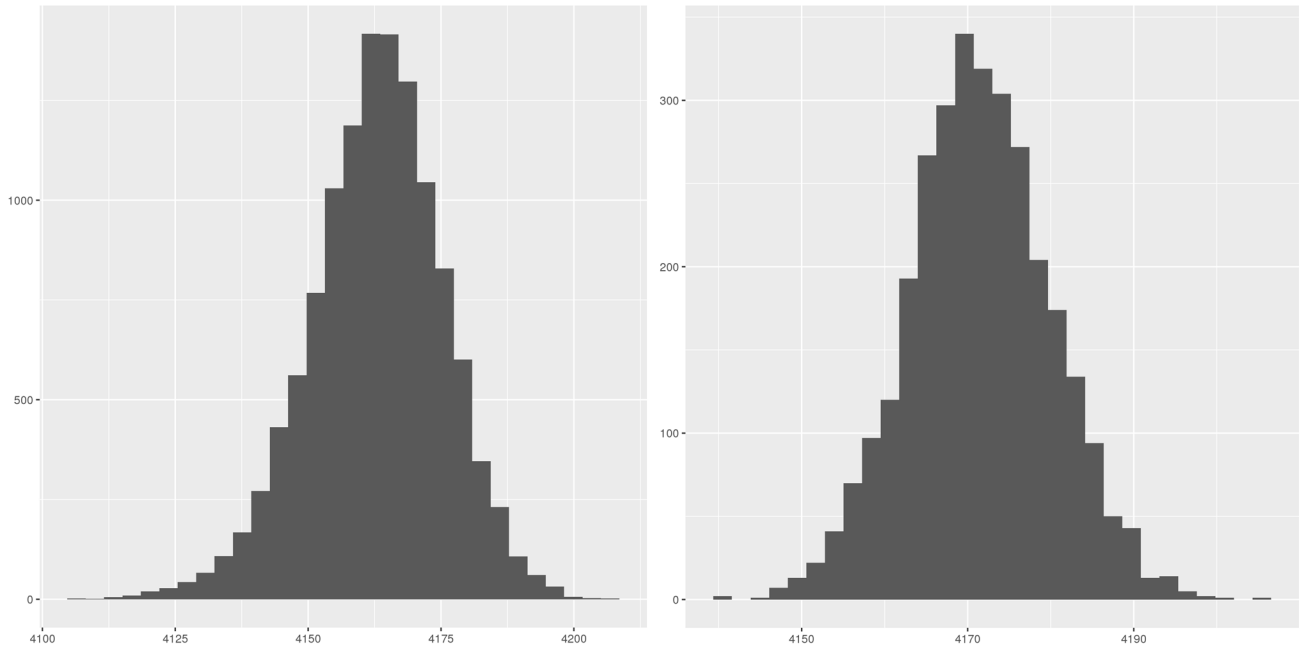
PGSs for waist circumference (WC) and waist-to-hip ratio (WHR) were created using results from a 2015 study conducted by the Genetic Investigation of ANthropometric Traits (GIANT) consortium. The GWAS meta-analysis files are publicly available on their data download page: https://www.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium_data_files (WC: GIANT 2015 WC COMBINED EUR.txt.gz, WHR: GIANT 2015 WHR COMBINED EUR.txt.gz).
GWAS meta-analysis was performed on a sample of 142,762 individuals from 57 studies across 2,507,022 SNPs, and separately in a Metabochip (MC) meta-analysis on a sample of 67,326 individuals from 44 studies across 124,196 SNPs. A joint GWAS and MC meta-analysis was then conducted on 210,088 individuals across 93,057 SNPs. The GWAS identified 49 loci associated with WHR and an additional 19 loci associated with WC at the genome-wide significance level (**Table 1**). Association analyses adjusted for age, age^2, study-specific covariates if necessary, and BMI.

The European ancestry PGSs for WC contain 765,699 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 764,462 SNPs. European ancestry PGSs for WHR contain 763,849 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs for WHR contain 762,193 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

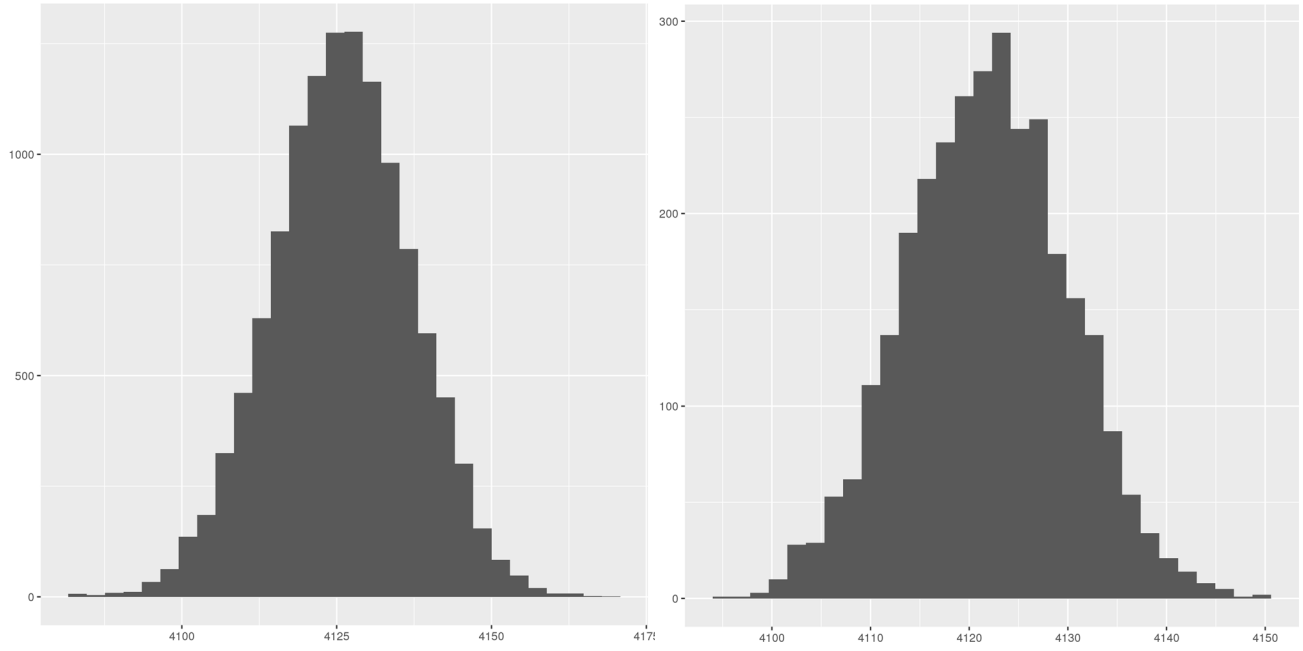
N.B.: These weights are from the joint analysis of GWAS and MC meta-analysis conducted on 210,088 individuals.
Please note that the GIANT results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Waist circumference						
	Sample Size	**Minimum**	**Maximum**	**Range**	**Median**	**Mean**	**SE (Mean)**
European ancestry	12090	4106.73	4207.14	100.41	4163.39	4162.86	0.11
African ancestry	3100	4140.13	4205.07	64.94	4171.38	4171.47	0.15
	Waist-to-Hip-ratio						
	Sample Size	**Minimum**	**Maximum**	**Range**	**Median**	**Mean**	**SE (Mean)**
European ancestry	12090	4082.30	4168.48	86.18	4125.87	4125.78	0.10
African ancestry	3100	4094.15	4148.85	54.70	4121.92	4121.78	0.15



European ancestry: Dist. of E4_WC_GIANT15 African ancestry: Dist. of A4_WC_GIANT15



European ancestry: Dist. of E4_WHR_GIANT15 African ancestry: Dist. of A4_WHR_GIANT15

References

Shungin, D., Winkler, T. W., Croteau-Chonka, D. C., Ferreira, T., Locke, A. E., Mägi, R., ... & Workalemahu, T. (2015). New genetic loci link adipose and insulin biology to body fat distribution. *Nature*, *518*(7538), 187.

H. Blood Pressure: Diastolic Blood Pressure (DBP), Systolic Blood Pressure (SBP), Pulse Pressure (PP), and Mean Arterial Pressure (MAP)

The PGSs for blood pressure have been removed from the second release of the PGSs due to a corruption of the Beta weights from the ICBP consortia. We are working on obtaining correct Beta weights but have not received them in time for this release of PGSs. **Please do not use the first version of the blood pressure PGSs**.

References

Ehret, G. B., Munroe, P. B., Rice, K. M., Bochud, M., Johnson, A. D., Chasman, D. I., ... & Okamura, T. (2011). Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. *Nature*, *478*(7367), 103-109.

Wain, L. V., Verwoert, G. C., O'Reilly, P. F., Shi, G., Johnson, T., Johnson, A. D., ... & Ehret, G. B. (2011). Genome-wide association study identifies six new loci influencing pulse pressure and mean arterial pressure. *Nature Genetics*, *43*(10), 1005-1011.

I. Alzheimer's Disease - International Genomics of Alzheimer's Project 2013

OUTDATED – INCLUDED FOR POSTERITY: The PGSs for Alzheimer's disease (AD) were created using results from a 2013 GWAS conducted by the International Genomics of Alzheimer's Project (IGAP): http://web.pasteur-lille.fr/en/recherche/u744/igap/igap_download.php. A GWAS meta-analysis of AD was conducted across 20 independent studies using data from four international consortia: Alzheimer 's Disease Genetic Consortium (ADGC), the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, the European Alzheimer's Disease Initiative (EADI), and the Genetic and Environmental Risk in Alzheimer's Disease (GERAD) Consortium. The stage 1 meta-analysis included 54,162 participants (N_{cases}=17,008 and $N_{controls}$=37,154) of European decent with a total of 7,055,881 SNPs imputed to 1000 Genomes (2010 release). The stage 2 replication sample included 19,884 participants of European ancestry (N_{cases}=8,572 and $N_{controls}$=11,312) with a total of 11,632 genotyped SNPs. In addition to the *APOE* locus (encoding apolipoprotein E), the two-stage combined discovery and replication GWAS revealed 19 SNPs that reached genome-wide significant associations with AD (**Table 2**). Adjustment covariates within each contributing cohort included age, sex, and genetic principal components.

The European ancestry PGSs contain 1,145,019 (1,145,021, adding the two ApoE status variants) SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,159,040 (1,159,042) SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

N.B.: There are TWO AD scores published here representing PGS with and without the two variants that contribute to ApoE status (rs7412, rs429358). The correlation between the two scores is 0.99992 for the European Ancestry sample and 0.99995 for the African Ancestry sample.

1) using genotyped data only, not including the ApoE status variants; and
2) using genotyped data, including the imputed ApoE status variants

Please note that the IGAP results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

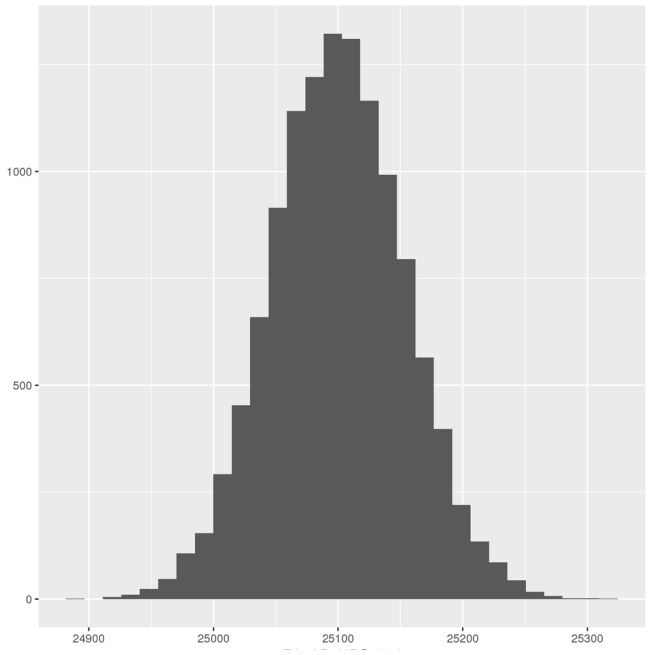
Raw PGS details are presented below.

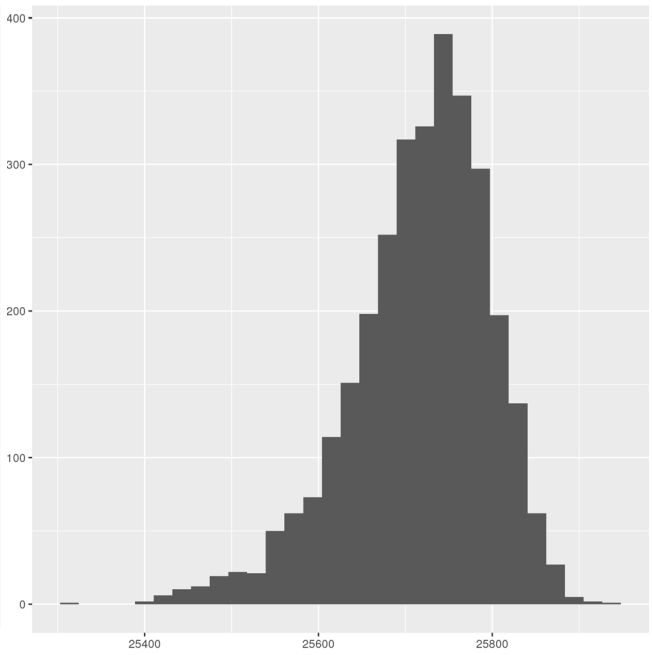
Alzheimer's Disease PGS without ApoE status variants (rs7412, rs429358)

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	24889.60	25317.20	427.60	25099.80	25099.94	0.48
African ancestry	3100	25321.70	25945.40	623.70	25727.50	25716.50	1.45

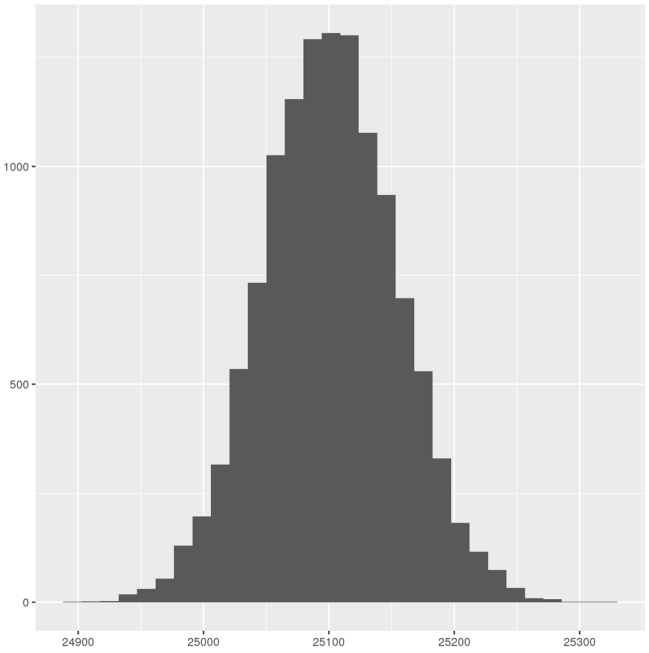
Alzheimer's Disease PGS with ApoE status variants (rs7412, rs429358)

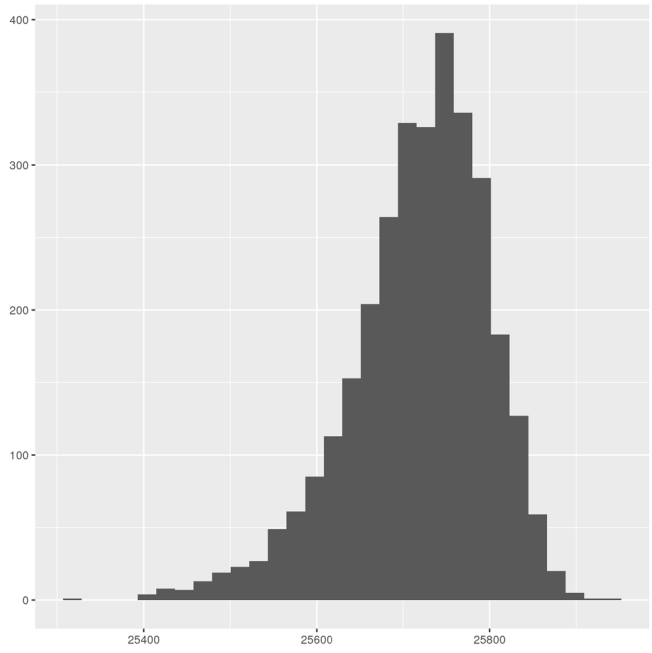
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	24890.40	25317.60	427.20	25100.80	25101.00	0.48
African ancestry	3100	25322.40	25946.20	623.80	25728.65	25717.70	1.45





European ancestry: Dist. of E4_AD_IGAP13 African ancestry: Dist. of A4_AD_IGAP13





European ancestry: Dist. of E4_AD2_IGAP13 African ancestry: Dist. of A4_AD2_IGAP13

References

Lambert JC, Ibrahim-Verbaas CA, Harold D, et al. Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. *Nature Genetics.* 2013;45(12):1452-1458.

J. General Cognition – Cohorts for Heart and Aging Research in Genomic Epidemiology 2015

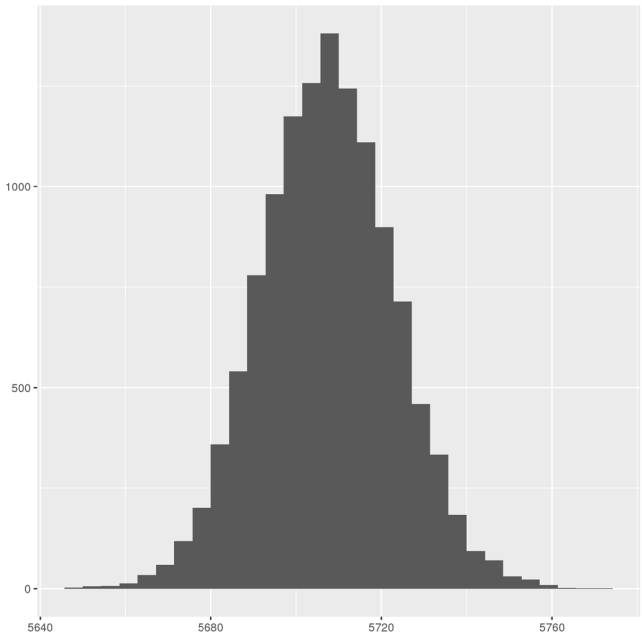
OUTDATED – INCLUDED FOR POSTERITY: The PGSs for general cognition were created using results from a 2015 GWAS conducted across 31 cohorts by the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium. A total of 53,949 participants undertook multiple, diverse cognitive tests from which a general cognitive function phenotype was created within each cohort by principal component analysis. Thirteen genome-wide significant SNPs in three separate regions previously associated with neuropsychiatric phenotypes were reported (**Supplementary Table S3**). The original GWAS included the HRS. To compute the PGSs for HRS respondents, weights were provided by the CHARGE consortium from a meta-analysis that excluded the HRS. Adjustments for age, sex, and population stratification were included in study-specific GWAS association analyses. Cohort-specific covariates—for example, site or familial relationships—were also fitted as required. A total of 2,478,500 SNPs were included in the meta-analysis.

The European ancestry PGSs contain 760,139 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 756,012 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

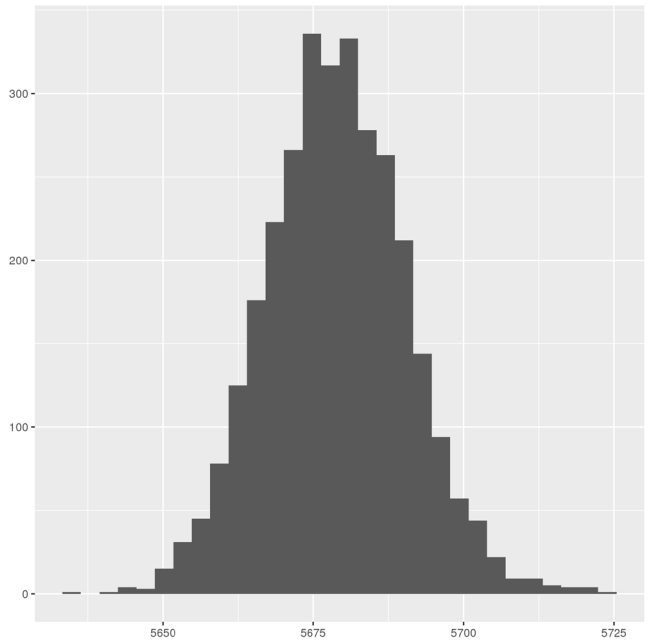
N.B.: The general cognition GWAS does not include the APOε4 variant so only one PGS is presented.
Please note that the CHARGE results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	5645.81	5770.08	124.27	5707.26	5707.36	0.14
African ancestry	3100	5635.26	5724.36	89.10	5678.59	5678.82	0.21



European ancestry: Dist. of E4_GenCog_CHARGE15



African ancestry: Dist. of A4_GenCog_CHARGE15

References

Davies, G., Armstrong, N., Bis, J. C., Bressler, J., Chouraki, V., Giddaluru, S., ... & Van Der Lee, S. J. (2015). Genetic contributions to variation in general cognitive function: a meta-analysis of genome-wide association studies in the CHARGE consortium (N= 53,949). *Molecular Psychiatry*, *20*(2), 183.

K. Schizophrenia – Psychiatric Genomics Consortium 2014

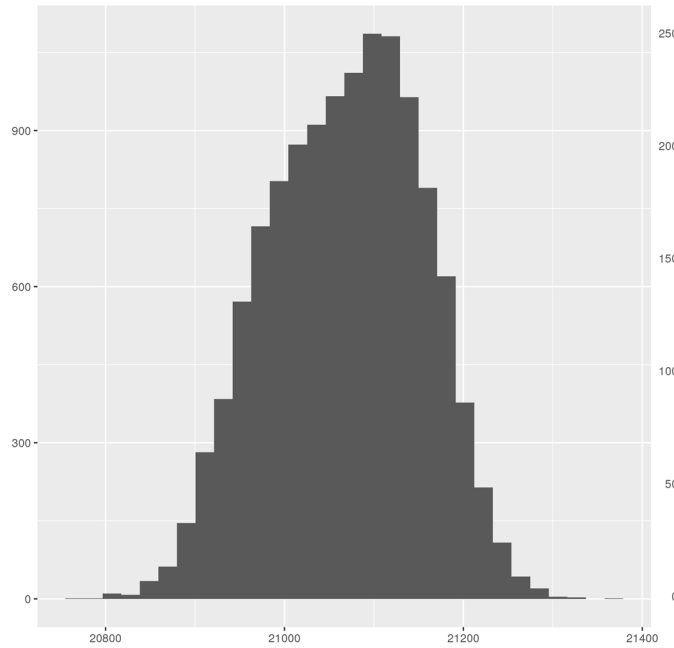
The PGSs for schizophrenia were created using results from a 2014 GWAS conducted by the Schizophrenia Working Group of the Psychiatric Genomics Consortium (PGC). The GWAS meta-analysis files are publicly available on their data download page: https://www.med.unc.edu/pgc/results-and-downloads (scz2.snp.results.txt.gz). The schizophrenia GWAS combined meta-analysis included 36,989 cases and 113,075 controls (N=150,064) and identified 128 loci that meet genome-wide significance (**Supplementary Table 2**). The replication sample consisted of 1,513 cases and 66,236 controls. After quality control, around 9.5 million SNPs were analyzed. To enable acquisition of large samples, some of the participating groups ascertained cases via clinician diagnosis rather than a research-based assessment. Genetic principal components and study identifiers were included as covariates.

The European ancestry PGSs contain 1,247,126 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,259,351 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

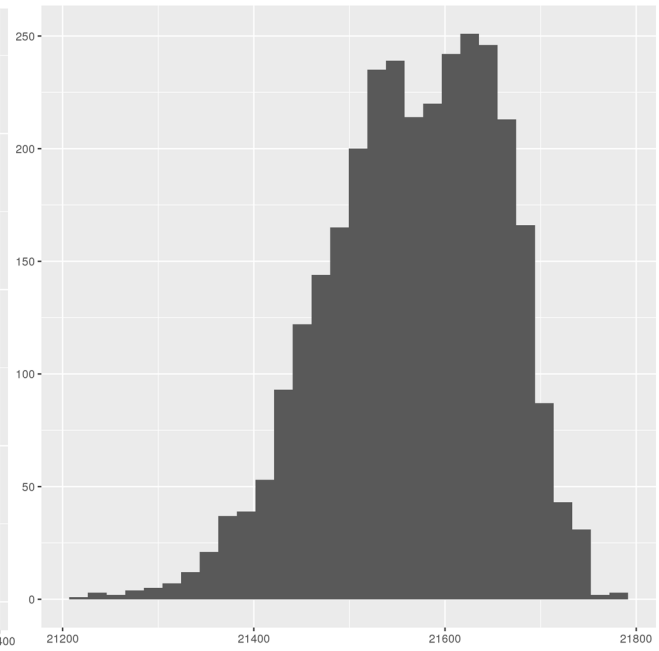
N.B.:
Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	20755.50	21358.30	602.80	21072.80	21067.82	0.77
African ancestry	3100	21225.20	21790.20	565.00	21572.75	21566.47	1.61



European ancestry: Dist. of E4_SCZ_PGC14



African ancestry: Dist. of A4_SCZ_PGC14

References

Ripke, S., Neale, B. M., Corvin, A., Walters, J. T., Farh, K. H., Holmans, P. A., ... & Pers, T. H. (2014). Biological insights from 108 schizophrenia-associated genetic loci. *Nature*, *511*(7510), 421-427.

L. Smoking Initiation (ever/never) – Tobacco and Genetics Consortium 2010

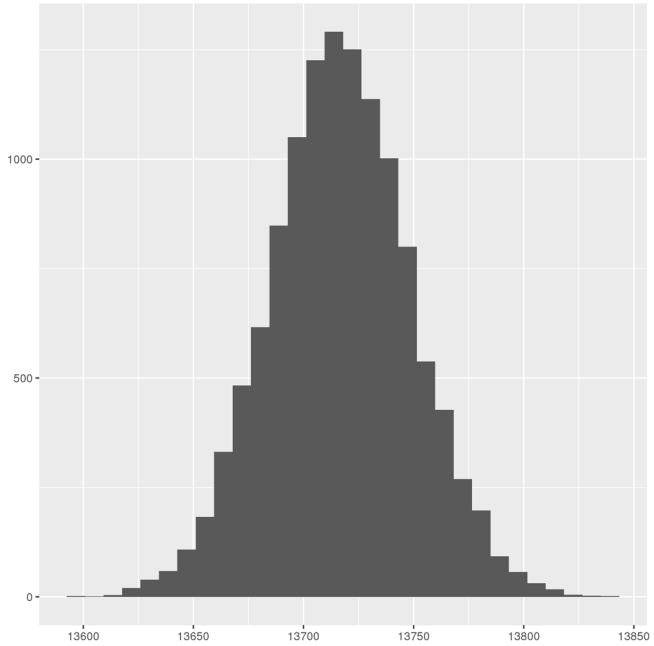
OUTDATED – INCLUDED FOR POSTERITY: The PGSs for smoking initiation were created using results from a 2010 GWAS conducted by the Tobacco and Genetics Consortium (TAG). The GWAS meta-analysis files are publicly available on the Psychiatric Genomics Consortium (PGC) website: https://www.med.unc.edu/pgc/results-and-downloads (tag.evrsmk.tbl.gz). A total of 74,053 participants were included in the discovery phase of the analysis, and 143,023 were included in a follow up meta-analysis of the 15 most significant regions. Eight SNPs exceeded genome-wide significance. HapMap-2 CEU was used as the imputation panel resulting in a common set of ~2.5 million SNPs across studies. Individuals who were recorded as having ever been regular smokers were defined as those who reported having smoked at least 100 cigarettes during their lifetime, and never regular smokers were defined as those who reported having smoked between 0 and 99 cigarettes during their lifetime. Study-specific GWASs controlled for imputed allele dosage for a SNP plus whether a subject was classified as a case in the primary study. If the primary study was case-control in design and the phenotype being studied was known to be associated with smoking, the GWAS adjusted for case status to reduce potential confounding. Analyses were run and meta-analyzed separately for males and females.

The European ancestry PGSs contain 710,288 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 707,989 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

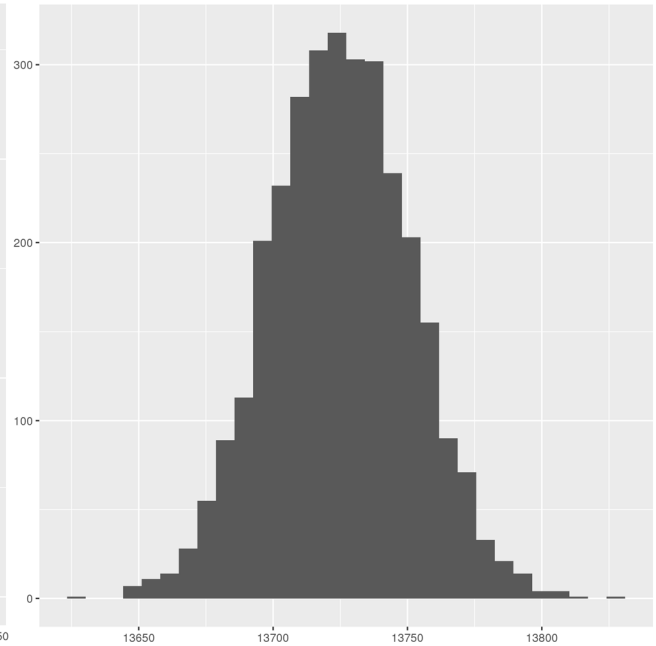
N.B.: **Please note that the TAG results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	13599.40	13841.90	242.50	13716.50	13716.86	0.29
African ancestry	3100	13626.30	13827.00	200.70	13724.60	13724.97	0.47



European ancestry: Dist. of E4_EvrSmk_TAG10



African ancestry: Dist. of A4_EvrSmk_TAG10

References

Tobacco and Genetics Consortium. (2010). Genome-wide meta-analyses identify multiple loci associated with smoking behavior. *Nature Genetics*, *42*(5), 441-447.

M. Subjective Wellbeing – Social Science Genetic Association Consortium 2016

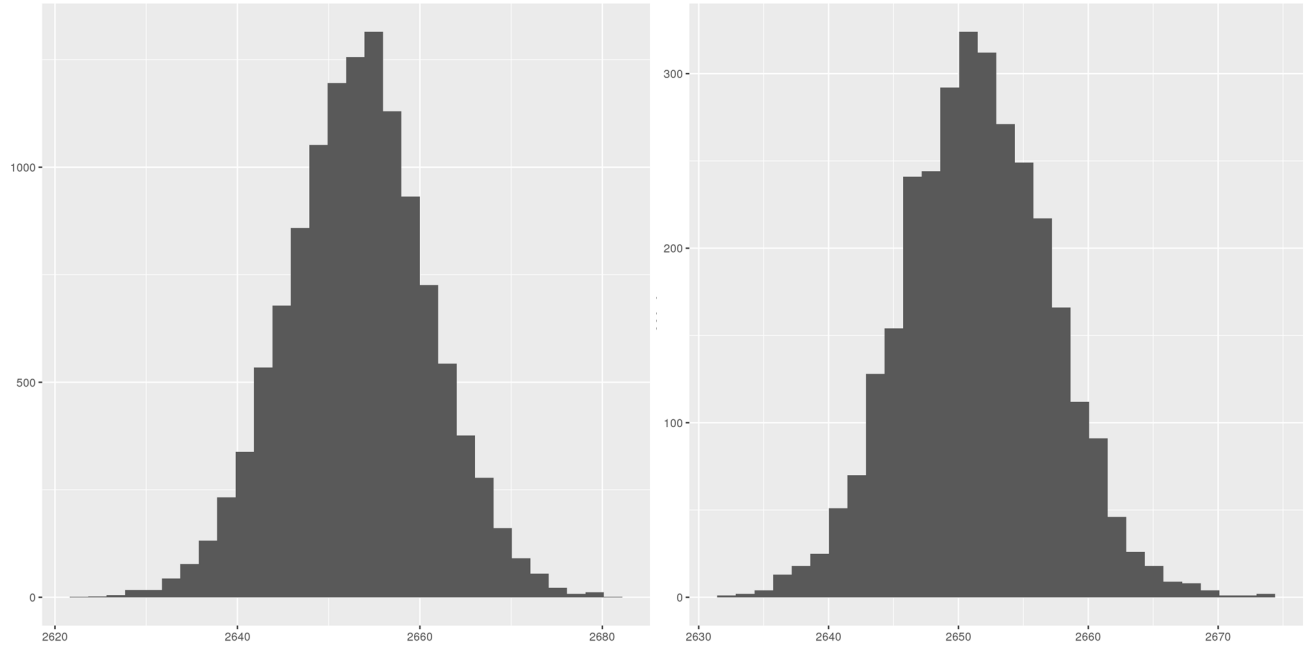
The PGSs for subjective wellbeing were created using results from a 2016 GWAS conducted by the Social Science Genetic Association Consortium (SSGAC). The subjective wellbeing analyses included 298,420 European ancestry individuals in the discovery sample. Genome-wide significant SNPs were identified in 3 loci (**Table 1**). A quasi-replication analysis tested whether these three SNPs were associated with depressive symptoms and neuroticism. The phenotype measure was life satisfaction, positive affect, or in some cohorts a measure combining both. Approximately 9.3 million SNPs were included in the analyses, with cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G) or the HapMap 2 Panel. Adjustments for age, age^2, sex, and population stratification (first four PCs from the genotypic data) were included in study-specific GWAS association analyses. Cohorts were also asked to include any study-specific covariates such as study site or batch effects. The original subjective wellbeing GWAS included the HRS. To compute PGSs for HRS respondents, the SSGAC provided SNP weights with the HRS and 23andMe results (due to data use agreements) removed (combined discovery + replication sample size without the HRS: N=288,478).

The European ancestry PGSs contain 710,288 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 707,989 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication. Included SNPs and weights are avaialable upon request. **Please note that the SSGAC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	2623.24	2681.79	58.55	2653.32	2653.22	0.07
African ancestry	3100	2632.63	2674.16	41.53	2651.39	2651.49	0.10



European ancestry: Dist. of E4_wellbeing_SSGAC16 African ancestry: Dist. of A4_wellbeing_SSGAC16

References

Okbay, A., Baselmans, B. M., De Neve, J. E., Turley, P., Nivard, M. G., Fontana, M. A., ... & Gratten, J. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics*, *48*(6), 624-633.

N. Neuroticism – Social Science Genetic Association Consortium 2016

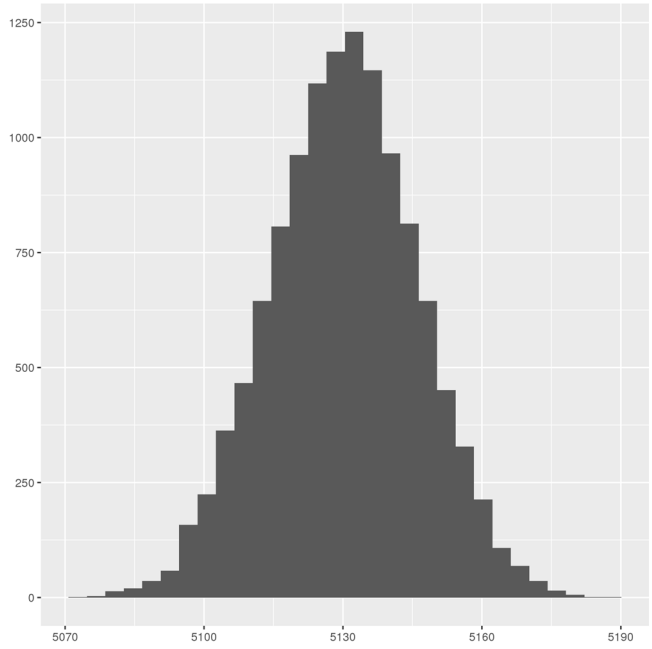
The PGSs for neuroticism were created using results from a 2016 auxiliary GWAS conducted by the Social Science Genetic Association Consortium (SSGAC) as part of their subjective wellbeing GWAS (see above). The GWAS meta-analysis files are publicly available on the SSGAC website: https://www.thessgac.org/data. The entire meta-analysis included 170,911 individuals. Meta-analysis was performed on publicly available results from the Genetics of Personality Consortium (GPC) (N=63,661) with results from UK Biobank data (N=107,245). The meta-analysis yielded 11 lead SNPs, 2 of which tag inversion polymorphisms (**Table 1**). A quasi-replication analysis tested whether these SNPs were associated with subjective wellbeing. A replication analysis was also performed using data from 23andMe (N=368,890). In UKB, the phenotype measure was the respondent's score on a 12-item version of the Eysenck Personality Inventory Neuroticism scale. The GPC harmonized different neuroticism batteries. In the UKB, analyses controlled for the first 15 PCs, indicator variables for genotyping array, sex, indicator variables for age ranges, and sex-by-age interactions. Model adjustments for the 29 cohorts contributing to the GPC meta-analysis varied (see de Moor et al., p. 644, 2015).

The European ancestry PGSs contain 1,134,281 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,130,293 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

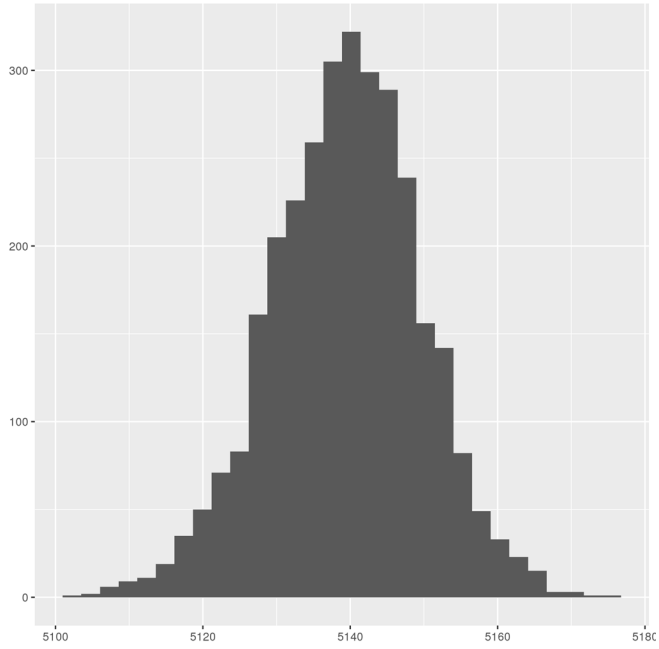
N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication. Included SNPs and weights are avaialable upon request. **Please note that the SSGAC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	5071.39	5186.77	115.38	5130.41	5130.16	0.14
African ancestry	3100	5102.11	5175.36	73.25	5139.68	5139.40	0.18



European ancestry: Dist. of E4_neuroticism_SSGAC16



African ancestry: Dist. of A4_neuroticism_SSGAC16

References

Okbay, A., Baselmans, B. M., De Neve, J. E., Turley, P., Nivard, M. G., Fontana, M. A., ... & Gratten, J. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics*, *48*(6), 624-633.

De Moor, M. H., Van Den Berg, S. M., Verweij, K. J., Krueger, R. F., Luciano, M., Vasquez, A. A., ... & Gordon, S. D. (2015). Meta-analysis of genome-wide association studies for neuroticism, and the polygenic association with major depressive disorder. *JAMA Psychiatry*, *72*(7), 642-650.

O. Depressive Symptoms – Social Science Genetic Association Consortium 2016

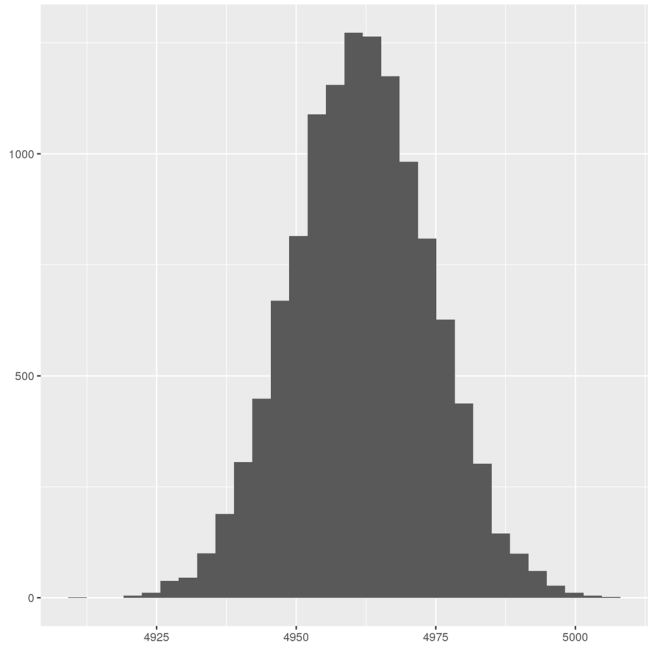
The PGSs for depressive symptoms were created using results from a 2016 auxiliary GWAS conducted by the Social Science Genetic Association Consortium (SSGAC) as part of their subjective wellbeing GWAS (see above). The GWAS meta-analysis files are publicly available on the SSGAC website: https://www.thessgac.org/data. The GWAS included 180,866 individuals and meta-analyzed publicly available results from a study performed by the Psychiatric Genomics Consortium (PGC) (Ncases = 9,240, Ncontrols = 9,519) with results from analyses of UK Biobank (UKB) data (N = 105,739), and the Resource for Genetic Epidemiology Research on Aging (GERA) Cohort (Ncases = 7,231, Ncontrols = 49,316). The meta-analysis identified two genome-wide significant SNPs (**Table 1**). A quasi-replication analysis tested whether these SNPs were associated with subjective wellbeing. A replication analysis was also performed using data from 23andMe (N=368,890). In UKB, a continuous phenotype measure was used that combined responses to two questions, which ask about the frequency in the past two weeks with which the respondent experienced feelings of unenthusiasm/disinterest and depression/hopelessness. The PGC and GERA cohorts utilized case-control data on major depressive disorder. In the UKB, analyses controlled for the first 15 PCs, indicator variables for genotyping array, sex, indicator variables for age ranges, and sex-by-age interactions. In GERA, analyses controlled for the first four PCs of the genotypic data, sex, and 14 indicator variables for age ranges. The PGC included controls for five PCs, sex, age, and cohort fixed effects (for details see Ripke et al., 2013).

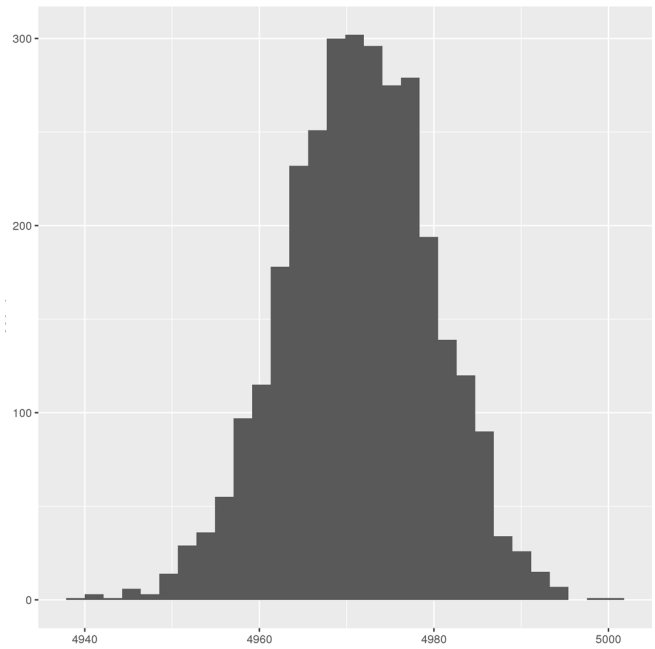
The European ancestry PGSs contain 1,130,606 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,127,901 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication. Included SNPs and weights are avaialable upon request. **Please note that the SSGAC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	4910.43	5006.01	95.58	4961.70	4961.69	0.11
African ancestry	3100	4938.18	4999.97	61.79	4971.48	4971.36	0.15





European ancestry: Dist. of E4_depsymp_SSGAC16 African ancestry: Dist. of A4_depsymp_SSGAC16

References

Okbay, A., Baselmans, B. M., De Neve, J. E., Turley, P., Nivard, M. G., Fontana, M. A., ... & Gratten, J. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics*, *48*(6), 624-633.

Ripke, S., Wray, N. R., Lewis, C. M., Hamilton, S. P., Weissman, M. M., Breen, G., ... & Heath, A. C. (2013). A mega-analysis of genome-wide association studies for major depressive disorder. *Molecular Psychiatry*, *18*(4), 497.

P. Longevity – Cohorts for Heart and Aging Research in Genomic Epidemiology 2015

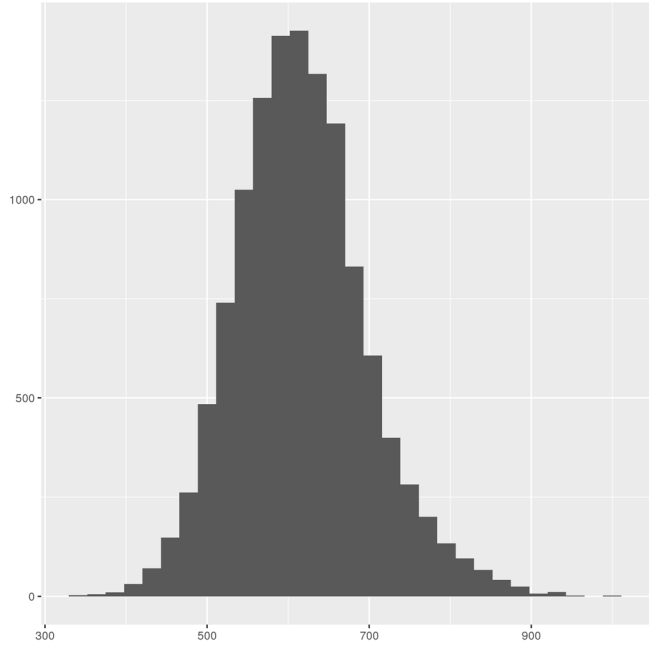
OUTDATED – INCLUDED FOR POSTERITY: The longetivy PGSs were created using summary statistics from a 2015 GWAS conducted by the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortia. The GWAS meta-analysis summary statistics were requested from the CHARGE consortia, after removing the HRS contribution. The meta-analysis includes 6,036 longevity cases (age ≥90 years) and 3,757 controls that died between ages 55 and 80 and were of European descent. Genetic measures were imputed to ~2.5 million SNPs using the HapMap 22 CEU (Build 36) genotyped samples as a reference. Logistic regression analyses were used to test each SNP for association with longevity using an additive model adjusting for sex and genetic principal components to adjust for population stratification. Meta-analysis raw results with HRS removed were filtered for HetPval>0.2 and HetDF>5.

The European ancestry PGS contains 577,249 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 571,377 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

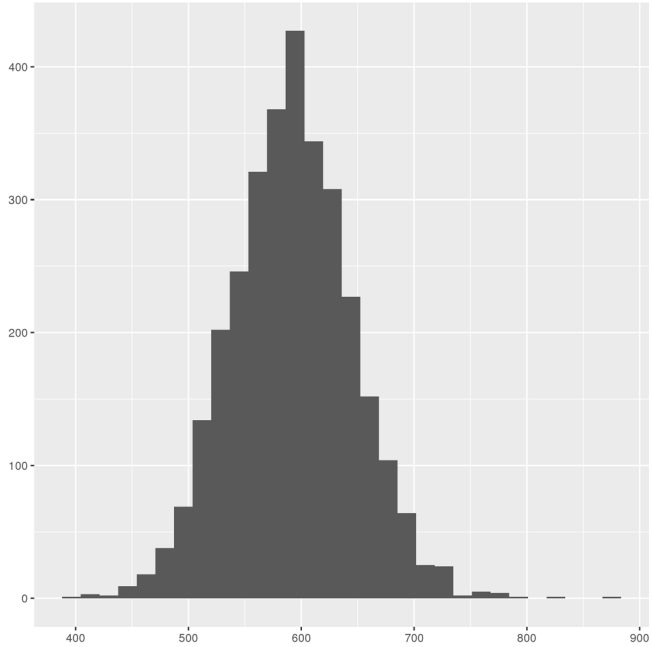
N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication. Included SNPs and weights are avaialable upon request. **Please note that the CHARGE results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	332.2	991.18	659	611.62	616.04	0.74
African ancestry	3100	393.97	872.86	478.9	591.33	591.62	0.96



European ancestry: Dist. of E4_longevity_CHARGE15



African ancestry: Dist. of A4_longevity_CHARGE15

References:

Broer L, Buchman, A. S., Deelen, J., Evans, D. S., Faul, J. D., Lunetta, K. L., ... & Yu, L. (2014). GWAS of longevity in CHARGE consortium confirms APOE and FOXO3 candidacy. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *70*(1), 110-118.

Q. Number of Cigarettes Smoked per Day – Toacco and Genetics Consortium 2010

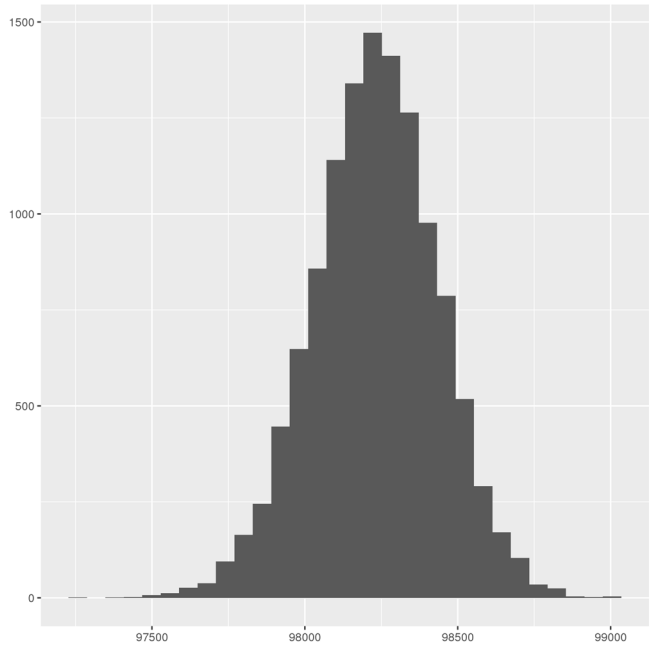
OUTDATED – INCLUDED FOR POSTERITY: PGSs for smoking quantity, measured as number of cigarettes smoked per day (CPD), were created using results from a 2010 GWAS conducted by the Tobacco and Genetics Consortium (TAG). The GWAS meta-analysis files are publicly available on the Psychiatric Genomics Consortium (PGC) website: https://www.med.unc.edu/pgc/results-and-downloads (tag.cpd.tbl.gz). A total of 74,053 participants were included in the discovery phase of the analysis, and 73,853 were included in a follow up meta-analysis of the 15 most significant regions. Three SNPs exceeded genome-wide significance (**Table 2**). HapMap-2 CEU was used as the imputation panel resulting in a common set of ~2.5 million SNPs across studies. CPD across studies was measured as either average CPD or maximum CPD. Study-specific GWAS controlled for imputed allele dosage for a SNP plus whether a subject was classified as a case in the primary study. If the primary study was case-control in design and the phenotype being studied was known to be associated with smoking, the GWAS adjusted for case status to reduce potential confounding. Analyses were run and meta-analyzed separately for males and females.

The European ancestry PGSs contain 767,171 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 761,843 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

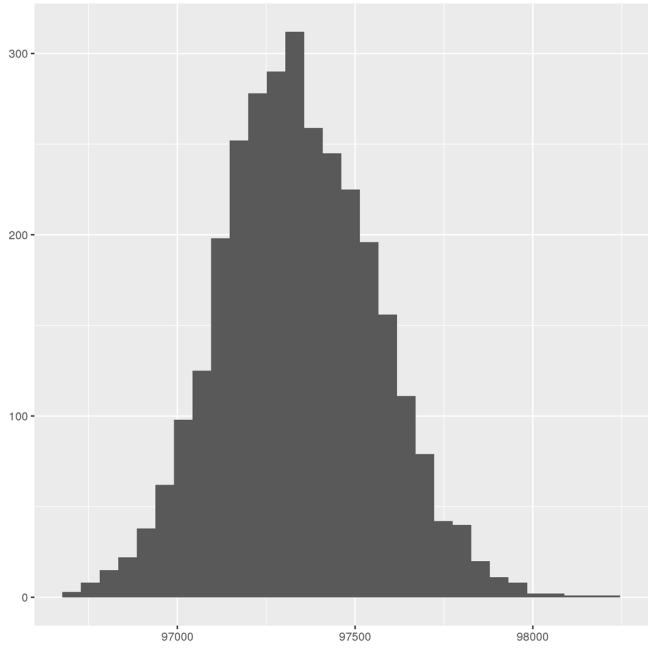
N.B.: **Please note that the TAG results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	97283.20	99030.70	1747.50	98233.05	98230.48	1.86
African ancestry	3100	96686.80	98203.50	1516.70	97331.45	97340.52	3.89



European ancestry: Dist. of E4_CPD_TAG10



African ancestry: Dist. of A4_CPD_TAG10

References

Tobacco and Genetics Consortium. (2010). Genome-wide meta-analyses identify multiple loci associated with smoking behavior. *Nature Genetics*, *42*(5), 441-447.

R. Coronary Artery Disease - Coronary ARtery DIsease Genome wide Replication and Meta-analysis 2011

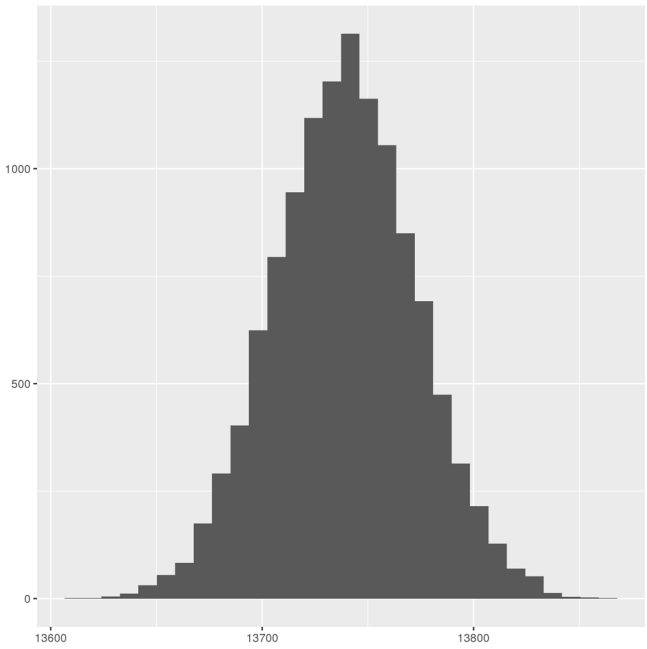
The PGSs for coronary artery disease (CAD) were created using results from a 2011 study conducted by the Coronary ARtery DIsease Genome wide Replication and Meta-analysis (CARDIoGRAM) consortium. The GWAS meta-analysis files are publicly available and can be downloaded from www.cardiogramplusc4d.org (cad.add.160614.website.txt). The GWAS meta-analysis consisted of 14 studies with a total of 22,233 individuals with CAD (cases) and 64,762 without CAD (controls) of European descent imputed to the HapMap3 CEU panel. Replication was performed in a sample of 56,682 individuals (approximately half cases and half controls). Analysis identified 13 new genome-wide significant loci and confirmed 10 previously reported CAD loci **(Tables 1 and 2)**. Study-specific GWAS adjusted for age of onset (cases) or age of recruitment (controls), gender, and genetic principal components.

The European ancestry PGSs contain 742,371 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 741,248 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1). Weights are represented as log(OR).

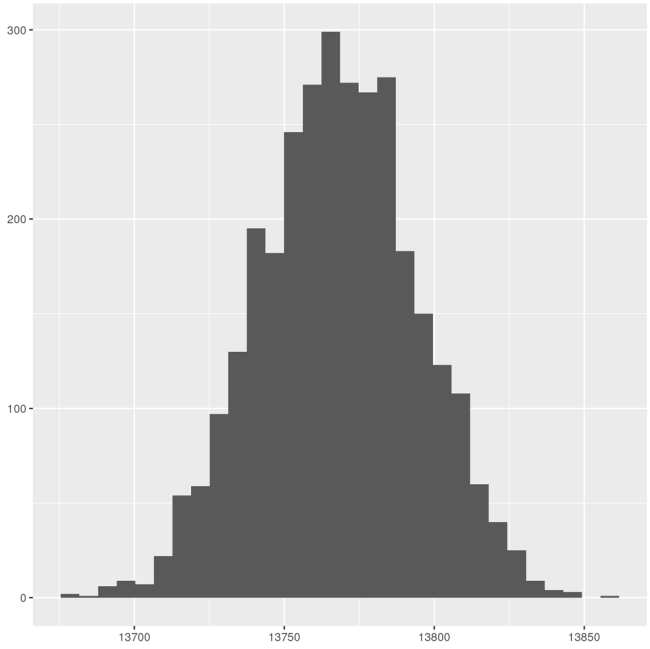
N.B.: **Please note that the CARDIoGRAM results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	13614.50	13867.20	252.70	13739.30	13739.09	0.30
African ancestry	3100	13677.60	13857.50	179.90	13767.80	13767.90	0.47



European ancestry: Dist. of E4_CAD_CARDIOGRAM11



African ancestry: Dist. of A4_CAD_CARDIOGRAM11

References

Schunkert, H., König, I. R., Kathiresan, S., Reilly, M. P., Assimes, T. L., Holm, H., ... & Absher, D. (2011). Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. *Nature Genetics*, *43*(4), 333-338.

S. Myocardial Infarction - Coronary ARtery DIsease Genome wide Replication and Meta-analysis 2015

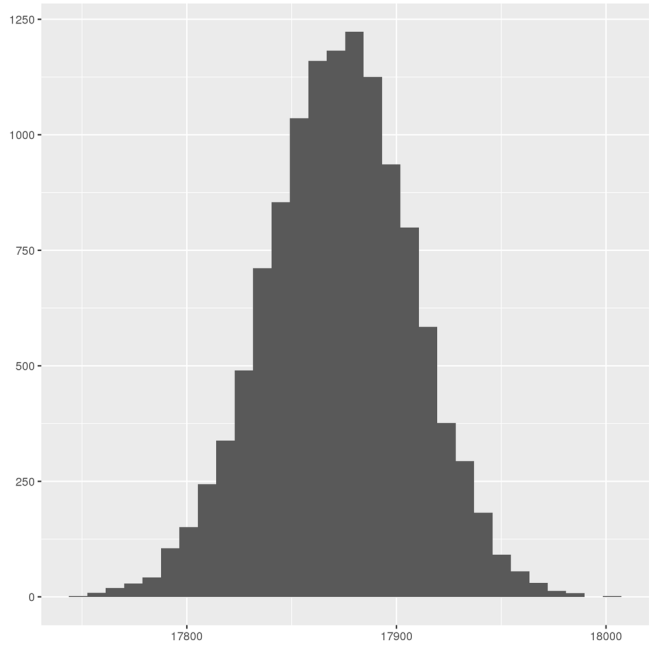
The PGSs for myocardial infarction (MI) were created using 2015 results from a subgroup analysis of coronary artery disease (CAD) conducted by the Coronary ARtery DIsease Genome wide Replication and Meta-analysis (CARDIoGRAM) consortium. The GWAS meta-analysis files are publicly available and can be downloaded from www.cardiogramplusc4d.org (mi.add.030315.website.txt). The GWAS is a meta-analysis of 48 studies of mainly European, South Asian, and East Asian, descent imputed using the 1000 Genomes phase 1 v3 training set with 38 million variants. The study interrogated 9.4 million variants and involved 60,801 CAD cases and 123,504 controls. Case status was defined by an inclusive CAD diagnosis (for example, myocardial infarction, acute coronary syndrome, chronic stable angina or coronary stenosis of >50%). Thirty-seven previous loci and ten new loci achieved genome-wide significance (**Supplementary Table 2**). MI subgroup analysis was performed in cases with a reported history of MI (~70% of the total number of cases). No additional loci reached genome-wide significance in the MI analysis.

The European ancestry PGSs contain 1,257,292 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,261,702 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1). Weights are represented as log(OR).

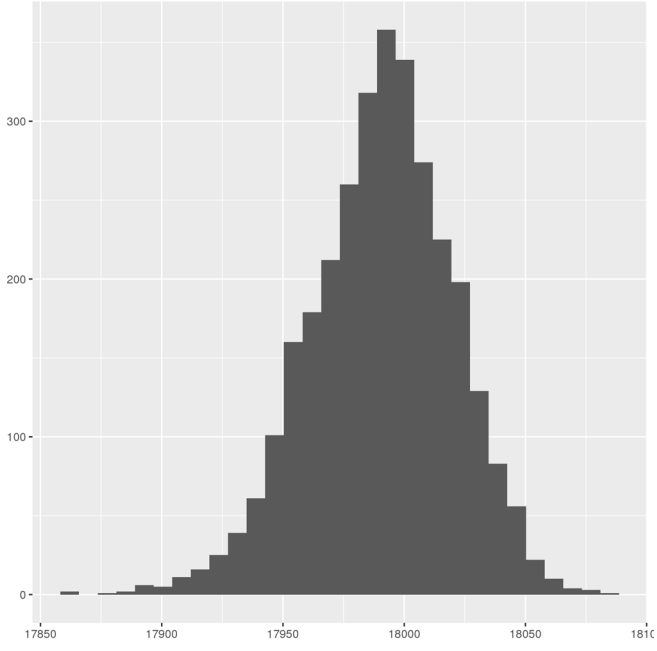
N.B.: **Please note that the CARDIoGRAM results are from a GWAS on individuals of mostly European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	17744.30	17999.10	254.80	17872.90	17872.64	0.32
African ancestry	3100	17862.50	18085.20	222.70	17992.05	17990.61	0.53



European ancestry: Dist. of E4_MI_CARDIOGRAM15



African ancestry: Dist. of A4_MI_CARDIOGRAM15

References

CARDIoGRAMplusC4D Consortium. (2015). A comprehensive 1000 Genomes-based genome-wide association

meta-analysis of coronary artery disease. *Nature Genetics*, *47*(10), 1121-1130.

T. Type II Diabetes – DIAbetes Genetics Replication and Meta-analysis 2012

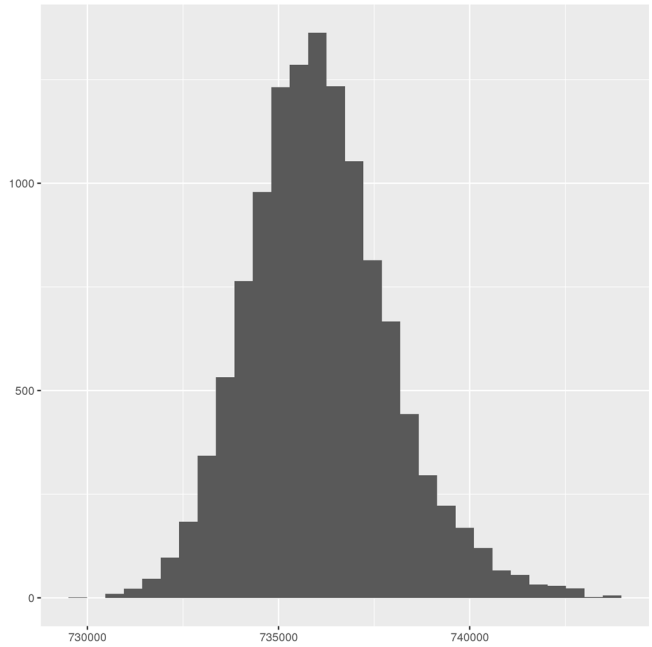
The PGSs for Type II Diabetes (T2D) were created using GWAS meta-analysis results from a 2012 study conducted by the DIAbetes Genetics Replication and Meta-analysis (DIAGRAM) Consortium. The GWAS meta-analysis files can be downloaded from the DIAGRAM Consortium website: http://www.diagram-consortium.org/downloads.html (DIAGRAMv3.2012DEC17.txt). The stage one (discovery) meta-analysis consists of 12,171 T2D cases and 56,862 controls across 12 GWAS from European descent populations. The stage two (replication) meta-analysis consisted of 22,669 cases and 58,119 controls, including 1,178 cases and 2,472 controls of Pakistani descent. The combined meta-analysis identified ten genome-wide significant loci (**Table 1**). HapMap-2 CEU was used as the imputation panel resulting in a common set of ~2.5 million SNPs across studies. Study-specific GWAS adjusted for age of onset (cases) or age of recruitment (controls), gender, and genetic principal components. The results of each GWAS were corrected for residual population structure using the genomic control inflation factor, as reported in Supplementary Table 1 of Morris et al. (2012).

The European ancestry PGSs contain 726,395 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 734,890 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

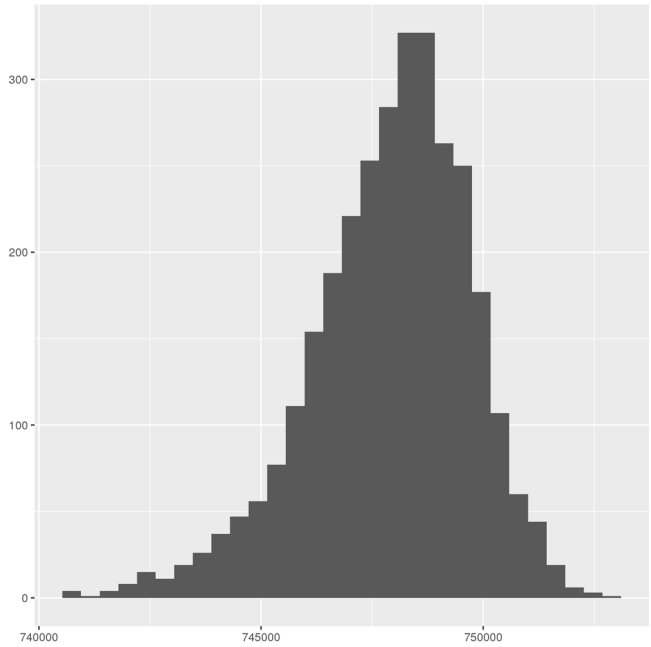
N.B.: The effect estimates for SNPs come from the discovery stage I meta-analysis of European descent individuals. **Note that the DIAGRAM results are from a GWAS on individuals of mostly European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	16202.70	16633.40	430.70	16380.60	16385.24	0.50
African ancestry	3100	16574.70	16983.20	408.50	16837.90	16830.60	1.12



European ancestry: Dist. of E4_T2D_DIAGRAM12



African ancestry: Dist. of A4_T2D_DIAGRAM12

References

Morris, A. P., Voight, B. F., Teslovich, T. M., Ferreira, T., Segre, A. V., Steinthorsdottir, V., ... & Prokopenko, I. (2012). Large-scale association analysis provides insights into the genetic architecture and pathophysiology of type 2 diabetes. *Nature Genetics*, *44*(9), 981-990.

U. Attention Deficit/Hyperactivity Disorder (ADHD) – Psychiatric Genomics Consortium 2010

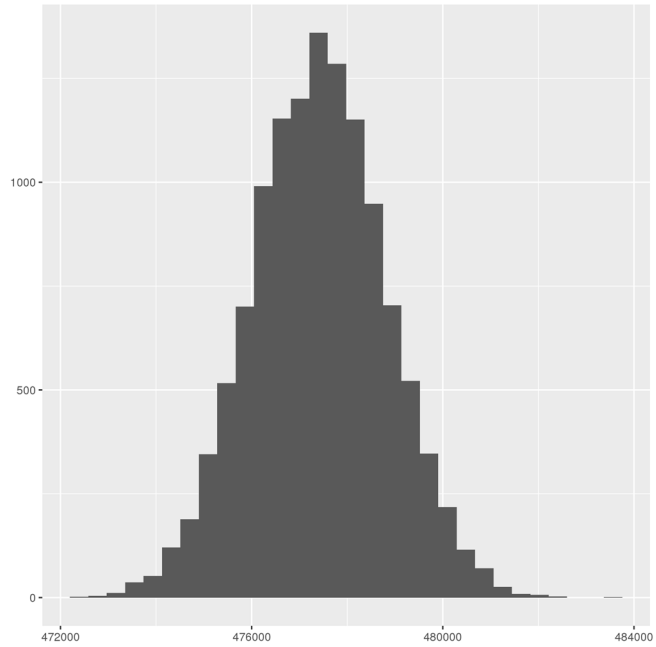
OUTDATED – INCLUDED FOR POSTERITY: The PGSs for ADHD were created using results from a 2010 GWAS conducted by the ADHD subgroup of the Psychiatric GWAS Consortium. The GWAS meta-analysis files are publicly available on the PGC website: http://www.med.unc.edu/pgc/results-and-downloads (pgc.adhd.full.2012-10.txt). The entire meta-analysis included 2,064 trios, 896 cases, and 2,455 controls. Samples were drawn from four projects: the Children's Hospital of Philadelphia (CHOP), phase I of the International Multisite ADHD Genetics Project (IMAGE), phase II of IMAGE (IMAGE II), and the Pfizer funded study from the University of California, Los Angeles, Washington University, and the Massachusetts General Hospital (PUWMa). No SNPs exceed genome-wide significance. There was not a replication sample. Phenotypes were harmonized across samples; all studies implemented a combination of semi-structured interveiews and parent and/or teacher report on questionnaires (see Neale et al., p. 3-5, 2010).

The European ancestry PGSs contain 598,468 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 592,973 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

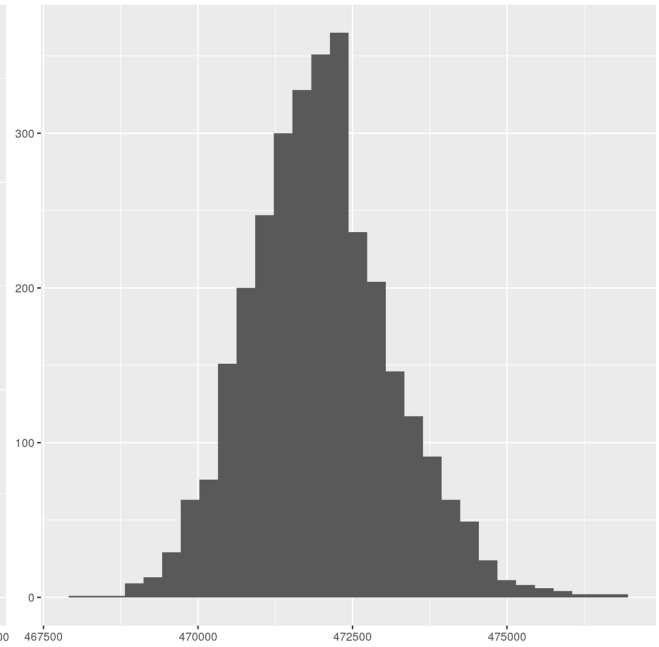
N.B.: The effect estimates for SNPs come from the full GWAS of European descent individuals.**Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	472367	483541	11174	477409	477407.03	12.67
African ancestry	3100	468167	476913	8746	471932	471983.74	20.71



European ancestry: Dist. of E4_ADHD_PGC10



African ancestry: Dist. of A4_ADHD_PGC10

References

Neale, B. M., Medland, S. E., Ripke, S., Asherson, P., Franke, B., Lesch, K. P., ... & Daly, M. (2010). Meta-analysis

of genome-wide association studies of attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *49*(9), 884-897.

V. Attention Deficit/Hyperactivity Disorder (ADHD) – Psychiatric Genomics Consortium 2019

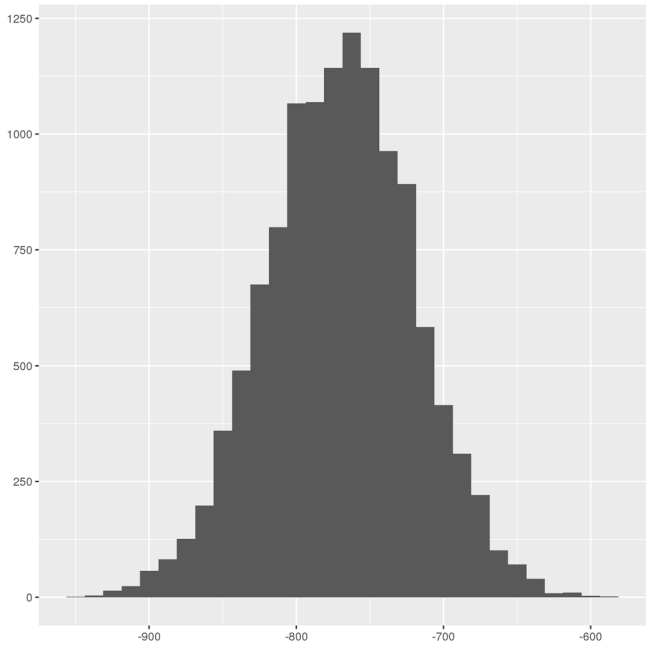
UPDATED FROM RELEASE 3: The 2019 ADHD PGSs were created using results from a Nature Genetics article by the Foundation Initiative for Integrative Psychiatric Research (iPSYCH) and Psychiatric Genomics Consortium (PGC). The GWAS meta-analysis files are publicly available on the PGC website: http://www.med.unc.edu/pgc/results-and-downloads. Genotype array data for 20,183 individuals with ADHD and 35,191 controls were collected from 12 cohorts (Supplementary Table 1). These samples included a population-based cohort of 14,584 individuals with ADHD and 22,492 controls from Denmark collected by the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH; Supplementary Fig. 1), and 11 European, North American and Chinese cohorts aggregated by the Psychiatric Genomics Consortium (PGC). The overall GWAS meta-analysis did not include the HRS. In the discovery sample, 12 loci met the genome-wide significance threshold for association with ADHD; 10 of these 12 loci were replicated in the replication sample. Study-specific GWASs controlled for ancestry principal components and relevant study-specific covariates.

The European ancestry PGSs contain 1,043,408 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,033,418 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

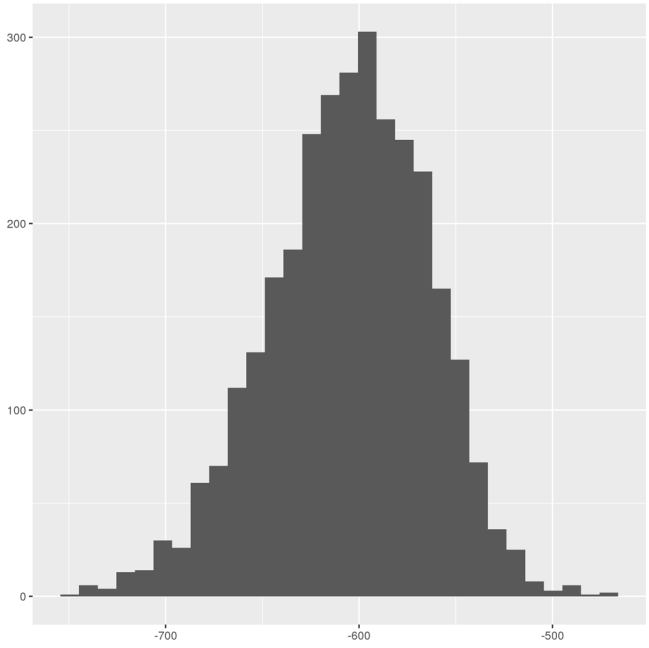
N.B.: The effect estimates for SNPs come from the full GWAS of mixed ancestry individuals**.**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	-948.58	-586.12	362.46	-769.22	-770.15	0.45
African ancestry	3100	-749.36	-470.68	278.68	-603.03	-605.43	0.74



European ancestry: Dist. of E4_ADHD_PGC17



African ancestry: Dist. of A4_ADHD_PGC17

References

Demontis, D., Walters, R. K., Martin, J., Mattheisen, M., Als, T. D., Agerbo, E., … Neale, B. M. (2017). Discovery Of The First Genome-Wide Significant Risk Loci For ADHD. *Nat Genet. 2019 Jan;51(1):63-75. doi: 10.1038/s41588-018-0269-7.*

W. Autism Spectrum Disorders – Psychiatric Genomics Consortium 2017

The PGSs for autism were created using results from a 2017 GWAS conducted by the Autism Spectrum Disorders Working Group of the Psychiatric Genomics Consortium. The GWAS meta-analysis files are publicly available on the PGC website: http://www.med.unc.edu/pgc/results-and-downloads. The phase I discovery sample included 7,387 Autism Spectrum Disorder (ASD) cases, and 8,567 controls. Samples were drawn from 14 independent cohorts. Covariates in the individual GWAS included genetic principal components. No SNPs exceeded genome-wide significance in the phase I discovery stage. Two independent samples were used for replication: the Danish iPSYCH Project (7,783 ASD cases, 11,359 controls) and a combined deCODE Collection and the Study to Explore Early Development (SEED) (1,369 ASD cases, 137,308 controls). Authors examined 180 LD-independent markers from the phase I discovery GWAS meta-analysis that were associated with ASD at $p < 5 \times 10^{-4}$ in both replication samples: 6.1% and 5% of the markers were associated with ASD after multiple comparison correction in the iPSYCH and deCODE/SEED samples, respectively.

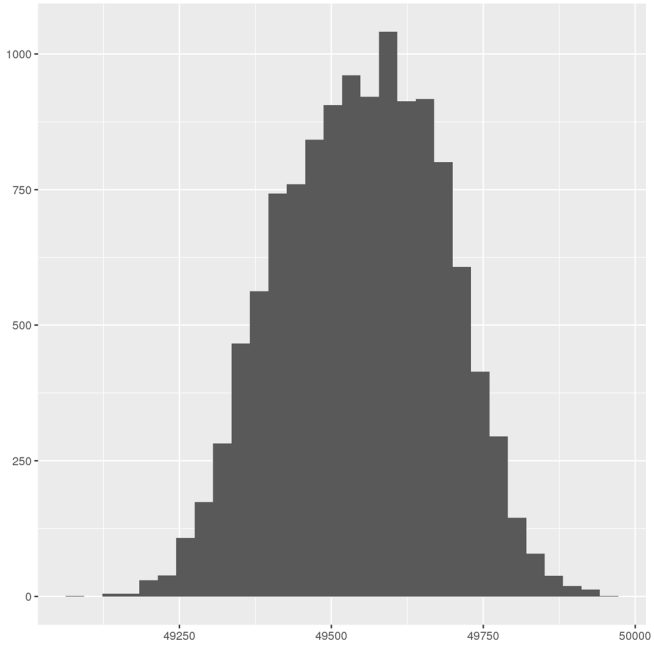
The European ancestry PGSs contain 1,290,830 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,284,072 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

N.B.: **Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups). Provided below is a CAUTION from the consortia regarding use of their summary statistics:**

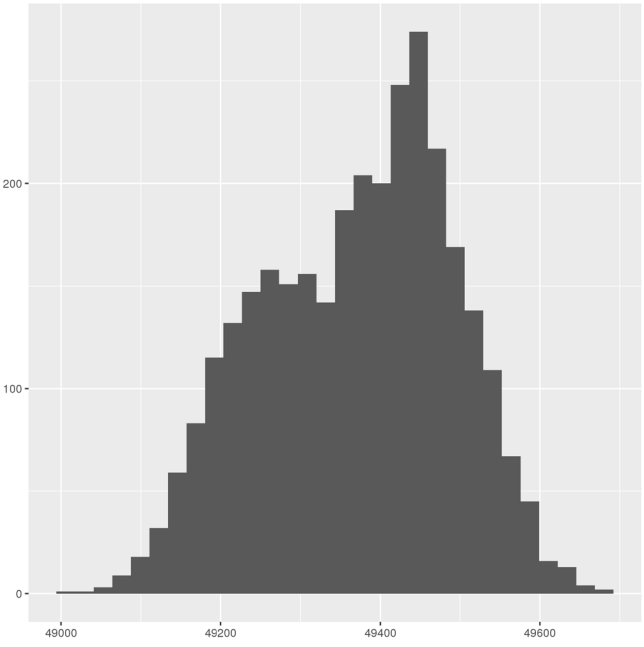
```
# CAUTION. Large meta-analyses often include overlapping studies of samples. The "shared-controls"
# phenomenon is becoming more pervasive (e.g., WTCCC/NIMH). If you wish to compare results between
# datasets, you must account for overlapping controls. If in doubt, run sanity-checks that included
# control x control and alternate-case x control comparisons. *GOTCHA WARNING* This is important
# in polygenic-risk-scoring approaches that do not account for overlap.
```

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	49082.60	49961.70	879.10	49553.00	49549.17	1.20
African ancestry	3100	49010.50	49685.00	674.50	49385.25	49370.47	2.16



European ancestry: Dist. of E4_Autism_PGC17



African ancestry: Dist. of A4_Autism_PGC17

References

Autism Spectrum Disorders Working Group of The Psychiatric Genomics Consortium, Anney, R. J., Ripke, S., Anttila, V., Grove, J., Holmans, P., ... & Neale, B. (2017). Meta-analysis of GWAS of over 16,000 individuals with autism spectrum disorder highlights a novel locus at 10q24. 32 and a significant overlap with schizophrenia. *Molecular Autism*, *8*, 1-17.

X. Bipolar Disorder (BIP) – Psychiatric Genomics Consortium 2011

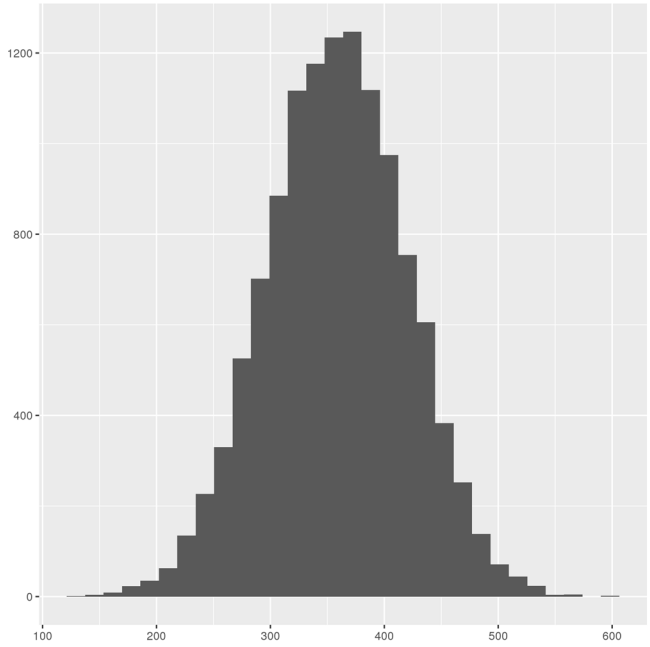
The PGSs for BP were created using results from a 2011 GWAS conducted by the Bipolar Disorder working group of the Psychiatric GWAS Consortium. The GWAS meta-analysis files are publicly available on the PGC website: http://www.med.unc.edu/pgc/results-and-downloads (pgc.bip.2012-04.zip). The discovery phase of the meta-analysis included 7,481 cases and 9,250 controls. Samples were drawn from 11 studies (see Skylar et al., Table 1 and supplemental materials, 2011). A follow up meta-analysis of the 34 most significant regions was conducted in a replication sample that included 4,496 independent cases and 42,422 independent controls. The combined GWAS meta-analysis yielded two genome-wide significance SNPs. BP case status was measured in all studies using standardized semi-structured interviews. Controls had a low probability of BP; some control selection criteria excluded individuals with a history of a mood disorder and other controls were unscreened. Meta-analyses were adjusted for the top five principal componets and 10 dummy variables to account for differences between the 11 studies.

The European ancestry PGSs contain 758,042 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 757,581 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

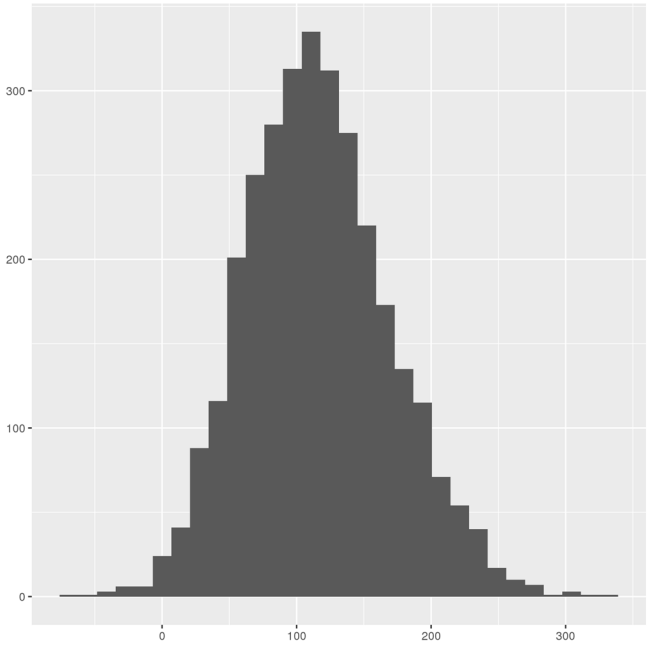
N.B.: **Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	130.79	599.69	468.90	358.03	357.87	0.56
African ancestry	3100	-72.01	329.23	401.24	113.31	115.78	0.96



European ancestry: Dist. of E4_BIP_PGC11



African ancestry: Dist. of A4_BIP_PGC11

References:

Psychiatric GWAS Consortium Bipolar Disorder Working Group. (2011). Large-scale genome-wide association analysis of bipolar disorder identifies a new susceptibility locus near ODZ4. *Nature Genetics*, *43*(10), 977-983.

Y. Mental health cross disorder – Psychiatric Genomics Consortium 2013

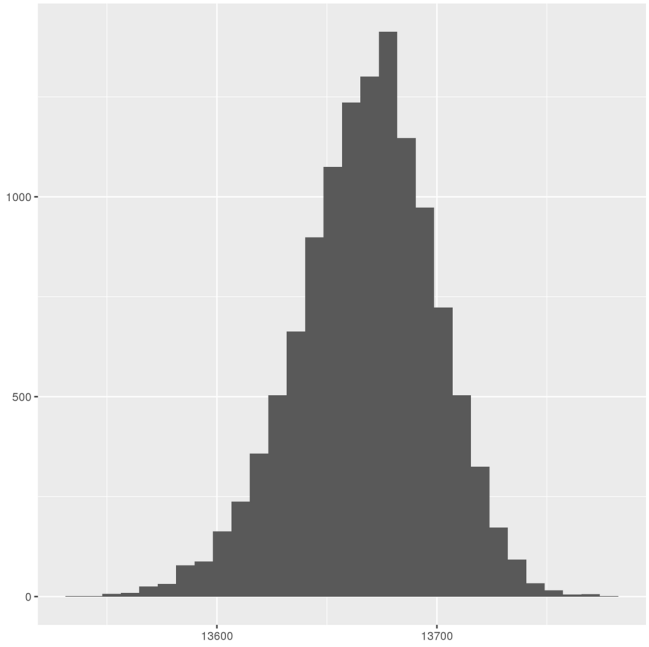
The PGSs for Mental Health Cross-Disorder were created using results from a 2013 GWAS conducted by the Cross Disorder working group of the Psychiatric Genomics Consortium. The GWAS meta-analysis files are publicly available on the PGC website: http://www.med.unc.edu/pgc/results-and-downloads (pgc.cross.full.2013-03.zip). The discovery phase of the meta-analysis included 33,342 cases and 27,888 controls. Disorders that were counted as cases (DSM-III-R or DSM-IV criteria) included autism spectrum disorder, attention deficit-hyperactivity disorder, bipolar disorder, major depressive disorder, and schizophrenia. Four SNPs surpassed the genome-wide significance threshold. Analyses were adjusted for the top seven genetic principal components.

The European ancestry PGSs contain 593,841 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 590,568 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

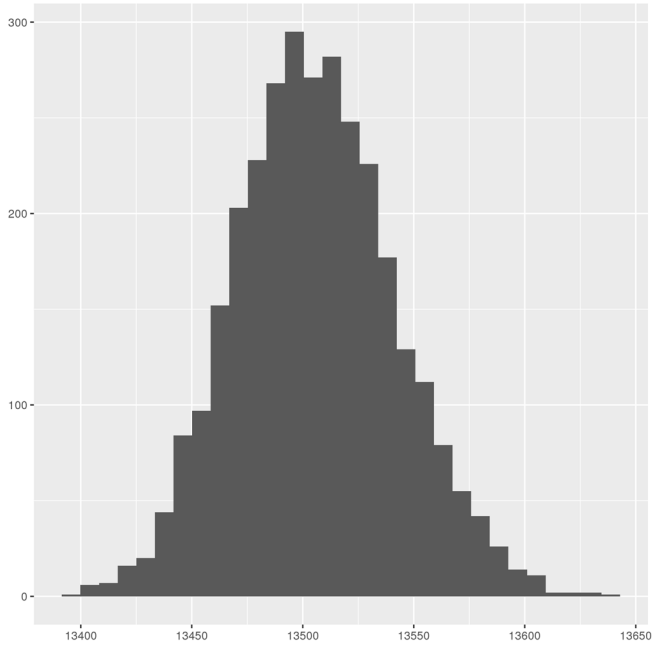
N.B.: **Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	13534.50	13777.40	242.90	13669.30	13667.79	0.28
African ancestry	3100	13393.20	13636.30	243.10	13504.90	13505.70	0.65



European ancestry: Dist. of E4_xdisorder_PGC13



African ancestry: Dist. of A4_xdisorder_PGC13

Refereces:

Cross-Disorder Group of the Psychiatric Genomics Consortium. (2013). Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *The Lancet*, *381*(9875), 1371-1379.

Z. Age at Menarche – REPROductive GENetics consortium 2014

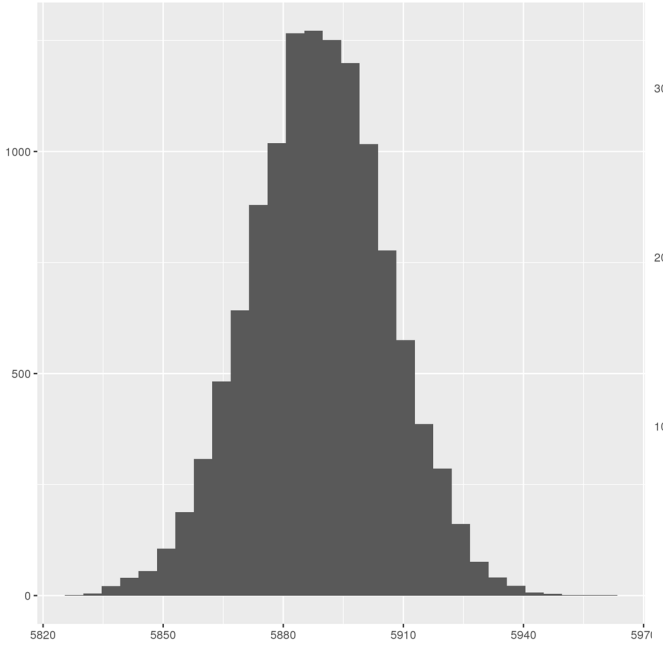
PGSs for age at menarche were created using results from a 2014 study conducted by the Reproductive Genetics (ReproGen) consortium. The GWAS meta-analysis files are publicly available on the ReproGen data download page: http://www.reprogen.org/data_download.html (Menarche_Nature2014_GWASMetaResults_17122014.txt). The ReproGen meta-analysis included 182,416 women of European descent from 57 studies imputed to HapMap Phase 2 CEU build 35 or 36 with at total of 2,441,815 autosomal SNPs. Birth year was the only covariate included to allow for the secular trends in menarche timing. The study reported 3,915 genome-wide significant SNPs (**Figure 1**). Of these, the authors identified 123 independent signals for age at menarche, which they assessed further in an independent sample of 8,689 women from the EPIC-InterAct study.

The European ancestry PGSs contain 753,289 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 747,702 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

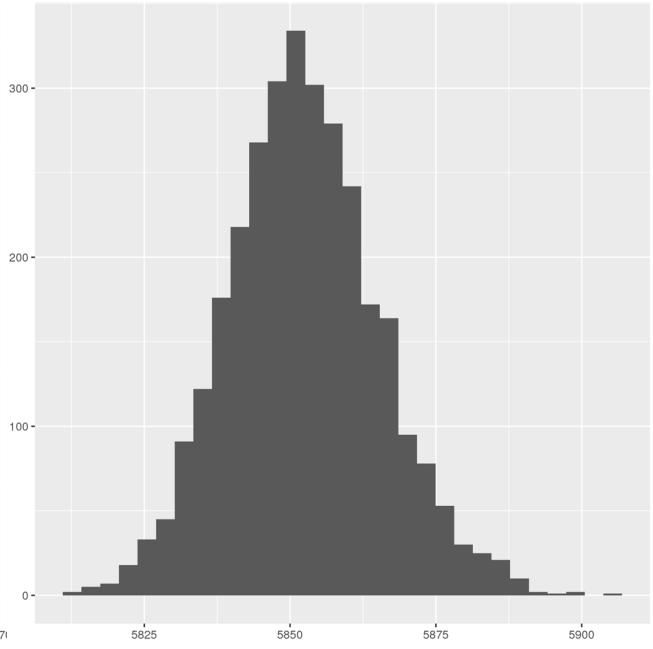
N.B.: Sample size for European Ancestry females = 6,894; Sample size for African Ancestry females = 1,910
Please note that the ReproGen results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	6894	5828.04	5961.43	133.39	5889.01	5888.94	0.16
African ancestry	1910	5811.35	5904.02	92.67	5852.03	5852.39	0.23



European ancestry: Dist. of E4_menarche_ReproGen14



African ancestry: Dist. of A4_menarche_ReproGen14

References:

Perry, J. R., Day, F., Elks, C. E., Sulem, P., Thompson, D. J., Ferreira, T., ... & Albrecht, E. (2014). Parent-of-origin-specific allelic associations among 106 genomic loci for age at menarche. *Nature*, *514*(7520), 92-97.

AA. Age at Menopause – REPROductive GENetics consortium 2015

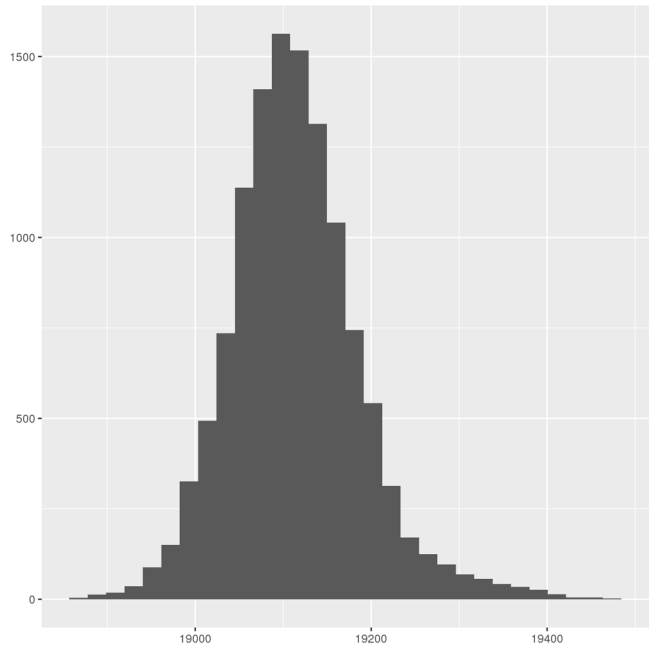
PGSs for age at menopause were created using results from a 2014 study conducted by the Reproductive Genetics (ReproGen) consortium. The GWAS meta-analysis files are publicly available on the ReproGen data download page: http://www.reprogen.org/data_download.html. The ReproGen meta-analysis included 69,360 women of European descent from 33 studies imputed to HapMap Phase 2 CEU build 35 or 36. The study reported 44 genome-wide significant regions (**Table 1**).

The European ancestry PGSs contain 742,458 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 736,696 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

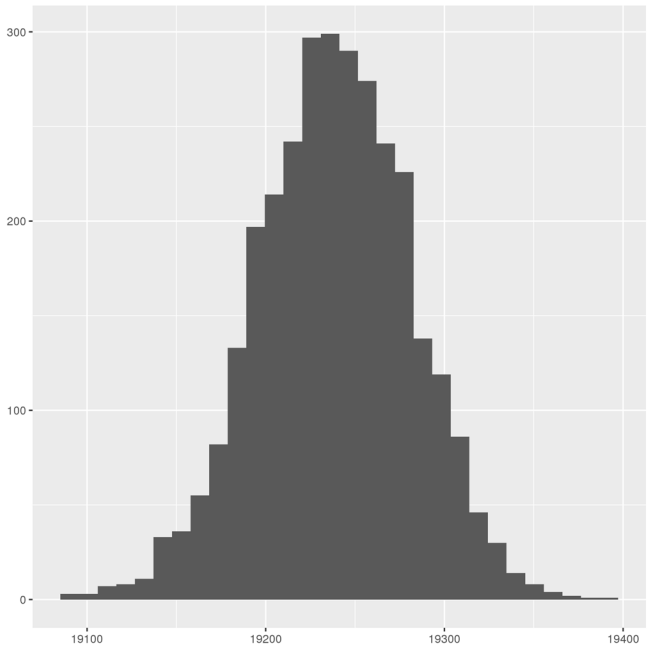
N.B.: Sample size for European Ancestry females = 6,894; Sample size for African Ancestry females = 1,910
Please note that the ReproGen results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	6894	18860.20	19466.80	606.60	19108.80	19113.47	0.67
African ancestry	1910	19086.40	19388.10	301.70	19238.90	19238.43	0.77



European ancestry: Dist. of E4_menopause_ReproGen15



African ancestry: Dist. of A4_menopause_ReproGen15

References:

Day, F. R., Ruth, K. S., Thompson, D. J., Lunetta, K. L., Pervjakova, N., Chasman, D. I., … Murray, A. (2015). Large-scale genomic analyses link reproductive ageing to hypothalamic signaling, breast cancer susceptibility and BRCA1-mediated DNA repair. Nature Genetics, 47(11), 1294–1303. http://doi.org/10.1038/ng.3412

BB. Plasma Cortisol – CORtisol NETwork 2014

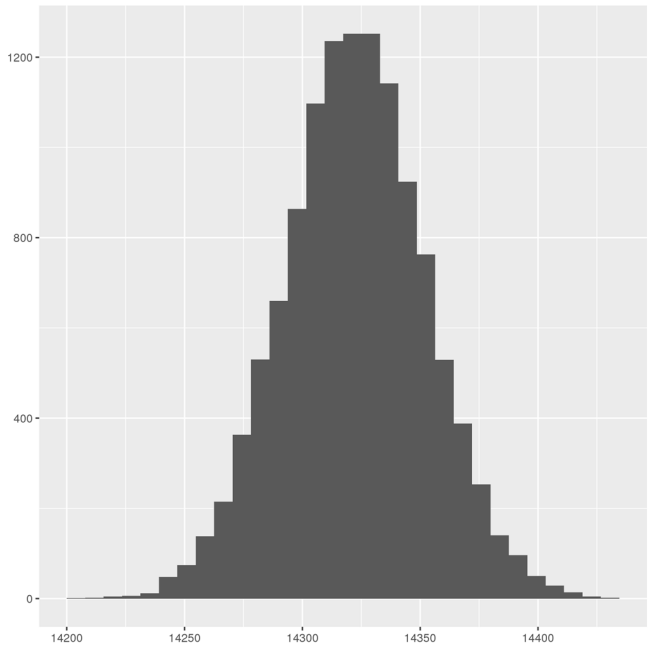
The PGSs for plasma corticol were created using results from a 2014 GWAS conducted by the CORtisol NETwork (CORNET). The GWAS meta-analysis files are available through CORNET by request only. The discovery phase of the meta-analysis included 12,597 Caucasian participants; the replication sample consisted of 2,795 participants. Samples from the discovery phase were drawn from 11 western European population-based cohorts, and samples in the replication phase were drawn from three independent cohorts (see Bolten et al., p. 8 and S1, 2014). The GWAS meta-analysis (phase 1) yielded two genome-wide significance SNPs. Cortisol was measured similarly in all cohorts, using a blood immunoassay; there were multiple inclusion and exclusion criteria (see Bolten et al., p. 8 and S1, 2014). Analyses were adjusted for age and sex; there were no differences when time of samping was also included as a covariate.

The European ancestry PGSs contain 796,779 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 794,626 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

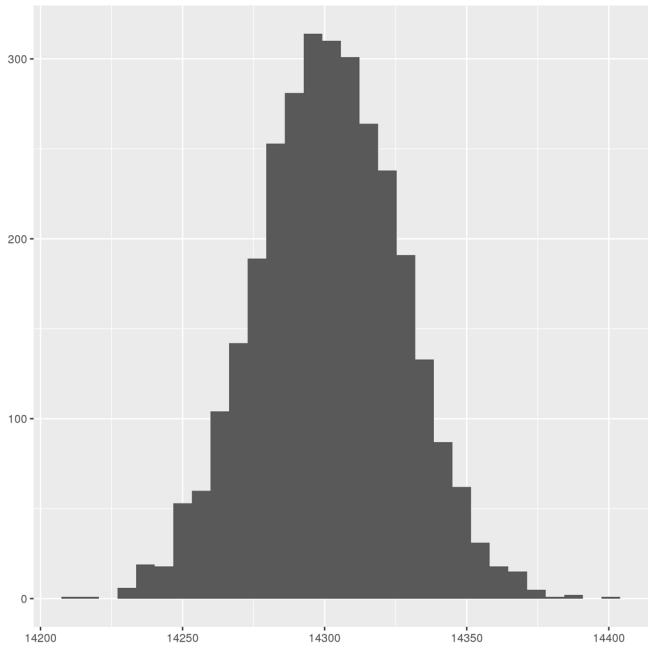
N.B.: The effect estimates for the GWAS by CORNET are only available through request to the CORNET consortia. **Please note that the CORNET results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	14201.60	14428.30	226.70	14322.30	14322.20	0.27
African ancestry	3100	14208.00	14398.00	190.00	14301.30	14301.45	0.46



European ancestry: Dist. of E4_cortisol_CORNET14



African ancestry: Dist. of A4_cortisol_CORNET14

References:

Bolton, J. L., Hayward, C., Direk, N., Lewis, J. G., Hammond, G. L., Hill, L. A., ... & Rudan, I. (2014). Genome wide association identifies common variants at the SERPINA6/SERPINA1 locus influencing plasma cortisol and corticosteroid binding globulin. *PLoS Genetics*, *10*(7), e1004474.

CC. Major Depressive Disorder (MDD) – Psychiatric Genomics Consortium 2013

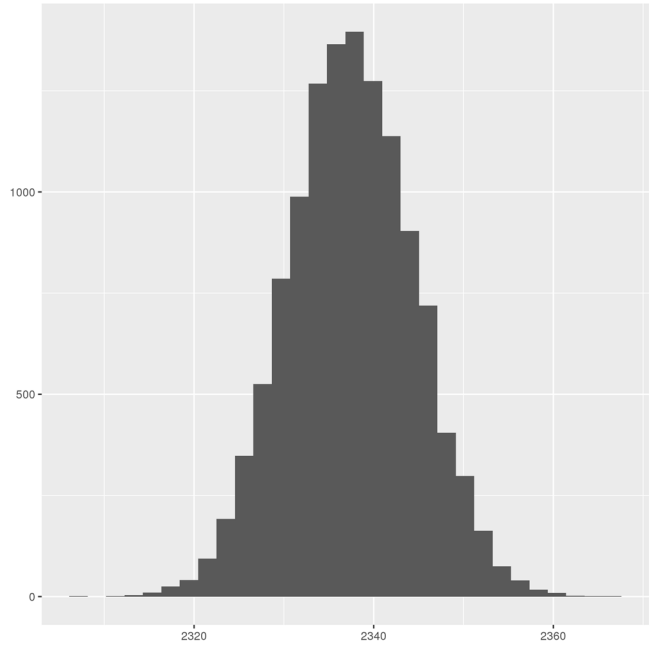
OUTDATED – INCLUDED FOR POSTERITY: The PGSs for MDD were created using results from a 2013 GWAS conducted by the MDD working group of the Psychiatric Genomics Consortium (PGC). The GWAS meta-analysis files are available on the PGC website: http://www.med.unc.edu/pgc/results-and-downloads (pgc.mdd.2012-04.zip). The discovery phase of the meta-analysis included 9,240 cases and 9,519 controls. A follow up meta-analysis of the 544 most significant SNPs was conducted in a replication sample that included 6,783 independent cases and 50,695 independent controls. No SNPs reached genome-wide significance in the discovery or replication phase. A MDD-bipolar cross-disorder analyses using 819 autosomal SNPs was further conducted in 9,238 MDD cases/8,039 controls and 6,998 BP cases/7,775 controls. Fifteen SNPs achieved genome-wide significance in the cross-disorder meta-analysis. MDD cases were required to have a DSM-IV lifetime MDD diagnosis that was collected by a clinician using structured interviews or clinician-administered DSM-IV checklists. Most controls were randomly selected and screened for lifetime MDD. Meta-analyses adjusted for the top 5 genetic principal components and study indicators.

The European ancestry PGSs contain 73,017 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 73,090 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

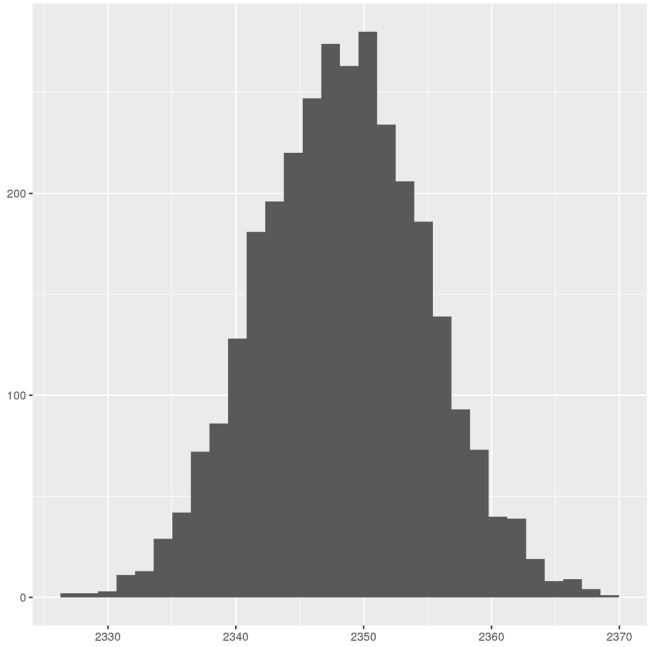
N.B.: The GWAS results have been heavily pruned by the PGC consortia therefore resulting in a low number of overlapping SNPs. **Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	2306.52	2365.94	59.42	2337.41	2337.49	0.06
African ancestry	3100	2326.79	2369.02	42.23	2348.37	2348.35	0.12



European ancestry: Dist. of E4_MDD_PGC13



African ancestry: Dist. of A4_MDD_PGC13

References

Ripke, S., Wray, N. R., Lewis, C. M., Hamilton, S. P., Weissman, M. M., Breen, G., ... & Heath, A. C. (2013). A mega-analysis of genome-wide association studies for major depressive disorder. *Molecular Psychiatry*, *18*(4), 497-511.

DD. Extraversion – Genetics of Personality Consortium 2016

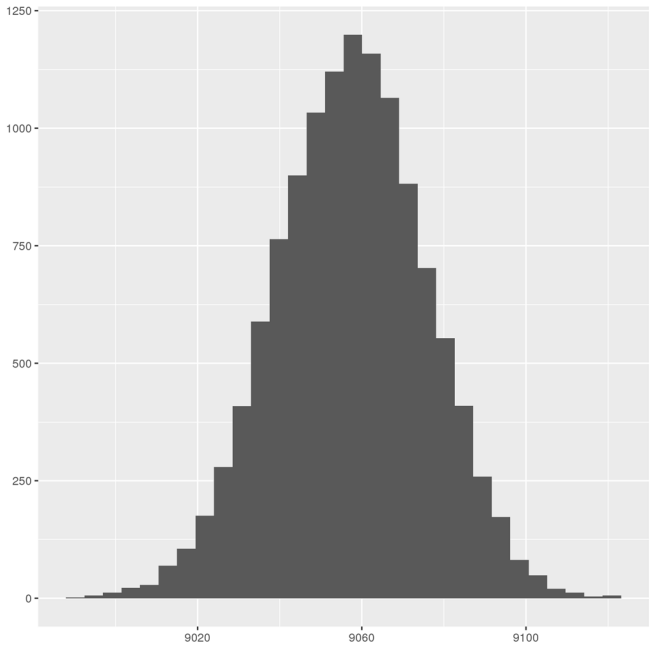
The extraversion PGSs were created using results from a 2016 study by the Genetics of Personality Consortium (GPC). The meta-analysis included 63,030 individuals of European ancestry from 29 cohorts in the discovery sample, and 9,783 individauls from one cohort in the replication sample. All datasets used a harmonized latent extraversion score as a continuous phenotype in study-specific GWAS. Summary statistics are freely available from the Netherlands Tweelingen register website (http://www.tweelingenregister.org/GPC/). Approximately 7.5 million SNPs were included in the meta-analyses, with all cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G). The GWAS meta-analysis did not include the HRS. No genome-wide significant SNPs were identified in the total sample; none of the 74 SNPs that were identified with a P-value < 1 x 10^{-5} were replicated in the replication sample. Study-specific GWASs accounted for sex and age; ancestry principal components were included as covariates at a study-specific determination.

The European ancestry PGSs contain 1,162,652 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,157,732 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

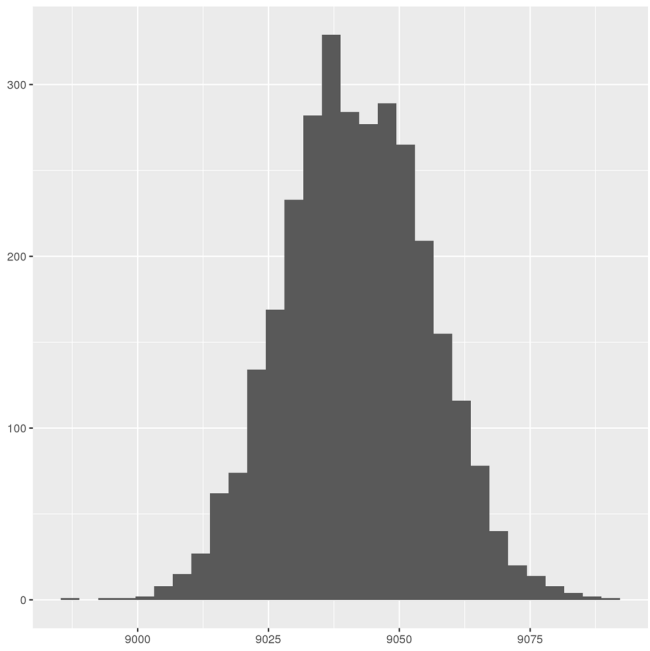
N.B.: **Please note that the PGC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below:

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	8990.73	9121.48	130.75	9057.52	9057.34	0.17
African ancestry	3100	8987.18	9090.48	103.30	9041.48	9041.70	0.25



European ancestry: Dist. of E4_extraversion_GPC16



African ancestry: Dist. of A4_extraversion_GPC16

References

van den Berg, S. M., de Moor, M. H. M., Verweij, K. J. H., Krueger, R. F., Luciano, M., Arias Vasquez, A., … Boomsma, D. I. (2016). Meta-analysis of Genome-Wide Association Studies for Extraversion: Findings from the Genetics of Personality Consortium. *Behavior Genetics*, *46*(2), 170–182. https://doi.org/10.1007/s10519-015-9735-5

EE. Antisocial Behavior – Broad Antisocial Behavior Consortium 2017

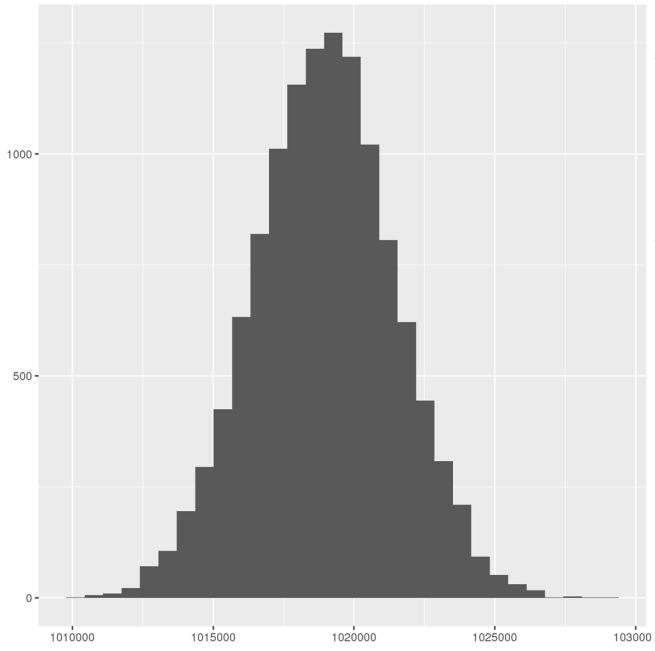
The antisocial behavior (AB) PGSs were created using results from a 2017 study by the Broad Antisocial Behavior Consortium. The meta-analysis included 16,400 individuals in the discovery sample and 9,381 individuals in the replication sample (both child and adult samples). All datasets used continuous phenotypes except for one study that used a case-control design (Tielbeek et al., 2017). Approximately 7.4 million SNPs were included in the meta-analyses, with all cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G) (except two of the replication cohorts, which were not imputed). The GWAS meta-analysis did not include the HRS. Sex-specific GWAS were also conducted. No genome-wide significant SNPs were identified in the total sample; three sex-discordant loci were identified just below the genome-wide significant p-value threshold, but were not replicated in the replication samples. Study-specific GWASs accounted for sex, age, the first four principal components, and study-specific covariates.

The European ancestry PGSs contain 1,289,915 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,285,962 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

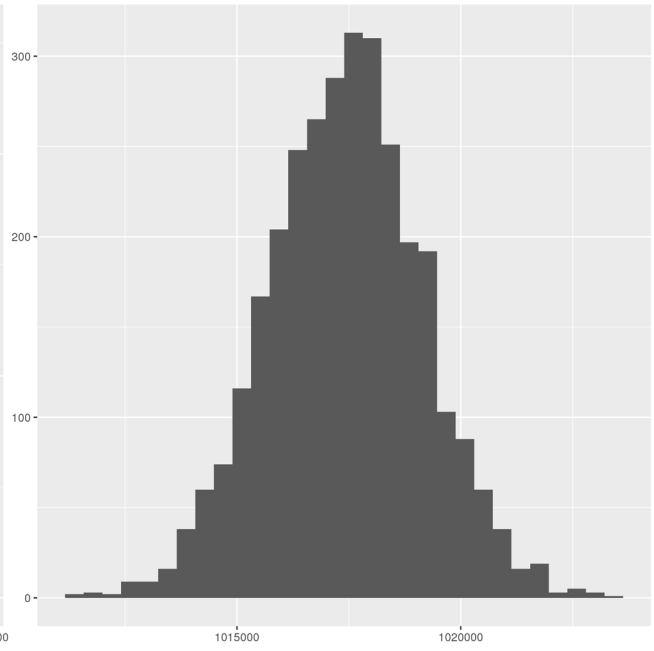
N.B.: **Please note that the Broad ABC are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below:

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	1010040	1029000	18960	1018960	1018948.2	22.61464
African ancestry	3100	1011170	1023220	12050	1017450	1017425.2	30.77879



European ancestry: Dist. of E4_AB_BROAD17



African ancestry: Dist. of A4_AB_BROAD17

References

Tielbeek, J. J., Johansson, A., Polderman, T. J. C., Rautiainen, M.-R., Jansen, P., Taylor, M., … Posthuma, D. (2017). Genome-Wide Association Studies of a Broad Spectrum of Antisocial Behavior. *JAMA Psychiatry*, *74*(12), 1242–1250. https://doi.org/10.1001/jamapsychiatry.2017.3069

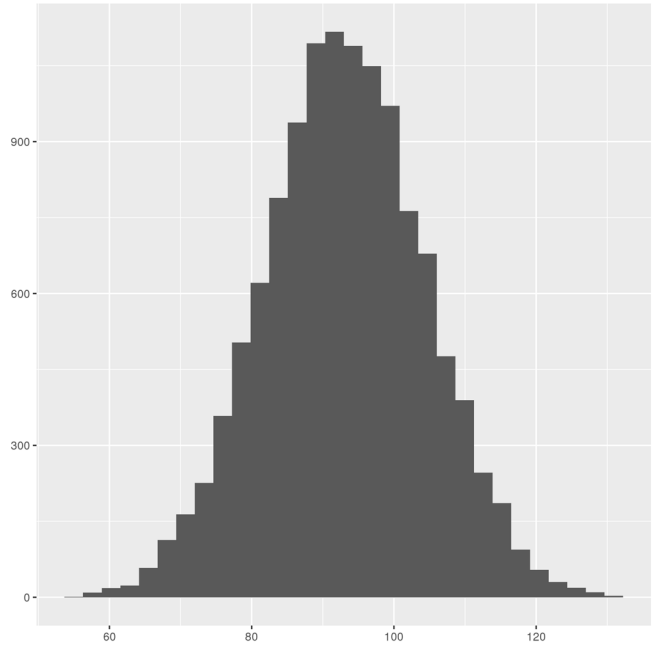
FF. Educational Attainment 3 – Social Science Genetic Association Consortium 2018

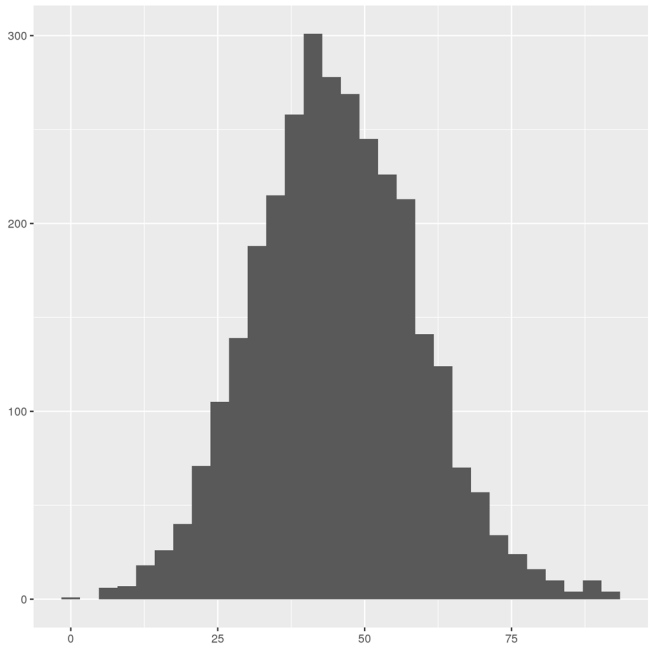
The educational attainment PGSs were created using results from a 2018 study by the Social Science Genetic Association Consortium (SSGAC). The meta-analysis included 405,073 individuals in the combined discovery and replication sample and 726,808 individuals that did not contribute to the analyses of the previous study and were used as replication in this study (total of 1,131,881 individuals). Genome-wide significant SNPs were identified in 1,271 loci (**Supplementary Information table 2** [1]). Approximately 10.2 million SNPs were included in the analyses, with all cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G). The original GWAS included the HRS. To compute the PGSs for HRS respondents, the SSGAC provided SNP weights with the HRS and 23andMe results removed (due to data use agreements). Study-specific GWASs controlled for the first ten principal components of the genotypic data, a third-order polynomial in age, an indicator for being female, interactions between age and female, and study-specific controls, including dummy variables for major events such as wars or policy changes that may have affected access to education in their specific sample.

The European ancestry PGSs contains 1,274,056 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,263,974 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication. Included SNPs and weights with the HRS and 23andMe removed are avaialable upon request to the SSGAC consortium contact@ssgac.org.
Please note that the SSGAC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).
Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	55.01	130.94	75.93	92.97	93.05	0.10
African ancestry	3100	0.87	92.76	91.88	44.82	45.25	0.25





European ancestry: Dist. of E4_EDU3_SSGAC18 African ancestry: Dist. of A4_EDU3_SSGAC18

References

Lee JJ, Wedow R, Okbay A, Kong E, Maghzian O, Zacher M, … & Cesarini D. (2016). Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nature genetics*, *doi: 10.1038/s41588-018-0147-3*

GG. Obsessive Compulsive Disorder (OCD) – International Obsessive Compulsive Disorder Foundation – Genetics Collaborative 2017

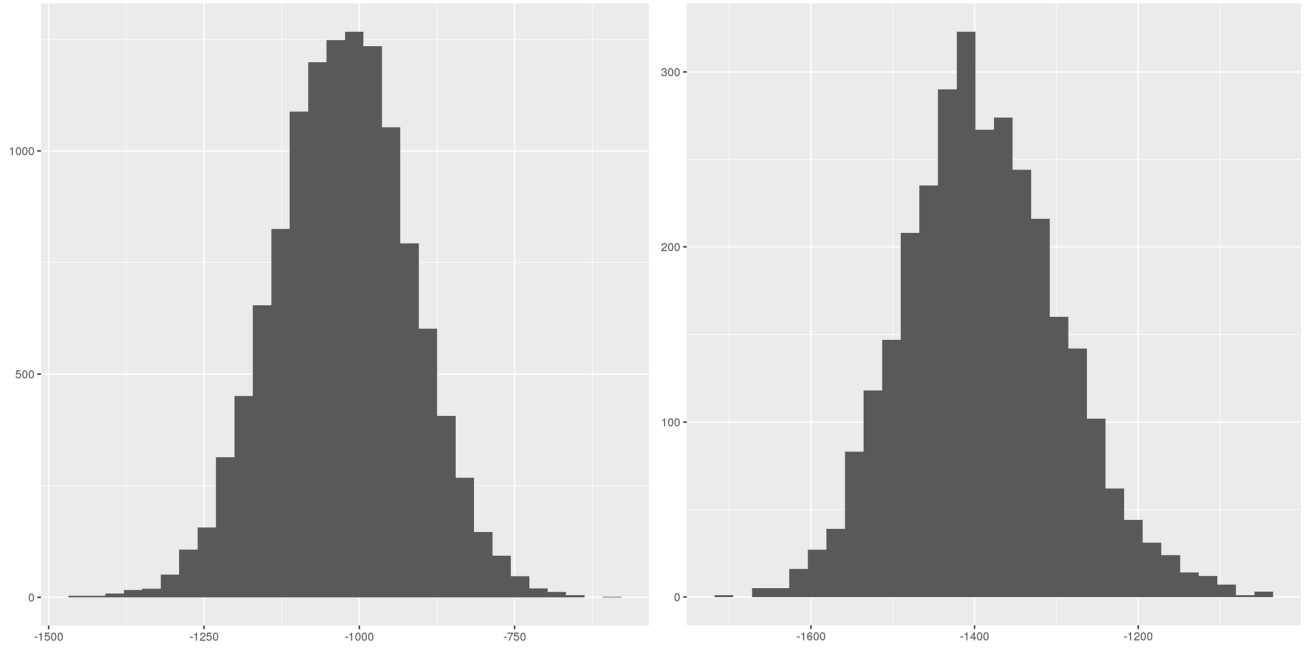
The obsessive-compulsive disorder (OCD) PGSs were created using results from a 2017 study by International Obsessive Compulsive Disorder Foundation Genetics Collaborative (IOCDF-GC) and OCD Collaborative Genetics Association Studies (OCGAS). The meta-analysis included 9,725 (2,688 OCD cases, 7037 controls) individuals. There was no replication sample for the GWAS analyses. No genome-wide significant SNPs were identified. Approximately 8.7 million SNPs were included in the analyses, with all cohorts using SNPs imputed to the 1000 genomes reference panel (1000G). The GWAS meta-analysis did not include HRS. Study-specific GWASs did not account for covariates; rather, separate association analyses were conducted for each case-control sub-population (i.e., identified using principal components analyses).

The European ancestry PGSs contains 1,274,056 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,263,974 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

N.B.: **Please note that the IOCDF-OCD are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	-1465.43	-605.46	859.97	-1025.59	-1026.25	1.00
African ancestry	3100	-1699.22	-1039.48	659.74	-1394.95	-1389.14	1.73



European ancestry: Dist. of E4_OCD_IOCDF17 African ancestry: Dist. of A4_OCD_IOCDF17

References

International Obsessive Compulsive Disorder Foundation Genetics Collaborative (IOCDF-GC) and OCD Collaborative Genetics Association Studies (OCGAS). (2017). Revealing the complex genetic architecture of obsessive-compulsive disorder using meta-analysis. Molecular Psychiatry. https://doi.org/10.1038/mp.2017.154

HH. Age at first birth (AFB) – Sociogenome consortium 2016

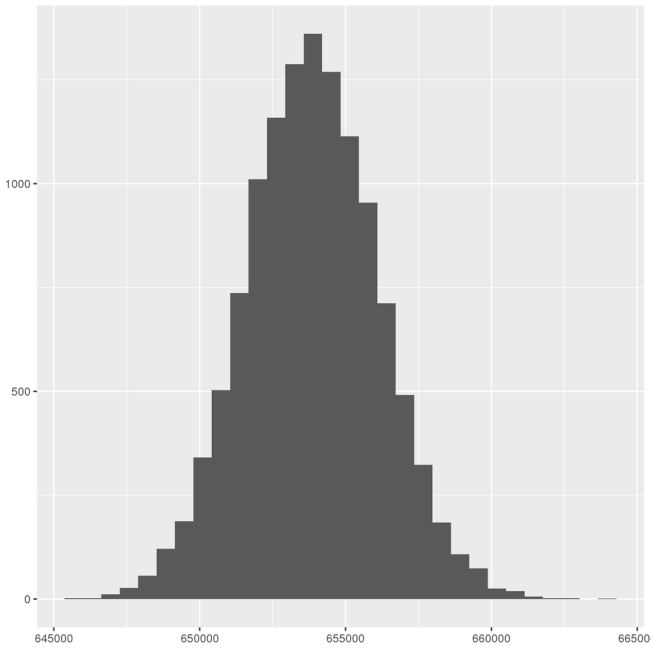
PGSs for age at first birth (AFB) were created using results from a 2016 study conducted by the Sociogenome consortium. The GWAS meta-analysis files are publicly available on the Sociogenome data download page: http://www.sociogenome.com//data/ (AgeFirstBirth_Pooled.txt; AgeFirstBirth_Female.txt; AgeFirstBirth_Male.txt). The meta-analysis included 251,151 men and women from a total of 62 cohorts of European ancestry. 2.4 million SNPs imputed from NCBI Build 37 HapMap phase 2 data passed quality control filters. Associations were adjusted for principal components to reduce confounding by population stratification, as well as for respondent birth year and its square and cube to control for nonlinear birth cohort effects. A single genomic control at the cohort level was applied and meta-analysis results were obtained using a sample-size-weighted fixed-effect method in METAL. AFB was only assessed for those who were parous. Meta-analysis results are reported for men and women combined and separately. The study identified ten genome-wide significant SNPs for combined results, nine of which were significantly associated in both sexes combined, and one of which was associated in women only (n=154,839) (**Figure 1a** and **Table 1**).

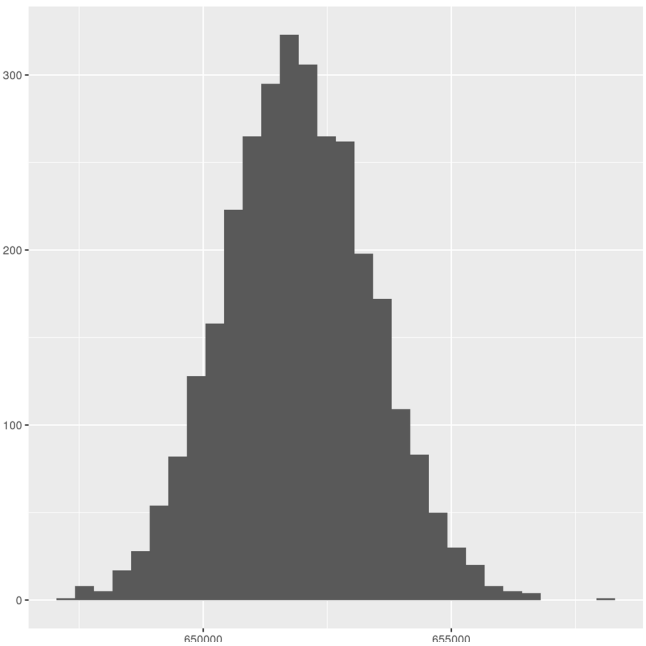
The European ancestry PGSs for the combined sample contain 761,196 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 757,179 SNPs. The European ancestry PGSs for the female sample contain 760,076 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 756,838 SNPs. The European ancestry PGSs for the male sample contain 755,629 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 755,336 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

N.B.: **Please note that the AFB are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

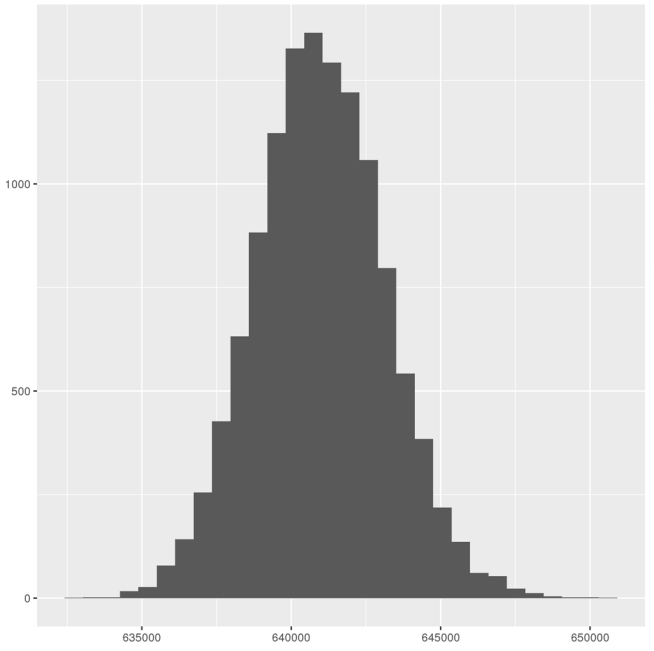
Raw PGS details are presented below.

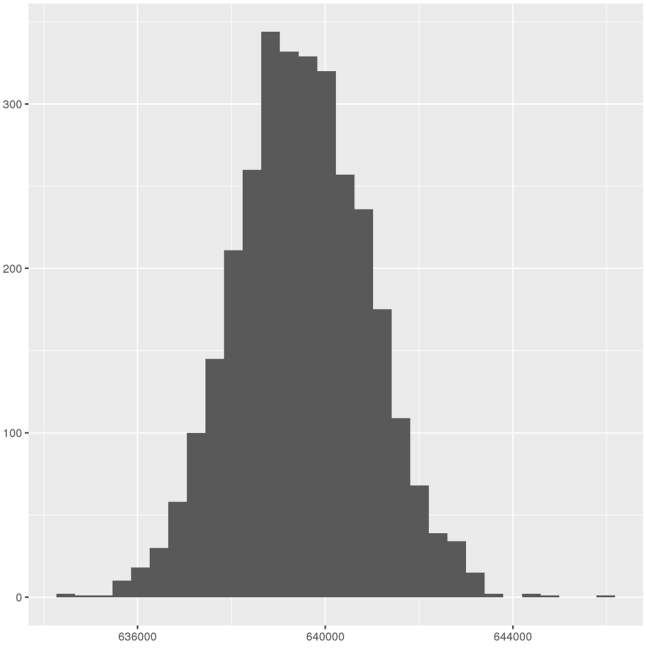
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
Combined sample							
European ancestry	12090	645582.00	663868.00	18286.00	653844.00	653864.38	20.54
African ancestry	3100	647400.00	658281.00	10881.00	651882.50	651907.75	26.53
Female Sample							
European ancestry	12090	632704.00	650588.00	17884.00	640933.00	640986.65	19.71
African ancestry	3100	634527.00	646034.00	11507.00	639471.00	639504.74	25.46
Male sample							
European ancestry	12090	602785.00	617445.00	14660.00	610140.50	610131.13	17.00
African ancestry	3100	605930.00	616006.00	10076.00	610649.00	610627.00	23.28



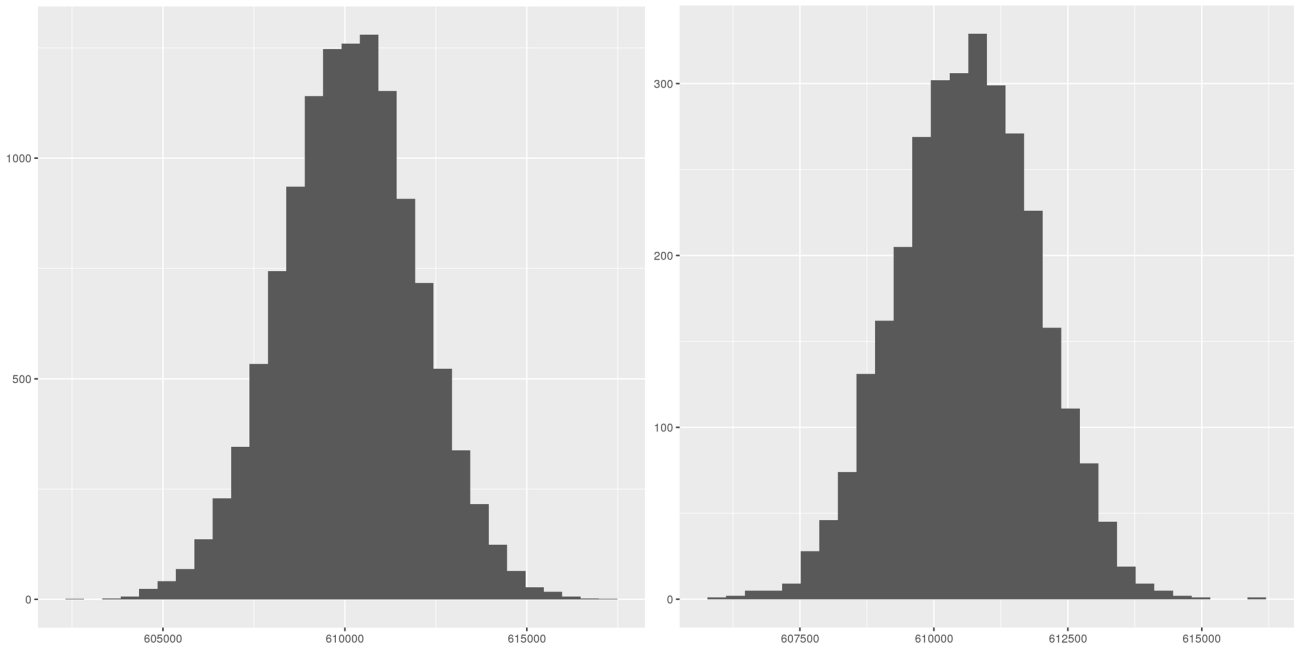


European ancestry: Dist. of E4_AFBc_socgen16 African ancestry: Dist. of A4_AFBc_socgen16





European ancestry: Dist. of E4_AFBf_socgen16 African ancestry: Dist. of A4_AFBf_socgen16



European ancestry: Dist. of E4_AFBm_socgen16 African ancestry: Dist. of A4_AFBm_socgen16

References

Barban, N., Jansen, R., De Vlaming, R., Vaez, A., Mandemakers, J. J., Tropf, F. C., ... & Tragante, V. (2016). Genome-wide analysis identifies 12 loci influencing human reproductive behavior. Nature genetics, 48(12), 1462.

II. Number of children ever born (NEB) – Sociogenome consortium 2016

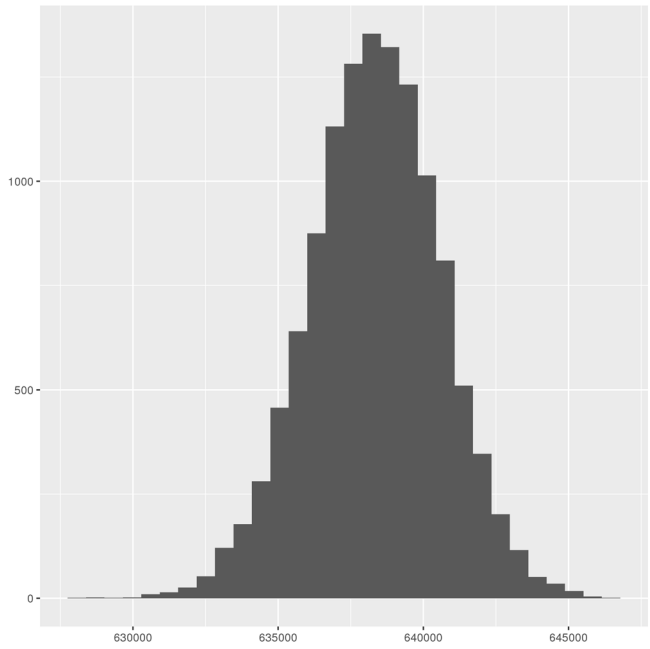
PGSs for number of children ever born (NEB) were created using results from a 2016 study conducted by the Sociogenome consortium. The GWAS meta-analysis files are publicly available on the Sociogenome data download page: http://www.sociogenome.com//data/ (NumberChildrenEverBorn_Pooled.txt; NumberChildrenEverBorn _Female.txt; NumberChildrenEverBorn _Male.txt). The Sociogenome meta-analysis included 343,072 men and women from a total of 62 cohorts of European ancestry. 2.4 million SNPs imputed from NCBI Build 37 HapMap phase 2 data passed quality control filters. Associations were adjusted for principal components to reduce confounding by population stratification, as well as for the birth year of the respondent and its square and cube to control for nonlinear birth cohort effects. A single genomic control at the cohort level was applied and meta-analysis results were obtained using a sample-size-weighted fixed-effect method in METAL. NEB was assessed only for those who had completed their reproductive period (age ≥45 years for women and ≥55 years for men). Meta-analysis results are reported for men and women combined and separately. Three loci were significantly associated at the genome-wide level with NEB: two in both sexes combined and one in men only (n = 103,736) (**Figure 1b, Table 1**, and **Supplementary Note**).

The European ancestry PGSs for the combined sample contain 764,577 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 758,283 SNPs. The European ancestry PGSs for the female sample contain 763,060 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 757,701 SNPs. The European ancestry PGSs for the male sample contain 763,620 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 759,159 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

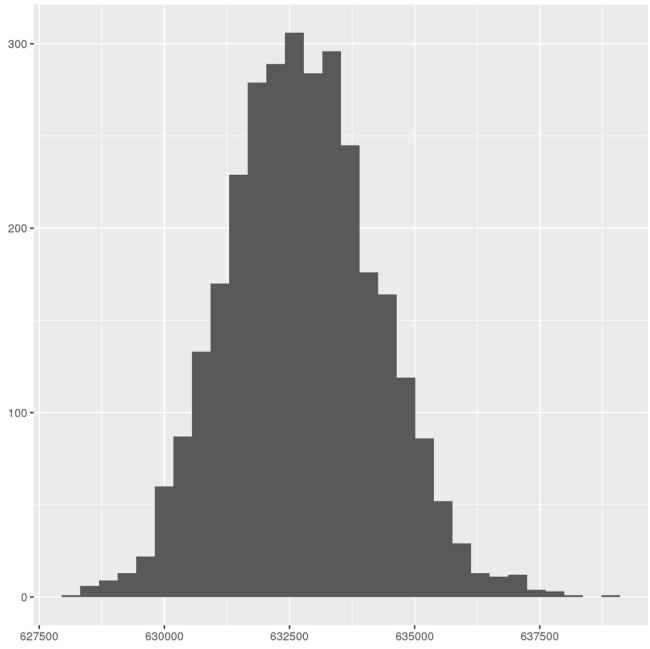
N.B.: **Please note that the NEB are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

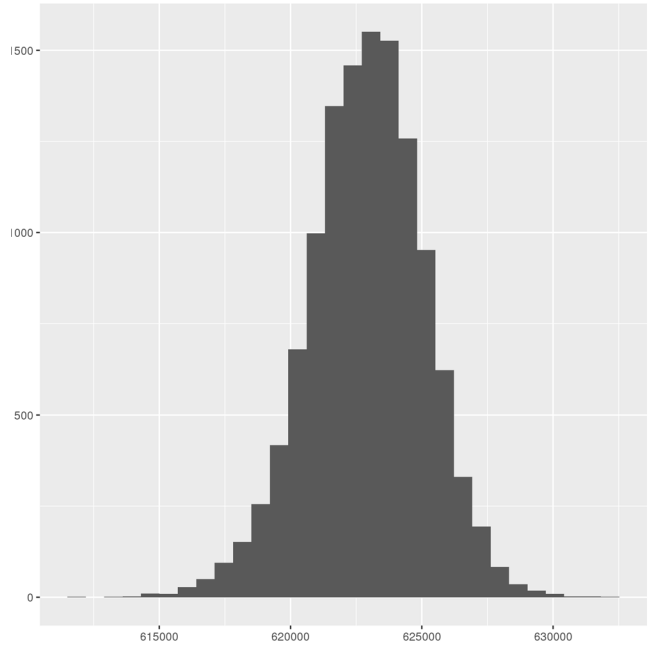
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
Combined sample							
European ancestry	12090	627833.00	646231.00	18398.00	638363.00	638330.93	20.52
African ancestry	3100	628249.00	639034.00	10785.00	632710.00	632759.33	26.77
Female Sample							
European ancestry	12090	611607.00	631932.00	20325.00	622960.00	622895.75	19.94
African ancestry	3100	612997.00	624388.00	11391.00	617576.00	617630.45	25.93
Male sample							
European ancestry	12090	608813.00	626786.00	17973.00	615736.00	615746.80	18.04
African ancestry	3100	609349.00	617771.00	8422.00	613394.00	613397.11	23.14



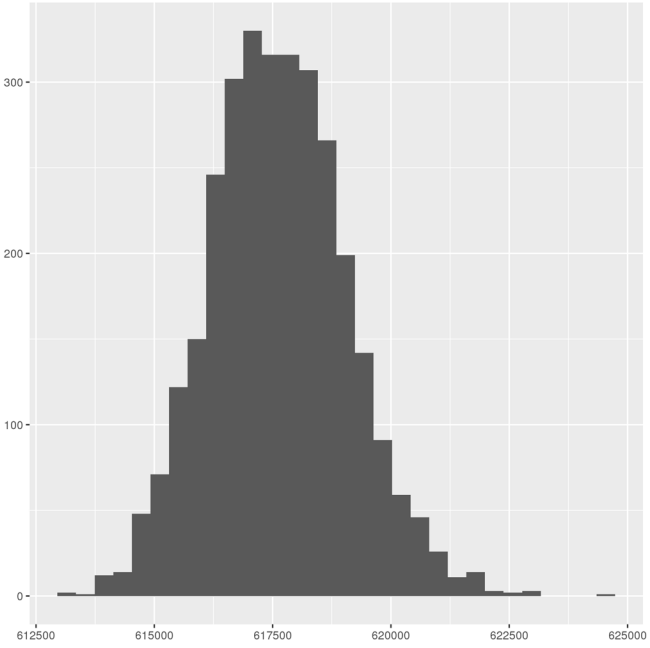
European ancestry: Dist. of E4_NEBa_socgen16



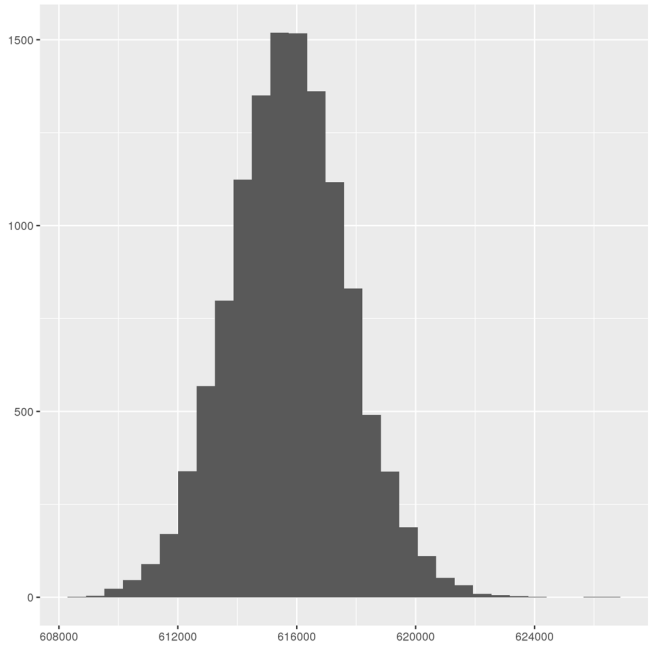
African ancestry: Dist. of A4_NEBa_socgen16



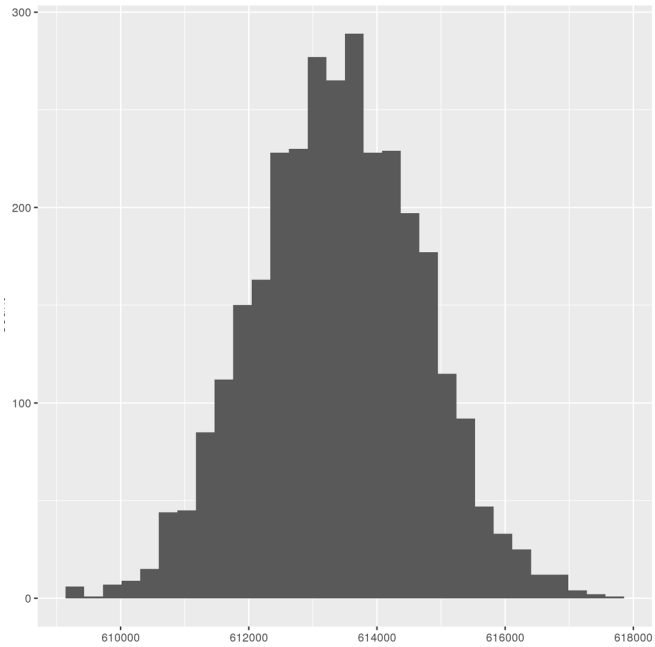
European ancestry: Dist. of E4_NEBf_socgen16



African ancestry: Dist. of A4_NEBf_socgen16



European ancestry: Dist. of E4_NEBm_socgen16



African ancestry: Dist. of A4_NEBm_socgen16

References

Barban, N., Jansen, R., De Vlaming, R., Vaez, A., Mandemakers, J. J., Tropf, F. C., ... & Tragante, V. (2016). Genome-wide analysis identifies 12 loci influencing human reproductive behavior. Nature genetics, 48(12), 1462.

JJ. Major Depressive Disorder 2 (MDD2) – Psychiatric Genomics Consortium 2018

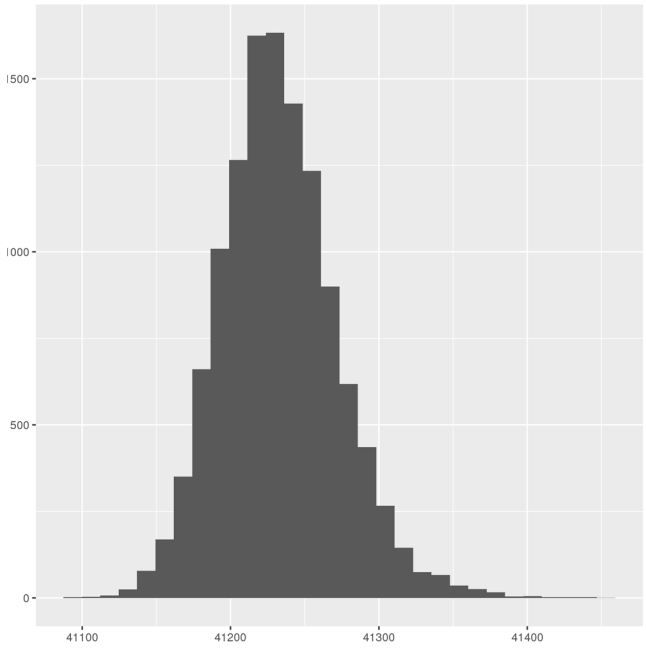
PGSs for major depressive disorder version 2 (MDD2) were created using results from a 2018 study conducted by the Psychiatric Genomics Consortium (PGC). The GWAS meta-analysis files are publicly available on the PGC data download page: https://www.med.unc.edu/pgc/results-and-downloads (daner_pgc_mdd_meta_no23andMe.gz). The PGC meta-analysis included 59,851 cases and 113,154 controls from European ancestry cohorts. Results from the full meta-analysis with 23andMe added an additional 75,607 cases and 231,747 controls. To compute the PGSs for HRS respondents, SNP weights were constructed from publicly available data and do not include results with 23andMe due to data use agreements. The GWAS meta-analysis included 9.6 million SNPs imputed to NCBI Build 37/UCSC hg 19. Inclusion/exclusion criteria for cases and controls for each cohort are available in **Supplementary Table 2**. Results from LD score regression did not reveal any evidence of residual population stratification. The study identified 44 independent genome-wide significant SNPs (**Table 2**). Of these 44 loci, 30 are new and 14 were significant in a prior study of MDD or depressive symptoms.

The European ancestry PGSs contains 1,340,536 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,346,587 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

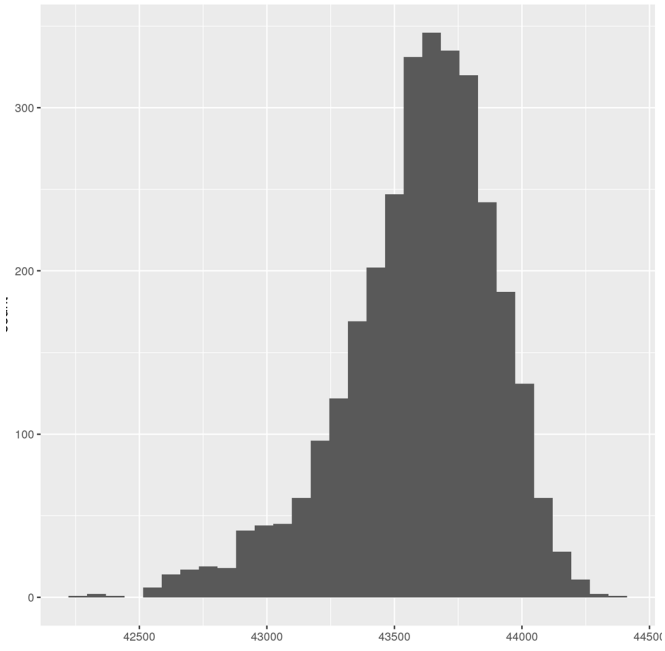
N.B.: **Please note that the PGC-MDD2 are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	41088.60	41448.20	359.60	41230.30	41232.77	0.36
African ancestry	3100	42286.60	44403.20	2116.60	43633.15	43595.44	5.37



European ancestry: Dist. of E4_MDD2_PGC18



African ancestry: Dist. of A4_MDD2_PGC18

References

Wray, N. R., Ripke, S., Mattheisen, M., Trzaskowski, M., Byrne, E. M., Abdellaoui, A., ... & Bacanu, S. A. (2018). Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. Nature Genetics, 50(5), 668.

KK. Post traumatic stress disorder (PTSD) – Psychiatric Genomics Consortium 2018

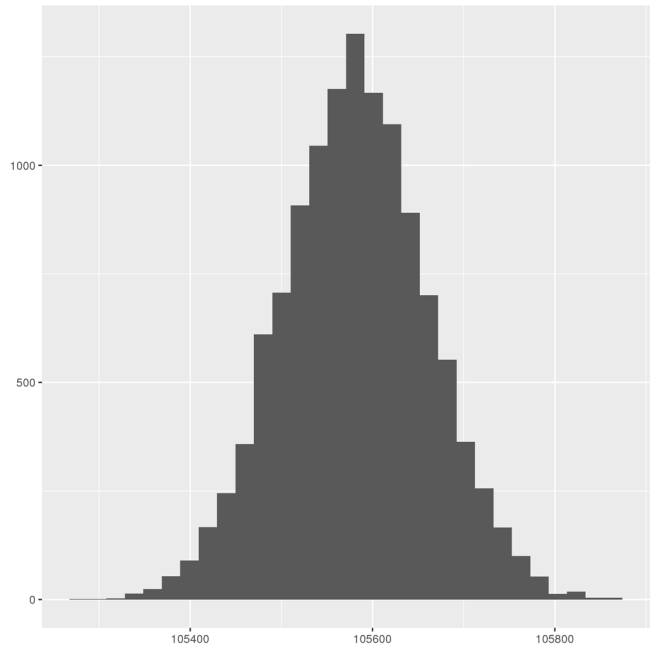
The PTSD PGSs were created using results from a 2018 study by the Psychiatric Genomics Consortium (Duncan et al., 2018). Authors conducted separate GWAS for European ancestry datasets (N_{cases} = 2,424, $N_{controls}$ = 7,113), African American datasets (N_{cases} = 2,479, $N_{controls}$ = 6,744), Latino/Hispanic datasets (N_{cases} = 98, $N_{controls}$ = 598), and South African datasets (N_{cases} = 130, $N_{controls}$ = 254), followed by a meta-analyses across all four ancestry groups (N_{cases} = 5,131, $N_{controls}$ = 15,092). Data sourced from 11 contributing studies; PTSD case status was measured using both self-report measures matched to DSM symptoms, clinician-administered questionnaires, and clinical interviews. Many of the controls were also exposed to trauma but did not meet PTSD criteria (Duncan et al., 2018). All cohorts imputed SNPs to the 1000 Genomes phase I reference panel. Approximately 21.2 million SNPs were included in the African American GWAS, 13.2 million SNPs in the European GWAS, and 25.5 million SNPs in the combined ancestry GWAS. None of the GWAS meta-analyses included the HRS. No genome-wide significant SNPs were identified in either the transethnic or European meta-analyses. In the African American meta-analysis, one SNP exceeded the genome-wide significance threshold. All GWAS analyses controlled for the top 10 principal components.

The European ancestry PGSs for the combined GWAS contain 1,660,513 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,665,738 SNPs. The European ancestry PGSs for the European GWAS contain 1,297,321 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,309,885 SNPs. The European ancestry PGSs for the African GWAS contain 1,660,565 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,657,852 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

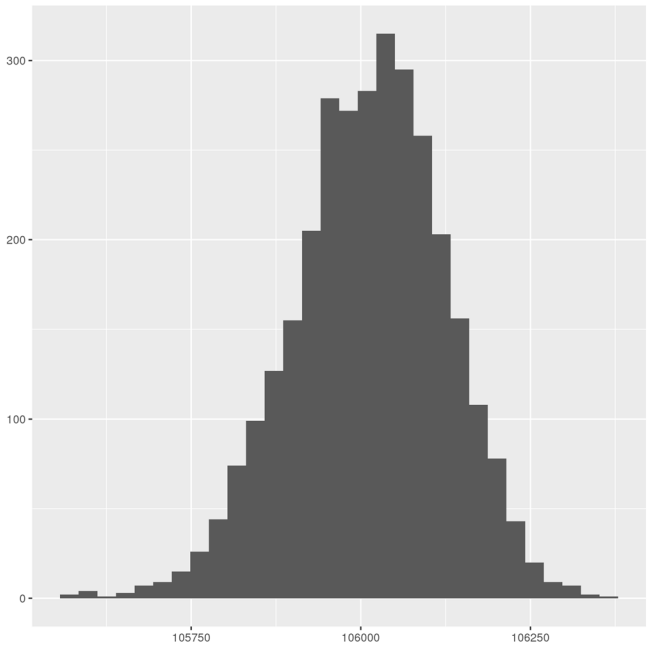
N.B.: **Please note that the PGC-PTSD results contain PGSs from multiple ancestry backgrounds (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

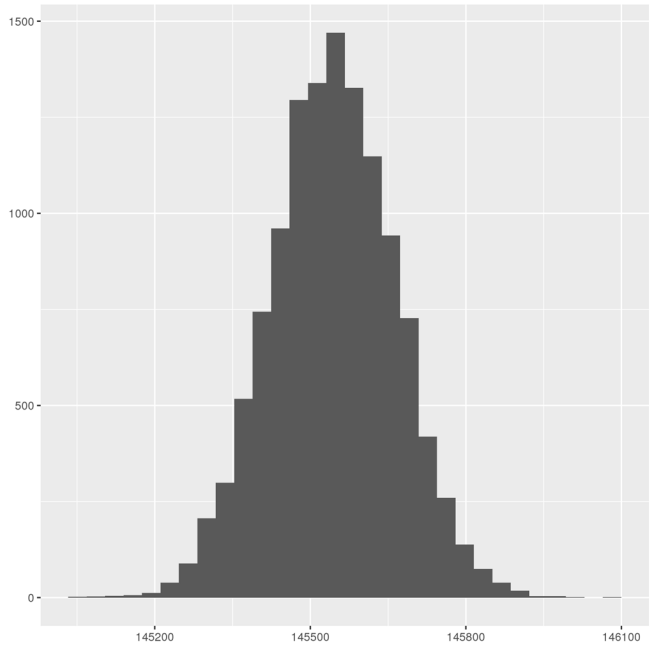
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
Combined sample							
European ancestry	12090	105287.00	105873.00	586.00	105581.00	105580.73	0.72
African ancestry	3100	105563.00	106358.00	795.00	106017.00	106011.85	2.01
European Sample							
European ancestry	12090	123181.00	125624.00	2443.00	123747.00	123771.16	1.81
African ancestry	3100	130586.00	149822.00	19236.00	144323.00	143899.82	44.83
African sample							
European ancestry	12090	145035.00	146066.00	1031.00	145543.00	145543.44	1.08
African ancestry	3100	144703.00	145938.00	1235.00	145346.00	145349.38	2.66



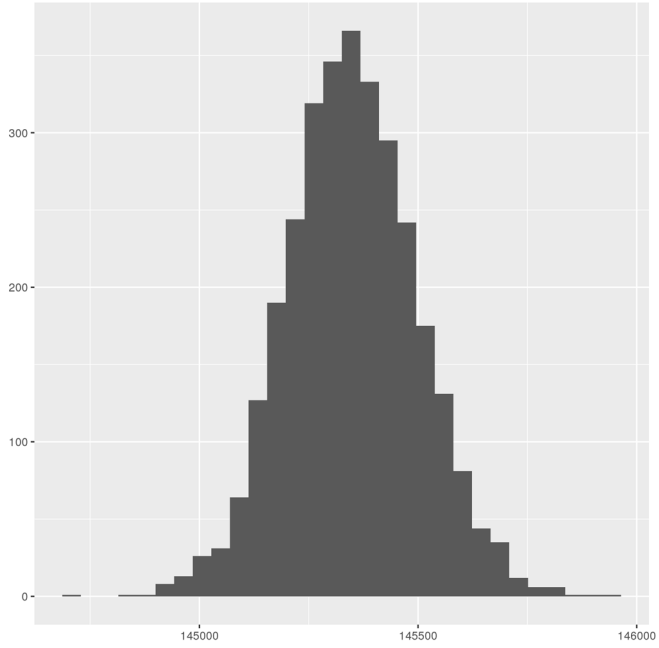
European ancestry: Dist. of E4_PTSDc_PGC18



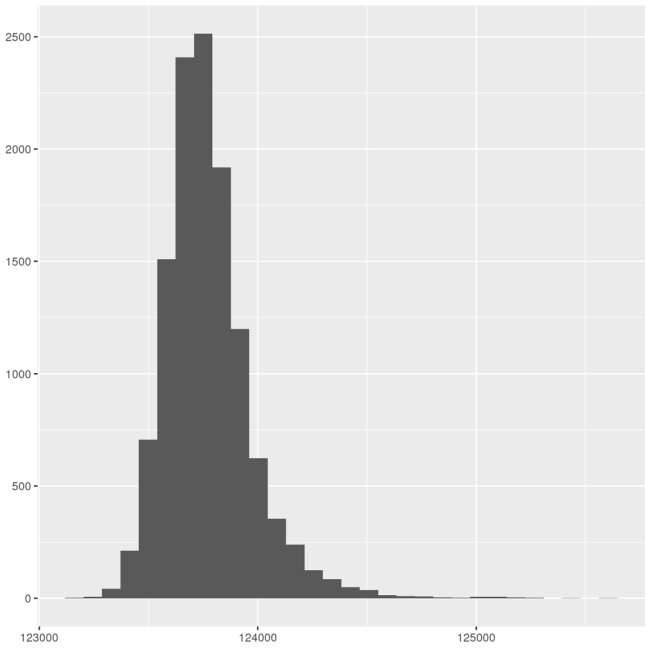
African ancestry: Dist. of A4_PTSDc_PGC18



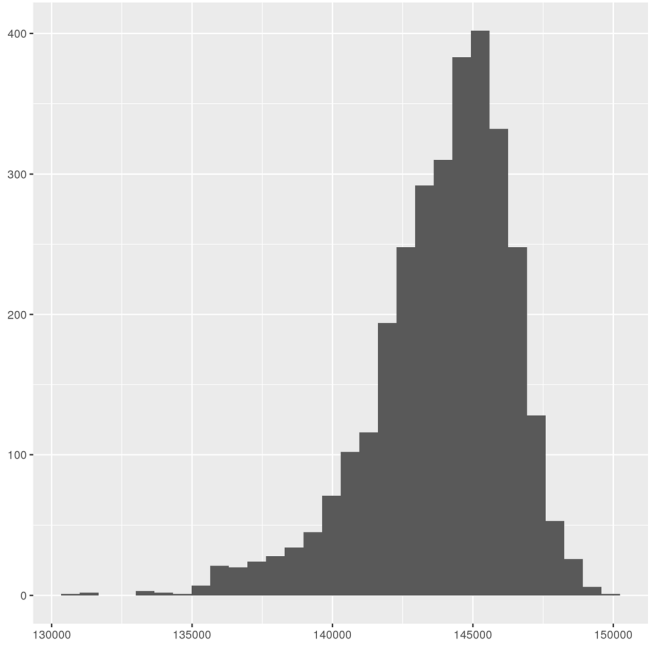
European ancestry: Dist. of E4_PTSDAA_PGC18



African ancestry: Dist. of A4_PTSDAA_PGC18



European ancestry: Dist. of E4_PTSDEA_PGC18



African ancestry: Dist. of A4_PTSDEA_PGC18

References

Duncan, L. E., Ratanatharathorn, A., Aiello, A. E., Almli, L. M., Amstadter, A. B., Ashley-Koch, A. E., ... & Bradley, B. (2018). Largest GWAS of PTSD (N= 20 070) yields genetic overlap with schizophrenia and sex differences in heritability. Molecular psychiatry, 23(3), 666

LL. Lipid traits (HDL, LDL, total cholesterol, triglycerides) – Global Lipid Genetics Consortium 2013

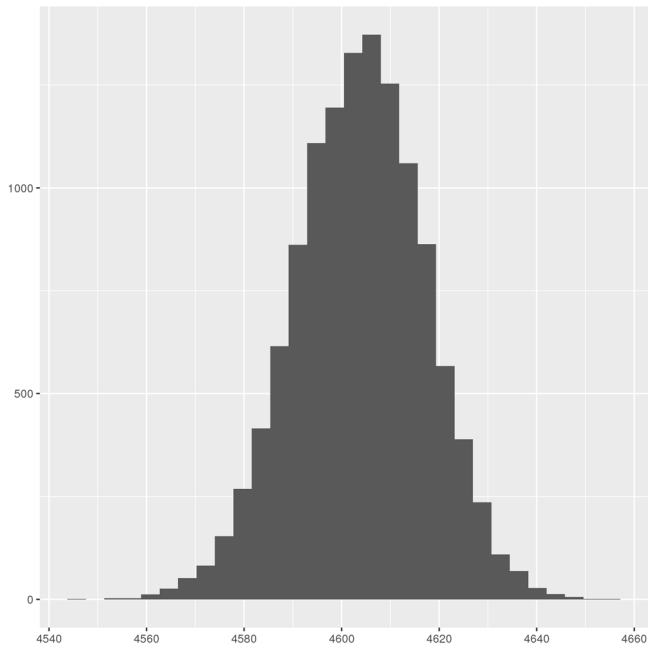
The HDL, LDL, and TC PGS were created using results from a 2013 study by the Global Lipid Genetics Consortium (Willer et al. 2013). Authors conducted separate GWAS for European (n=188,578) and non-European (n=7,898) ancestries followed by a meta-analysis of 7,168 individuals in a single ancestry group. Only European samples were used for discovery of novel genome-wide significant loci; non-European samples were meta-analyzed and examined only for fine-mapping analyses. Results are available for download directly from the Center for Statistical Genetic's website (http://csg.sph.umich.edu/willer/public/lipids2013/) and results from the joint analysis of metabochip and GWAS data were used to create the PGSs. Results files were slightly modified on 11/26/2013. Sites with N<50,000 were removed from the joint meta-analysis results, sites with N<20,000 were removed from the Metabochip-only results and an rsid column was added to each dataset. Data was sourced by collecting summary statistics from 23 studies of European ancestry genotyped with GWAS arrays and 46 studies genotyped with Metabochip arrays, of which 37 studies consisted primarily of individuals of European ancestry. Nine studies using Metabochip arrays were of non-European ancestry: two studies were South Asian, two studies were East Asian, and five studies were African. Blood lipid levels were typically measured after > 8 hours of fasting and individuals known to be on lipid-lowering medication were excluded when possible. Hapmap release 22 CEU reference was used. In cases where Metabochip and GWAS array data were available for the same individuals, Metabochip data was used to ensure key variants were directly genotyped, rather than imputed. None of the GWAS meta-analyses included HRS. The study identified 157 loci associated with lipid levels at P <5×01-8, including 62 loci not previously associated with lipid levels in humans. Adjustments for population structure using principal component analysis or mixed model approaches were carried out in 24 studies (35% of individuals).

The European ancestry PGSs for the HDL GWAS contain 739,945 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 736,292 SNPs. The European ancestry PGSs for the LDL GWAS contain 736,927 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 737,224 SNPs. The European ancestry PGSs for the total cholesterol GWAS contain 739,175 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 738,878 SNPs. The posted PGSs have been standardized within ethnicity, to a standard normal curve (mean=0, standard deviation = 1).

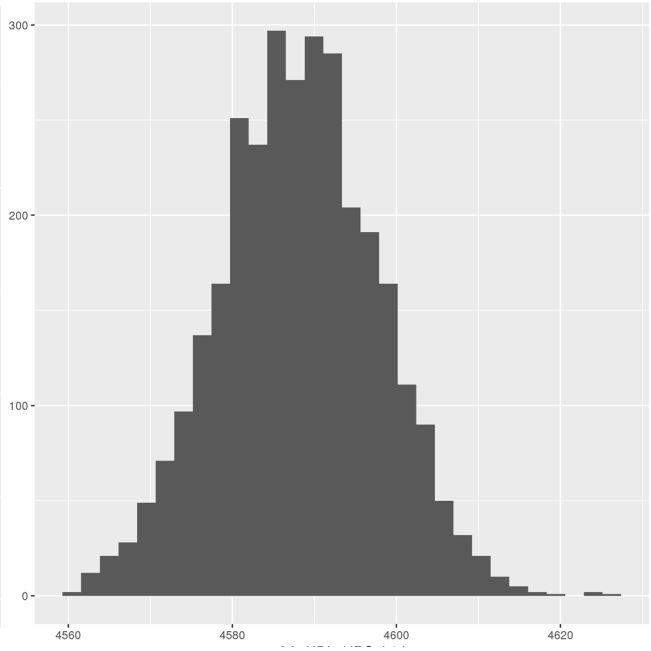
N.B.: **Please note that the GLGC-lipid results contain PGSs from European ancestry backgrounds (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

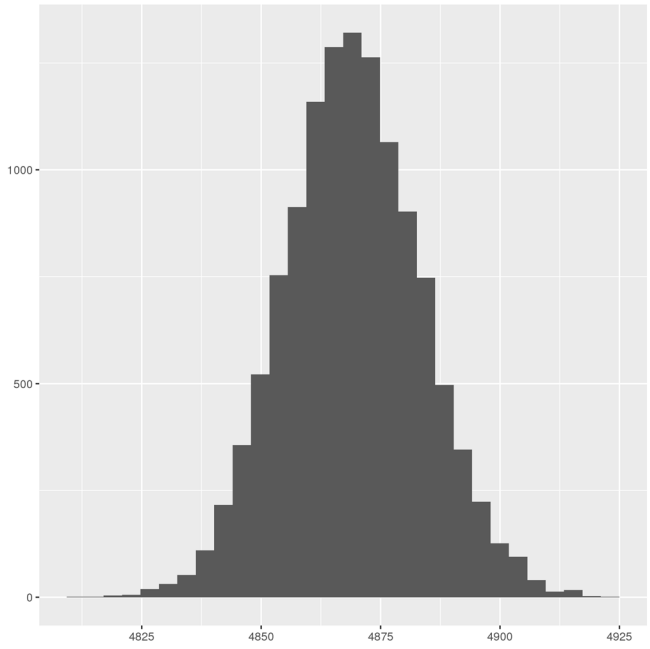
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
HDL cholesterol							
European ancestry	12090	12090	4544.20	4653.78	109.58	4604.01	4603.76
African ancestry	3100	3100	4559.69	4625.52	65.83	4588.13	4588.09
LDL cholesterol							
European ancestry	12090	12090	4812.75	4924.55	111.80	4868.96	4869.17
African ancestry	3100	3100	4845.56	4923.47	77.91	4892.23	4891.86
Total cholesterol							
European ancestry	12090	12090	4768.46	4882.72	114.26	4827.83	4827.99
African ancestry	3100	3100	4793.51	4882.98	89.47	4846.71	4846.49



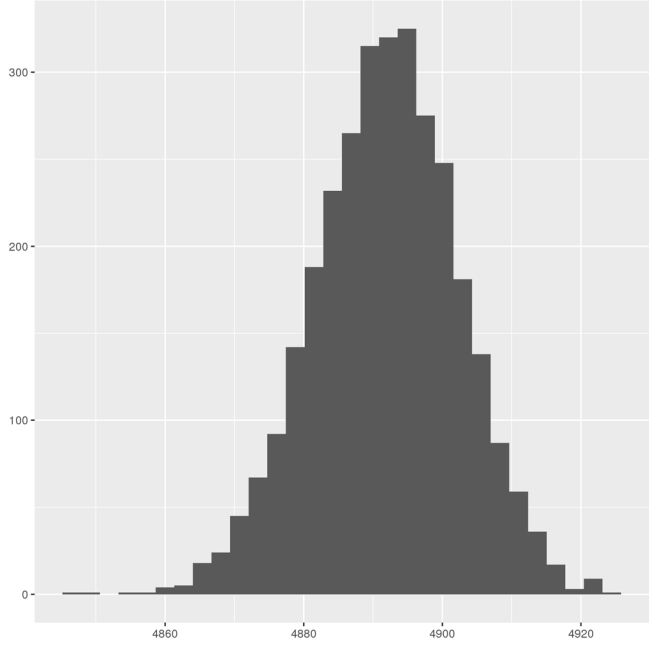
European ancestry: Dist. of E4_HDL_GLGC13



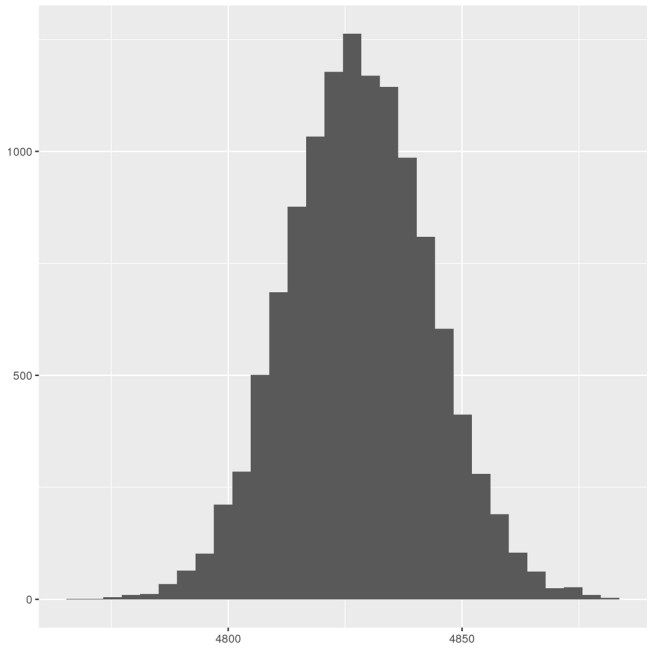
African ancestry: Dist. of A4_HDL_GLGC13



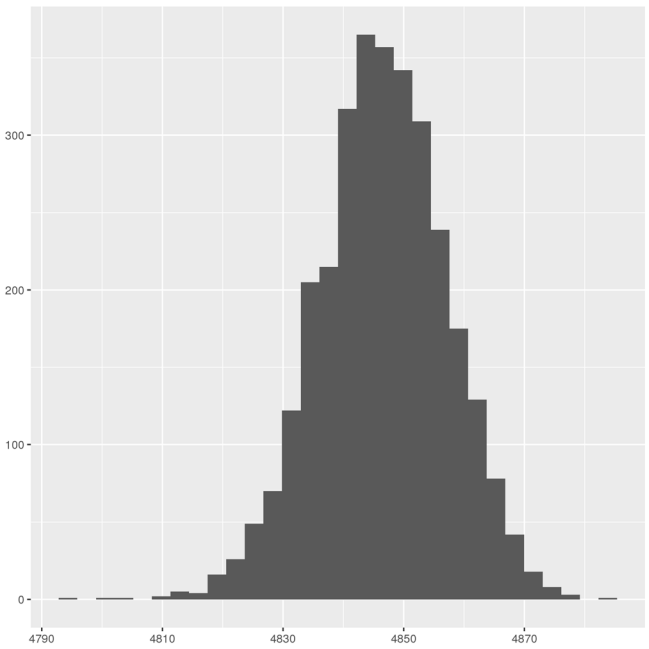
European ancestry: Dist. of E4_LDL_GLGC13



African ancestry: Dist. of A4_LDL_GLGC13



European ancestry: Dist. of E4_TC_GLGC13



African ancestry: Dist. of A4_TC_GLGC13

References

Willer, C.J., Schmidt, E.M., Sengupta, S., Peloso, G.M., Gustafsson, S., … & Global Lipids Genetic Consortium. (2013) Discovery and Refinement of Loci Associated with Lipid Levels. Nat Genet. 45(11), 1274-1283. doi:10.1038/ng.2797.

MM. Anxiety (case-control, factor score) – Anxiety NeuroGenetics Study 2016

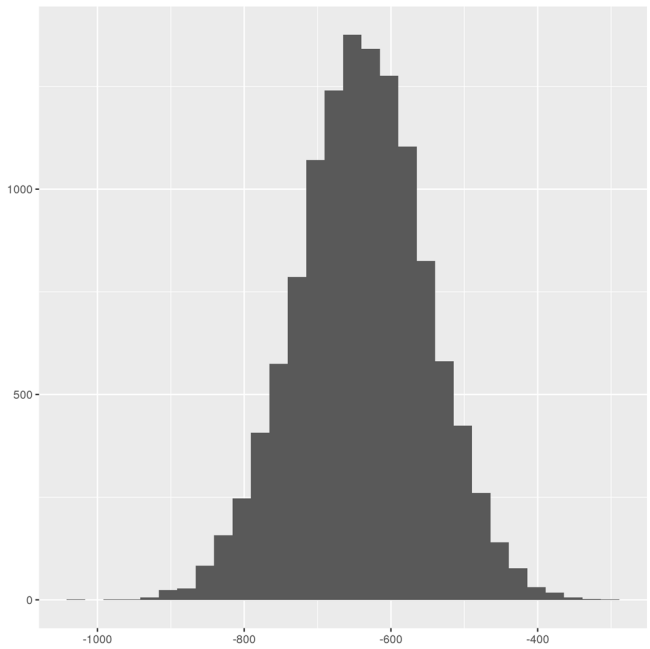
The Anxiety PGSs were created using results from a 2016 study by the Anxiety NeuroGenetics Study (ANGST) Consortium (Otowa et al., 2016). Summary statistics are available from the PGC data download website (https://www.med.unc.edu/pgc/results-and-downloads). Data sourced 9 samples of European ancestry individuals, where each contributing cohort used standardized instruments to assess DSM-based anxiety disorder diagnoses (i.e., generalized anxiety disorder, panic disorder, social phobia, agoraphobia, and/or specific phobia). Parallel GWAS were conducted in each cohort (both in a case-control design and using a continuous factor score), followed by meta-analysis across all cohorts. The combined case-control meta-analysis included N=17,310 and the continuous factor score GWAS included N=18,186. All cohorts imputed SNPs to the 1000 Genomes Project references data (release v3, March 2012) and approximately 6.5 million SNPs were included in the combined meta-analysis. The GWAS meta-analyses did not include the HRS. Sex and age at interview were included in the sample-specific GWAS and ancestry principal components were included on a "… sample-by-sample basis depending on their correlation with the outcome phenotypes" (Otowa et al., 2016). No genome-wide significant SNPs were identified in the GWAS meta-analyses.

The European ancestry PGSs for the case-control GWAS contain 1,022,580 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,011,145 SNPs. The European ancestry PGSs for the factor score GWAS contain 1,079,599 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,075,483 SNPs.

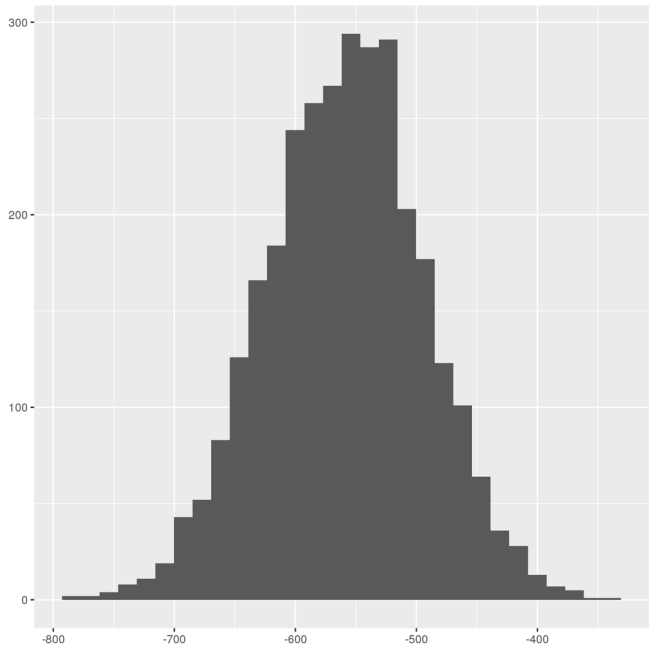
N.B.: **Please note that the GLGC-lipid results contain PGSs from European ancestry backgrounds (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

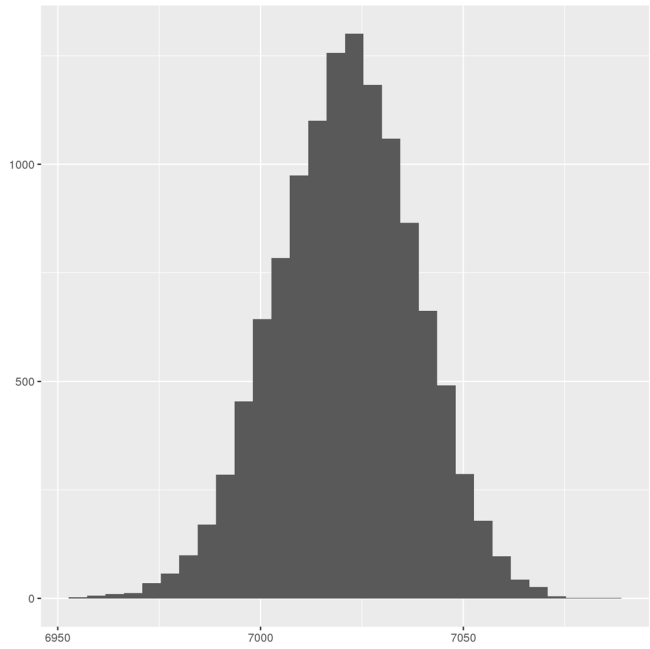
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
Anxiety – case-control							
European ancestry	12090	-1018.44	-290.39	728.06	-639.43	-639.72	0.80
African ancestry	3100	-788.06	-341.70	446.36	-558.21	-559.34	1.17
Anxiety – factor-score							
European ancestry	12090	6954.15	7085.89	131.74	7021.32	7021.00	0.16
African ancestry	3100	6955.45	7053.83	98.38	7003.96	7004.06	0.22



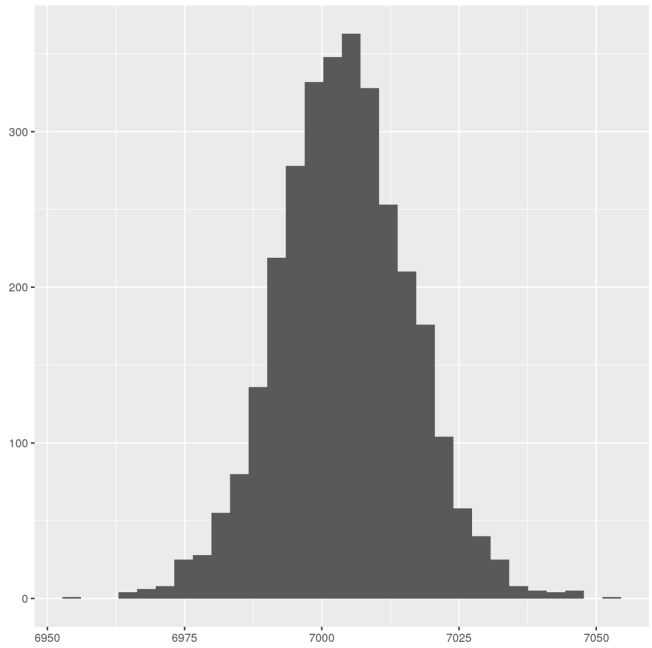
European ancestry: Dist. of E4_AnxCC_ANGST16



African ancestry: Dist. of A4_AnxCC_ANGST16



European ancestry: Dist. of E4_AnxFS_ANGST16



African ancestry: Dist. of A4_AnxFS_ANGST16

References

Otowa, T., Hek, K., Lee, M., Byrne, E. M., Mirza, S. S., Nivard, M. G., ... & Fanous, A. (2016). Meta-analysis of genome-wide association studies of anxiety disorders. Molecular psychiatry, 21(10), 1391.

NN. General Cognition 2 (Gencog2) – Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE), the Cognitive Genomics Consortium (COGENT) consortia, and UK Biobank 2018

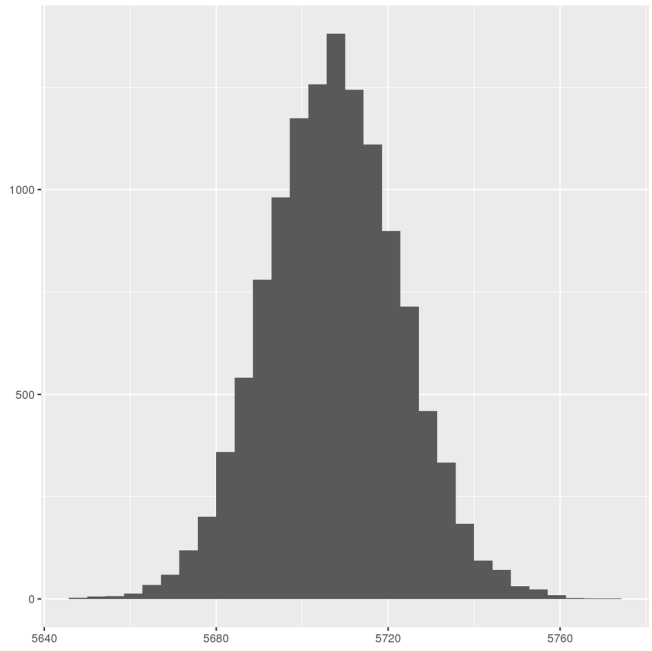
PGSs for general cognitive function were created using results from a 2018 study conducted by the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE), the Cognitive Genomics Consortium (COGENT) consortia, and UK Biobank. Access to the full GWAS summary results for general cognitive function can be requested by application to the chairs of the CHARGE and COGENT consortia. The general cognition GWAS meta-analysis included 300,486 individuals age 16-102 of European ancestry. To compute the PGSs for HRS respondents, we used SNPs weights from a GWAS with several NHLBI cohorts, and the Health and Retirement Study removed from the meta-analysis. There are 12,871,898 SNPs in the summary statistics file imputed to NCBI Build 37/UCSC hg 19. Inclusion/exclusion criteria for cases and controls for each cohort are available in **Supplementary Data 18**. The study identified 148 loci with 434 independent genome-wide significant SNPs (**Supplementary Data 1 and 2**).

The European ancestry PGSs contains 1,382,609 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,382,609 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

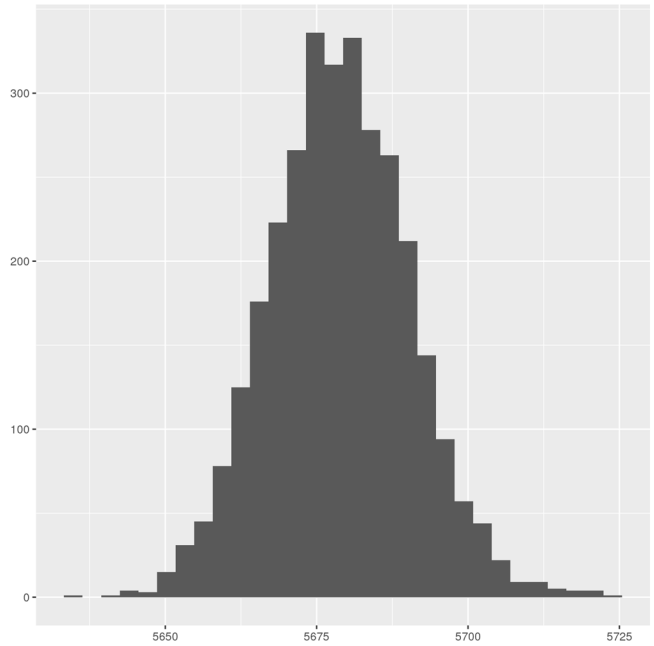
N.B.: **Please note that the CHARGE-Gencog2 weights are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).** The HRS was removed from the meta-analysis GWAS upon request to the consortia. The following CHARGE cohorts requested that their data be removed due to restrictions on their use: The Aging Gene-Environment Susceptibility - Reykjavik Study (AGES), The Atherosclerosis Risk in Communities Study (ARIC), The Cardiovascular Health Study (CHS), The Framingham Heart Study (FHS), and The Genetic Epidemiology Network of Arteriopathy (GENOA).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	5645.81	5770.08	124.27	5707.26	5707.36	0.14
African ancestry	3100	5635.26	5724.36	89.10	5678.59	5678.82	0.21



European ancestry: Dist. of E4_GenCog2_CHARGE18



African ancestry: Dist. of A4_GenCog2_CHARGE18

References

Davies, G., Lam, M., Harris, S. E., Trampush, J. W., Luciano, M., Hill, W. D., … Deary, I. J. (2018). Study of 300,486 individuals identifies 148 independent genetic loci influencing general cognitive function. Nature Communications, 9, 2098. http://doi.org/10.1038/s41467-018-04362-x

OO. Kidney function – Chronic Kidney Disease Genetics consortium 2019

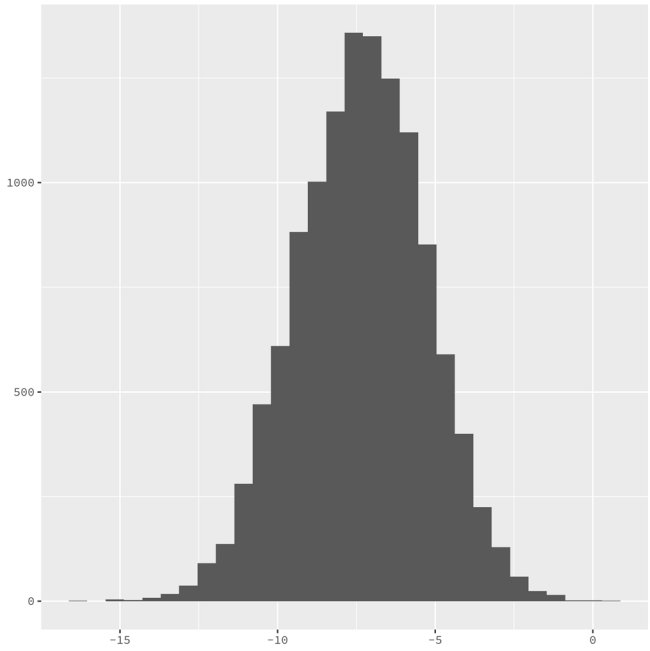
PGSs for kidney function phenotypes were created using results from a 2019 study conducted by the Chronic Kidney Disease Genetics (CKDGen) consrotium. The GWAS meta-analysis files are publicly available on the CKDGen data download page: http://ckdgen.imbi.uni-freiburg.de/ (20171016_MW_eGFR_overall_ALL_nstud61.dbgap.txt.gz, 20171017_MW_eGFR_overall_EA_nstud42.dbgap.txt.gz, BUN_overall_ALL_YL_20171017_METAL1_nstud_33.dbgap.txt.gz, BUN_overall_EA_YL_20171108_METAL1_nstud24.dbgap.txt.gz, CKD_overall_ALL_JW_20180223_nstud30.dbgap.txt.gz, CKD_overall_EA_JW_20180223_nstud23.dbgap.txt.gz). The CKDGen meta-analysis included GWAS on estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN) and chronic kidney disease (CKD) using a European ancestry only sample and also a trans-ethnic sample encompassing individuals of European, East Asian, African, South Asian, and Hispanic ancestry. The trans-ethnic GWAS of eGFR included 121 studies with an n of 765,348 and found 308 loci associated with eGFR. The European ancestry eGFR GWAS included 85 studies and an n of 567,460 with 256 discovered loci. The trans-ethnic BUN discovery analysis included an n of 416,178. The European ancestry BUN GWAS included an n of 243,029. The CKD trans-ethnic anlaysis included 625,219 individuals. The European ancestry CKD analysis included 480,698 individuals (41,395 cases and 439,303 controls). The GWAS meta-analyses included ~9 million imputed SNPs on NCBI Build 37/UCSC hg 19.

The HRS PGSs (for both African and European ancestry participants) contains 1,315,819 (BUN), 1,332,919 (CKD), and 1,326,635 (eGFR) SNPs that overlapped between the HRS genetic database in the European-ancestry based GWAS meta-analysis; and 1,308,547 (BUN), 1,355,733 (CKD), and 1,312,534 (eGFR) SNPs that overlapped between the HRS genetic database and the trans-ancestry based GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

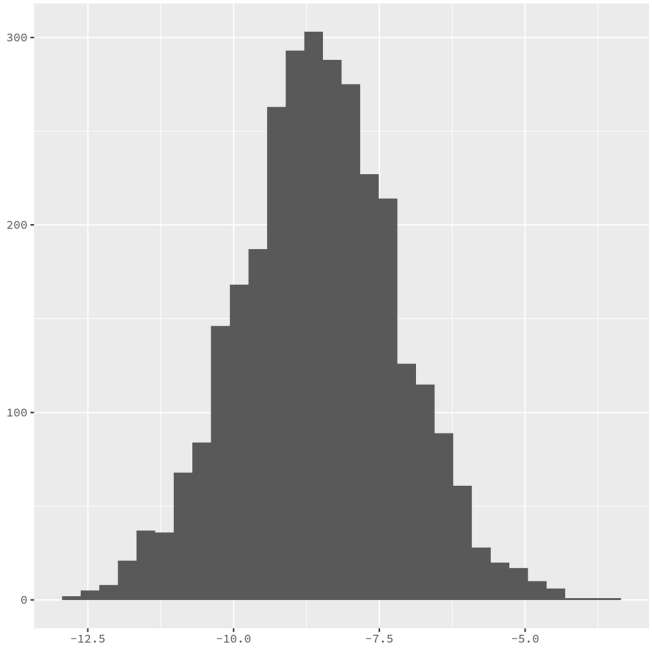
N.B.: **Please note that the European ancestry based summary statistics are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

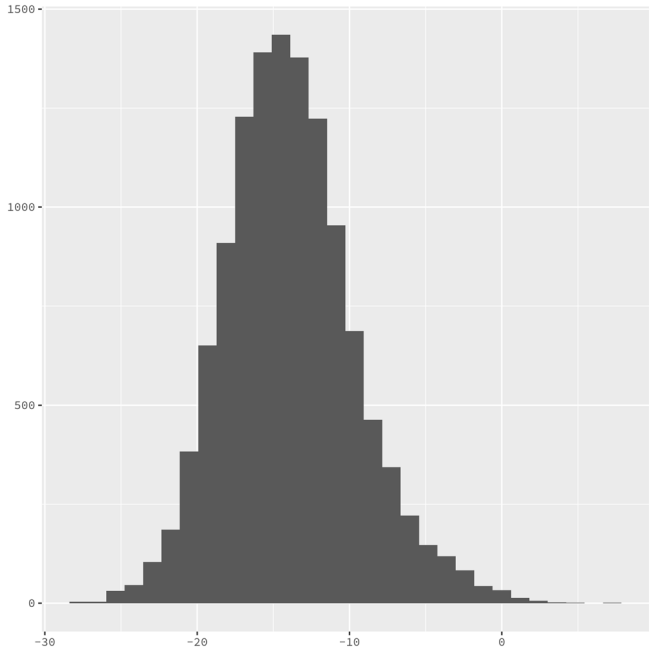
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry-based GWAS							
eGFR							
European ancestry	12090	-16.08	0.83	16.92	-7.30	-7.35	0.02
African ancestry	3100	-12.91	-3.64	9.27	-8.53	-8.53	0.02
BUN							
European ancestry	12090	-28.20	6.834	35.03	-14.16	-13.90	0.04
African ancestry	3100	-18.62	2.49	21.11	-8.69	-8.69	0.05
CKD							
European ancestry	12090	-4920.58	-4531.73	388.85	-4771.71	-4767.19	0.43
African ancestry	3100	-4296.34	-3618.85	677.49	-3839.29	-3856.80	1.97
Trans-ancestry-based GWAS							
eGFR							
European ancestry	12090	-13.12	1.37	14.49	-5.29	-5.32	0.02
African ancestry	3100	-10.68	-1.37	9.31	-6.48	-6.47	0.02
BUN							
European ancestry	12090	-16.08	12.32	28.40	-3.61	-3.44	0.03
African ancestry	3100	-14.11	5.23	19.34	-2.61	-2.64	0.04
CKD							
European ancestry	12090	-4093.75	-3799.88	293.87	-3974.82	-3972.37	0.33
African ancestry	3100	-3736.28	-3334.69	401.59	-3475.095	-3484.11	1.11



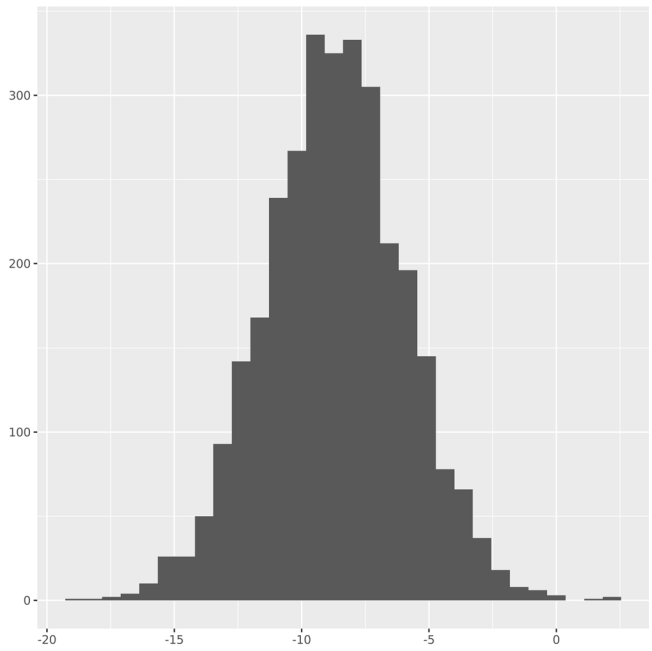
European ancestry: Dist. of E4_EGFR_CKDGEN19



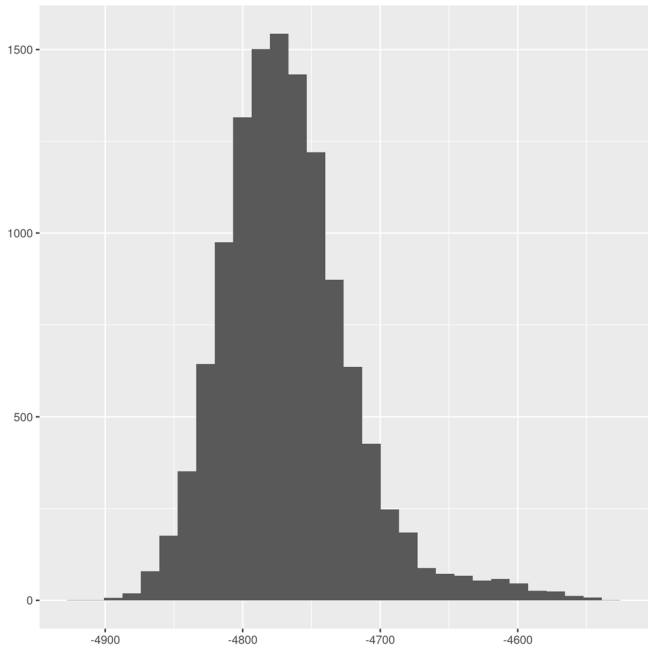
African ancestry: Dist. of A4_EGFR_CKDGEN19



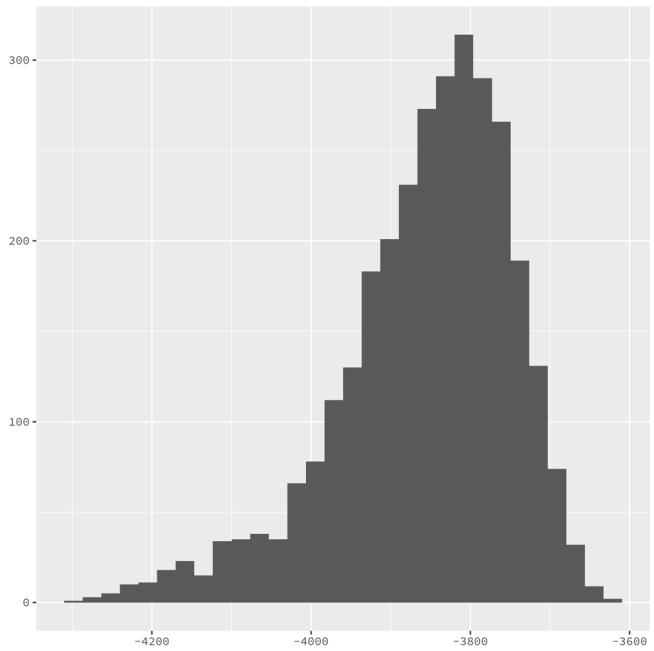
European ancestry: Dist. of E4_BUN_CKDGEN19



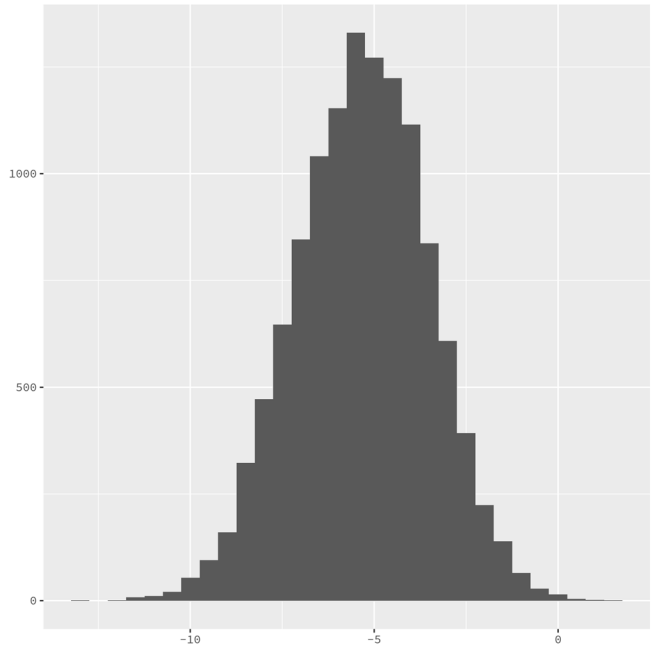
African ancestry: Dist. of A4_BUN_CKDGEN19



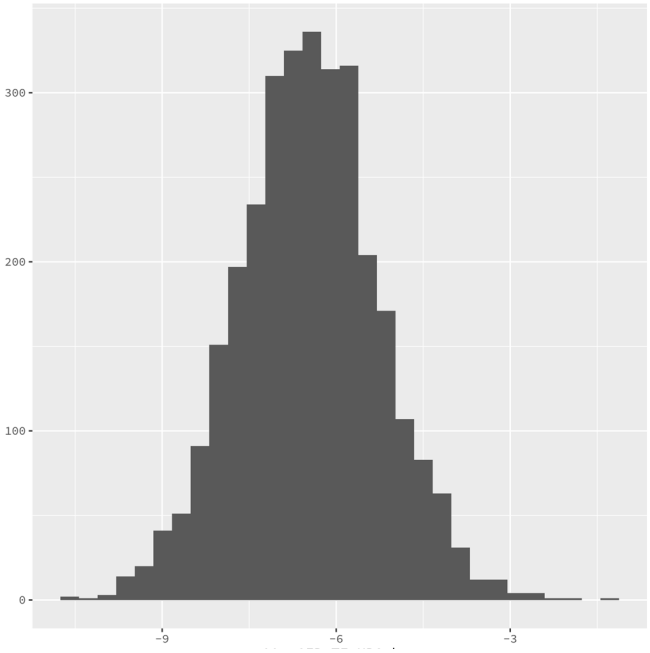
European ancestry: Dist. of E4_CKD_CKDGEN19



African ancestry: Dist. of A4_CKD_CKDGEN19



European ancestry: Dist. of E4_EGFRTE_CKDGEN19



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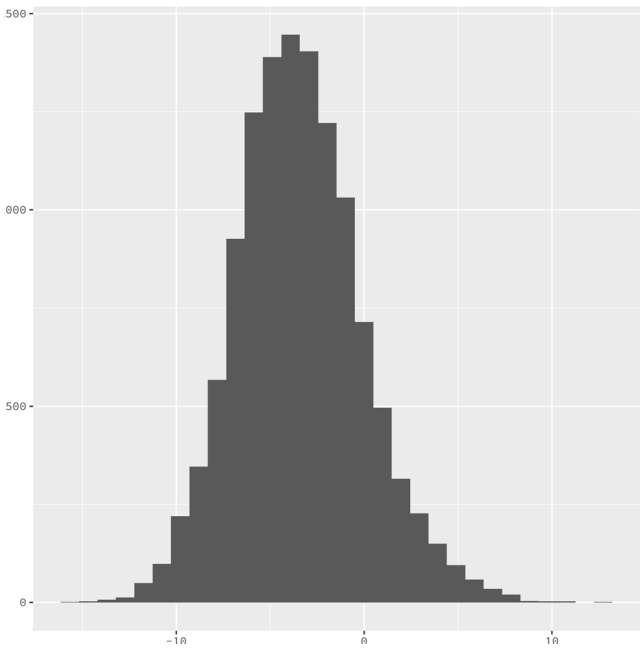

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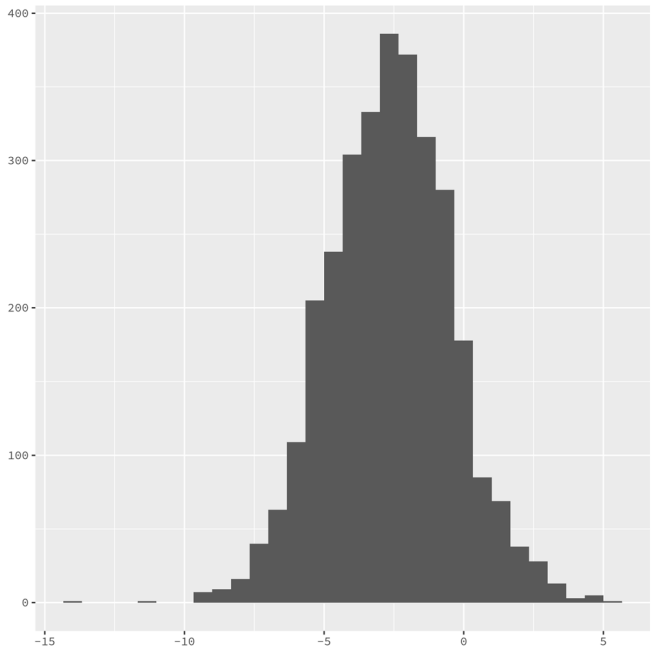
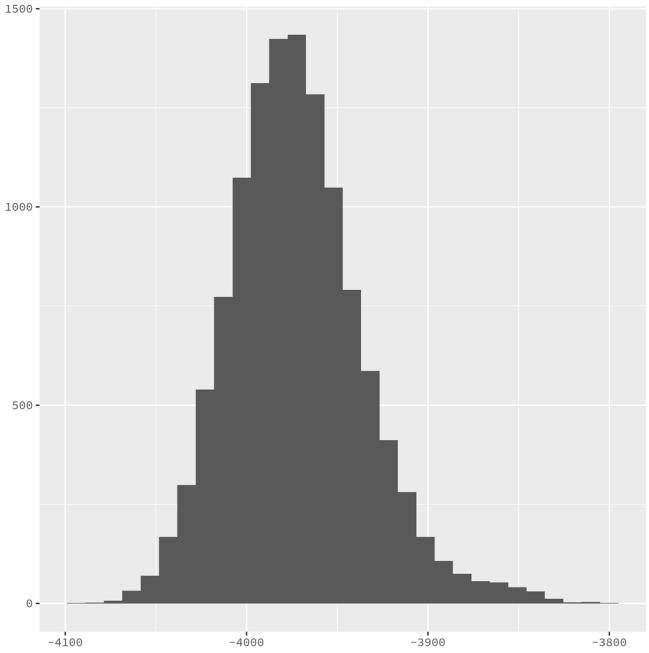
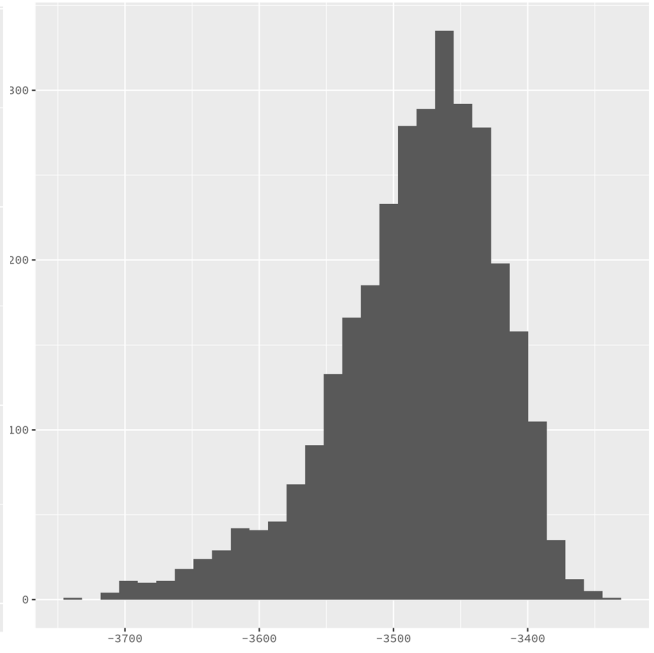


African ancestry: Dist. of A4_BUNTE_CKDGEN19



European ancestry: Dist. of E4_CKDTE_CKDGEN19



African ancestry: Dist. of A4_CKDTE_CKDGEN19

References

Wuttke M, Li Y, Li M, et al. A catalog of genetic loci associated with kidney function from analyses of a million individuals. Nat Genet. 2019;51(6):957–972. doi:10.1038/s41588-019-0407-x

PP. Blood Pressure in African-ancestry – Continental Origins and Genetic Epidemiology Network 2017

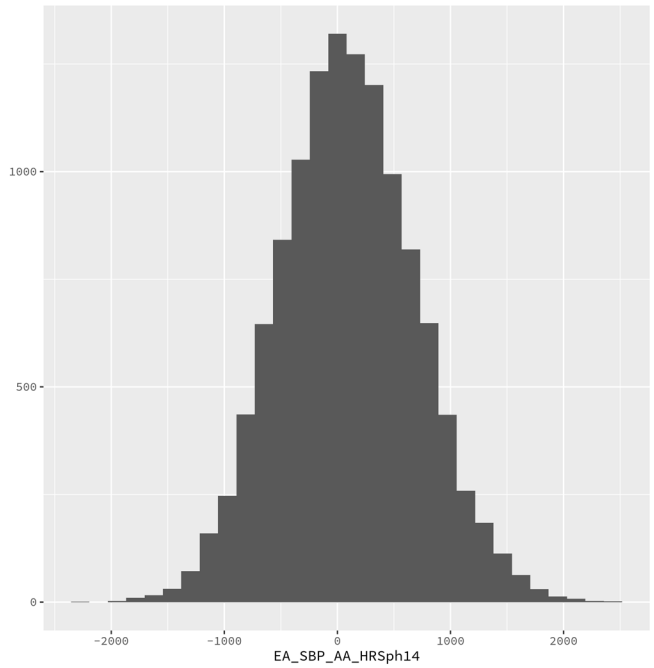
PGSs for four blood pressure traits (systolic (SBP), diastolic (DBP), and pulse pressure (PP), and hypertension) were created using results from a 2017 study conducted by the Continental Origins and Genetic Epidemiology Network (COGENT)-blood pressure (BP) consortium. The GWAS meta-analysis files were obtained through request and approval of the consortium members and the HRS was removed from the meta-analysis. COGENT-BP analyzed 21 genome-wide association studies comprised of 31,968 individuals of African ancestry and validated their results in an additional 54,395 individuals from multi-ethnic studies. Study descriptions can be found in (**S1 Table**). Analyses identified nine loci with 11 independent variants at genome-wide significance. The GWAS meta-analyses included ~21.5 million SNPs imputed to NCBI Build 37/UCSC hg 19 using the Phase 1 integrated (March 2012 release) multi-ethnic reference panel from the 1000G Consortium. For individuals taking antihypertensive medications, we added 15 and 10 mm Hg to measured SBP and DBP, respectively, a standard method used in other BP GWAS. PP was calculated as the difference between SBP and DBP after addition of the constant values. HTN was defined by a SBP ≥ 140 mm Hg, a DBP ≥ 90 mm Hg, or use of antihypertensive drugs (Liang et al. 2017).

The HRS PGSs (for both African and European ancestry participants) contains 1,829,800 (SBP) 1,831,285 (DBP), 1,831,158 (PP), and 1,830,745 (HTN) SNPs that overlapped between the HRS genetic database in the African-ancestry based GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

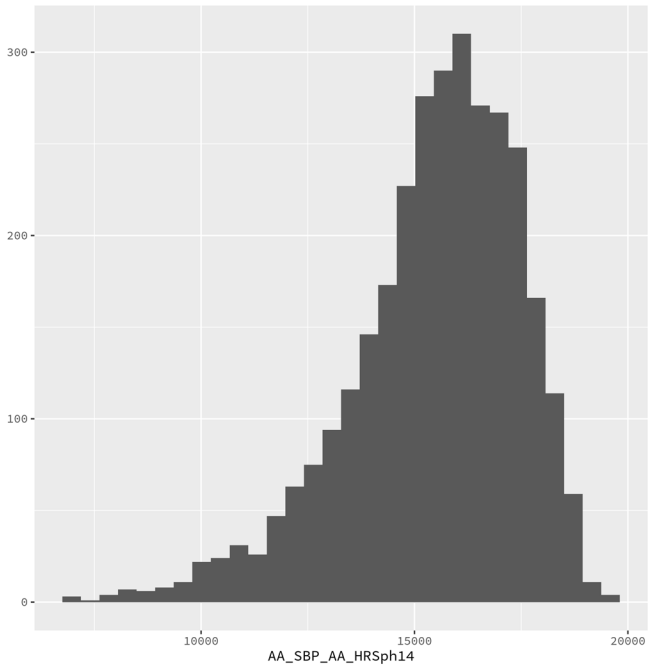
N.B.: **Please note that the COGENT-BP trait summary statistics are from a GWAS on individuals of African ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

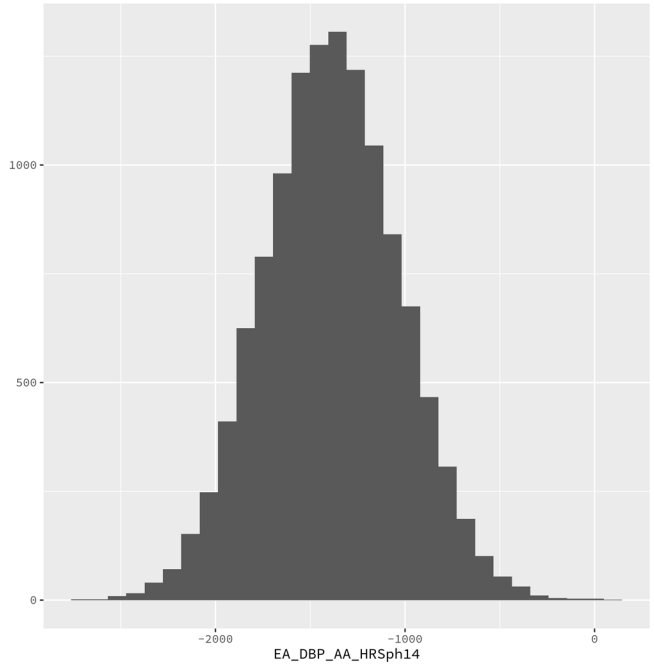
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
Systolic Blood Pressure (SBP)							
European ancestry	12090	-2327.59	2383.45	4711.04	81.33	94.32	5.45
African ancestry	3100	6849.54	19475.80	12626.26	15749.90	15457.50	36.06
Diastolic Blood Pressure (DBP)							
European ancestry	12090	-2728.82	81.50	2810.32	-1389.74	-1387.17	3.25
African ancestry	3100	1604.28	8070.97	6466.69	6122.21	5982.52	18.50
Pulse Pressure (PP)							
European ancestry	12090	-2927.7	709.81	3637.51	-1230.34	-1224.21	3.87
African ancestry	3100	1747.81	9861.03	8113.22	7237.41	7086.65	20.49
Hypertension (HTN)							
European ancestry	12090	-813.447	-243.894	569.55	-536.67	-536.14	0.64
African ancestry	3100	-660.18	112.06	772.24	-251.66	-254.43	1.90



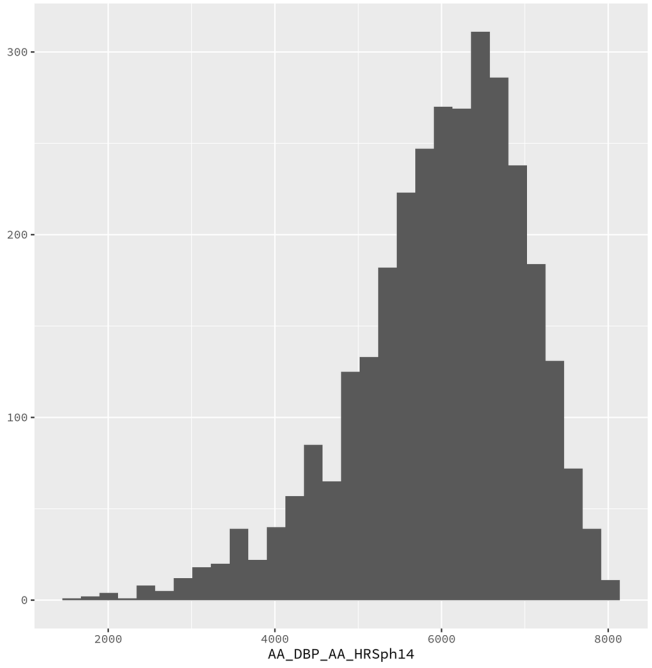
European ancestry: Dist. of E4_SBP_COGENT17



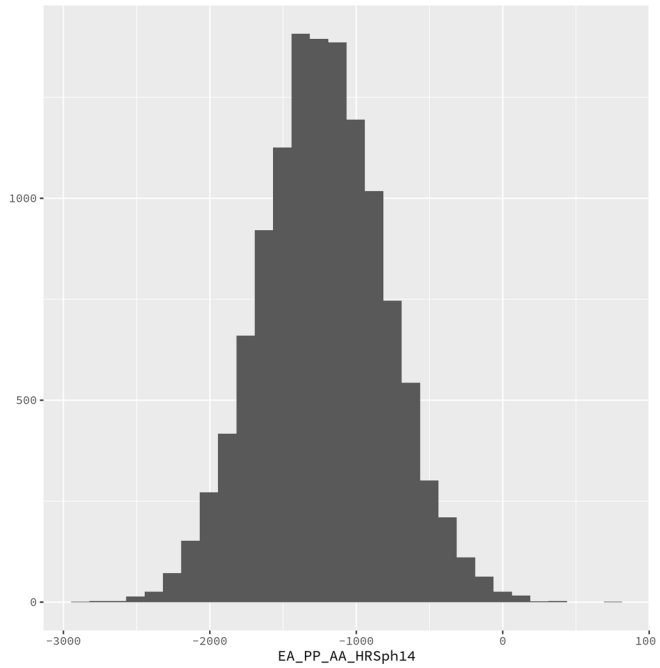
African ancestry: Dist. of A4_SBP_COGENT17



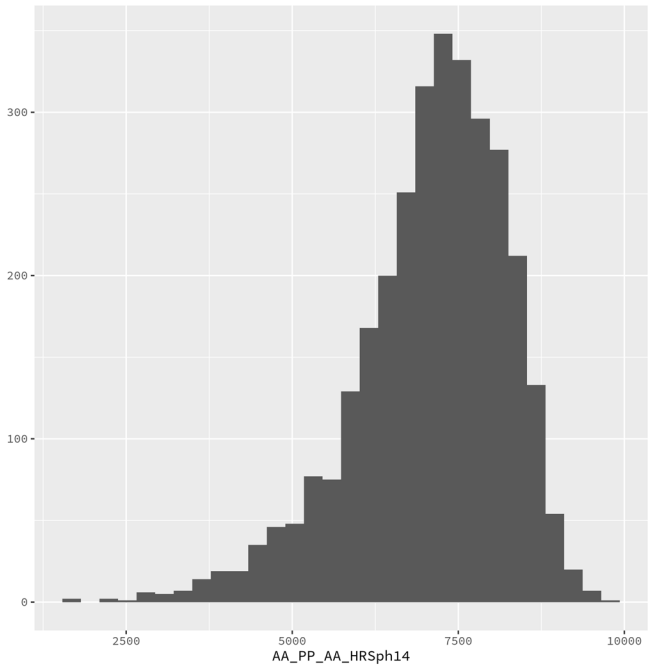
European ancestry: Dist. of E4_DBP_COGENT17



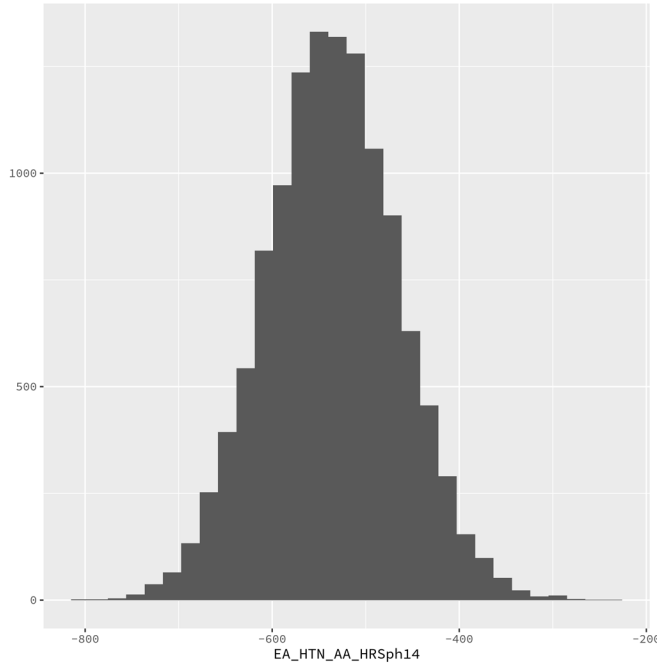
African ancestry: Dist. of A4_DBP_COGENT17



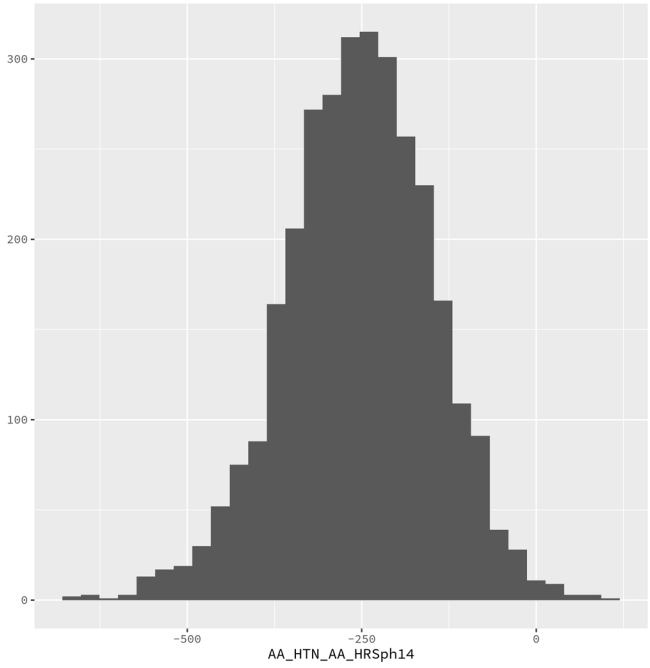
European ancestry: Dist. of E4_PP_COGENT17



African ancestry: Dist. of A4_PP_COGENT17



European ancestry: Dist. of E4_HTN_COGENT17



African ancestry: Dist. of A4_HTN_COGENT17

References

Liang J, Le TH, Edwards DRV, et al. Single-trait and multi-trait genome-wide association analyses identify novel loci for blood pressure in African-ancestry populations [published correction appears in PLoS Genet. 2018 May 11;14 (5):e1007345]. PLoS Genet. 2017;13(5):e1006728. Published 2017 May 12. doi:10.1371/journal.pgen.1006728

QQ. Body Mass Index 2 (BMI2) – Genetic Investigation of ANthropometric Traits 2018

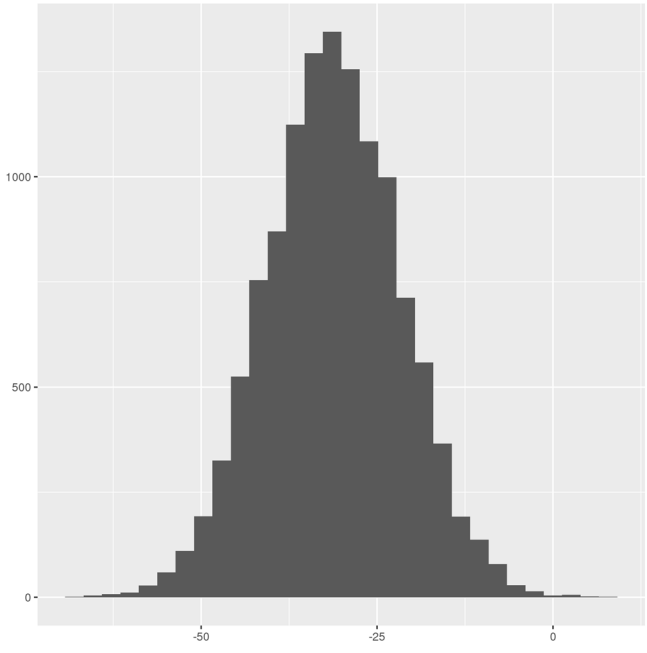
PGSs for body mass index (BMI) were created using results from a 2018 study conducted by the GIANT consortium. The GWAS meta-analysis files are publicly available on the Broad Institute data download page: (https://portals.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium_data_files#2018_GIANT_and_UK_BioBank_Meta-analysis). The meta-analysis included 681,275 participants from a total of 15 cohorts of European ancestry. The 15 cohorts include the UK Biobank (UKB) and 14 cohorts from the previous GIANT GWAS of BMI (Locke et al., 2015; *Nature*). Authors performed a fixed effect inverse-variance weighted meta-analysis of the UKB results with GWAS summary statistics from Locke et al. (2015). 2,334,002 SNPs imputed from NCBI Build 37 HapMap phase 2 data were included in the meta-analysis. The GWAS of BMI in UKB was conducted in 456,426 participants of European Ancestry, using 16,653,239 SNPs imputed to the Haplotype Reference Consortium imputation reference panel. Associations were adjusted for 10 principal components to reduce confounding by population stratification, as well as for age, sex, recruitment center, and genotyping batch. See section F in this documentation for detailed about the GWAS conducted by Locke et al. (2015). The study identified 941 genome-wide significant SNPs ($P < 10^{-8}$) (**Figure 1** and **Table 1**).

The GIANT BMI2 PGSs contains 711,273 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

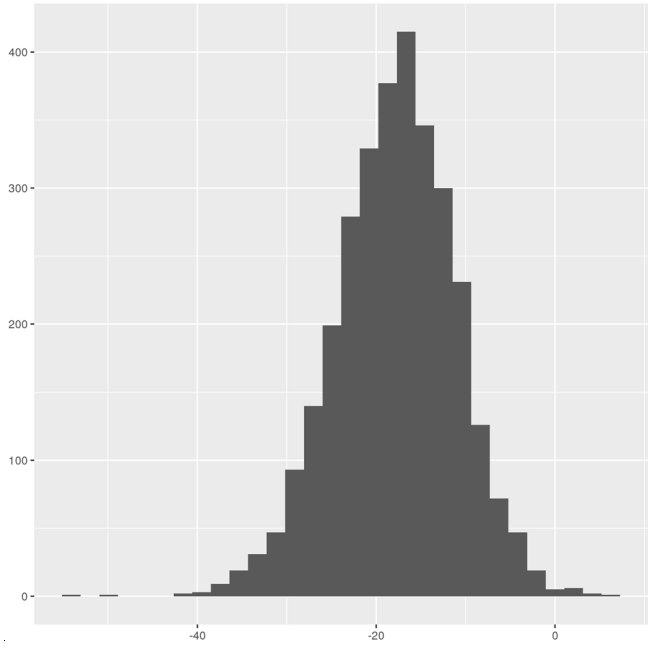
N.B.: **Please note that the GIANT-BMI2 summary statistics are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	-68.24	7.62	75.86	-31.23	-31.18	0.09
African ancestry	3100	-53.70	6.63	60.33	-17.59	-17.86	0.12



European ancestry: Dist. of E4_BMI2_GIANT18



African ancestry: Dist. of A4_BMI2_GIANT18

References

Yengo L, Sidorenko J, Kemper KE, et al. Meta-analysis of genome-wide association studies for height and body mass index in ∼700000 individuals of European ancestry. Hum Mol Genet. 2018;27(20):3641–3649. doi:10.1093/hmg/ddy271

RR. Height 2 (Height2) – Genetic Investigation of ANthropometric Traits 2018

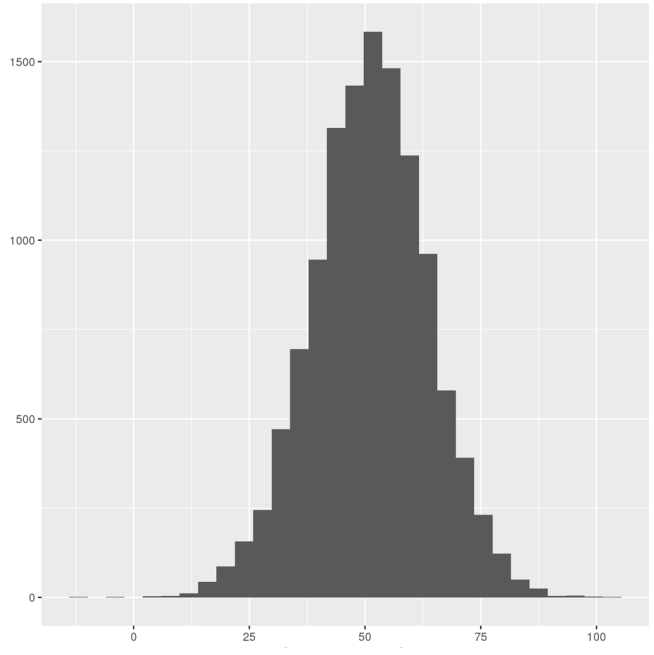
PGSs for Height were created using results from a 2018 study conducted by the GIANT consortium. The GWAS meta-analysis files are publicly available on the Broad Institute data download page: (https://portals.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium_data_files#2018_GIANT_and_UK_BioBank_Meta-analysis). The GIANT meta-analysis included 693,529 participants from a total of 6 cohorts of European ancestry. The 6 cohorts include the UK Biobank (UKB) and 5 cohorts from the previous GIANT GWAS of Height (Wood et al., 2014; *Nature Genetics*). Authors performed a fixed effect inverse-variance weighted meta-analysis of the UKB results with GWAS summary statistics from Wood et al. (2014). XXXXXX SNPs imputed from NCBI Build 37 HapMap phase 2 data were included in the meta-analysis. The GWAS of Height in UKB was conducted in 456,426 participants of European Ancestry, using 16,653,239 SNPs imputed to the Haplotype Reference Consortium imputation reference panel. Associations were adjusted for 10 principal components to reduce confounding by population stratification, as well as for age, sex, recruitment center, and genotyping batch. See section E in this documentation for detailed about the GWAS conducted by Wood et al. (2014). The study identified 3,290 genome-wide significant SNPs ($P < 10^{-8}$) (**Figure 1** and **Table 1**).

The GIANT Height2 PGSs contains 710,954 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

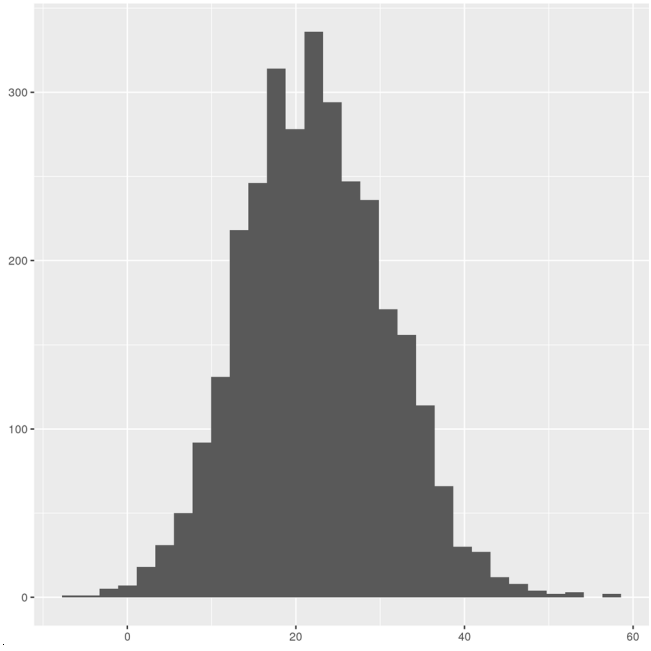
N.B.: **Please note that the GIANT Height2 summary statistics are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	-11.19	104.13	115.32	51.27	51.10	0.11
African ancestry	3100	-6.85	57.25	64.10	22.03	22.31	0.15



European ancestry: Dist. of E4_ HEIGHT2_GIANT18



African ancestry: Dist. of A4_HEIGHT2_GIANT18

References

Yengo L, Sidorenko J, Kemper KE, et al. Meta-analysis of genome-wide association studies for height and body mass index in ∼700000 individuals of European ancestry. Hum Mol Genet. 2018;27(20):3641–3649. doi:10.1093/hmg/ddy271

SS. Smoking behaivors – GWAS & Sequencing Consortium of Alcohol and Nicotine 2019

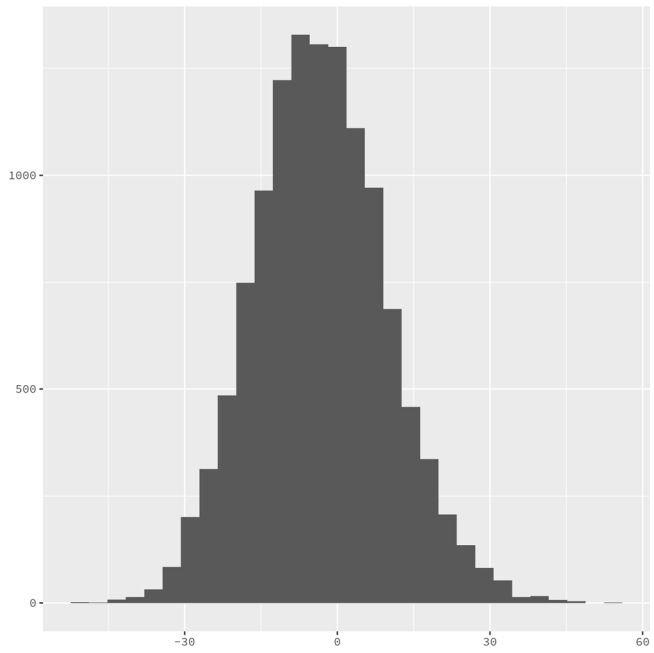
The substance behaviors PGSs were created using results from a 2019 study by the GWAS & Sequencing Consortium of Alcohol and Nicotine use (GSCAN) consortium. PGSs were created for smoking initiation (SI), cigarettes per day (CPD), smoking cessation (SC), age of initiation of regular smoking (AI), and drinks per day (DPW). SI was a binary phenotype indicating whether an individual had ever smoked regularly; the SI meta-analysis included 1,232,091 individuals of European ancestry. CPD captured heaviness of smoking, either as a current or former smoker; the CPD meta-analysis included 337,334 individuals of European ancestry. SC was a binary phenotype indicating whether an individual was a current smoker or former smoker, with never smokers coded as missing; the SC meta-analysis included 547,219 individuals of European ancestry. AI was measured as the age when an individual started smoking regularly; the AI meta-analysis included 341,427 individuals of European ancestry. DPW was defined as the average number of drinks a participant reported drinking each week, aggregated across all types of alcohol; the DPW meta-analysis 941,280 individuals of European ancestry. Genome-wide significant SNPs were identified in all of the meta-analyses: SI (N = 378), CPD (N = 55), SC (N = 24), AI (N = 10), and DPW (N = 99) (**Supplementary Tables 1 – 5; Supplemental Figures 2 – 12**). To compute the PGSs for HRS respondents, the GSCAN consortium provided SNP weights with the HRS and 23andMe results removed (due to data use agreements). In the original analysis, 23andMe contributed 78,437 (SI), 73,380 (CPD), 403,931 (DPW), 234,398 (SC), 599,289 (SI).

The age at smoking initiation PGSs contain 1,410,087 SNP variants that overlapped between the HRS genetic database and the GWAS meta-analysis; The cigarettes per day PGSs contain 1,411,187 SNP variants that overlapped between the HRS genetic database and the GWAS meta-analysis; The drinks per week PGSs contain 1,399,824 SNP variants that overlapped between the HRS genetic database and the GWAS meta-analysis; The smoking cessation PGSs contain 1,408,650 SNP variants that overlapped between the HRS genetic database and the GWAS meta-analysis; The smoking initiation PGSs contain 1,395,832 SNP variants that overlapped between the HRS genetic database and the GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

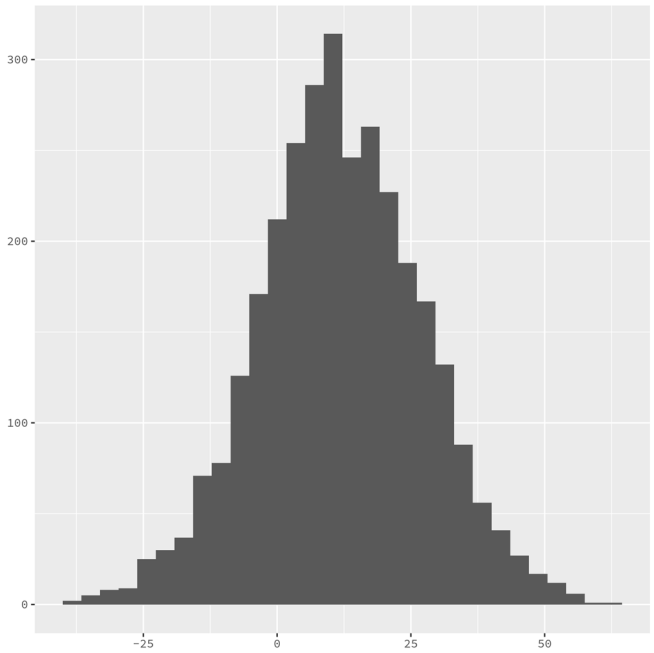
N.B.: **Please note that the GSCAN smoking behaviors summary statistics are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

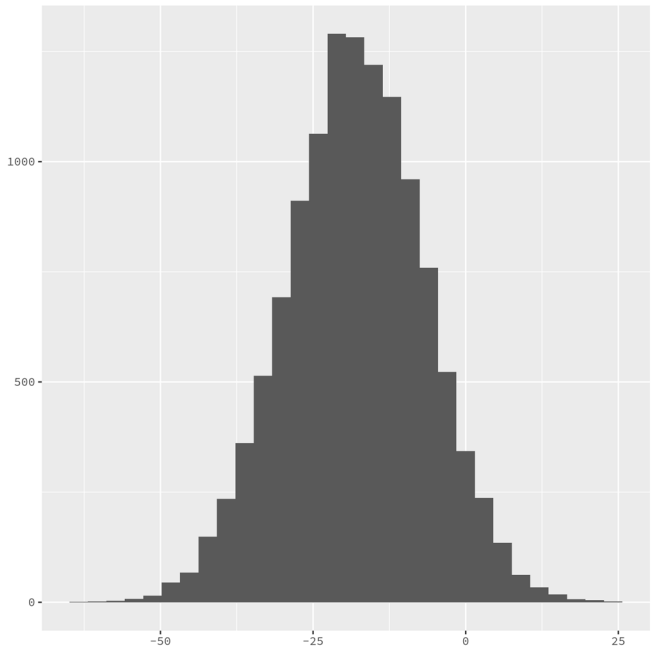
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
Age at smoking initiation							
European ancestry	12090	-51.73	53.09	104.82	-3.67	-3.25	0.12
African ancestry	3100	-38.88	62.16	101.03	11.36	11.78	0.28
Cigarettes per day							
European ancestry	12090	-64.41	23.14	87.55	-18.04	-18.06	0.10
African ancestry	3100	4.31	148.68	144.36	84.83	84.21	0.35
Drinks per week							
European ancestry	12090	-42.12	22.87	64.98	-9.96	-9.92	0.08
African ancestry	3100	-62.02	10.09	72.11	-28.85	-28.76	0.18
Smoking cessation							
European ancestry	12090	-81.52	2.67	84.19	-35.36	-35.54	0.10
African ancestry	3100	-4.21	143.97	148.18	67.21	66.21	0.34
Smoking initiation							
European ancestry	12090	-57.08	11.38	68.47	-23.26	-23.19	0.08
African ancestry	3100	-10.31	77.35	87.66	41.10	40.49	0.23



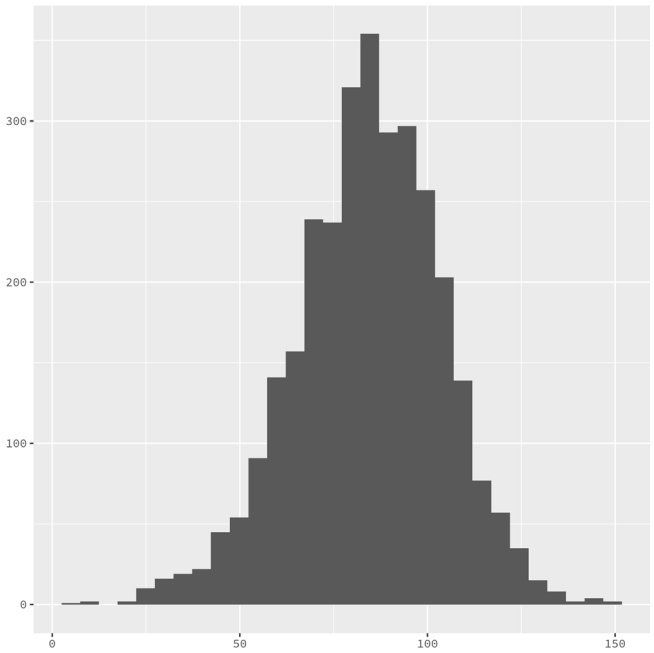
European ancestry: Dist. of E4_AI_GSCAN19



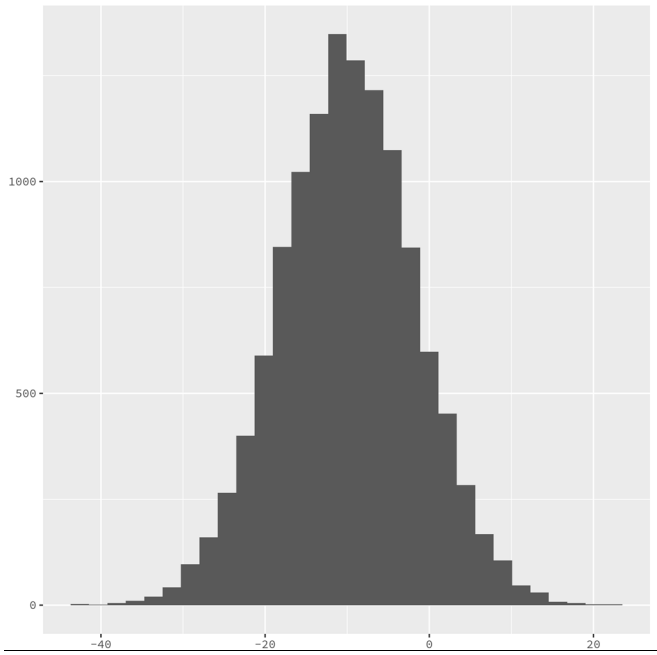
African ancestry: Dist. of A4_ AI_GSCAN19



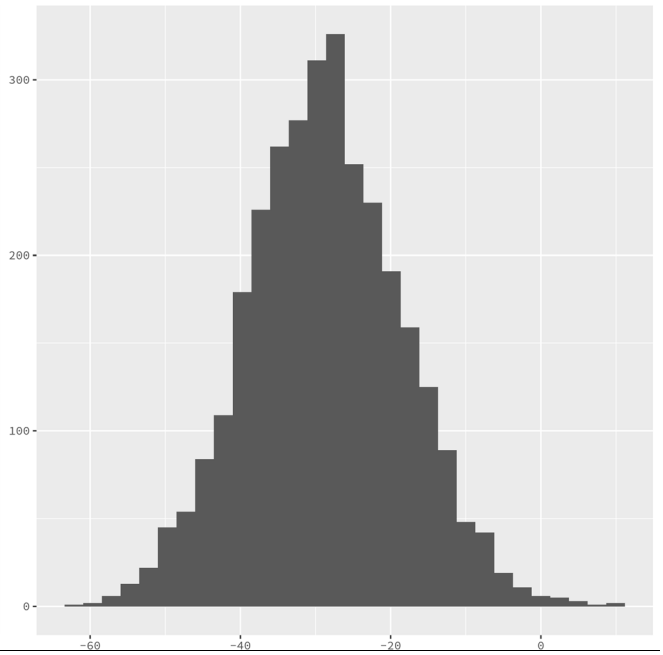
European ancestry: Dist. of E4_CPD_GSCAN19



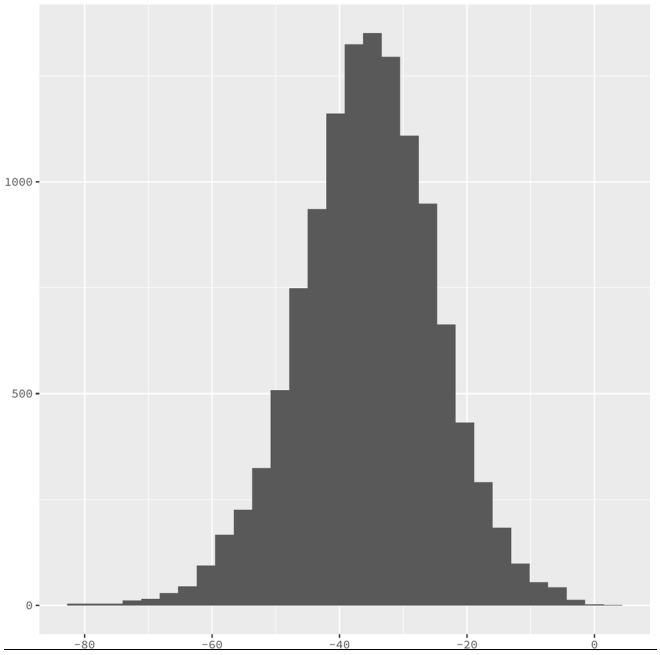
African ancestry: Dist. of A4_CPD_GSCAN19



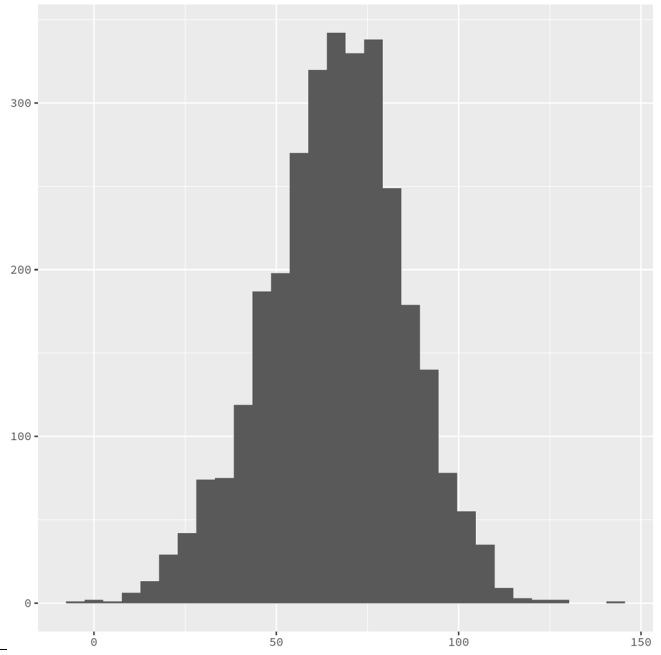
European ancestry: Dist. of E4_DPW_GSCAN19



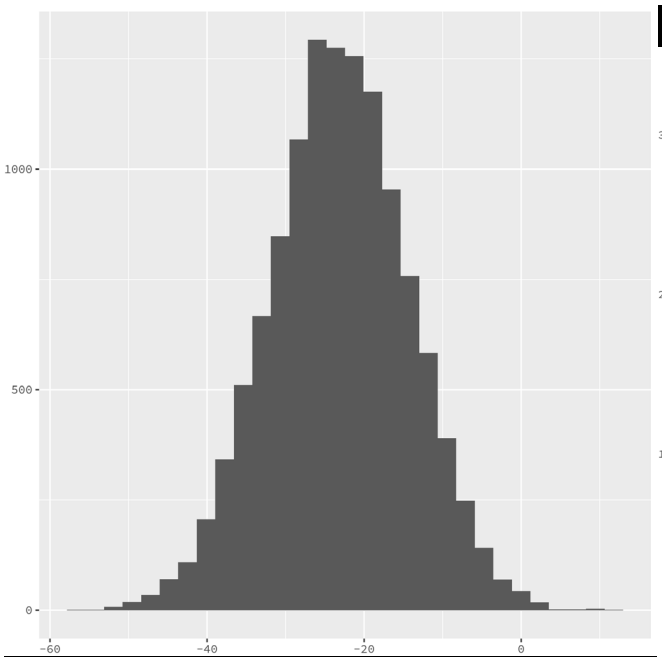
African ancestry: Dist. of A4_ DPW_GSCAN19



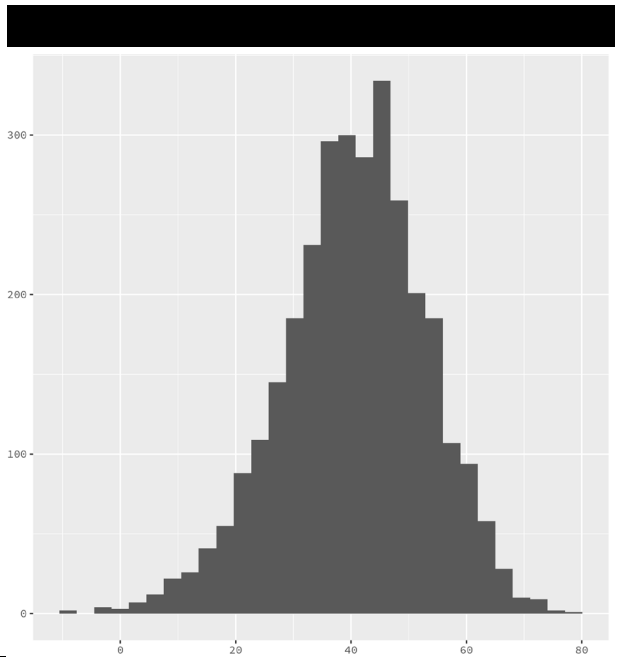
European ancestry: Dist. of E4_SC_GSCAN19



African ancestry: Dist. of A4_ SC_GSCAN19



European ancestry: Dist. of E4_SI_GSCAN19



African ancestry: Dist. of A4_ SI_GSCAN19

References

Liu M, Jiang Y, Wedow R, et al. Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use. Nat Genet. 2019;51(2):237–244. doi:10.1038/s41588-018-0307-5

TT. Lifetime cannabis use – International Cannabis Consortium + UKBiobank 2019

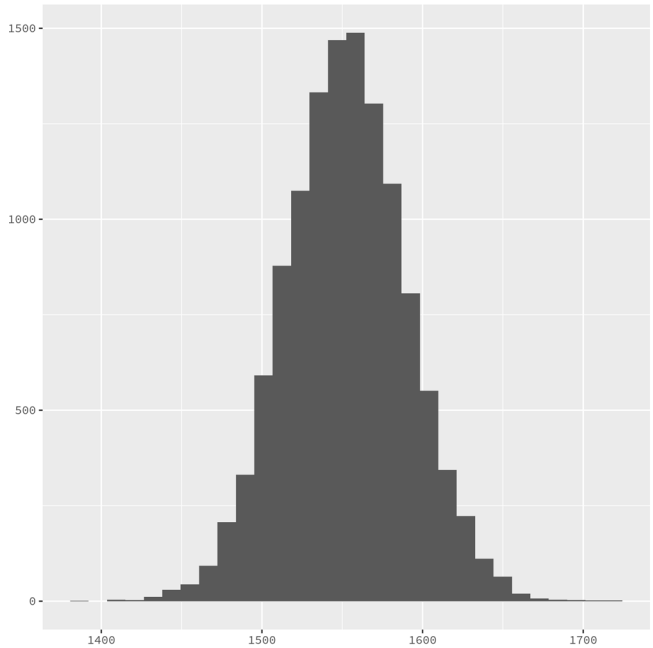
PGSs for lifetime cannabis use (CANNA) were created using results from a 2018 study conducted by the International Cannabis Consortium. The GWAS meta-analysis files are publicly available on the ICC data download page: https://www.ru.nl/bsi/research/group-pages/substance-use-addiction-food-saf/vm-saf/genetics/international-cannabis-consortium-icc/. The meta-analysis included 184,765 participants of European ancestry, from the ICC, 23andMe, and UK Biobank cohorts. To compute the PGSs for HRS respondents, SNP weights were constructed from publicly available data and do not include results with 23andMe due to data use agreements. Thus, the PGSs for HRS respondents are based on a GWAS of 162,082 participants of European Ancestry from the ICC cohorts and the UK Biobank (see cannabis readme on ICC documentation page; website link above). For the CANNABIS phenotype, self-report data were available on whether the participant had ever used cannabis during their lifetime: yes (1) versus no (0); slightly different wording was used in each cohort (see Pasman et al., 2018). The GWAS in the ICC cohorts was based on 6,643,927 SNPs in 35,297 participants; covariates included age, sex, principal components to account for population stratification, birth cohort, and batch effects. The GWAS in the UKB was based on 10,827,718 SNPs in 126,785 participants; covariates included age, age^2, sex, genotype array, and ancestry principal components to account for population stratification. This GWAS meta-analysis of the ICC cohorts and UKB (N = 162,082) included 11,733,371 million SNPs imputed to Haplotype Reference Consortium imputation reference panel. The study identified 8 genome-wide significant SNPs ($P < 10^{-8}$) (**Figure 1** and **Table 1**).

The ICCUKB cannabis use PGSs contains 1,445,349 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

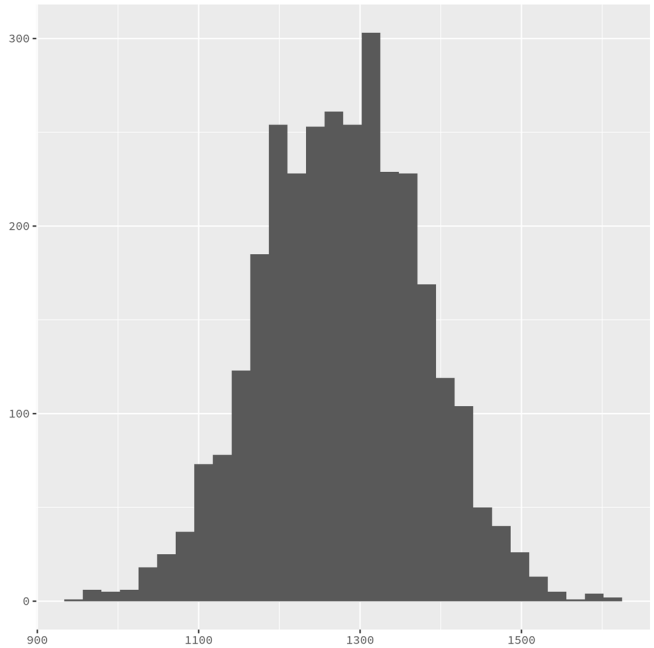
N.B.: **Please note that the ICCUKB weights are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	1386.93	1719.2	332.27	1552.36	1552.53	0.34
African ancestry	3100	953.32	1621.65	668.33	1278.79	1277.40	1.78



European ancestry: Dist. of E4_CANNABIS_ICC18



African ancestry: Dist. of A4_CANNABIS_ICC18

References

Pasman JA, Verweij KJH, Gerring Z, et al. GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal influence of schizophrenia [published correction appears in Nat Neurosci. 2019 Jul;22(7):1196]. Nat Neurosci. 2018;21(9):1161–1170. doi:10.1038/s41593-018-0206-1

UU. Alzheimer's disease 2 – International Genomics of Alzheimer's Project 2019

PGSs for Alzheimer's disease version 2 (AD2) were created using results from a 2019 study conducted by the International Genomics of Alzheimer's Project (IGAP). The GWAS meta-analysis files are publicly available through the National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS: https://www.niagads.org/datasets/ng00075; https://www.niagads.org/system/tdf/public_docs/Kunkle_etal_Stage1_results.txt?file=1&type=field_collection_item&id=121&force=). This meta-analysis confirmed 20 previous late-onset Alzeimer's diseases risk loci and identify five new genome-wide loci. The researchers conducted a GWAS meta-analysis of non-Hispanic Whites using a larger Stage 1 discovery sample (17 new, 46 total datasets; n = 21,982 cases, 41,944 cognitively normal controls) from the International Genomics of Alzheimer's Project (IGAP) (composed of four consortia: Alzheimer Disease Genetics Consortium (ADGC), Cohorts for Heart and Aging Research in Genomic Epidemiology Consortium (CHARGE), The European Alzheimer's Disease Initiative (EADI), and Genetic and Environmental Risk in AD/Defining Genetic, Polygenic and Environmental Risk for Alzheimer's Disease Consortium (GERAD/PERADES) (**Supplementary Tables 1 and 2, and Supplementary Note**).

N.B.: A total of four PGSs for the IGAP AD2 PGSs are being released including: PGSs at two different p-value thresholds (one PGS with all variants that overlap; one PGS with only variants that reached an association p-value between the variant and the outcome in the GWAS at 0.01), and PGSs with the *APOE/TOMM40* genomic region (45,384,477 to 45,432,606, build 37/hg 19) removed from the summary statistics or PGSs with the *APOE/TOMM40* genomic region included in the summary statistics + the two imputed variants that comprise *APOE-ε4* status (rs7412, rs429358). These options are provided for researchers based on discussions by the HRS genomics core and work by Ware et al 2019 (https://www.medrxiv.org/content/10.1101/2019.12.10.19014365v1).

Variable names for each Alzheimer's disease polygenic score:

	Treatment of the APOE/TOMM40 region and *APOE-ε4* variants	
P-value threshold for SNP inclusion (pT)	All variants that overlap, plus two imputed SNPs (rs7412, rs429358)	**REMOVED:** *APOE/TOMM40* genomic region (45,384,477 to 45,432,606, build 37/hg 19)
pT = 1.0	_GWAD2WA_IGAP19	_GWAD2NA_IGAP19
pT = 0.01	_01AD2WA_IGAP19	_01AD2NA_IGAP19

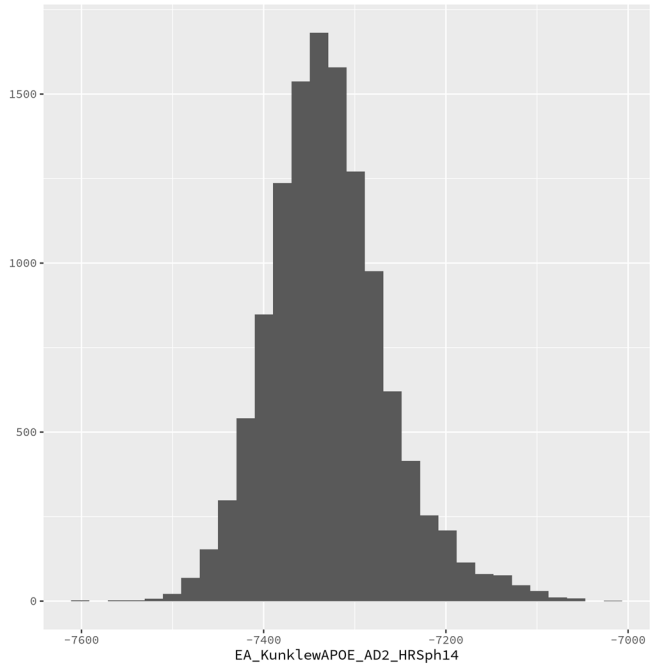
The IGAP-AD2 genome-wide (pT=1) PGSs contains 1,406,839 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; IGAP-AD2 genome-wide (pT=1) PGSs *without the APOE region* contains 1,406,784 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; The IGAP-AD2 at pT=0.01 PGSs contains 12,174 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; IGAP-AD2 at pT=0.01 PGSs *without the APOE region* contains 18,824 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

N.B.: **Please note that the IGAP-AD2 PGSs are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

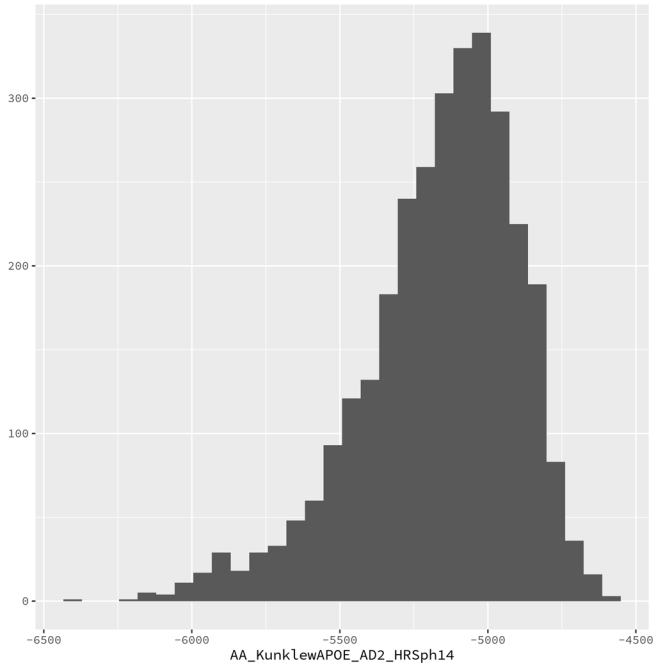
Raw PGS details are presented below.

	Sample Size	**Minimum**	**Maximum**	**Range**	**Median**	**Mean**	**SE (Mean)**
PGS with APOE/TOMM40 region, plus rs7412 and rs429358							
pT=1.0							
European ancestry	12090	-7611.10	-7026.38	584.72	-7333.59	-7328.85	0.60
African ancestry	3100	-6396.8	-4576.42	1820.38	-5122.625	-5164.45	4.77

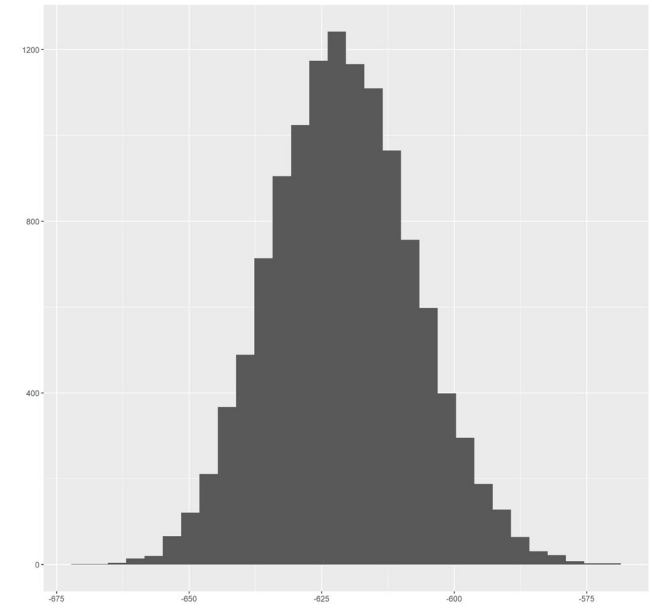
pT=0.01							
European ancestry	12090	-669.36	-569.13	100.23	-621.18	-621.00	5.11
African ancestry	3100	-559.98	-379.22	180.76	-459.75	-461.88	9.72
PGS without APOE/TOMM40 region							
pT=1.0							
European ancestry	12090	-7605.32	-7021.37	583.95	-7330.705	-7325.68	0.60
African ancestry	3100	-6393.49	-4576.66	1816.83	-5119.91	-5161.20	4.77
pT=0.01							
European ancestry	12090	-662.40	-568.15	94.25	-617.81	-617.68	4.84
African ancestry	3100	-553.48	-375.13	178.35	-456.65	-458.52	9.68



European ancestry: Dist. of E4_GWAD2WA_IGAP19



African ancestry: Dist. of A4_GWAD2WA_IGAP19



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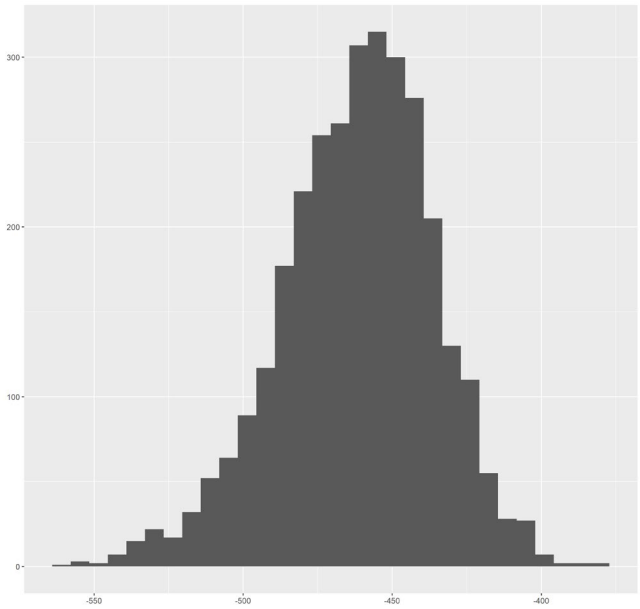

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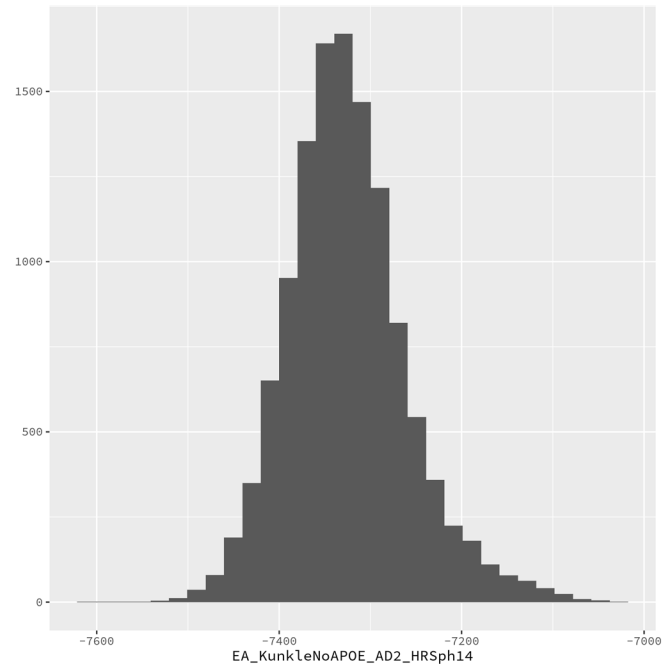
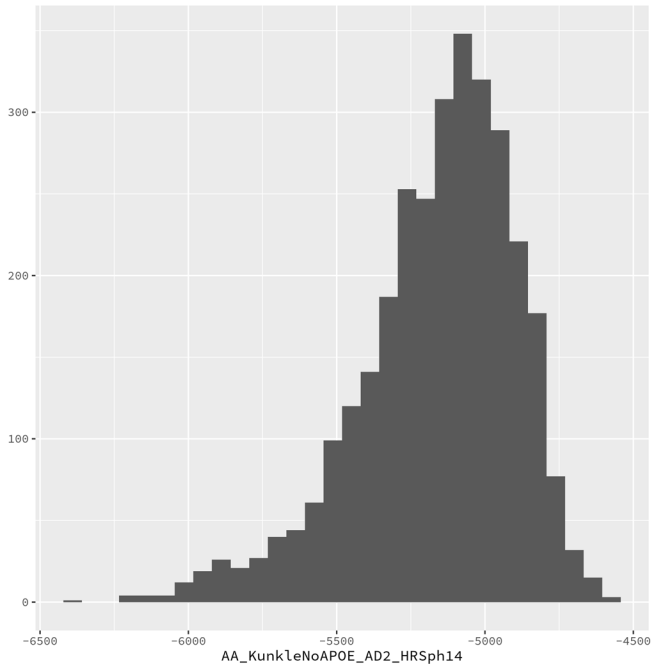


European ancestry: Dist. of E4_GWAD2NA_IGAP19



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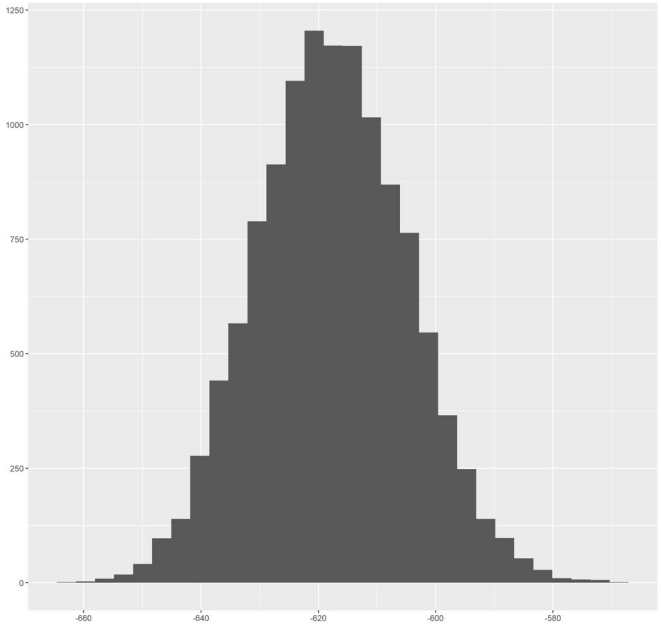

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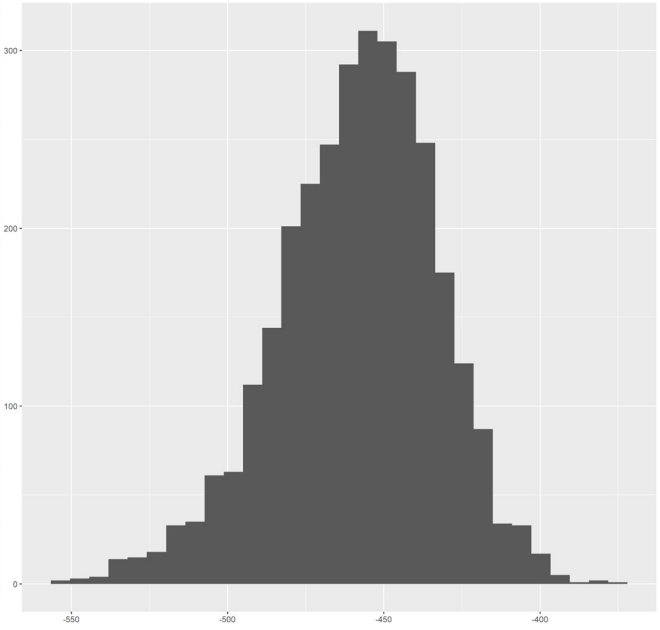


African ancestry: Dist. of A4_01AD2NA_IGAP19

References

Kunkle BW, Grenier-Boley B, Sims R, Bis JC, Damotte V, Naj A, et al. Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates Aβ, tau, immunity and lipid processing. Nat Genet. 2019 Mar;51(3):414-430. doi: 10.1038/s41588-019-0358-2.

Ware EB, Faul JD, Mitchell CM, Bakulski KM. Considering the APOE locus in polygenic scores for Alzheimer's disease. medRxiv 2019.12.10.19014365; doi: https://doi.org/10.1101/2019.12.10.19014365

VV. HbA1c – Meta-Analyses of Glucose and Insulin-related traits Consortium 2017

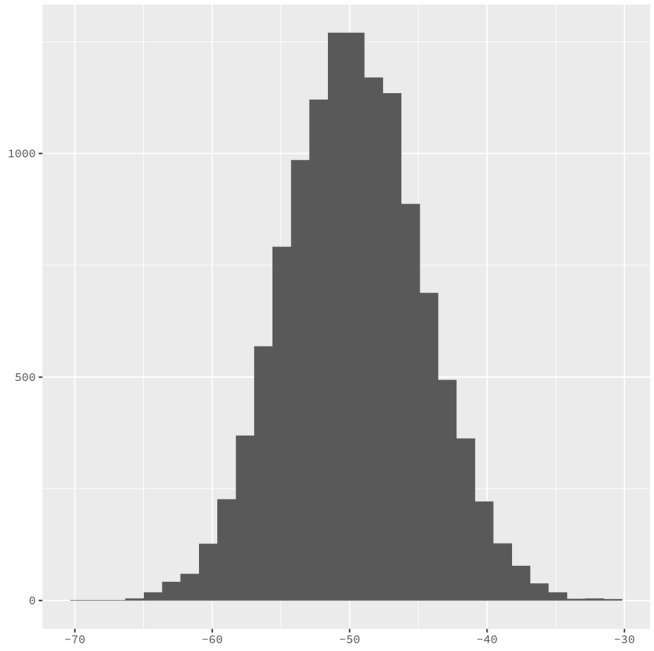
PGS for glycated hemoglobin A1c (HbA1c) were created using results from a 2017 study conducted by the Meta-Analyses of Glucose and Insluin-related traits Consortium (MAGIC). The GWAS meta-analysis files are publicly available on the MAGIC investigators download page (https://www.magicinvestigators.org/downloads/; ftp://ftp.sanger.ac.uk/pub/magic/HbA1c_METAL_AfricanAmerican_updatedSept2018.txt.gz, and ftp://ftp.sanger.ac.uk/pub/magic/HbA1c_METAL_European.txt.gz). Ancestry-specific and transethnic genome-wide meta-analysis summary statistics for association with HbA1c in up to 159,940 individuals from 82 cohorts of European (N=123,665), African (N=7,564), East Asian (N=20,838) and South Asian (N=8,874) ancestry. HbA1c trait values are untransformed and adjusted for age, sex and study-specific covariates. To compute the PGSs for HRS respondents, SNP weights were constructed from publicly available datafor the European and African-based discovery analysis. The GWAS meta-analysis included 3,009,839 million SNPs (African-based discovery results) and 2,586,698 million SNPs (European-based discovery results) imputed to NCBI Build 37/UCSC hg 19. The GWAS meta-analysis identified 60 common genetic variants associated with HbA1c. Variants were classified as implicated in glycemic, erythrocytic, or unclassified biology. Where possible, studies reported HbA1c as a National Glycohemoglobin Standardization Program (NGSP) percent (**S1 Table**).

The PGSs created from the European-based GWAS summary statistics contained 789,140 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; the PGSs created from the African-based GWAS summary statistics contained 869,686 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

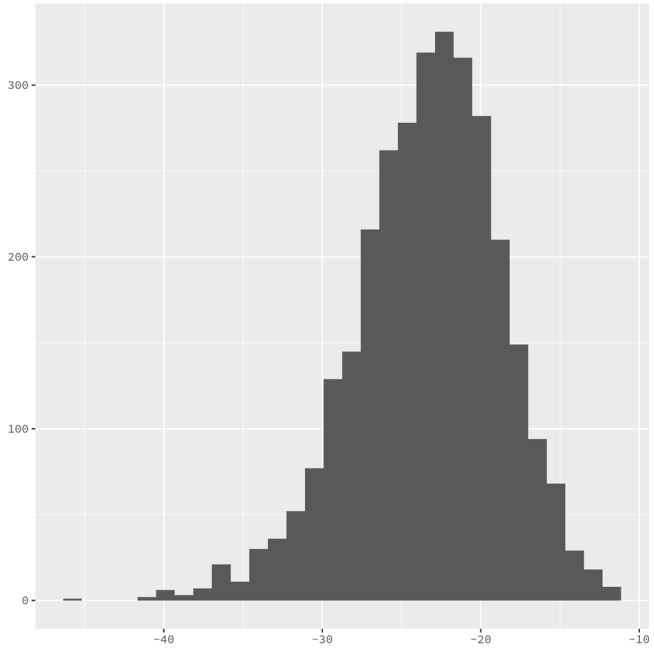
N.B.: **Please note that the MAGIC-HbA1c weights are from ancestry-specific discovery GWAS (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

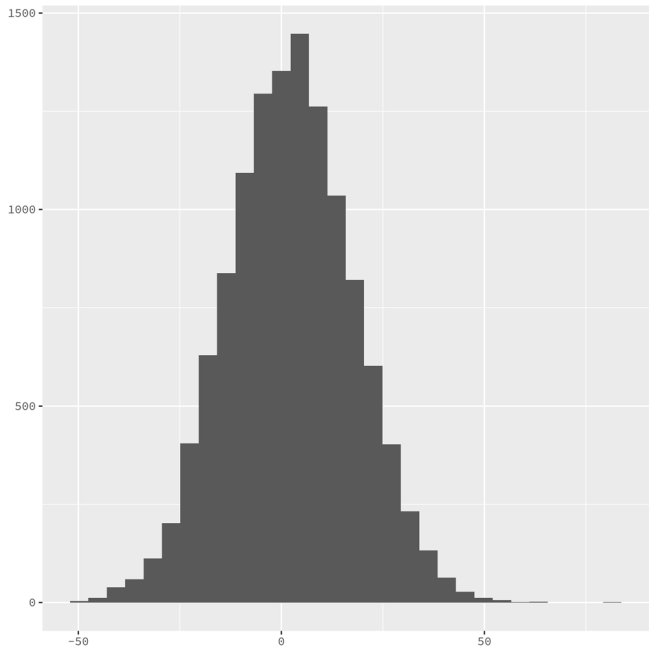
	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European-ancestry GWAS							
European ancestry	12090	-69.79	-30.93	38.86	-49.76	-49.69	0.05
African ancestry	3100	-45.26	-11.23	34.03	-23.03	-23.37	0.08
African-ancestry GWAS							
European ancestry	12090	-49.45	81.81	131.27	2.27	2.27	0.14
African ancestry	3100	-57.11	164.06	221.17	89.24	87.86	0.45



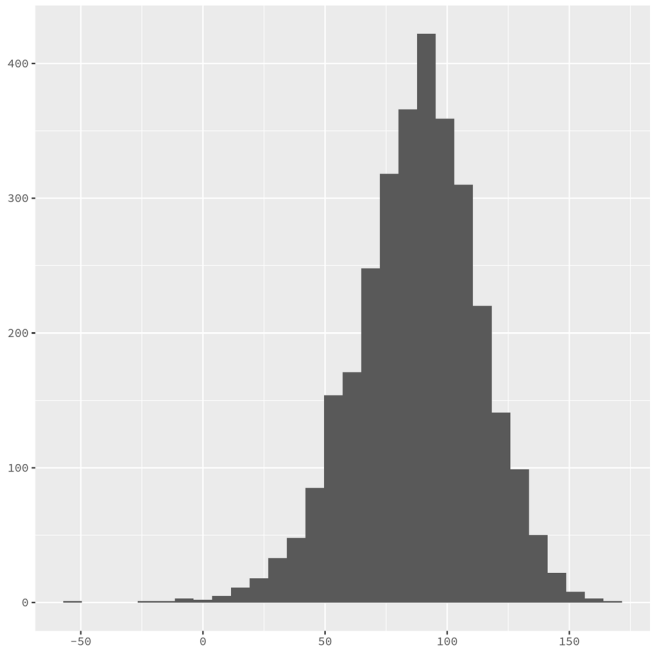
European ancestry: Dist. of E4_HBA1CEA_MAGIC17



African ancestry: Dist. of A4_HBA1CEA_MAGIC17



European ancestry: Dist. of E4_HBA1CAA_MAGIC17



African ancestry: Dist. of A4_HBA1CAA_MAGIC17

References

Wheeler E, Leong A, Liu CT, et al. Impact of common genetic determinants of Hemoglobin A1c on type 2 diabetes risk and diagnosis in ancestrally diverse populations: A transethnic genome-wide meta-analysis. PLoS Med. 2017;14(9):e1002383. Published 2017 Sep 12. doi:10.1371/journal.pmed.1002383

WW. Alcohol dependence – Psychiatric Genomics Consortium 2018

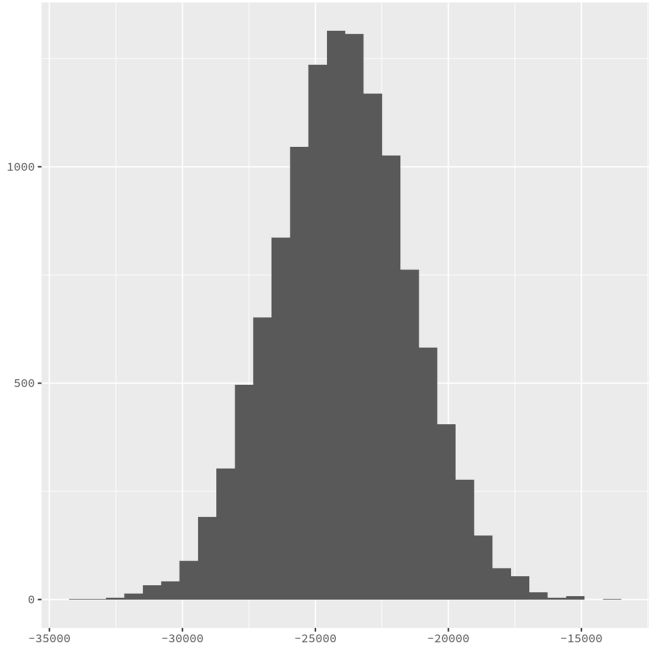
The alcohol dependence PGSs were created using results from a 2018 study by the Psychiatric Genomics **Consortium Substance Use Disorder workgroup. Results from several GWAS were reported. The unrelated European ancestry GWAS meta-analysis included 11,569 cases and 34,999 controls from 27 cohorts; three SNPs** reached genome-wide significance. Approximately ~9 million SNPs were included in the analyses, with all cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G). Three replication cohorts were used: FINRISK (1,232 cases, 22,614 controls); Yale-Penn 2 (911 cases, 599 controls); and COGA African-American Family GWAS (880 cases, 1,814 controls). The original GWAS did not include the HRS. Study-specific GWASs controlled for sex and between five and ten principal components of the genotypic data in the European cohorts.

The HRS PGSs from the unrelated, European GWAS meta-analysis contain 1,279,450 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

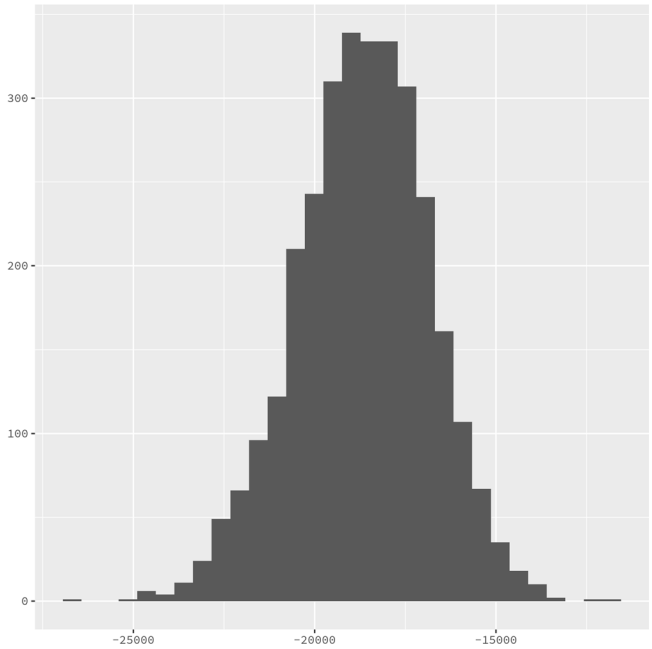
N.B.: **Please note that the PGC Alcohol Dependence weights are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).**

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	-34032.30	-13961.40	20070.90	-23993.4	-23989.35	23.15
African ancestry	3100	-26571.60	-11687.20	14884.40	-18625.15	-18685.97	32.93



European ancestry: Dist. of E4_ALC_PGC18



African ancestry: Dist. of A4_ ALC_PGC18

References

Walters RK, Polimanti R, Johnson EC, et al. Transancestral GWAS of alcohol dependence reveals common genetic underpinnings with psychiatric disorders. Nat Neurosci. 2018;21(12):1656–1669. doi:10.1038/s41593-018-0275-1

XX. Educational Attainment 3 – Social Science Genetic Association Consortium 2018 WITH 23andMe summary statistics

The educational attainment PGSs were created using results from a 2018 study by the Social Science Genetic Association Consortium (SSGAC) *including data provided by 23andMe*. The meta-analysis included 405,073 individuals in the combined discovery and replication sample and 726,808 individuals that did not contribute to the analyses of the previous study and were used as replication in this study (total of 1,131,881 individuals). Genome-wide significant SNPs were identified in 1,271 loci (**Supplementary Information table 2** [1]). Approximately 10.2 million SNPs were included in the analyses, with all cohorts utilizing SNPs imputed to the 1000 genomes reference panel (1000G). The original GWAS included the HRS. To compute the PGSs for HRS respondents, the SSGAC provided SNP weights with the HRS and 23andMe results removed (due to data use agreements). Study-specific GWASs controlled for the first ten principal components of the genotypic data, a third-order polynomial in age, an indicator for being female, interactions between age and female, and study-specific controls, including dummy variables for major events such as wars or policy changes that may have affected access to education in their specific sample. After a data request to 23andMe, the educational attainment summary statistics from 23andMe were then meta-analyzed with the summary statistics provided by SSGAC without HRS.

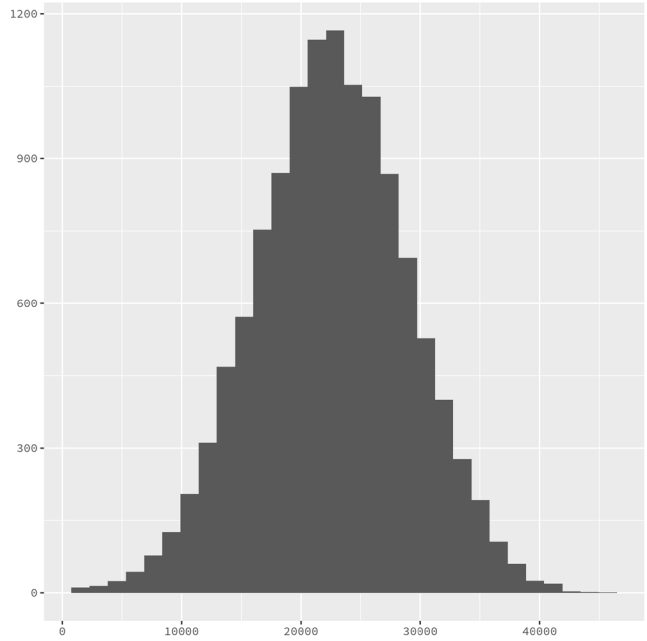
The European ancestry PGSs contains 1,308,344 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis; African ancestry PGSs contain 1,298,357 SNPs. The posted PGSs have been standardized within ethnicity to a standard normal curve (mean=0, standard deviation = 1).

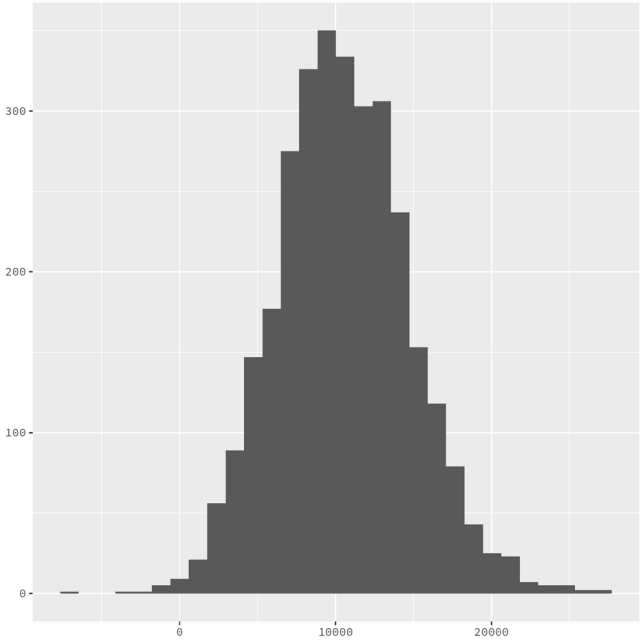
N.B.: As this GWAS required the removal of the HRS cohort from the summary statistics, estimates do not 100% align with the corresponding publication Included SNPs and weights are avaialable upon request to the SSGAC consortium contact@ssgac.org. Please contact dataset-request@23andme.com for more information about applying to access 23andMe data.

Please note that the SSGAC results are from a GWAS on individuals of European ancestry (see Section C. "Notes about the use of PGSs" for more information on the use of PGSs in other ancestry groups).

Raw PGS details are presented below.

	Sample Size	Minimum	Maximum	Range	Median	Mean	SE (Mean)
European ancestry	12090	1141.70	45332.30	44190.60	22623.25	22576.48	58.23
African ancestry	3100	-7312.63	26880.80	34193.43	10359.40	10505.12	75.53





References

Lee JJ, Wedow R, Okbay A, Kong E, Maghzian O, Zacher M, … & Cesarini D. (2016). Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nature genetics*, *doi: 10.1038/s41588-018-0147-3*

III. Setup

By downloading this freely provided data set, you agree to use its contents only for research and statistical purposes, making no effort to identify the respondents. You also agree inform HRS of any papers, publications, or presentations based on this data set. Please send a copy of such publications in PDF format via e-mail to *hrsquestions@umich.edu* with "Attn: Papers and Publications" in the subject line. If you wish, you may include a bibliographical reference. As an alternative, you may transmit publications in paper format by postal mail:

```
Health and Retirement Study
Attn: Papers and Publications
The Institute for Social Research
P.O. Box 1248
Ann Arbor, Michigan  48106-1248
```

A. Distribution Set

The *HRS Polygenic Scores* data set is packaged for distribution in a ZIP file, **`PGENSCORE.zip`**. The .zip file contains two data files, PGENSCOREA_R (African Ancestry) and PGENSCOREE_R (European Ancestry). Both files are keyed on HRS Household Identifier (HHID) and Person Number (PN). To use these data, extract the data files, the program statement files that matches your analysis environment, the data description (this file), and the codebook files.

If you have problems when downloading this data product or in extracting its contents, please contact the HRS Help Desk. See Table 1 (below) for a description of the .zip file contents as well as a suggested subdirectory structure.

Table 1: Contents of the Distribution Package

Directory[3]	File Type	Polygenic Scores	File Name
c:\polys\docs\	Codebook (ASCII text)		PGENSCORE.txt
	Data Description (this document)		PGENSCORESDD.pdf
c:\polys\data\	Data files (ASCII text)	AFRICAN ANCESTRY	PGENSCOREA_R.da (n=3100)
		EUROPEAN ANCESTRY	PGENSCOREE_R.da (n=12090)
c:\polys\sas\	SAS program statements	AFRICAN ANCESTRY	PGENSCOREA_R.sas
		EUROPEAN ANCESTRY	PGENSCOREE_R.sas
c:\polys\spss\	SPSS program statements	AFRICAN ANCESTRY	PGENSCOREA_R.sps
		EUROPEAN ANCESTRY	PGENSCOREE_R.sps
c:\polys\stata\	Stata dictionary/"do" files	AFRICAN ANCESTRY	PGENSCOREA_R.dct/.do
		EUROPEAN ANCESTRY	PGENSCOREE_R.dct/.do

[3] When using HRS data products, you should feel free to create the directory structure that is most suitable for your needs. By using the suggested directory structure (or a Unix equivalent), you will not have to change the path name references in the data descriptor files. If you want to use a different structure, just change the directory references in the program files.

B. Program Statements

Each data file comes with associated SPSS, SAS, or Stata program statements to read the data. Files containing SPSS statements are named with an .sps extension, those with SAS statements with an .sas extension, and those with Stata statements with .do and .dct extensions.

1. Using the Files with SAS

To create a SAS system file for this data set, load the .sas program statement files into the SAS Program Editor and reference the appropriate .da data files. If the *.sas file is located in 'c:\polys\sas" and the data file is located in 'c:\polys\data", you can run the file as is. A SAS system file will be saved to directory 'c:\polys\sas". If the files are not located in the specified directories, you will need to edit the *.sas file to reflect the proper path names prior to running the file.

2. Using the Files with SPSS

To create an SPSS system file for this data set, load the .sps program statement files into the SPSS syntax editor window, reference the appropriate .da data files, and select the *Run>All* option. If the *.sps file is located in 'c:\polys\spss" and the data file is located in 'c:\polys\data", you can run the file as is. An SPSS system file (*.sav) will be saved to directory 'c:\polys\spss". If the files are not located in the specified directories, you will need to edit the *.sps file to reflect the proper path names prior to running the file.

3. Using the Files with Stata

To use Stata with this data set, three file types must be present for that data set: .dct, .do, and .da. Files with the suffix ".da" contain the raw data for Stata to read. Files with the suffix ".dct" are Stata dictionaries used by Stata to describe the data. Files with the suffix ".do" are short Stata programs ("do files") which you may use to read in the data. Load the .do file into Stata and then submit it. If the *.do and .dct files are located in 'c:\polys\stata" and the data file is located in 'c:\polys\data", you can run the .do file as is. If the files are not located in these directories, you must edit the *.do and *.dct files to reflect the proper path names before you run the files.

C. Non-Windows Environments

Non-Microsoft users should modify the default Windows file structure syntax to match that of their own operating system. The following examples should work for both Macintosh OS X and any Unix/Linux distribution. Open the SAS program file(s), SPSS syntax file(s) or the Stata do/dct files in an ASCII editor and make the changes indicated below.

1. SPSS in an OSX environment

In this example, we assume that the user has downloaded the region dataset and placed the files in a **Desktop** folder called **Polys** with the ASCII data file stored in subfolder **data** and the syntax file in subfolder **spss**. Then the commands in the syntax file that reads PGENSCOREA_R.da would be modified to look like this:

```
FILE HANDLE polys /name='Desktop/Polys/data/PGENSCOREA_R.da' LRECL=431.
DATA LIST FILE= polys/
HHID 1-6(A)
[rest of syntax file goes here]
.
execute.
SAVE /outfile 'Desktop/Polys/spss/PGENSCOREA_R.sav'. Execute.
```

2. STATA in an OS X Environment

In the following example we assume that:

- The username is “user1”
- The zip file containing tracker information has been downloaded to the user’s desktop from the HRS file download site
- The user has decompressed the zip file (use Stuffit for OS X) into a desktop folder named **Polys**
- The statistical package is stata

File `PGENSCOREA_R.do` should be modified as follows:

Change…

```
infile using c:\polys\stata\PGENSCOREA_R.dct
```

To…

```
infile using /Users/user1/Desktop/Polys/stata/PGENSCOREA_R.dct
```

Change…

```
save c:\polys\stata\PGENSCOREA_R.dta
```

To…

```
save /Users/user1/Desktop/Polys/stata/PGENSCOREA_R.dta
```

File `PGENSCOREA_R.dct` should be modified as follows

Change…

```
dictionary using c:\polys\data\PGENSCOREA_R.da {
```

To…

```
dictionary using /Users/user1/Desktop/Polys/data/PGENSCOREA_R.da {
```

IV. If You Need to Know More

This document is intended to serve as a brief overview to provide guidelines for using the *HRS Polygenic Scores* data product. If you have questions or concerns that are not adequately covered here or on our Web site, or if you have any comments, please contact us. We will do our best to provide answers.

A. HRS Internet Site

Health and Retirement Study public release data and additional information about the study are available on the Internet. To access public data or to find out more about restricted data products and procedures, visit the HRS Web site.

B. Contact Information

If you need to contact us, you may do so by one of the methods listed below.

Internet: Help Desk at the HRS Web site (http://hrsonline.isr.umich.edu)

E-mail: hrsquestions@umich.edu

Postal Service:
Health and Retirement Study
The Institute for Social Research
The University of Michigan
P.O. Box 1248
Ann Arbor, Michigan 48106-1248
FAX: (734) 647-1186

C. Citing this Document

Please include the following citation in any research reports, papers, or publications based on these data along with the citiation for the reference GWAS:

In text:

"The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (NIA U01AG009740) and is conducted by the University of Michigan. "

In references:

"Ware EB, Gard AM, Schmitz LL, Faul JD. HRS Polygenic Scores – Release 4. Ann Arbor, MI: Survey Research Center, Institute for Social Research, University of Michigan; 2020."