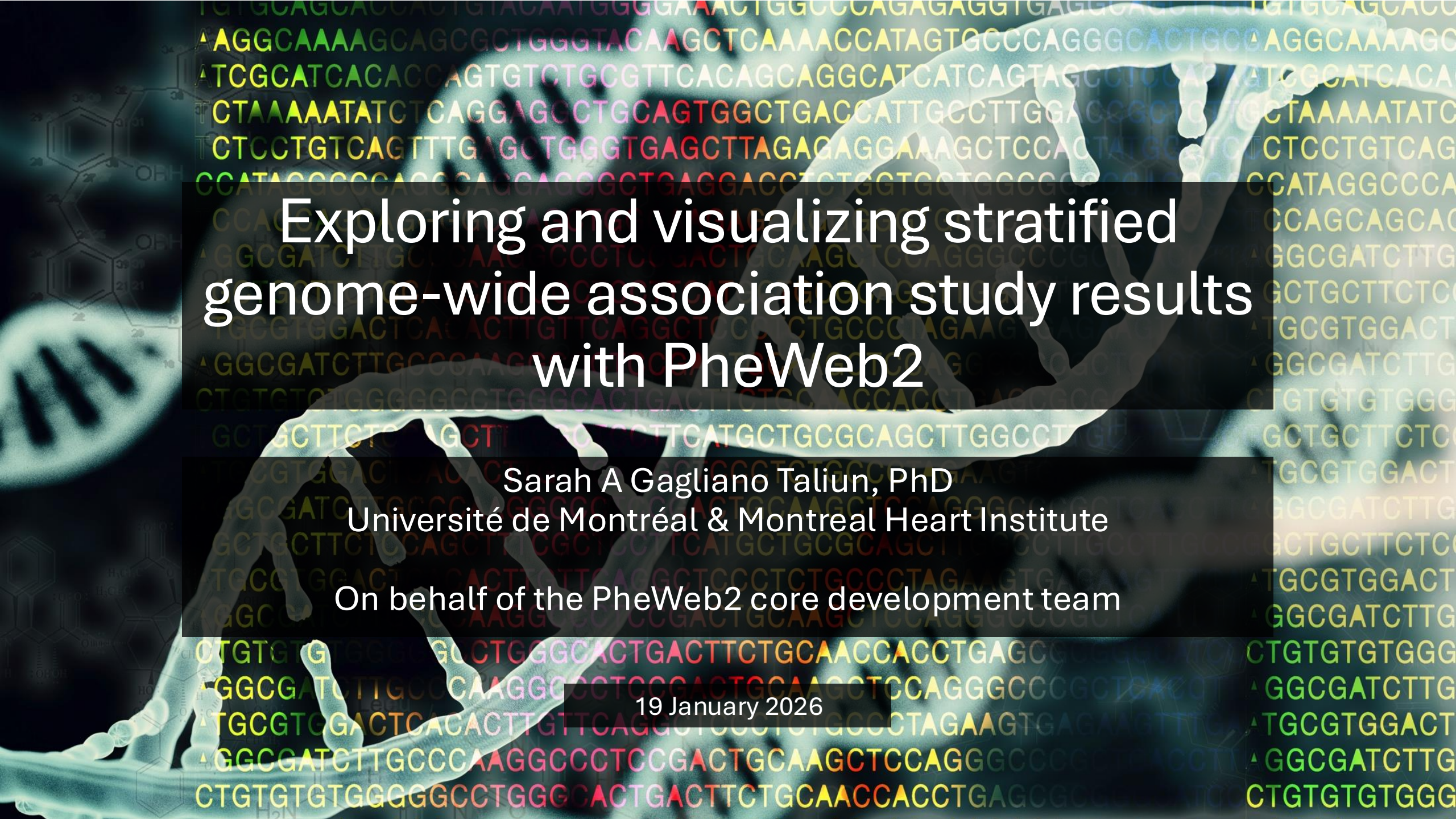


Exploring and visualizing stratified genome-wide association study results with PheWeb2

Sarah A Gagliano Taliun, PhD
Université de Montréal & Montreal Heart Institute

On behalf of the PheWeb2 core development team

19 January 2026

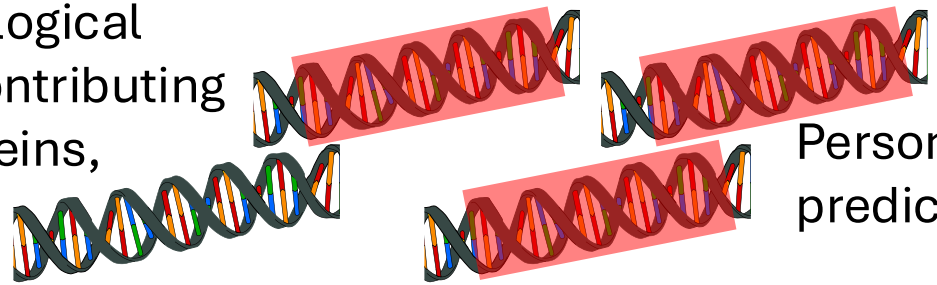
What we'll talk about today

- **GWAS and visualization with PheWeb**
- What's new with PheWeb2
- Using CLSA to showcase PheWeb2's features

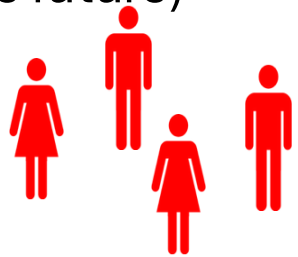
A genome-wide association study (GWAS) identifies DNA regions **associated** with a complex disease or trait of interest

Why identify genetic variants that influence complex traits/diseases?

Understand biological mechanisms contributing to the trait: proteins, tissues



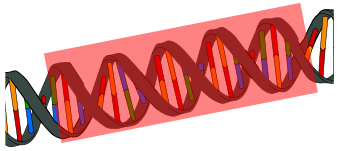
Personalized medicine/ prediction (for the future)

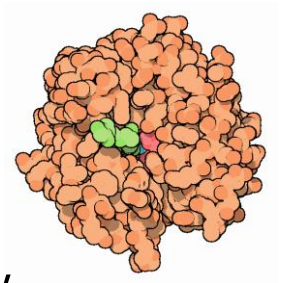


with diabetes

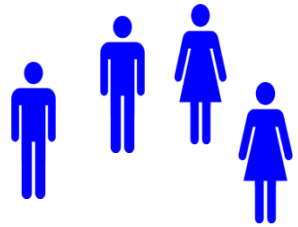
Many genes + intergenic and intronic regions

Gene ⟶ ⟶ Protein ⟶ ⟶ Complex Trait





New targets for the development of new medications



without diabetes

Environment

Case-control GWAS design: is the allele more common in cases vs. controls (or vice versa)?

Without diabetes ("Controls")

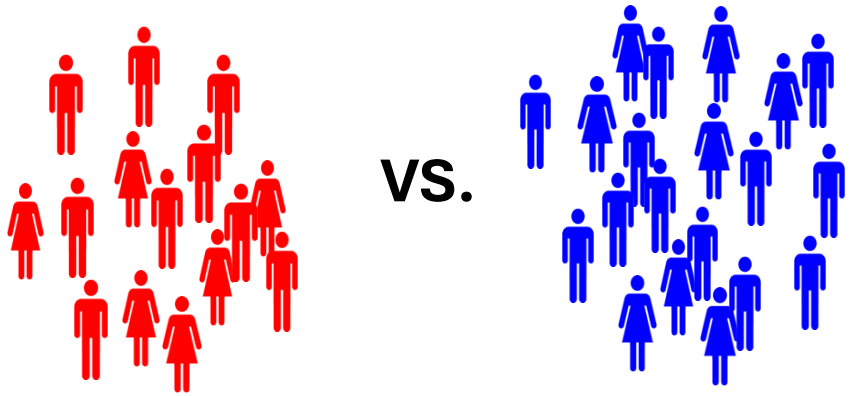
With diabetes ("Cases")

Test for a statistical difference.
Repeat for each genetic variant.

Variant 1

…A C C T A G C T A T C C T…
…A C C T A G C T A T C C T…
…A C C T A G C T A T C C T…
…A C C G A G C T A T C C T…
…A C C T A G C T A T C C T…
…A C C T A G C T A T C C T…
…A C C T A G C T A T C C T…
…A C C G A G C T A T C C T…
…A C C T A G C T A T C C T…
…A C C G A G C T A T C C T…

Variant 1: frequency of allele G



Cases
2000/4000 = 50%

VS.

Controls
1000/6000 = 16.7%

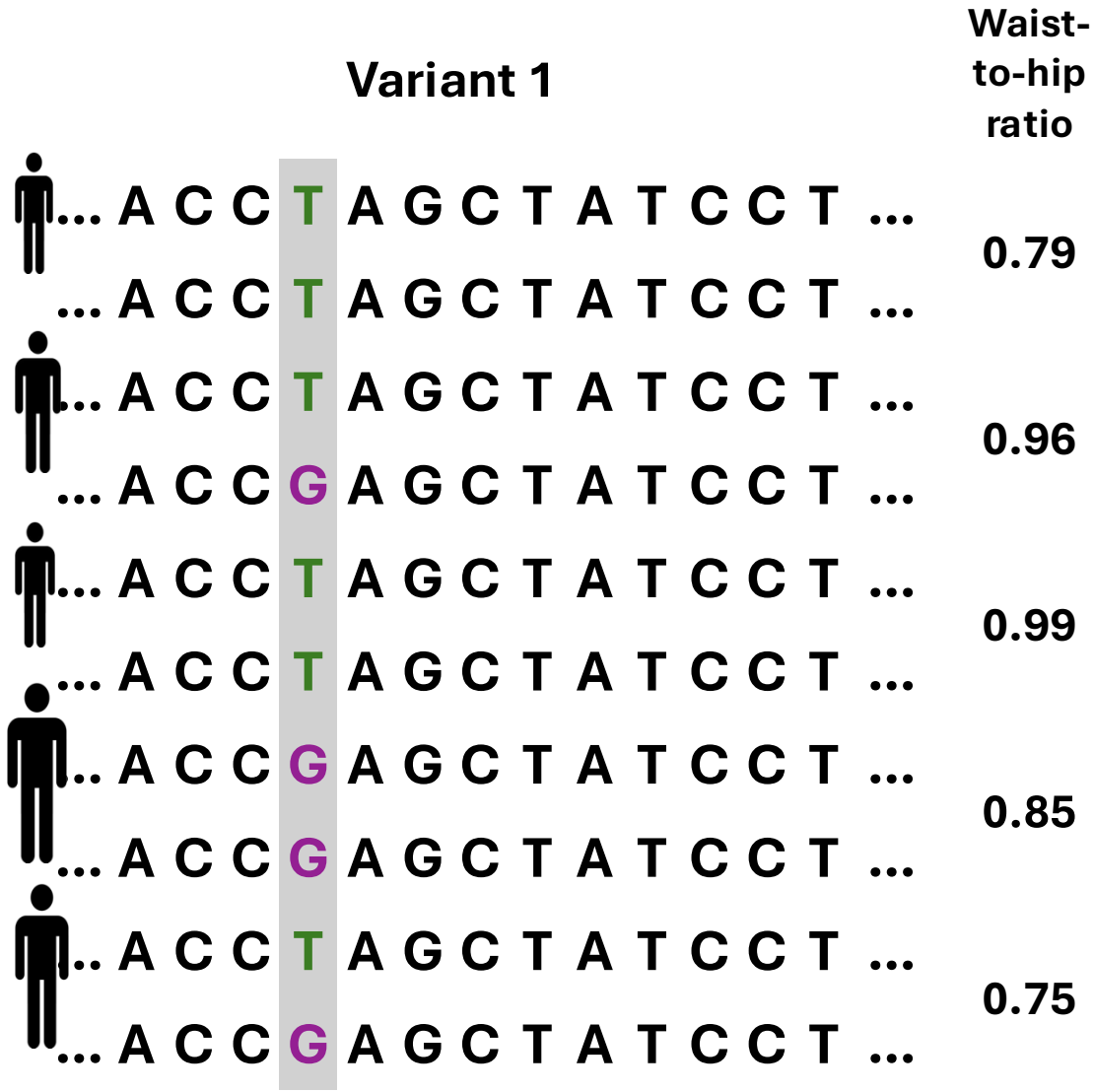
Logistic regression

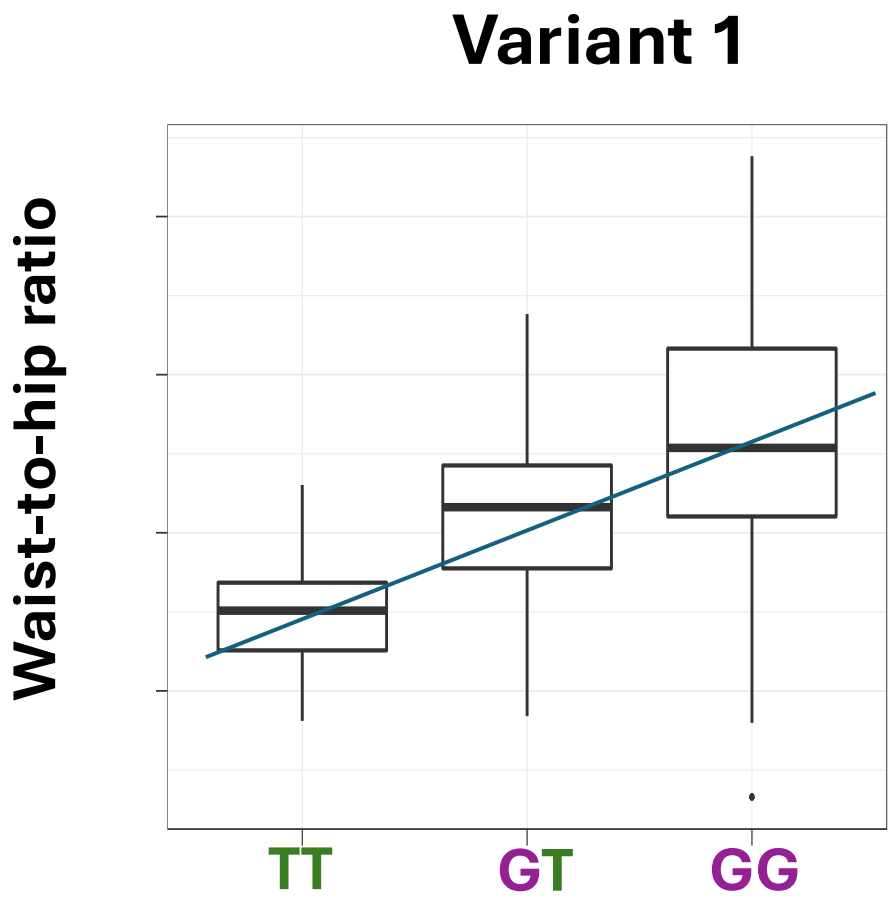
$H_0 : Freq_{cases} = Freq_{controls}$

$H_1 : Freq_{cases} \neq Freq_{controls}$

Obtain p-value & effect size

Quantitative/continuous trait GWAS: is the frequency of the allele associated with the trait?





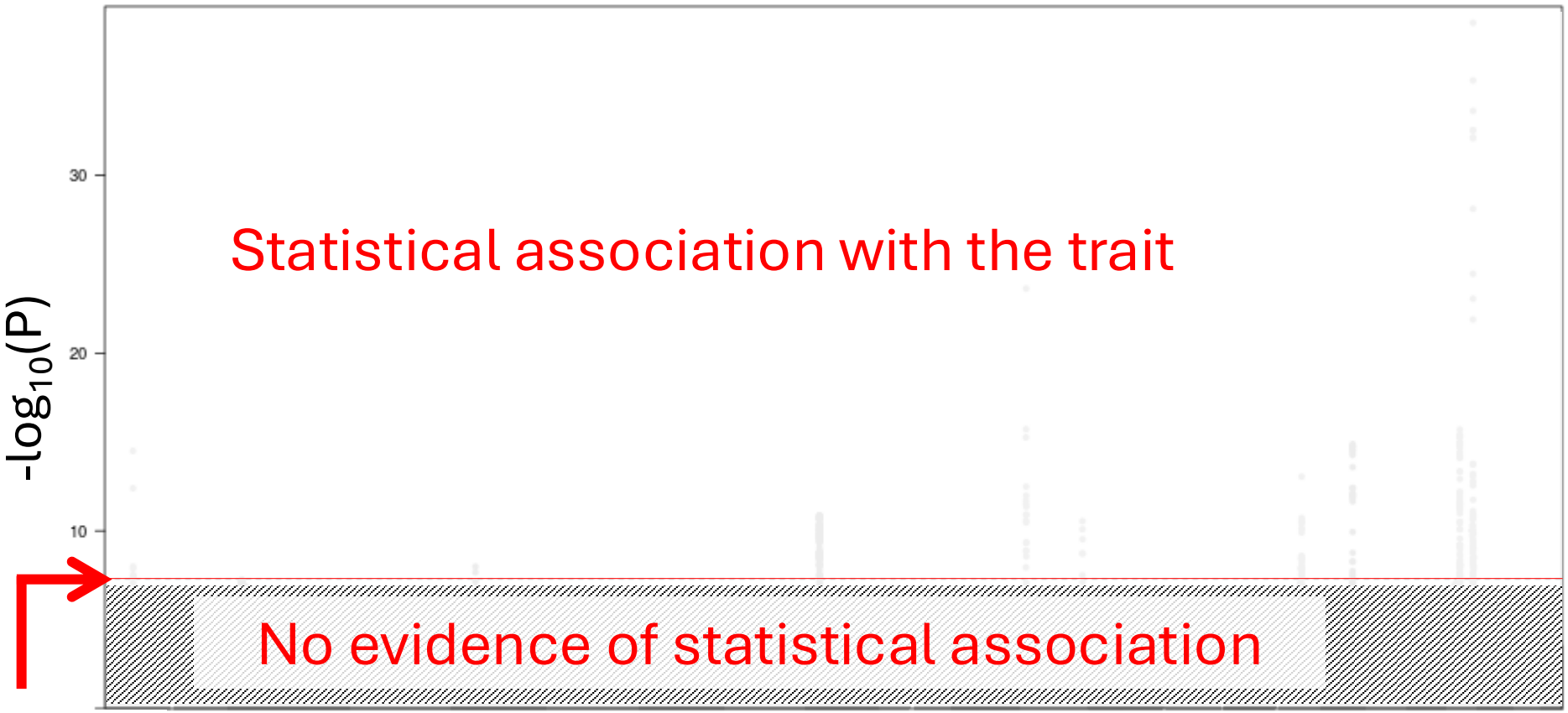
Linear regression

$H_0 : \beta=0$

$H_1 : \beta\neq0$

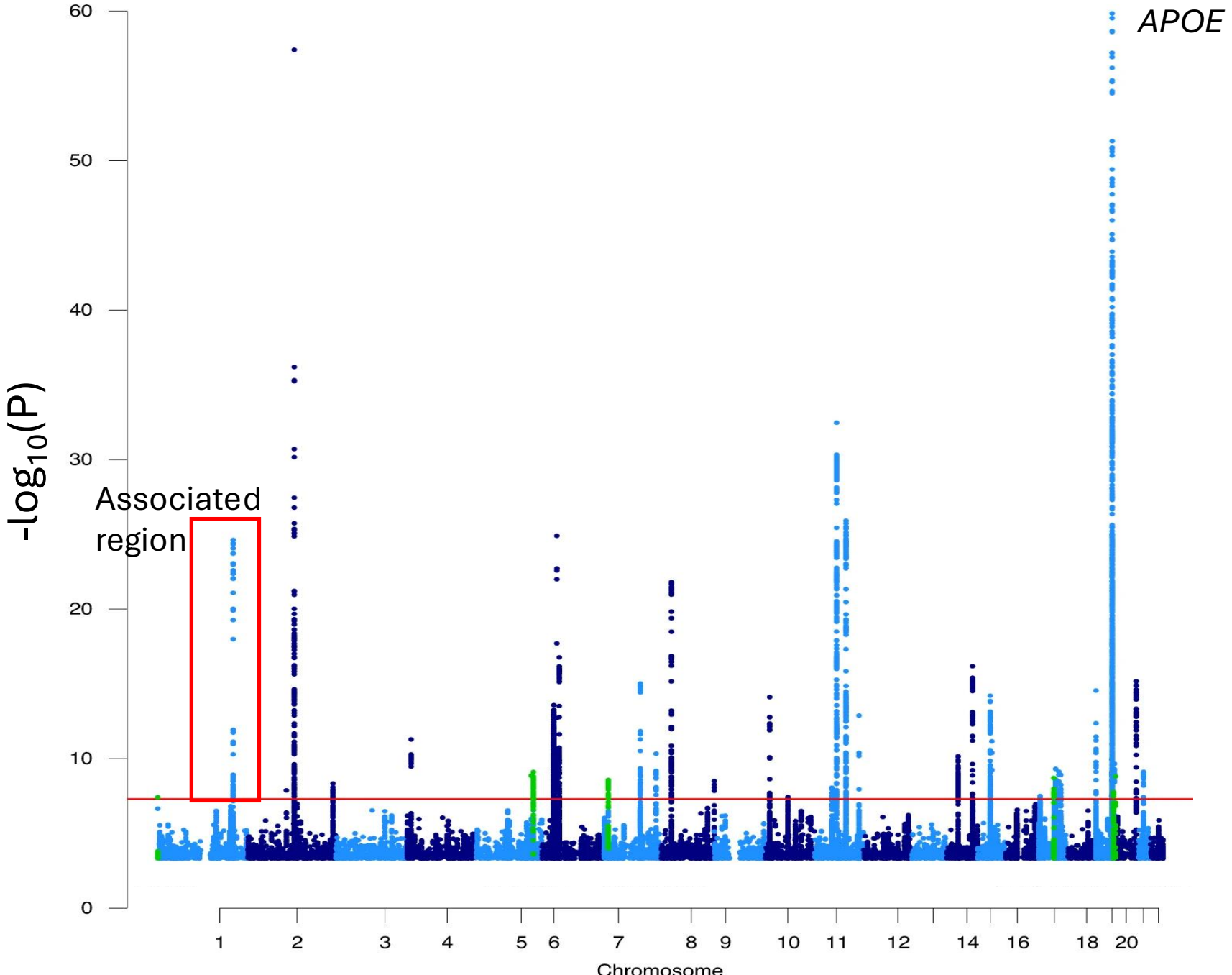
Obtain p-value & effect size

“Manhattan plot” to visualize the associations across the genome



p=significance threshold

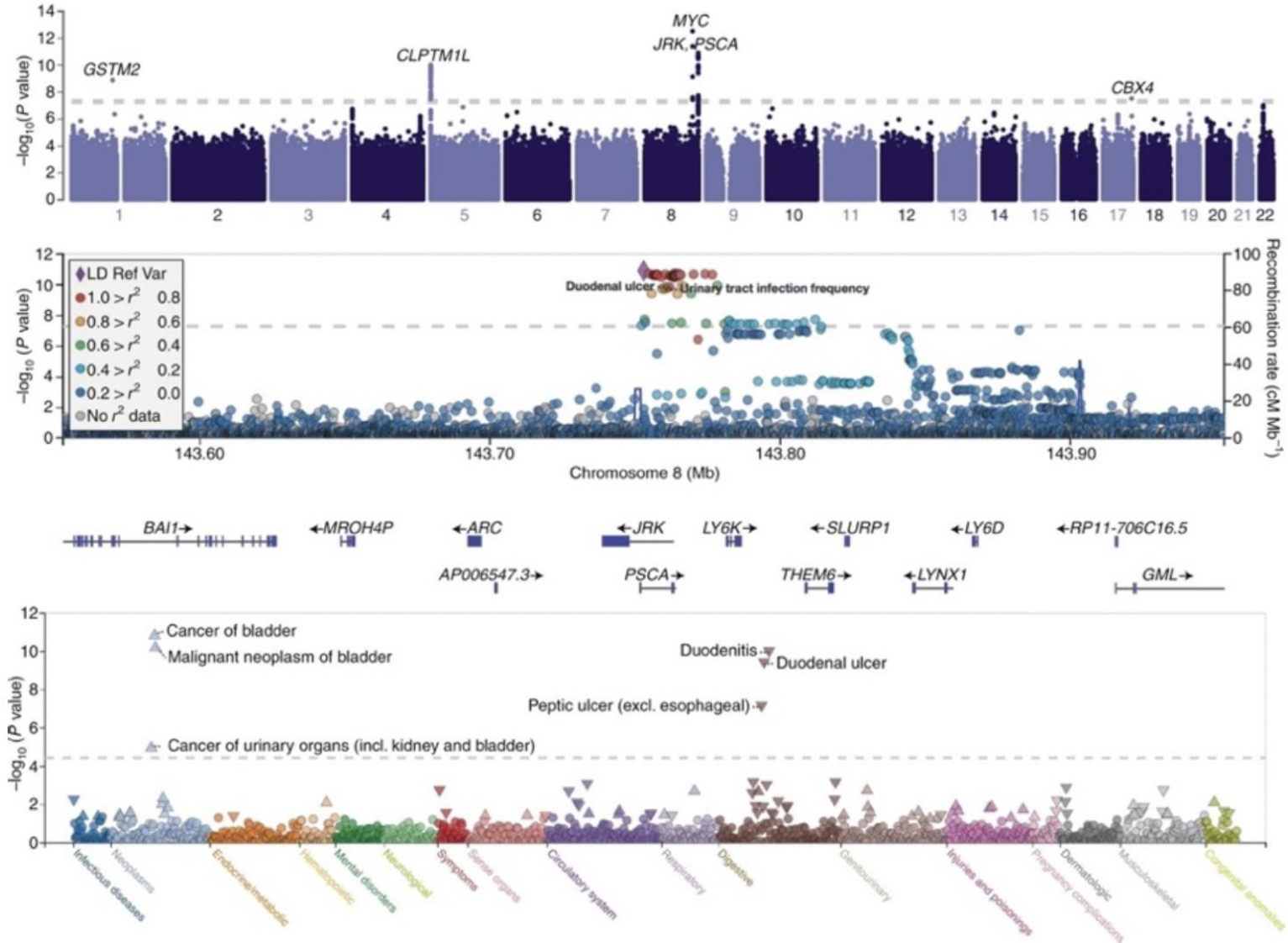
Alzheimer's Disease GWAS (Wightman et al *Nat Genetics* 2022)



1 cohort – many traits to run GWAS

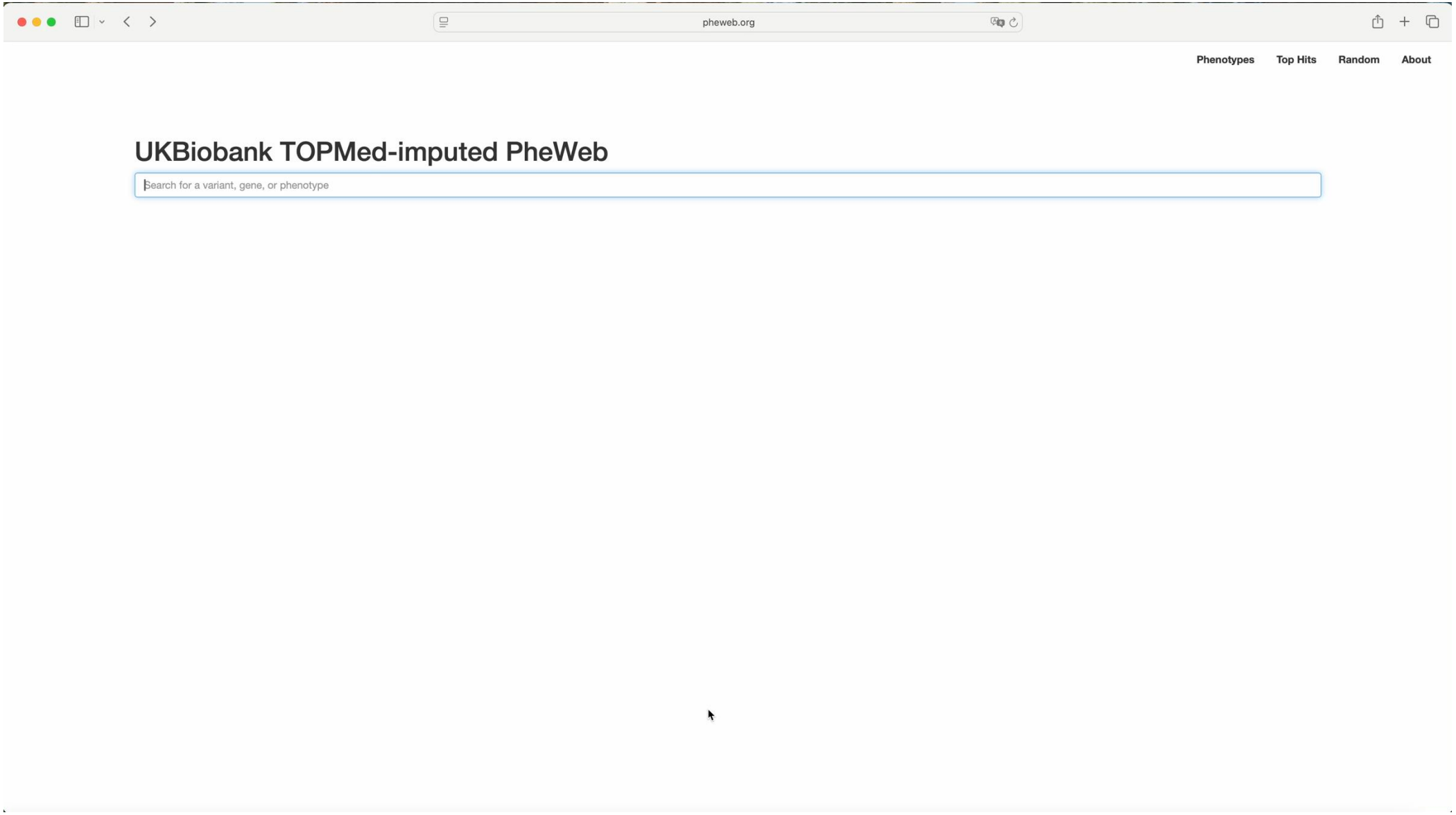
PheWeb: fast & intuitive GWAS browser

- Explore 100s GWASs
- Generate new hypotheses
- Replicate
- Share results
- Collaborate



Gagliano Taliun, VandeHaar, … et al. (2020) *Nature Genetics* PMID: 32504056

UK Biobank PheWeb – 1400 GWAS run in the white British subset (480K)



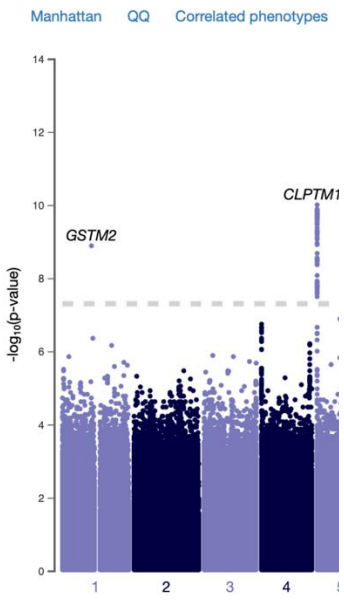
Stratified GWAS results (by ancestry or sex) are becoming available in large biobanks

- UK Biobank
- Million Veterans Program
- All of Us
- …
- CLSA

The original PheWeb is designed for 1 GWAS per trait …

The original PheWeb is designed for 1 GWAS per trait …

Cancer – All cohort

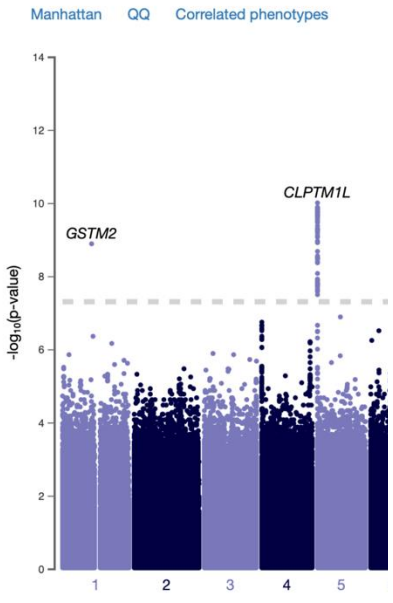


Top Loci:

Search... "TCF7L2", "rs1861867", etc.

Variant
8:128,719,884 A / T (rs10094872)
8:143,752,994 T / C (rs2976384)
5:1,315,660 G / A (rs4975616)

Cancer – Female-only

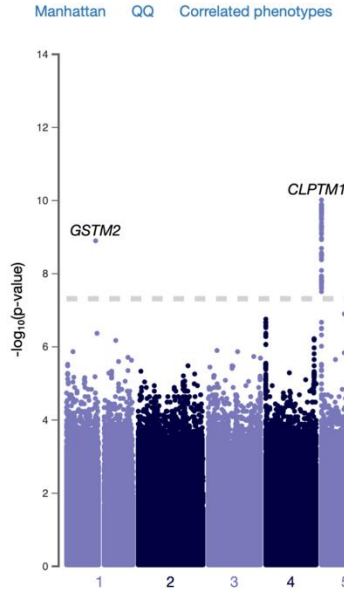


Top Loci:

Search... "TCF7L2", "rs1861867", etc.

Variant	Nea
8:128,719,884 A / T (rs10094872)	MYC
8:143,752,994 T / C (rs2976384)	JRK
5:1,315,660 G / A (rs4975616)	CLP

Cancer – Male-only

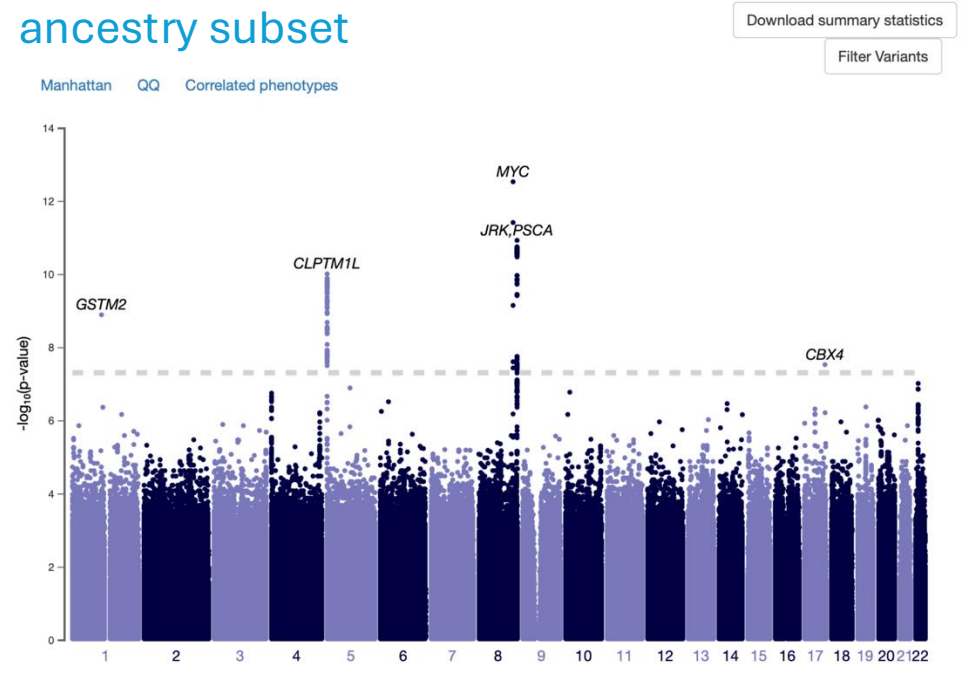


Top Loci:

Search... "TCF7L2", "rs1861867", etc.

Variant
8:128,719,884 A / T (rs10094872)
8:143,752,994 T / C (rs2976384)
5:1,315,660 G / A (rs4975616)

Cancer – European ancestry subset



Top Loci:

Search... "TCF7L2", "rs1861867", etc.

23 total variants

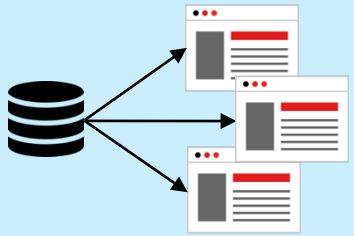
Variant	Nearest Gene(s)	MAF	P-value	Effect Size (se)
8:128,719,884 A / T (rs10094872)	*MYC*	0.37	3.0e-13	0.22 (0.030)
8:143,752,994 T / C (rs2976384)	*JRK, PSCA*	0.44	1.2e-11	0.20 (0.029)
5:1,315,660 G / A (rs4975616)	*CLPTM1L*	0.42	9.9e-11	0.19 (0.029)

What we'll talk about today

- GWAS and visualization with PheWeb
- **What's new with PheWeb2**
- Using CLSA to showcase PheWeb2's features

Base PheWeb

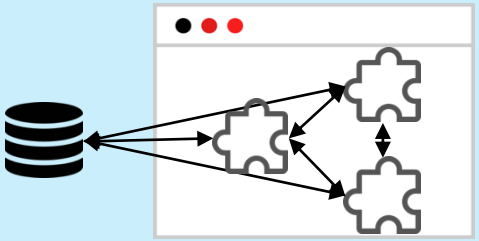
Static HTML templates + JavaScript



VS

PheWeb2

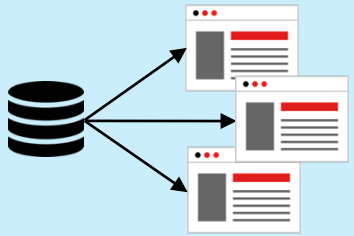
Independent dynamic JavaScript/HTML



Base PheWeb

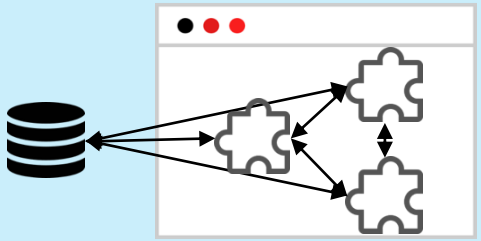
PheWeb2

Static HTML templates + JavaScript

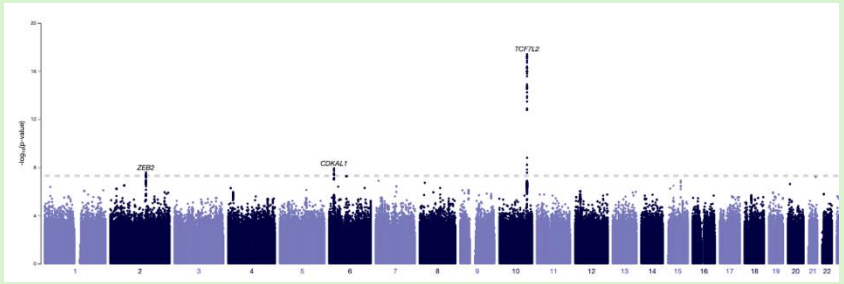


VS

Independent dynamic JavaScript/HTML

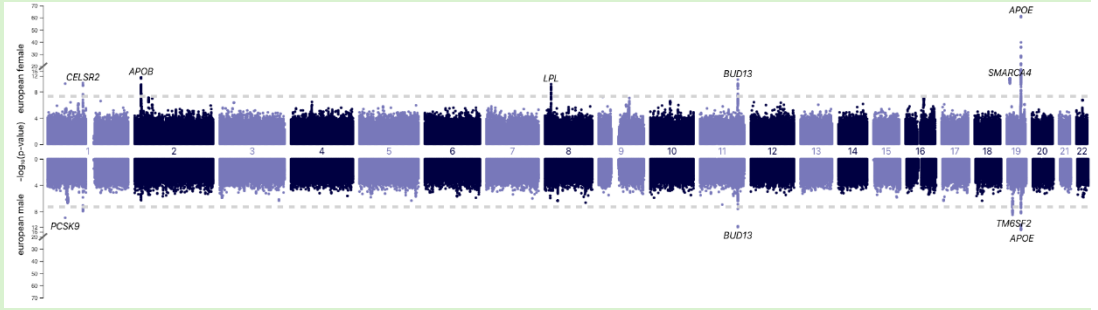


One interactive GWAS plot at a time



VS

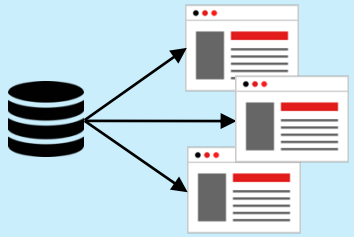
Interactive side-by-side comparisons of multiple GWASs



Base PheWeb

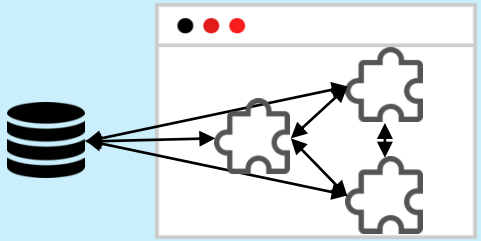
PheWeb2

Static HTML templates + JavaScript

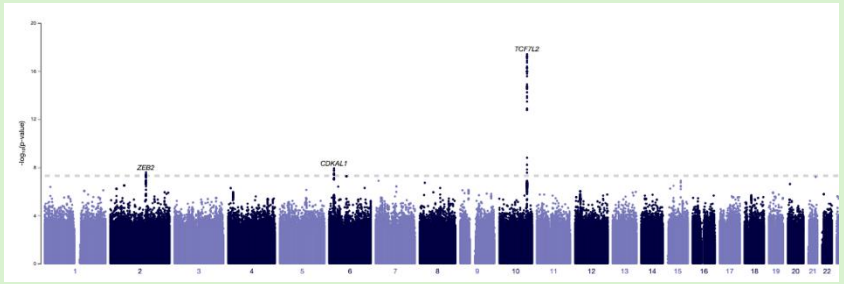


VS

Independent dynamic JavaScript/HTML

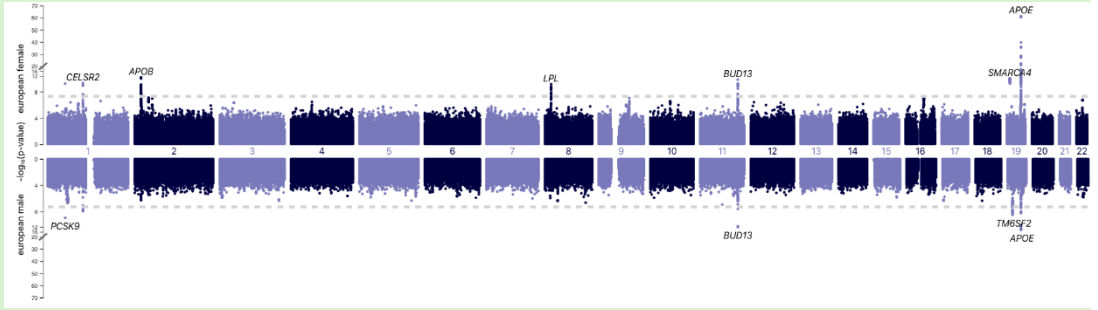


One interactive GWAS plot at a time

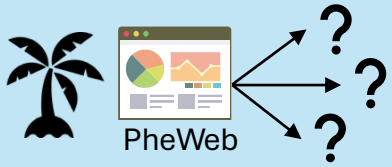


VS

Interactive side-by-side comparisons of multiple GWASs



Isolated



VS

Connected: Application Programming Interface (API)

nature genetics

Correspondence | Published: 19 January 2026

Exploring and visualizing stratified GWAS results with PheWeb2

Justin Bellavance, Hongyu Xiao, Le Chang, Mehrdad Kazemi, Seyla Wickramasinghe, Alexandra J. Mayhew, Parminder Raina, Peter VandeHaar, Daniel Taliun ✉ & Sarah A. Gagliano Taliun ✉

Nature Genetics (2026) | Cite this article

What we'll talk about today

- GWAS and visualization with PheWeb
- What's new with PheWeb2
- **Using CLSA to showcase PheWeb2's features**

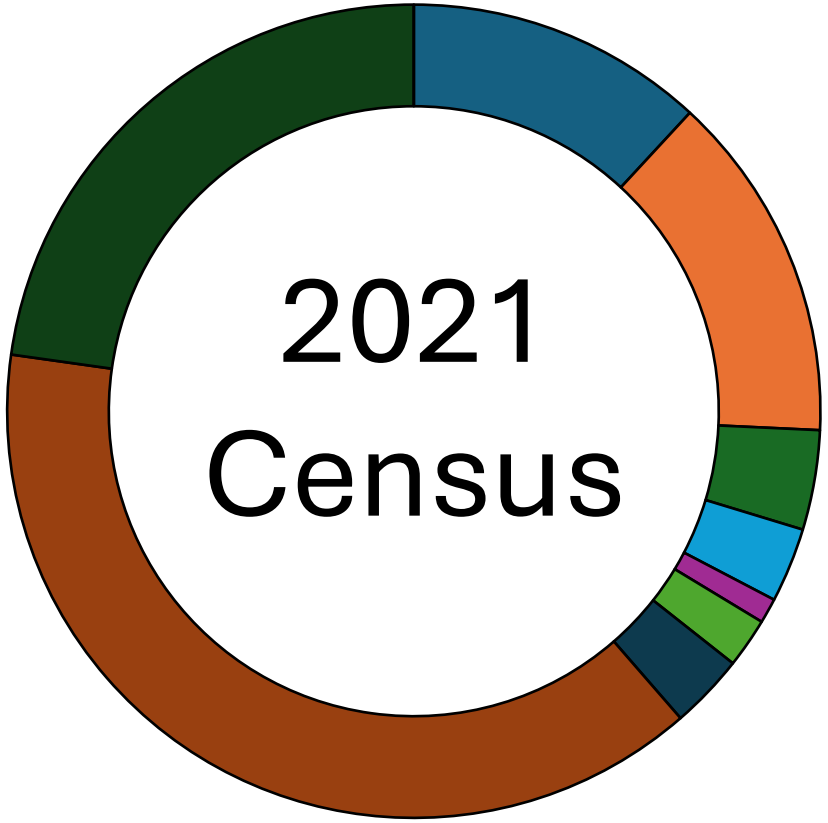
We applied PheWeb2 to the Canadian Longitudinal Study on Aging (CLSA)

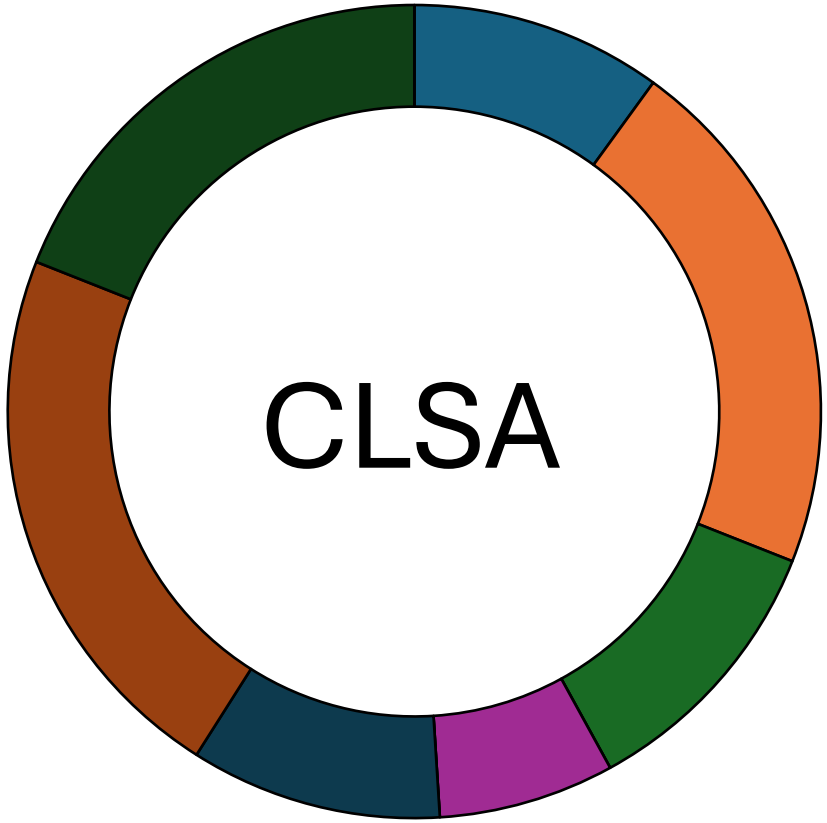
26,622 participants with genetic data (45-85 years old)

100s phenotypes available at baseline (questionnaires, labs, DXA scans, etc.)

Currently continuous traits at baseline assessed in PheWeb2 (n = 225)

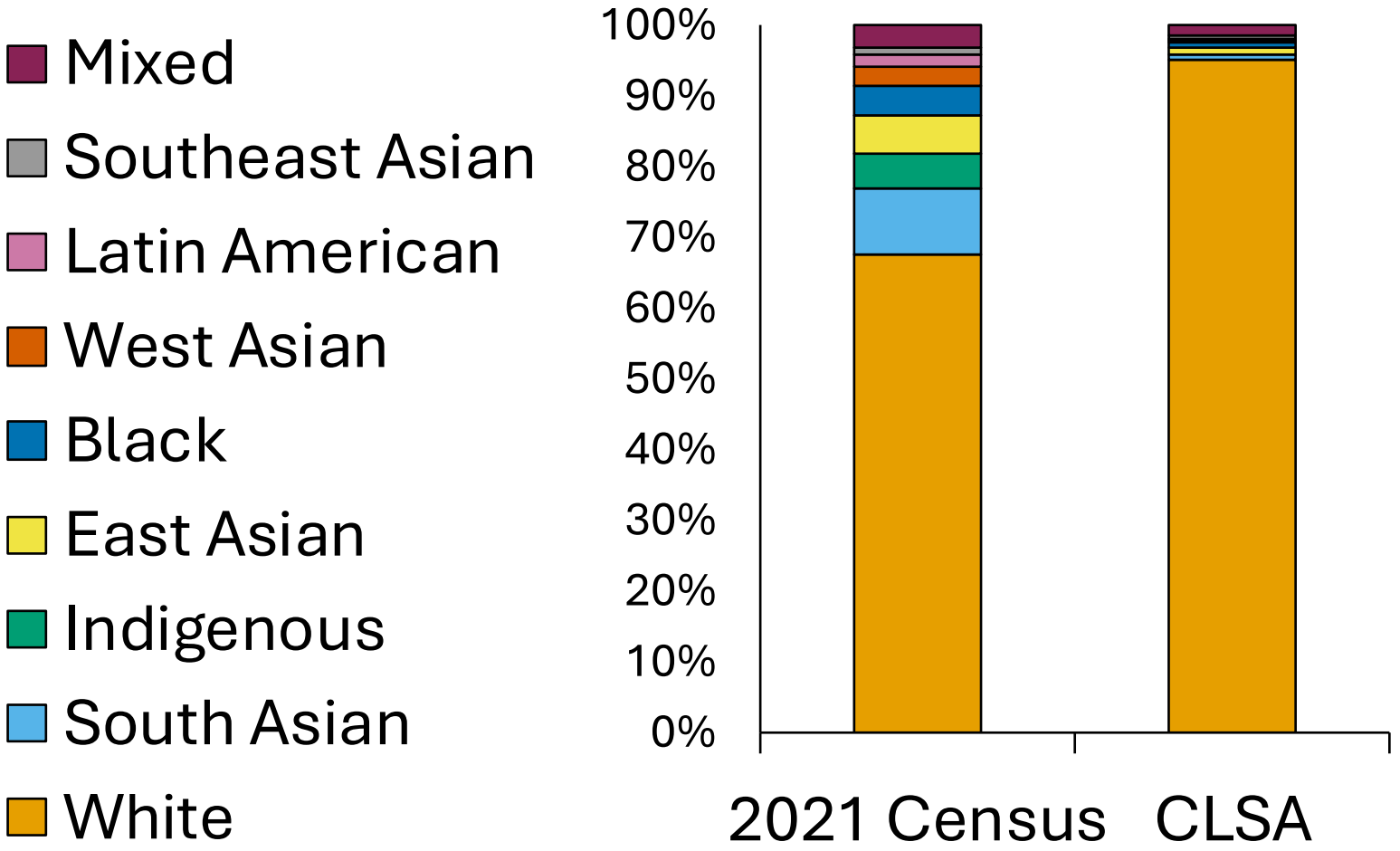
CLSA recruitment is generally representative of Canada

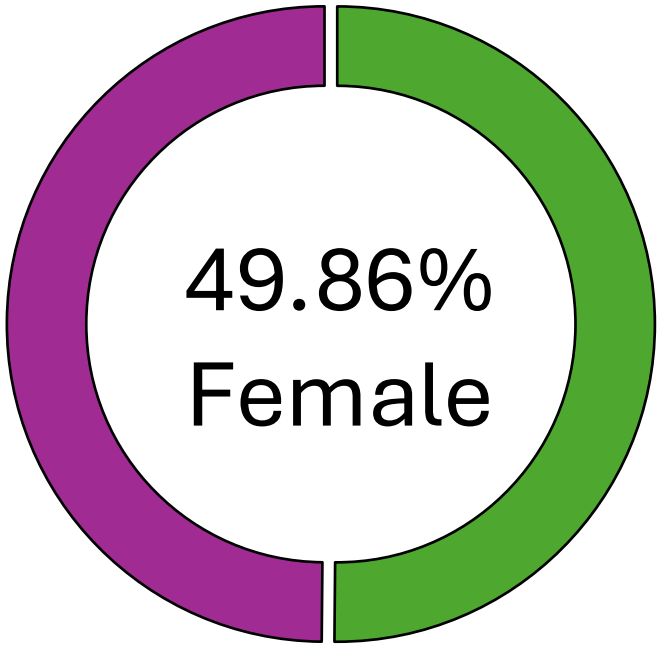




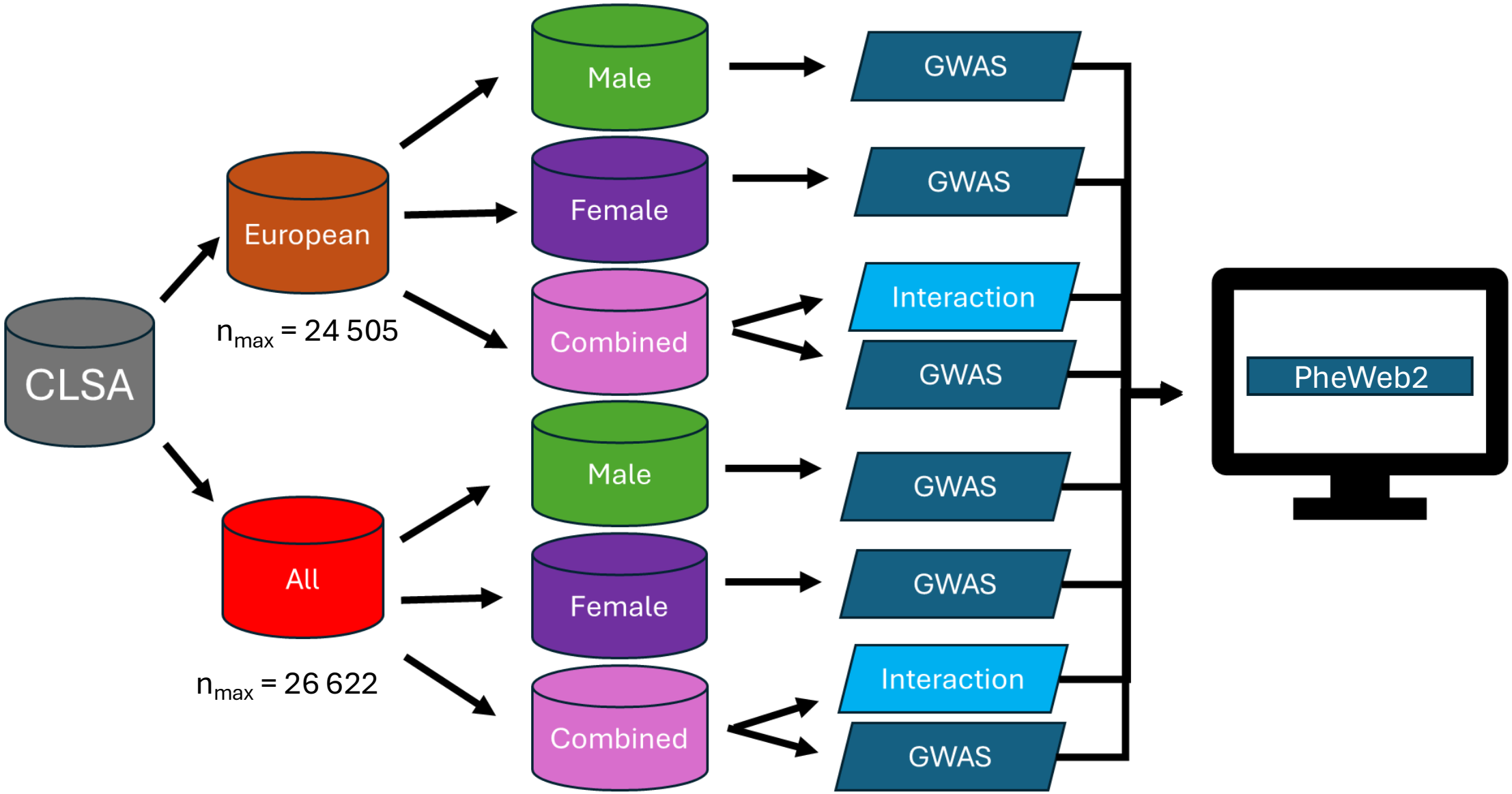
- Alberta
- British Columbia
- Manitoba
- Saskatchewan
- Newfoundland and Labrador
- New Brunswick
- Nova Scotia
- Ontario
- Quebec
- Prince Edward Island

Self-Reported ‘Ethnicity’ and Genetic Sex of CLSA participants





6 stratifications for CLSA PheWeb2

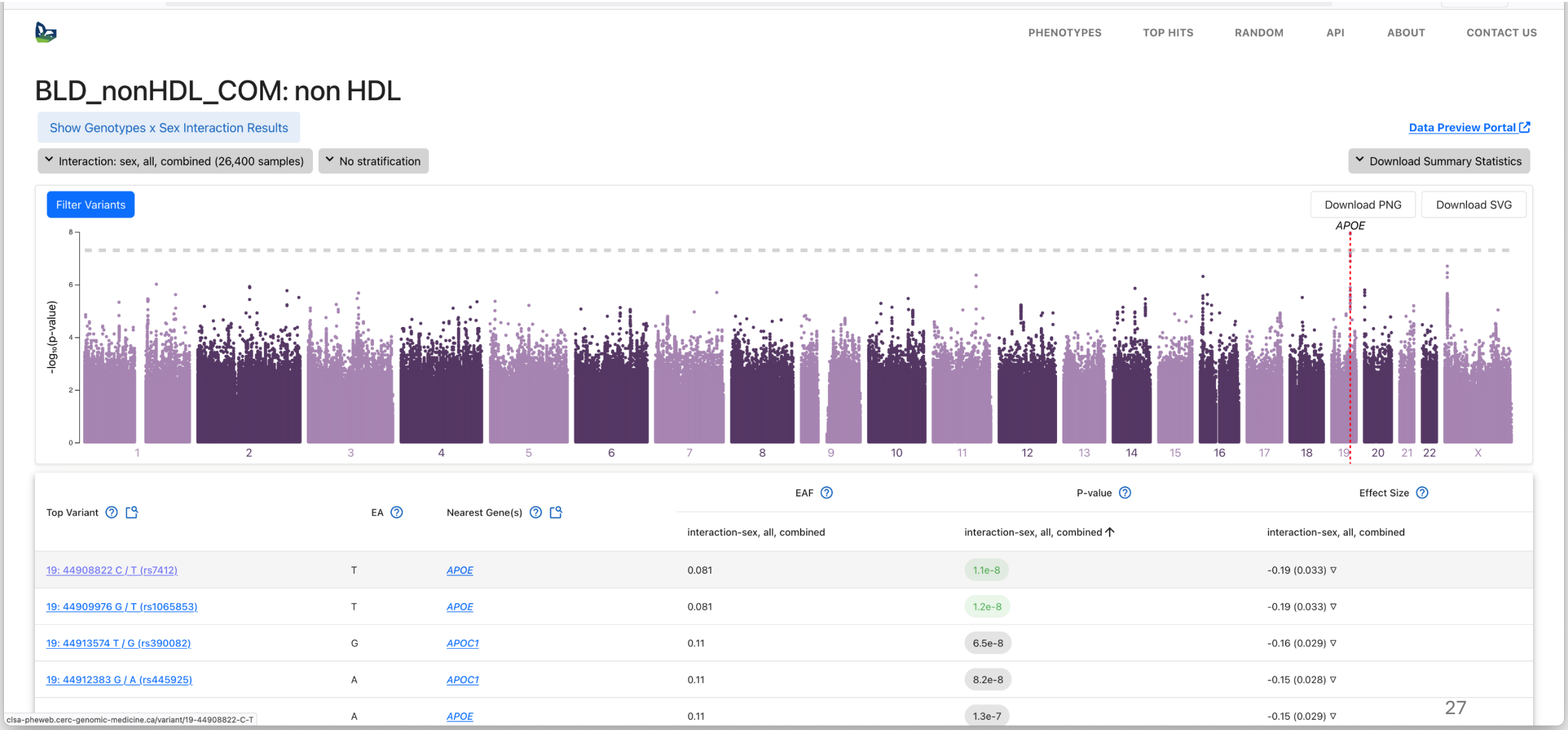


Message 1: Value of testing for sex differential effects

Miami view and table for non HDL cholesterol: a potential stronger effect in females than in males at *APOE* rs7412 (T)

Top Variant	EA	Nearest Gene(s)	EAF		P-value		Effect Size	
			european, female	european, male	european, female	european, male	european, female	european, male
19: 44908822 C / T (rs7412)	T	*APOE*	0.085	0.078	7.00e-62	6.10e-15	-0.37 (0.023)	-0.18 (0.023)
19: 44909976 G / T (rs1065853)	T	*APOE*	0.085	0.078	4.80e-61	6.30e-15	-0.37 (0.023)	-0.18 (0.023)

Sex-by-genotype interaction: sex-differential effects at *APOE* rs7412 for non HDL cholesterol



Top Variant	EA	Nearest Gene(s)	EAF	P-value	Effect Size
			interaction-sex, all, combined	interaction-sex, all, combined ↑	interaction-sex, all, combined
19: 44908822 C / T (rs7412)	T	*APOE*	0.081	1.1e-8	-0.19 (0.033) ▽
19: 44909976 G / T (rs1065853)	T	*APOE*	0.081	1.2e-8	-0.19 (0.033) ▽
19: 44913574 T / G (rs390082)	G	*APOC1*	0.11	6.5e-8	-0.16 (0.029) ▽
19: 44912383 G / A (rs445925)	A	*APOC1*	0.11	8.2e-8	-0.15 (0.028) ▽
	A	*APOE*	0.11	1.3e-7	-0.15 (0.029) ▽

rs7412 (T; *APOE* ε2) is associated with decreased levels of non HDL cholesterol

Protective effect for cognitive decline and total cholesterol; increases triglycerides

Variant and risk allele	P-value	P-value annotation	RAF	OR	Beta	CI	Mapped gene	Reported trait
								non HDL
rs7412-T	1×10^{-91}	-	NR	-	0.466 unit decrease	[0.42-0.51]	APOE	Non-HDL cholesterol levels
rs7412-T	2×10^{-403}	-	0.0752	-	0.3395 unit decrease	[0.32-0.35]	APOE	Remnant cholesterol (non-HDL, non-LDL - cholesterol)
rs7412-T	8×10^{-16}	-	0.0203201	-	0.390475 unit decrease	[0.3-0.49]	APOE	Non-HDL cholesterol levels
rs7412-T	6×10^{-174}	-	0.0793135	-	0.463006 unit decrease	[0.43-0.49]	APOE	Non-HDL cholesterol levels

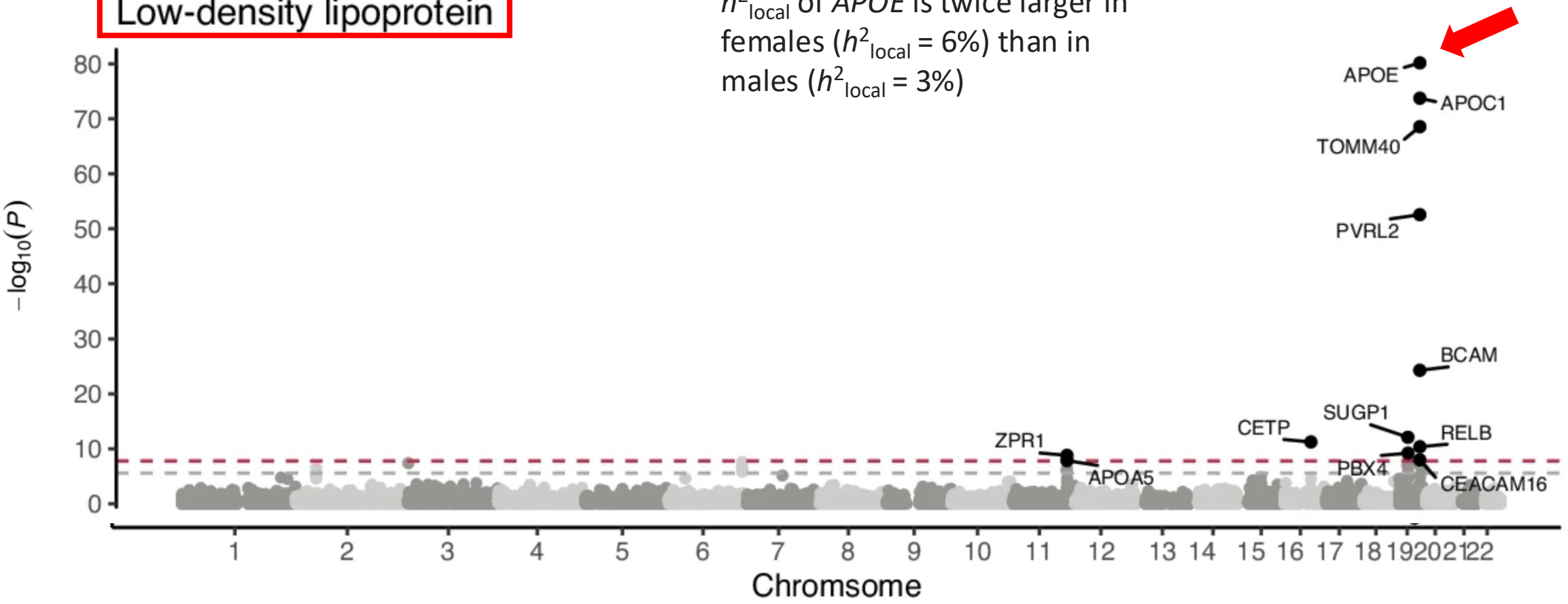
GWAS Catalog

Evidence of potential sex-differences for LDL in UK Biobank

Test of equal genetic effects at each gene

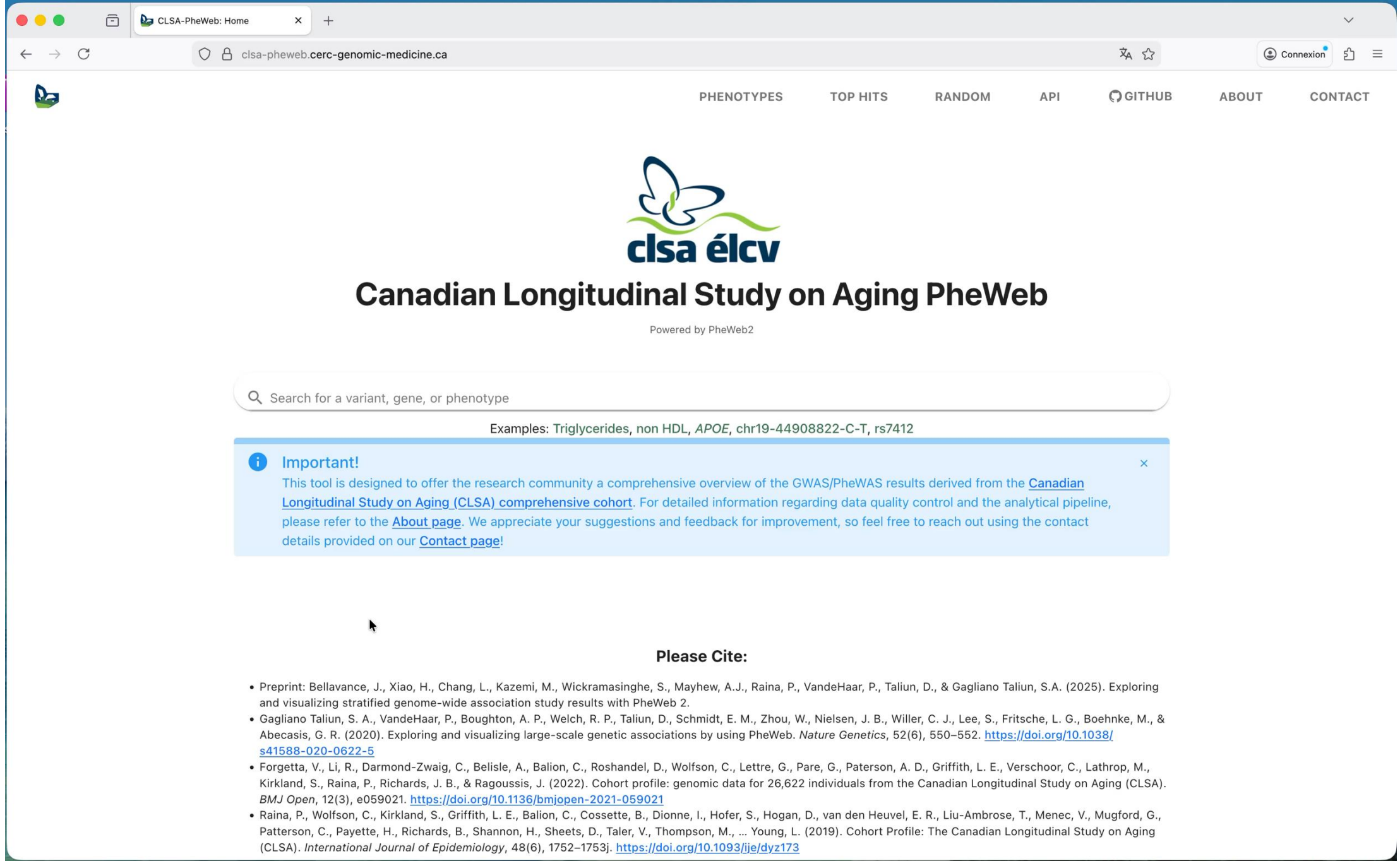
Low-density lipoprotein

h^2_{local} of *APOE* is twice larger in females (h^2_{local} = 6%) than in males (h^2_{local} = 3%)



Adapted Fig. 6 from Uffelmann, de Leeuw, Schipper & Postuma. (2025) *Nat Comms*. PMID: 40770183

Also: Sex-differential effects at rs7412 for nonHDL and LDL Kanoni et al. (2022) *Genome Biology*. PMID: 36575460


CLSA-PheWeb: Home
clsa-pheweb.cerc-genomic-medicine.ca
Connexion
PHENOTYPES
TOP HITS
RANDOM
API
GITHUB
ABOUT
CONTACT
clsa élcv
Canadian Longitudinal Study on Aging PheWeb
Powered by PheWeb2
Search for a variant, gene, or phenotype
Examples: Triglycerides, non HDL, APOE, chr19-44908822-C-T, rs7412
Important!
This tool is designed to offer the research community a comprehensive overview of the GWAS/PheWAS results derived from the Canadian Longitudinal Study on Aging (CLSA) comprehensive cohort. For detailed information regarding data quality control and the analytical pipeline, please refer to the About page. We appreciate your suggestions and feedback for improvement, so feel free to reach out using the contact details provided on our Contact page!
Please Cite:
• Preprint: Bellavance, J., Xiao, H., Chang, L., Kazemi, M., Wickramasinghe, S., Mayhew, A.J., Raina, P., VandeHaar, P., Taliun, D., & Gagliano Taliun, S.A. (2025). Exploring and visualizing stratified genome-wide association study results with PheWeb 2.
• Gagliano Taliun, S. A., VandeHaar, P., Boughton, A. P., Welch, R. P., Taliun, D., Schmidt, E. M., Zhou, W., Nielsen, J. B., Willer, C. J., Lee, S., Fritsche, L. G., Boehnke, M., & Abecasis, G. R. (2020). Exploring and visualizing large-scale genetic associations by using PheWeb. Nature Genetics, 52(6), 550–552. https://doi.org/10.1038/s41588-020-0622-5
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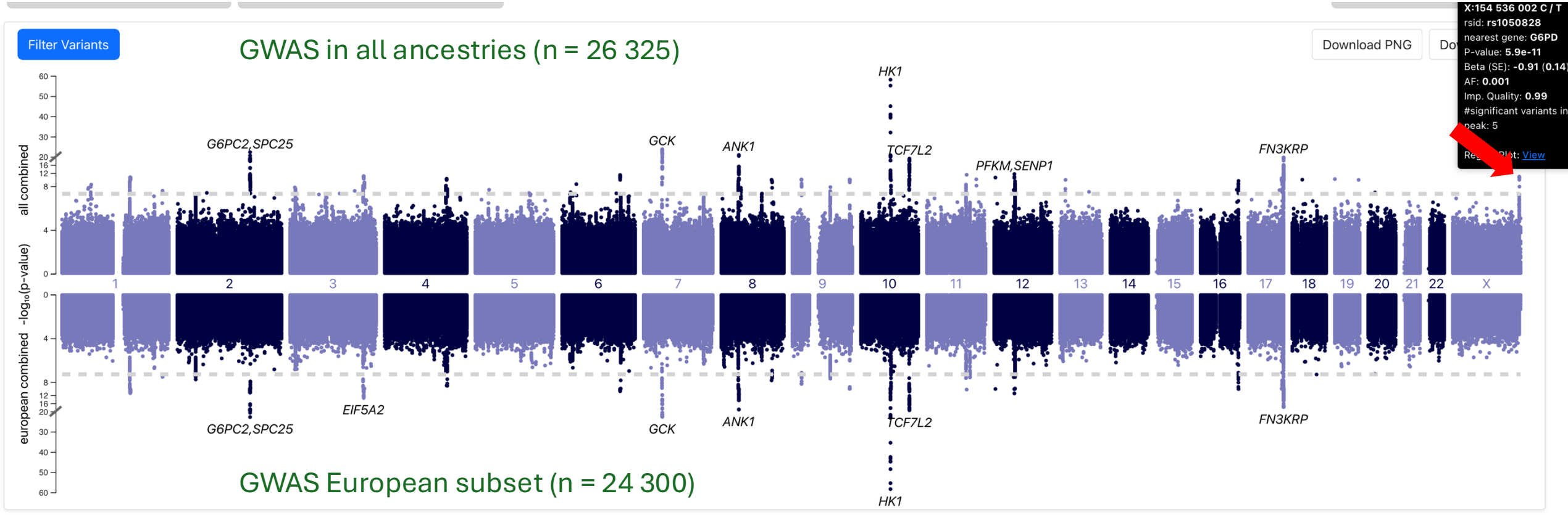
Message 2: Utility of carrying out GWAS in all ancestries

Message 3: Importance of testing variants on chromsome X

“All ancestry” GWAS for hemoglobin A1c levels : Missense variant (T) lowers HbA1c levels



Top Variant	EA	Nearest Gene(s)	EAF		P-value		Effect Size (SE)	
			All, Combined	European, Combined	All, Combined ↑	European, Combined	All, Combined	European, Combined
X: 154536002 C / T (rs1050828)	T	G6PD	0.001	NA	5.90e-11	NA	-0.91 (0.14) ▽	NA

Causes hemolytic anemia due to Glucose-6-phosphate dehydrogenase (G6PD) deficiency

Variation	Gene (Protein Change)	Type (Consequence)	Condition	Classification, Review status
NM_001360016.2(G6PD):c.[202G>A;871G>A]	G6PD (V291M +3 more)	Single nucleotide variant (missense variant)	Anemia, nonspherocytic hemolytic, due to G6PD deficiency	Likely pathogenic ★
NM_001360016.2(G6PD):c.[1264C>G;202G>A376A>G]	G6PD (V68M +5 more)	Single nucleotide variant (missense variant)	Anemia, nonspherocytic hemolytic, due to G6PD deficiency	Likely pathogenic ★
NM_000402.4(G6PD):c.292G>A (p.Val98Met)	G6PD (V68M +1 more)	Single nucleotide variant (missense variant)	not specified +5 more	Pathogenic/Likely pathogenic ★★
G6PD A-	G6PD (V68M +3 more)	Single nucleotide variant (missense variant)	Anemia, nonspherocytic hemolytic, due to G6PD deficiency	Likely pathogenic/Established risk allele ★★
NM_001360016.2(G6PD):c.[143T>C;202G>A]	G6PD (I48T +3 more)	Single nucleotide variant (missense variant)	Anemia, nonspherocytic hemolytic, due to G6PD deficiency	Likely pathogenic ★

ClinVar

Missense variant rs1050828 is common in African genetic ancestry groups (~12%)

Genetic Ancestry Group	Allele Frequency
African	0.1176
Central/South Asian	0.004950
Middle Eastern	0.004695
East Asian	0.000
European	0.000
Native American	0.000
Oceanian	0.000

Source : gnomad v4.1.0

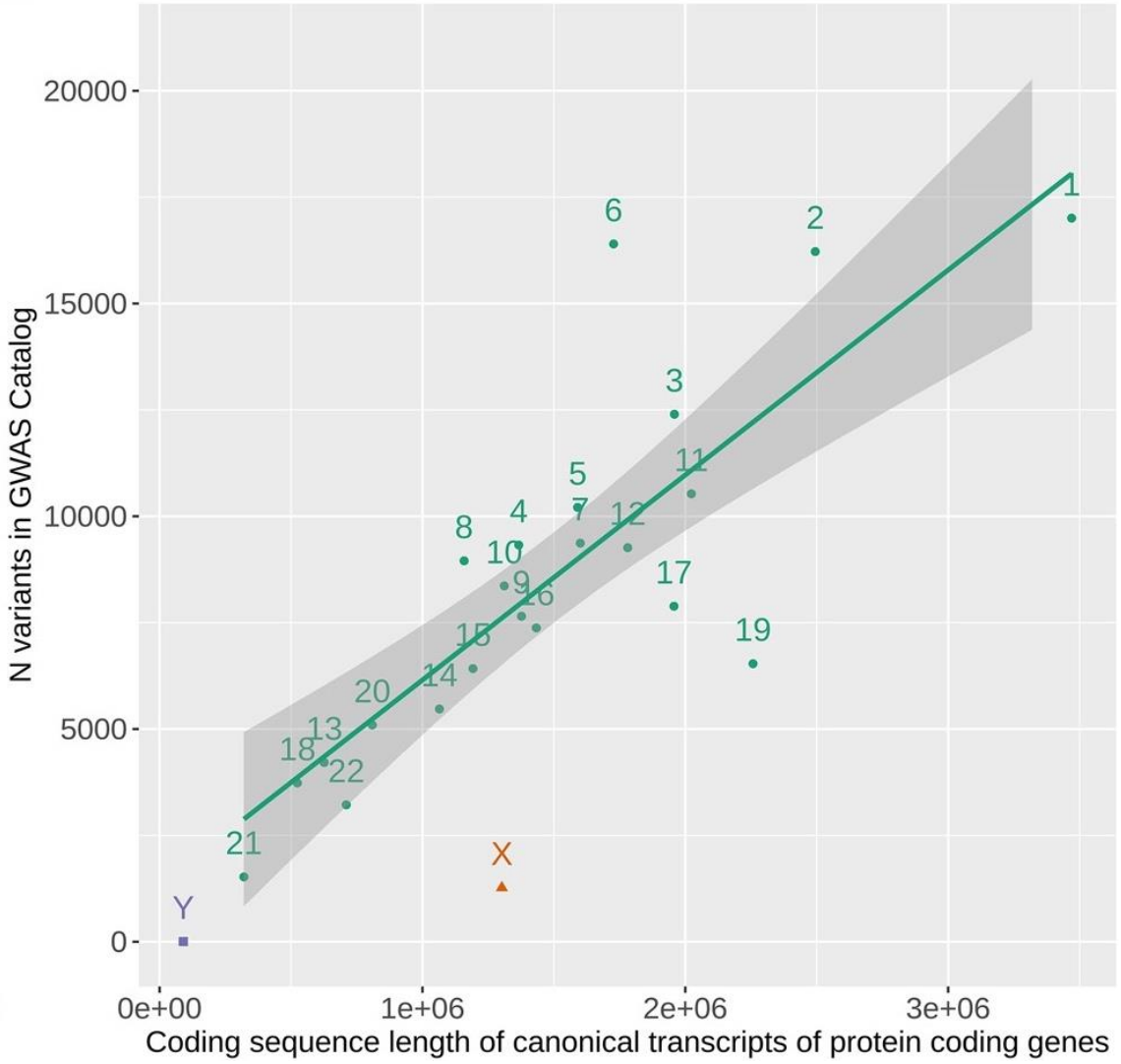
TOPMed African American Hemoglobin GWAS in 3K individuals

African-Americans				
N	T allele freq	Beta	SE	*p Value*
3,123	0.12	−0.41	0.01	8.4E- 205

Sarnowski et al. (2019) *AJHG* PMID: 31564435

Pan-UK Biobank all ancestry analysis in 500K individuals
Karczewski et al. (2025) *Nature Genetics* PMID: 40968291

Chromosome X is (still) understudied in GWAS



Neale, Lona-Durazo, Ryten & Gagliano Taliun
Brain Commun, 6(3), 2024, fcae192,
https://doi.org/10.1093/braincomms/fcae192

PheWeb2 allows for intuitive visualization, sharing and comparison of **stratified GWAS results**.

How will you use PheWeb2?

- Scan through stratified GWAS results in CLSA at baseline

- Make your own instance of PheWeb2

GitHub

- Stay-tuned for updated versions of CLSA PheWeb2 (add binary traits, ordinal traits at baseline)

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Questions? Comments? Let's get in touch!

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