University of Colorado **Boulder**

Institute for Behavioral Genetics

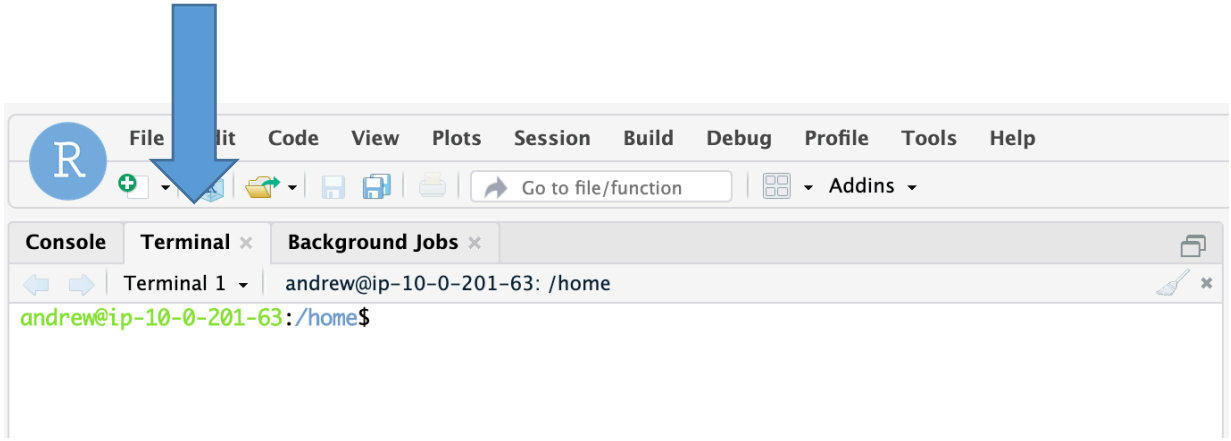
Genomic SEM Practical

ISG Workshop 2024

Let's start by going to:

https://workshop.colorado.edu/rstudio/

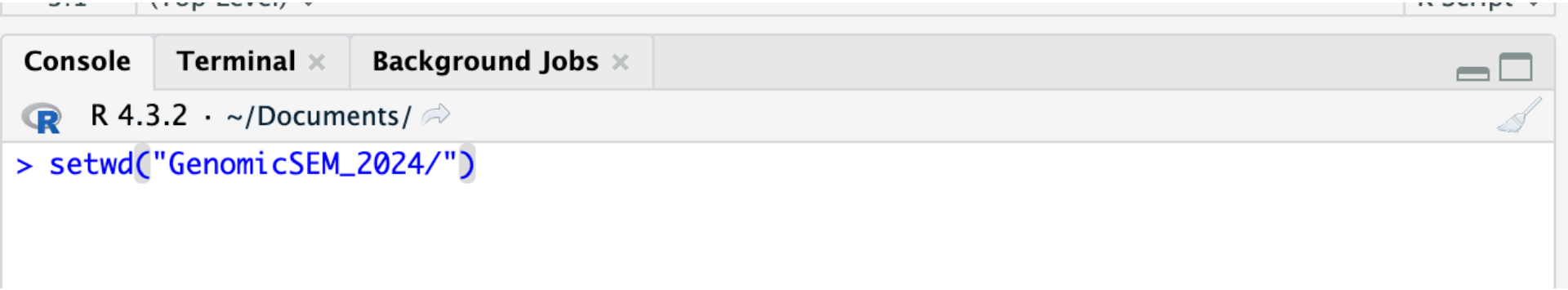
And clicking on the terminal tab.



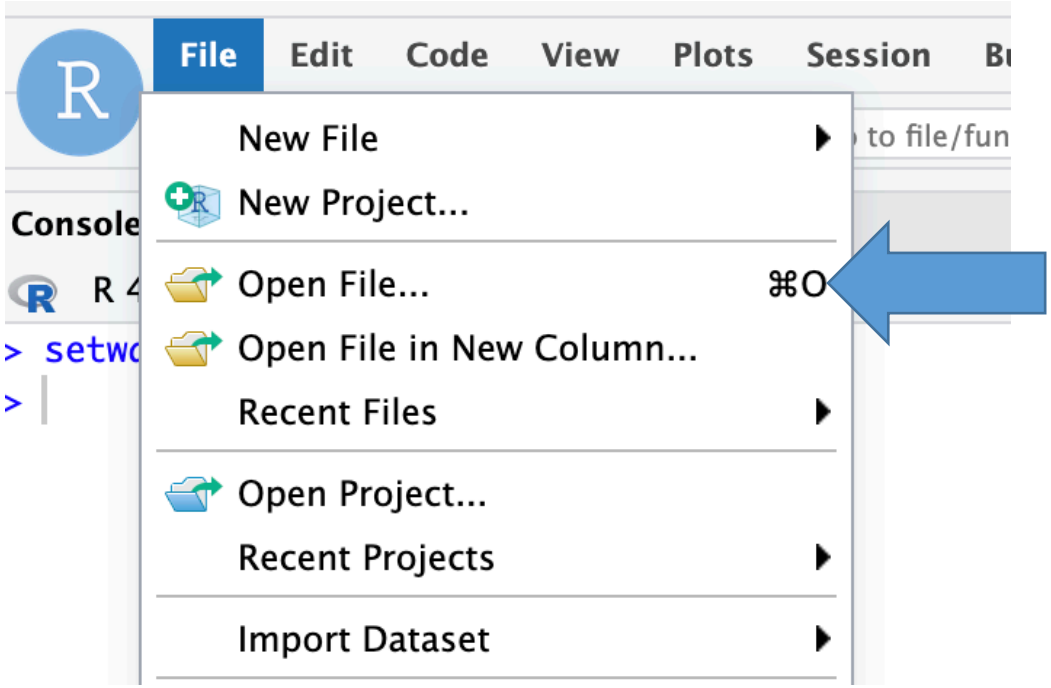
cp -r /faculty/andrew/GenomicSEM_2024 .

cd GenomicSEM_2024/

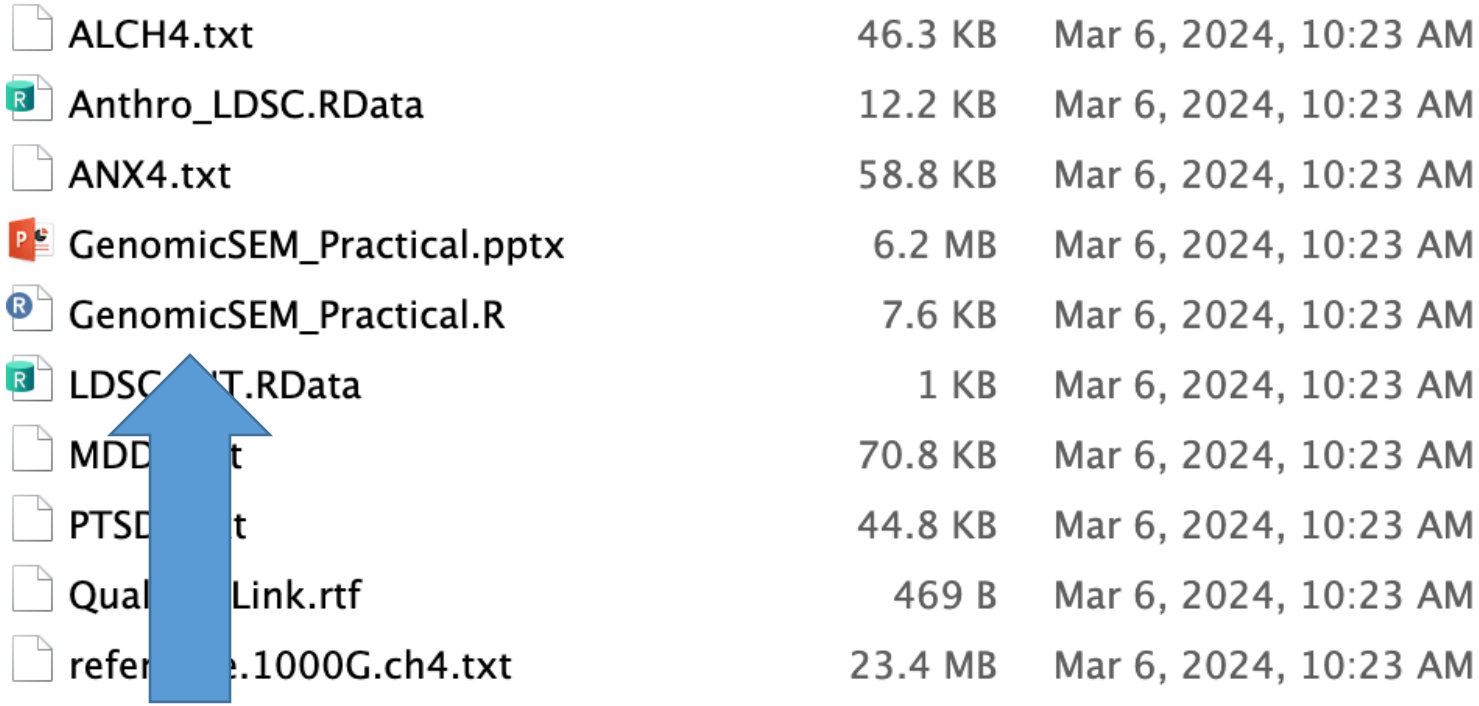
Now let's go over to the console and *setwd* for this new folder you just copied



Now let's go to File at the top and open the .R script with the commands we will be running



Open the R script "GenomicSEM_Practical.R"



Line 2 of R code: the Qualtrics link

https://qimr.az1.qualtrics.com/jfe/form/SV_72kzAByH72t9URo

Practical outline

I. Background and Sales Pitch

II. Estimating genome-wide models

III. Estimating multivariate GWAS in Genomic SEM

IV. More practice with genome-wide models

I. Background and Sales Pitch

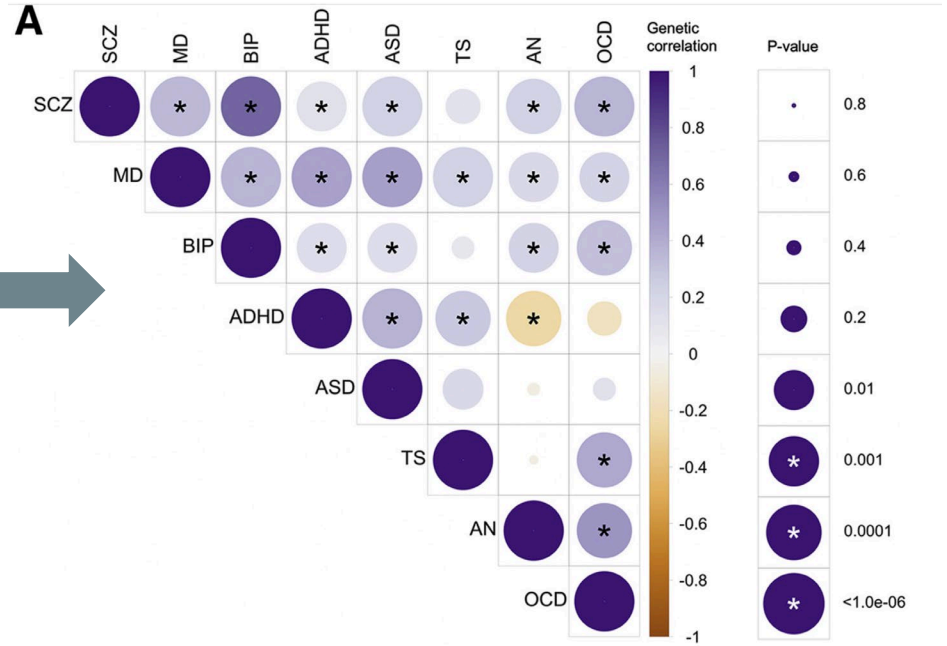
Pervasive Overlap Necessitates Methods for Analyzing Genetic Co-Morbidity

An atlas of genetic correlations across human diseases and traits

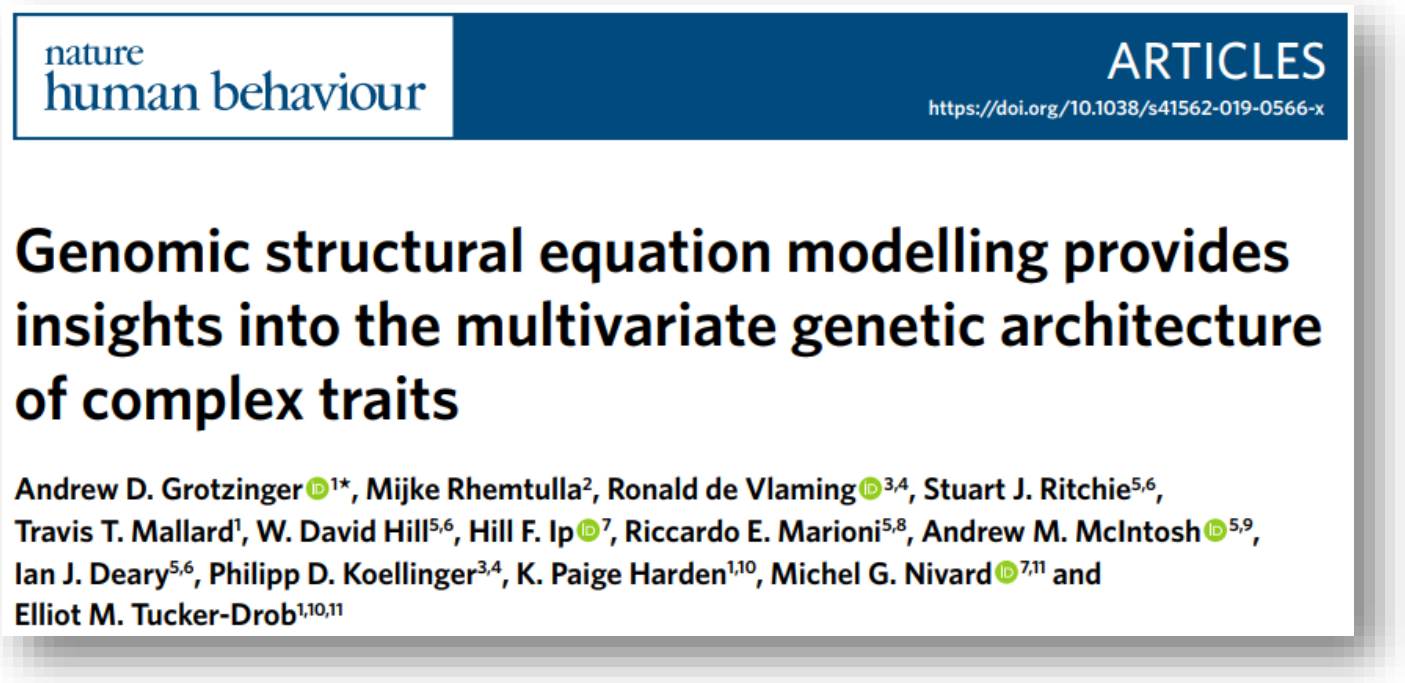
Brendan Bulik-Sullivan, Hilary K Finucane, Verneri Anttila, Alexander Gusev, Felix R Day, Po-Ru Loh, ReproGen Consortium, Psychiatric Genomics Consortium, Genetic Consortium for Anorexia Nervosa of the Wellcome Trust Case Control Consortium 3, Laramie Duncan, John R B Perry, Nick Patterson, Elise B Robinson, Mark J Daly, Alkes L Price & Benjamin M Neale

Nature Genetics **47**, 1236–1241 (2015) | Download Citation

Estimates genetic correlations between samples with varying degrees of sample overlap using publicly available data



Genomic SEM



nature human behaviour

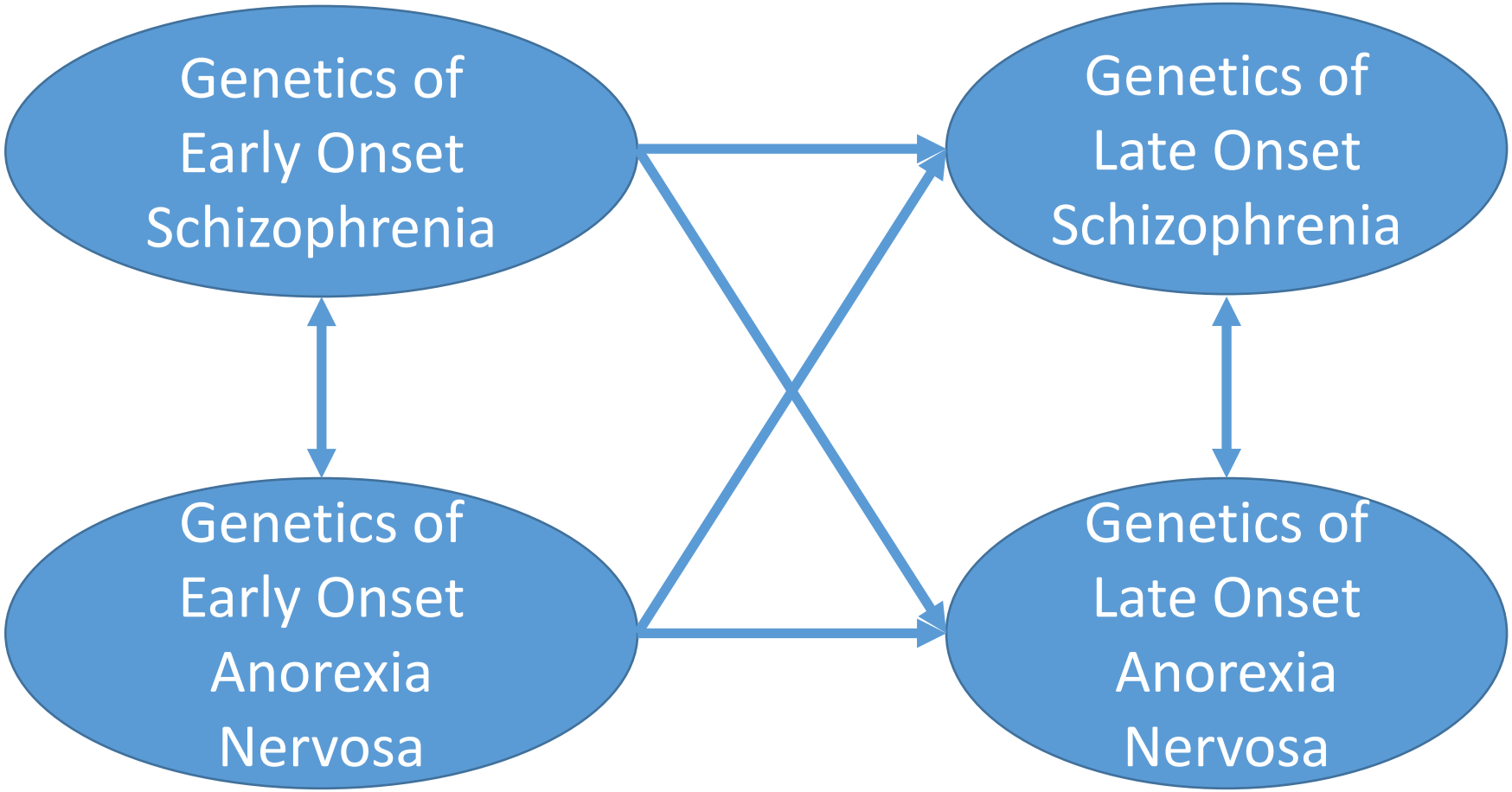
ARTICLES

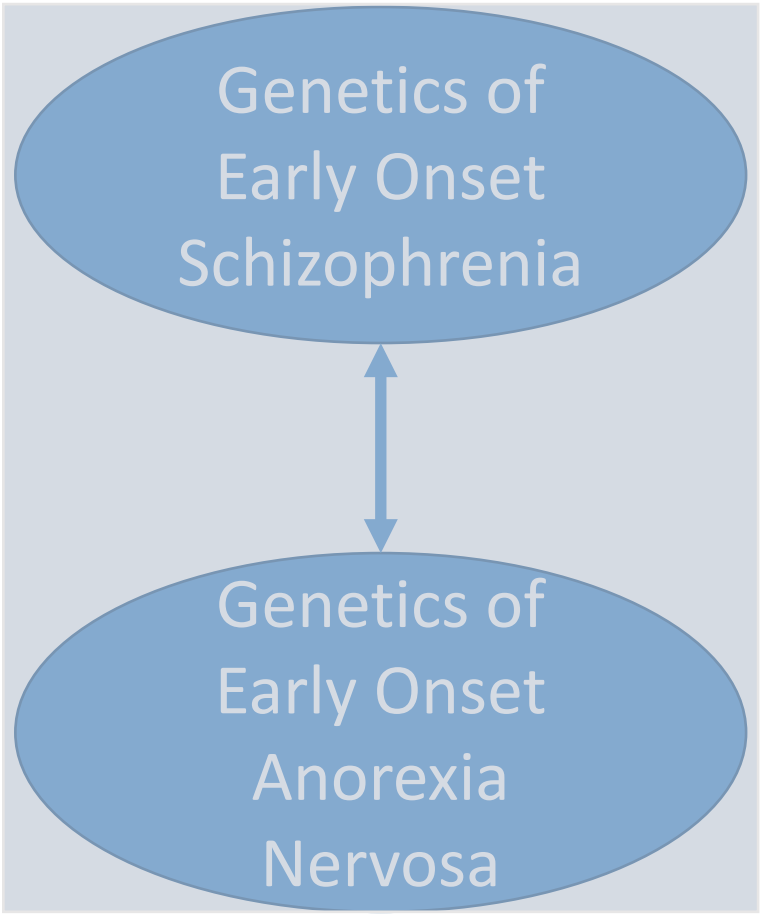
https://doi.org/10.1038/s41562-019-0566-x

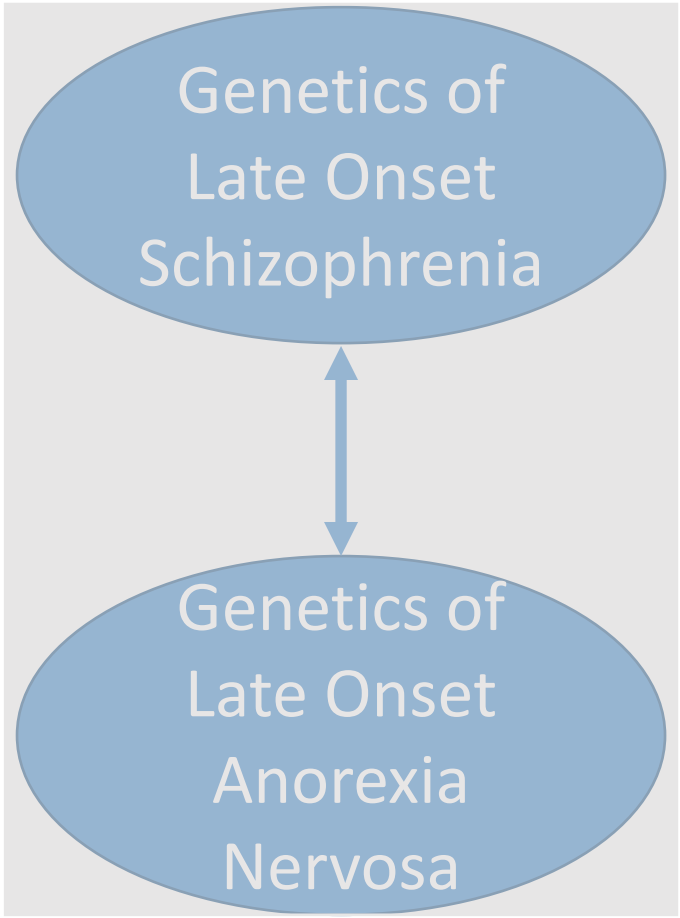
Genomic structural equation modelling provides insights into the multivariate genetic architecture of complex traits

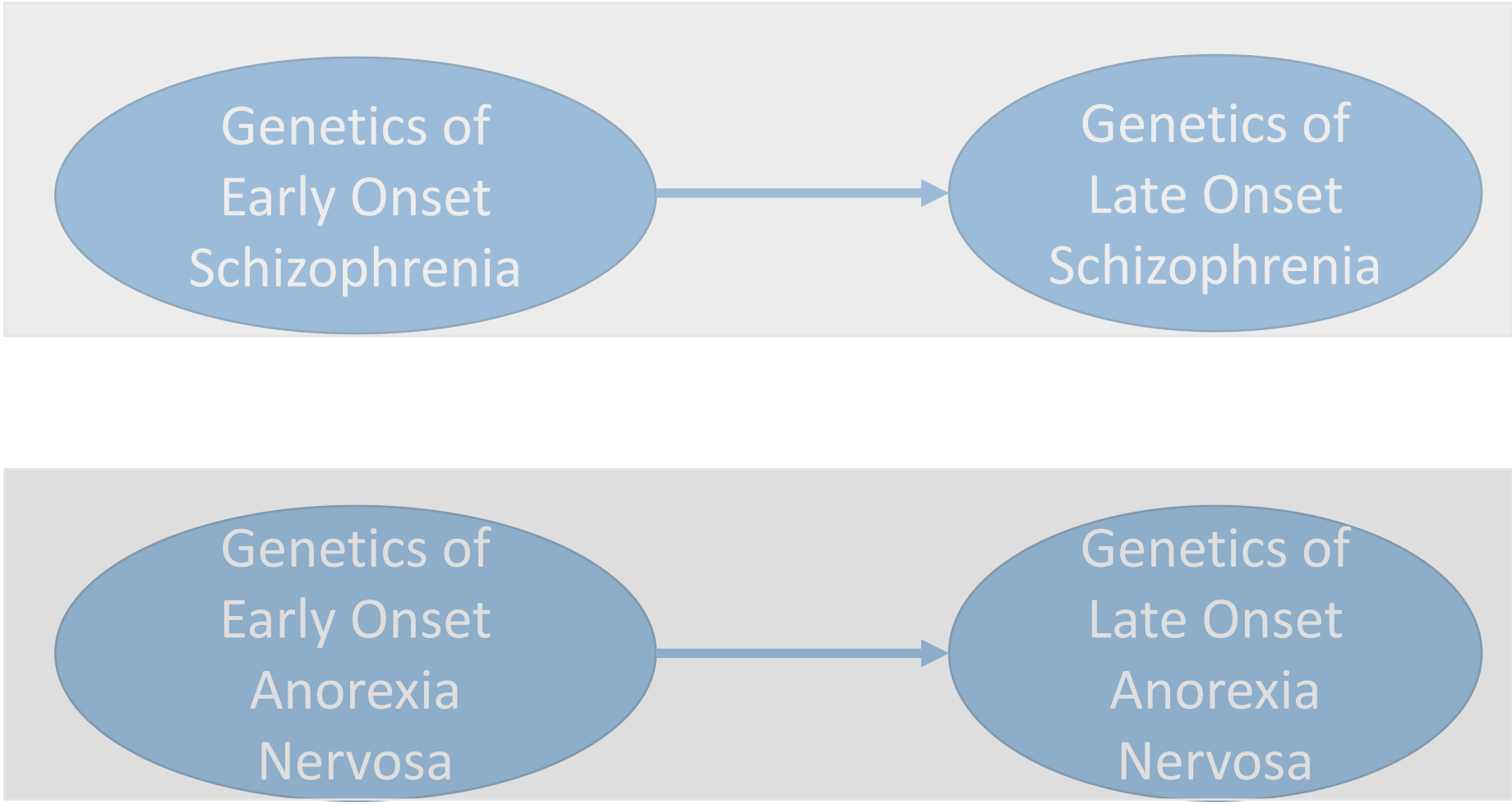
Andrew D. Grotzinger[1*], Mijke Rhemtulla[2], Ronald de Vlaming[3,4], Stuart J. Ritchie[5,6], Travis T. Mallard[1], W. David Hill[5,6], Hill F. Ip[7], Riccardo E. Marioni[5,8], Andrew M. McIntosh[5,9], Ian J. Deary[5,6], Philipp D. Koellinger[3,4], K. Paige Harden[1,10], Michel G. Nivard[7,11] and Elliot M. Tucker-Drob[1,10,11]

Genomic SEM provides flexible framework for estimating limitless number of structural equation models using multivariate genetic data from GWAS summary statistics for even mutually exclusive traits


Genetics of Early Onset Schizophrenia
Genetics of Late Onset Schizophrenia
Genetics of Early Onset Anorexia Nervosa
Genetics of Late Onset Anorexia Nervosa


Genetics of Early Onset Schizophrenia
Genetics of Early Onset Anorexia Nervosa


Genetics of Late Onset Schizophrenia
Genetics of Late Onset Anorexia Nervosa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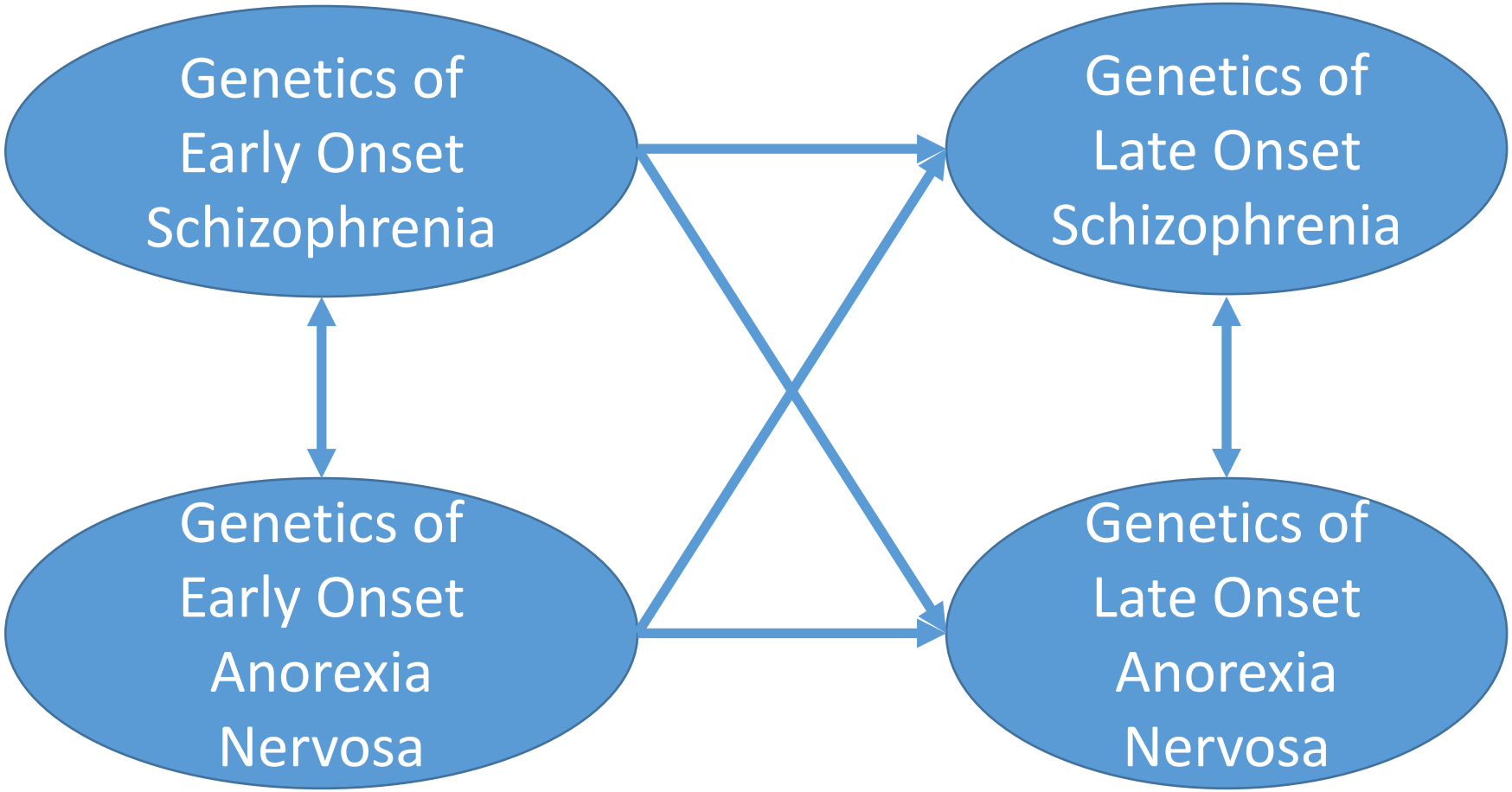
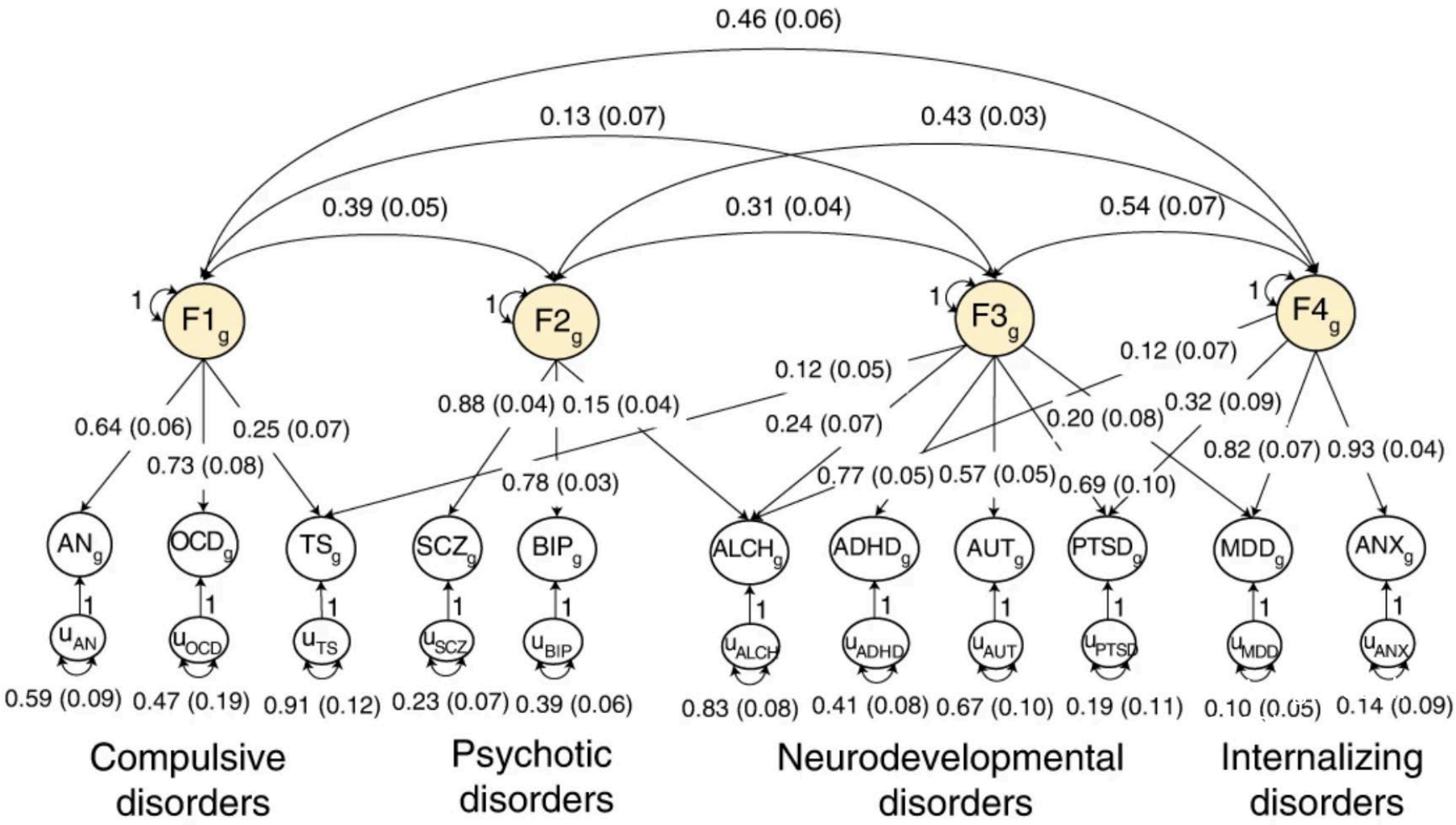

Genetics of Early Onset Schizophrenia
Genetics of Late Onset Schizophrenia
Genetics of Early Onset Anorexia Nervosa
Genetics of Late Onset Anorexia Nervosa

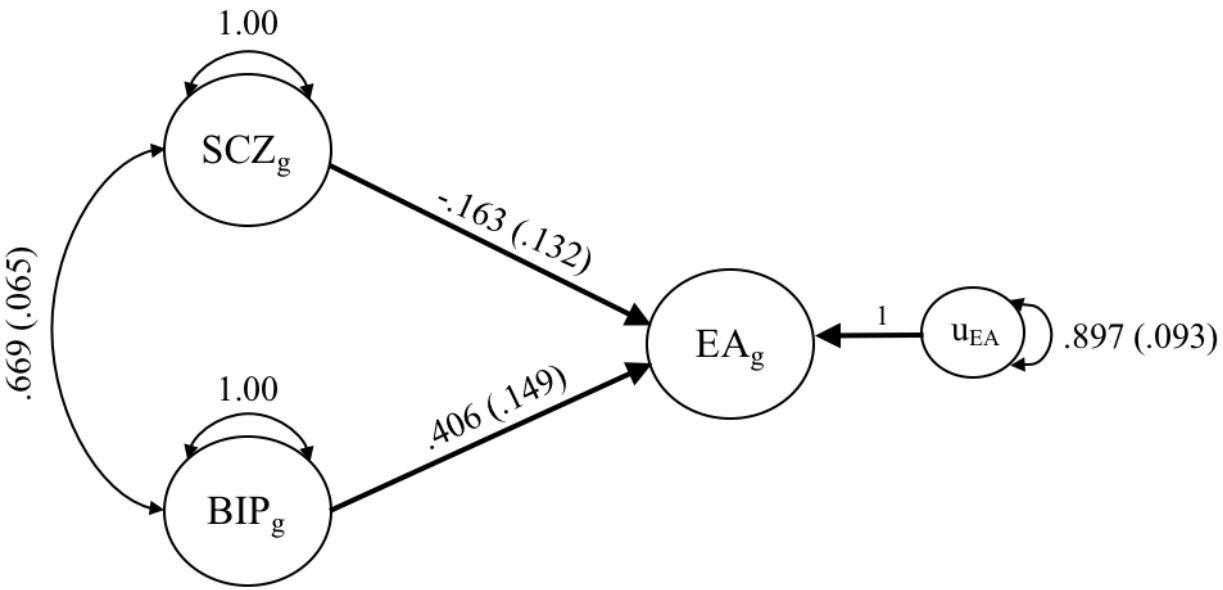
Can estimate genomic factor models



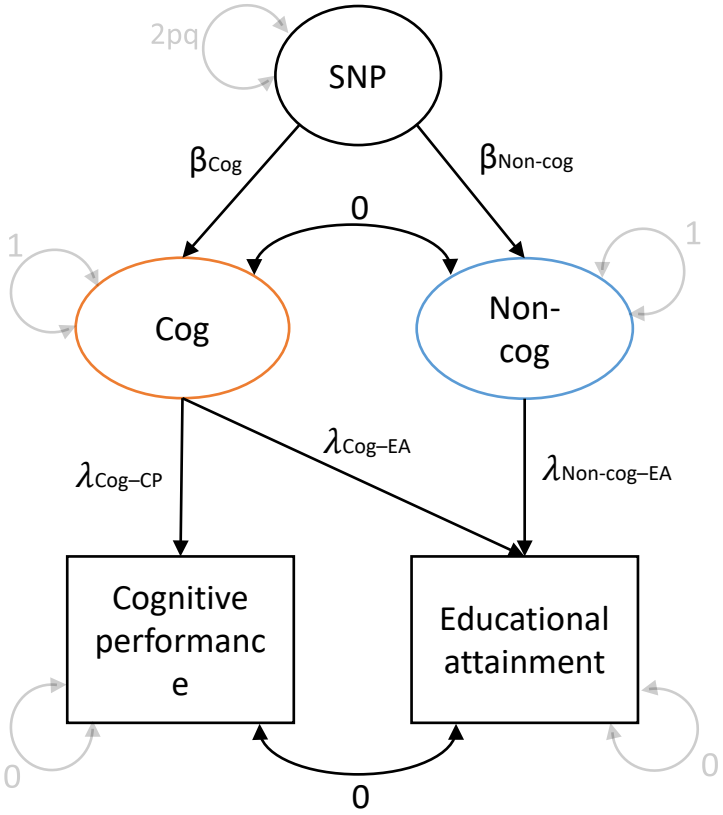
Genetic Multiple Regression

SCZ		
.67	BIP	
.11	.30	EA

$$EA_g = b_1 \times SCZ_g + b_2 \times BIP_g + u$$



GWAS-by-subtraction



nature genetics
ARTICLES
https://doi.org/10.1038/s41588-020-00754-2
Check for updates

Investigating the genetic architecture of noncognitive skills using GWAS-by-subtraction

Perline A. Demange[1,2,3,20], Margherita Malanchini[4,5,6,20], Travis T. Mallard[6], Pietro Biroli[7], Simon R. Cox[8], Andrew D. Grotzinger[6], Elliot M. Tucker-Drob[6,9], Abdel Abdellaoui[1,10], Louise Arseneault[5], Elsje van Bergen[1,3], Dorret I. Boomsma[1], Avshalom Caspi[5,11,12,13], David L. Corcoran[12], Benjamin W. Domingue[14], Kathleen Mullan Harris[15], Hill F. Ip[1], Colter Mitchell[16], Terrie E. Moffitt[5,11,12,13], Richie Poulton[17], Joseph A. Prinz[12], Karen Sugden[11], Jasmin Wertz[11], Benjamin S. Williams[11], Eveline L. de Zeeuw[1,3], Daniel W. Belsky[18,19,21] ✉, K. Paige Harden[6,21] ✉ and Michel G. Nivard[1,21] ✉

RESEARCH ARTICLE | HUMAN GENETICS

The genetic architecture and evolution of the human skeletal form

Psychologic

EUCHARIST KUN, EMILY M. JAVAN, OLIVIA SMITH, FARIS GULAMALI, [...], AND VAGHEESH M. NARASIMHAN +8 authors Authors Info & Affiliations

nature > nature mental health > articles > article

Article | Published: 22 March 2023

Multivariate genome-wide association meta-analysis of over 1 million subjects identifies loci underlying multiple substance use disorders

Alexander S. Hatoum, Sarah M. C. Colbert, Emma C. Johnson, Spencer B. Huggett, Joseph D. Deak, Gita A. Pathak, Mariela V. Jennings, Sarah E. Paul, Nicole R. Karcher, Isabella Hansen, David A. A. Baranger, Alexis Edwards, Andrew D. Grotzinger, Substance Use Disorder Working Group of the Psychiatric Genomics Consortium, Elliot M. Tucker-Drob, Henry R. Kranzler, Lea K. Davis, Sandra Sanchez-Roige, Renato Polimanti, Joel Gelernter, Howard J. Edenberg, Ryan Bogdan & Arpana Agrawal

Nature Mental Health **1**, 210–223 (2023) | Cite this article

genetics

Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use

Mengzhen Liu, Yu Jiang, [...] Scott Vrieze

PAPER

ic risk shared across 24 ic pain conditions: identification and characterization with genomic structural equation modeling

Zorina-Lichtenwalter, Katerina[a,*]; Bango, Carmen I.[b]; Van Oudenhove, Lukas[c]; Čeko, Marta[d]; Lindquist, Martin A.[e]; Grotzinger, Andrew D.[f]; Keller, Matthew C.[f]; Friedman, Naomi P.[f]; Wager, Tor D.[b]

Author Information

PAIN 164(10):p 2239-2252, October 2023. | *DOI:* 10.1097/j.pain.0000000000002922

Molecular Psychiatry **24**, 819–827 (2019) | Download Citation

Genetic st

nature genetics

Article https://dc

Genetic insights into human corti organization and development through genome-wide analyses of neuroimaging phenotypes

Selling the product

Now

Selling the product

I know what the grad students in the audience must be thinking

Selling the product

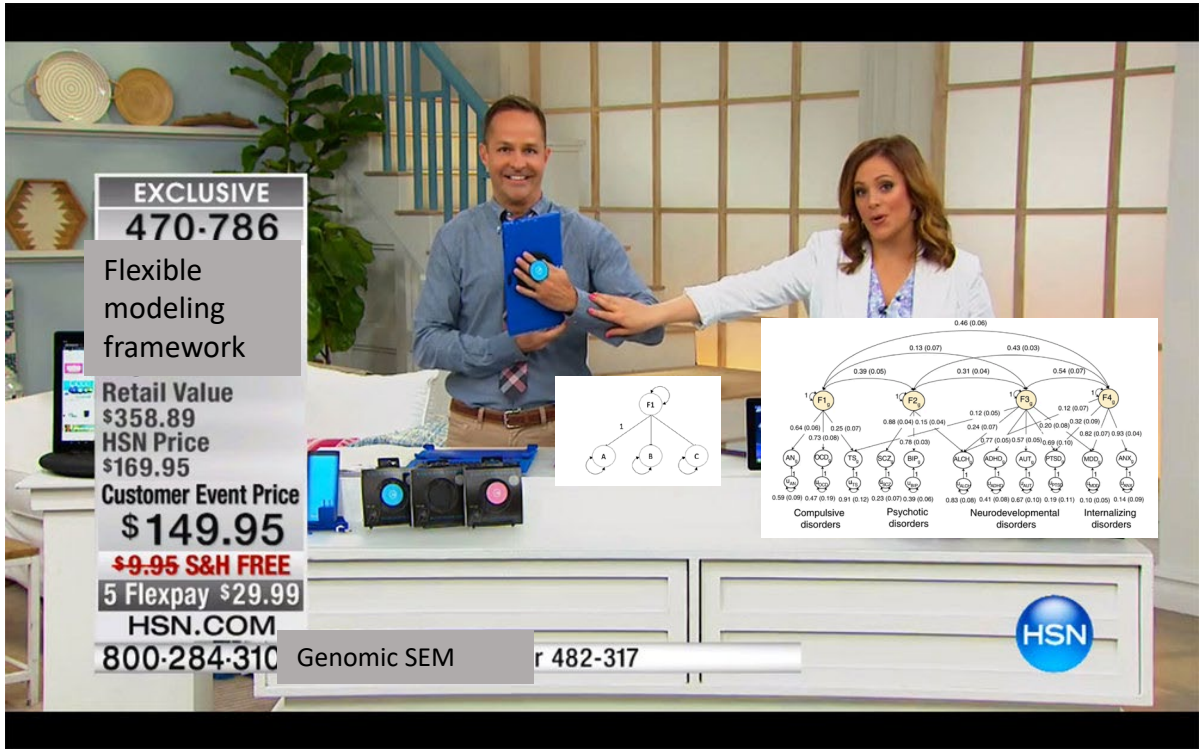
You're selling us an amazing tool to flexibly model genetic overlap across ***even mutually exclusive traits.***

But I can barely pay rent and my bar tab, there's no way I can afford this

Selling the product

But you know what…

Selling the product



I like this group and I'm feeling generous so I'm going to slash our prices just for you

Selling the product

*Staged call

Selling the product

Ya'll, at these prices we are practically (literally) giving the product away:

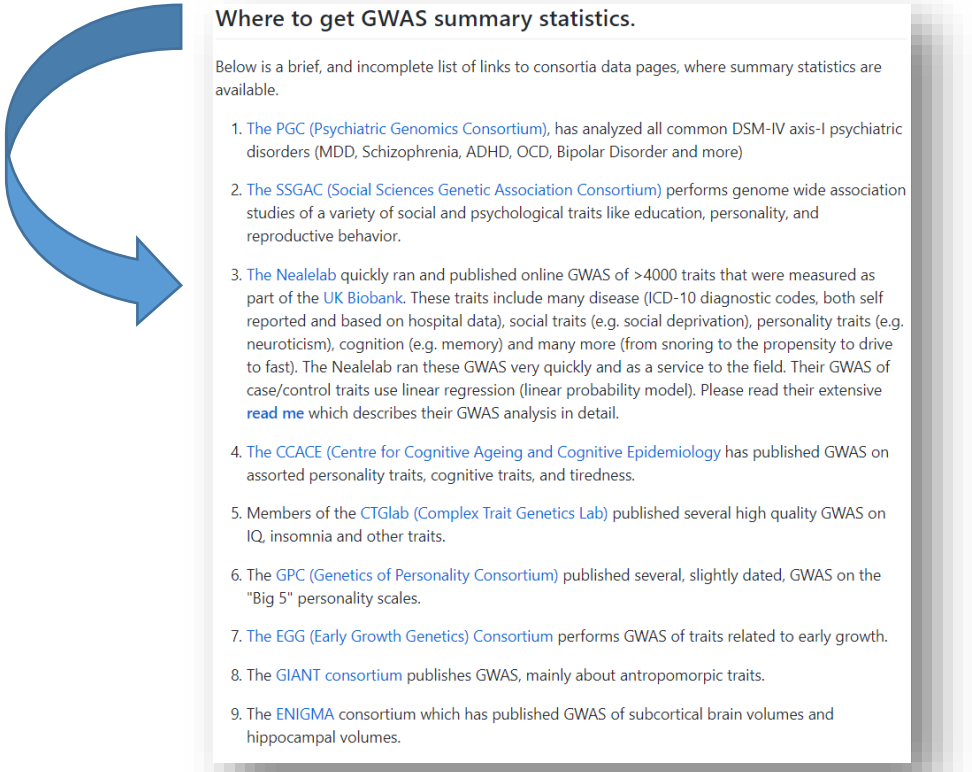
$0 down
$0 monthly payment
No annual fees

Selling the product

Alright, but what about the data? That costs money doesn’t it?

Where to get FREE summary statistics

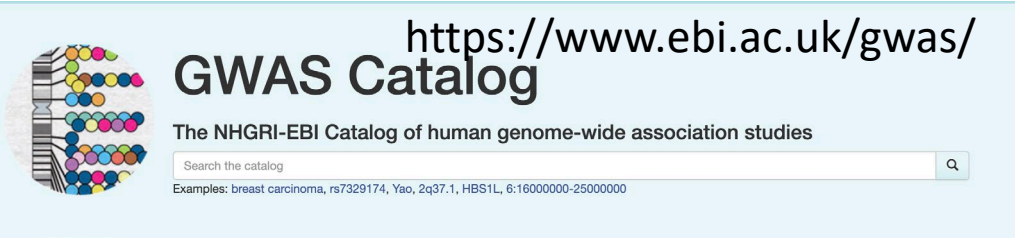
- List lots of resources on the Genomic SEM Wiki: https://github.com/GenomicSEM/GenomicSEM/wiki/2.-Important-resources-and-key-information



Where to get GWAS summary statistics.

Below is a brief, and incomplete list of links to consortia data pages, where summary statistics are available.

1. The PGC (Psychiatric Genomics Consortium), has analyzed all common DSM-IV axis-I psychiatric disorders (MDD, Schizophrenia, ADHD, OCD, Bipolar Disorder and more)
2. The SSGAC (Social Sciences Genetic Association Consortium) performs genome wide association studies of a variety of social and psychological traits like education, personality, and reproductive behavior.
3. The Nealelab quickly ran and published online GWAS of >4000 traits that were measured as part of the UK Biobank. These traits include many disease (ICD-10 diagnostic codes, both self reported and based on hospital data), social traits (e.g. social deprivation), personality traits (e.g. neuroticism), cognition (e.g. memory) and many more (from snoring to the propensity to drive to fast). The Nealelab ran these GWAS very quickly and as a service to the field. Their GWAS of case/control traits use linear regression (linear probability model). Please read their extensive **read me** which describes their GWAS analysis in detail.
4. The CCACE (Centre for Cognitive Ageing and Cognitive Epidemiology has published GWAS on assorted personality traits, cognitive traits, and tiredness.
5. Members of the CTGlab (Complex Trait Genetics Lab) published several high quality GWAS on IQ, insomnia and other traits.
6. The GPC (Genetics of Personality Consortium) published several, slightly dated, GWAS on the "Big 5" personality scales.
7. The EGG (Early Growth Genetics) Consortium performs GWAS of traits related to early growth.
8. The GIANT consortium publishes GWAS, mainly about antropomorpic traits.
9. The ENIGMA consortium which has published GWAS of subcortical brain volumes and hippocampal volumes.



https://www.ebi.ac.uk/gwas/

BioBank Japan PheWeb (PheWeb.jp)

https://pheweb.jp/

FINNGEN https://www.finngen.fi/en/access_results

Pan-UK Biobank

Pan-ancestry genetic analysis of the UK Biobank

https://docs.google.com/spreadsheets/d/1AeeADtT0U1AukliiNyiVzVRdLYPkTbruQSk38DeutU8/edit#gid=268241601

PGC Psychiatric Genomics Consortium

https://pgc.unc.edu/for-researchers/download-results/

https://enigma.ini.usc.edu/research/download-enigma-gwas-results/

You aren’t dreaming
this product is as good as it sounds

II. Estimating Genome-wide Models

Three Primary Steps

1. Munge the summary statistics *(**munge**)*

2. Run LD-Score Regression to obtain the genetic covariance and sampling covariance matrices *(**ldsc**)*

3. Specify and run the model (***usermodel***)

Lab

Using GWAS summary statistics for:

- Major Depressive Disorder (Cases = 170,756; Controls = 329,443; Howard et al., 2019)
- Anxiety Disorders (Cases = 31,977; Controls = 82,114; Purves et al., 2020)
- Alcohol use disorder (Cases = 8,485; Controls = 20,272; Walters et al., 2018)
- PTSD (Cases = 2,424; Controls = 7,113; Duncan et al., 2018)

We are going to start with **Step 3**: Estimating the genome-wide model

How to specify a model in lavaan

We use the lavaan formula language, slightly extended:

Regression:

A ~ B

(Co)variance:

A ~~ A; A ~~ B

Factor:

F1 =~ A + B + C + D

Fix a parameter:

A ~~ 1*B (the covariance between A and B is 1)

Name a parameter:

A ~~ a*B (the covariance between A and B = parameter label a)

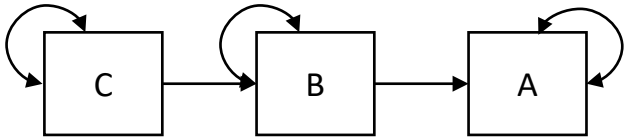
Allows you to use model constraints for this parameter:

a > .001

Let’s make that a bit more specific

Model1 <- “ A ~ B

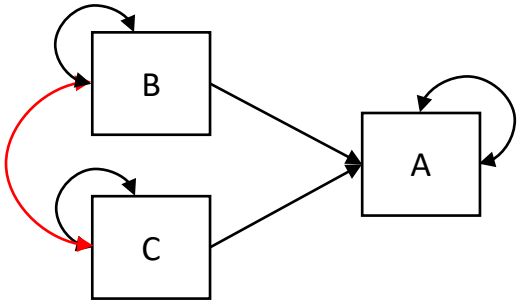
B ~ C”



Model2 <- “ A ~ B

A ~ C

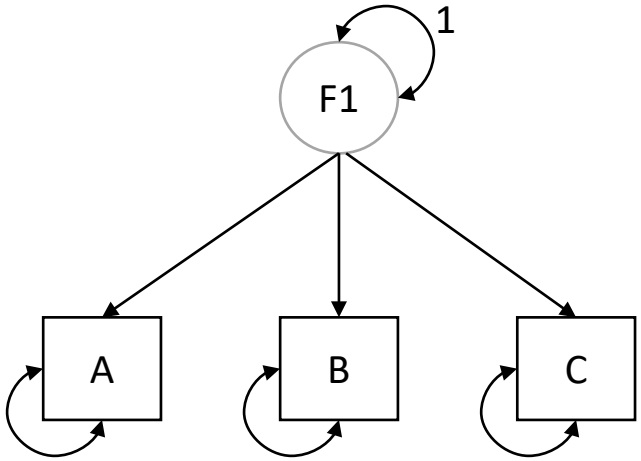
B ~~ C”



Identifying the factor option 1: Unit variance identification

Model3 <- " F1 =~ NA*A + B + C

F1 ~~ 1*F1"



Note that the above is the same as running

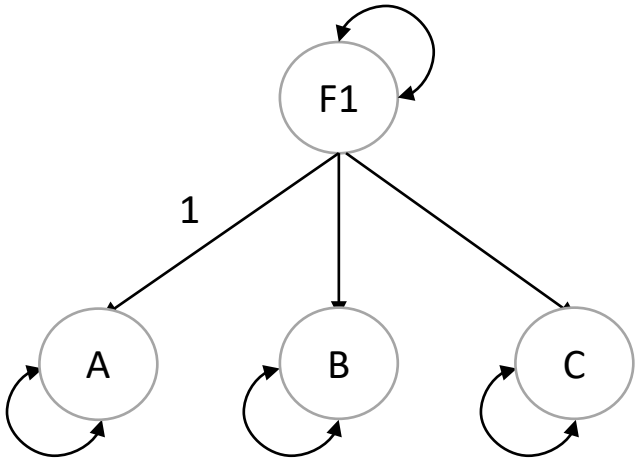
Model3 <- " F1 =~ A + B + C"

And setting the argument std.lv = TRUE

Where std.lv denotes standardized latent variables

Identifying the factor option 2: Unit loading identification

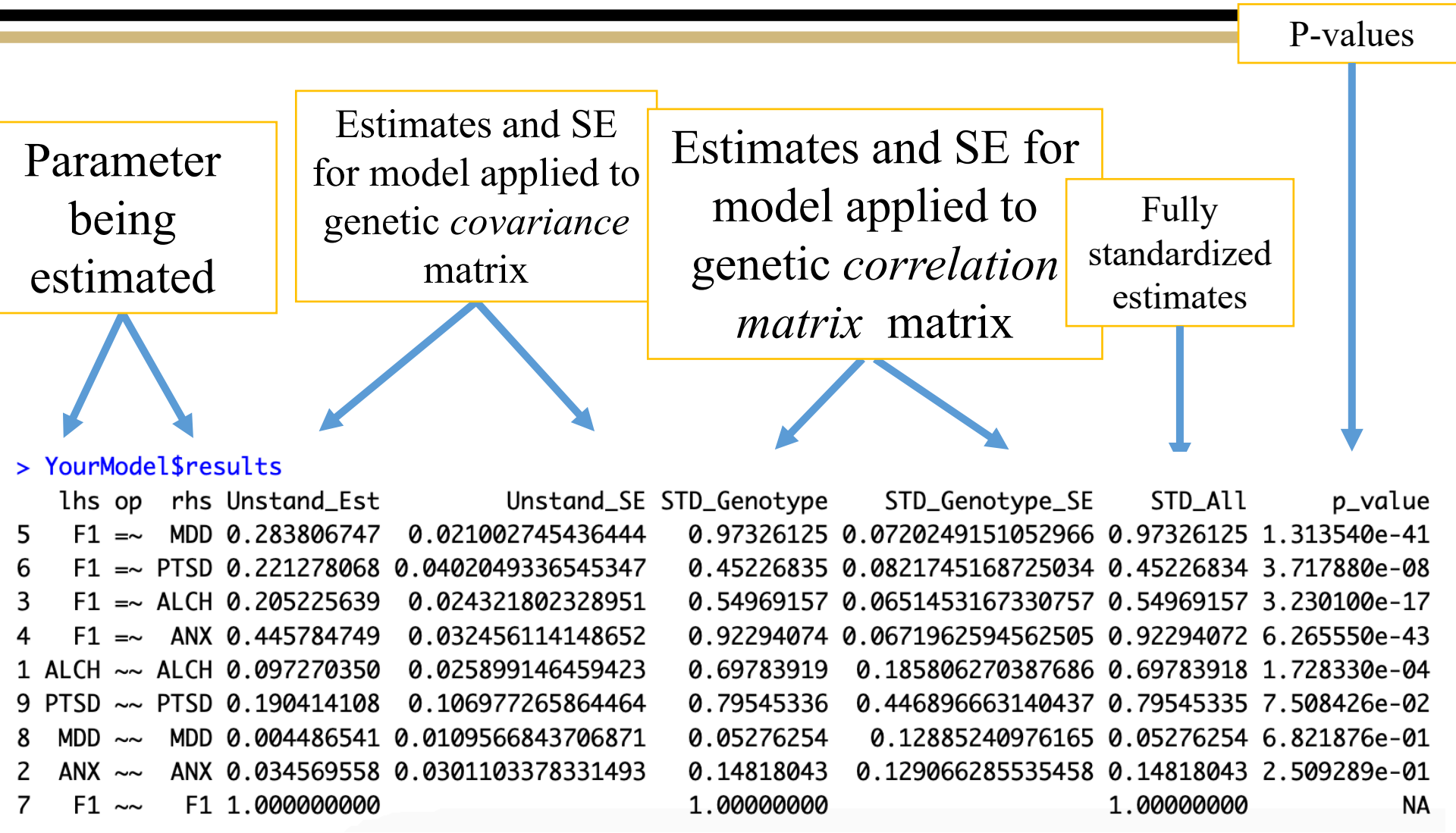
Model3 <- " F1 =~ 1*A + B + C"



Specifying Arguments in *usermodel*

```
#load in the LDSC object made in step 2 above
load("LDSC_INT.RData")

#Takes two necessary arguments:
#1. covstruc: the output from multivariable ldsc
covstruc<-LDSC_INT

#2. model: the user specified model
#here we specify a common factor model
INT.model<-"F1=~MDD+PTSD+ALCH+ANX"

#std.lv: optional argument specifying whether variances of latent variables should be set to 1
std.lv=TRUE

#Run your model
IntResults <- usermodel(covstruc=covstruc, model=INT.model,std.lv=std.lv)
```

IntResults$results




```
> YourModel$results
   lhs op  rhs Unstand_Est         Unstand_SE STD_Genotype    STD_Genotype_SE     STD_All      p_value
5   F1 =~  MDD 0.283806747  0.021002745436444   0.97326125 0.0720249151052966 0.97326125 1.313540e-41
6   F1 =~ PTSD 0.221278068 0.0402049336545347   0.45226835 0.0821745168725034 0.45226834 3.717880e-08
3   F1 =~ ALCH 0.205225639  0.024321802328951   0.54969157 0.0651453167330757 0.54969157 3.230100e-17
4   F1 =~  ANX 0.445784749  0.032456114148652   0.92294074 0.0671962594562505 0.92294072 6.265550e-43
1 ALCH ~~ ALCH 0.097270350  0.025899146459423   0.69783919  0.185806270387686 0.69783918 1.728330e-04
9 PTSD ~~ PTSD 0.190414108  0.106977265864464   0.79545336  0.446896663140437 0.79545335 7.508426e-02
8  MDD ~~  MDD 0.004486541 0.0109566843706871   0.05276254   0.12885240976165 0.05276254 6.821876e-01
2  ANX ~~  ANX 0.034569558 0.0301103378331493   0.14818043  0.129066285535458 0.14818043 2.509289e-01
7   F1 ~~   F1 1.000000000                     1.00000000                    1.00000000           NA
```

IntResults$modelfit

chisq	df	p_chisq	AIC	CFI	SRMR
1.283452	2	0.526383	17.28345	1	0.03621695

- **chisq:** The model chi-square, reflecting index of exact fit to observed data, with lower values indicating better fit.
  - **df and p_chisq:** The degrees of freedom and p-value for the model chi-square.
- **AIC:** Akaike Information Criterion. Can be used to compare models regardless of whether they are nested.
- **CFI:** Comparative Fit Index. Higher = better. > .90 = acceptable fit; > .95 = good model fit
- **SRMR:** Standardized Room Mean Square Residual. Lower = better. < .10 = acceptable fit; < .05 = good fit

Let’s go to the code and fill out the Qualtrics questions for genome-wide models

III. Multivariate GWAS in Genomic SEM

Four Primary Steps

1. Munge the summary statistics *(**munge**)*
2. Run LD-Score Regression to obtain the genetic covariance and sampling covariance matrices *(**ldsc**)*
3. Prepare the summary statistics for multivariate GWAS *(**sumstats**)*
4. Run the multivariate GWAS *(**userGWAS**)*

These two steps mirror that for models without SNP effects and need not be run again for the same traits

Step 3: *sumstats* example code
Note that the traits need to be in the same order as for LDSC

```
#1. files = the name of the summary statistics file
##**note that these are a drastically reduced subsets of SNPs for the practical ONLY
##*that reflect a selected set of chromosome 4 variants
##*Also note that these need to be in the same order as your ldsc object
files<-c("ALCH4.txt", "PTSD4.txt", "MDD4.txt", "ANX4.txt")

#2. ref = the name of the reference file used to obtain SNP MAF
#**note again that this is a drastically reduced subset of SNPs for chromosome 4
#the full reference set is available on our github
ref <- "reference.1000G.ch4.txt"

#3. trait.names = the name of the traits to use for column labeling
trait.names<-c("ALCH","PTSD", "MDD", "ANX")

#4. se.logit = whether the standard errors are on an logistic scale
se.logit<-c(F,T,T,T)

#5. linprob: whether it was a binary outcome that was analyzed as continuoue -or-
#it is a file with only Z-statistics. This is true for ALCH for our data
linprob<-c(T,F,F,F)

#6. sample size. This is only needed for continuous outcomes or outcomes where linprob is TRUE
#we do not provide sample size for ALCH as it is already a column in the GWAS data
N<-c(NA,NA,NA,NA)

#run sumstats putting these pieces together
INT_sumstats<-sumstats(files=files,ref=ref,trait.names=trait.names,se.logit=se.logit,linprob=linprob,N=N)
```

Flowchart on github to help you figure out arguments for sumstats

The linear probability model argument for ALCH

sumstats needs a beta and SE to perform analyses, but sometimes the summary data only has a Z-statistic (or it was a binary outcome analyzed as continuous).

In these cases, linprob is set as TRUE for that trait and the sum of effective sample size is needed

	CHR	SNP	BP	A1	A2	Z	P	Weight
1	1	rs10799799	23973601	T	G	-0.190	0.8495	21857.28
2	1	rs200328701	57729103	CT	C	-0.278	0.7807	18324.09
3	1	rs75245025	151716030	C	G	0.710	0.4779	22791.88
4	1	rs146090341	211396305	T	G	-0.092	0.9265	18999.23
5	1	rs188551793	215407827	A	T	0.321	0.7482	11611.03
6	1	rs2490387	237279677	T	C	-1.216	0.2239	20769.08

Examine the .log file for MDD

```
Preparing summary statistics for file: MDD4.txt
Found an NEFF column for sample size.

Please note that this is likely effective sample size and should only be used for liability h^2 conversion for binary traits and that it should reflect the
sum of effective sample sizes across cohorts.

Be aware that some NEFF columns reflect half of the effective sample size; the function will automatically double the column names if recognized [check
above in .log file to determine if this is the case].
If the Neff value is halved in the summary stats, but not recognized by the munge function, this should be manually doubled prior to running munge.
Interpreting the MARKERNAME column as the SNP column.
Interpreting the A1 column as the A1 column.
Interpreting the A2 column as the A2 column.
Interpreting the LOGOR column as the effect column.
Interpreting the P column as the P column.
Interpreting the NEFF column as the N column.
Interpreting the MAF column as the MAF column.
Interpreting the STDERRLOGOR column as the SE column.
0 rows were removed from the MDD4.txt summary statistics file due to entries that were duplicated for rsID. These are removed as they likely reflect
multiallelic variants.
Merging file: MDD4.txt with the reference file: reference.1000G.ch4.txt
1400 rows present in the full MDD4.txt summary statistics file.
20 rows were removed from the MDD4.txt summary statistics file as the rsIDs for these SNPs were not present in the reference file.
The effect column was determined NOT to be coded as an odds ratio (OR) for the MDD4.txt summary statistics file based on the median of the effect column
being close to 0.
5rows were removed from theMDD4.txtsummary statistics file due to effect values estimated at exactly 0 as this causes problems for matrix inversion
necessary for later Genomic SEM analyses.
No INFO column, cannot filter on INFO, which may influence results
Performing transformation under the assumption that the effect column is either an odds ratio or logistic beta (please see output above to determine
whether it was interpreted as an odds ratio) and the SE column is a logistic SE (i.e., NOT the SE of the odds ratio) for:MDD4.txt
1375 SNPs are left in the summary statistics file MDD4.txt after QC and merging with the reference file.
```

Step 4: *userGWAS* example code

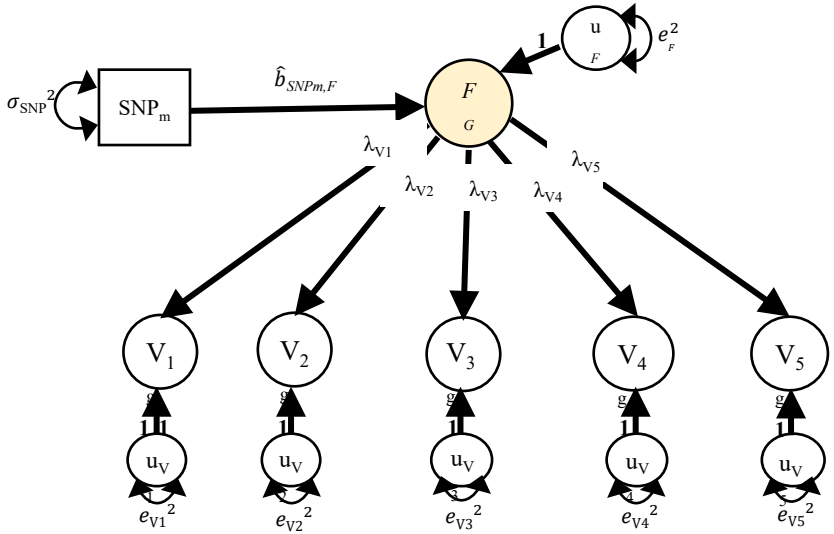
```
#STEP 4: RUN A USER SPECIFIED MULTIVARIATE GWAS
#userGWAS takes three necessary arguments:
#1. covstruc = the output from the ldsc function
covstruc<-LDSC_INT

#2. SNPs = output from sumstats function
SNPs<-INT_sumstats

#3. model = the model to be run
#going to troubleshoot estimated ov variances are negative for 4 SNPs
#by adding model constraint for all residuals to be above 0
model<-"F1=~MDD+PTSD+ALCH+ANX
F1~SNP"
```

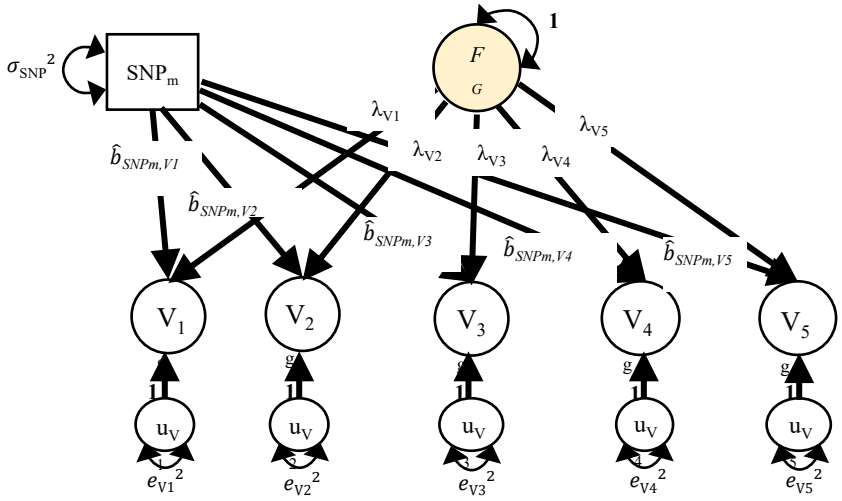
Step 4: *userGWAS* example code

```
#4. sub = optional argument specifying component of model output to be saved
sub<-"F1~SNP"

#5. parallel = optional argument specifying whether it should be run in parallel
#set to FALSE here just for the practical
parallel<-FALSE

#6. Q_SNP = optional argument specifying whether you want
#the heterogeneity index calculated for your factors
Q_SNP<-TRUE

#run the multivariate GWAS below
INT_GWAS<-userGWAS(covstruc=covstruc, SNPs=SNPs, model=model, sub=sub, parallel=parallel, Q_SNP=Q_SNP)
```

Estimates of SNP level heterogeneity (Q_{SNP})

- Asks to what extent the effect of the SNP operates through the common factor
- χ^2 distributed test statistic, indexing fit of the common pathways model against independent pathways model



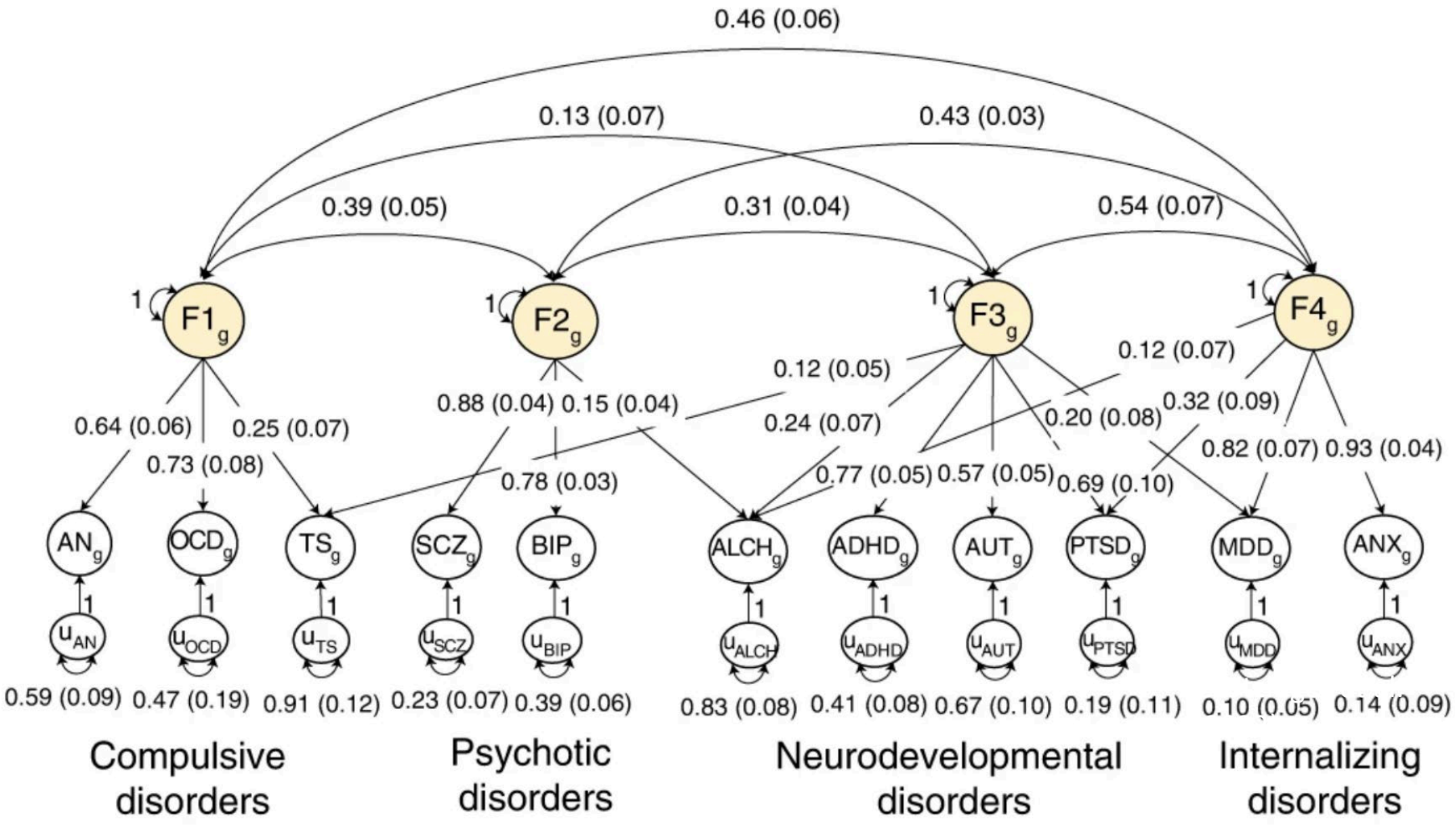


Q_{SNP} : QC Metric and a Result

- For some projects, you might just use Q_{SNP} to prune your factor GWAS results for SNPs that are unlikely to operate via the factor

- In other instances, your traits might be so highly correlated, but currently considered distinct phenotypes, such that your research question includes investigating what SNPs differentiate your traits

If you have multiple factors, you can get a Q_{SNP} specific metric for each factor. For example, you could have a SNP that fits one factor well, but is very disorder-specific for another factor



Q_{SNP} : Better, Faster, Stronger

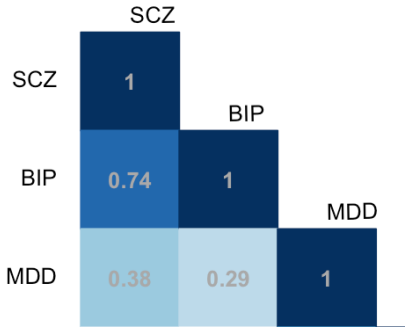
- It used to be that you had to estimate a separate independent pathways follow-up model.
  - This was slow, error prone, not computationally efficient

- ***Introducing today*** that Q_{SNP} is now an argument for *userGWAS* that will automatically calculate this metric for every factor that is predicted by a SNP without estimating a follow-up model

Behind the scenes

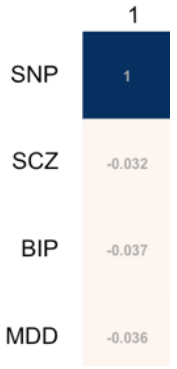
- *userGWAS* combines output from Steps 2 (*ldsc*) and 3 (*sumstats*) to be able to specify a model with SNP effects
- Creates as many covariance matrices as there are SNPs across traits
- **Introducing today:** the measurement model (the factor loadings and correlations) is fixed across SNPs as a default to speed up analysis and improve interpretability (can be turned on/off with *fix_measurement* argument)

Step 2: Run *ldsc*



+

Step 3: Run ***sumstats***



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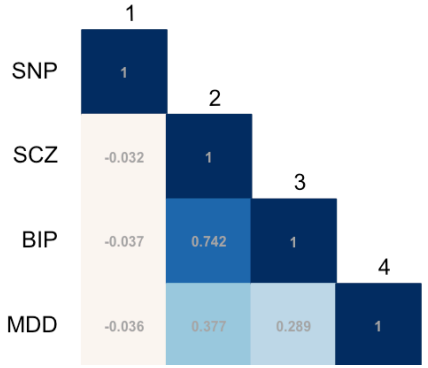
Step 4: *userGWAS* combines the two



First five rows of the output

The parameter being estimates (SNP effect on factor)

Beta and SE of SNP effect on factor

Multivariate GWAS *p*-value

	SNP	CHR	BP	MAF	A1	A2	lhs	op	rhs	free	label	est	SE	Z_Estimate	Pval_Estimate
1	rs10030871	4	68786	0.0765408	T	C	F1	~	SNP	6		9.072847e-04	0.004121185	0.22015141	0.8257532
2	rs6599368	4	69567	0.0755467	A	T	F1	~	SNP	6		1.009838e-03	0.004110347	0.24568182	0.8059285
3	rs7678633	4	69713	0.0755467	G	A	F1	~	SNP	6		1.051503e-03	0.004106863	0.25603562	0.7979233
4	rs13130581	4	70392	0.0725646	A	G	F1	~	SNP	6		8.299511e-05	0.004146428	0.02001605	0.9840306
5	rs13125929	4	71566	0.0725646	T	C	F1	~	SNP	6		4.857205e-04	0.004153705	0.11693667	0.9069102

	chisq	chisq_df	chisq_pval	AIC	Q_SNP	Q_SNP_df	Q_SNP_pval	error	warning
1	4.905573	8	0.7676193	18.90557	3.622121	3	0.3052654	0	0
2	4.839514	8	0.7745834	18.83951	3.556060	3	0.3135638	0	0
3	4.901617	8	0.7680379	18.90162	3.618163	3	0.3057570	0	0
4	5.029482	8	0.7544204	19.02948	3.746031	3	0.2902263	0	0
5	5.787667	8	0.6710025	19.78767	4.504214	3	0.2119147	0	0

Q_{SNP} *p*-value

Let’s go to the code and fill out the Qualtrics questions for multivariate GWAS

If you finish early, go onto next slides/section of code to play around more with specifying your own model at the genome-wide level

Anthropometric traits

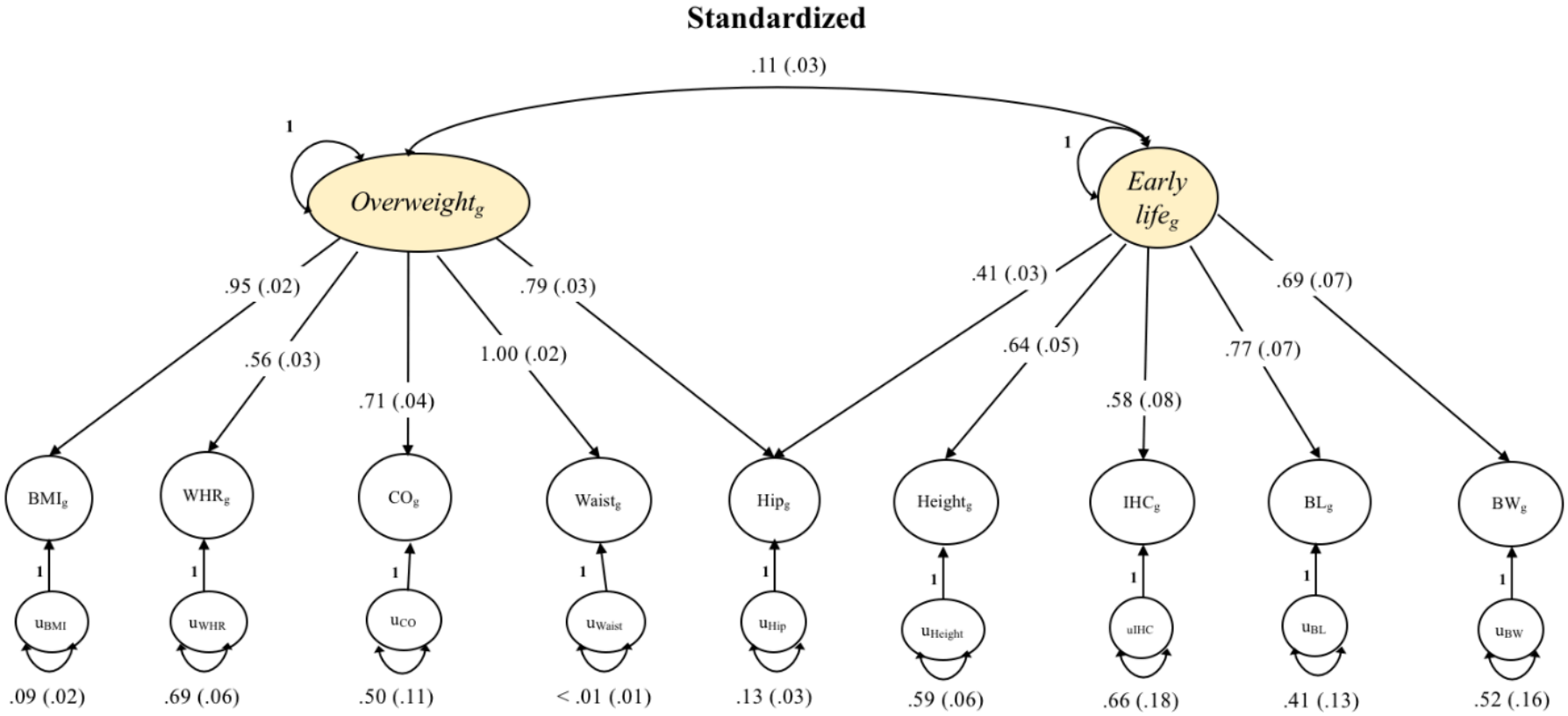
```
###IF theres time
load("Anthro_LDSC.RData")
colnames(anthro$S)

covstruc<-anthro

#2. model = the user specified model
anthro.model<-""

#estimation = an optional third argument specifying the estimation method to use
estimation<-"DWLS"

#std.lv = optional fourth argument specifying whether variances of latent variables should be set to 1
std.lv=FALSE

#Run your model
AnthroModel<- usermodel(covstruc=covstruc, model=anthro.model,estimation=estimation,std.lv=std.lv)
```

Note that you do not need to include all variables in the model

Variable Names

- BMI = Body Mass Index
- WHR = Waist Hip Ratio
- Waist = Waist Circumference
- Hip = Hip circumference
- CO = childhood obesity
- Height = Height
- BL = Birth Length
- BW = Birth Weight
- IHC = Infant Head Circumference

Example model that could be fit to the data (but you should fit your own)



Pre-register your model by writing it down on paper beforehand.

The goal is ***not*** to just pick models until you get “a result”

Rather, we want to test theories or take a documented data-driven approach

Final Notes

- Parallel processing and MPI for **`userGWAS`** is available
- Parallel is the same as serial processing, except that it takes an additional cores argument specifying how many cores to use
- Ideal run-time scenario: split jobs across computing nodes on a cluster and run in-parallel
  - All runs are independent of one another!

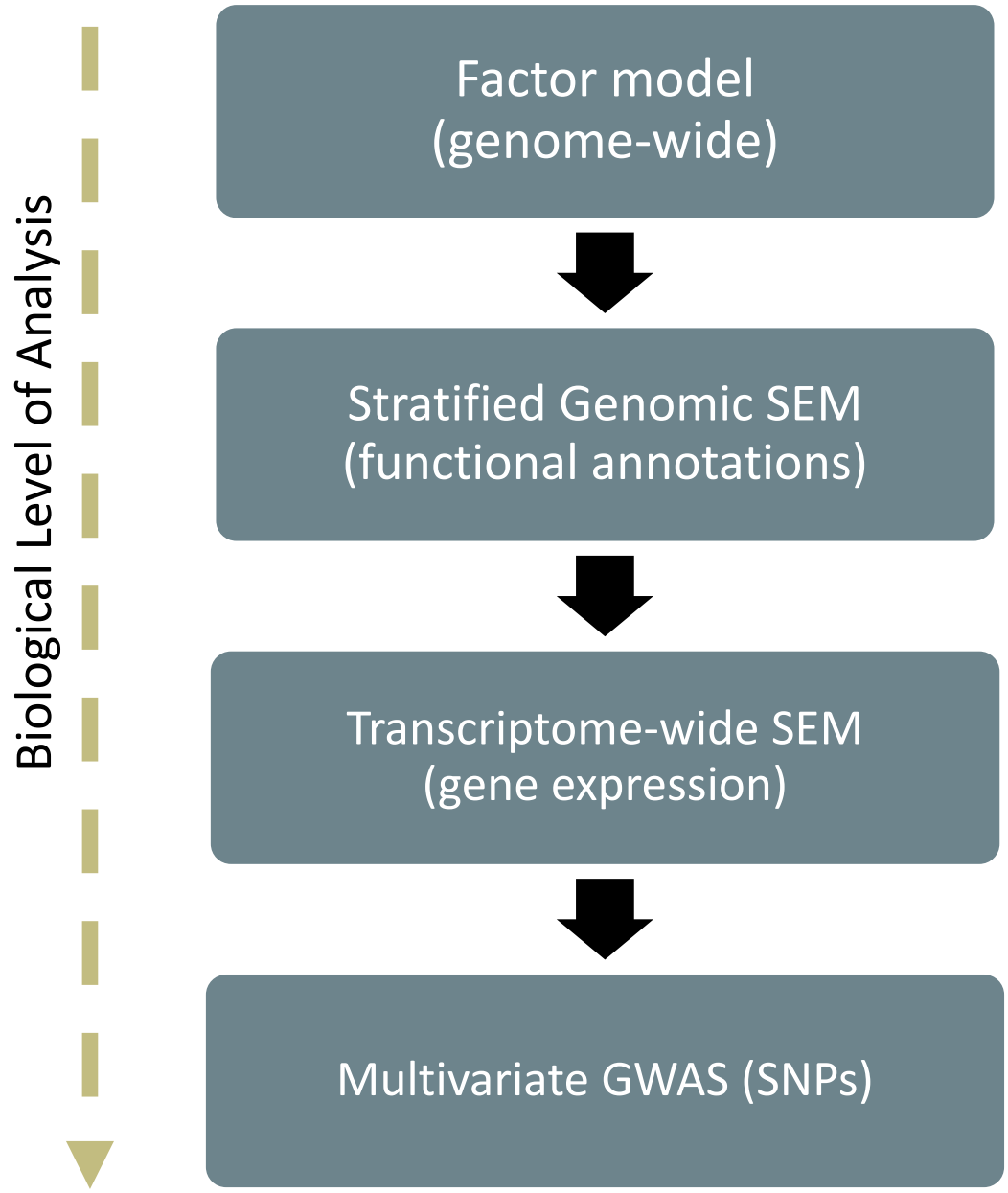
Overview

Ask questions on our google forum

- https://groups.google.com/forum/#!forum/genomic-sem-users

- Lots can be done using existing, openly available GWAS summary statistics

- Models are flexible and up to the user



We've gone over factor models and multivariate GWAS but two additional sets of functions are available for functional annotations and gene expression analyses

Resources

- See paper at: rdcu.be/bvn7t
- See github at: https://github.com/GenomicSEM/GenomicSEM
- See tutorials at: https://github.com/GenomicSEM/GenomicSEM/wiki