Amsterdam UMC
University Medical Centers

History of Biometrical Genetics: Causes of Individual Differences

Abdel Abdellaoui

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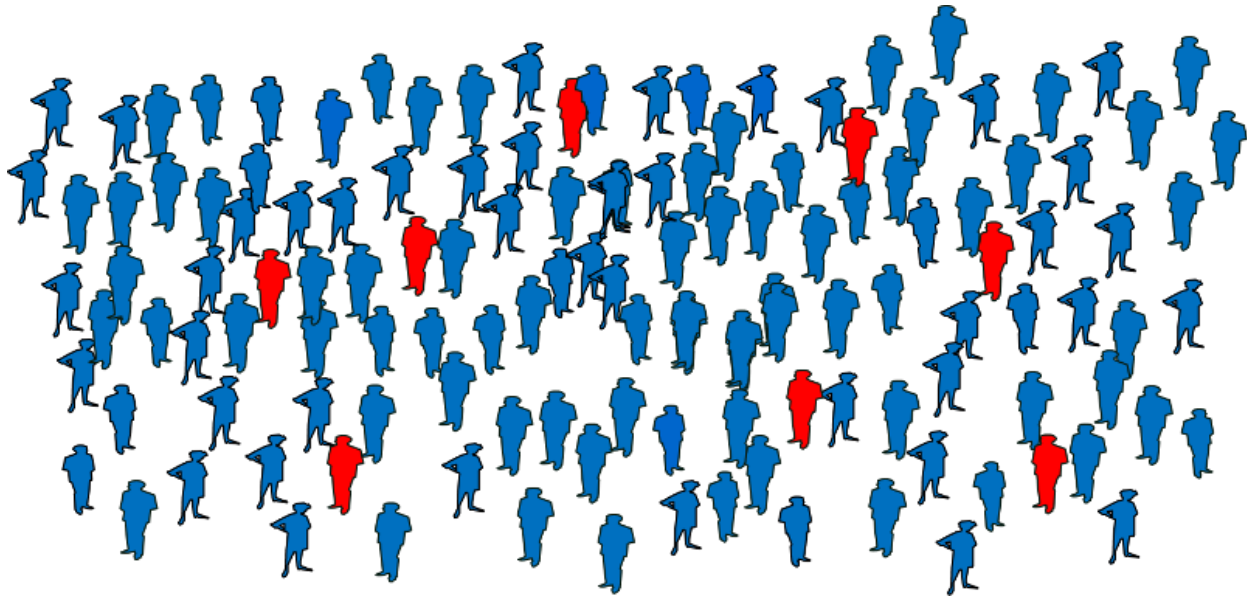
a.abdellaoui@amsterdamumc.nl

GENETICS NETWORK AMSTERDAM

Where do differences between individuals come from?



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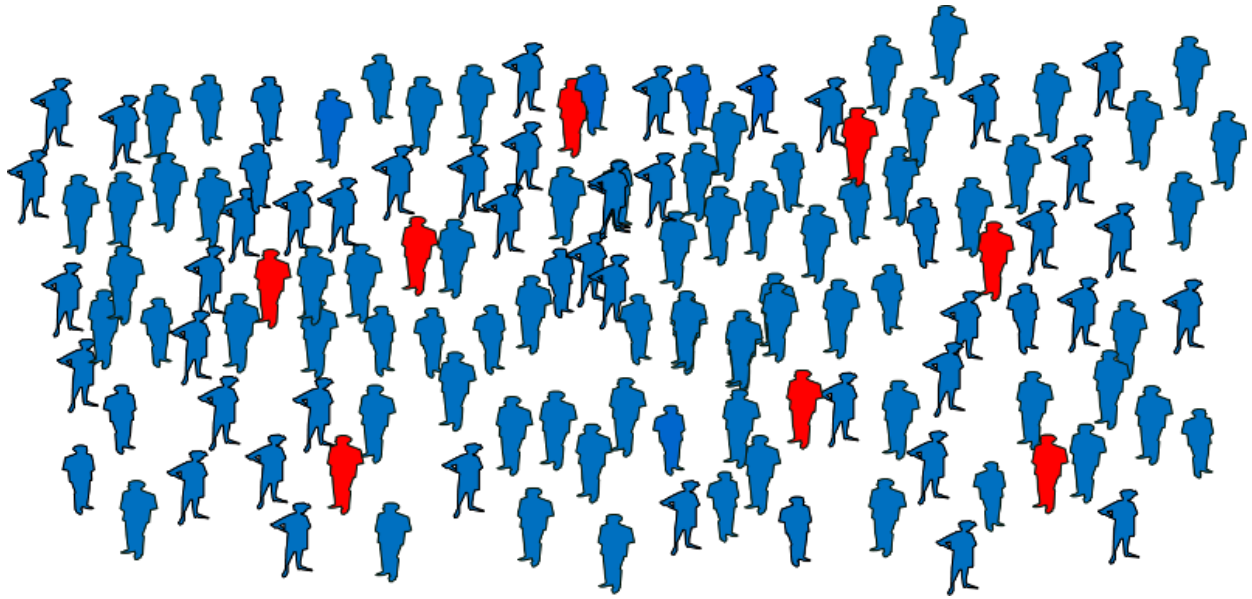

International Journal of Epidemiology 2001;**30**:427–432

REITERATION

Sick individuals and sick populations

Geoffrey Rose

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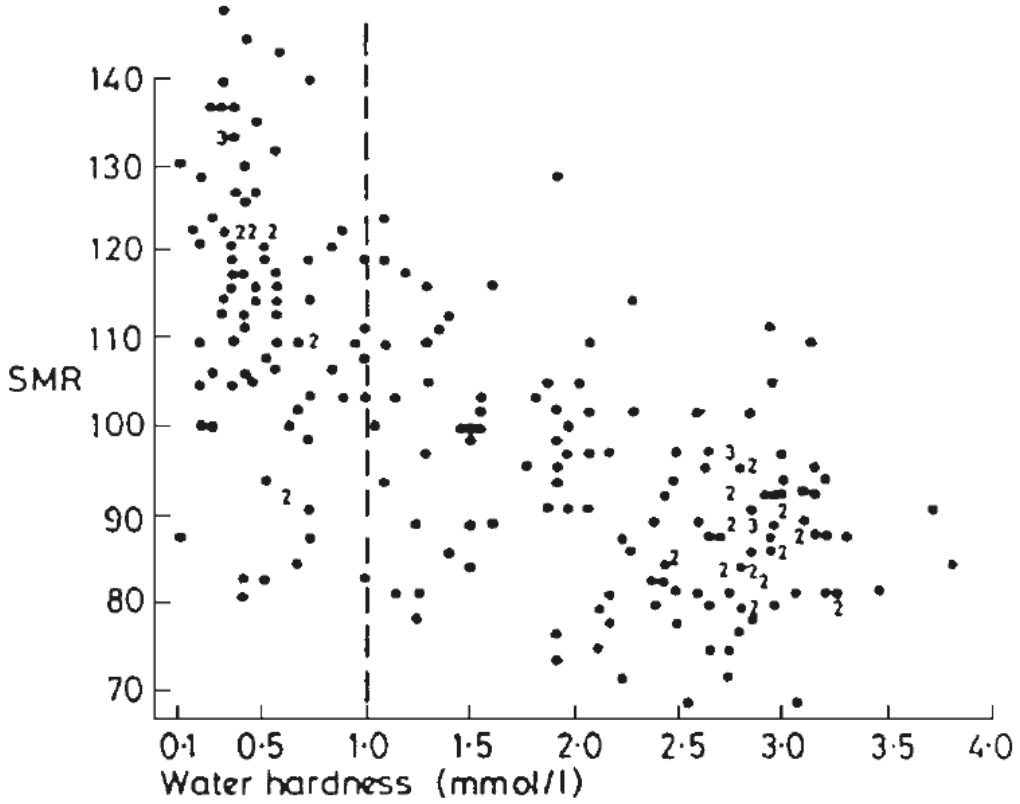


Figure 1 Relation between water quality and cardiovascular mortality in towns of the UK[1]

Where do differences between individuals come from?

International Journal of Epidemiology 2001;**30**:427–432

REITERATION

Sick individuals and sick populations

Geoffrey Rose

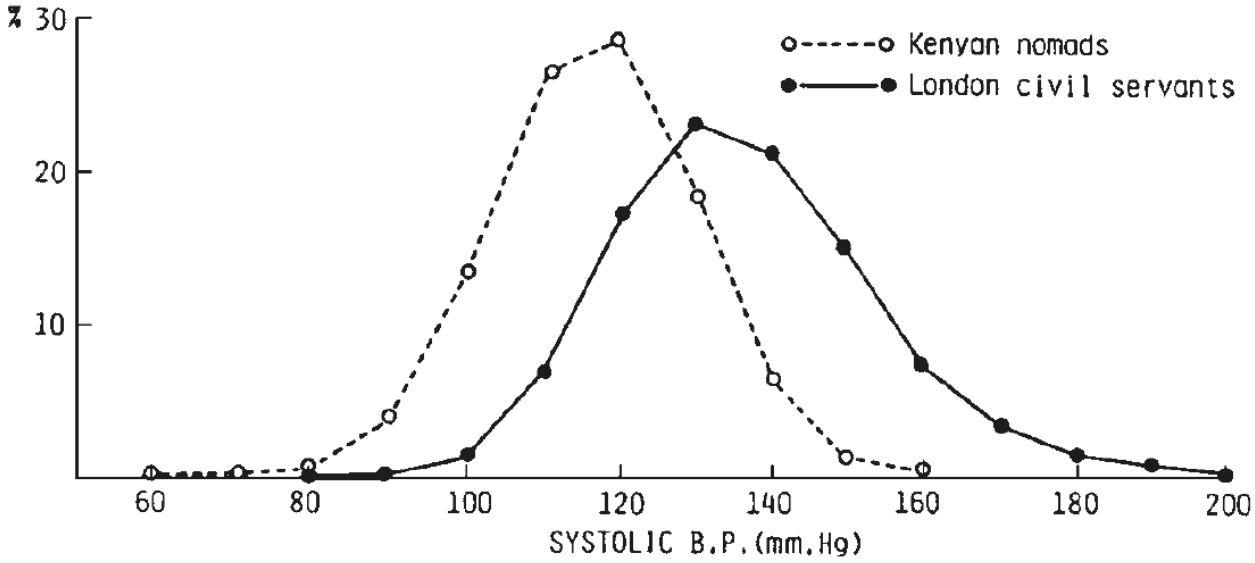
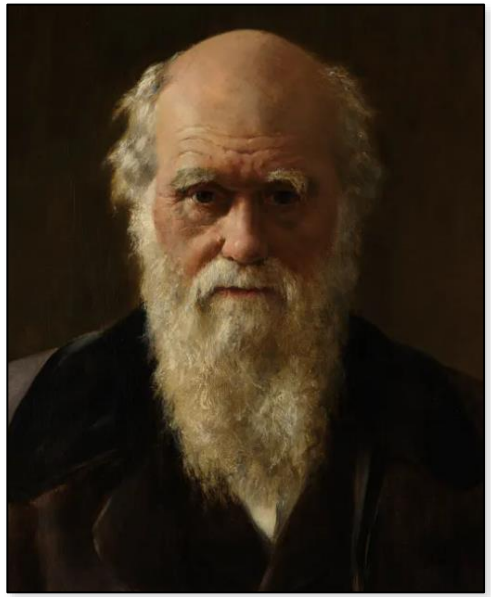
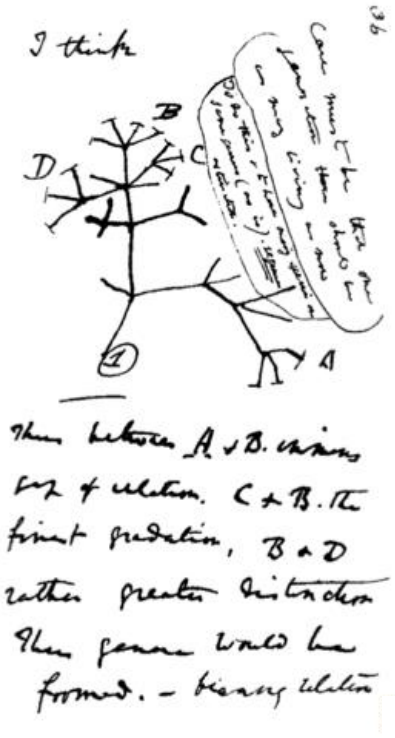
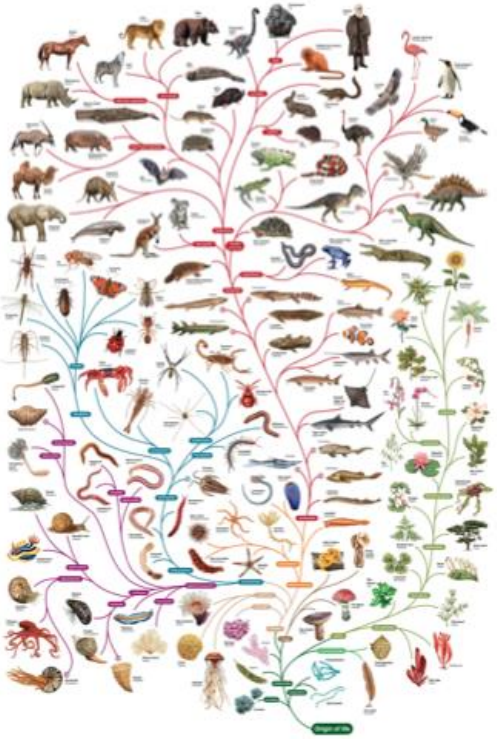


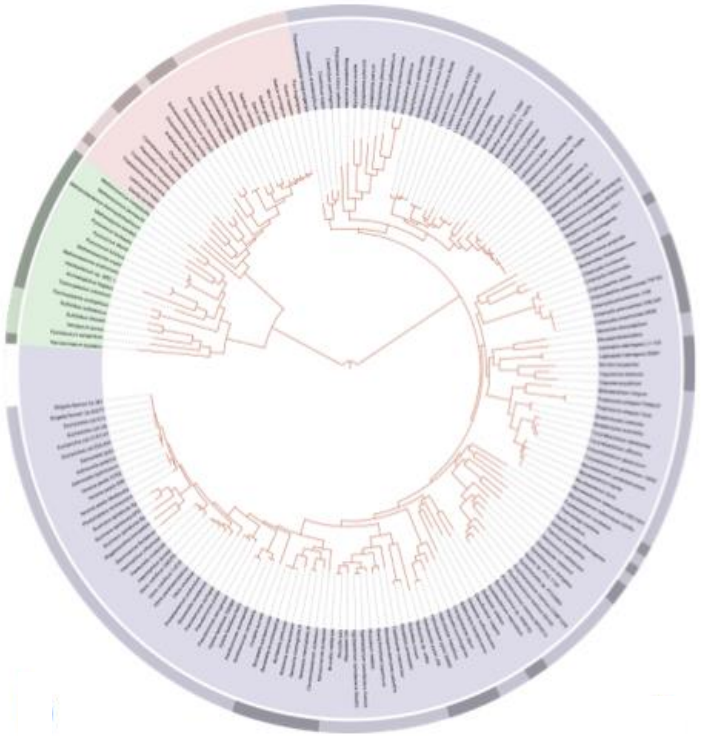
Figure 2 Distributions of systolic blood pressure in middle-aged men in two populations[2,3]

On the Origin of Species (Darwin, 1859)



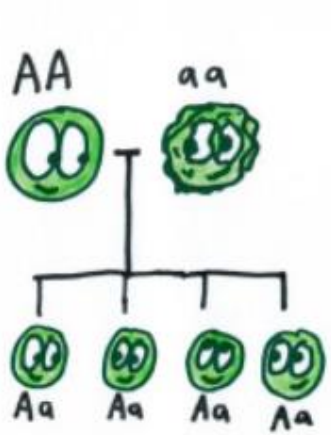


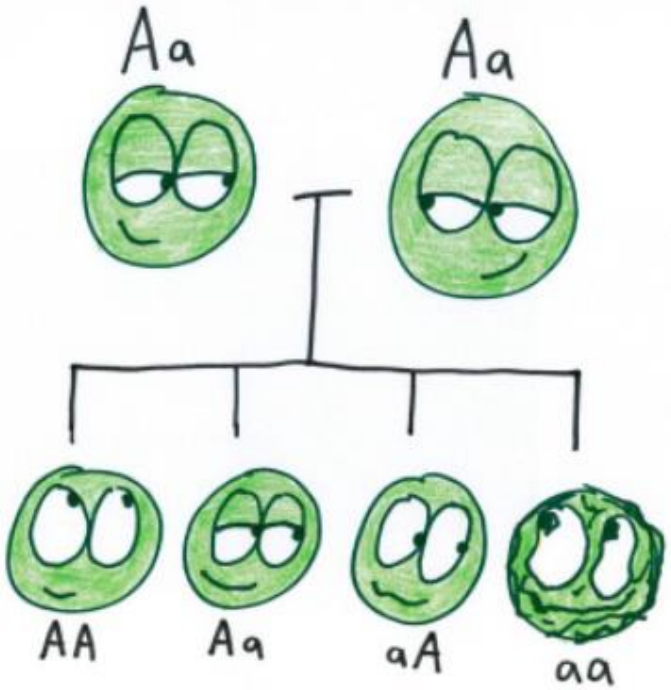


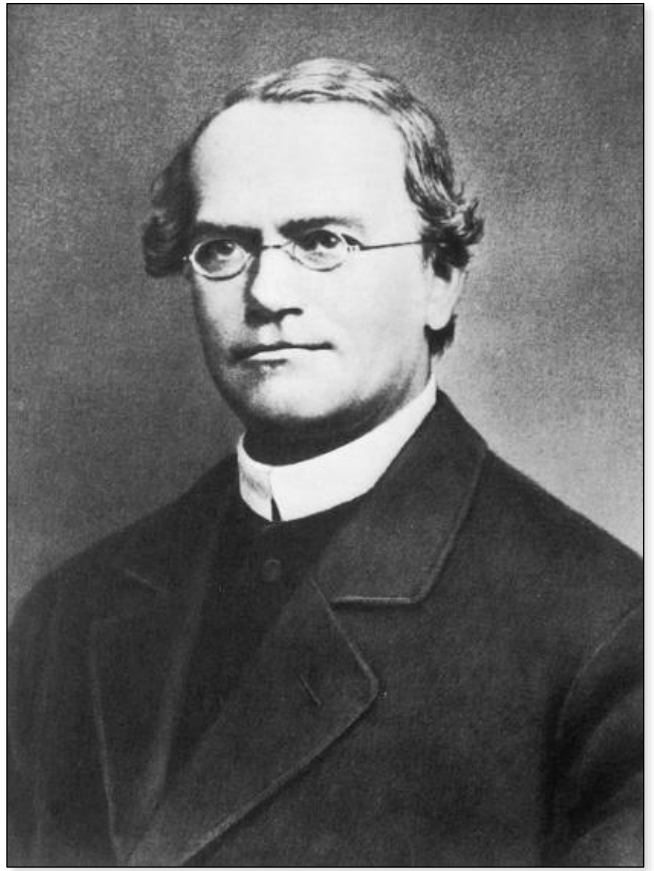


1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

Laws of **Mendel**







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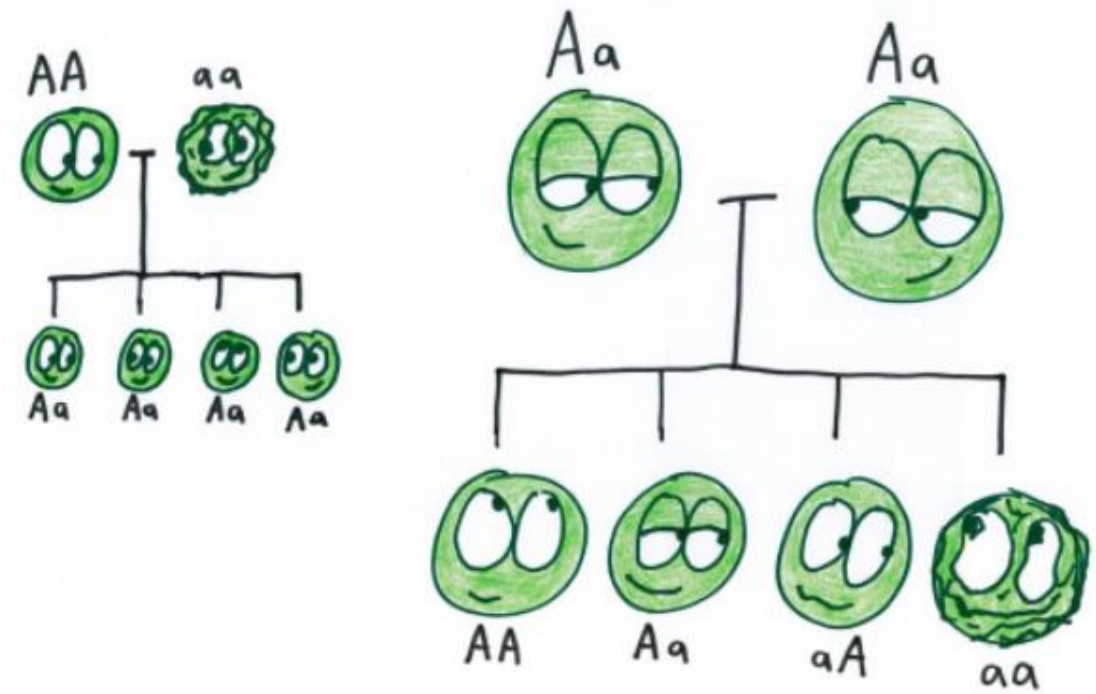
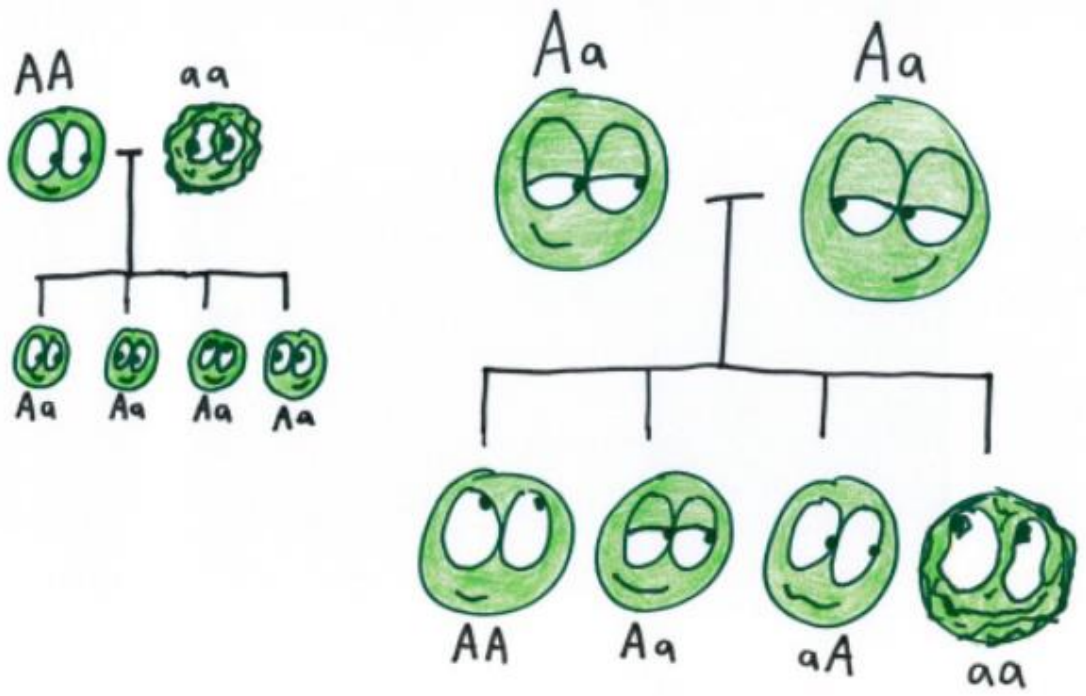


- Law of segregation:
  - One out of two alleles is passed down by each parent

Laws of **Mendel**



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  - Some alleles are dominant or recessive. An organism with at least one dominant allele will display the effect of the dominant allele

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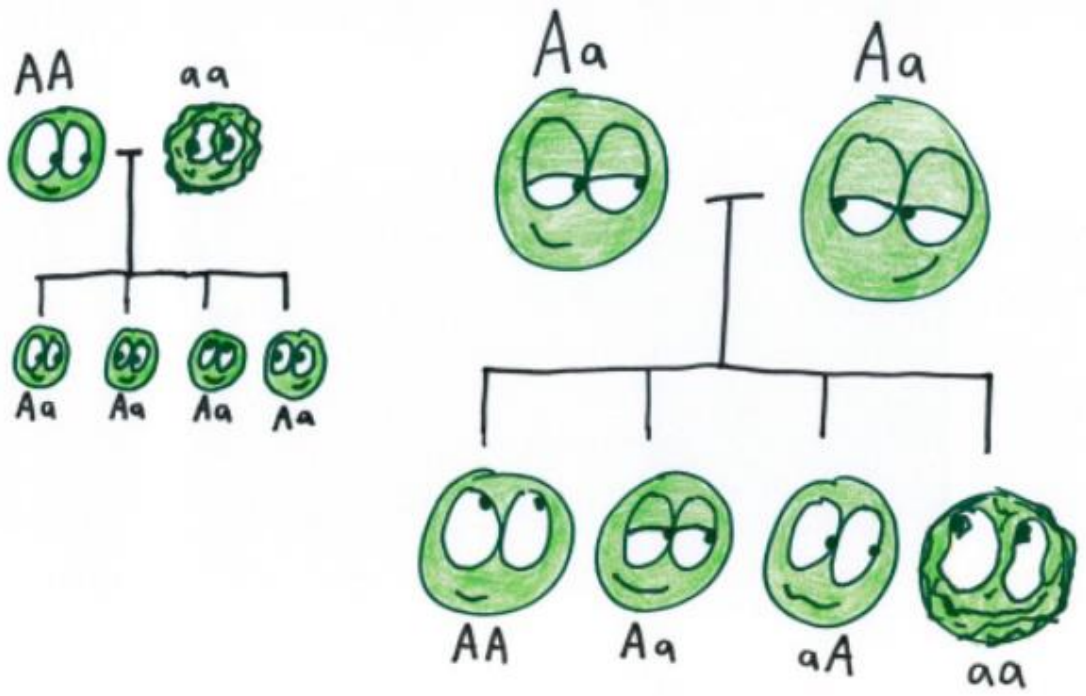
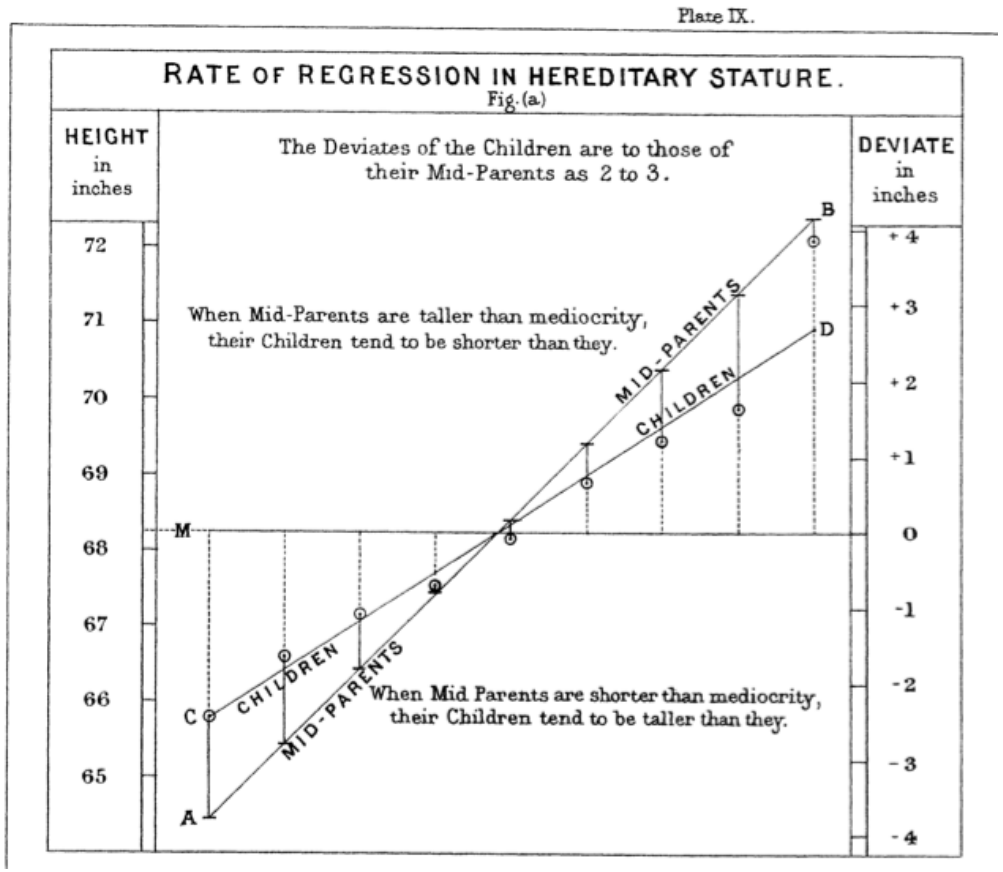
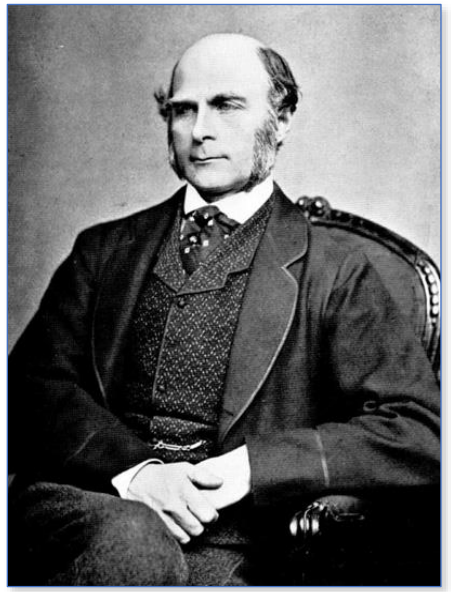
Laws of **Mendel**



- Law of segregation:
  - One out of two alleles is passed down by each parent
- Law of dominance:
  - Some alleles are dominant or recessive. An organism with at least one dominant allele will display the effect of the dominant allele
- Law of independent assortment:
  - Genes for different traits are passed down independently from each other

Regression toward mediocrity in hereditary stature (Galton 1886)





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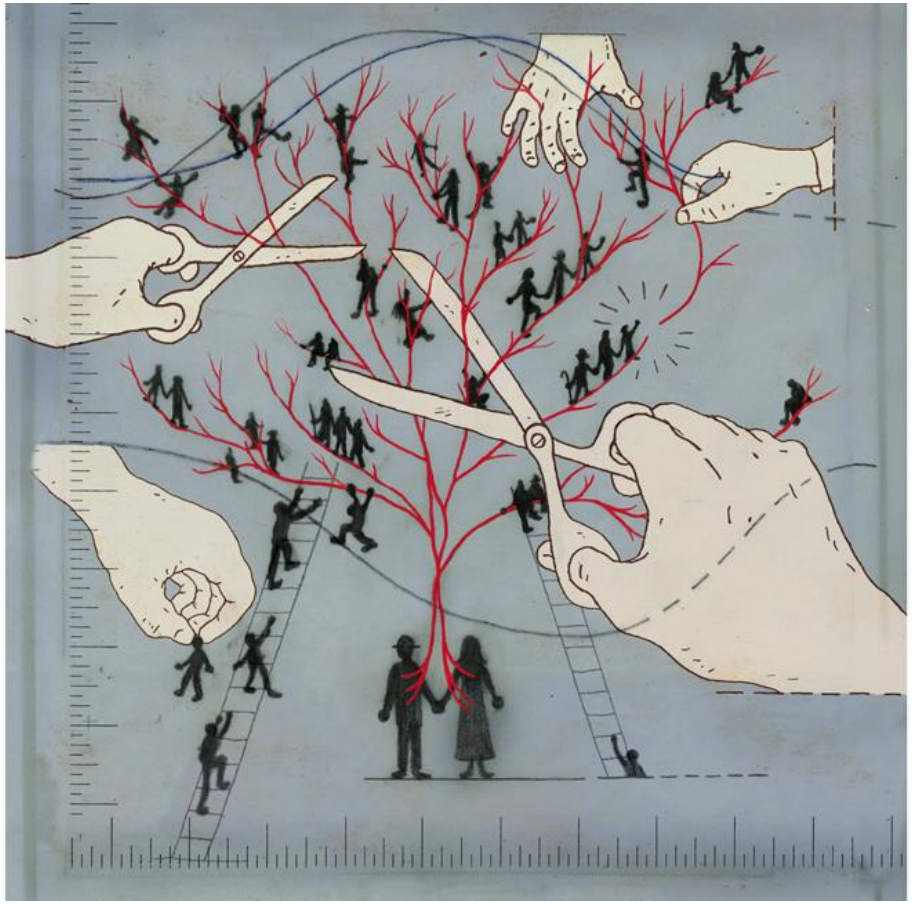
Galton also invented **Eugenics**:
Improving the “genetic quality” of the population through selective parenthood.

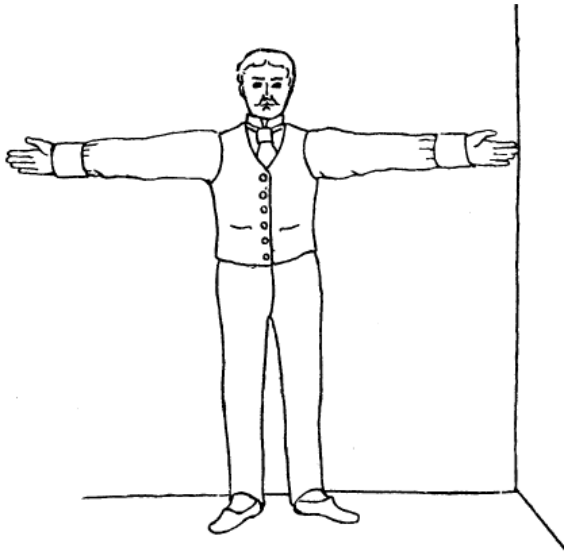


VOLUME II NOVEMBER, 1903 No. 4

ON THE LAWS OF INHERITANCE IN MAN*.

I. INHERITANCE OF PHYSICAL CHARACTERS.

BY KARL PEARSON, F.R.S., assisted by ALICE LEE, D.Sc.
University College, London.



FAMILY MEASUREMENTS.

Professor KARL PEARSON, of University College, London, would esteem it a great favour if any persons in a position to do so, would assist him by making one set (or if possible several sets) of anthropometric measurements on their own family, or on families with whom they are acquainted. The measurements are to be made use of for testing theories of heredity, no names, except that of the recorder, are required, but the Professor trusts to the *bona fides* of each recorder to send only correct results.

Each family should consist of a father, mother, and at least one son or daughter, not necessarily the eldest. The sons or daughters are to be at least 18 years of age, and measurements are to be made on not more than two sons and two daughters of the same family. If more than two sons or two daughters are easily accessible, then not the tallest but the eldest of those accessible should be selected.

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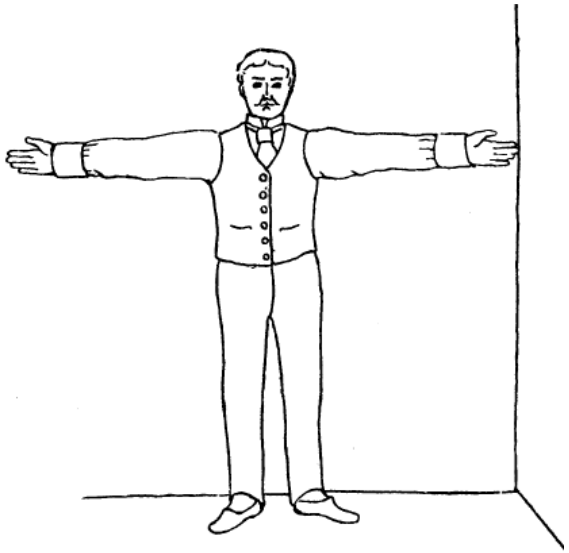

I. *Family Record Series.* About 1893 I drew up in conjunction with my then colleague, W. F. R. Weldon, the directions for family measurement which are described below. The measurements were in great part carried out by college students*, and I largely owe the success of this series to the energy and time devoted to the collection of the data by Dr Alice Lee. In the course of four to five years about 1100 cards were filled in. The tabling of the data on these cards and the calculation of the statistical constants, some 78 tables in all, are due entirely to Dr Lee, and occupied her spare time for nearly two years.

RA Fisher (1918). Transactions of the Royal Society of Edinburgh **52**: 399-433

XV.—**The Correlation between Relatives on the Supposition of Mendelian Inheritance.** By **R. A. Fisher**, B.A. *Communicated by* Professor J. Arthur Thomson. (With Four Figures in Text.)

(MS. received June 15, 1918. Read July 8, 1918. Issued separately October 1, 1918.)

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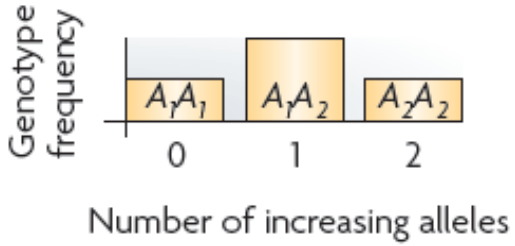
GENETICS | PERSPECTIVES

From R.A. Fisher's 1918 Paper to GWAS a Century Later

Peter M. Visscher*,† and Michael E. Goddard‡,§

Ronald Fisher reconciles Mendel's laws & quantitative traits



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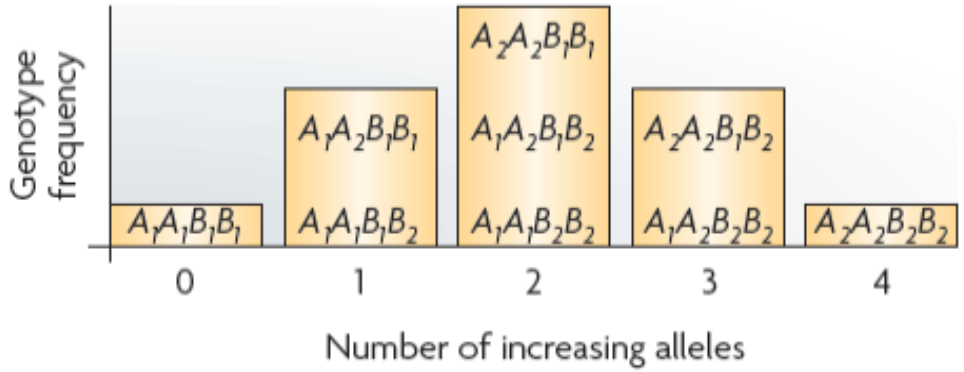

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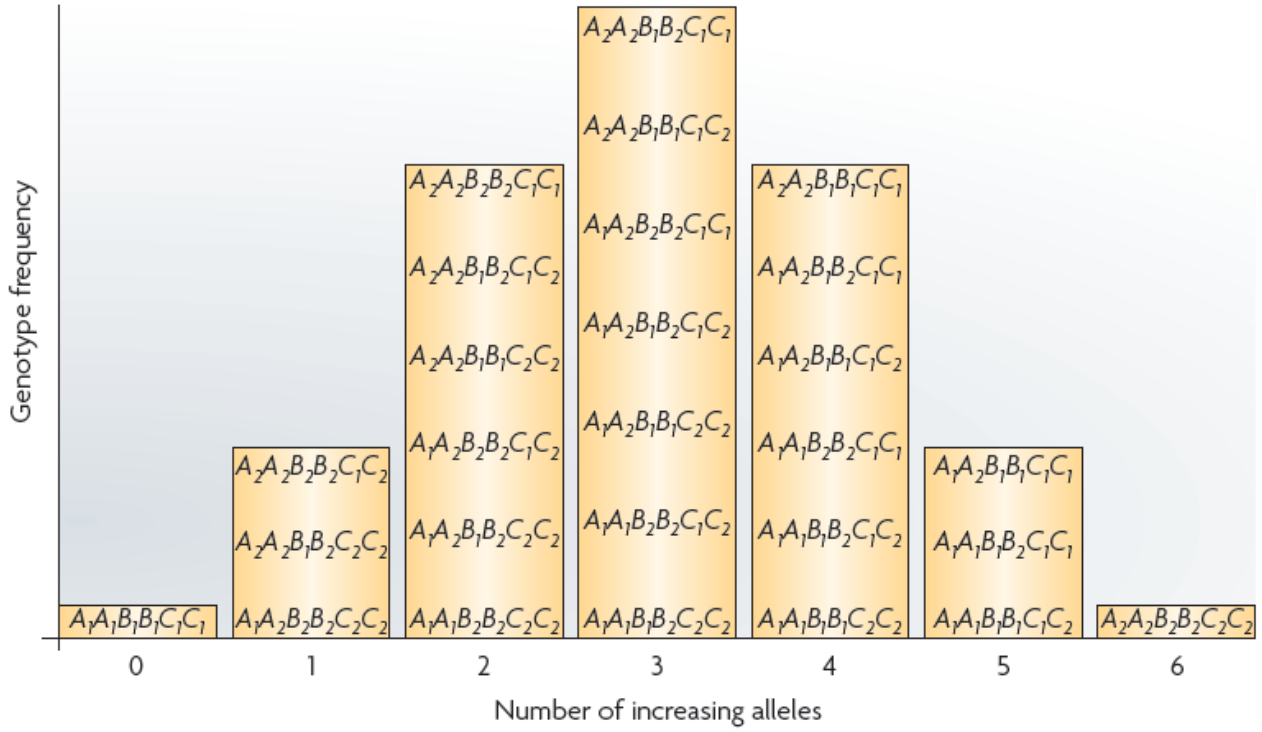

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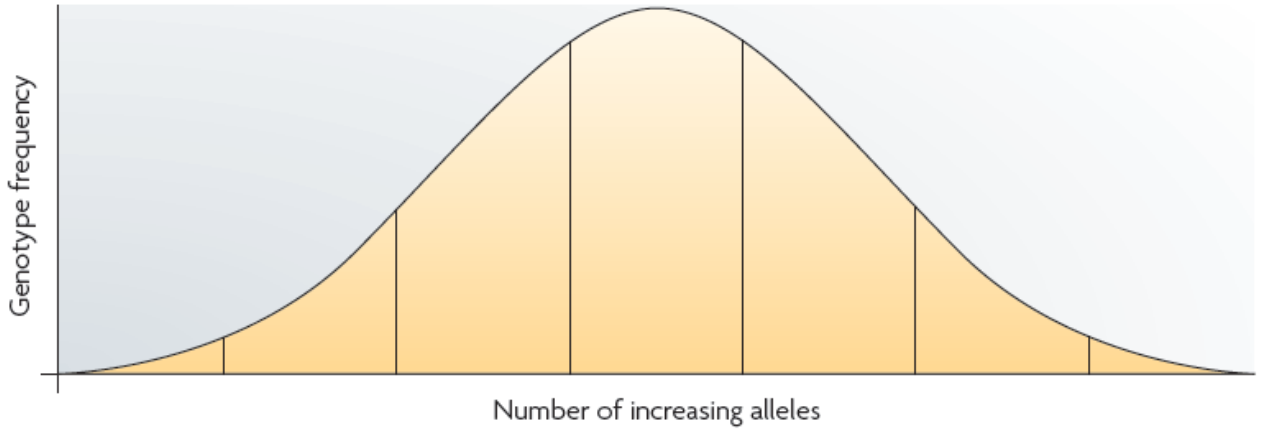

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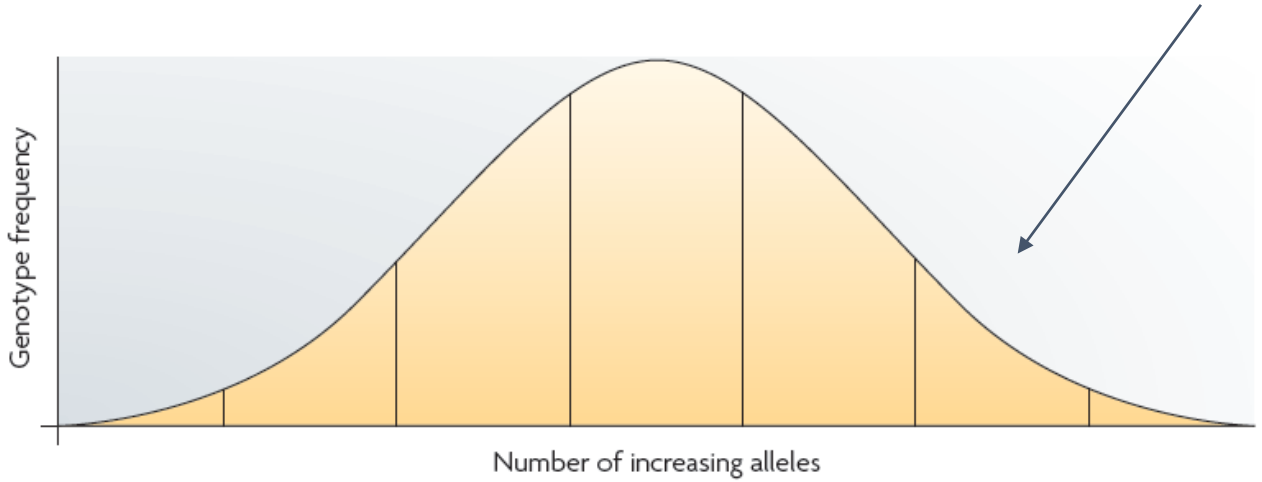
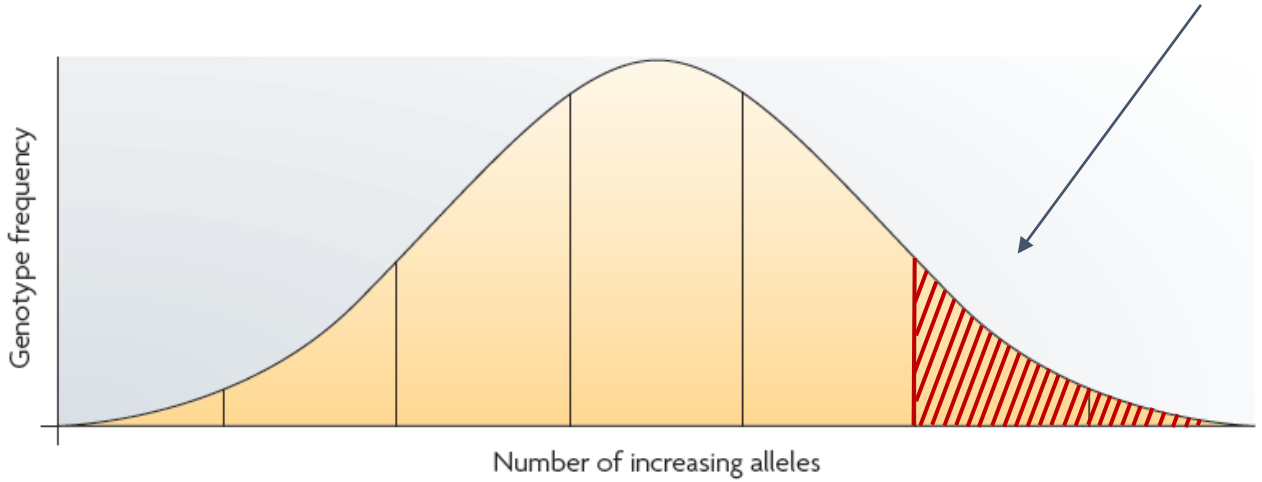
Ronald Fisher reconciles Mendel's laws & quantitative traits

Complex trait =
many genes + environment



Ronald Fisher reconciles Mendel's laws & quantitative traits

Complex disease =
many genes + environment



Liability threshold model

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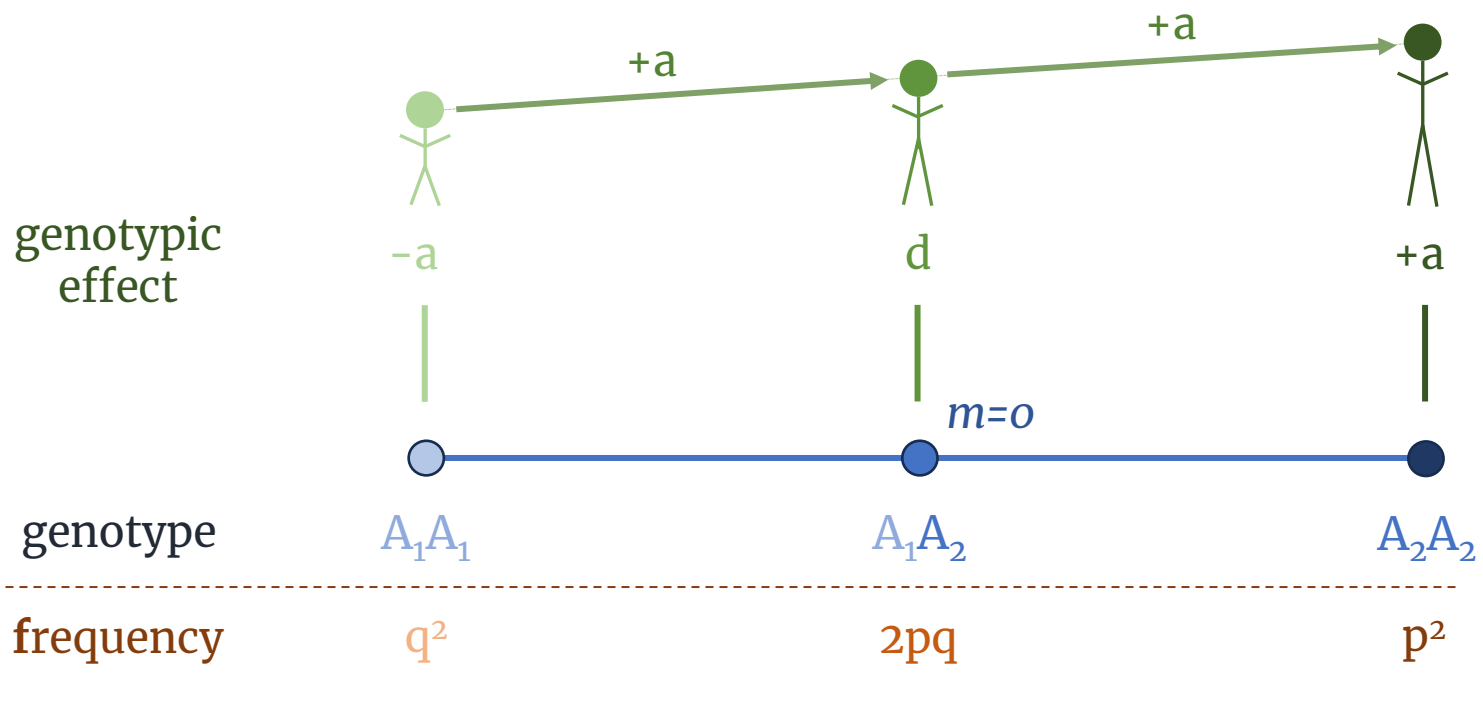
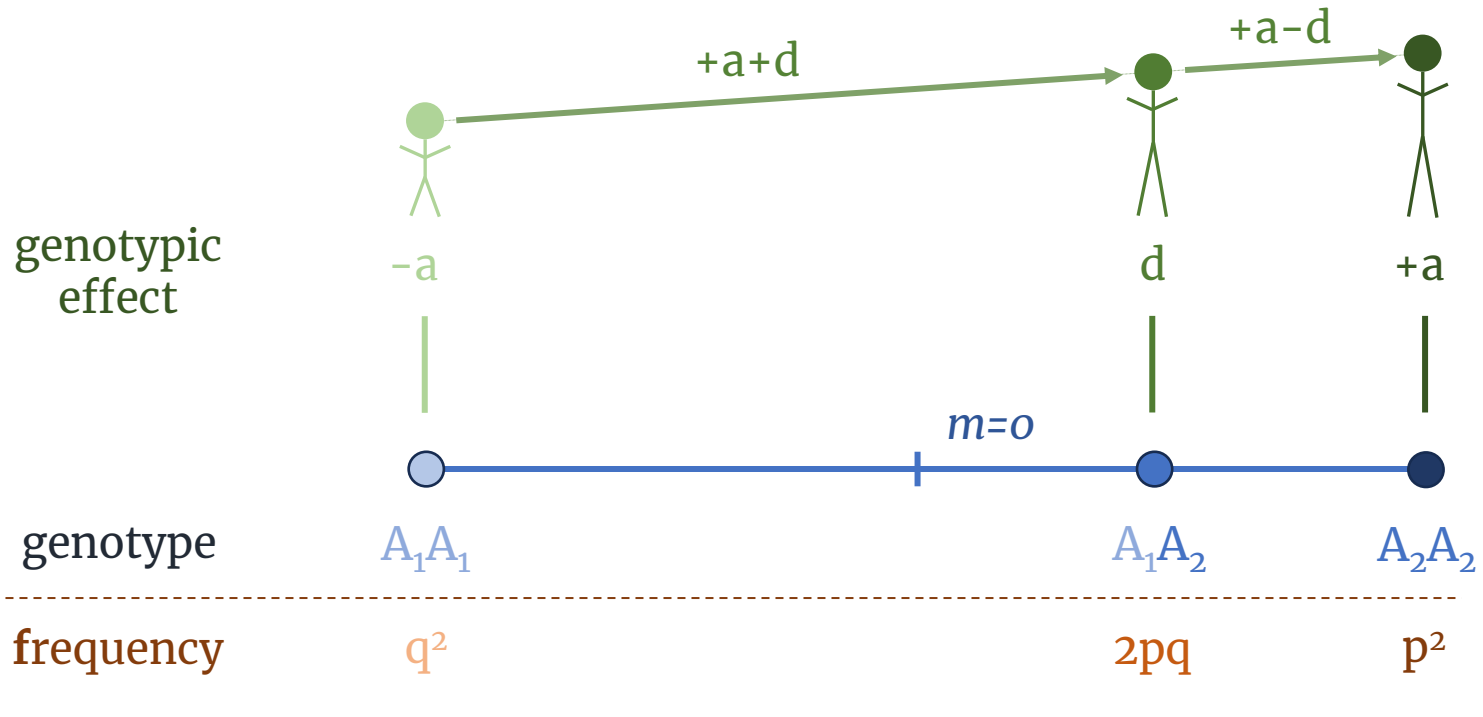
biometrical model

genotype with an additive effect (**d=0**)



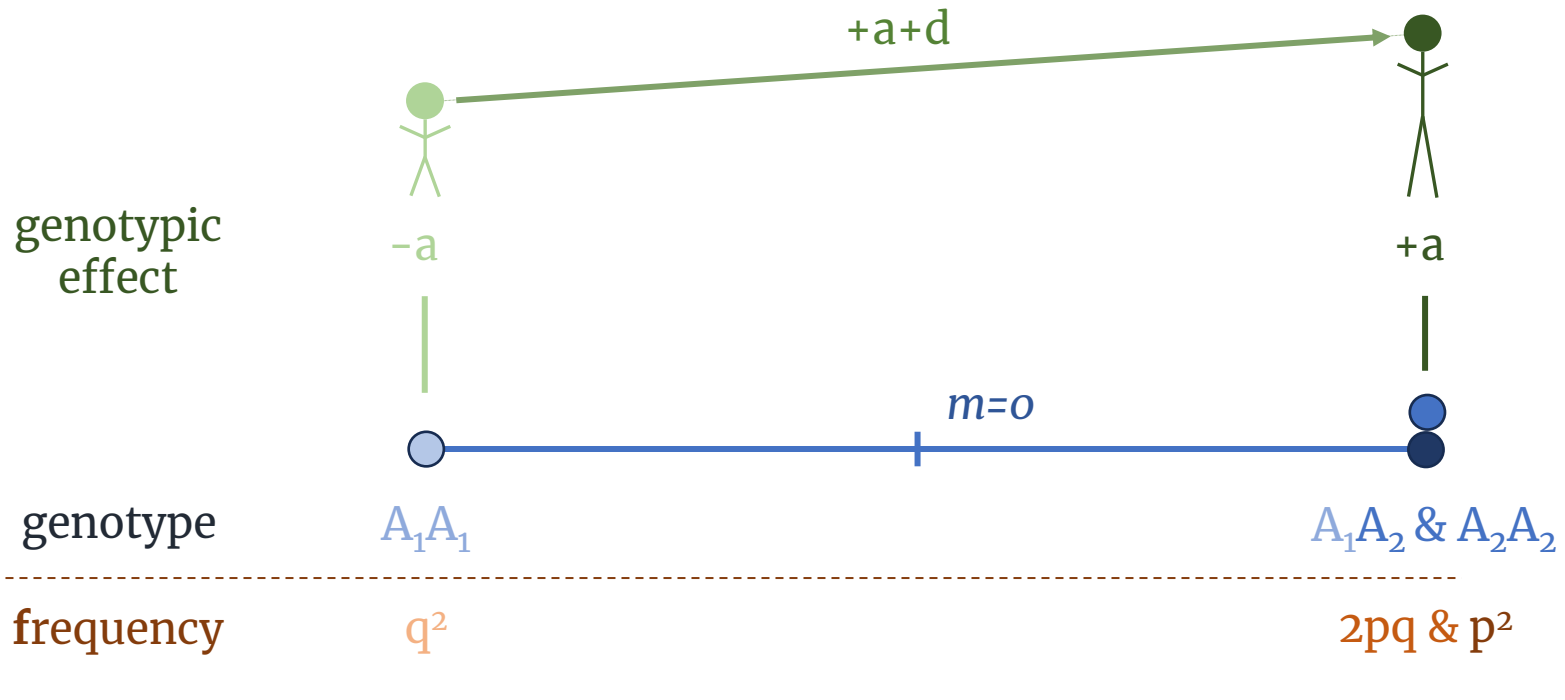
biometrical model

genotype with an additive and dominance effect (**d>o**)



biometrical model

genotype with a complete dominance effect (**d=a**)



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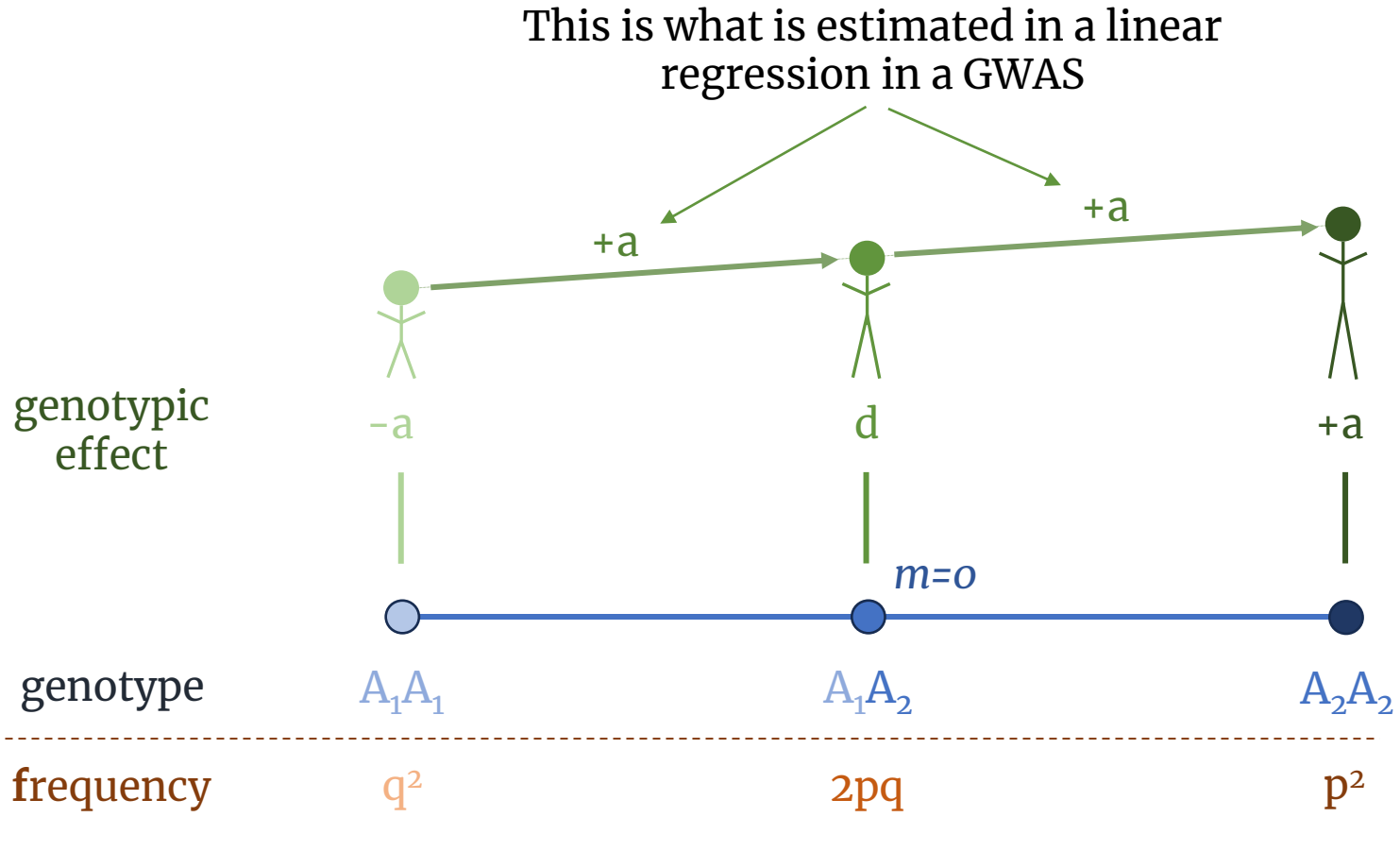
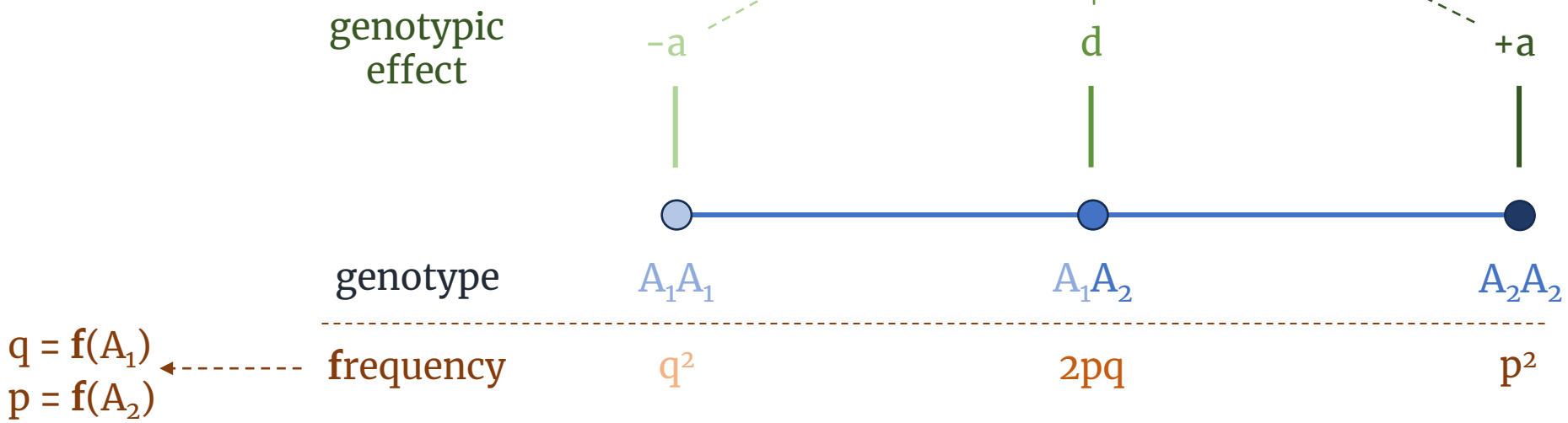


biometrical model

contribution of the locus to the Mean (X) $\longrightarrow$ $\mu = \sum_i x_i f(x_i)$

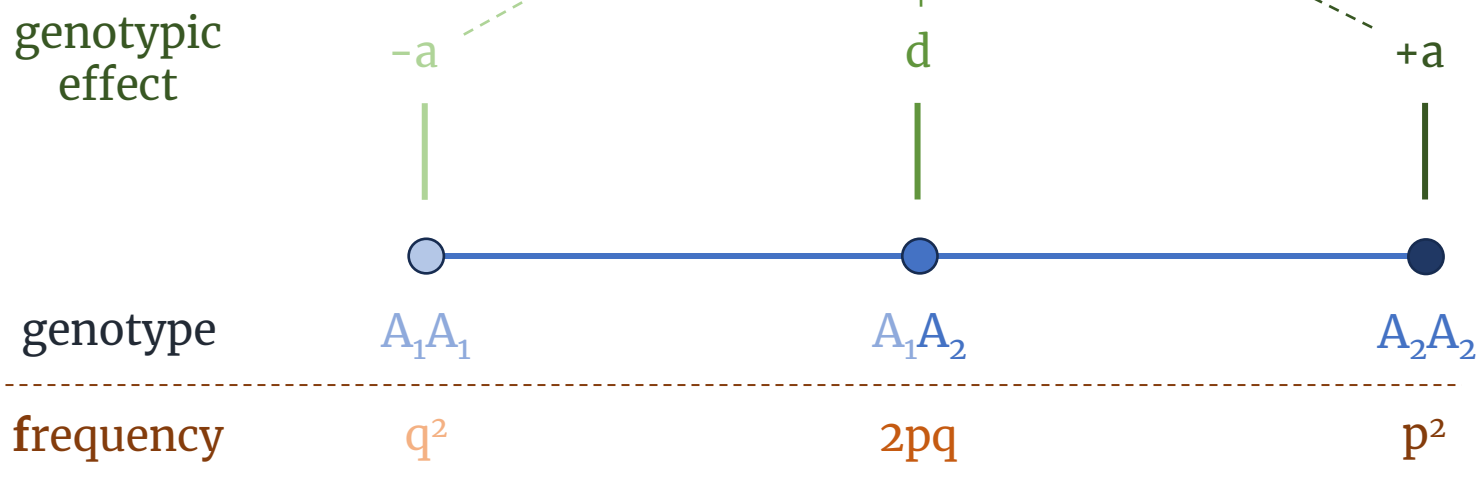
Mean (X) = $-a(q^2) + d(2pq) + a(p^2)$



biometrical model

contribution of the locus to the Mean (X) $\longrightarrow$ $\mu = \sum_i x_i f(x_i)$

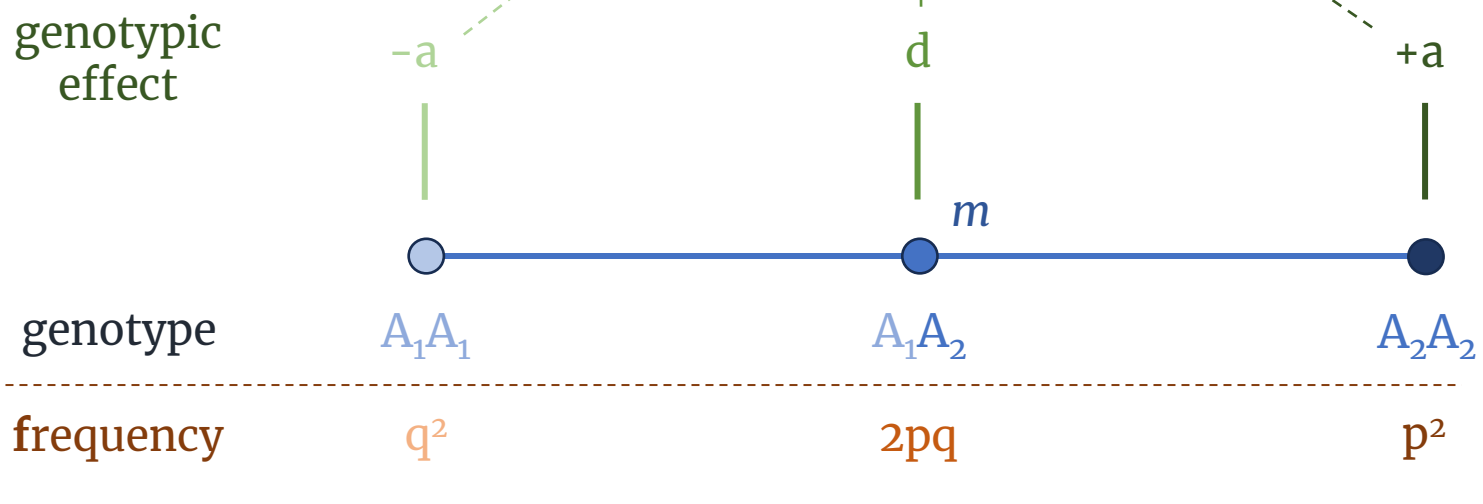
Mean (X) = $-a(q^2) + d(2pq) + a(p^2) = a(p-q) + 2pqd$



biometrical model

contribution of the locus to the Variance (X) ⟶ $Var = \sum_i (x_i - \mu)^2 f(x_i)$

Variance (X) = $(-a-m)^2q^2 + (d-m)^2 2pq + (a-m)^2p^2 = V_{QTL}$

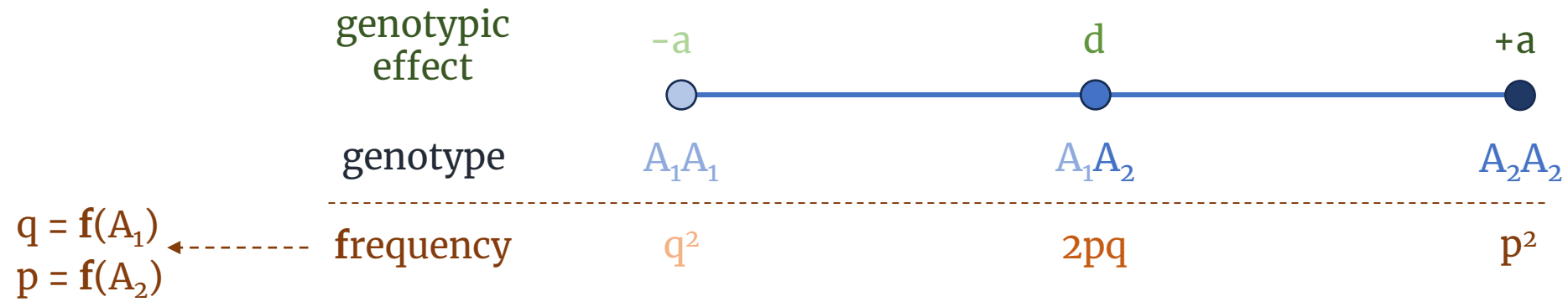


biometrical model

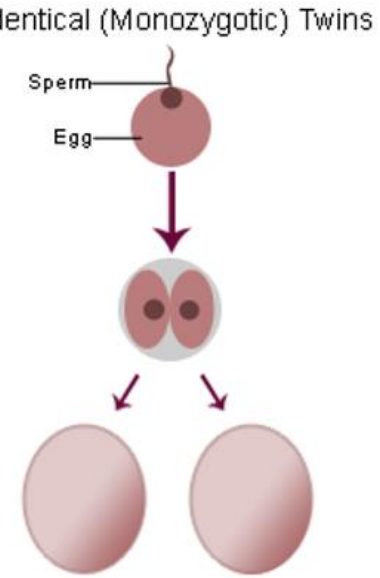
contribution of the locus to the Variance (X) ⟶ $Var = \sum_i (x_i - \mu)^2 f(x_i)$

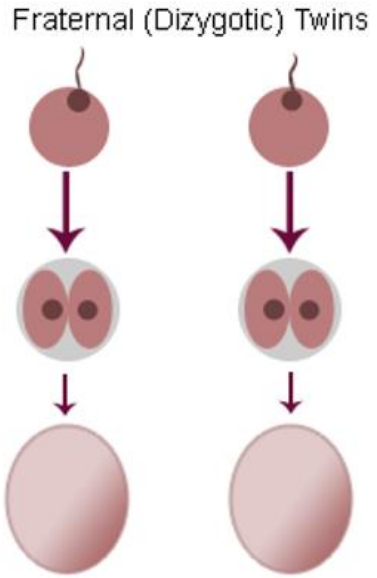
$$\text{Variance (X)} = (-a-m)^2q^2 + (d-m)^2 2pq + (a-m)^2p^2 = V_{QTL}$$

$$= \underbrace{2pq[a+(q-p)d]^2}_{V_{A_{QTL}}} + \underbrace{(2pqd)^2}_{V_{D_{QTL}}}$$



First classical twin studies (monozygotic [MZ] vs dizygotic [DZ] twins) were done in the late 1920s on intelligence.





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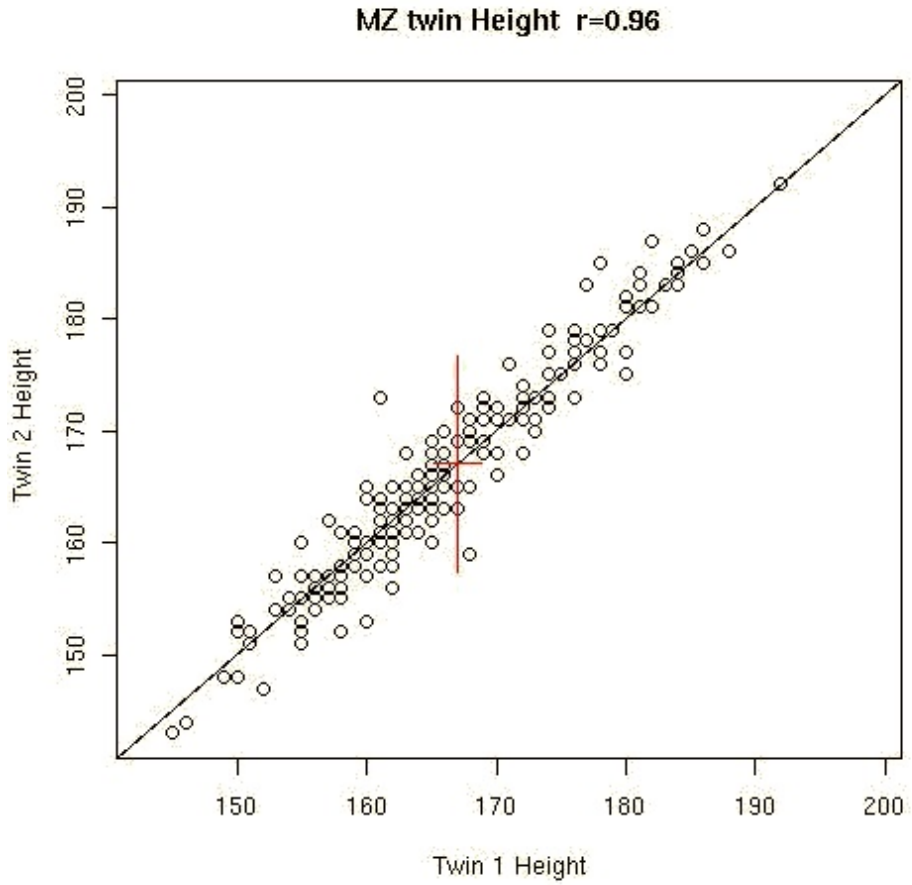
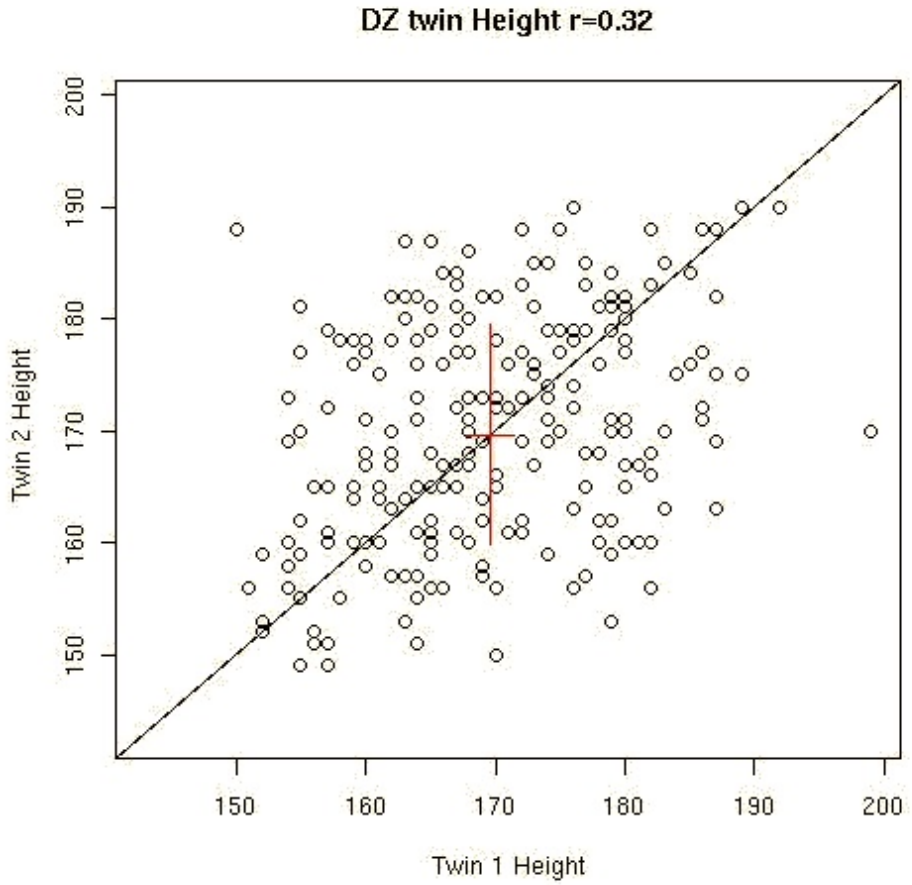
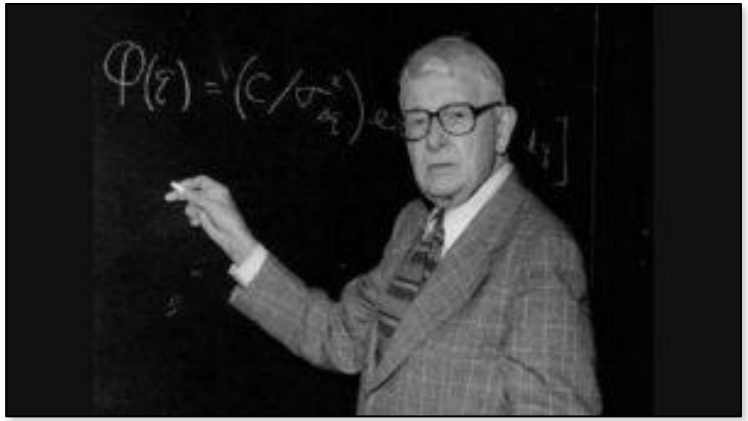

MZ twin Height r=0.96
Twin 2 Height
Twin 1 Height
150
160
170
180
190
200


DZ twin Height r=0.32
Twin 2 Height
Twin 1 Height
150
160
170
180
190
200


1859
1865
1886
1903
1918
1920s
1953
1970s
1980s
1990s
2000s
2010s
2020s

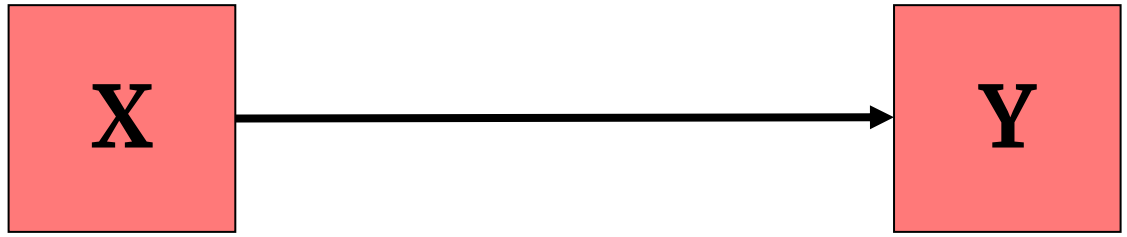
Structural Equation Modeling, 1921, Sewall Wright



Structural Equation Modeling, 1921, Sewall Wright

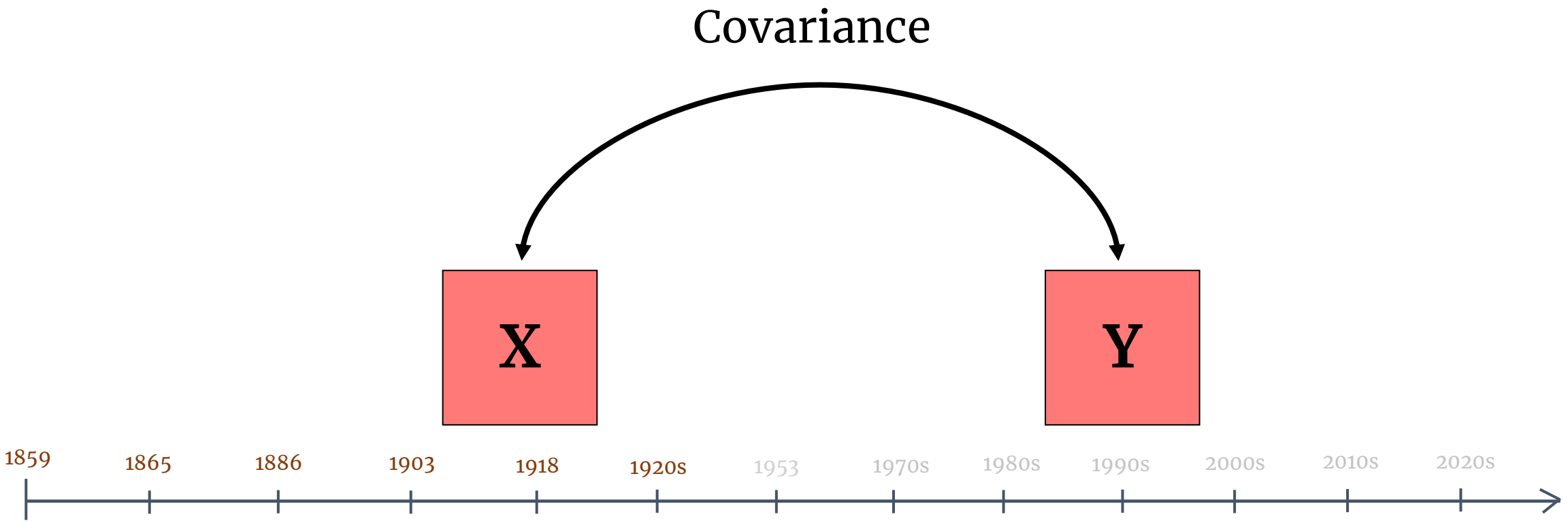
Types of relationships:

Linear Regression ("X causes Y")



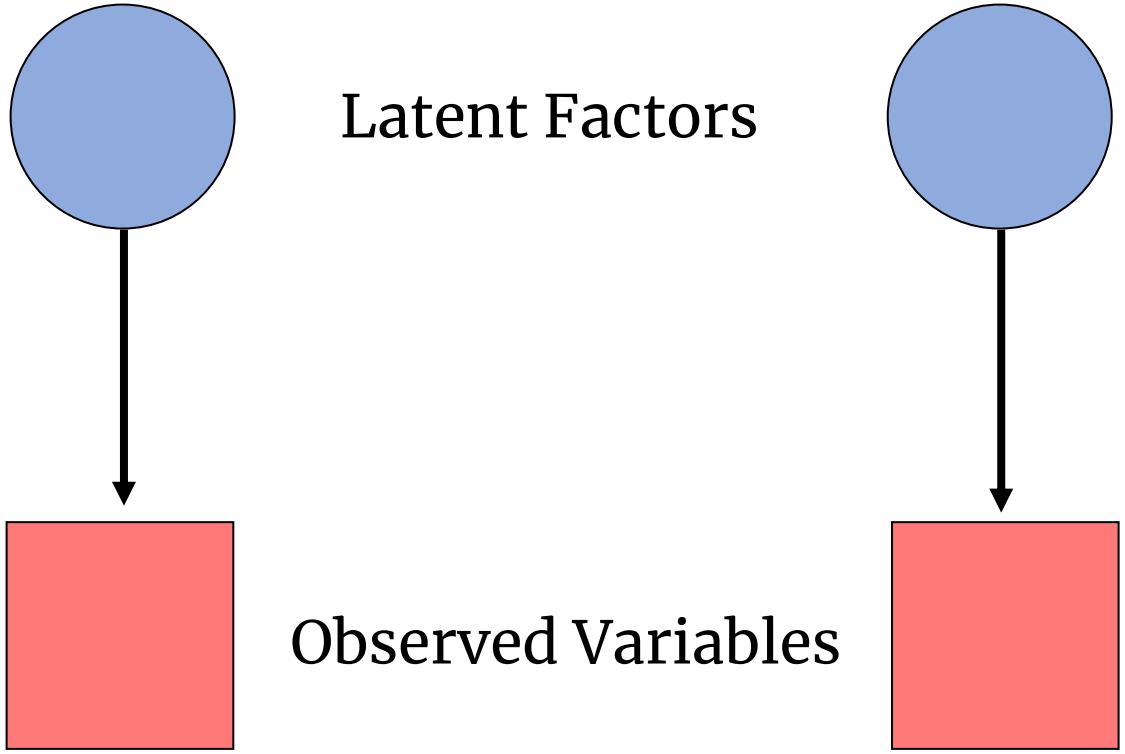
Structural Equation Modeling, 1921, Sewall Wright

Types of relationships:



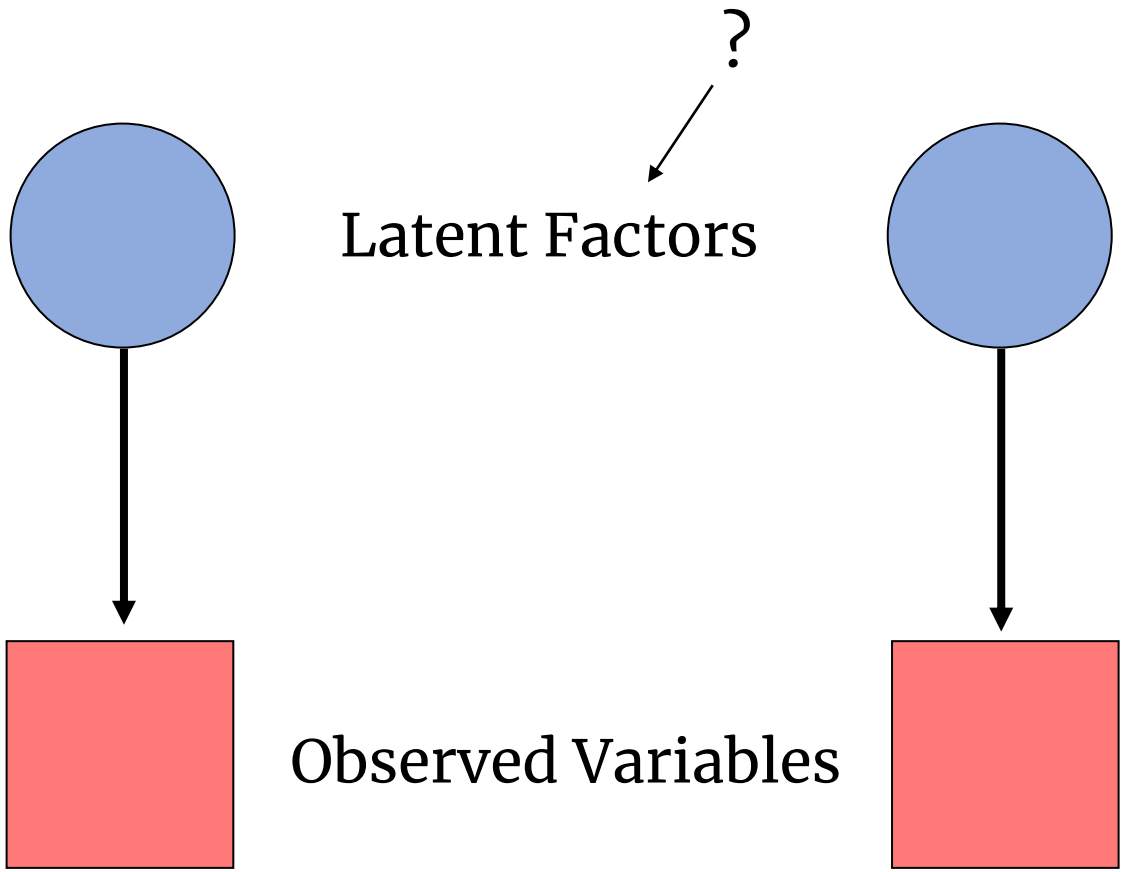
Structural Equation Modeling, 1921, Sewall Wright

Types of variables:

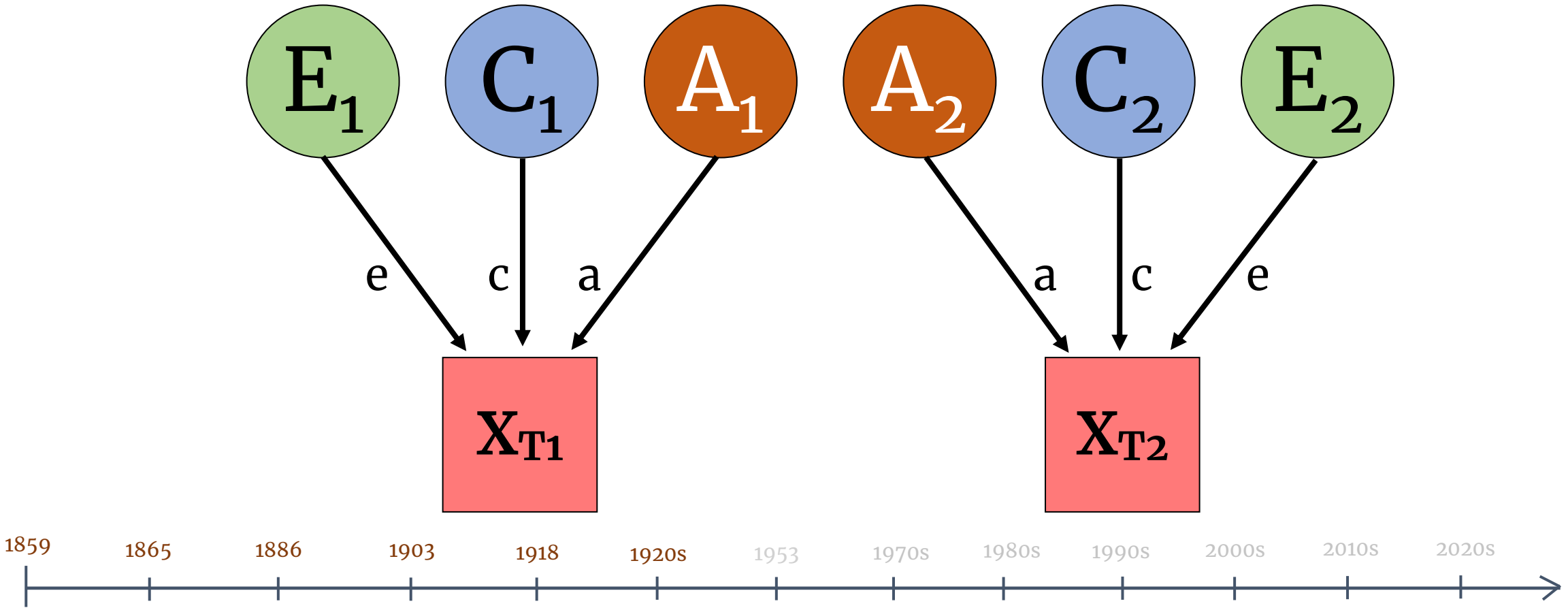


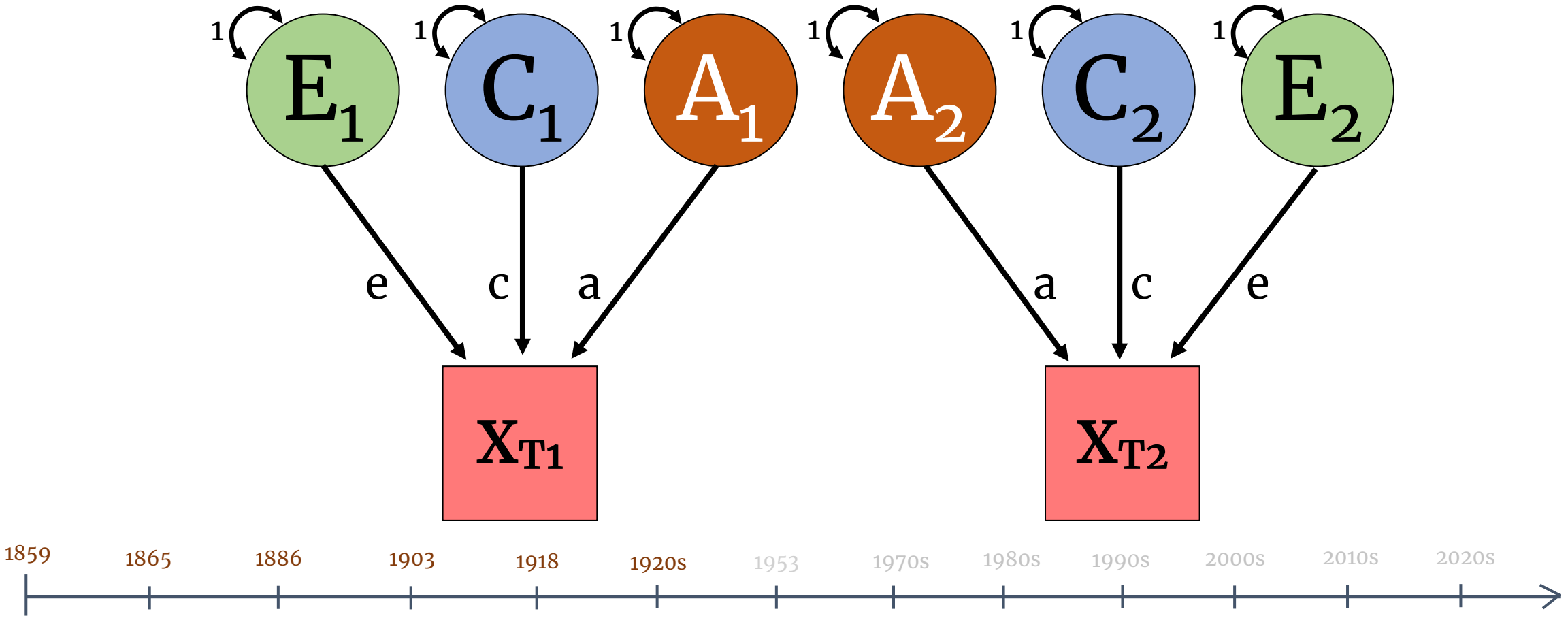
Structural Equation Modeling, 1921, Sewall Wright

Types of variables:



A = Additive Genetic Effects
C = Common Environment
E = Unique Environment (includes measurement error)




1
1
1
1
1
1
E_1
C_1
A_1
A_2
C_2
E_2
e
c
a
a
c
e
X_{T1}
X_{T2}
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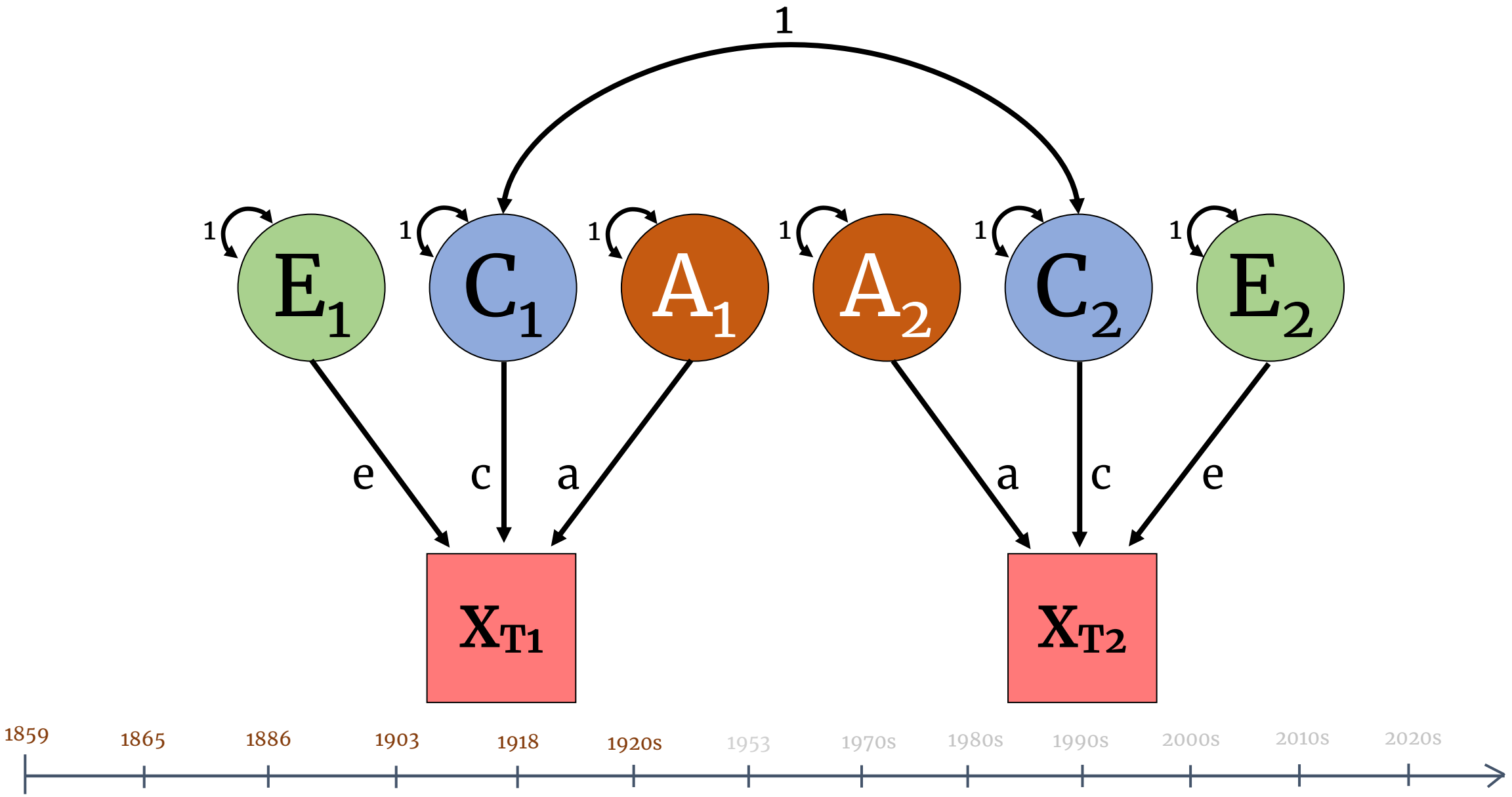
2020s


1
1
1
1
1
1
1
E1
C1
A1
A2
C2
E2
e
c
a
a
c
e
XT1
XT2
1859
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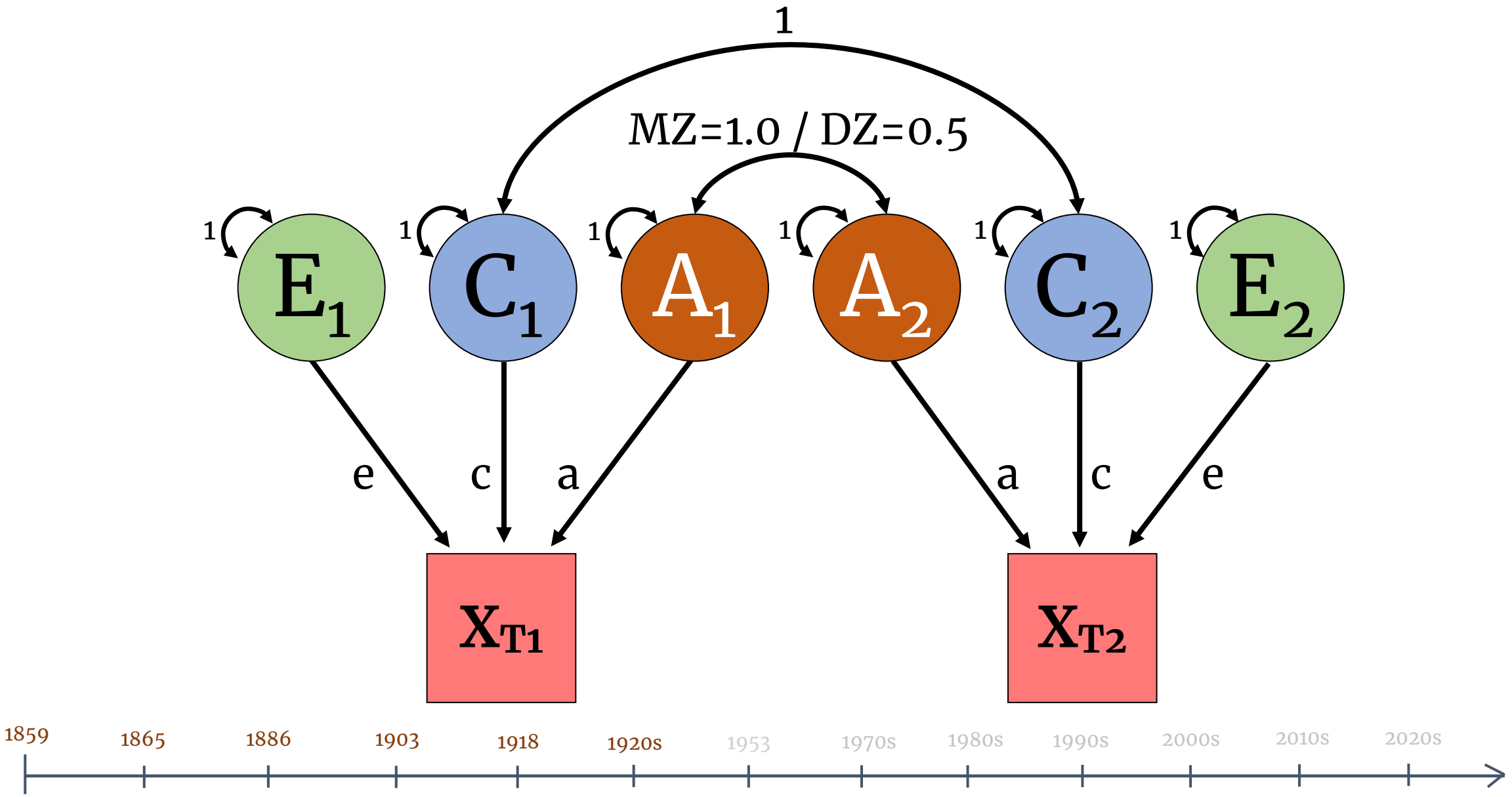
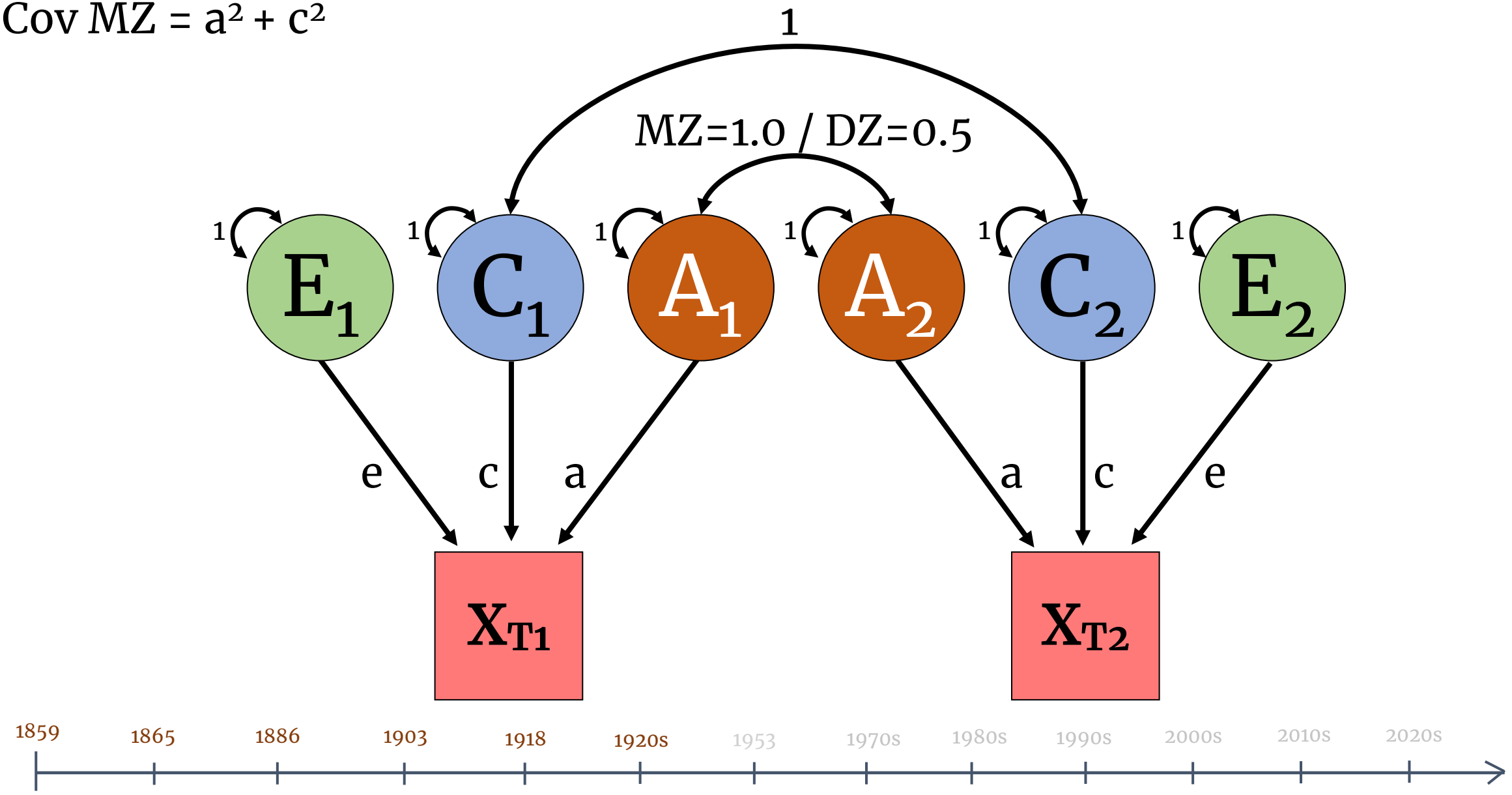
2020s


1
MZ=1.0 / DZ=0.5
1
1
1
1
1
1
E1
C1
A1
A2
C2
E2
e
c
a
a
c
e
XT1
XT2
1859
1865
1886
1903
1918
1920s
1953
1970s
1980s
1990s
2000s
2010s
2020s

Cov MZ = $a^2 + c^2$


1
MZ=1.0 / DZ=0.5
1
1
1
1
1
1
E1
C1
A1
A2
C2
E2
e
c
a
a
c
e
XT1
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1859
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1920s
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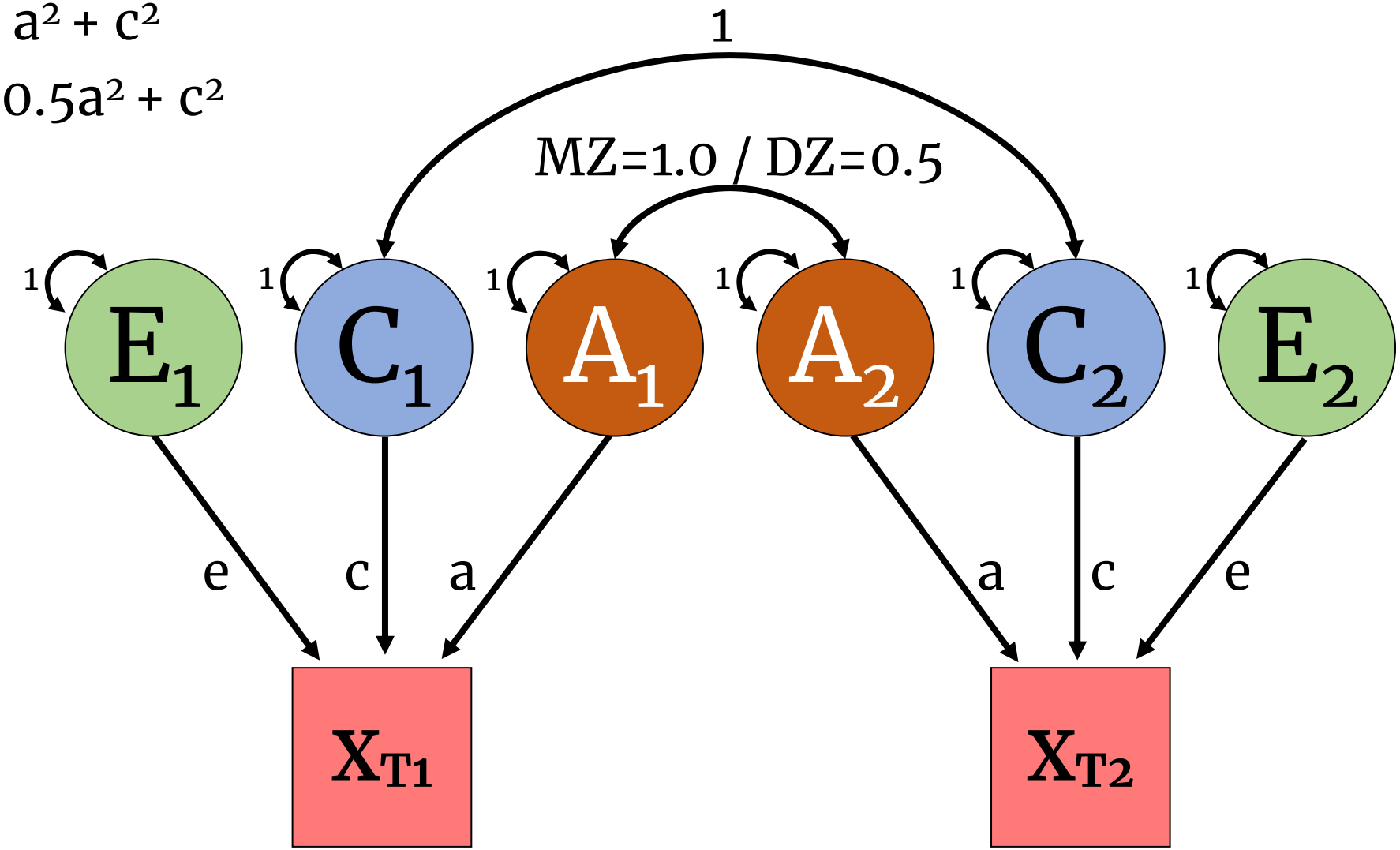
2010s
2020s

Cov MZ = $a^2 + c^2$

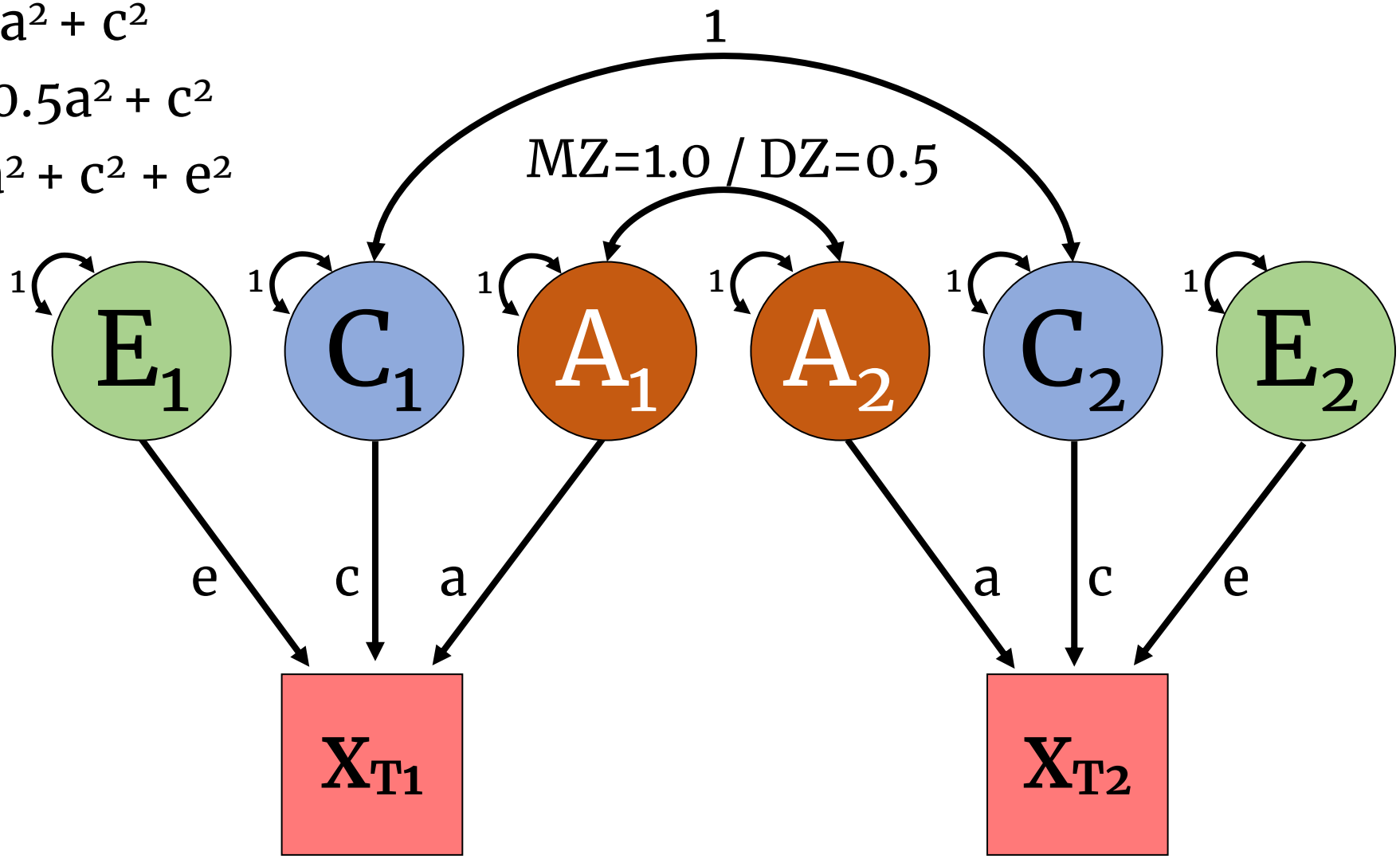
Cov DZ = $0.5a^2 + c^2$



Cov MZ = $a^2 + c^2$

Cov DZ = $0.5a^2 + c^2$

Var(X) = $a^2 + c^2 + e^2$



Heredity (1978), **41** (3), 249-320

MODEL-FITTING APPROACHES TO THE ANALYSIS OF HUMAN BEHAVIOUR

L. J. EAVES, KRYSTYNA A. LAST, P. A. YOUNG and N. G. MARTIN*
Department of Genetics, University of Birmingham, Birmingham B15 2TT

1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

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THE POWER OF THE CLASSICAL TWIN STUDY

N. G. MARTIN,* L. J. EAVES,* M. J. KEARSEY* and P. DAVIES†
**Department of Genetics and †Department of Mathematical Statistics,*
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Received 5.v.77

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THE GENETICAL ANALYSIS OF COVARIANCE STRUCTURE

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Received 9.ix.76

Behavior Genetics, Vol. 23, No. 1, 1993

Testing Hypotheses About Direction of Causation Using Cross-Sectional Family Data

A. C. Heath,[1] R. C. Kessler,[2] M. C. Neale,[3] J. K. Hewitt,[3] L. J. Eaves,[3,4] and K. S. Kendler[3,4]

Behavior Genetics (2021) 51:170–180
https://doi.org/10.1007/s10519-021-10049-9

ORIGINAL RESEARCH

Notes on Three Decades of Methodology Workshops

Hermine H. Maes[1,2,3,4]

Behavior Genetics (2021) 51:170–180
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ORIGINAL RESEARCH

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Hermine H. Maes[1,2,3,4]

1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

1987: LISREL > 1990: Mx > 2008: OpenMx

Mike Neale

'classic'Mx

graphical interface

MxGui

OpenMx Team

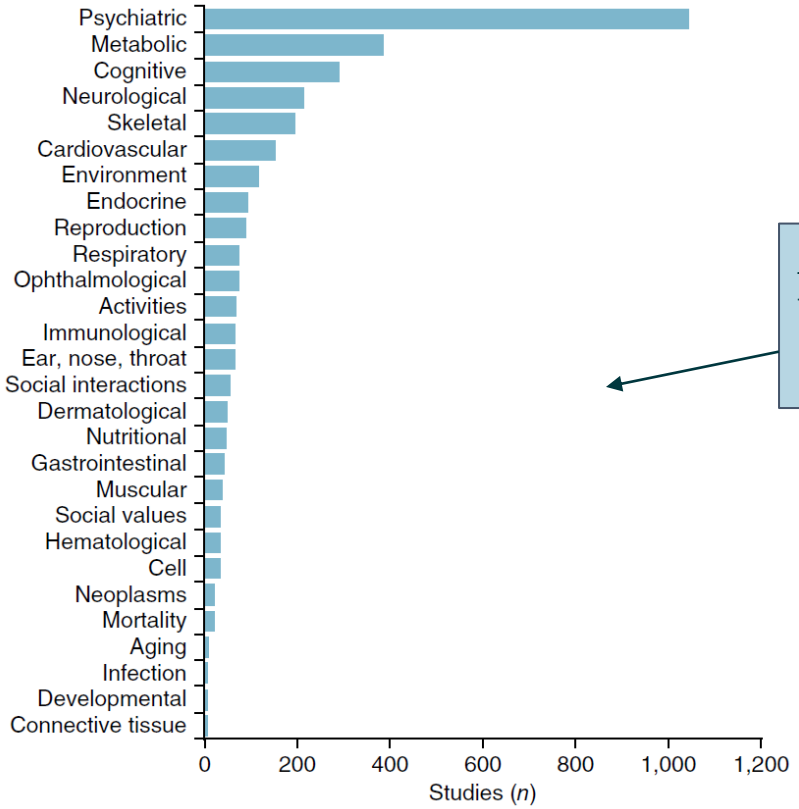
1993 Boulder TC5

“First law of behavior genetics”:
All human behavioral traits are heritable.

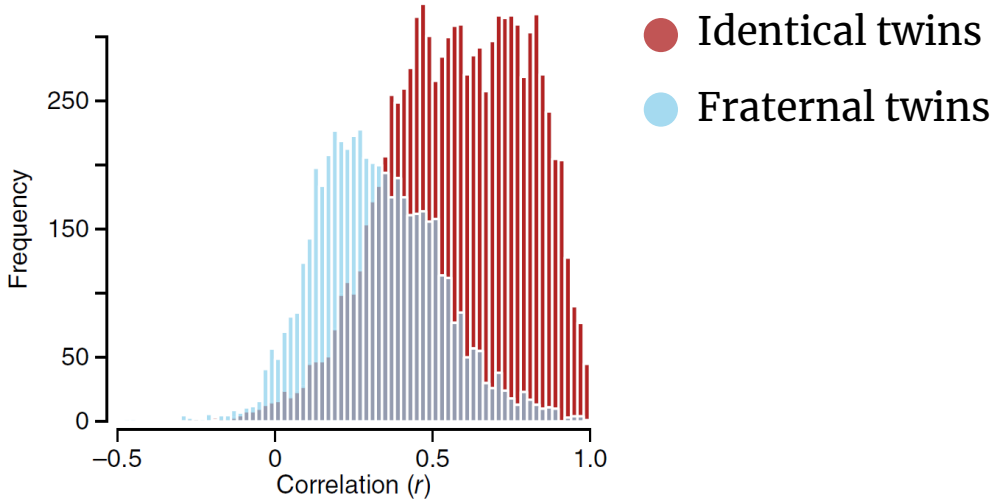
NATURE REVIEWS | GENETICS

CLASSICAL TWIN STUDIES AND BEYOND

Dorret Boomsma, Andreas Busjahn‡ and Leena Peltonen§*



All twin studies between 1958 & 2012



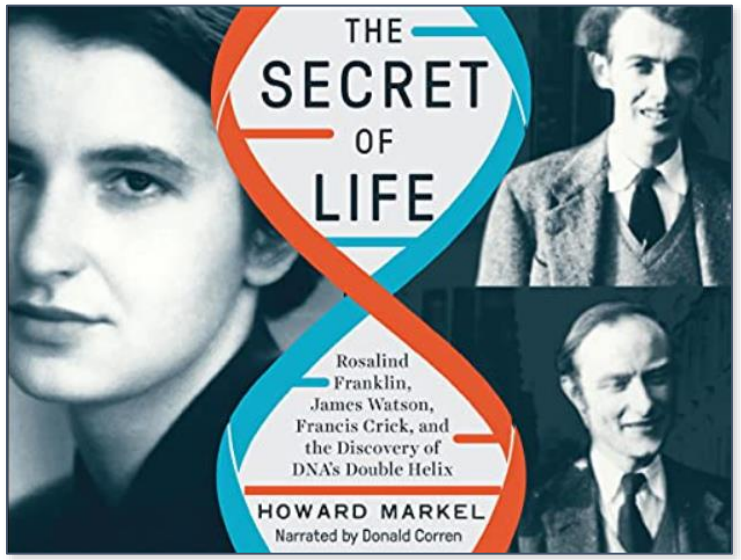
nature genetics

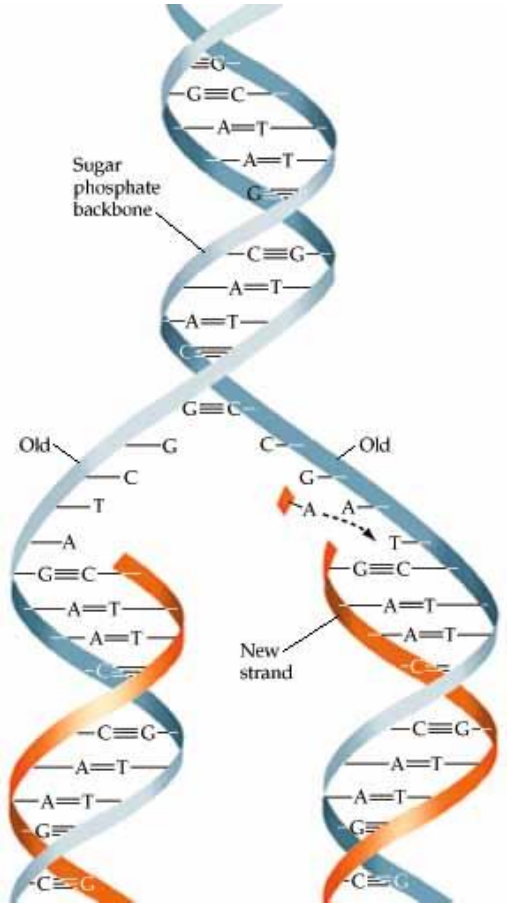
Meta-analysis of the heritability of human traits based on fifty years of twin studies

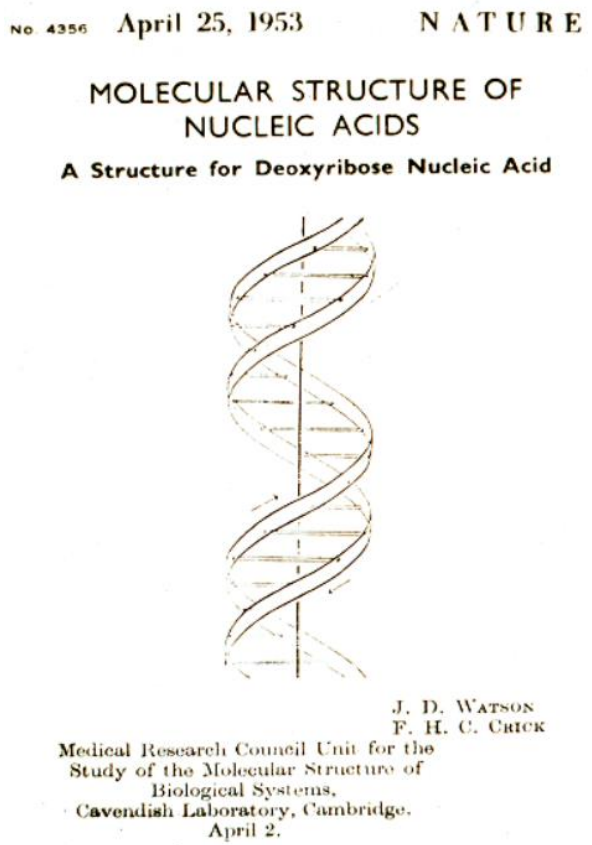
Tinca J C Polderman[1,10], Beben Benyamin[2,10], Christiaan A de Leeuw[1,3], Patrick F Sullivan[4–6], Arjen van Bochoven[7], Peter M Visscher[2,8,11] & Danielle Posthuma[1,9,11]

1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

DNA = double helix!







No 4356 April 25, 1953 NATURE

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

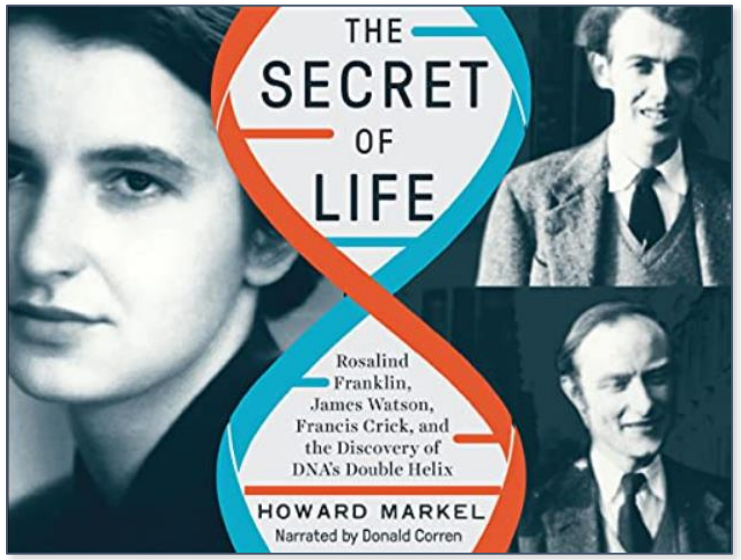
A Structure for Deoxyribose Nucleic Acid

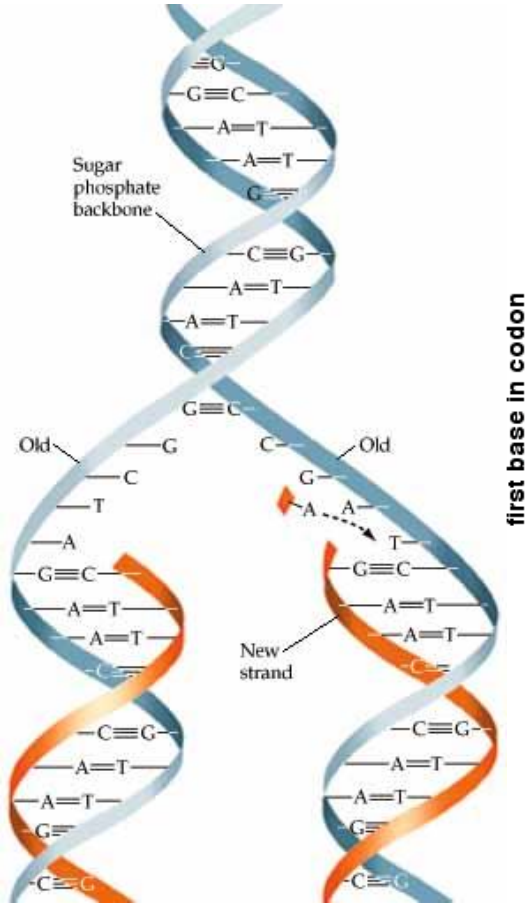
J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge. April 2.

1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

DNA = double helix!





first base in codon	second base in codon: T	second base in codon: C	second base in codon: A	second base in codon: G	third base in codon
T	TTT Phe	TCT Ser	TAT Tyr	TGT Cys	T
	TTC Phe	TCC Ser	TAC Tyr	TGC Cys	C
	TTA Leu	TCA Ser	TAA stop	TGA stop	A
	TTG Leu	TCG Ser	TAG stop	TGG Trp	G
C	CTT Leu	CCT Pro	CAT His	CGT Arg	T
	CTC Leu	CCC Pro	CAC His	CGC Arg	C
	CTA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CTG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	ATT Ile	ACT Thr	AAT Asn	AGT Ser	T
	ATC Ile	ACC Thr	AAC Asn	AGC Ser	C
	ATA Ile	ACA Thr	AAA Lys	AGA Arg	A
	ATG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GTT Val	GCT Ala	GAT Asp	GGT Gly	T
	GTC Val	GCC Ala	GAC Asp	GGC Gly	C
	GTA Val	GCA Ala	GAA Glu	GGA Gly	A
	GTG Val	GCG Ala	GAG Glu	GGG Gly	G

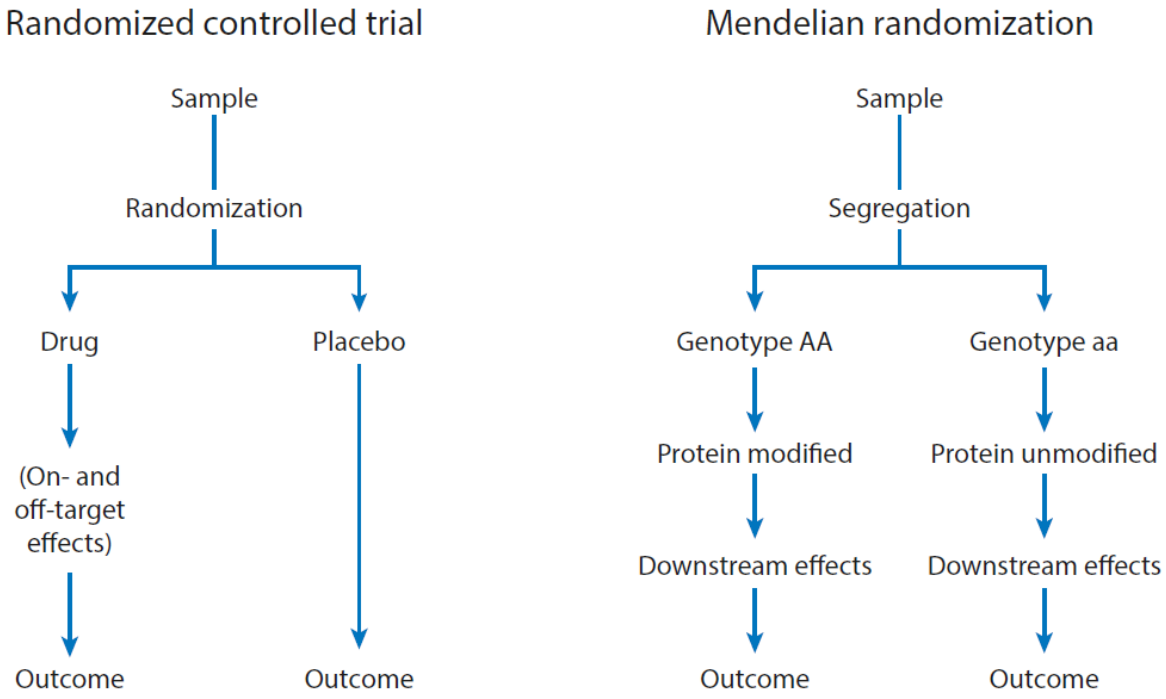
There are 20 amino-acids coded for in three letter words called "codons"

1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

Mendelian Randomization: New Applications in the Coming Age of Hypothesis-Free Causality

David M. Evans[1,2] and George Davey Smith[2]

www.annualreviews.org

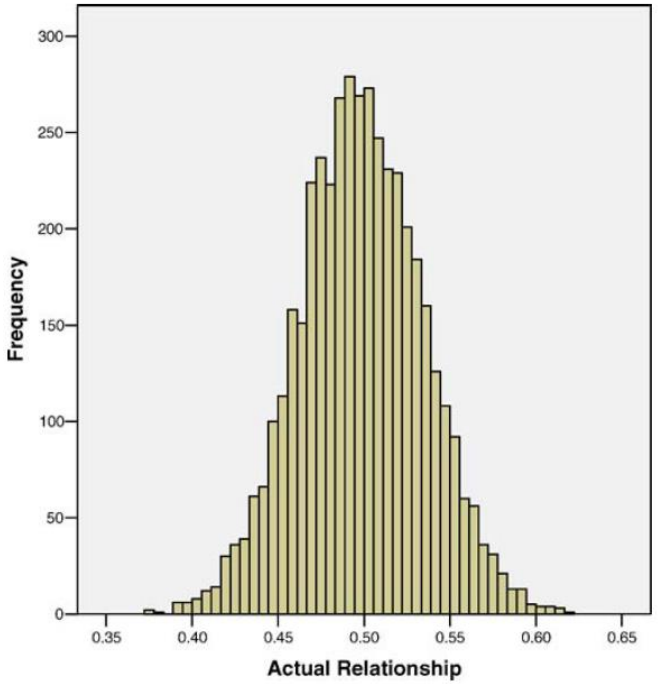


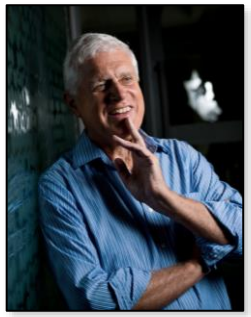
OPEN ACCESS Freely available online PLOS GENETICS

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





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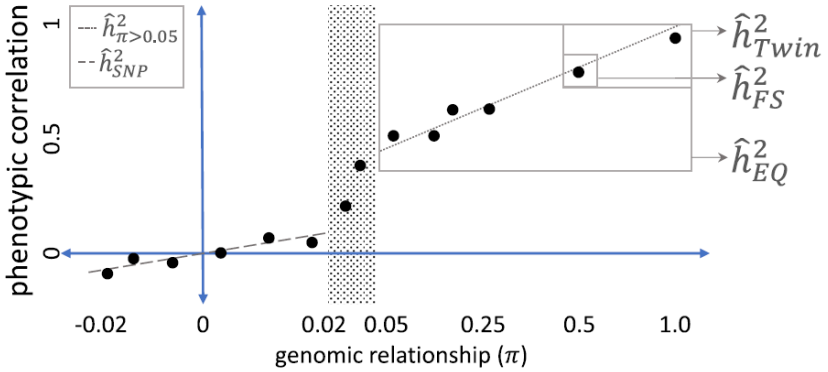
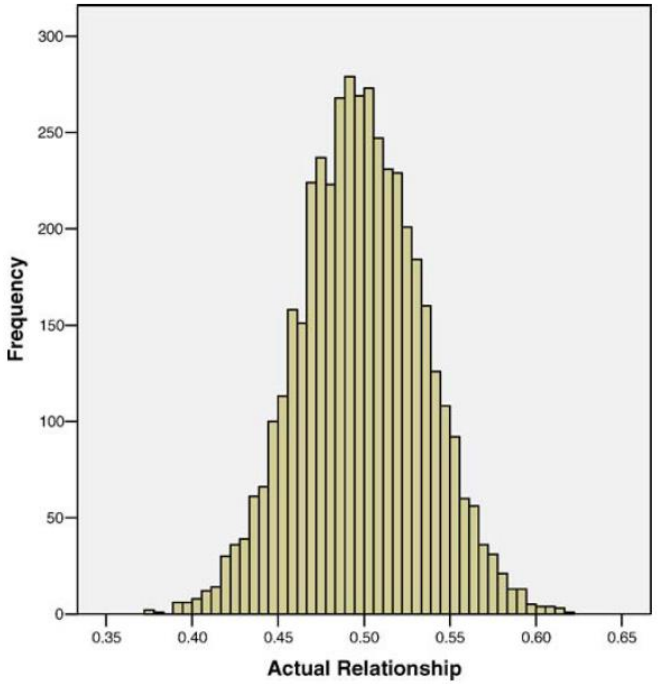
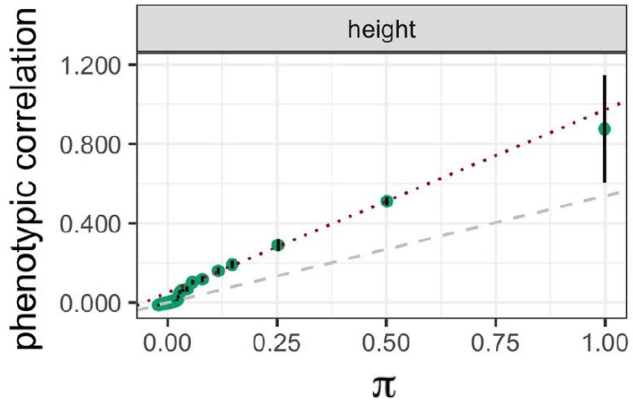






ARTICLE

https://doi.org/10.1038/s41467-021-21283-4 OPEN

Check for updates

Phenotypic covariance across the entire spectrum of relatedness for 86 billion pairs of individuals

Kathryn E. Kemper[1✉], Loic Yengo[1], Zhili Zheng[1], Abdel Abdellaoui[2], Matthew C. Keller[3,4], Michael E. Goddard[5,6], Naomi R. Wray[1,7], Jian Yang[1] & Peter M. Visscher[1,7✉]

1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

SCIENCE • VOL. 273 • 13 SEPTEMBER 1996

The Future of Genetic Studies of Complex Human Diseases

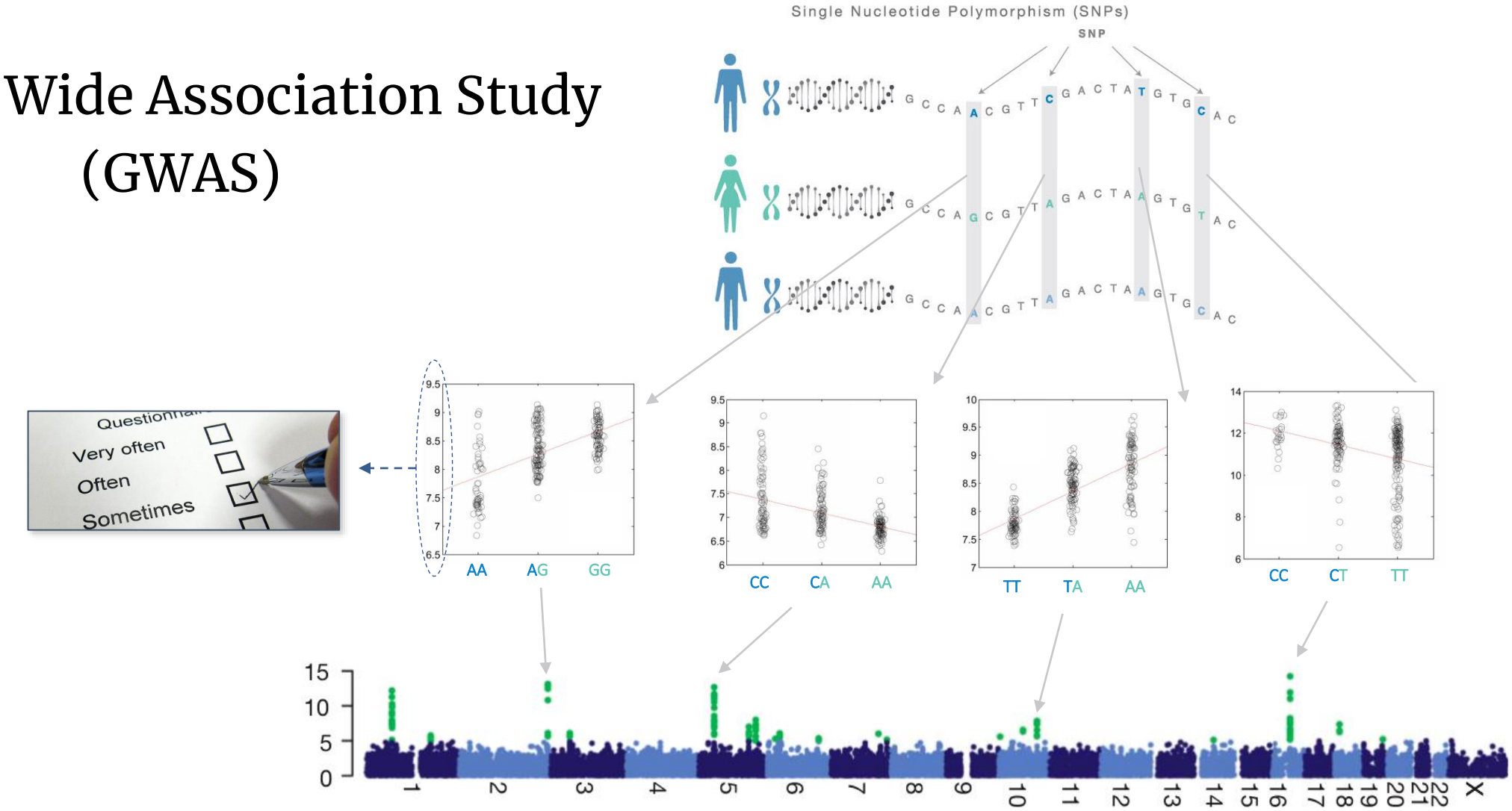
Neil Risch and Kathleen Merikangas

		Linkage			Association			
					Singletons		Sib pairs	
Genotypic risk ratio (γ)	Frequency of disease allele A (p)	Probability of allele sharing (Y)	No. of families required (N)	Probability of transmitting disease allele A P(tr-A)	Proportion of heterozygous parents (Het)	(N)	(Het)	(N)
4.0	0.01	0.520	4260	0.800	0.048	1098	0.112	235
	0.10	0.597	185	0.800	0.346	150	0.537	48
	0.50	0.576	297	0.800	0.500	103	0.424	61
	0.80	0.529	2013	0.800	0.235	222	0.163	161
2.0	0.01	0.502	296,710	0.667	0.029	5823	0.043	1970
	0.10	0.518	5382	0.667	0.245	695	0.323	264
	0.50	0.526	2498	0.667	0.500	340	0.474	180
	0.80	0.512	11,917	0.667	0.267	640	0.217	394
1.5	0.01	0.501	4,620,807	0.600	0.025	19,320	0.031	7776
	0.10	0.505	67,816	0.600	0.197	2218	0.253	941
	0.50	0.510	17,997	0.600	0.500	949	0.490	484
	0.80	0.505	67,816	0.600	0.286	1663	0.253	941

Comparison of linkage and association studies. Number of families needed for identification of a disease gene.

Thus, the primary limitation of genome-wide association tests is not a statistical one but a technological one. A large number of genes (up to 100,000) and polymorphisms (preferentially ones that create alterations in derived proteins or their expression) must first be identified, and an extremely large number of such polymorphisms will need to be tested. Although testing such a large number of polymorphisms on several hundred, or even a thousand families, might currently seem implausible in scope, more efficient methods of screening a large number of polymorphisms (for example, sample pooling) may be possible.

Genome-Wide Association Study (GWAS)



2016

PRESS RELEASES / 01.26.16

Genetic study provides first-ever insight into biological origin of schizophrenia

ARTICLE

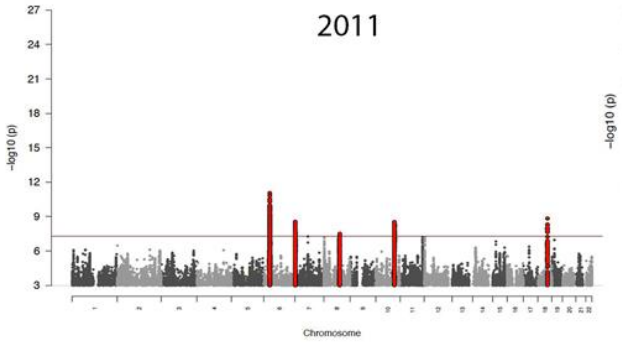
doi:10.1038/nature16549

Schizophrenia risk from complex variation of complement component 4

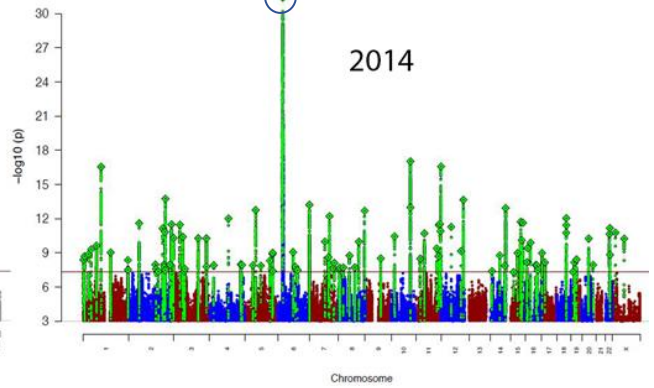
Aswin Sekar[1,2,3], Allison R. Bialas[4,5], Heather de Rivera[1,2], Avery Davis[1,2], Timothy R. Hammond[4], Nolan Kamitaki[1,2], Katherine Tooley[1,2], Jessy Presumey[5], Matthew Baum[1,2,3,4], Vanessa Van Doren[1], Giulio Genovese[1,2], Samuel A. Rose[2], Robert E. Handsaker[1,2], Schizophrenia Working Group of the Psychiatric Genomics Consortium*, Mark J. Daly[2,6], Michael C. Carroll[5], Beth Stevens[2,4] & Steven A. McCarroll[1,2]

Schizophrenia is a heritable brain illness with unknown pathogenic mechanisms. Schizophrenia's strongest genetic association at a population level involves variation in the major histocompatibility complex (MHC) locus, but the genes and molecular mechanisms accounting for this have been challenging to identify. Here we show that this association arises in part from many structurally diverse alleles of the complement component 4 (*C4*) genes. We found that these alleles generated widely varying levels of *C4A* and *C4B* expression in the brain, with each common *C4* allele associating with schizophrenia in proportion to its tendency to generate greater expression of *C4A*. Human C4 protein localized to neuronal synapses, dendrites, axons, and cell bodies. In mice, C4 mediated synapse elimination during postnatal development. These results implicate excessive complement activity in the development of schizophrenia and may help explain the reduced numbers of synapses in the brains of individuals with schizophrenia.

Influences "synaptic pruning" — the elimination of connections between neurons



N ~50,000



N ~150,000

PGC

Psychiatric Genomics Consortium

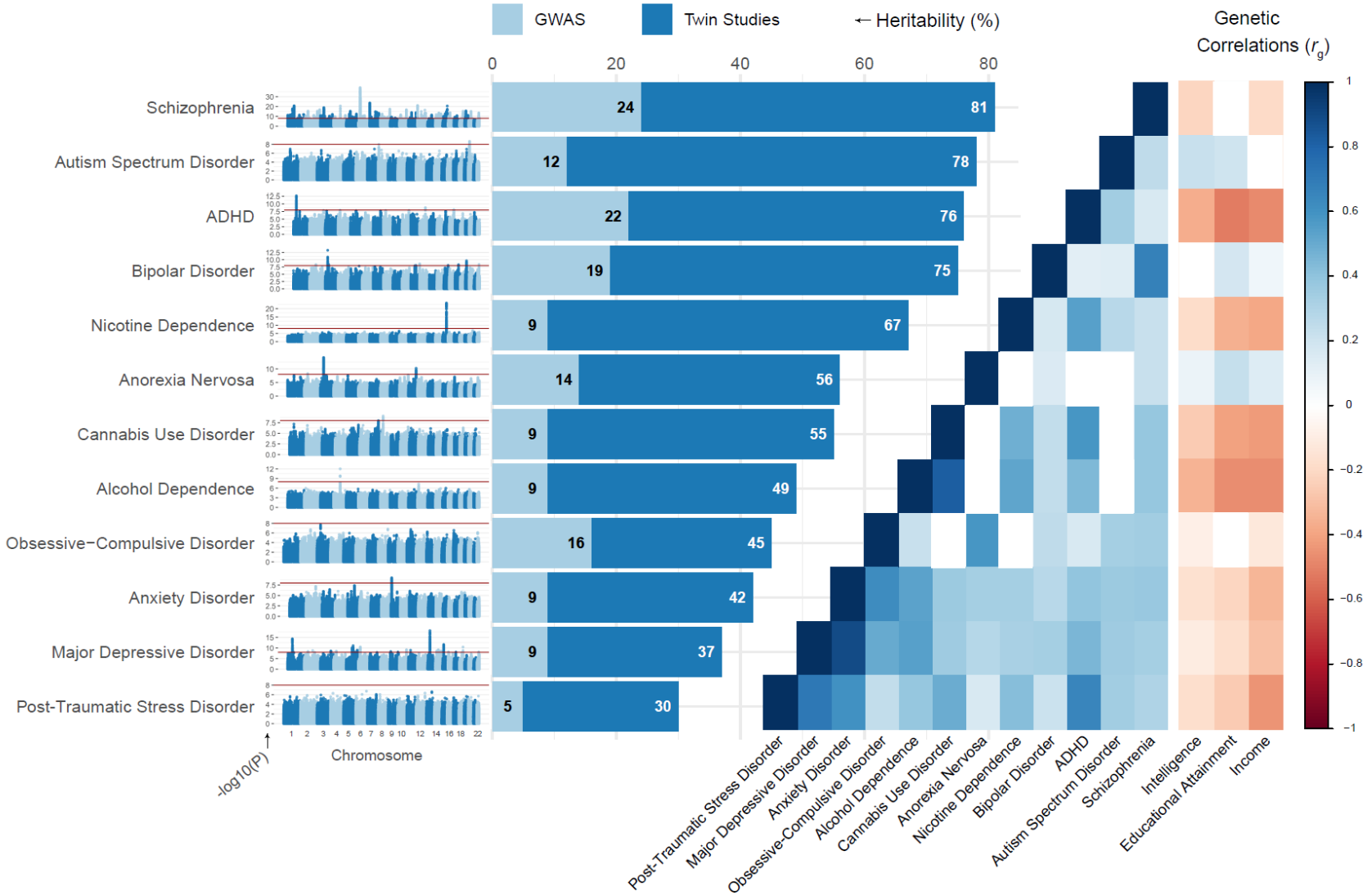
1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

TIJDSCHRIFT VOOR PSYCHIATRIE - JAARGANG 64 - MEI 2022

Genetica en psychiatrie

A. Abdellaoui, K.J.H. Verweij

PGC
Psychiatric Genomics Consortium



1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

nature genetics

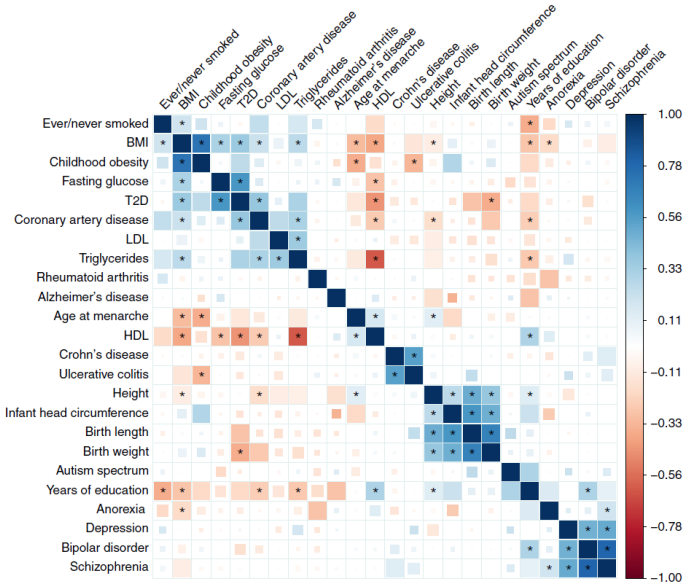
LD Score regression distinguishes confounding from polygenicity in genome-wide association studies

Brendan K Bulik-Sullivan[1–3], Po-Ru Loh[1,4], Hilary K Finucane[4,5], Stephan Ripke[2,3], Jian Yang[6], Schizophrenia Working Group of the Psychiatric Genomics Consortium[7], Nick Patterson[1], Mark J Daly[1–3], Alkes L Price[1,4,8] & Benjamin M Neale[1–3]

nature genetics

An atlas of genetic correlations across human diseases and traits

Brendan Bulik-Sullivan[1–3,9], Hilary K Finucane[4,9], Verneri Anttila[1–3], Alexander Gusev[5,6], Felix R Day[7], Po-Ru Loh[1,5], ReproGen Consortium[8], Psychiatric Genomics Consortium[8], Genetic Consortium for Anorexia Nervosa of the Wellcome Trust Case Control Consortium 3[8], Laramie Duncan[1–3], John R B Perry[7], Nick Patterson[1], Elise B Robinson[1–3], Mark J Daly[1–3], Alkes L Price[1,5,6,10] & Benjamin M Neale[1–3,10]



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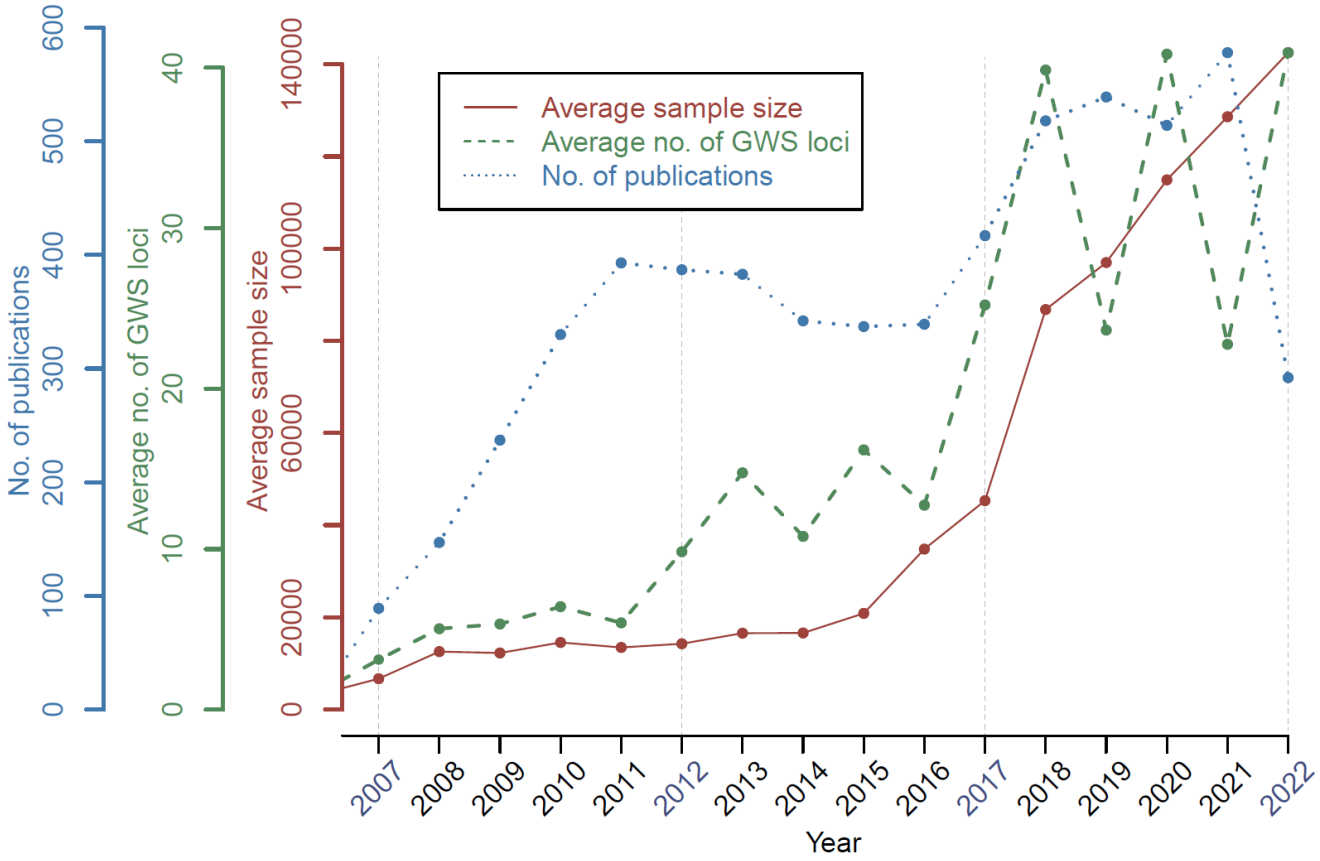


The American Journal of Human Genetics **REVIEW**

15 years of GWAS discovery: Realizing the promise

Abdel Abdellaoui,[1,*] Loic Yengo,[2] Karin J.H. Verweij,[1] and Peter M. Visscher[2]

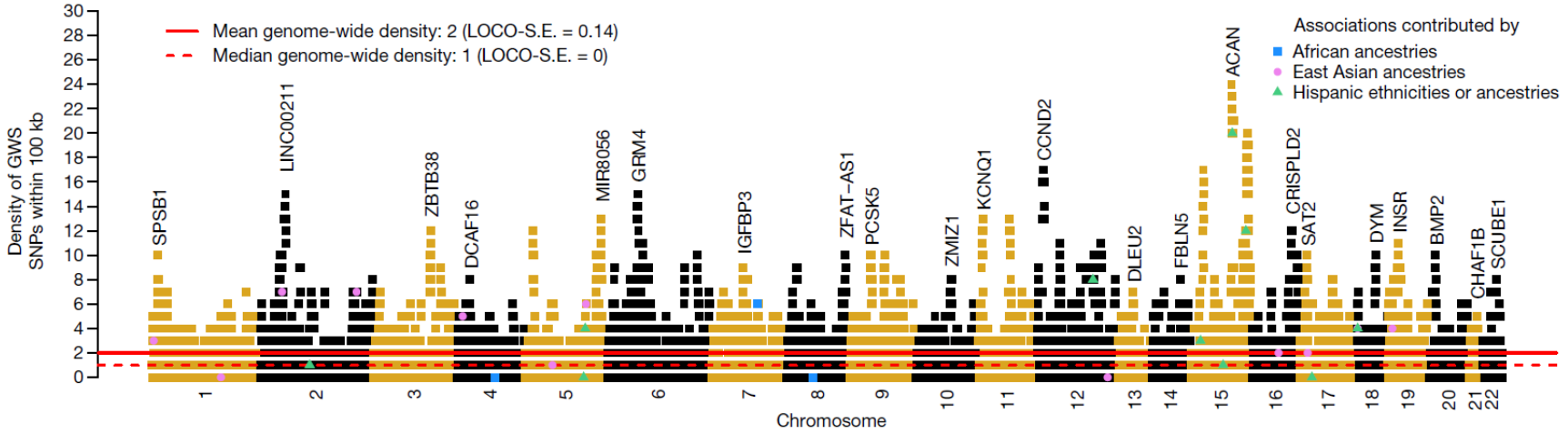
1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

Article

A saturated map of common genetic variants associated with human height

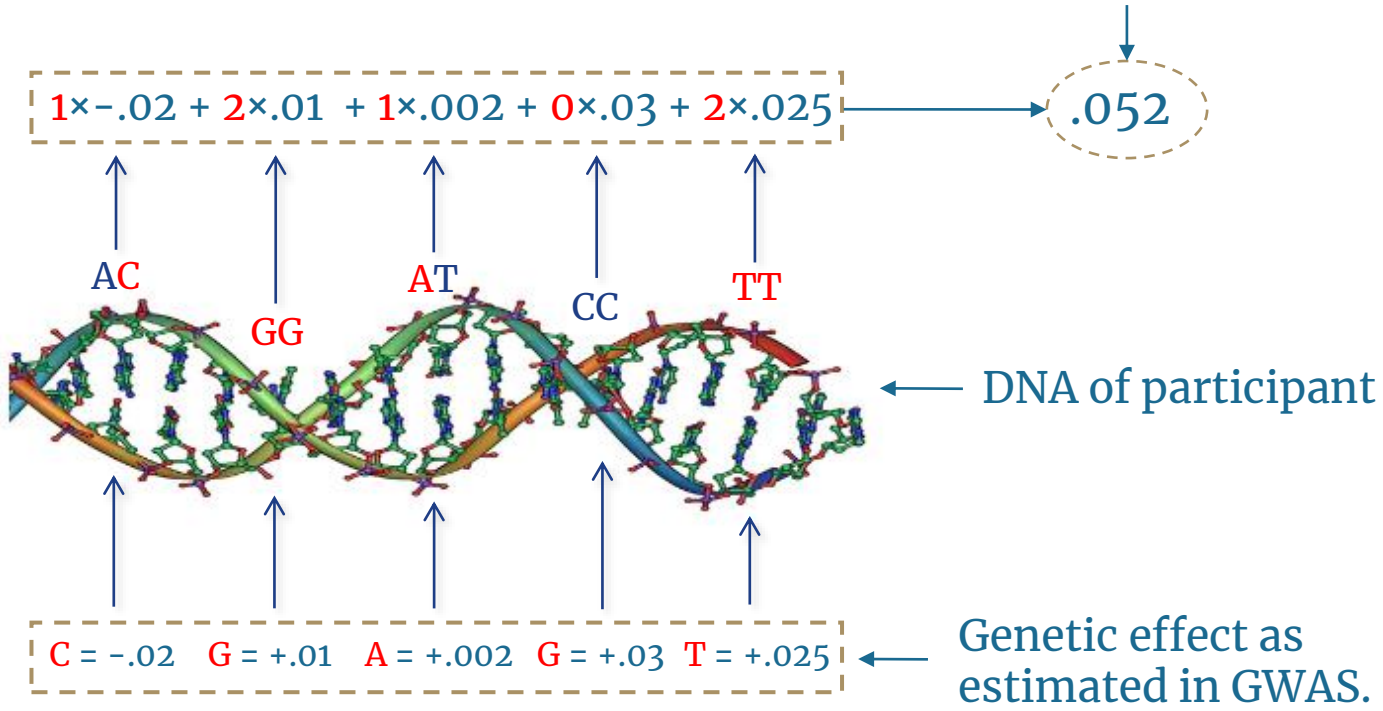
Nature | Vol 610 | 27 October 2022

N = 5.4 million

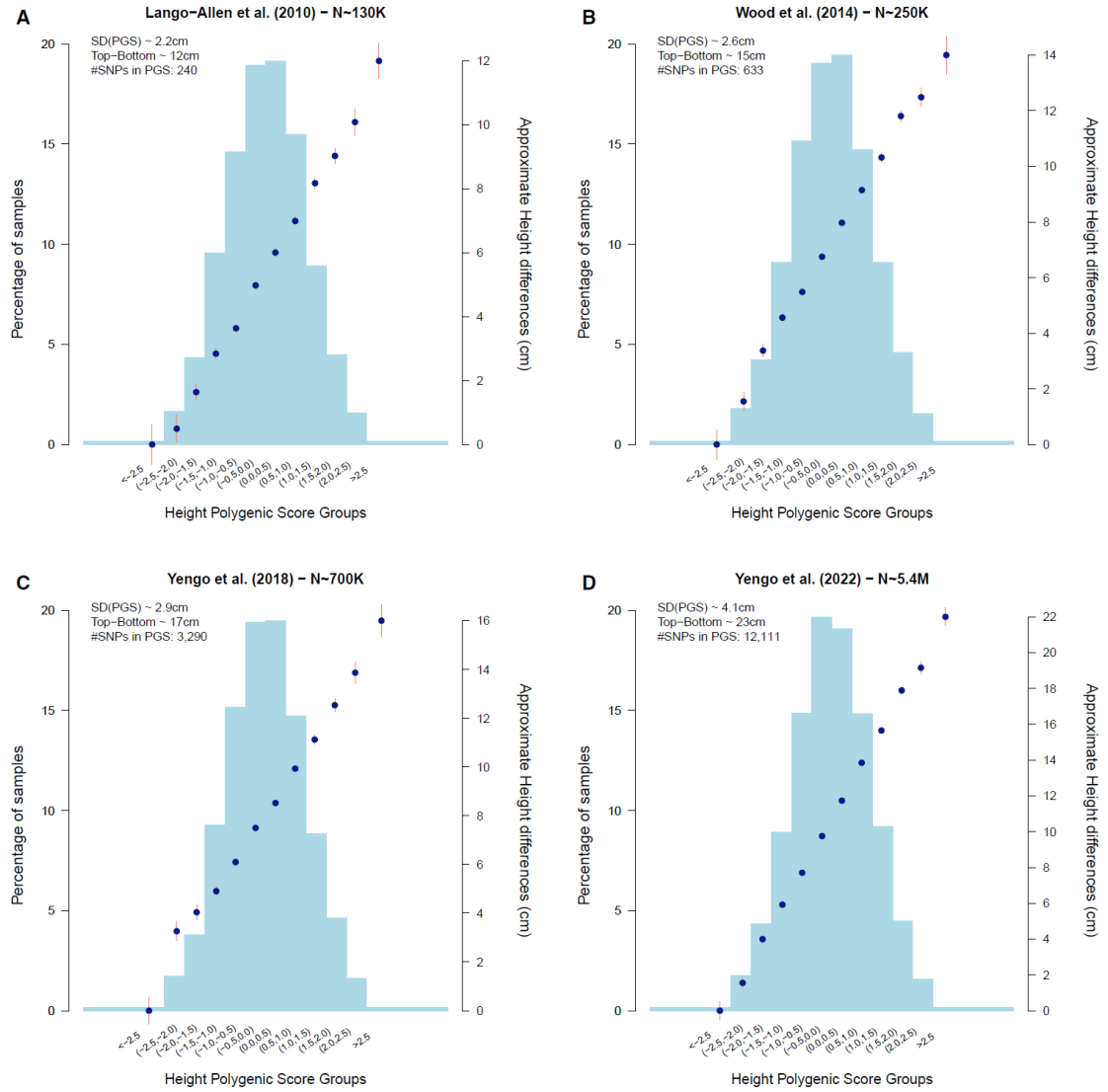


1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

Polygenic Score



Polygenic Score Prediction



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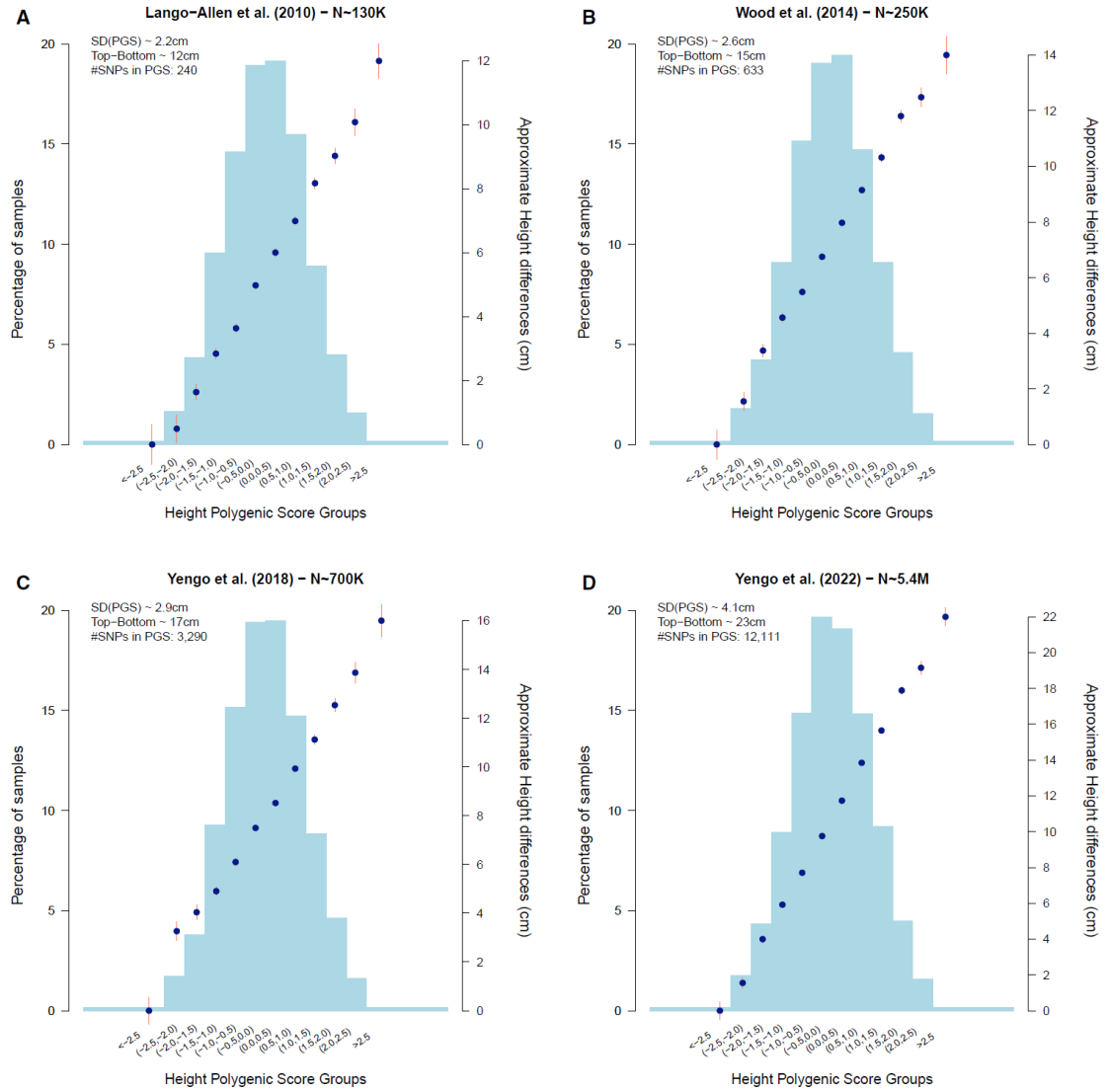
Polygenic Score Prediction

SD of outcome around the prediction:

$$\sigma_Y\sqrt{1-R^2}$$



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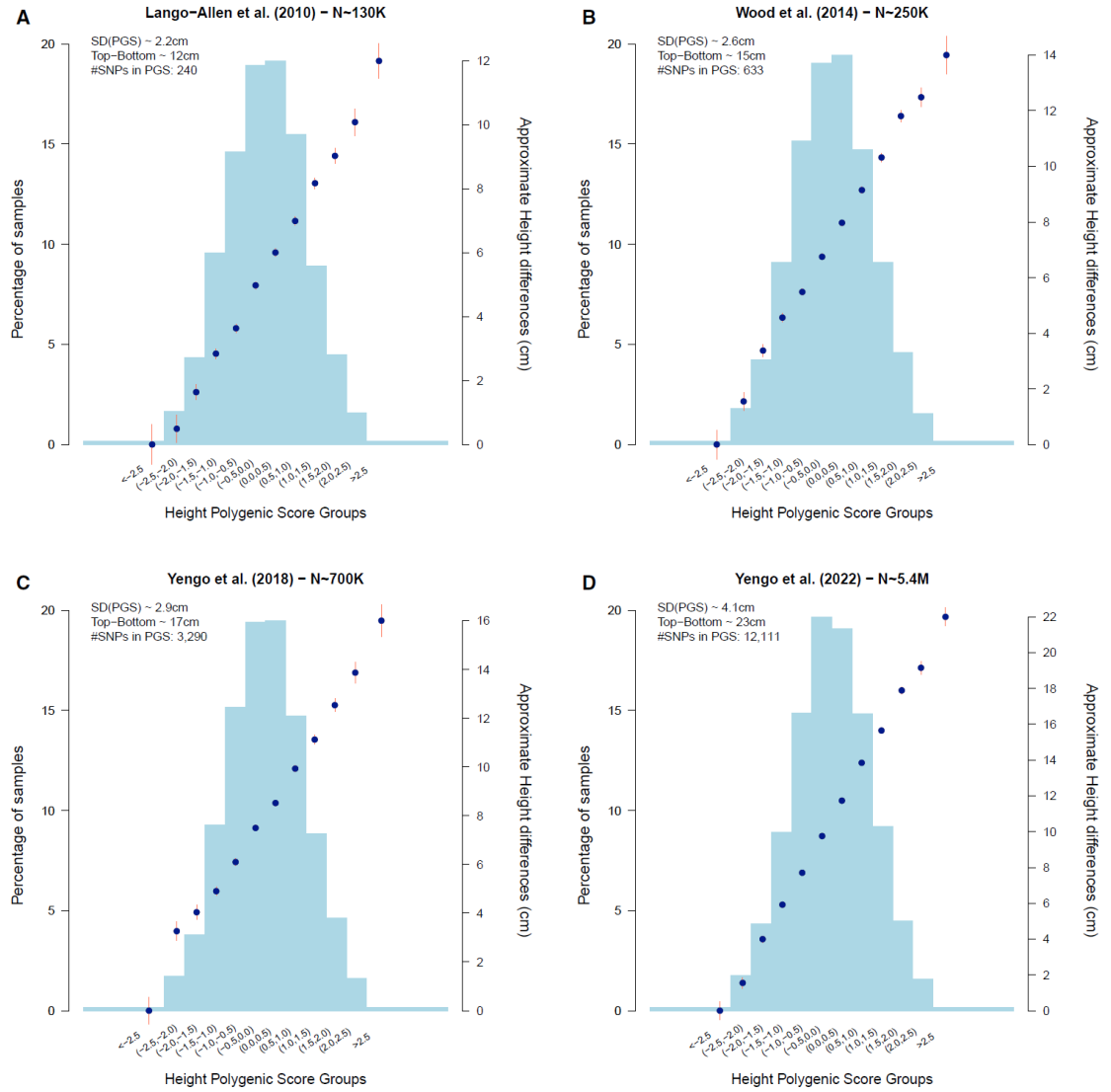
SD of outcome around the prediction:

$$\sigma_Y\sqrt{1-R^2}$$

Upper bound (maximum predictive power):

$$\sigma_Y\sqrt{1-h^2}$$



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Polygenic Score Prediction

SD of outcome around the prediction:

$$\sigma_Y\sqrt{1-R^2}$$

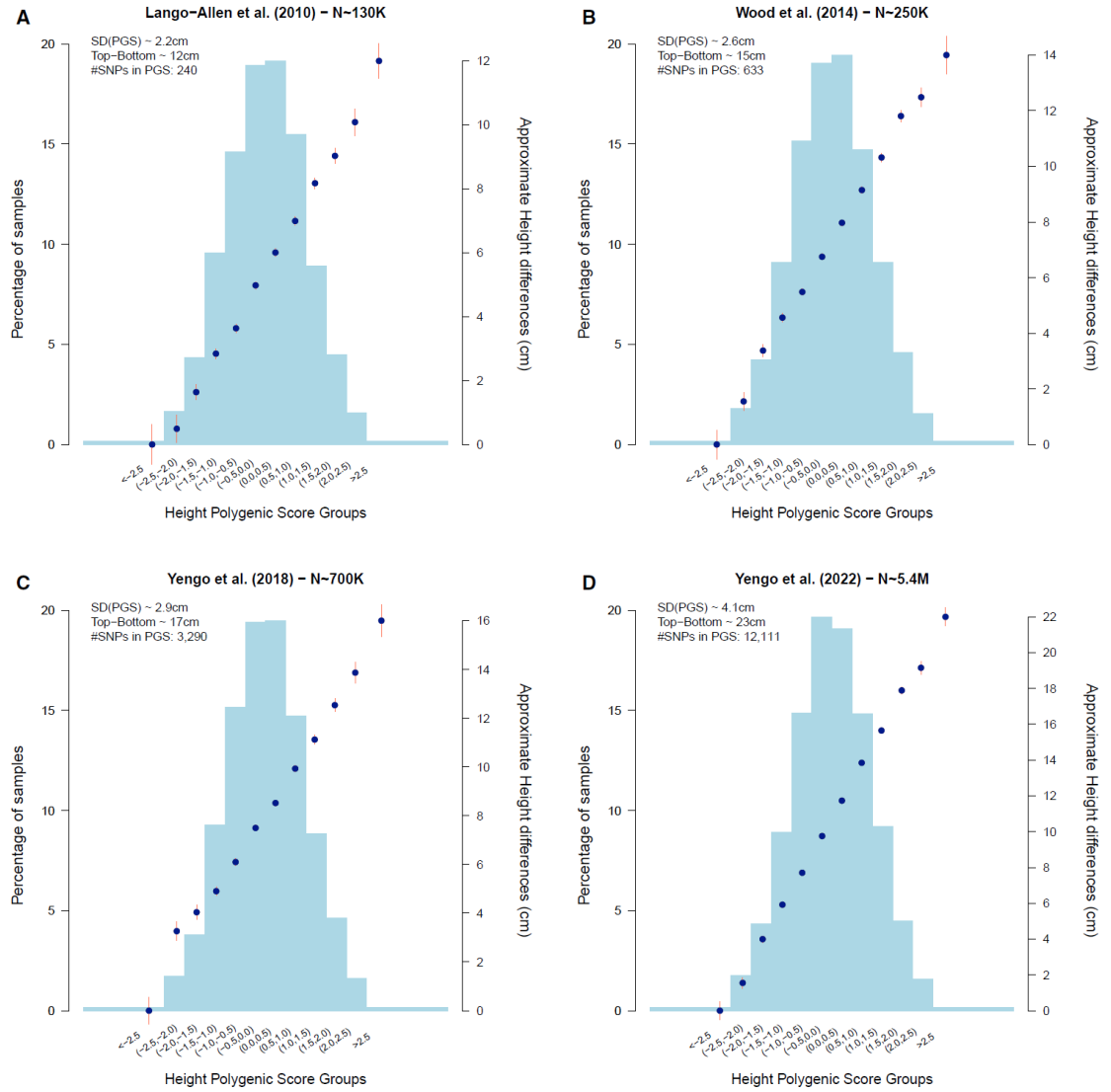
Upper bound (maximum predictive power):

$$\sigma_Y\sqrt{1-h^2}$$

Height has heritability of ~0.8 and standard deviation of ~6.5 cm

$$6.5cm \times \sqrt{1-0.8} \approx 3cm$$

Equivalent to 95% confidence interval of ~**12cm**



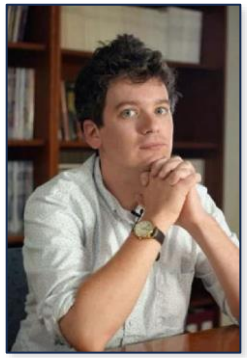
nature human behaviour

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]



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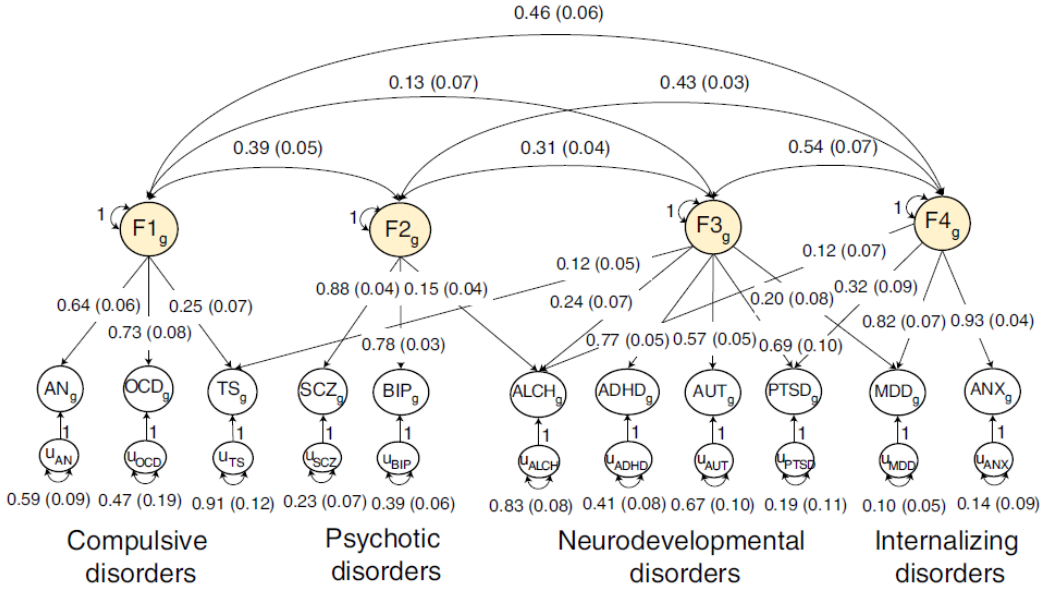
ARTICLES
https://doi.org/10.1038/s41588-022-01057-4

nature genetics

Check for updates

Genetic architecture of 11 major psychiatric disorders at biobehavioral, functional genomic and molecular genetic levels of analysis

Andrew D. Grotzinger[1,2] ✉, Travis T. Mallard[3], Wonuola A. Akingbuwa[4,5], Hill F. Ip[4], Mark J. Adams[6], Cathryn M. Lewis[7,8], Andrew M. McIntosh[6], Jakob Grove[9,10,11,12], Søren Dalsgaard[13], Klaus-Peter Lesch[14,15,16], Nora Strom[17,18,19], Sandra M. Meier[10,20], Manuel Mattheisen[10,17,19,20,21,22], Anders D. Børglum[9,10,11], Ole Mors[9,23], Gerome Breen[7,8], iPSYCH*, Tourette Syndrome and Obsessive Compulsive Disorder Working Group of the Psychiatric Genetics Consortium*, Bipolar Disorder Working Group of the Psychiatric Genetics Consortium*, Major Depressive Disorder Working Group of the Psychiatric Genetics Consortium*, Schizophrenia Working Group of the Psychiatric Genetics Consortium*, Phil H. Lee[24,25], Kenneth S. Kendler[26], Jordan W. Smoller[24,25], Elliot M. Tucker-Drob[3,27,28] and Michel G. Nivard[4,28]



nature genetics
ARTICLES
https://doi.org/10.1038/s41588-022-01062-7
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OPEN

Within-sibship genome-wide association analyses decrease bias in estimates of direct genetic effects

ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

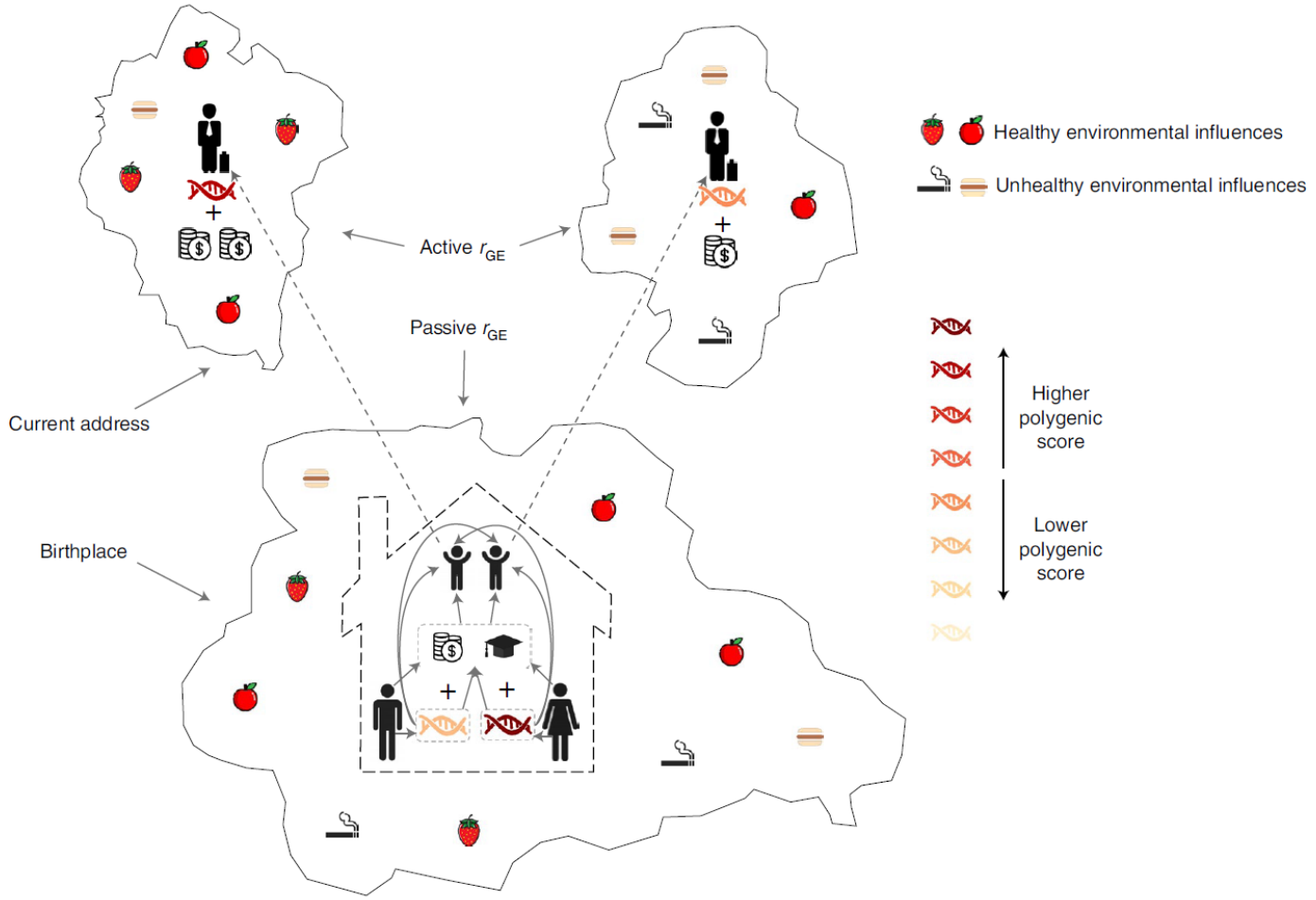
Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]

nature genetics
ARTICLES
https://doi.org/10.1038/s41588-022-01158-0
Check for updates

OPEN

Gene–environment correlations across geographic regions affect genome-wide association studies

Abdel Abdellaoui[1✉], Conor V. Dolan[2], Karin J. H. Verweij[1] and Michel G. Nivard[2]



1859 1865 1886 1903 1918 1920s 1953 1970s 1980s 1990s 2000s 2010s 2020s

Workshop Program

Day 1: Fundamentals

Day 2: Univariate

Day 3: Multivariate

Day 4: Gene-environment correlations

Day 5: Causality