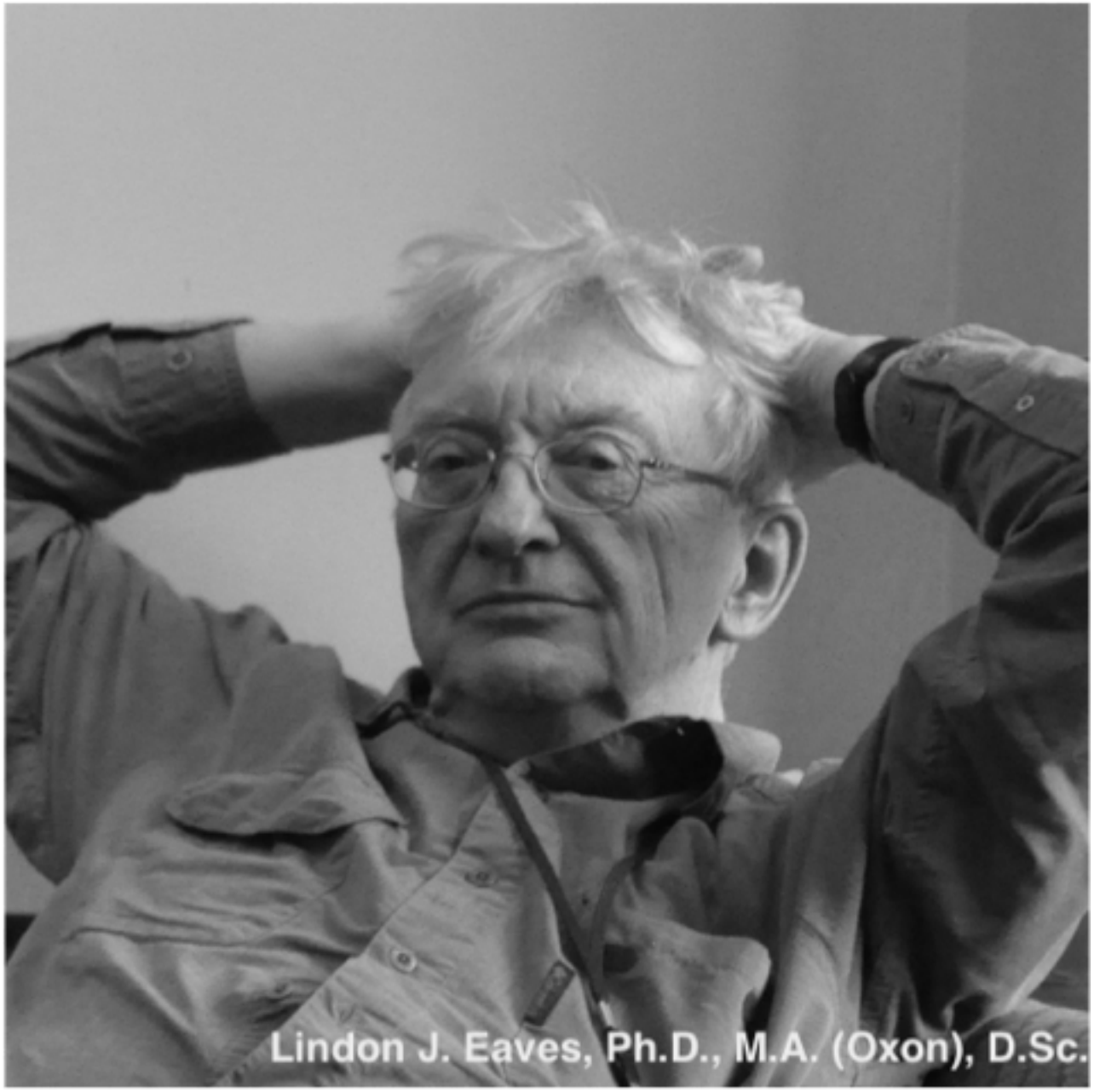
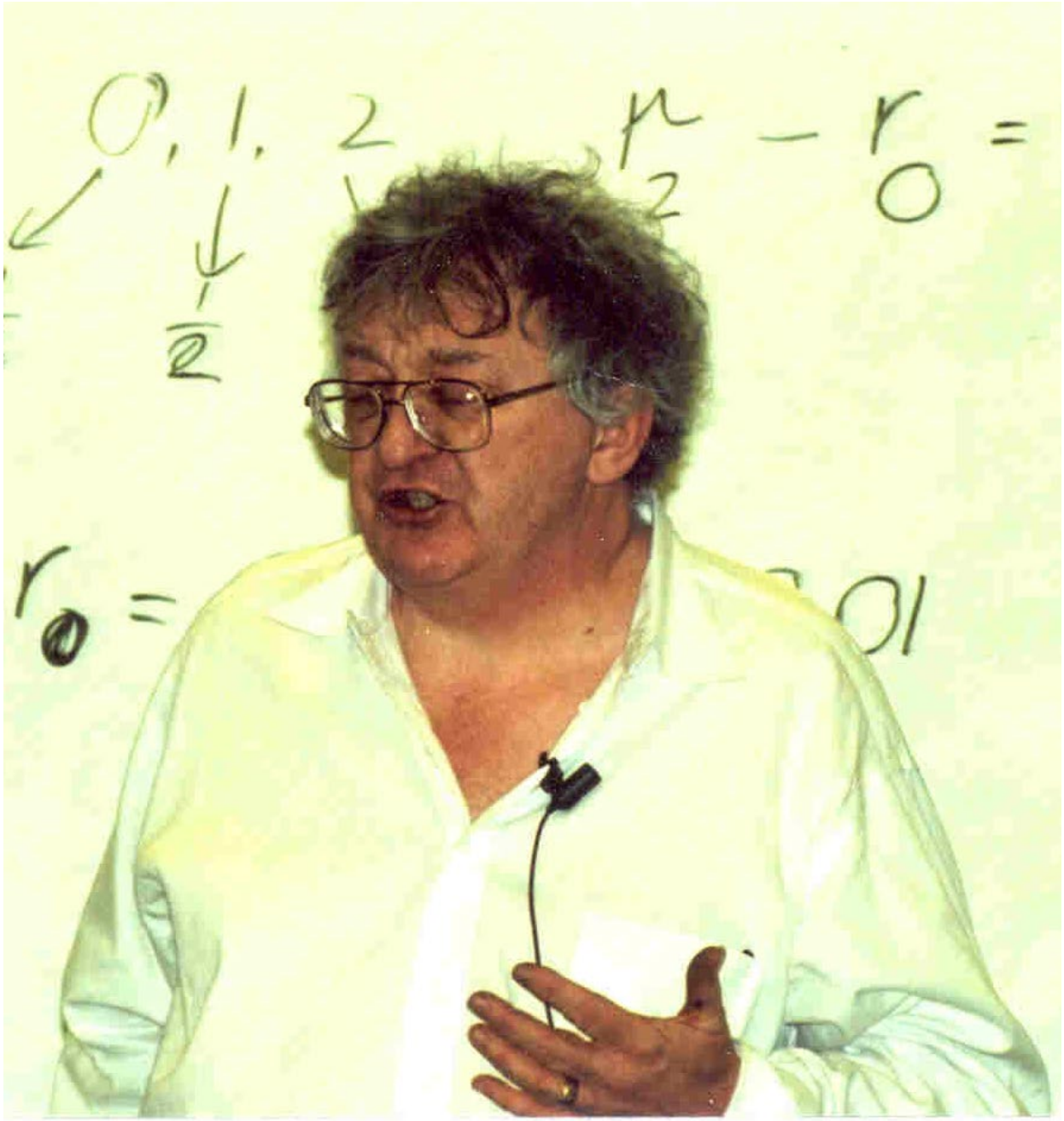
# 37nd International Statistical Genetics [ISG] Workshop

- Ben Neale (codirector)
- David Evans (codirector)
- Nick Martin
- Dorret Boomsma
- Mike Neale
- Hermine Maes
- Sarah Medland
- Brittany Mitchell
- John Kemp
- Wei Zhou
- Michel Nivard
- Abdel Abdellaoui
- Elizabeth Prom-Wormley
- Matt Keller (host)
- John Hewitt
- Jeff Lessem
- Luke Evans
- Andrew Grotzinger
- Dan Gustavson
- Dan Howrigan
- Tim Poterba
- Dan King
- Danielle Posthuma
- Aysu Okbay
- Loic Yengo
- Tim Thornton


Lindon J. Eaves, Ph.D., M.A. (Oxon), D.Sc.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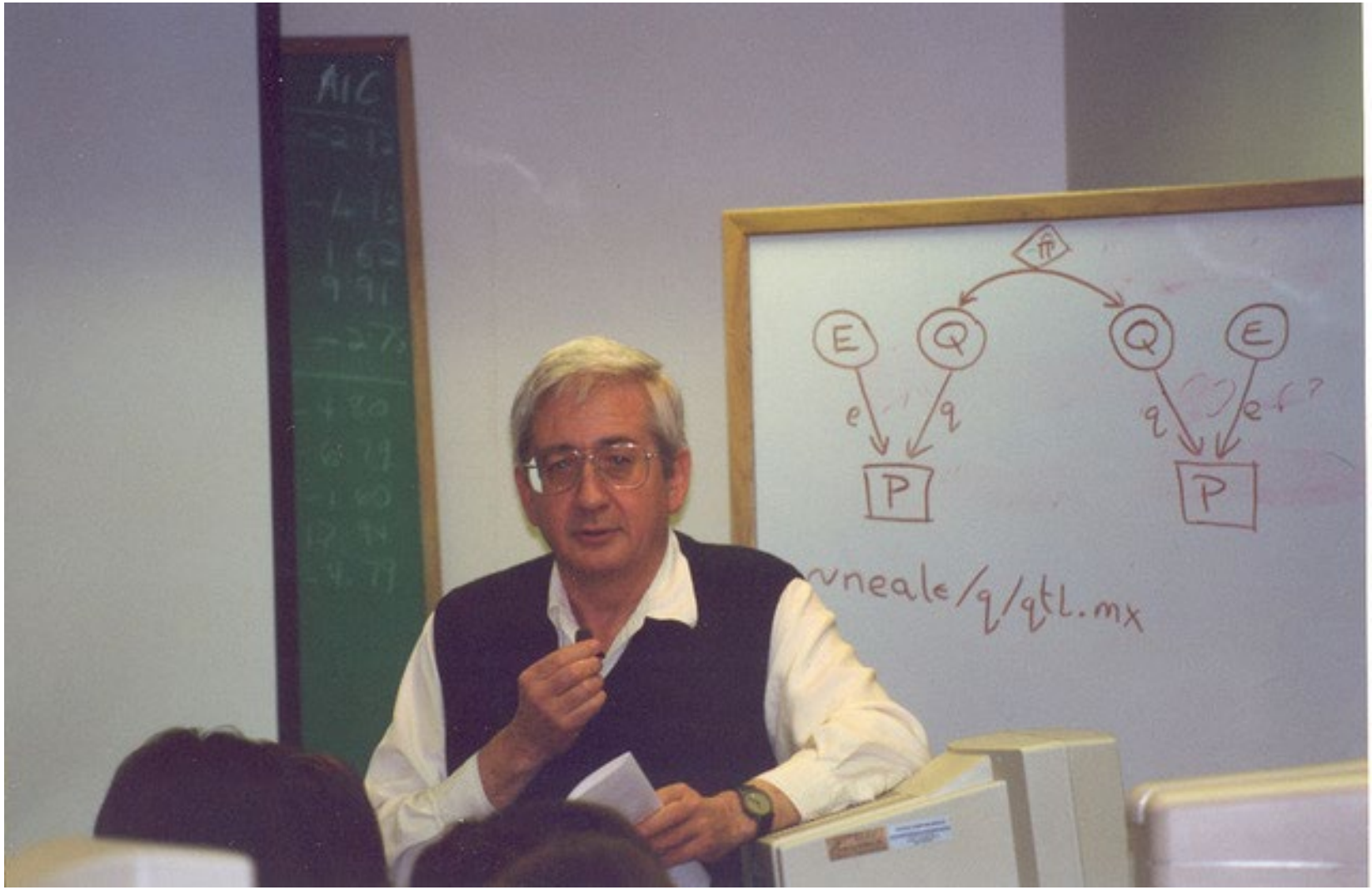
$\frac{1}{2}$
$r_2 - r_0 =$
$r_0 =$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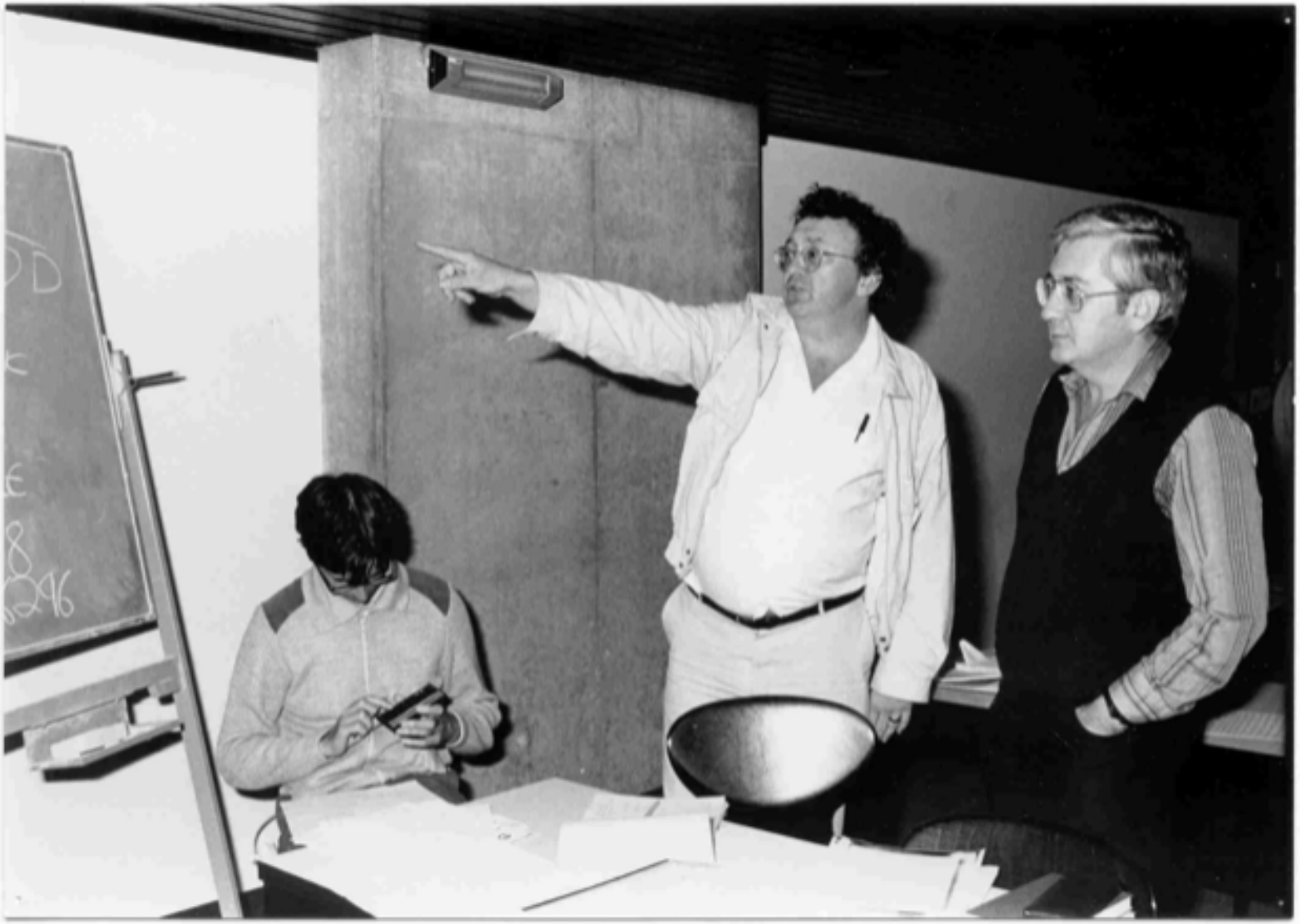
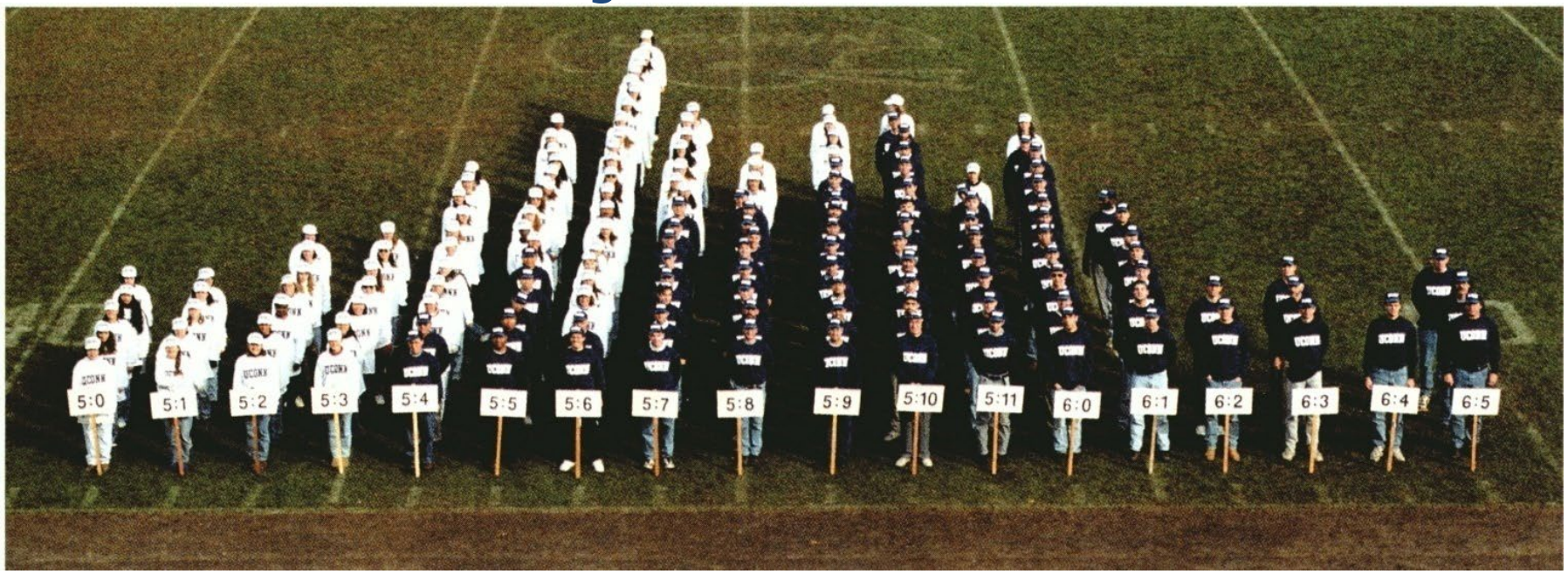


# The genetics of complex traits:
## historical context and current challenges

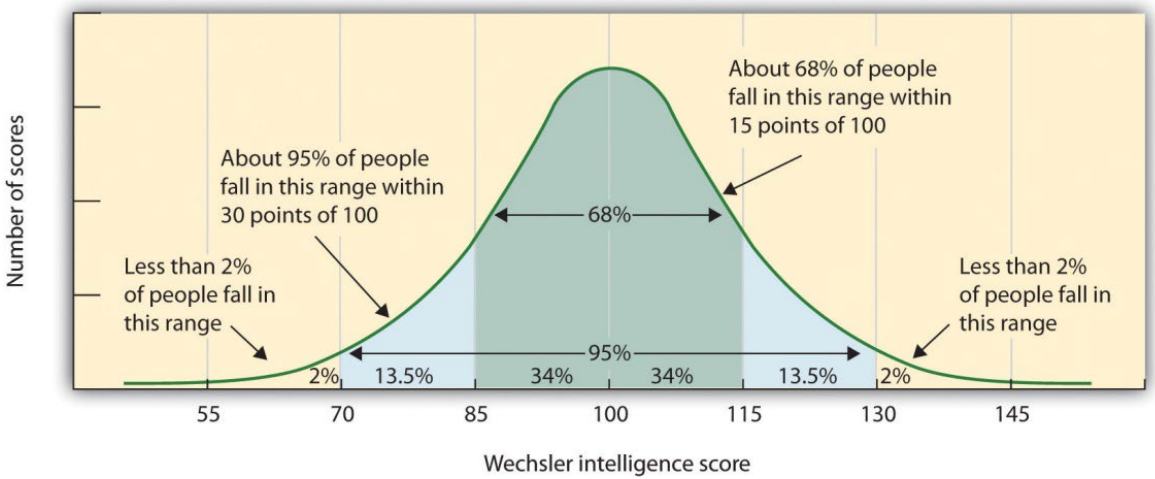
Nick Martin
Queensland Institute
of Medical Research
Brisbane

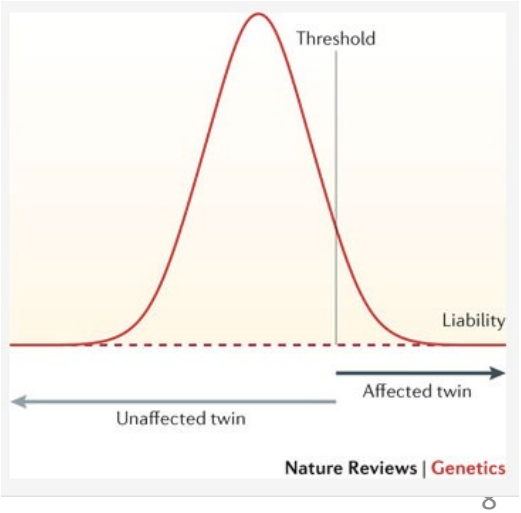
Boulder workshop
March 6, 2023

# Human variation: Height



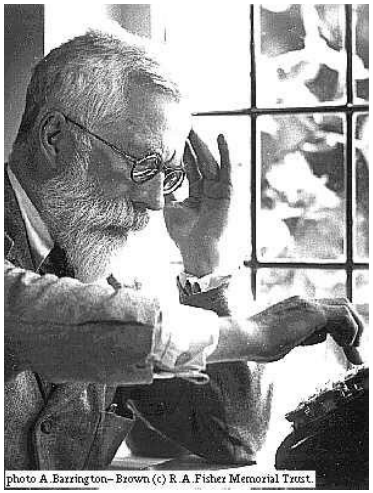

# Human variation: IQ



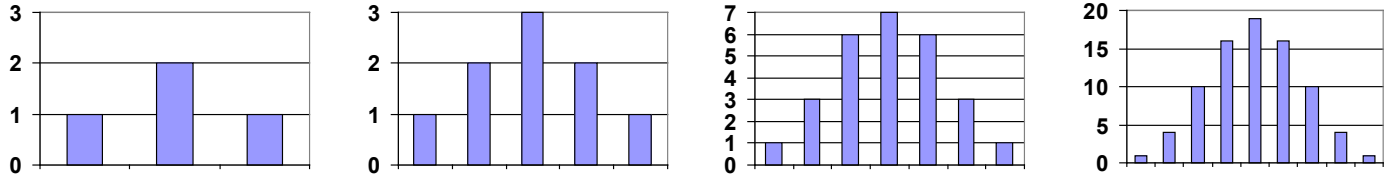



# R.A. Fisher, 1918

## The explanation of quantitative inheritance in Mendelian terms



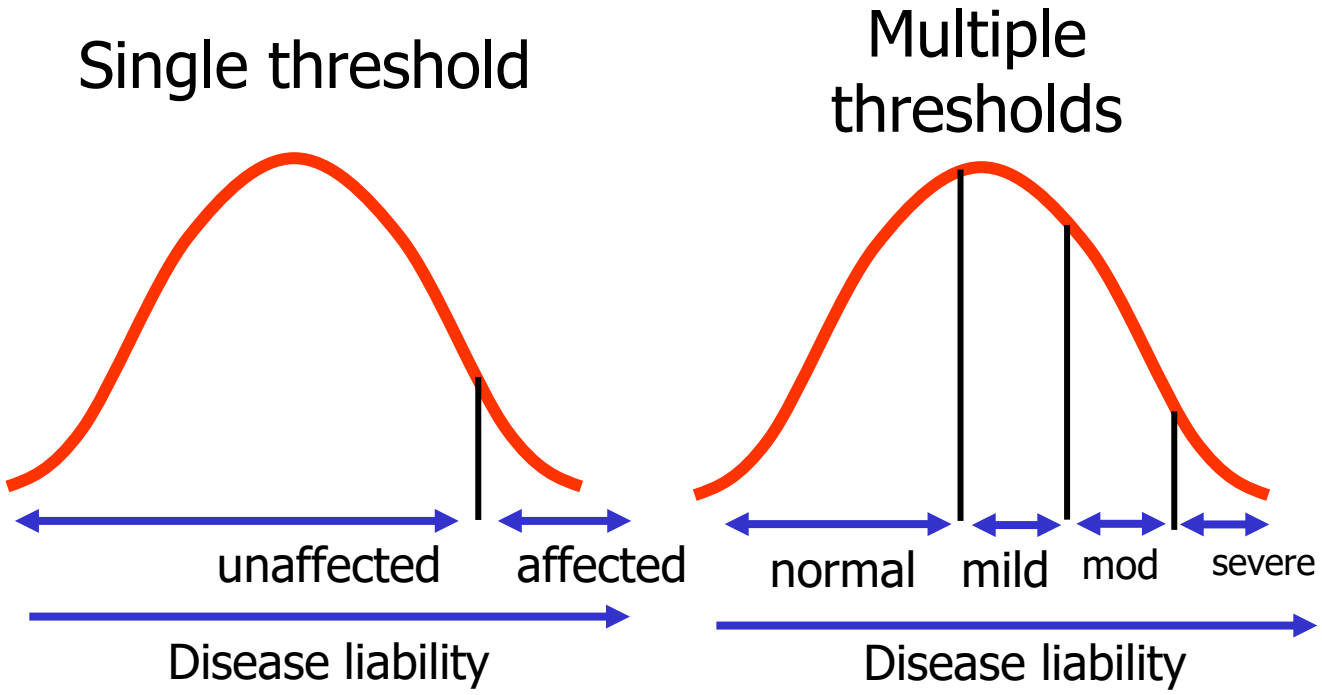

| 1 Gene | 2 Genes | 3 Genes | 4 Genes |
|---|---|---|---|
| → 3 Genotypes | → 9 Genotypes | → 27 Genotypes | → 81 Genotypes |
| → 3 Phenotypes | → 5 Phenotypes | → 7 Phenotypes | → 9 Phenotypes |



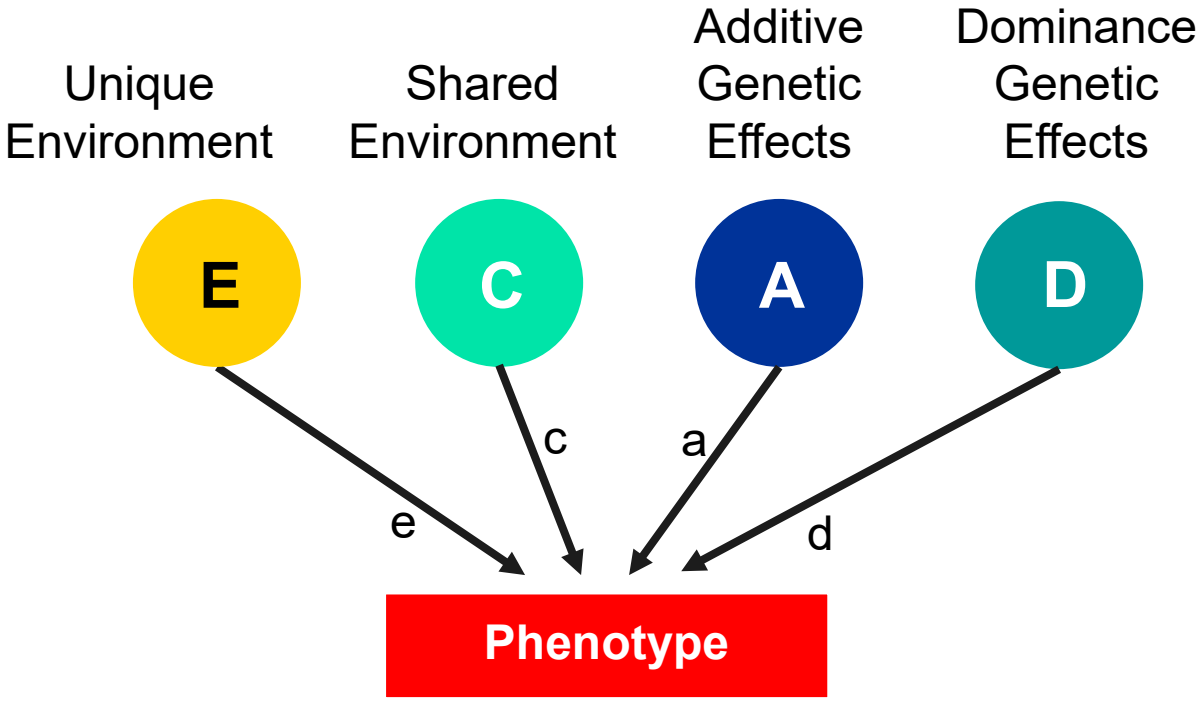
# Complex disorders account for most health burden

- Examples
  - Ischaemic heart disease (30-50%, F-M)
  - Breast cancer (12%, F)
  - Colorectal cancer (5%)
  - Recurrent major depression (10%)
  - ADHD (5%)
  - Bipolar (2%)
  - Schizophrenia (1%)
  - Non-insulin dependent diabetes (5%)
  - Asthma (10%)
  - Essential hypertension (10-25%)
  - etc…..

# Multifactorial Threshold Model of Disease – normally distributed "liability"



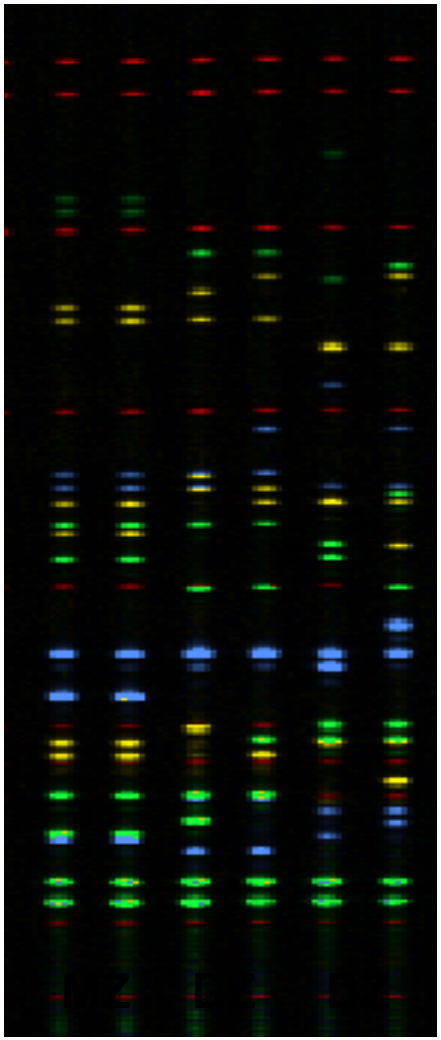
# Variance components




$$P = eE + aA + cC + dD$$

# Genetic Epidemiology: Stages of Genetic Mapping

- Are there genes influencing this trait?
  - Genetic epidemiological (twin / family) studies OR heritability based on measured genetic variants
- Where are those genes?
  - Linkage analysis
- What are those genes?
  - Association analysis (meta-analysis / pathway)
- How do they work beyond the sequence?
  - Epigenetics, transcriptomics, proteomics
- What can we do with them ?
  - Translational medicine



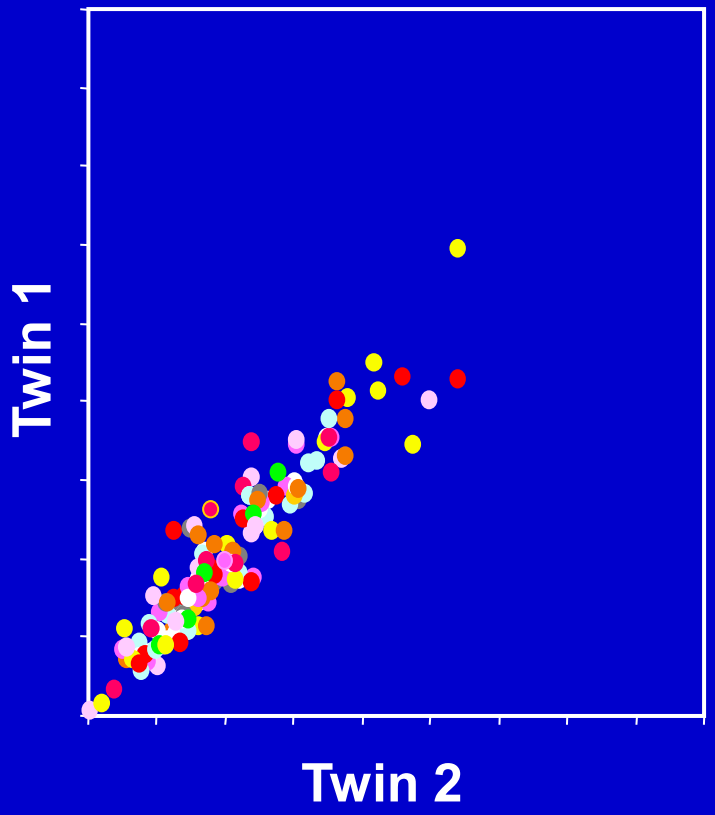
# The value of twins to estimate genetic and environmental variance

## MZ and DZ twins: determining zygosity using ABI Profiler™ genotyping

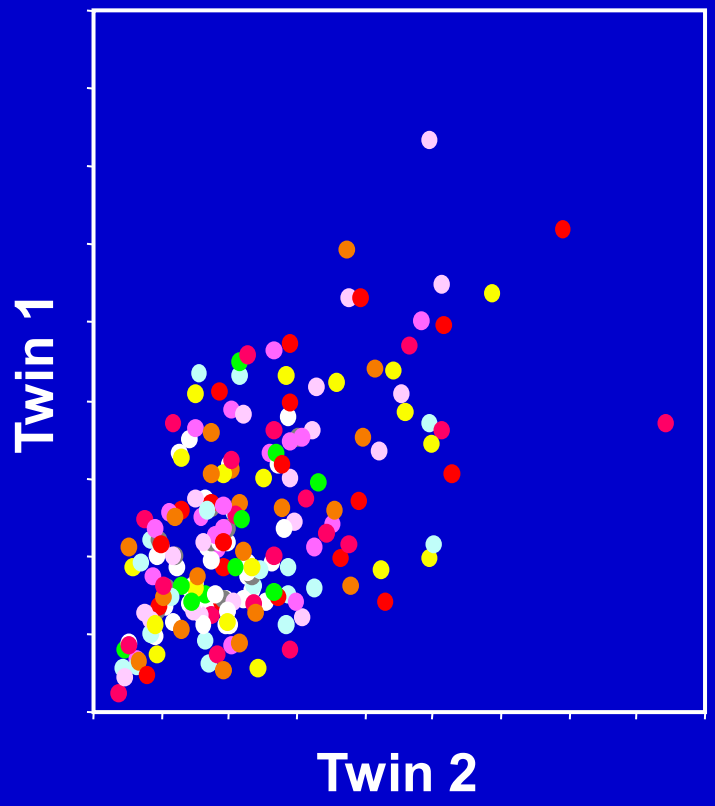
## (9 STR markers + sex)

# Height for 12yo MZ and DZ twins

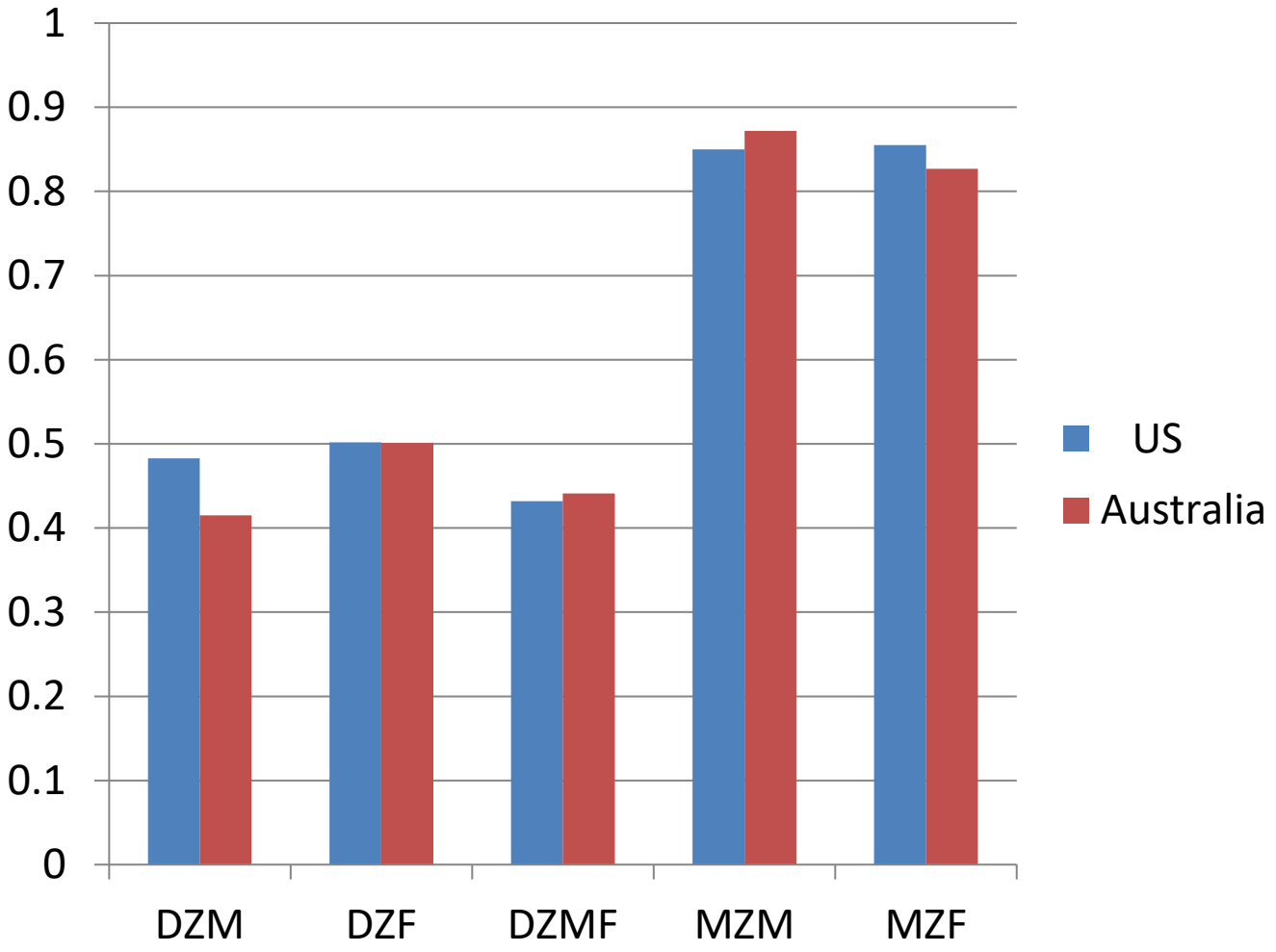
MZ twins - 153 pairs, r = 0.94



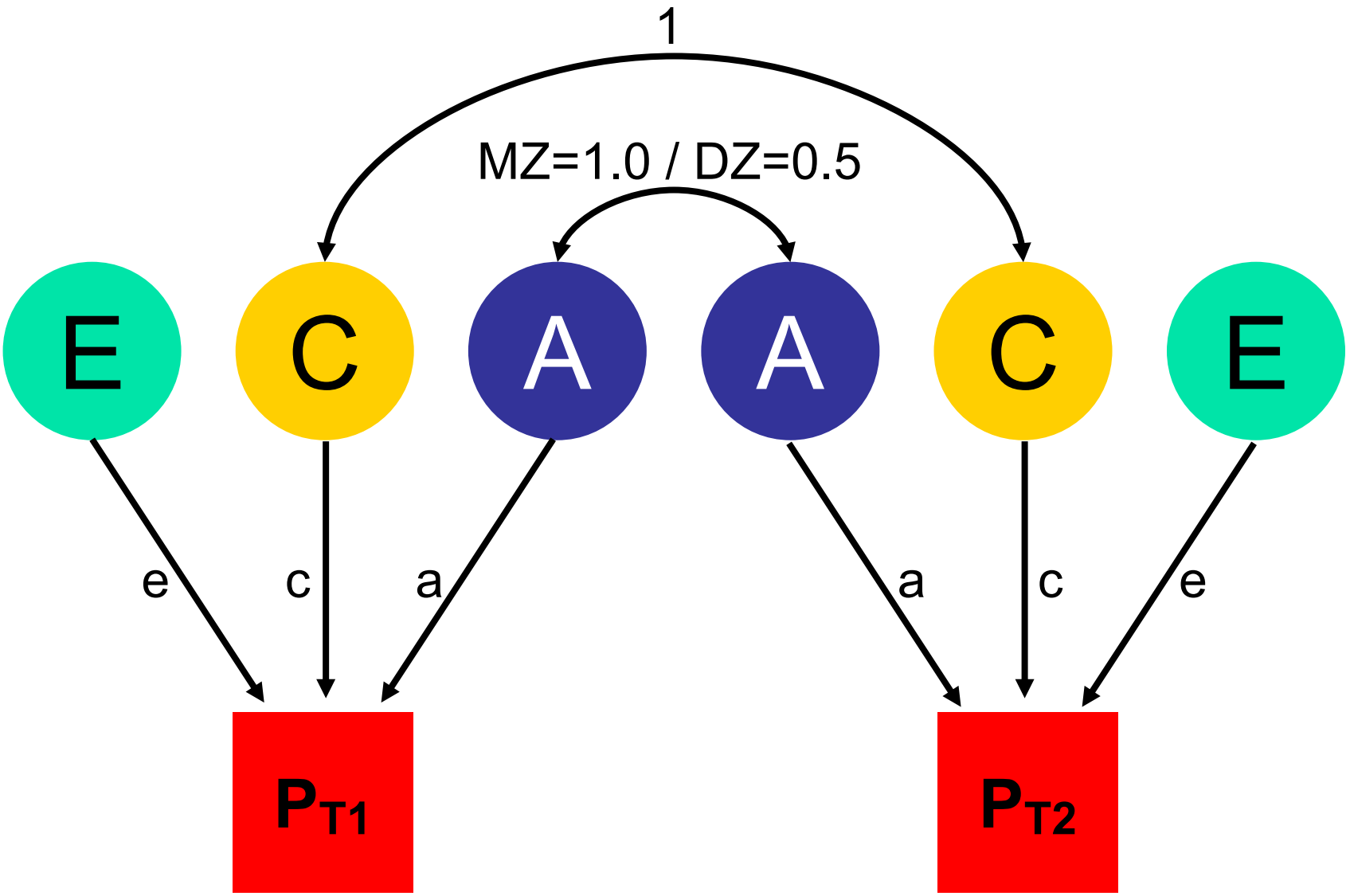

DZ twins - 199 pairs, r = 0.60



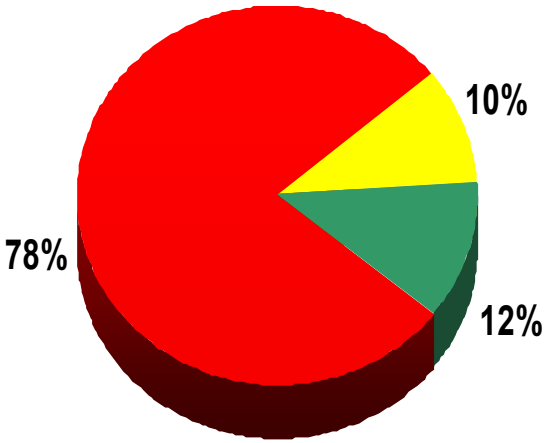
# Twin Correlations for Adult Stature (Virginia 30,000 and Australia 22,000)



# ACE Model for twin data



# Sources of variation in height




So total /twin /family /pedigree heritability ~80%

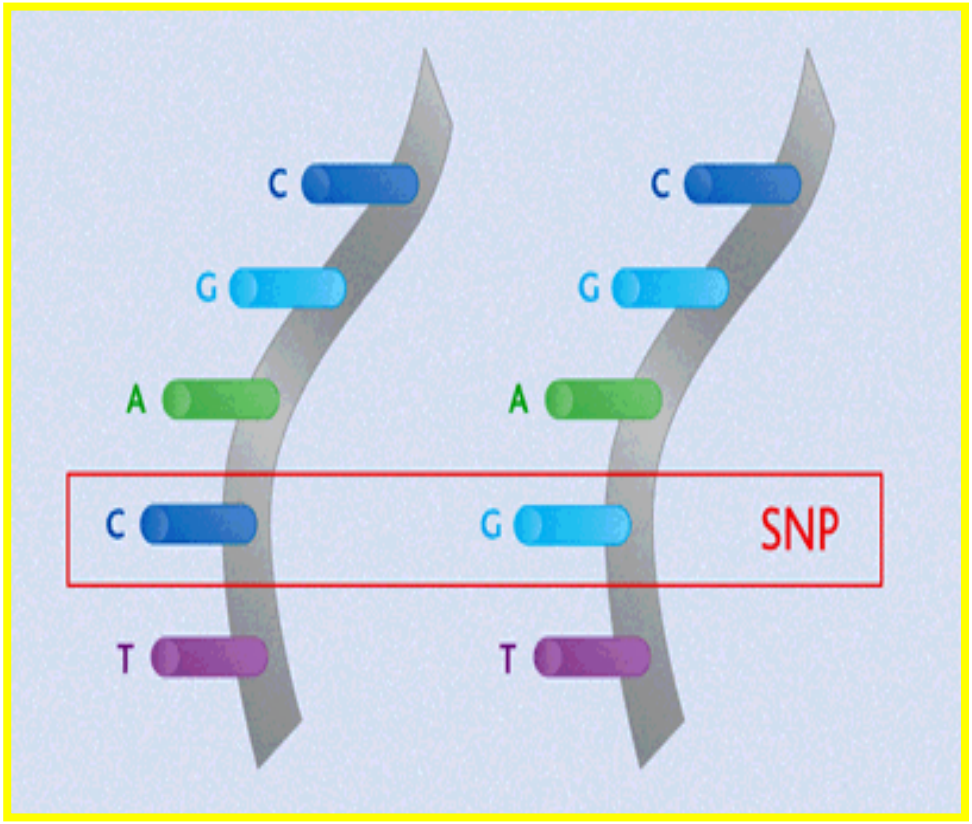
Additive genetic

AM / Shared environment

Non-shared environment

# Finding the genes - association

Looks for correlation between specific alleles and phenotype (trait value, disease risk) using single nucleotide polymorphisms (SNPs)

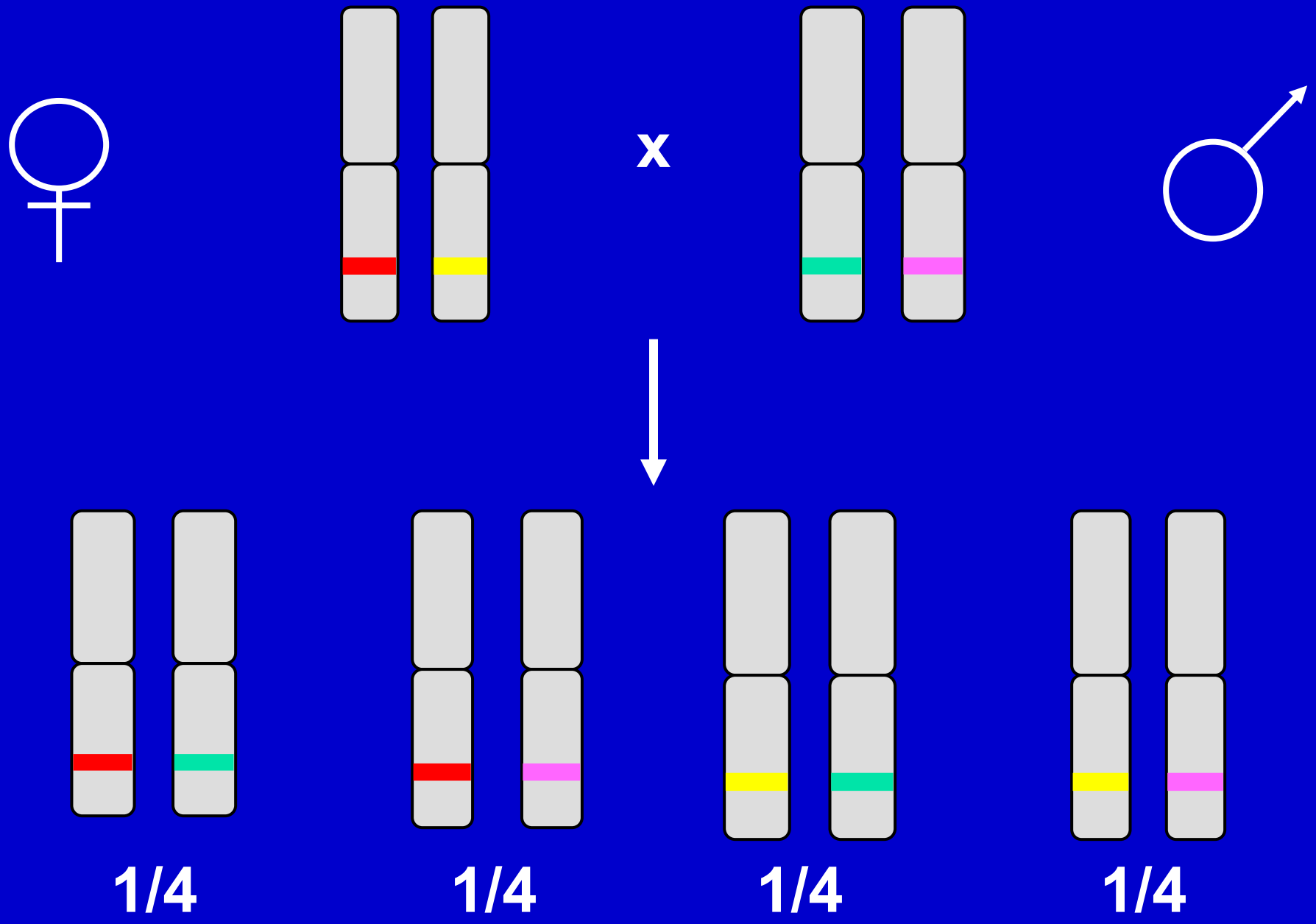


# Classical twin design revisited: Heritability estimation without MZ twins

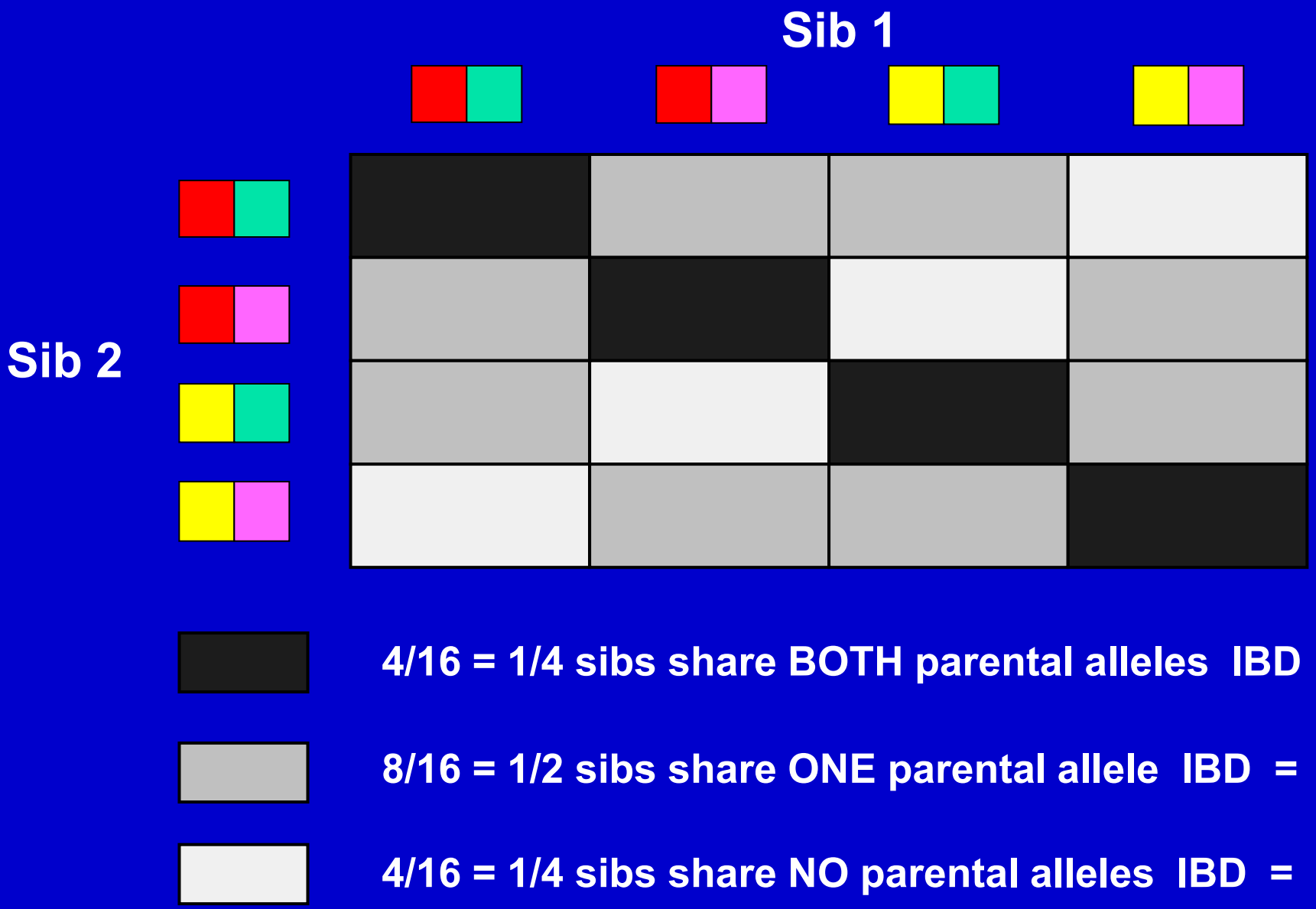
Why do we use the average sib values of

$r_a = 0.5$ and $r_d = 0.25$

when we can estimate the (almost) exact values for each sib pair from marker data ?


x
1/4
1/4
1/4
1/4

# IDENTITY BY DESCENT



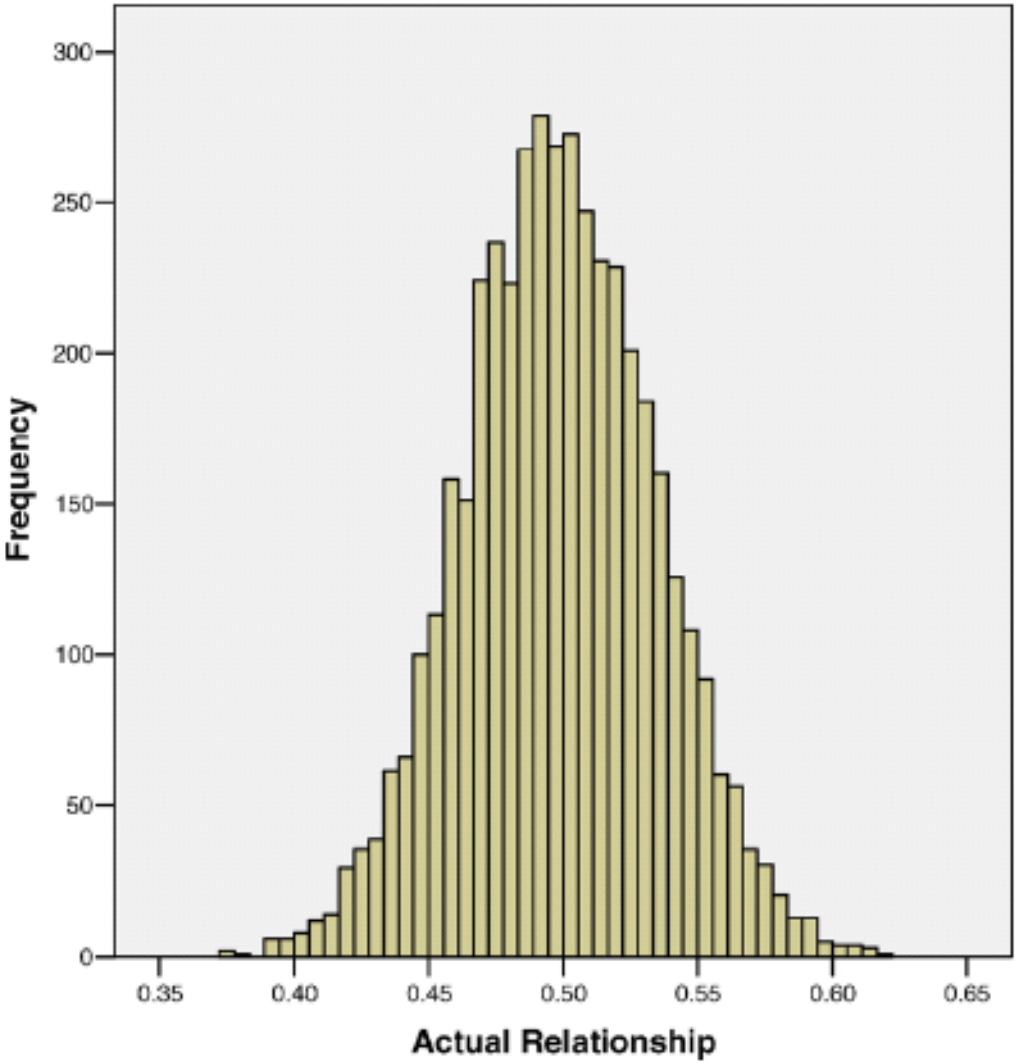


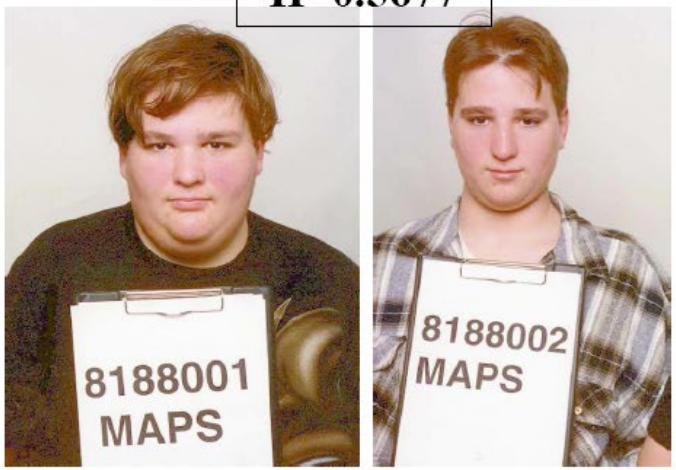

**Figure 1.** Empirical Distribution of Actual Additive Genetic Relationships of 4,401 Quasi-Independent Pairs of Full Sibs

Histogram of the genome-wide additive genetic relationships of full-sib pairs estimated from genetic markers.

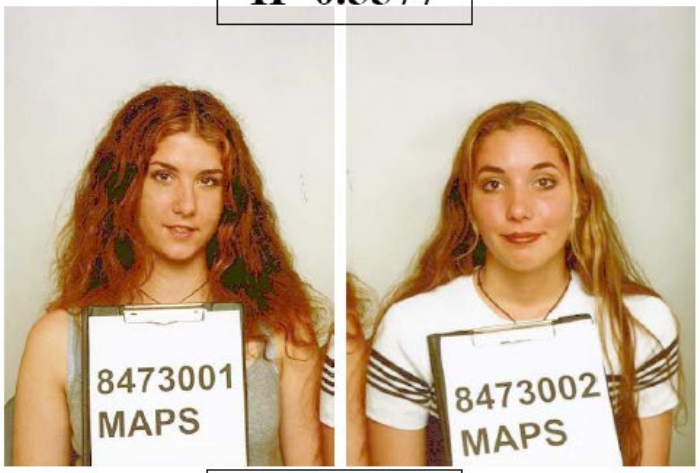
DOI: 10.1371/journal.pgen.0020041.g001

# Do these high IBD-sharing DZ twins look more similar……

**8188001,02**
**H=0.5677**




**8473001,02**
**H=0.5577**




**8300001,02**
**H=0.5719**


**8582601,02**
**H=0.5640**

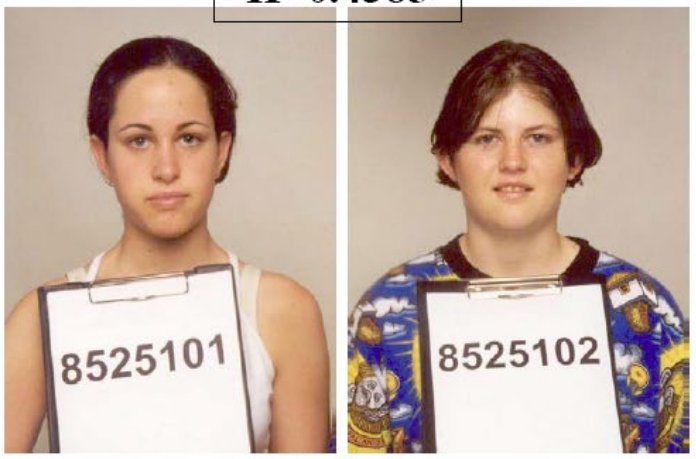
# ….than these low IBD sharing DZ twins ?

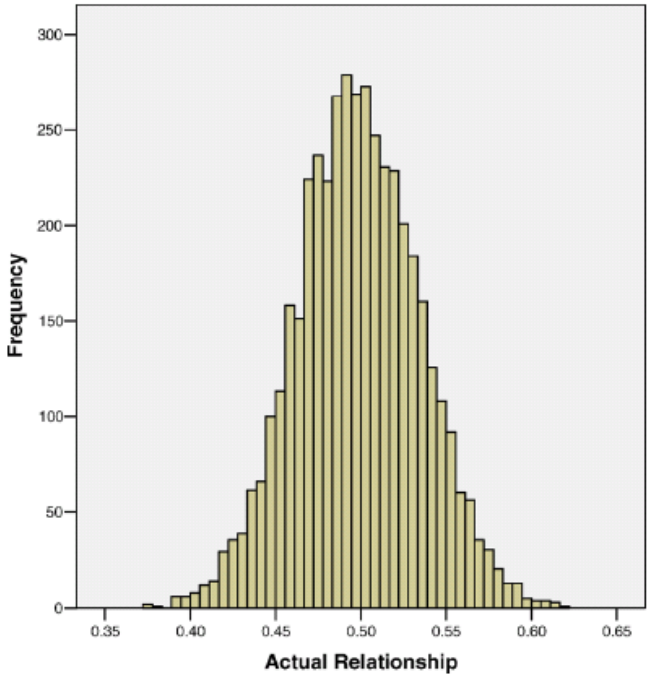
8040201,02
H=0.4351


8069101,02
H=0.4291


8315101,02
H=0.4320


8525101,02
H=0.4385



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Histogram of the genome-wide additive genetic relationships of full-sib pairs estimated from genetic markers.

DOI: 10.1371/journal.pgen.0020041.g001

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# Assumption-Free Estimation of Heritability from Genome-Wide Identity-by-Descent Sharing between Full Siblings

Peter M. Visscher*, Sarah E. Medland, Manuel A. R. Ferreira, Katherine I. Morley, Gu Zhu, Belinda K. Cornes, Grant W. Montgomery, Nicholas G. Martin

Genetic Epidemiology Group, Queensland Institute of Medical Research, Brisbane, Australia

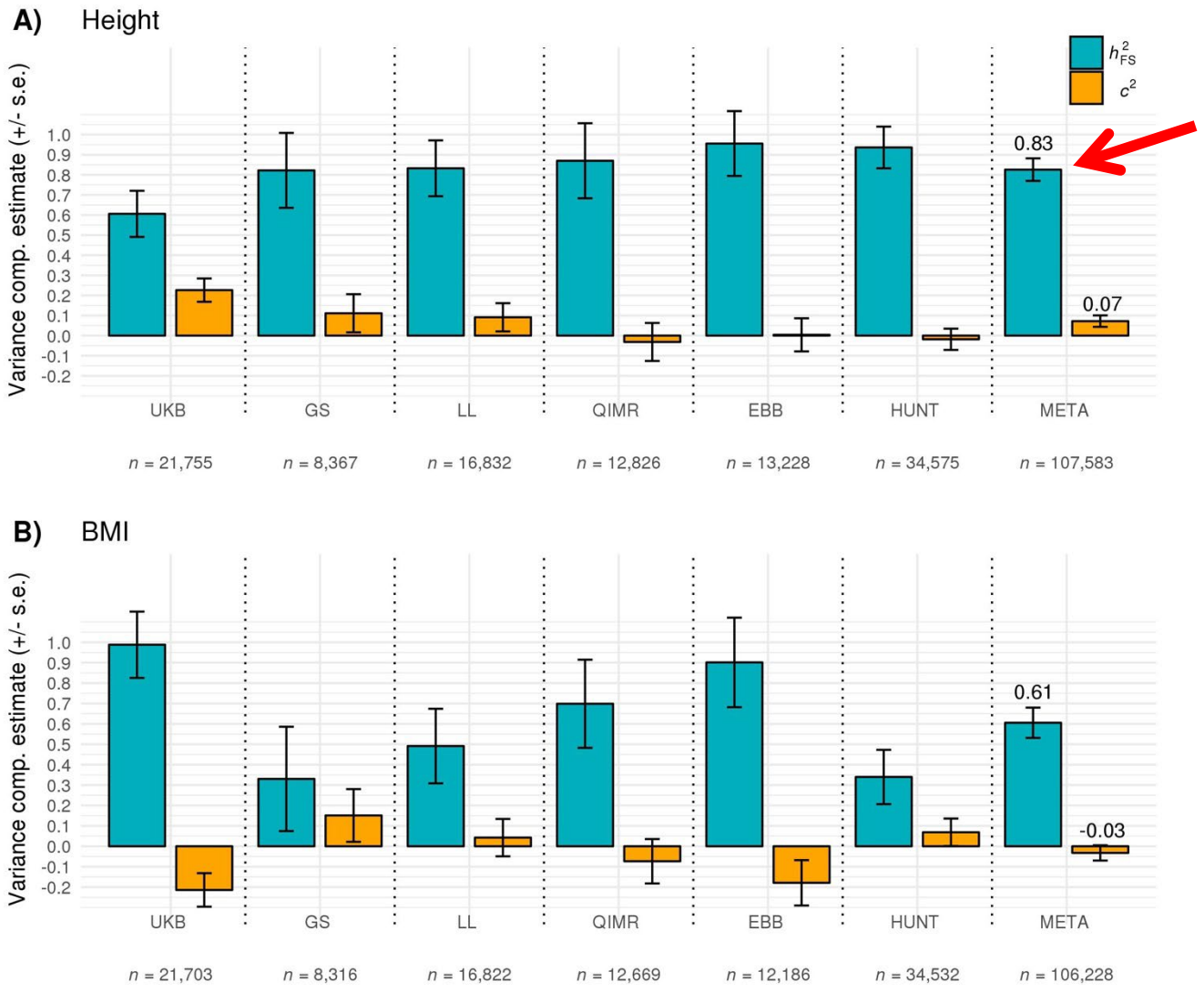
2006

From genotyped sibs alone (3375 pairs) we can estimate $h^2$ = 0.80 (.46-.85)

**Table 2.** ML Estimates of Heritability of Height from Genome-Wide IBD Sharing between Sib Pairs

| Data | Model | Estimates (95% CI) | |
|---|---|---|---|
| | | $f^2$ | $h^2$ |
| Adolescents ($n$ = 931) | FAE | 0.00 (0.00–0.43) | 0.80 (0.00–0.90) |
| | FE | 0.40 (0.34–0.45) | |
| Adults ($n$ = 2,444 ) | FAE | 0.00 (0.00–0.18) | 0.80 (0.43–0.86) |
| | FE | 0.39 (0.36–0.43) | |
| Combined ($n$ = 3,375) | FAE | 0.00 (0.00–0.17) | 0.80 (0.46–0.85) |
| | FE | 0.39 (0.36–0.42) | |

**Reconciling Linkage and Association Studies of Complex Traits Using 107,000 Sibling Pairs**




2023

Visscher, Yengo, Sidorenko et al, in press

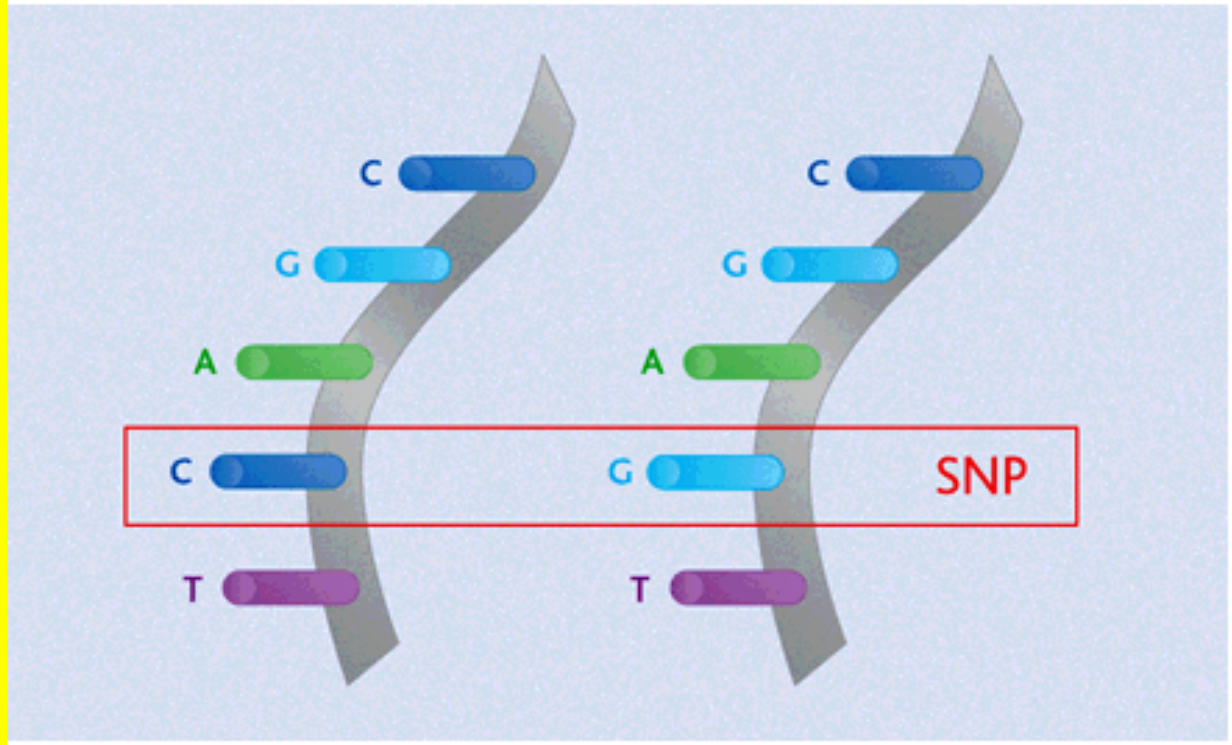
# 4 Stages of Genetic Mapping

- Are there genes influencing this trait?
  - Genetic epidemiological studies
- Where are those genes?
  - Linkage analysis
- What are those genes?
  - Association analysis
- What can we do with them ?
  - Translational medicine

# Association analysis

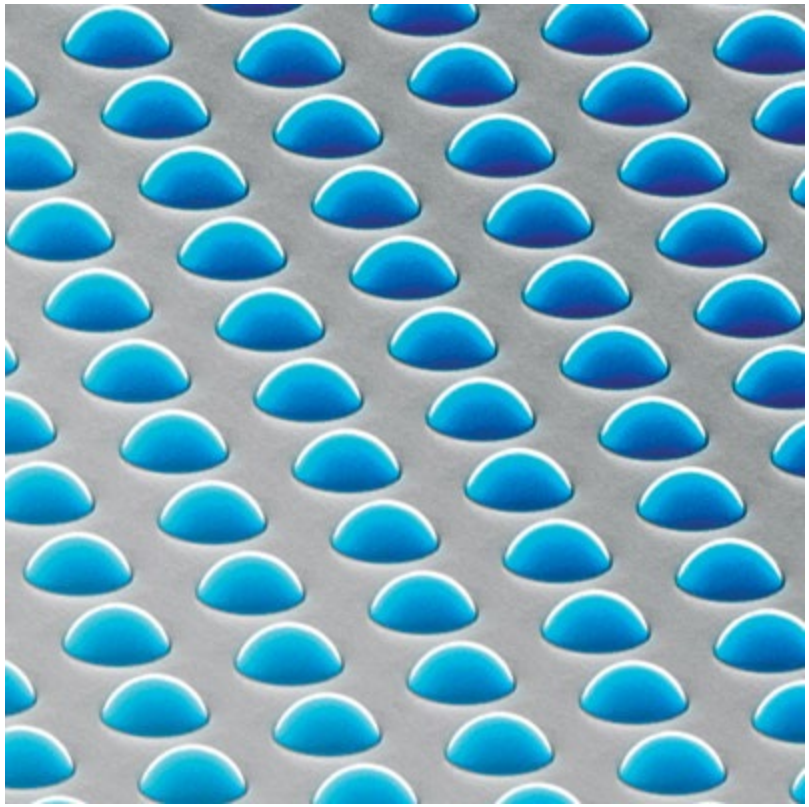
looks for correlation between specific alleles and phenotype (trait value, disease risk)

## Single Nucleotide Polymorphisms (SNPs)

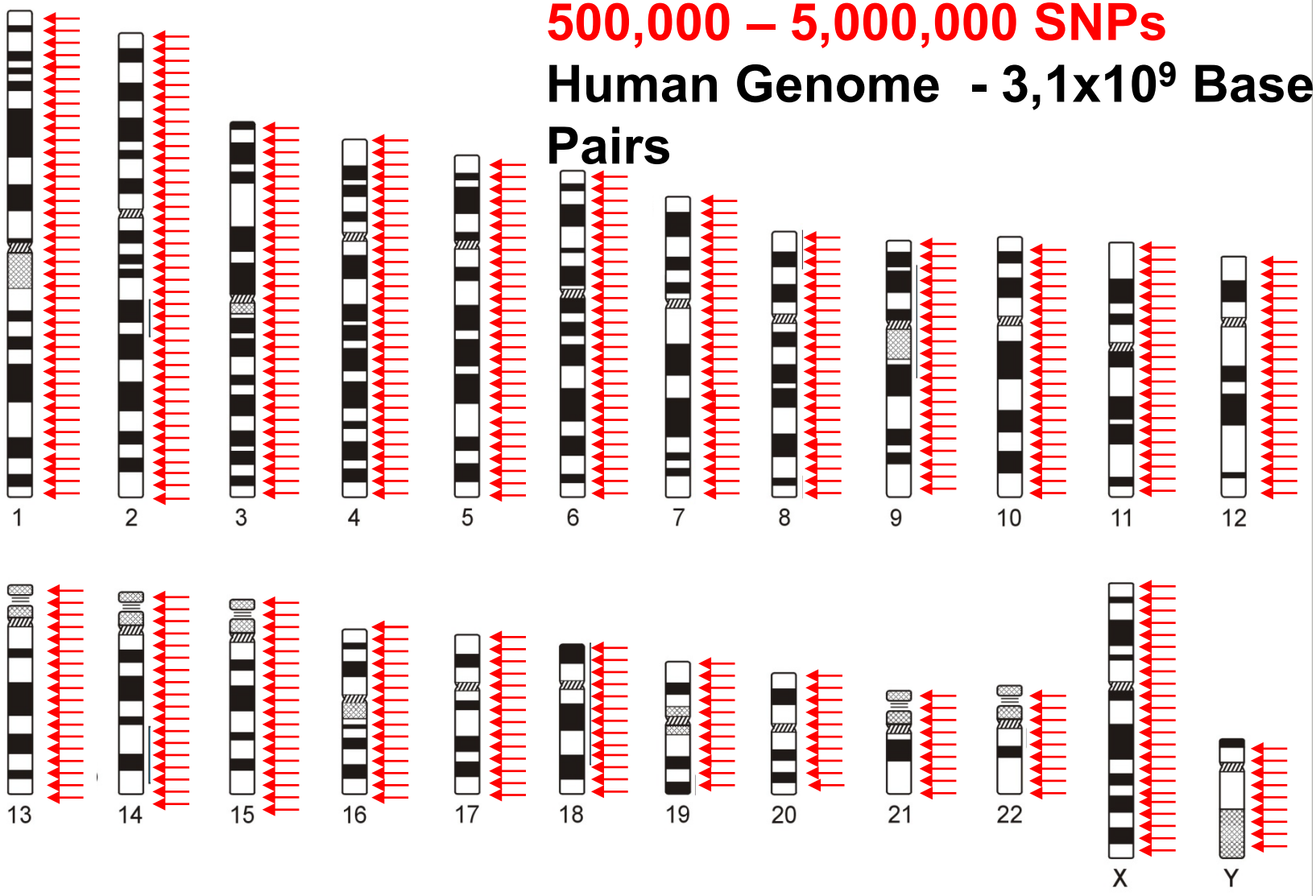



**Complex disease marker?** SNPs are single-base differences in DNA.

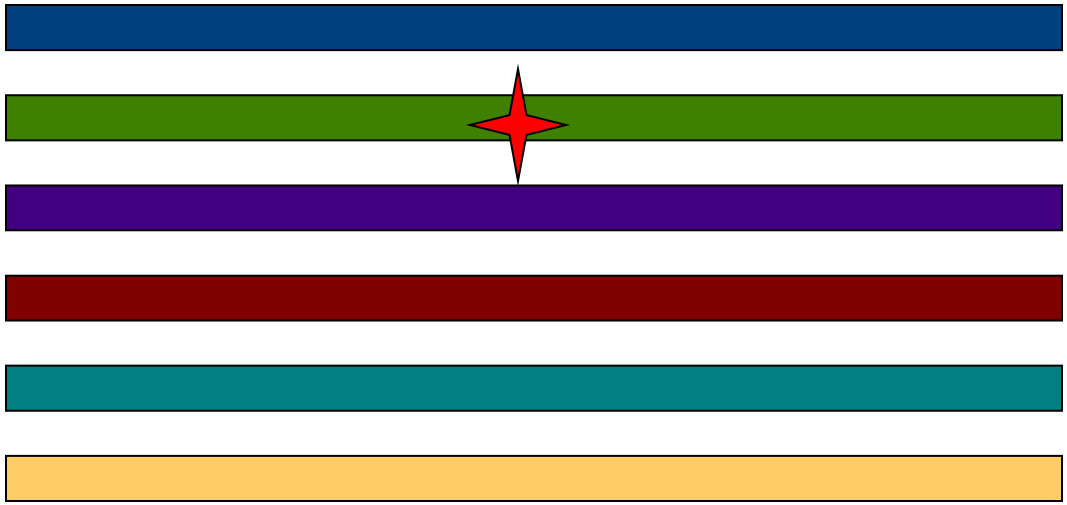
# High density SNP arrays – up to 1 million SNPs

# Genome-Wide Association Studies

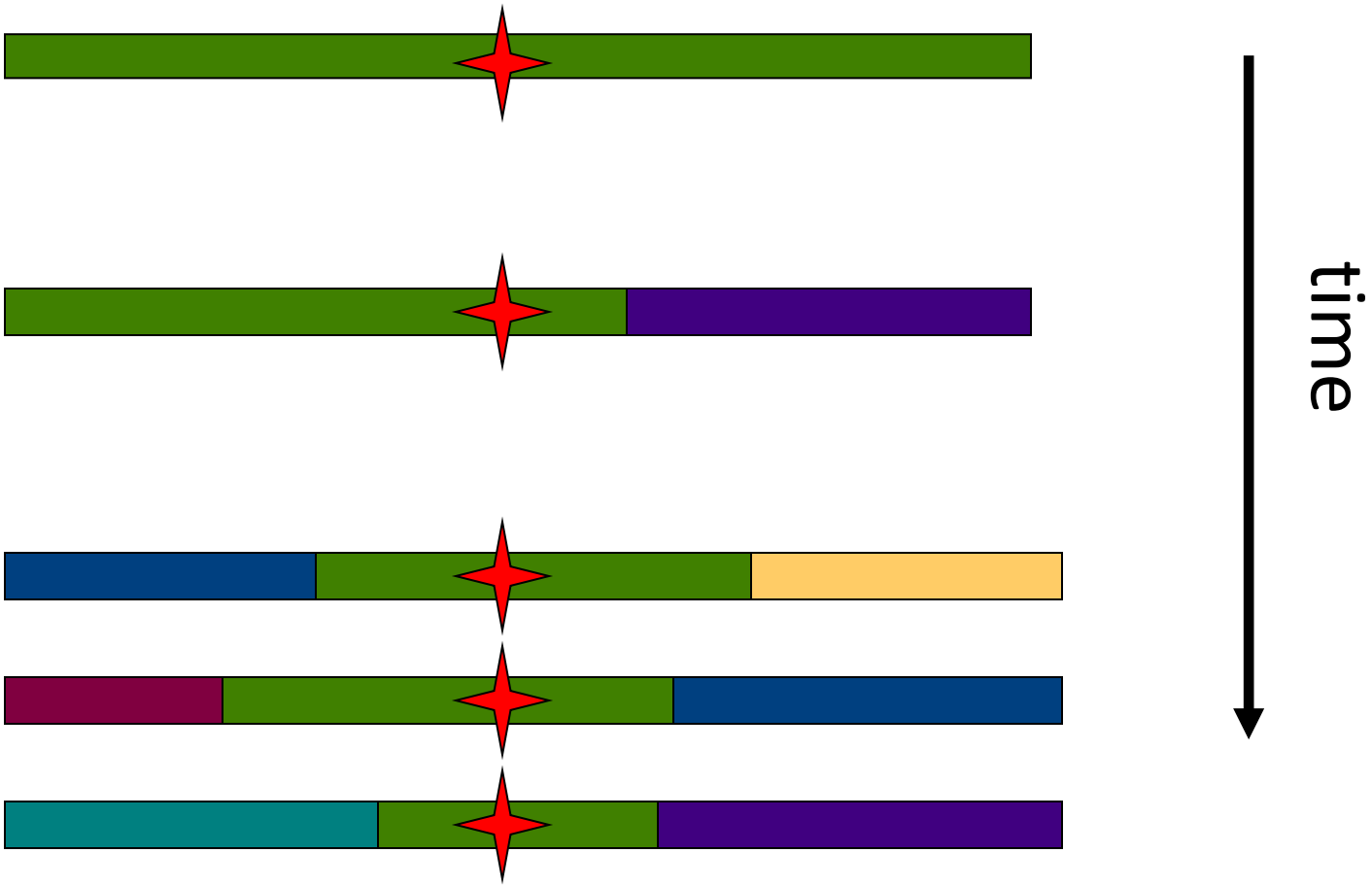


# Linkage disequilibrium

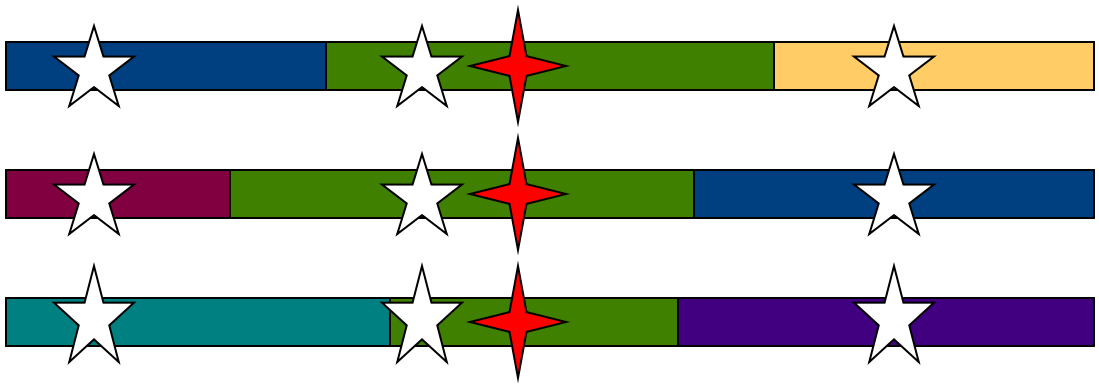


David Evans

# Linkage disequilibrium

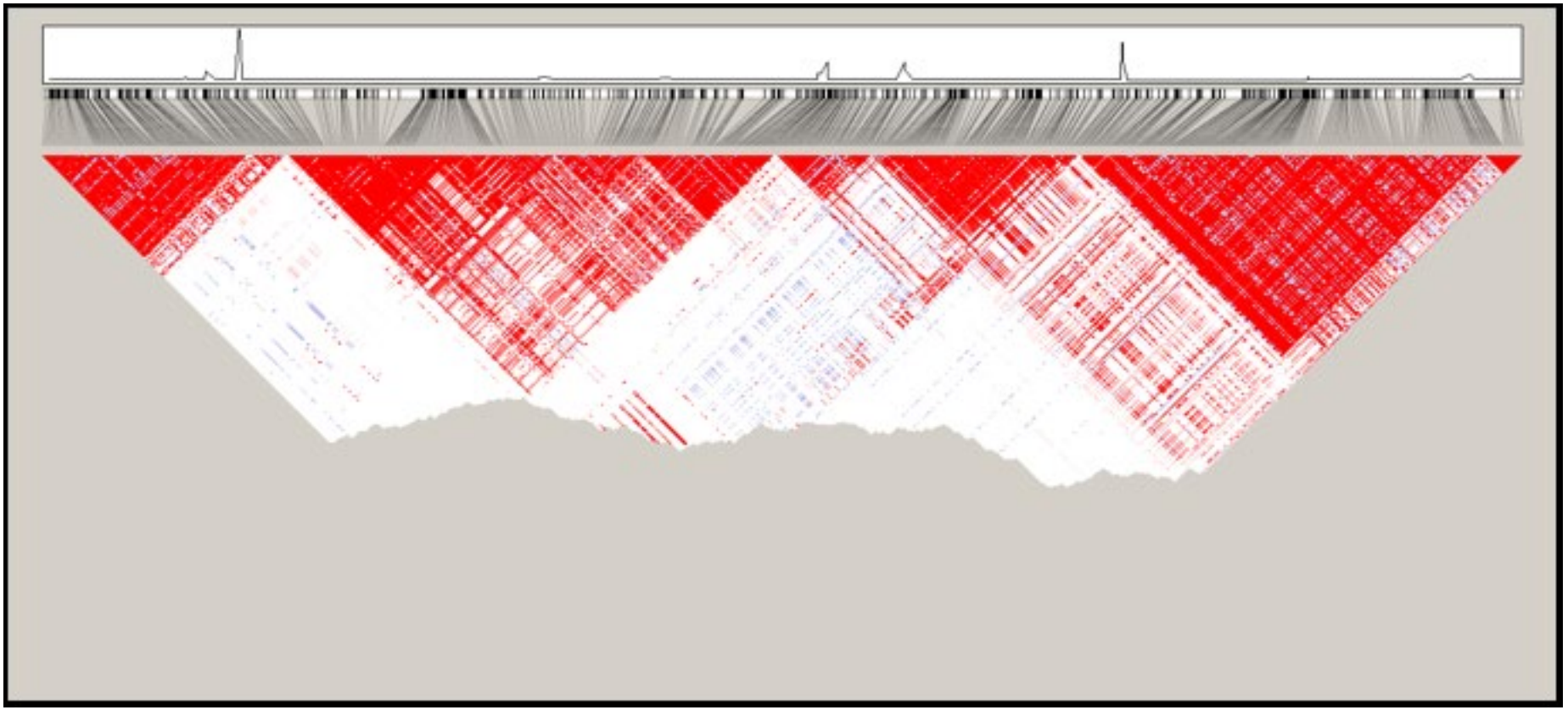


# Indirect association



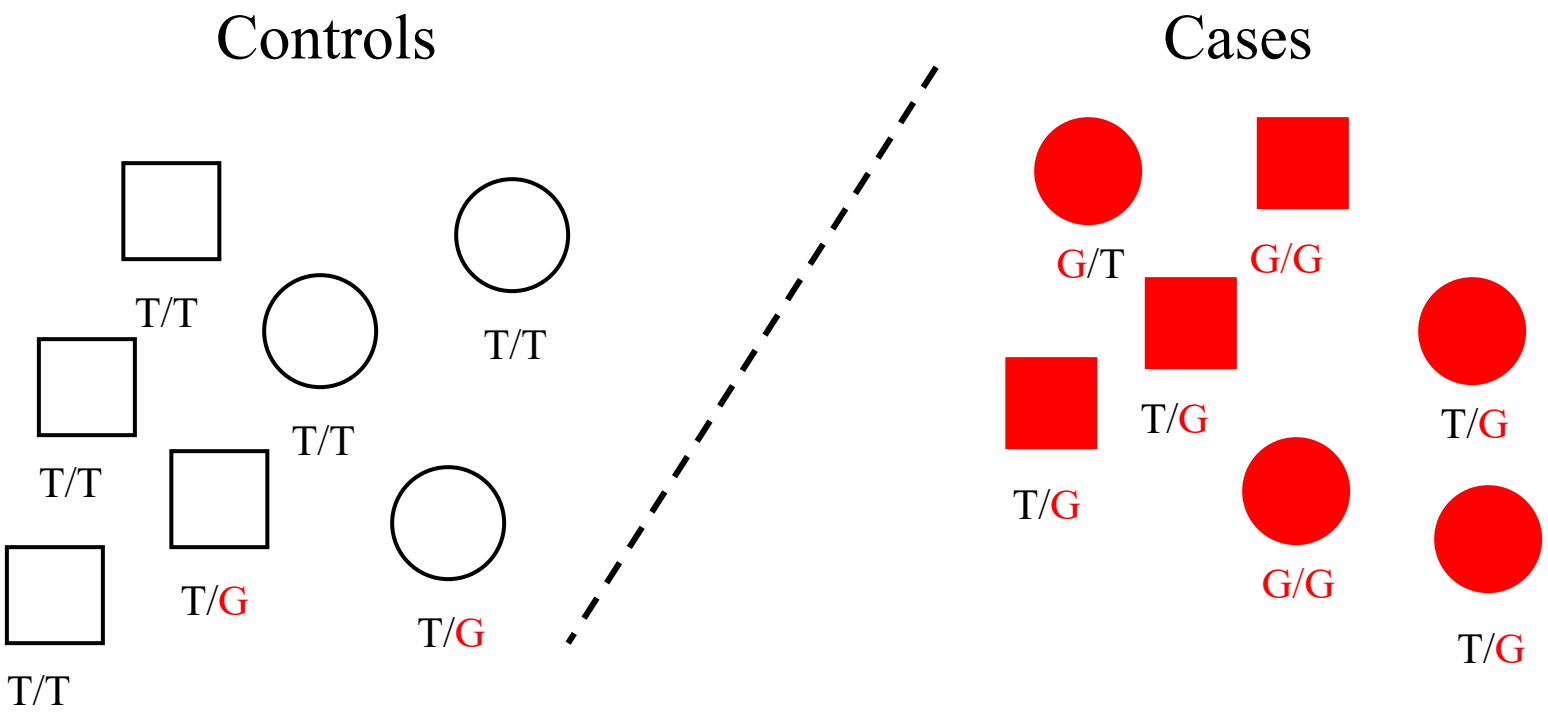
this SNP will be associated with disease

# Linkage disequilibrium blocks



Jeff Barrett

# *Genetic Case Control Study*




Allele G is ‘associated’ with disease

# Allele-based tests (case-control)

- Each individual contributes two counts to 2x2 table.
- Test of association

$$X^2 = \sum_{i=0,1} \sum_{j=A,U} \frac{\left(n_{ij} - E\left[n_{ij}\right]\right)^2}{E\left[n_{ij}\right]}$$

where

$$E\left[n_{ij}\right] = \frac{n_{i\cdot} n_{\cdot j}}{n_{\cdot\cdot}}$$

| | Cases | Controls | Total |
|---|---|---|---|
| G | $n_{1A}$ | $n_{1U}$ | $n_{1\cdot}$ |
| T | $n_{0A}$ | $n_{0U}$ | $n_{0\cdot}$ |
| Total | $n_{\cdot A}$ | $n_{\cdot U}$ | $n_{\cdot\cdot}$ |

- $X^2$ has $\chi^2$ distribution with 1 degrees of freedom under null hypothesis.

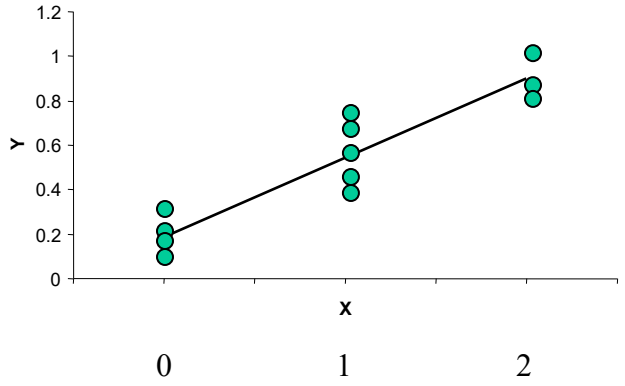
# Simple Regression Model of Association (continuous trait)

$$Y_i = \alpha + \beta X_i + e_i$$

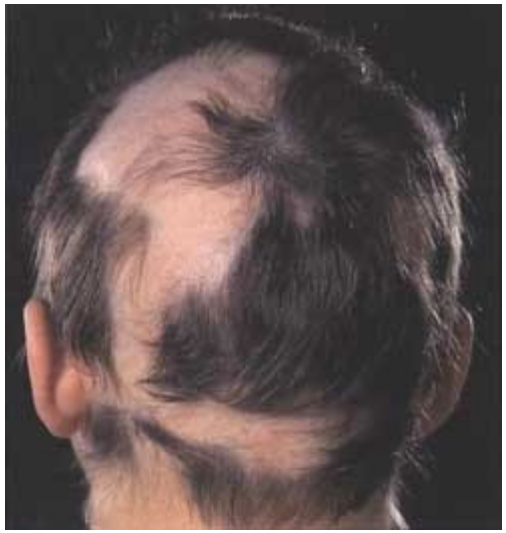
where

$Y_i =$ trait value for individual i

$X_i =$ number of 'A' alleles an individual has




Association test is whether $\beta > 0$



# Genome-wide association study in alopecia areata implicates both innate and adaptive immunity

Lynn Petukhova[1], Madeleine Duvic[2], Maria Hordinsky[3], David Norris[4], Vera Price[5], Yutaka Shimomura[1], Hyunmi Kim[1], Pallavi Singh[1], Annette Lee[6], Wei V. Chen[7], Katja C. Meyer[8], Ralf Paus[8,9], Colin A. B. Jahoda[10], Christopher I. Amos[7], Peter K. Gregersen[6] & Angela M. Christiano[1,11]

NATURE | Vol 466 | 1 July 2010

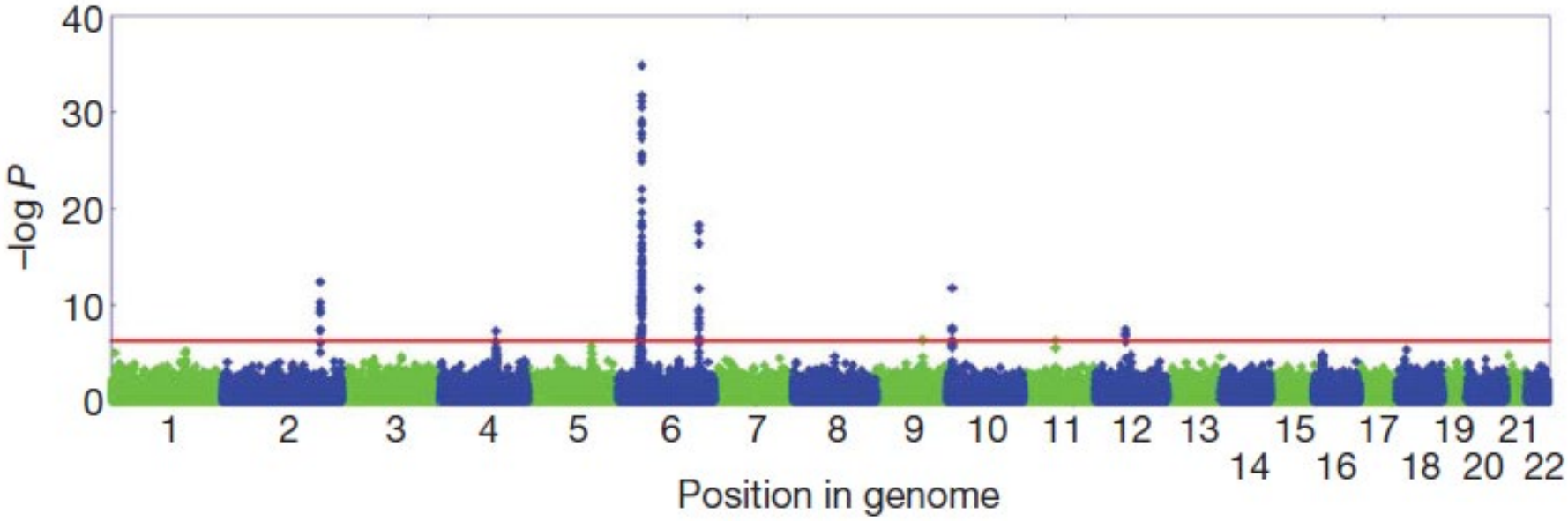
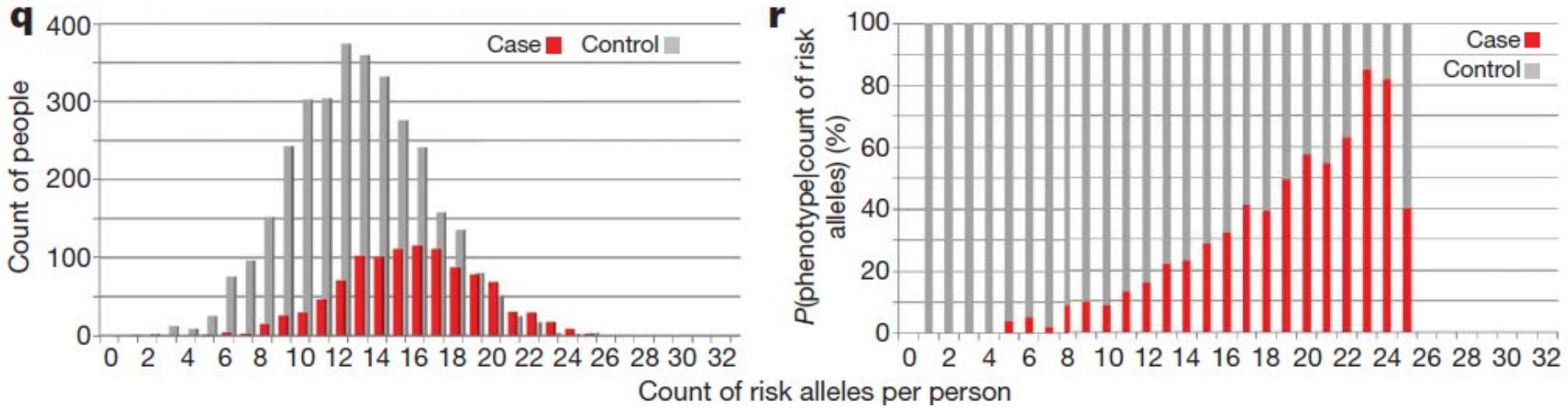


**Table 1 | Genes with significant association to AA**

| Region | Gene | Function | Strongest association (*P* value) | Maximum odds ratio | Involved in other autoimmune disease |
|---|---|---|---|---|---|
| 2q33.2 | *CTLA4* | Co-stimulatory family | $3.55 \times 10^{-13}$ | 1.44 | T1D, RA, CeD, MS, SLE, GD |
| | *ICOS* | Co-stimulatory family | $4.33 \times 10^{-8}$ | 1.32 | |
| 4q27 | *IL-21/IL-2* | T-, B- and NK-cell proliferation | $4.27 \times 10^{-8}$ | 1.34 | T1D, RA, CeD, PS |
| 6q25.1 | *ULBP6* | NKG2D activating ligand | $4.49 \times 10^{-19}$ | 1.65 | None |
| | *ULBP3* | NKG2D activating ligand | $4.43 \times 10^{-17}$ | 1.52 | None |
| 9q31.1 | *STX17* | Premature hair greying | $3.60 \times 10^{-7}$ | 1.33 | None |
| 10p15.1 | *IL-2RA* | T-cell proliferation | $1.74 \times 10^{-12}$ | 1.41 | T1D, MS, GD, GV |
| 11q13 | *PRDX5* | Antioxidant enzyme | $4.14 \times 10^{-7}$ | 1.33 | MS |
| 12q13 | *Eos (IKZF4)* | $T_{reg}$ transcription factor | $3.21 \times 10^{-8}$ | 1.34 | T1D, SLE |
| | *ERBB3* | Epidermal growth factor receptor | $1.27 \times 10^{-7}$ | 1.34 | T1D, SLE |
| 6p21.32 | *MICA* | NKG2D activating ligand | $1.19 \times 10^{-7}$ | 1.44 | T1D, RA, CeD, UC, PS, SLE |
| (HLA) | *NOTCH4* | Haematopoietic differentiation | $1.03 \times 10^{-8}$ | 1.61 | T1D, RA, MS |
| | *C6orf10* | Unknown | $1.45 \times 10^{-16}$ | 2.36 | T1D, RA, PS, GV |
| | *BTNL2* | Co-stimulatory family | $2.11 \times 10^{-26}$ | 2.70 | T1D, RA, UC, CD, SLE, MS, GV |
| | *HLA-DRA* | Antigen presentation | $2.93 \times 10^{-31}$ | 2.62 | T1D, RA, CeD, MS, GV |
| | *HLA-DQA1* | Antigen presentation | $3.60 \times 10^{-17}$ | 2.15 | T1D, RA, CeD, MS, SLE, PS, CD, UC, GD |
| | *HLA-DQA2* | Antigen presentation | $1.38 \times 10^{-35}$ | 5.43 | T1D, RA |
| | *HLA-DQB2* | Antigen presentation | $1.73 \times 10^{-13}$ | 1.60 | RA |

Each of the eight regions implicated in our study contains multiple significant SNPs, which are detailed in Supplementary Tables 1 and 2. Here we display candidate genes within the implicated regions, and include the *P* value of the most significant SNP, and the odds ratio for the SNP with the largest effect estimate. Diseases are listed for which a GWAS or previous candidate gene study identified the same region (http://www.genome.gov/gwastudies, http://www.cdc.gov/genomics/hugenet): Crohn's disease (CD), celiac disease (CeD), Graves disease (GD), generalized vitiligo (GV), multiple sclerosis (MS), psoriasis (PS), rheumatoid arthritis (RA), system lupus erythematosus (SLE), type I diabetes (T1D), and ulcerative colitis (UC).



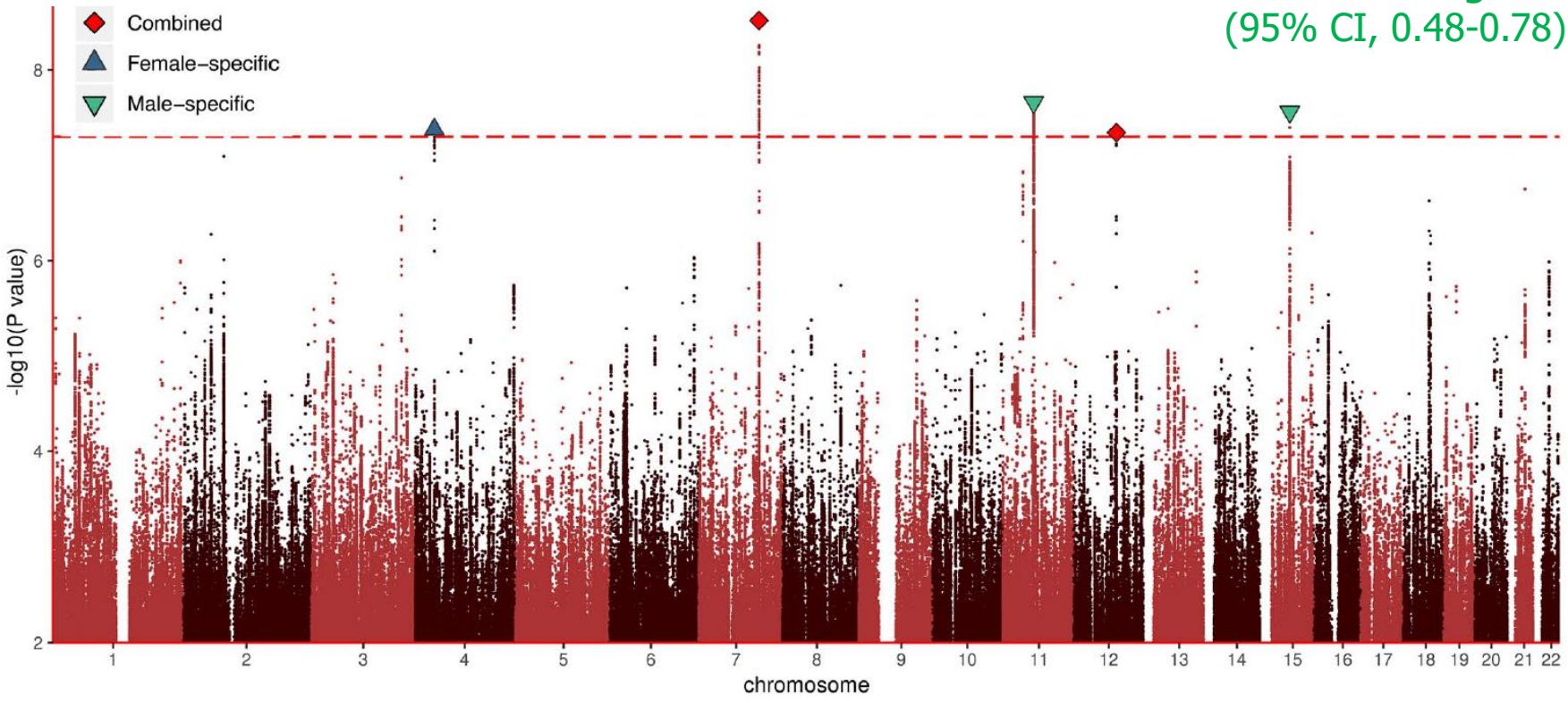
# Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior

**Total n = 477,522 (26,827 reporting same-sex sexual behavior)**

**Andrea Ganna[1,2,3,4]*, Karin J. H. Verweij[5]*, Michel G. Nivard[6], Robert Maier[1,2,3], Robbee Wedow[1,3,7,8,9,10,11], Alexander S. Busch[12,13,14], Abdel Abdellaoui[5], Shengru Guo[15], J. Fah Sathirapongsasuti[16], 23andMe Research Team[16], Paul Lichtenstein[4], Sebastian Lundström[17], Niklas Långström[4], Adam Auton[16], Kathleen Mullan Harris[18,19], Gary W. Beecham[15], Eden R. Martin[15], Alan R. Sanders[20,21], John R. B. Perry[12]†, Benjamin M. Neale[1,2,3]†, Brendan P. Zietsch[22]†‡**

GCTA $h^2$ = 32.4%
(95% CI 10.6 - 54.3)

Across sex Rg = 0.63
(95% CI, 0.48-0.78)



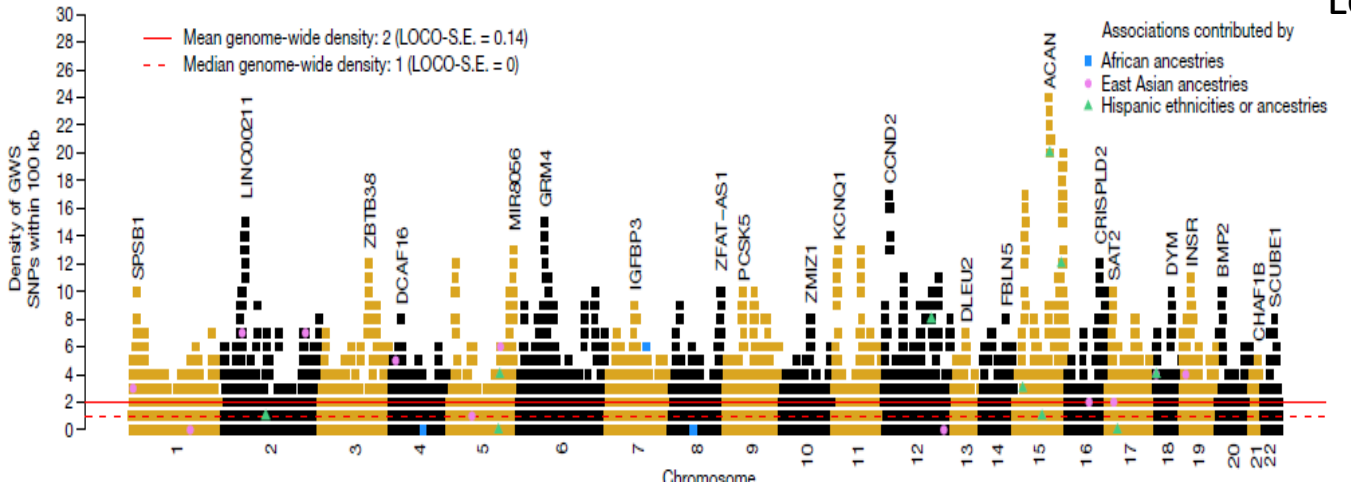

Ganna *et al.*, *Science* **365**, 882 (2019) 30 August 2019

# A saturated map of common genetic variants associated with human height

Nature | Vol 610 | 27 October 2022

Loic Yengo, UQ

**N = 5,314,291 !!**




- GWAS of 5.4 million individuals of diverse ancestries
  ➡ 12,111 independent common SNPs gw significant

- Account for **45% of phenotypic variance** in Europeans but only around 14–24% in other ancestries

- Reduced prediction accuracy likely due to ancestry differences in LD and MAF

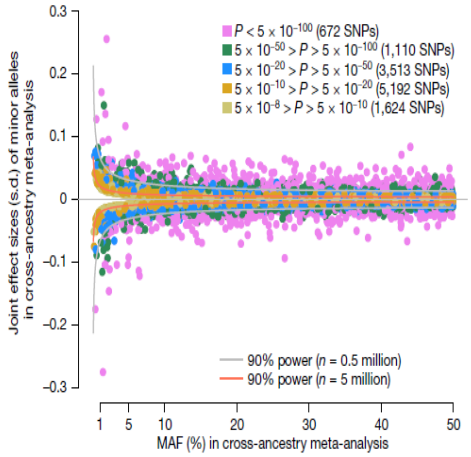


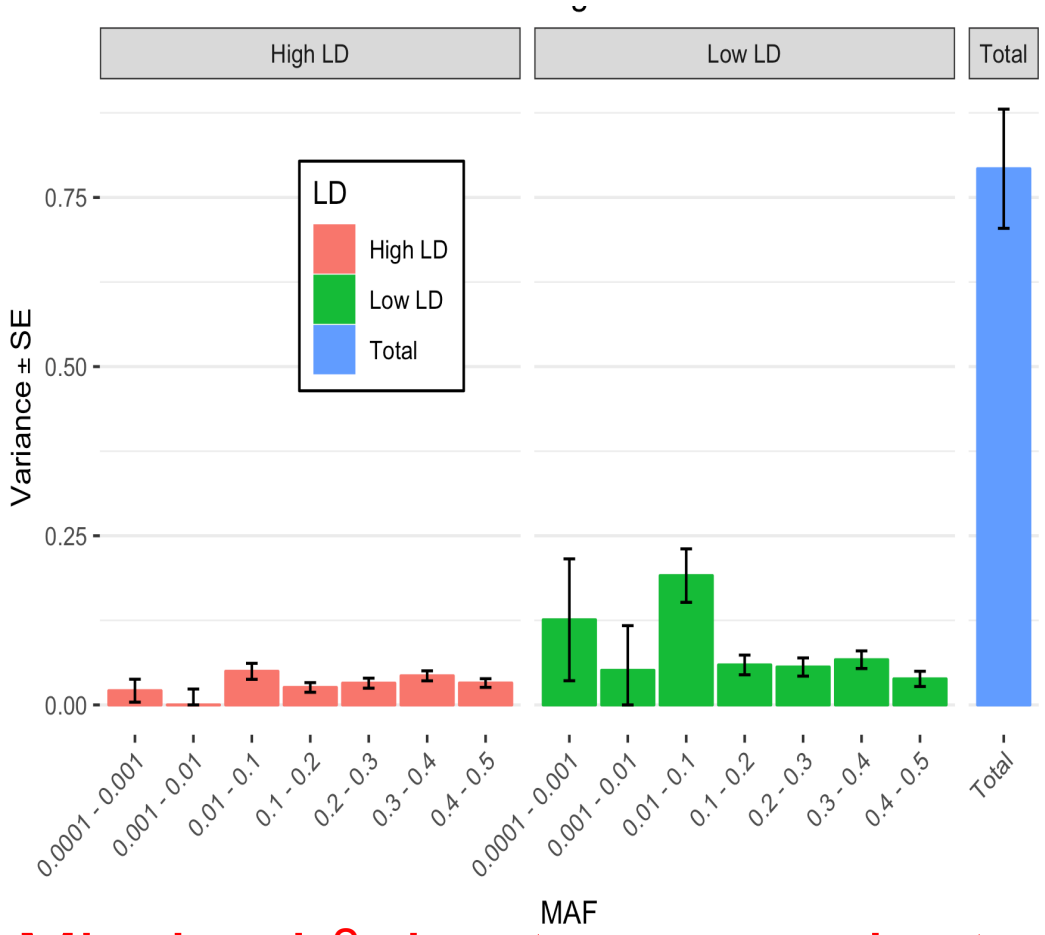

Fig. 1 | Relationship between frequency and estimated effect sizes of minor

What about the other

80 – 45 = 35%

“missing heritability” ?

# Using whole-genome sequence WGS data to recover the pedigree heritability?



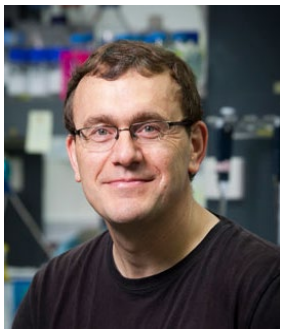

Missing $h^2$ due to rare variants of large effect in low LD with array SNPs

Estimates using 20PCs as fixed effec

- Height: $h^2_{WGS} = 0.79\ (0.09)$

Estimate close to pedigree estimate

Large role for low LD and low MAF variants



Peter Visscher

Pierrick Wainschtein

Nat Genet. 2022 March ; 54(3): 263

# Ways to increase power

Imputation

# Imputation

```
a g a g t t g a g g g a a c c t g a g a a
t g a g a c g a g g g a a a t t g a g a c
t g c g a c g g t g a t t c t c c a g a c
a g c g a c g a t g g t a c t t g a t c a
t a a g t t a g t a a t t c c c g a g c a
t g c a a t g a g g g a a a t t g t t a a
a g a g a c g g g g g a a a t t c t g c c
```

```
  g       a     g   g       t     a     a
  g       c     t   a       t     t     c

  a       t     g   g       t     t     a
  g       c     g   g       c     a     a

  g       c     t   g       t     t     c
  g       c     g   g       c     a     a

  g       t     g   g       t     a     c
  a       t     t   a       c     a     a
```

**Reference haplotypes via sequencing studies**

eg. 1000 Genomes Project

Slide from Jonathan Marchini

# Imputation

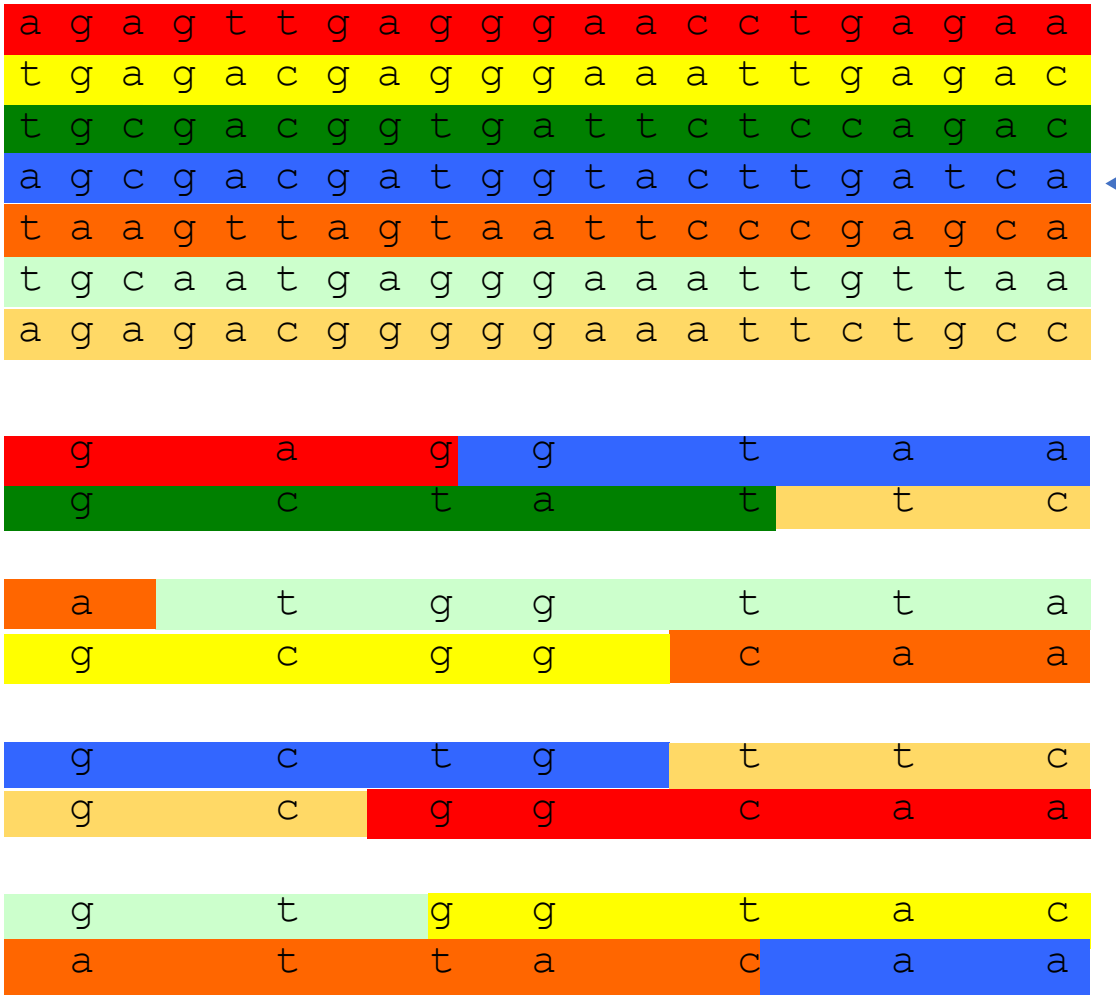
```
a g a g t t g a g g g a a c c t g a g a a
t g a g a c g a g g g a a a t t g a g a c
t g c g a c g g t g a t t c t c c a g a c
a g c g a c g a t g g t a c t t g a t c a
t a a g t t a g t a a t t c c c g a g c a
t g c a a t g a g g g a a a t t g t t a a
a g a g a c g g g g g a a a t t c t g c c

? g ? ? ? a ? ? g ? g ? ? ? t ? ? a ? ? a
? g ? ? ? c ? ? t ? a ? ? ? t ? ? t ? ? c

? a ? ? ? t ? ? g ? g ? ? ? t ? ? t ? ? a
? g ? ? ? c ? ? g ? g ? ? ? c ? ? a ? ? a

? g ? ? ? c ? ? t ? g ? ? ? t ? ? t ? ? c
? g ? ? ? c ? ? g ? g ? ? ? c ? ? a ? ? a

? g ? ? ? t ? ? g ? g ? ? ? t ? ? a ? ? c
? a ? ? ? t ? ? t ? a ? ? ? c ? ? a ? ? a
```

**Reference haplotypes via sequencing studies**

eg. 1000 Genomes Project

Slide from Jonathan Marchini

# Imputation




**Reference haplotypes via sequencing studies**

eg. 1000 Genomes Project

**Imputation of unobserved alleles via matching of shared haplotypes**

Slide from Jonathan Marchini

# Imputation

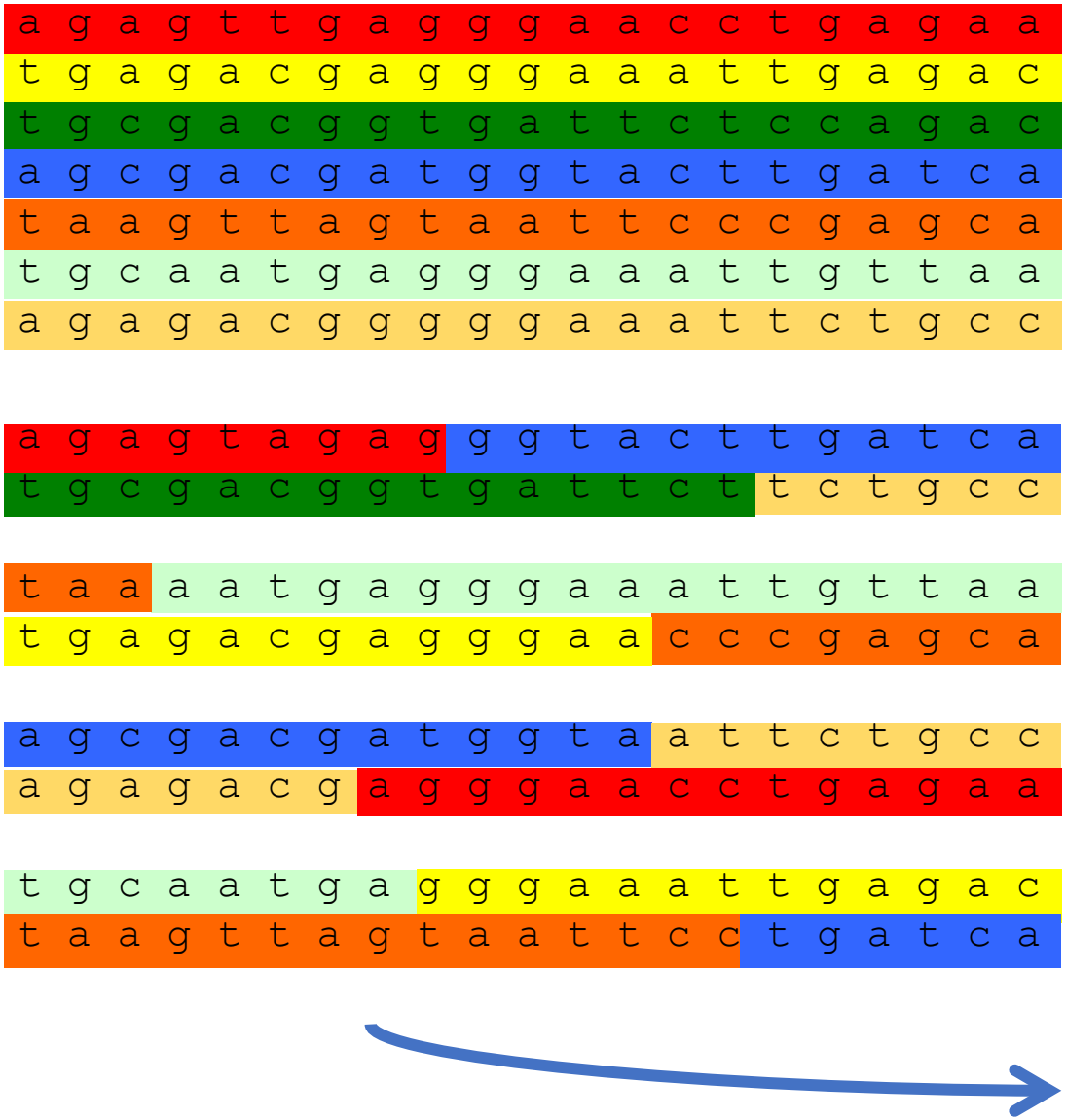

**Reference haplotypes via sequencing studies**

eg. 1000 Genomes Project

**Imputation of unobserved alleles via matching of shared haplotypes**

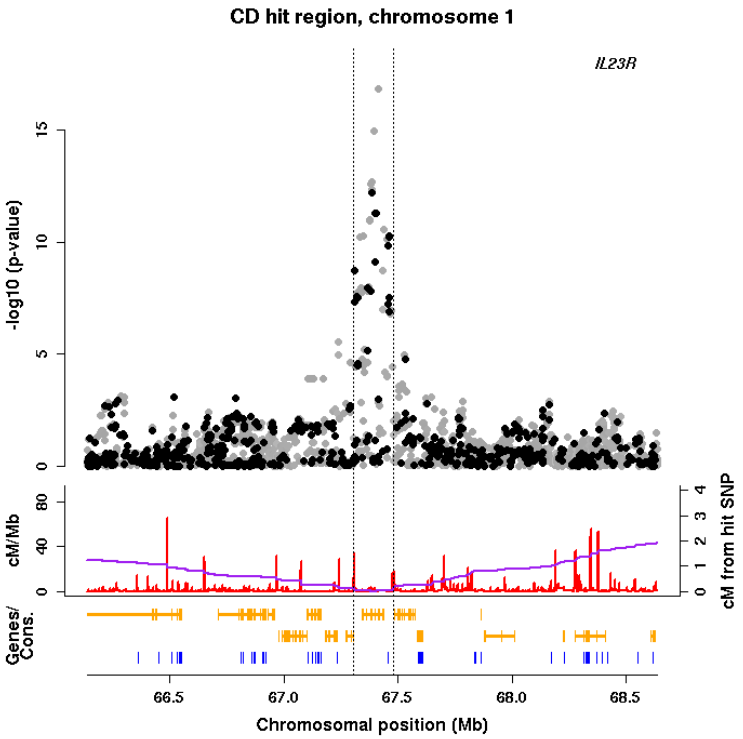
Slide from Jonathan Marchini

# Imputation




## GWAS of imputed genotypes

- Increased power
- Better resolution
- Facilitates meta-analysis

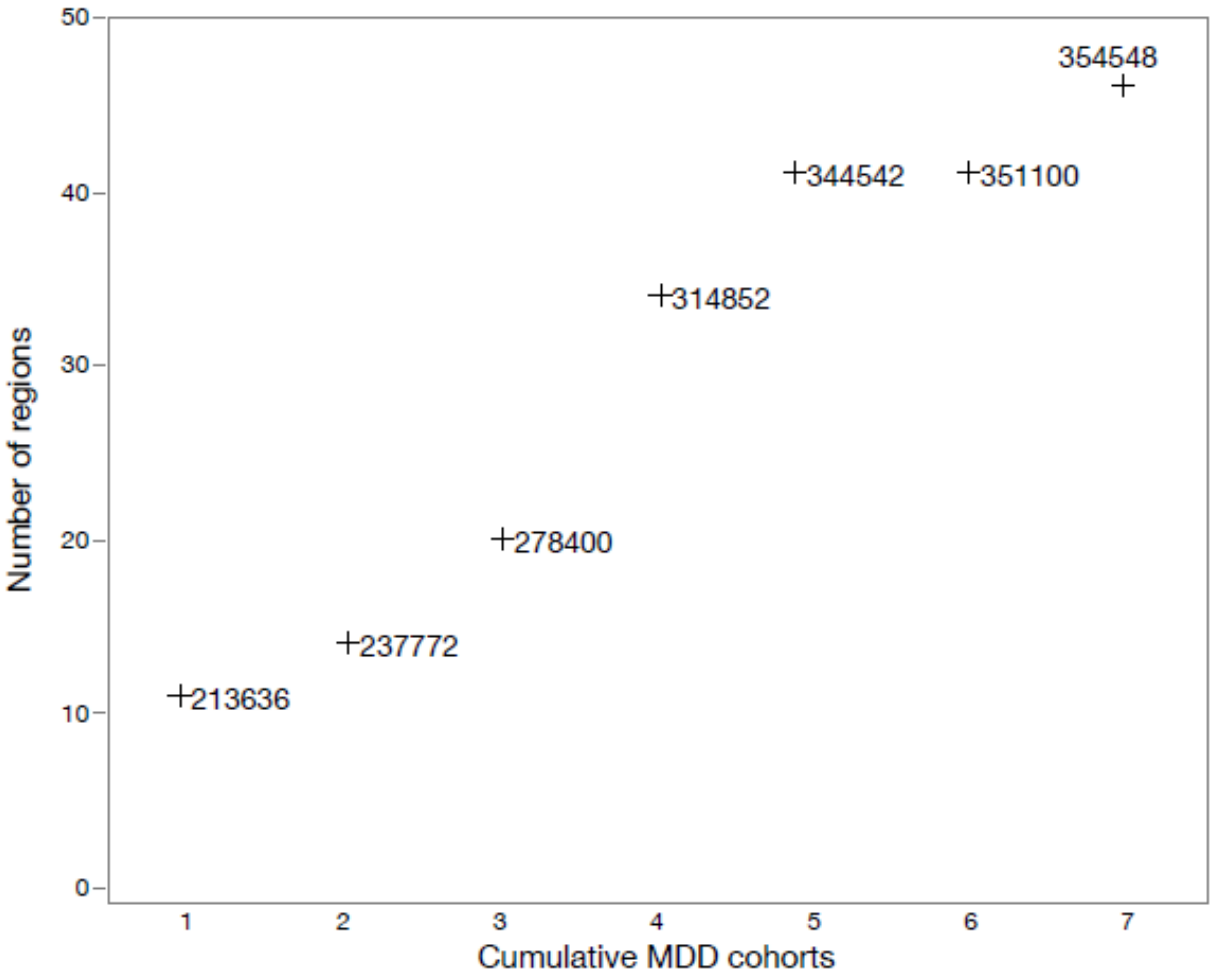



Slide from Jonathan Marchini

# Ways to increase power

Increase sample size

# Larger samples lead to more SNP discovery

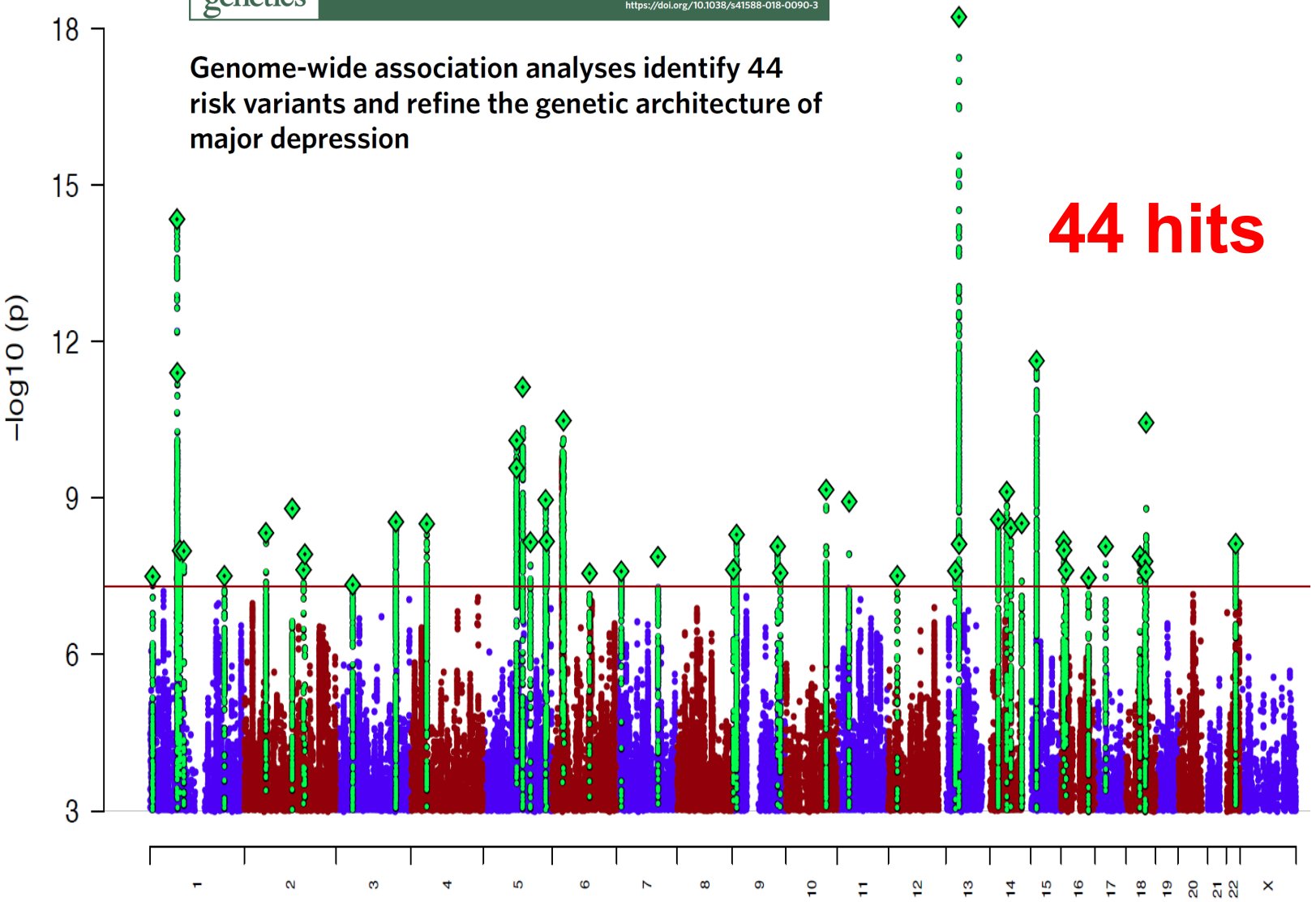



*Results of GWA meta-analysis of seven cohorts for MDD. (a) Relation between adding cohorts and number of genome-wide significant genomic regions. Beginning with the largest cohort (1), added the next largest cohort (2) until all cohorts were included (7). The number next to each point shows the total effective sample size.*

# Depression : 135K MDD Cases and 345K Controls

nature genetics
ARTICLES
https://doi.org/10.1038/s41588-018-0090-3

Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression



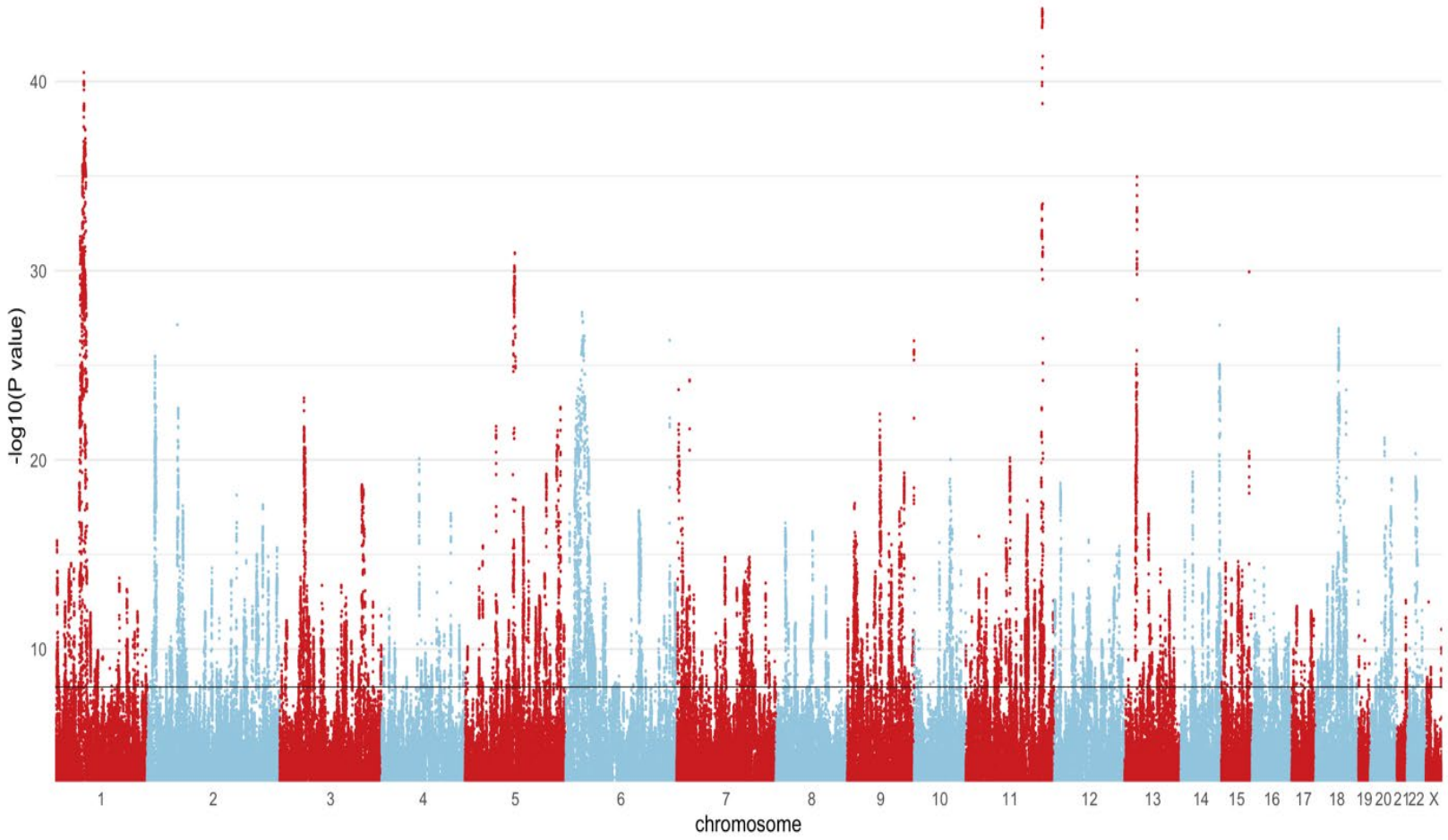

**44 hits**

Nat Genet. 2018 May;50(5):635-637.

Led by Naomi Wray

**PGC MDD3 GWAS meta-analysis: 525,197 MD cases and 3,362,335 controls**

**SNPs = 713 regions (500kb) = 510 (without AGDS = 460)**




# NEWS & VIEWS

HUMAN GENOMICS

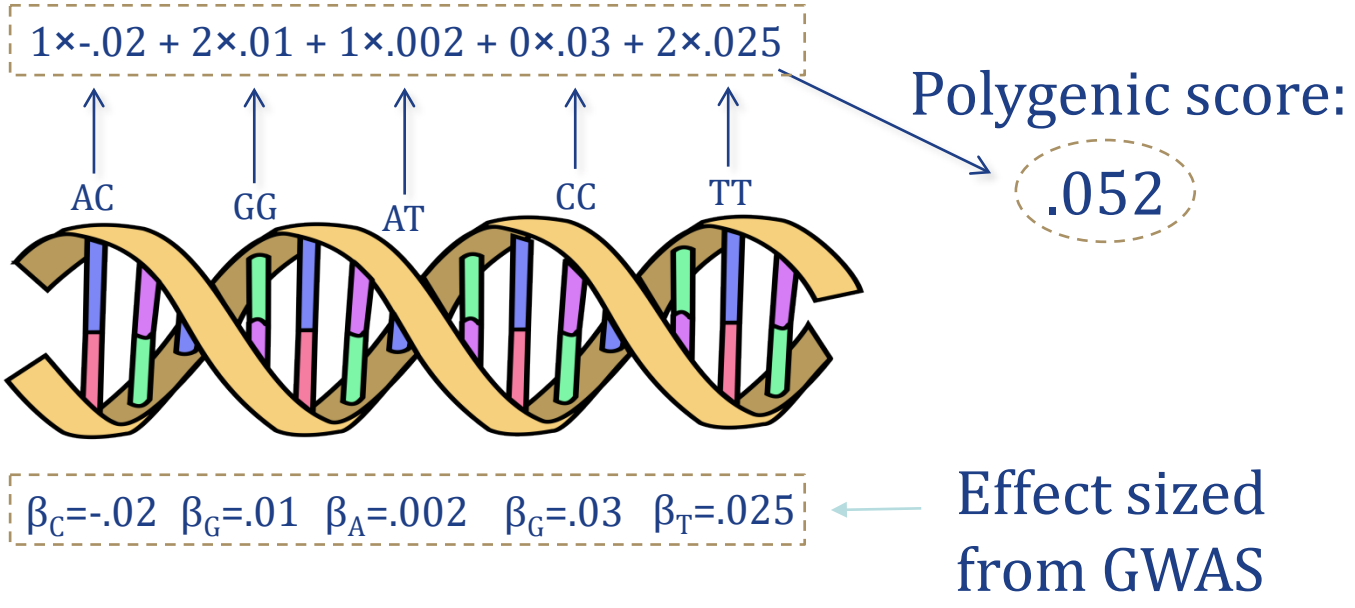
## Biobank for the masses

**UK Biobank contains a wealth of data on genetics, health and more from 500,000 participants.**

NATURE | VOL 562 | 11 OCTOBER 2018

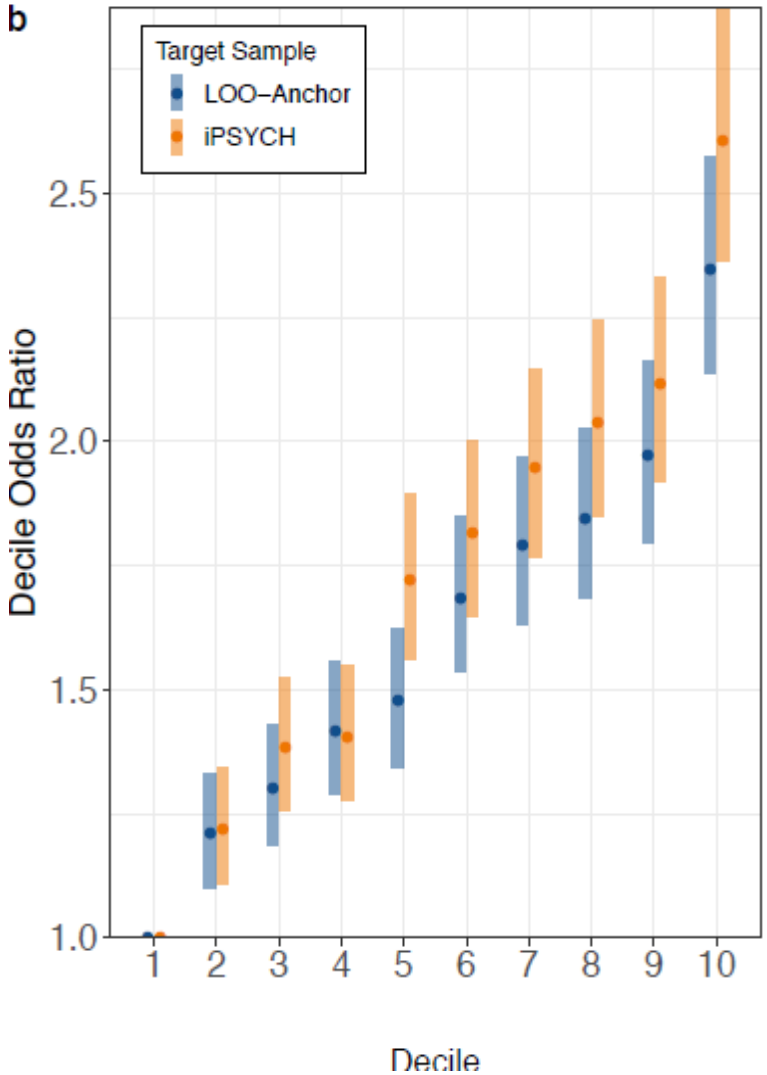
# Polygenic Risk Scores

Polygenic Risk Scores capture (part of) someone's genetic "risk" by summing all risk alleles weighted by the effect sizes estimated in a Genome-Wide Association Study (GWAS)




Wray, Visscher, Goddard, 2007 – Oz!

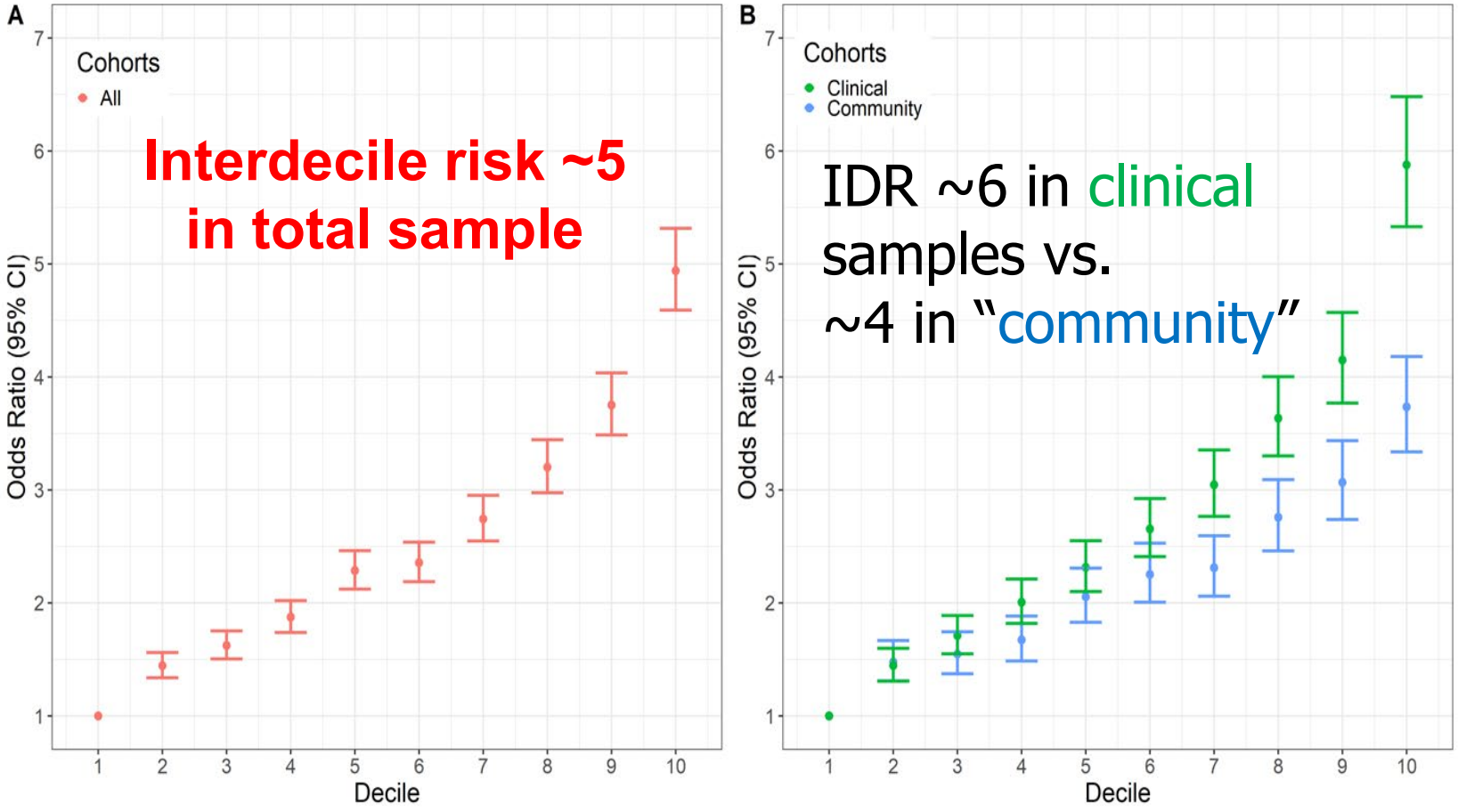
# MDD2 Polygenic Risk Score predicts risk in independent samples




*Odd ratios of MDD per PRS decile relative to the first decile for iPSYCH and anchor cohorts.*

**Interdecile risk ~2.5**

# MDD3: MD risk in outsamples by PGS decile



# Ways to increase power

Refine the phenotype

**Human Reproduction, Vol.25, No.6 pp. 1569–1580, 2010**
Advanced Access publication on April 8, 2010 doi:10.1093/humrep/deq084

human reproduction

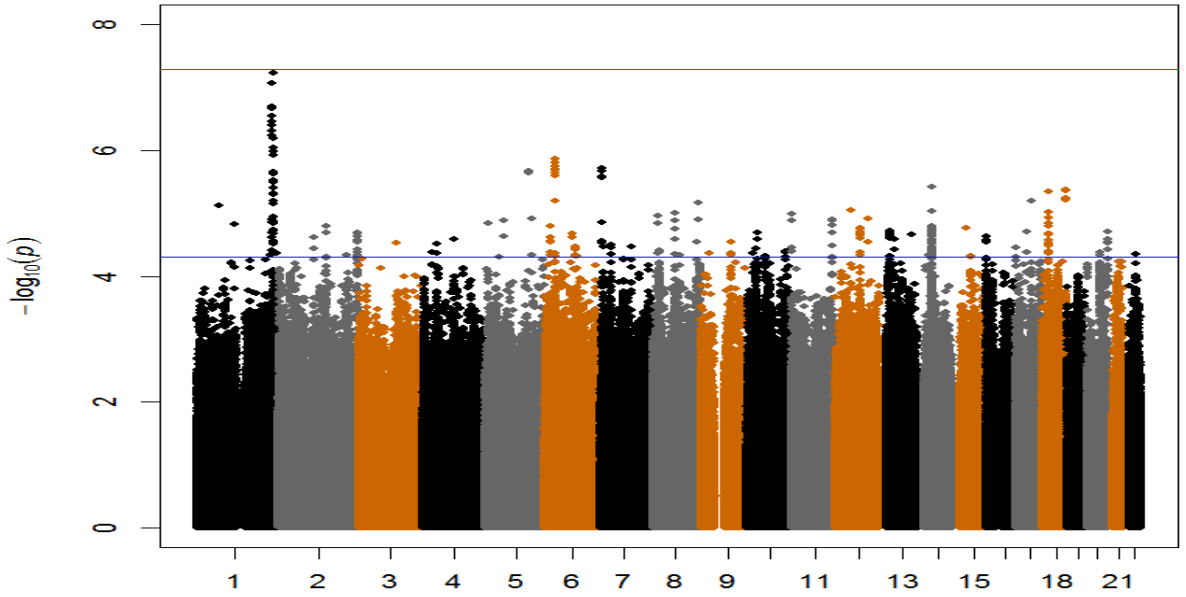
ORIGINAL ARTICLE *Reproductive genetics*

# A genome wide linkage scan for dizygotic twinning in 525 families of mothers of dizygotic twins

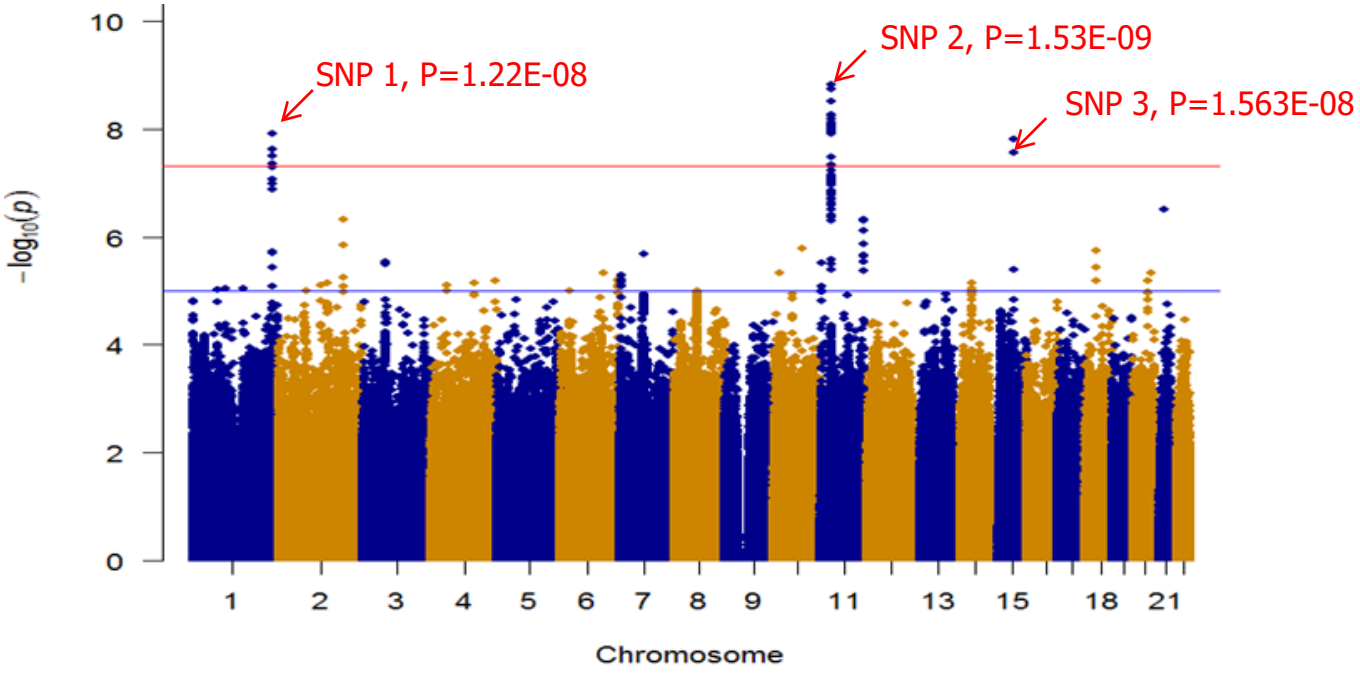
**Jodie N. Painter[1,*], Gonneke Willemsen[2], Dale Nyholt[1], Chantal Hoekstra[2], David L. Duffy[1], Anjali K. Henders[1], Leanne Wallace[1], Sue Healey[1], Lisa A. Cannon-Albright[3], Mark Skolnick[3], Nicholas G. Martin[1], Dorret I. Boomsma[2,†], and Grant W. Montgomery[1,†]**

# The importance of accurate phenotyping: GWAS for Being a Mother of DZ Twins - Before and after removing mothers who had used assisted reproductive technology

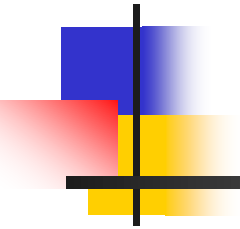
ART +




ART --




Hamdi Mbarek



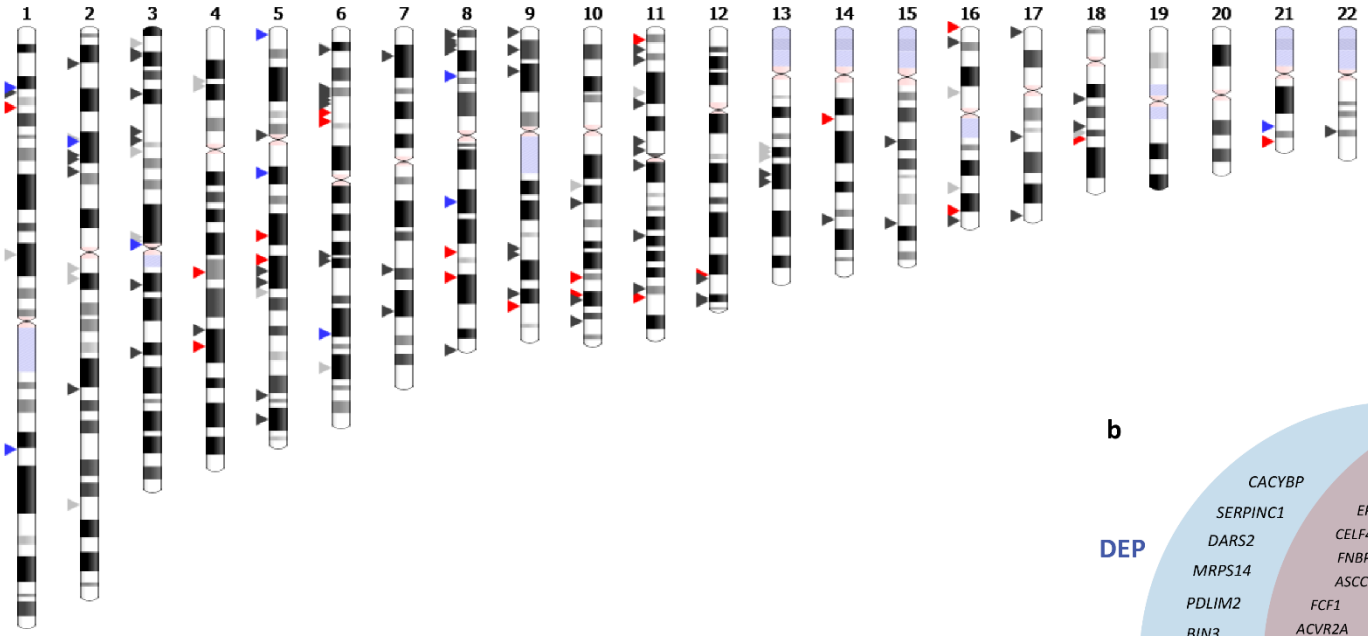
# Ways to increase power

Combine related phenotypes

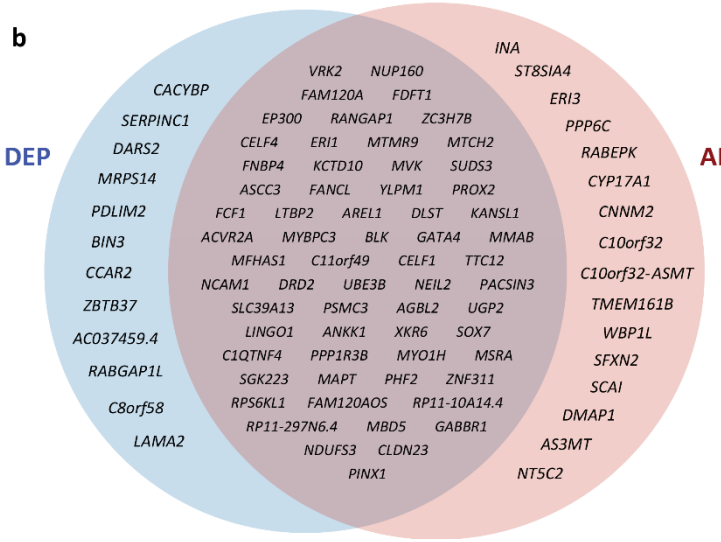
# Genes in common – and specific - for Depression and Anxiety

Jackson Thorp

a




b

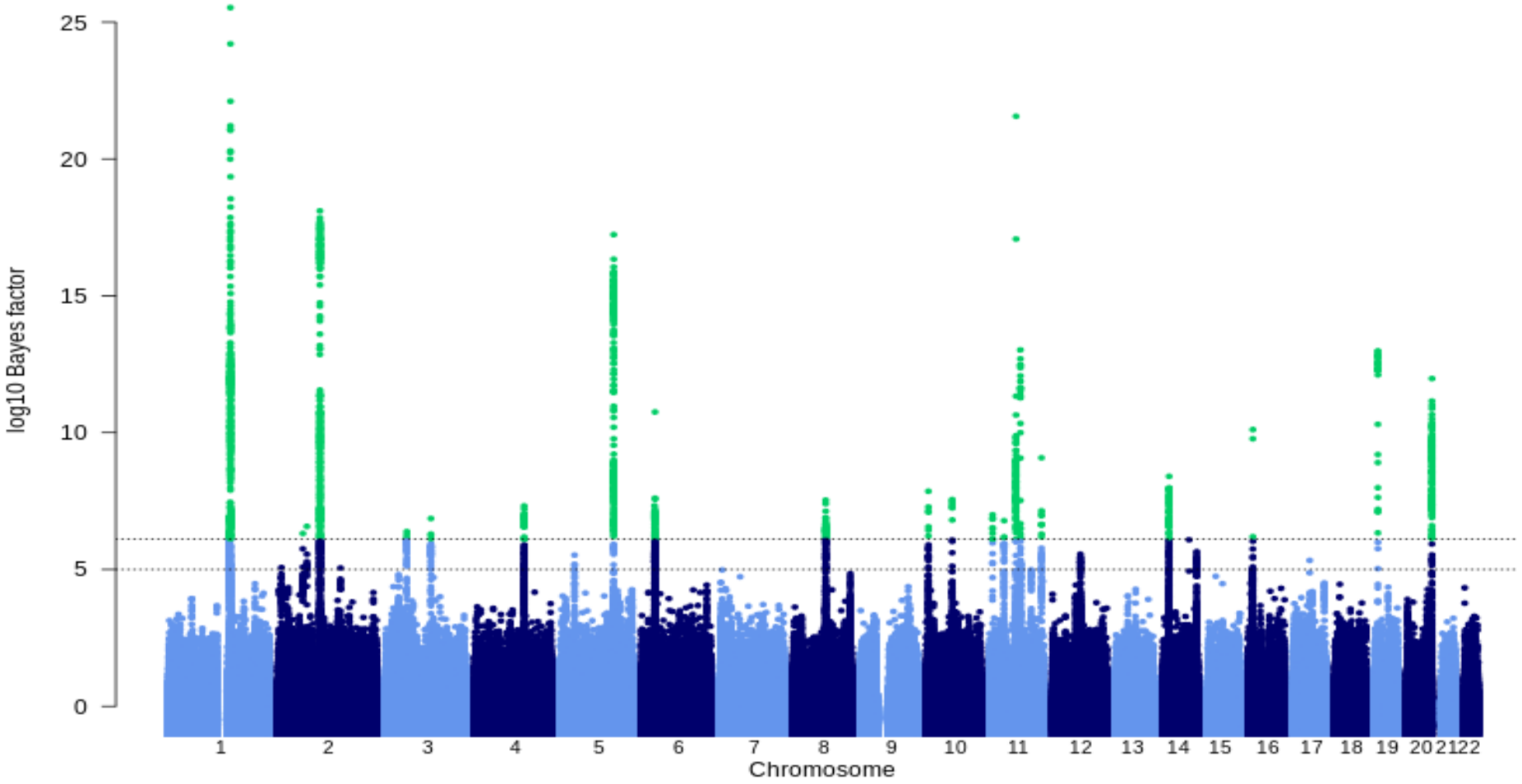



| | |
|---|---|
| DEP only | 10 regions; 63 mapped genes |
| ANX only | 20 regions; 102 mapped genes |
| Shared | 71 regions; 509 mapped genes |
| Separate | 22 regions |

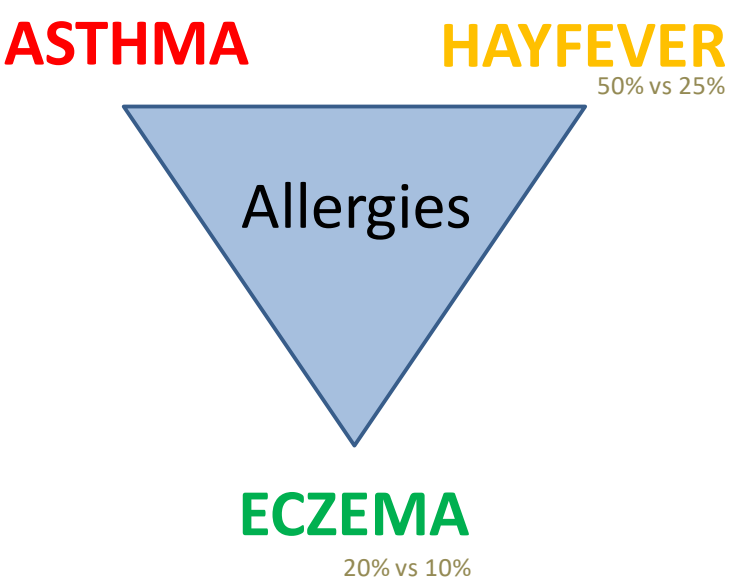
*Nature Human Behaviour* 5, 1432–1442, 2021

We define genome-wide significance as .05/1 million effective tests = $5 \times 10^{-8}$

# **GWAS for eczema** (21k cases, 98k controls, 27 hits)

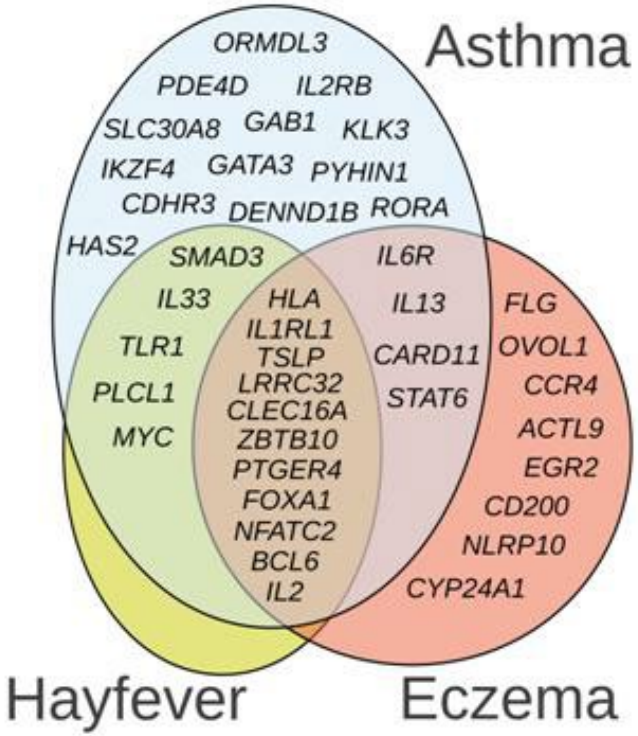



Lavinia Paternoster




## Risk factors overlap

(Thomsen 2006; van Beijsterveldt 2007)




**ENVIRONMENTAL risk factors:**

**20% to 70% shared**

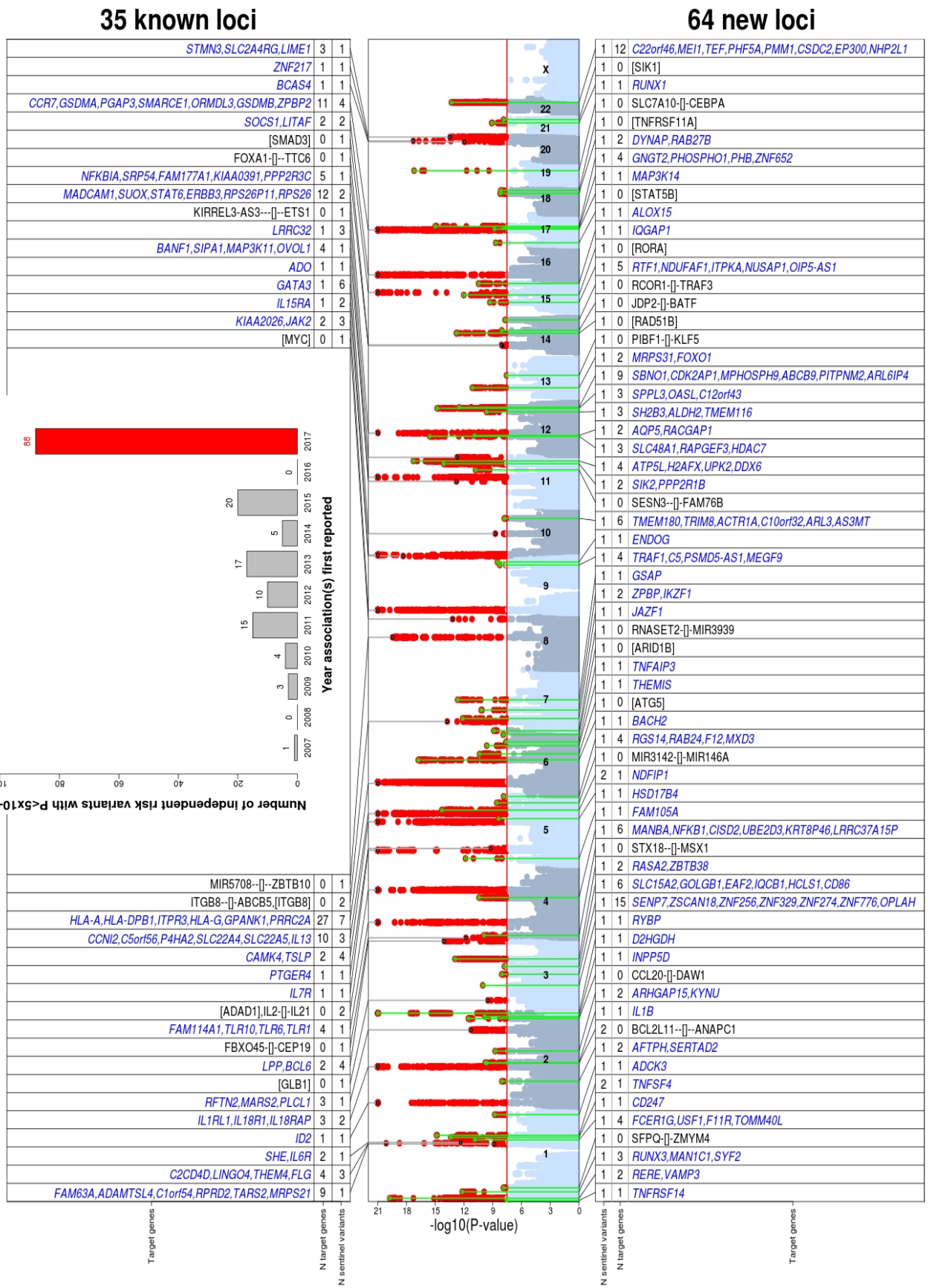
***COMMON TRIGGERS***

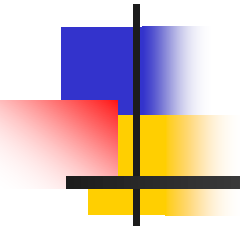
**GENETIC risk factors:**

**40% to 60% shared**

***COMMON MOLECULAR MECHANISMS***

Manuel Ferreira


35 known loci
64 new loci
Manuel Ferreira
Year association(s) first reported
Number of independent risk variants with P<5x10-8
-log10(P-value)
Target genes
N target genes
N sentinel variants



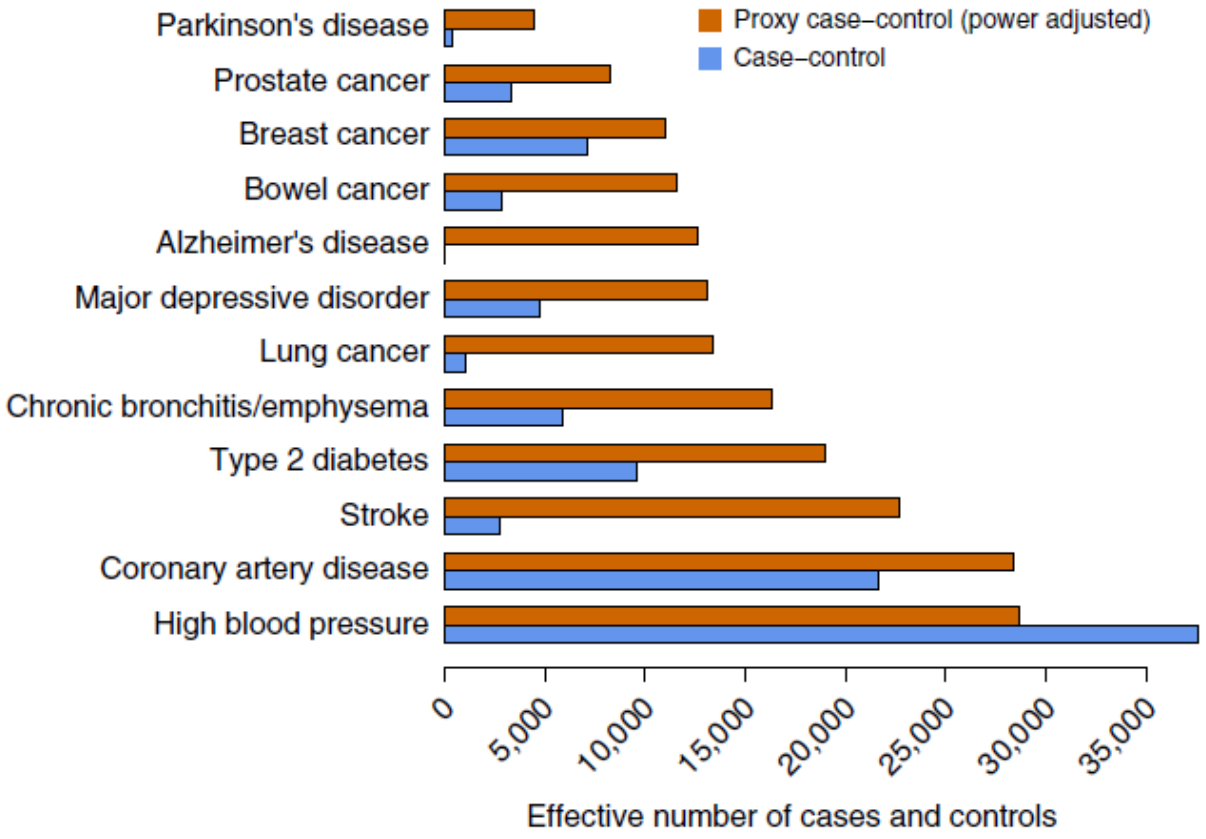
# Ways to increase power

Use ungenotyped relatives as proxy cases (GWAX)

# Case–control association mapping by proxy using family history of disease • (**GWAX**)

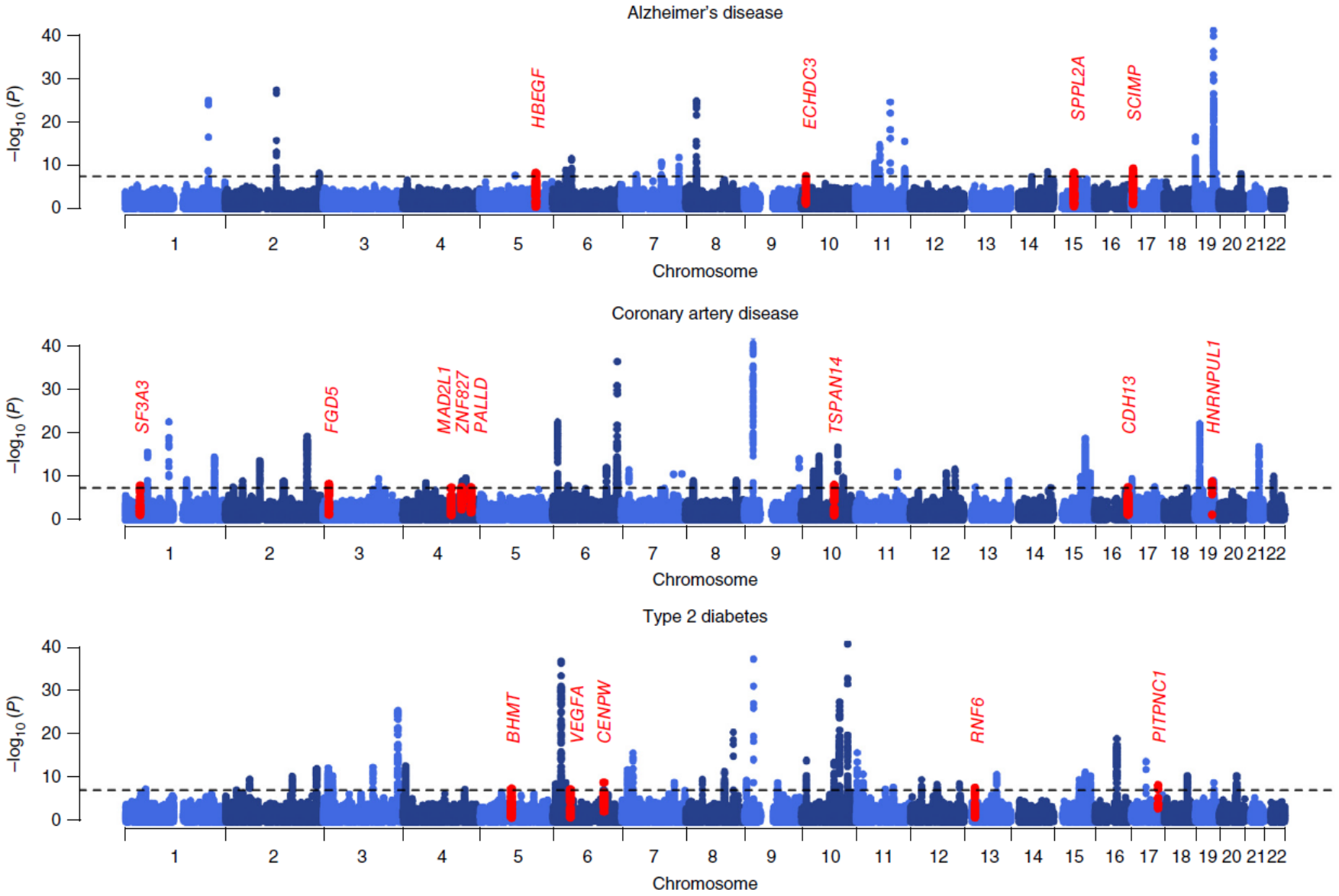
Jimmy Z Liu[1], Yaniv Erlich[1,2] & Joseph K Pickrell[1,3]

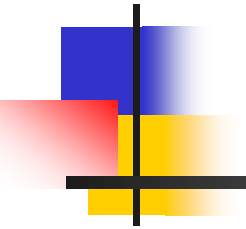
For late-onset or rapidly lethal diseases it may be more practical to identify family members of cases.




NATURE GENETICS VOLUME 49 | NUMBER 3 | MARCH 2017

# Meta-analysis results for GWAX + case-control studies
# New hits are shown in red

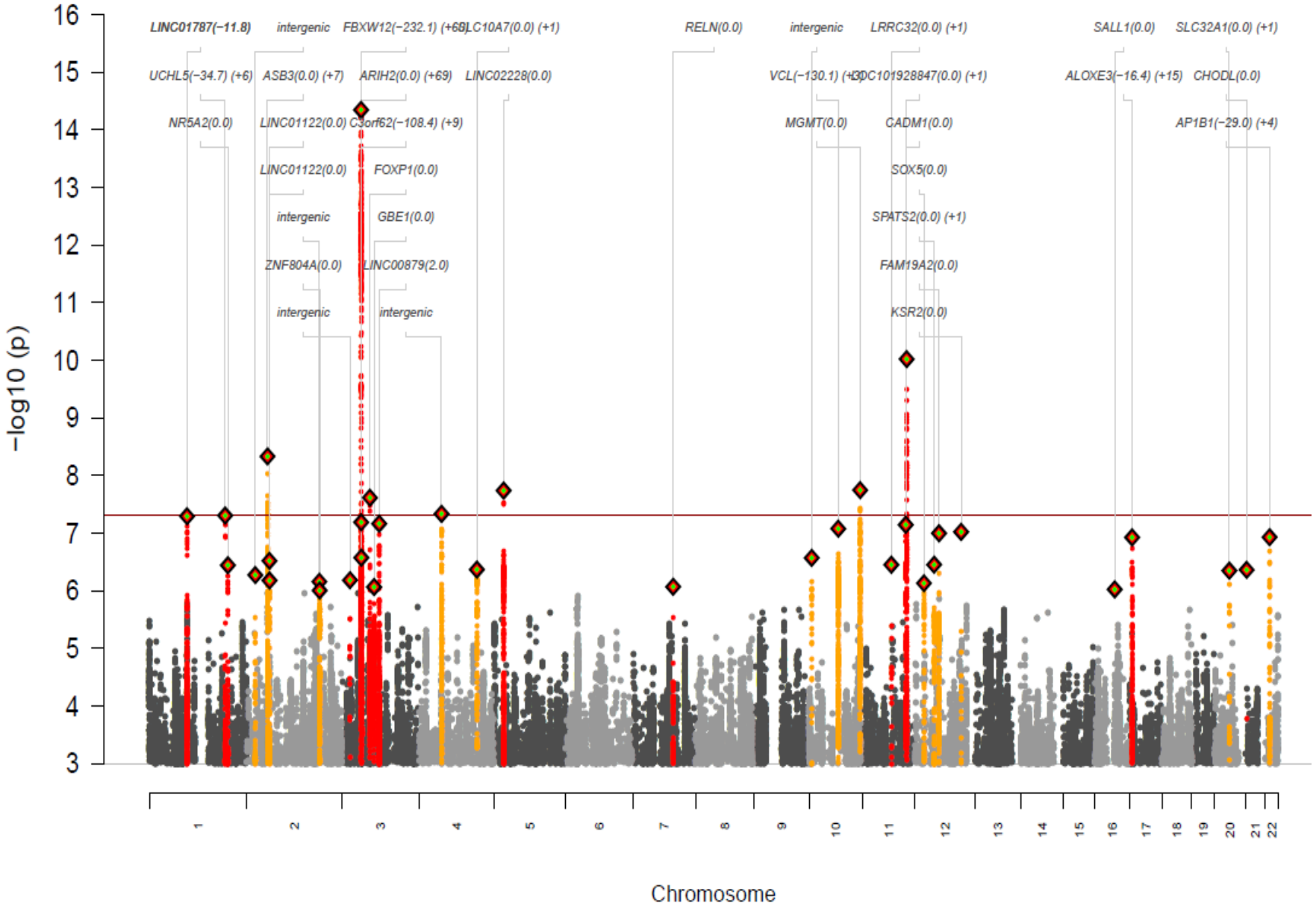




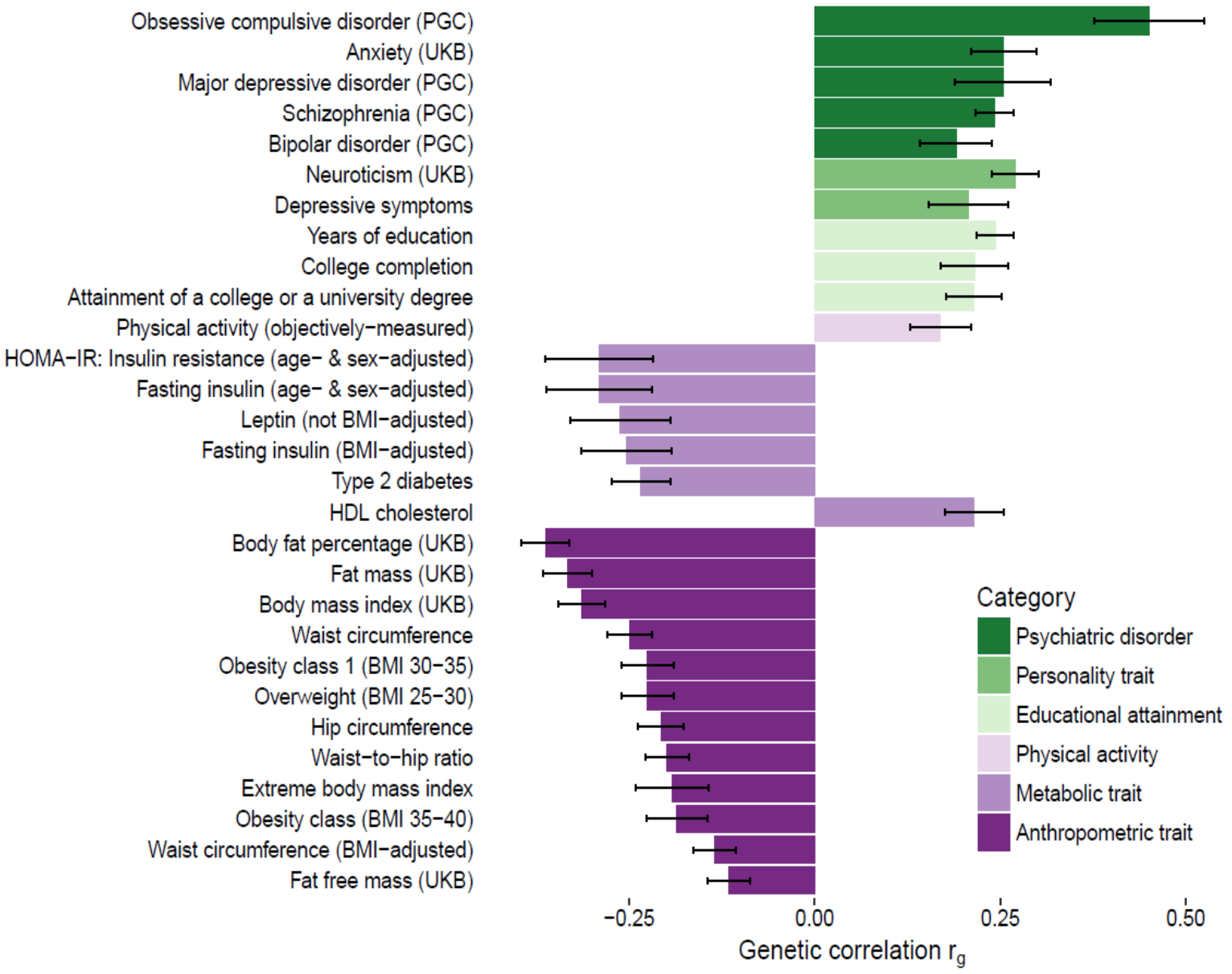
# Applications of GWAS

- Investigate genetic correlation
- The genetics of nurture
- Direction of causation

# GWAS meta-analysis of anorexia nervosa (17k cases, 56k controls)

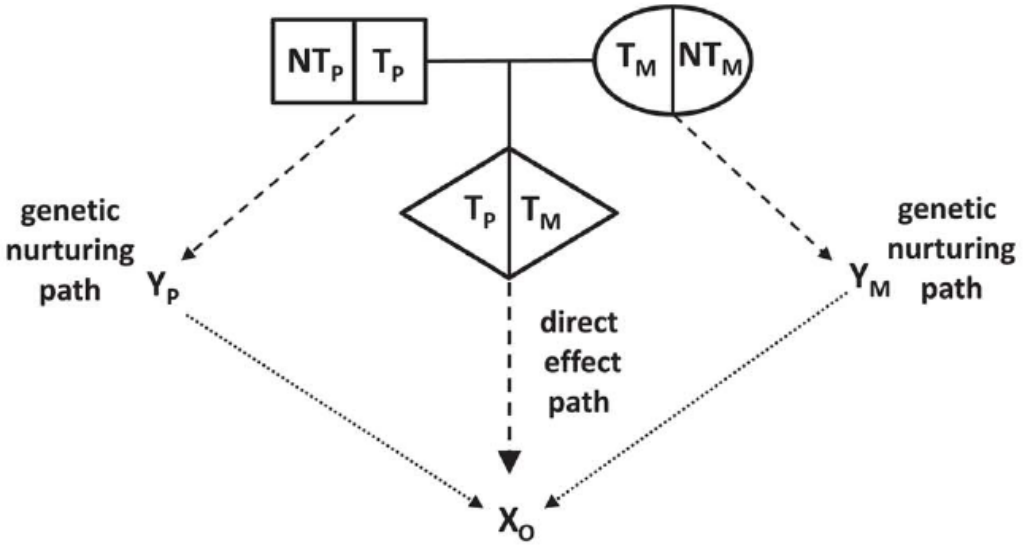


# Significant genetic correlations (SNP-Rg) and 95% confidence intervals (error bars) between anorexia nervosa and traits, as estimated by LD score regression



# The nature of nurture: Effects of parental genotypes

Augustine Kong …….Kari Stefansson




Nontransmitted alleles can affect a child through their impacts on the parents and other relatives, a phenomenon we call “genetic nurture.” Using results from a meta-analysis of educational attainment, we find that the polygenic score computed for the nontransmitted alleles of 21,637 probands with at least one parent genotyped has an estimated effect on the educational attainment of the proband that is 29.9% ($P = 1.6 \times 10^{-14}$) of that of the transmitted polygenic score.

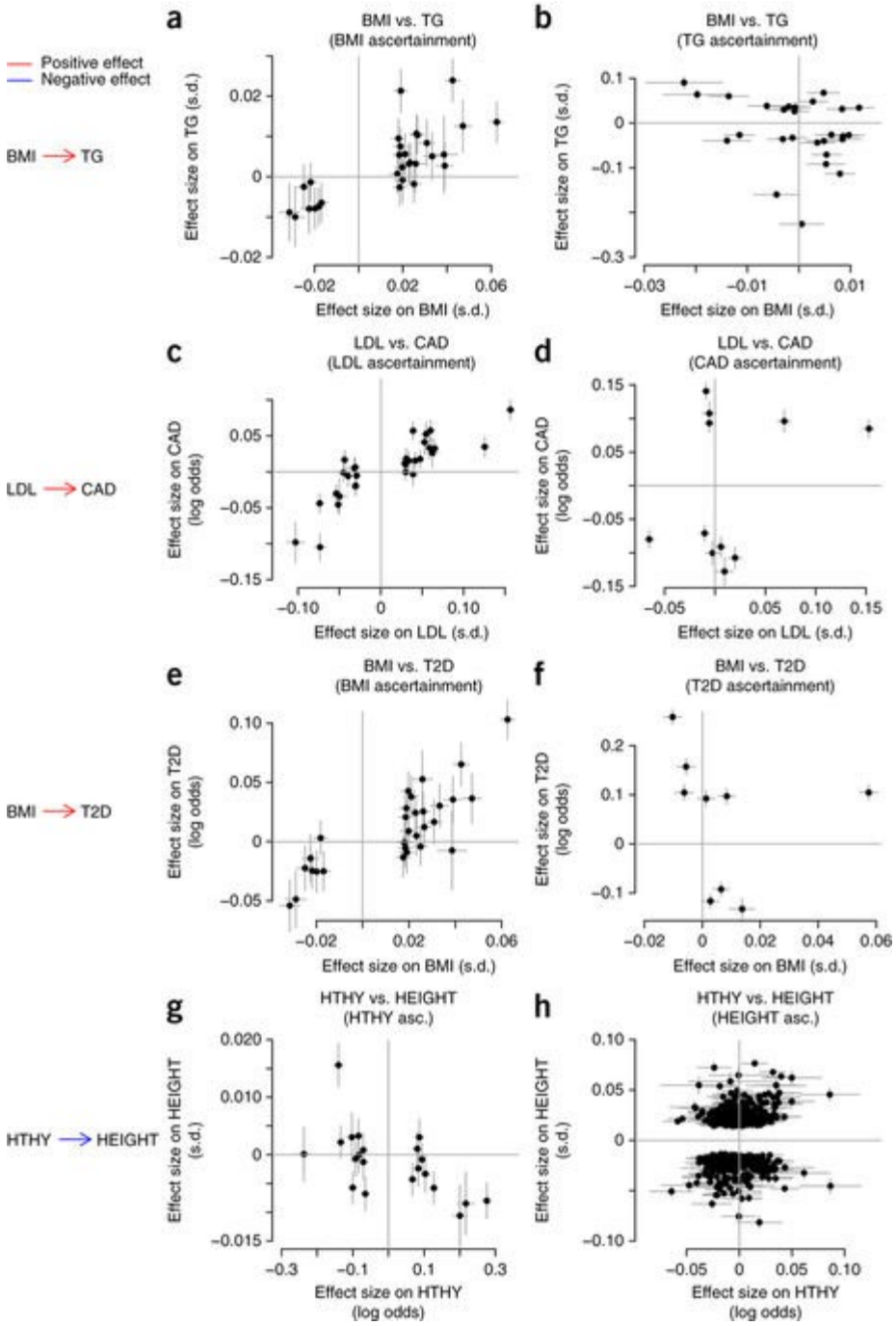
Kong *et al.*, *Science* **359**, 424–428 (2018) 26 January 2018

**Detection and interpretation of shared genetic influences on 42 human traits**

Joseph K Pickrell, Tomaz Berisa, Jimmy Z Liu, Laure Ségurel, Joyce Y Tung & David A Hinds.

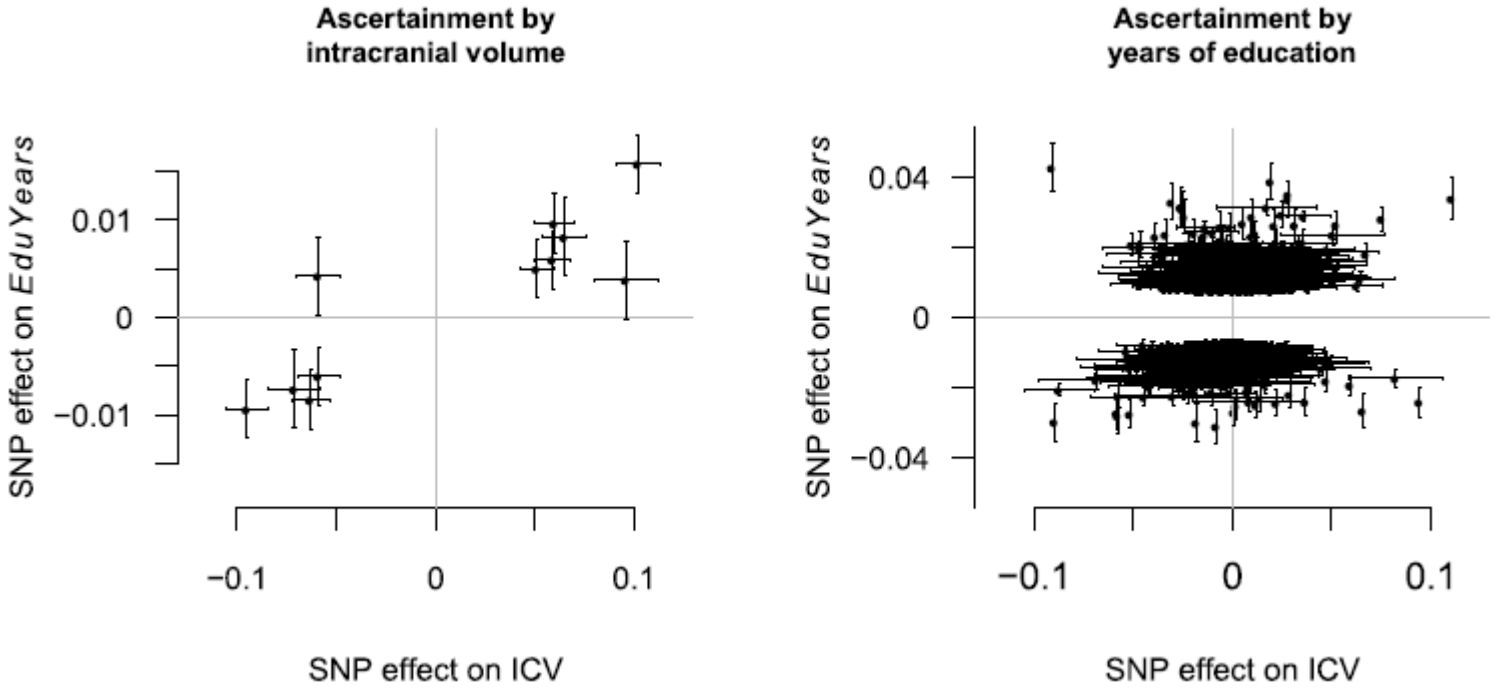
*Nature Genetics* 48; 709–717, 2016

**Powerful GWAS for traits A and B can help determine direction of causation**



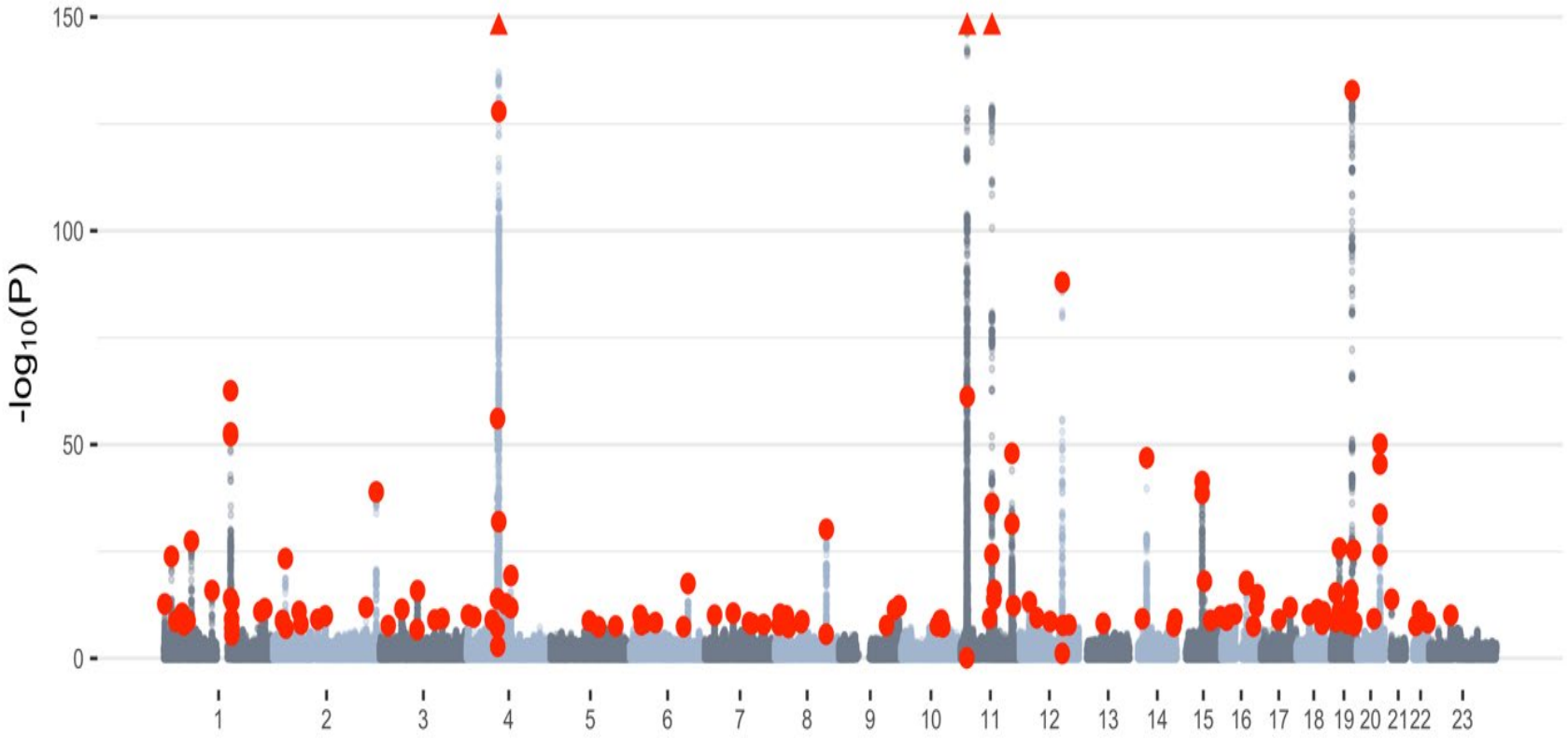
# The causal influence of brain size on human intelligence: Evidence from within-family phenotypic associations and GWAS modeling

James J. Lee[a,*], Matt McGue[a], William G. Iacono[a], Andrew M. Michael[b,c], Christopher F. Chabris[b]



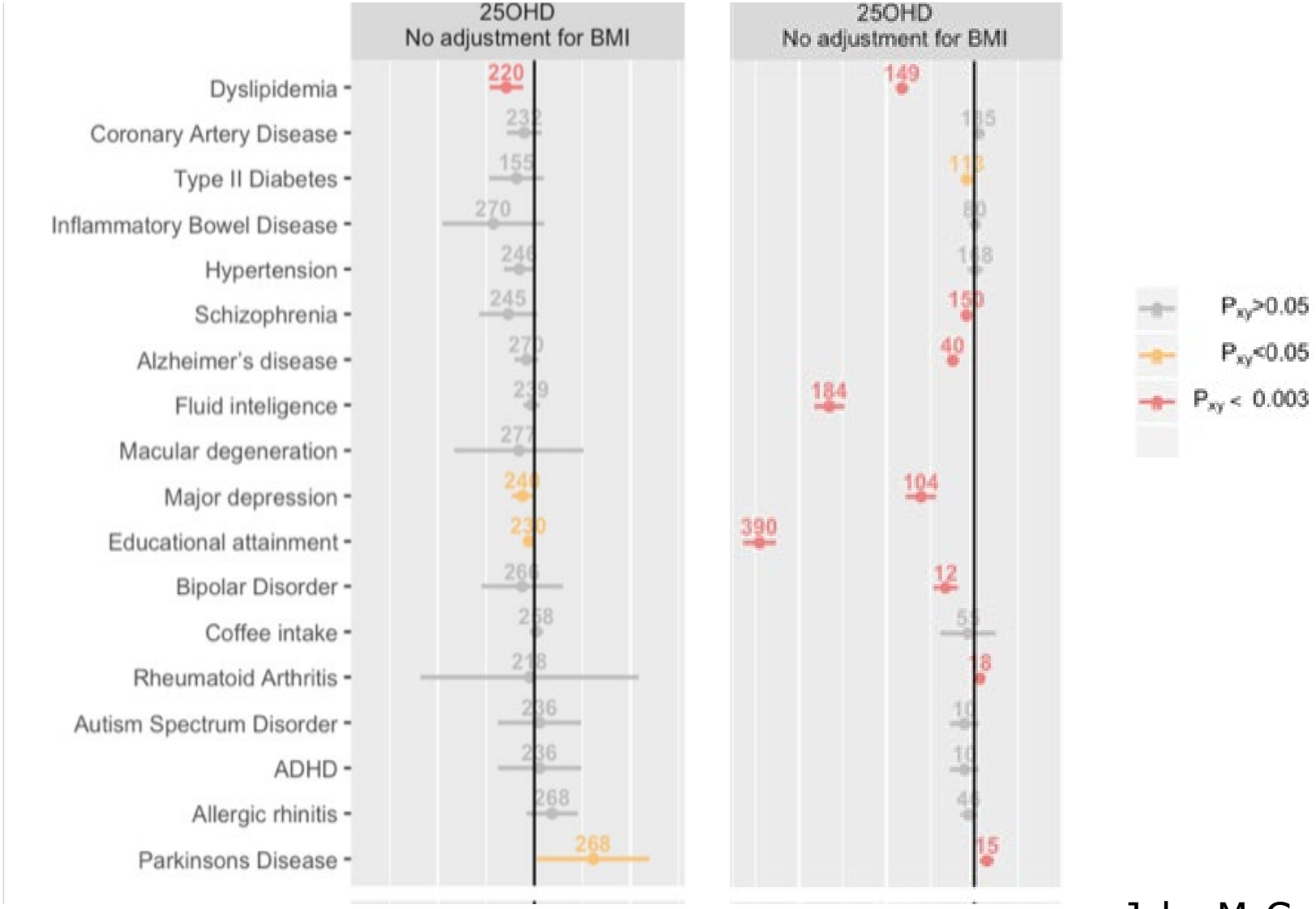

Intelligence 75 (2019) 48–58

**Manhattan plot of the 25OHD (vitamin D) GWAS in the UK Biobank:** n=417,580, 143 loci




John McGrath

**Bidirectional Generalized Summary data level Mendelian Randomization (GSMR) between 25 hydroxyvitamin D concentrations and selected phenotypes**

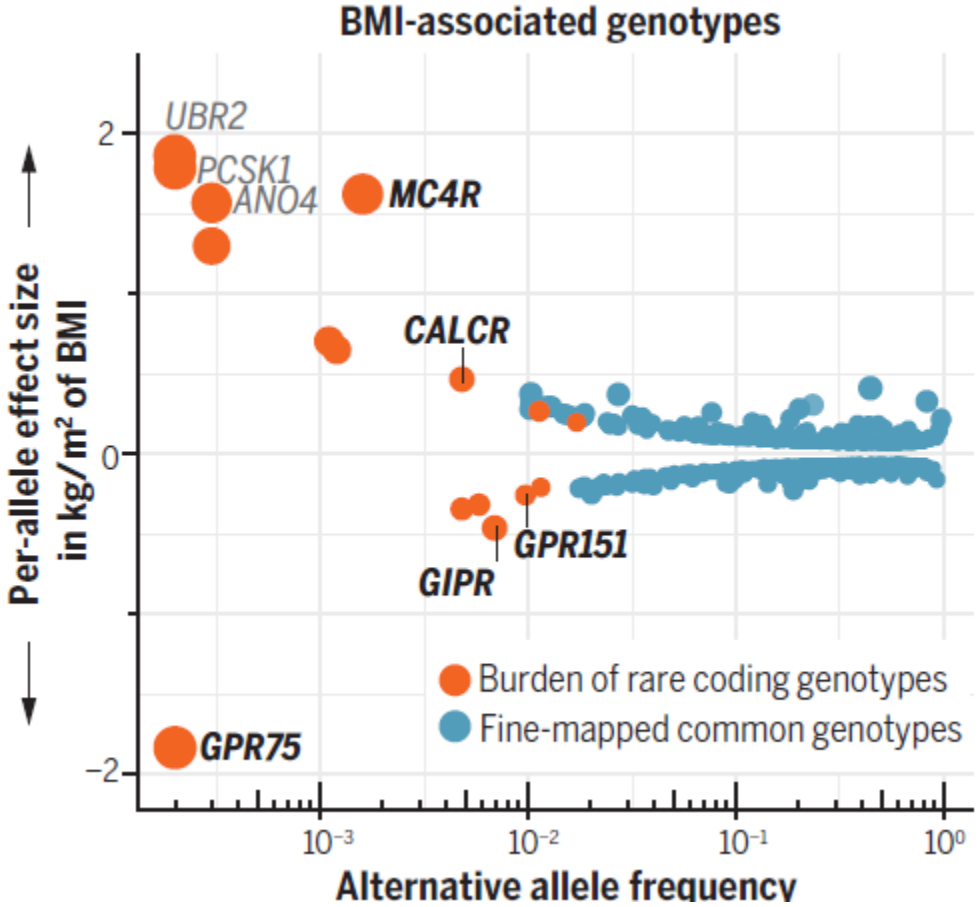


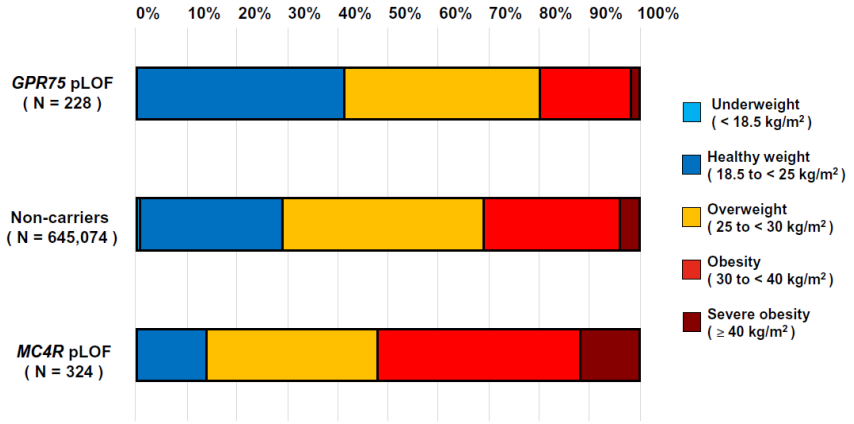

John McGrath

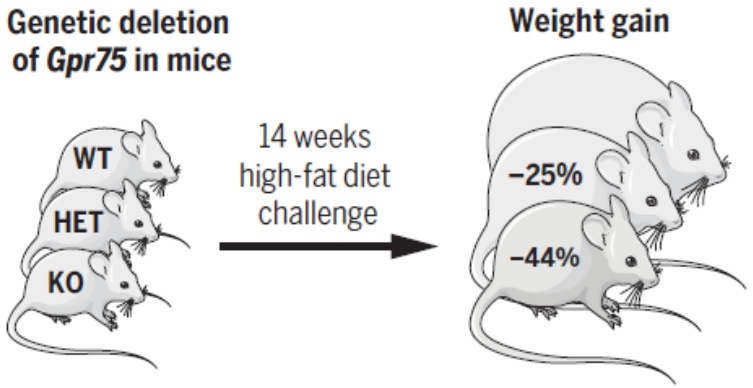
# Pushing power to the limit

Search for rare variants

# Sequencing of 640,000 exomes identifies *GPR75* variants associated with protection from obesity



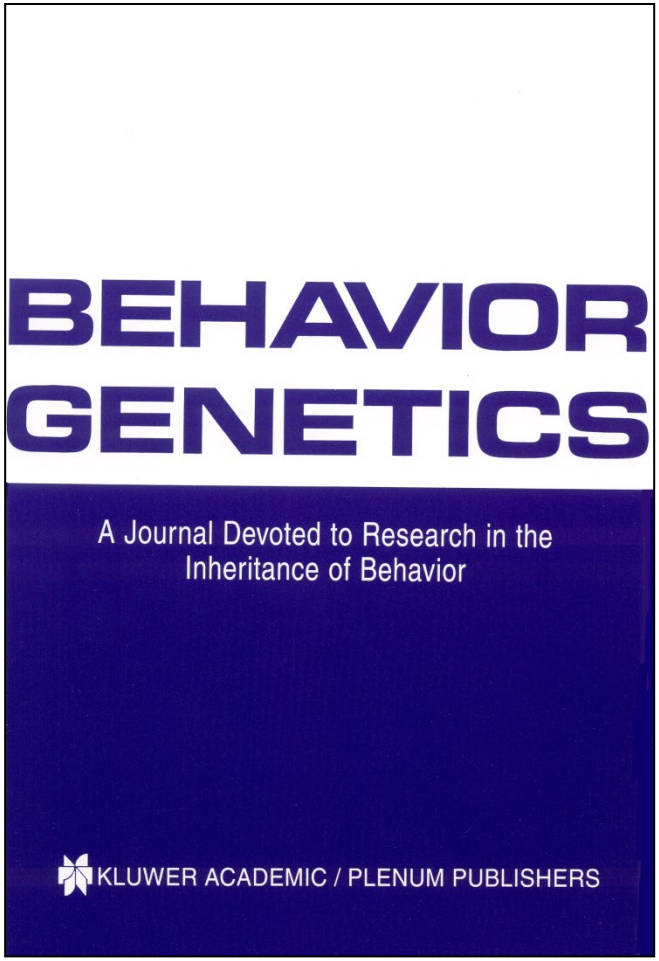




Led by Goncalo Abecasis, Manuel Ferreira
@ Regeneron Inc – ex Boulder

Akbari *et al.*, *Science* **373**, 73 (2021) 2 July 2021

# We also run two journals (1)




- Executive Editor: John K Hewitt
- Managing Editor: Christina A Hewitt
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- Editor: Nick Martin
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- Fast turnaround
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15-17 June 2023
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## 2023 BGA Annual Meeting: Murcia, Spain

**Wednesday June 21 – Saturday June 24**

Local hosts: Juan Ordoñana & Jose Morosoli

Please visit http://eventos.um.es/go/bga-in-spain for more information about the venue, hotel accommodations, and travel to Murcia.

Egmond aan Zee, October 8, 2004


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