

# Genetics as a key to understanding and improved treatment of mental disorders

Prof Martin Kennedy

Department of Pathology & Biomedical Science

University of Otago, Christchurch (8/10/19)



University of Otago, Christchurch







# THE AMERICAN JOURNAL OF PSYCHIATRY

Vol. 110 April 25, 1953

NATURE

## MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribonucleic Acid

With an appendix, a description for the joint  
American, British, and U.S.A. The  
structure of the nucleic acid, etc. of nucleic acids  
and their

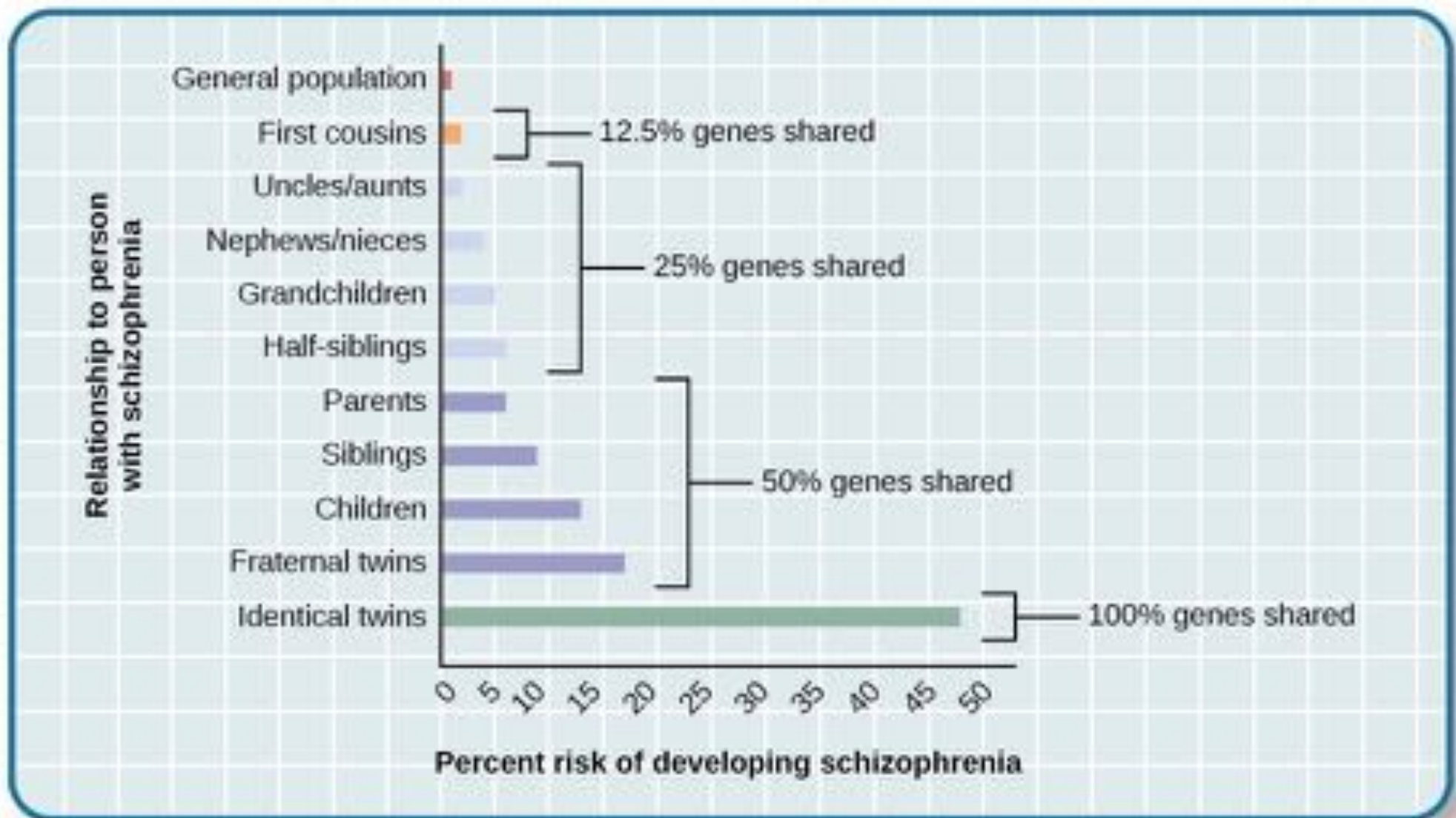


Watson Crick

This film is partly  
documentary. The two  
filmmakers reproduce the  
two guanine-uracil  
pairs, and the two  
metal rods for parts of  
base holding the double  
together. The vertical  
rod marks the film with

Official  
Journal of the  
AMERICAN  
PSYCHIATRIC  
ASSOCIATION  
Volume 110  
Number 4  
April  
1953

# Schizophrenia and genetic risks in families



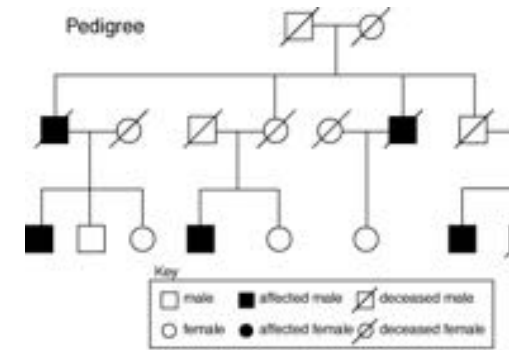
# Categories of genetic conditions

## 1. Mendelian

- one gene causes disease
- minor environmental influences

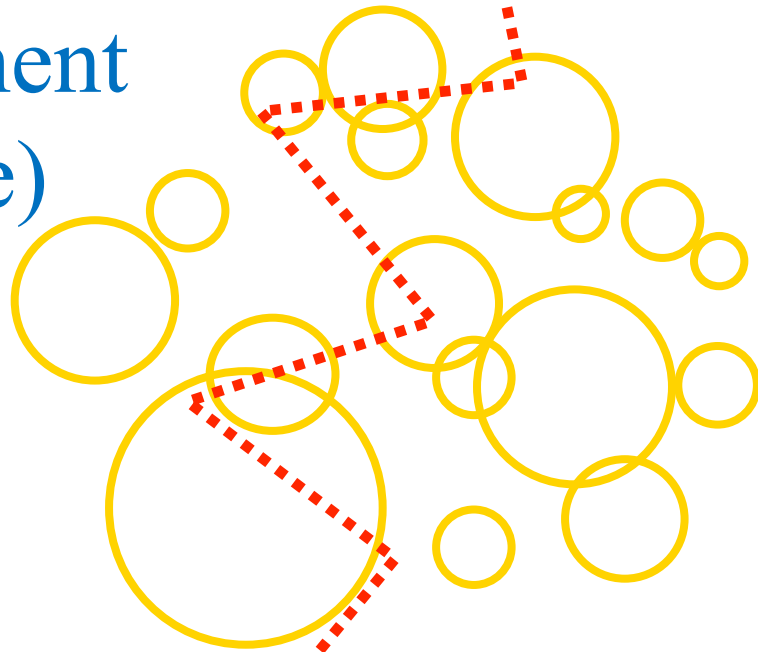
## 2. Complex

- multiple genes
- each gene contributes small risk
- major environmental influences

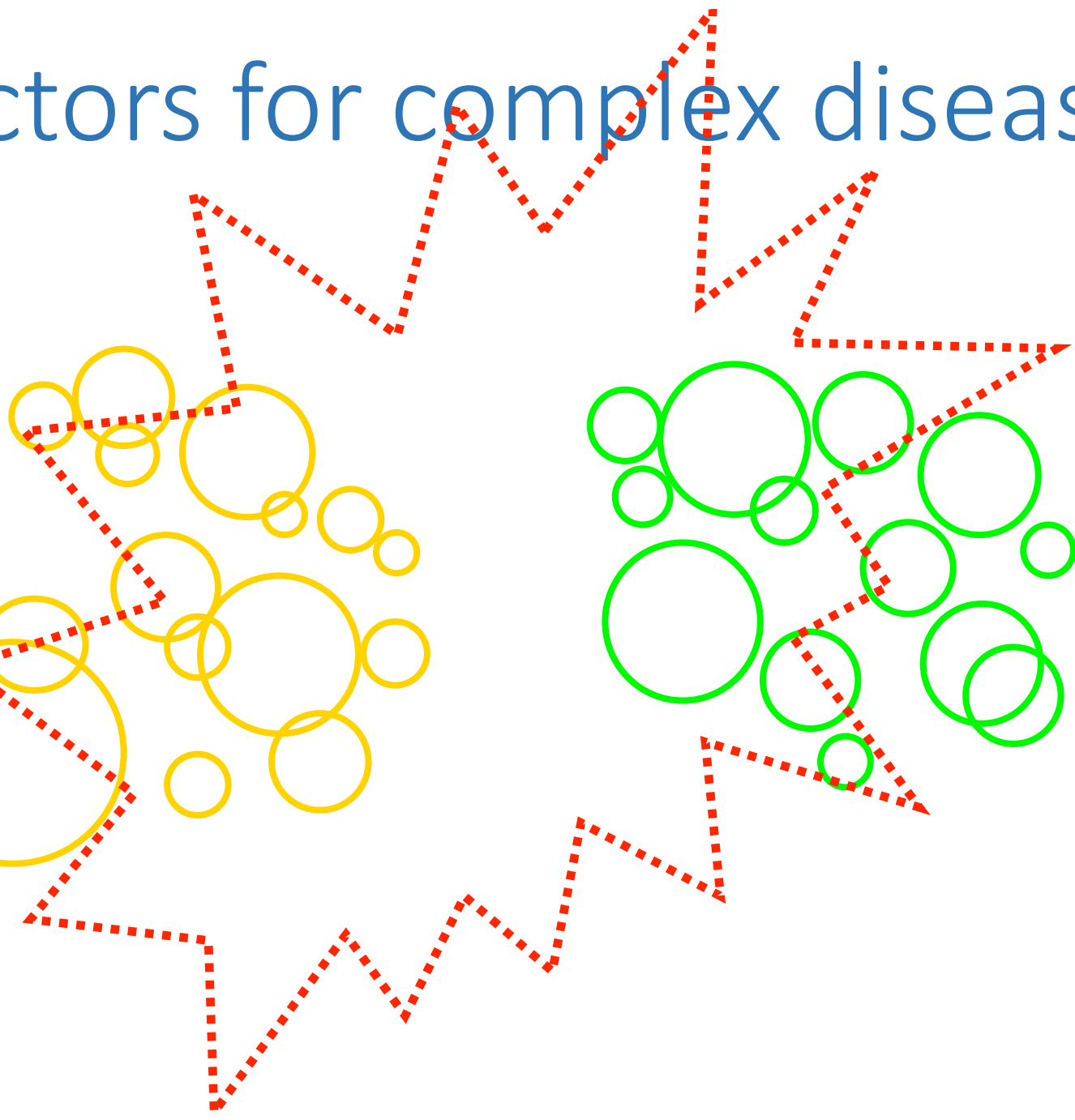
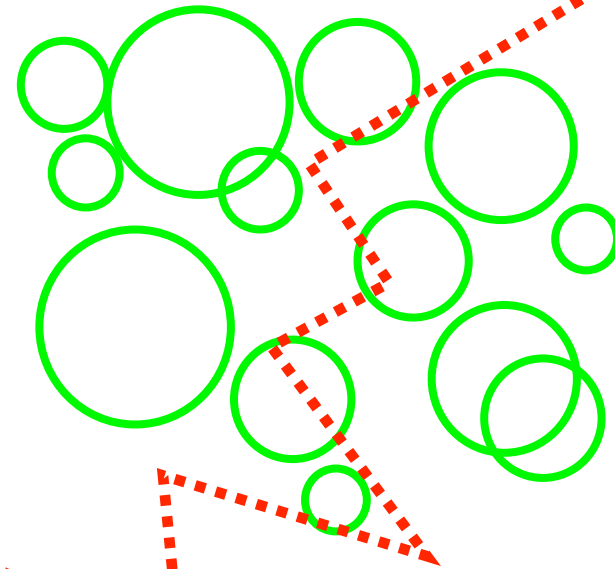


# Risk factors for complex disease

Environment  
(nurture)



Genes  
(nature)



# Single nucleotide polymorphisms (SNPs)

...CGGTACT**T**GAGGGCTAA...

...CGGTACT**C**GAGGGCTAA...

- We each have ~10 million SNPs
- Over 140 million human SNPs now catalogued



# Genome wide association studies (GWAS)

**Biological insights from 108  
schizophrenia-associated genetic loci**

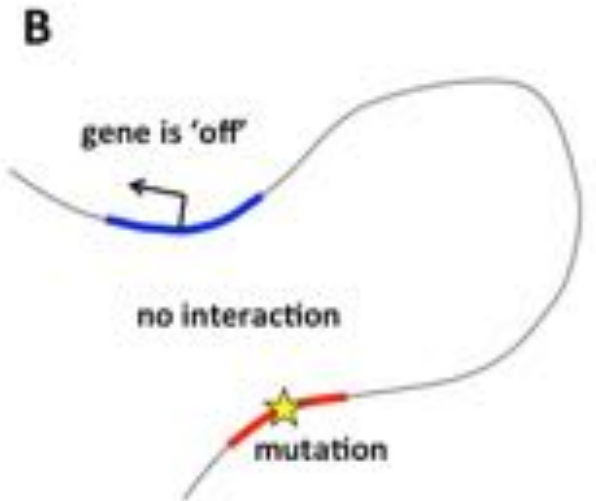
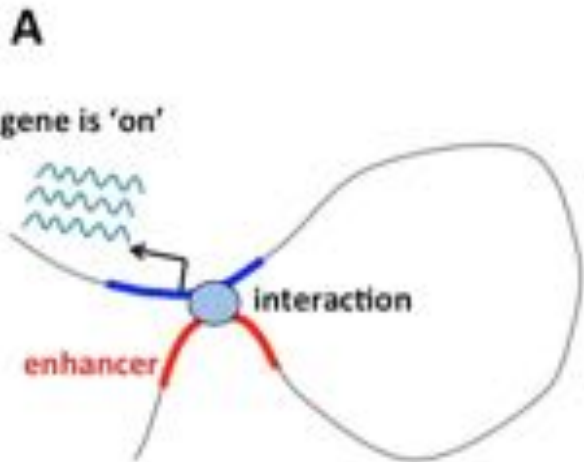
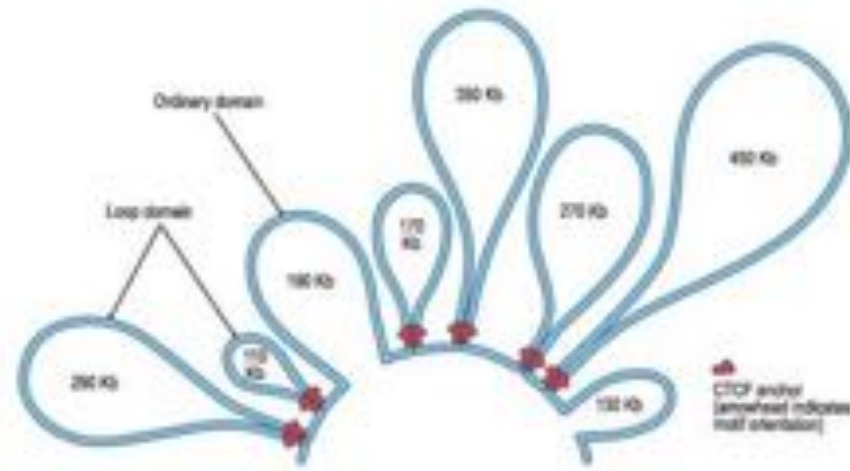
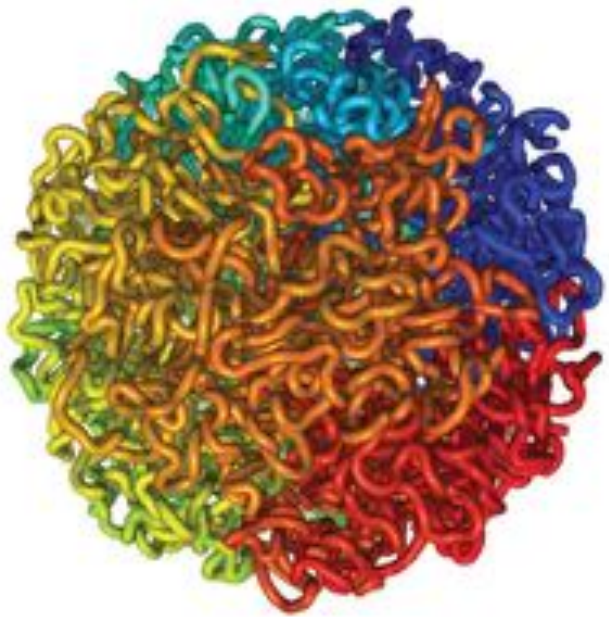
37,000 cases  
113,000 controls

Schizophrenia Working Group of the Psychiatric Genomics Consortium\*





# GWAS variants impact 3D structure of genome



# Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa

Hunna J. Watson et al.\*

- Recruited 3414 Australians and 543 New Zealanders with anorexia nervosa
- Largest cohort with anorexia nervosa ever collected in Australia and NZ



Prof Cynthia Bulik  
UNC/Karolinska



Prof Nick Martin  
QIMR Berghofer

>17K cases  
>55K controls



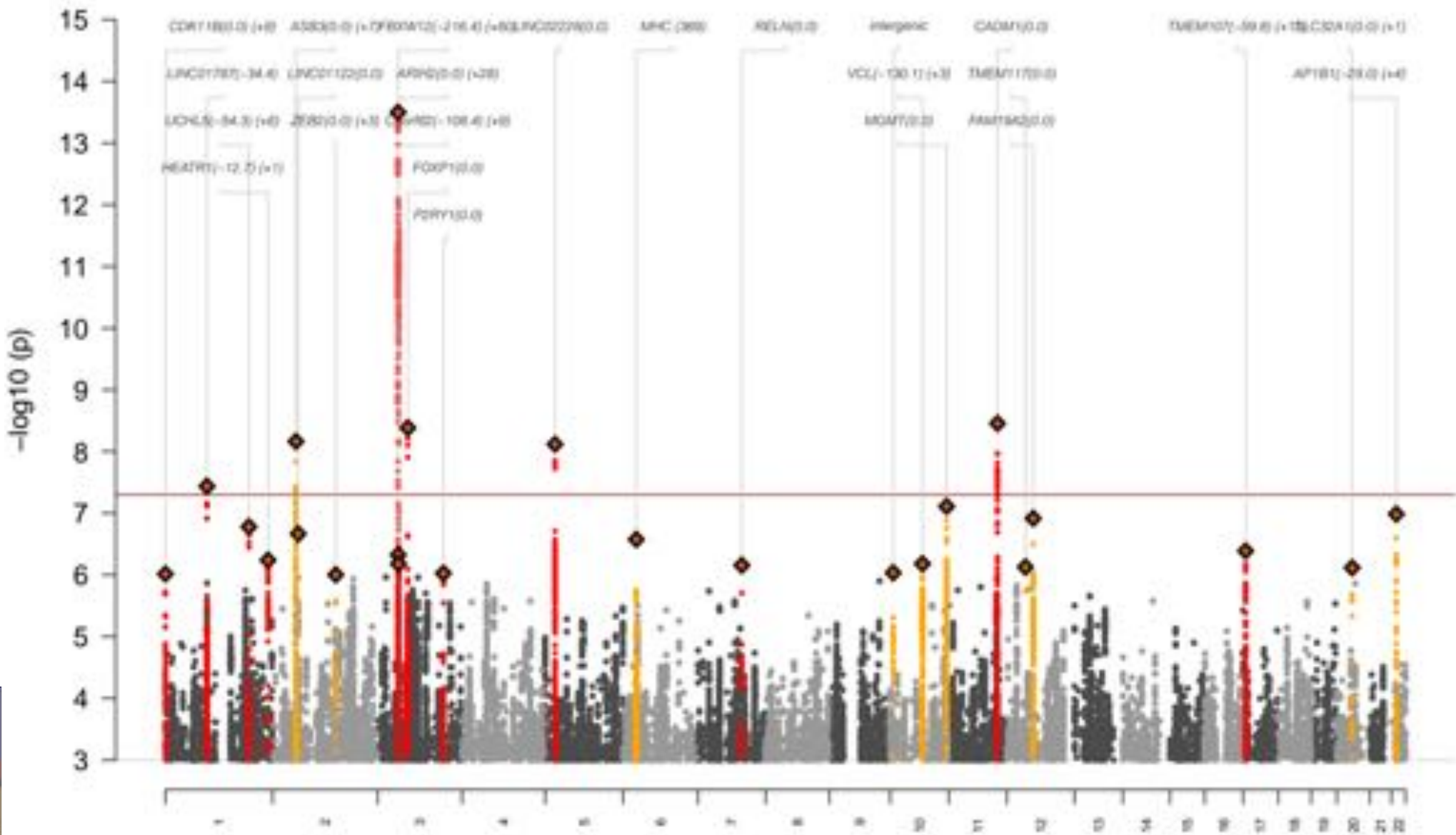
Dr Jenny Jordahl  
Psych Med. UO



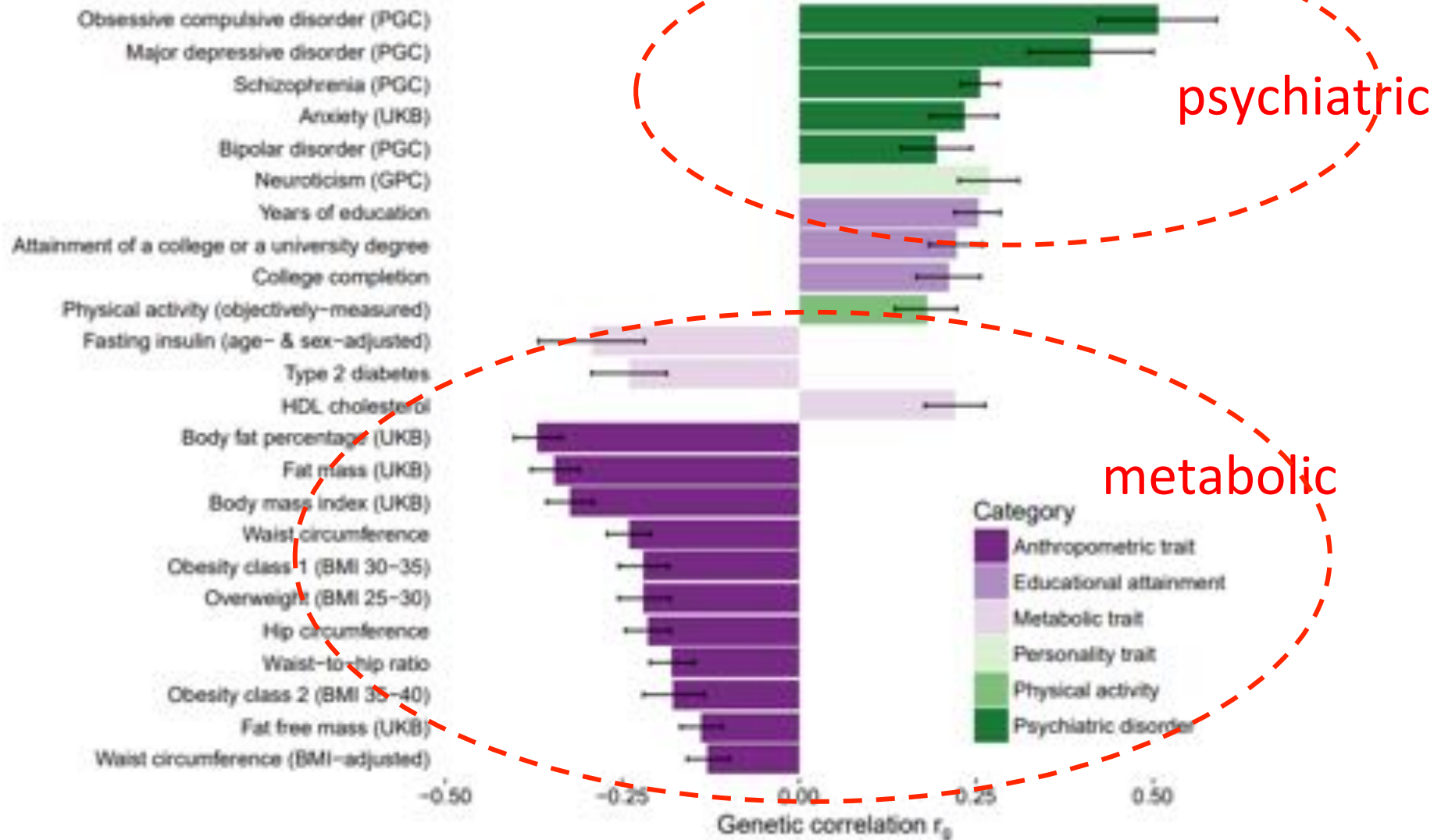
Prof Martin Kenyon  
Pathology, UO

# WAS - Anorexia nervosa

17K cases  
55K controls



# Genetic correlations between anorexia nervosa and other traits



from genetics to biology

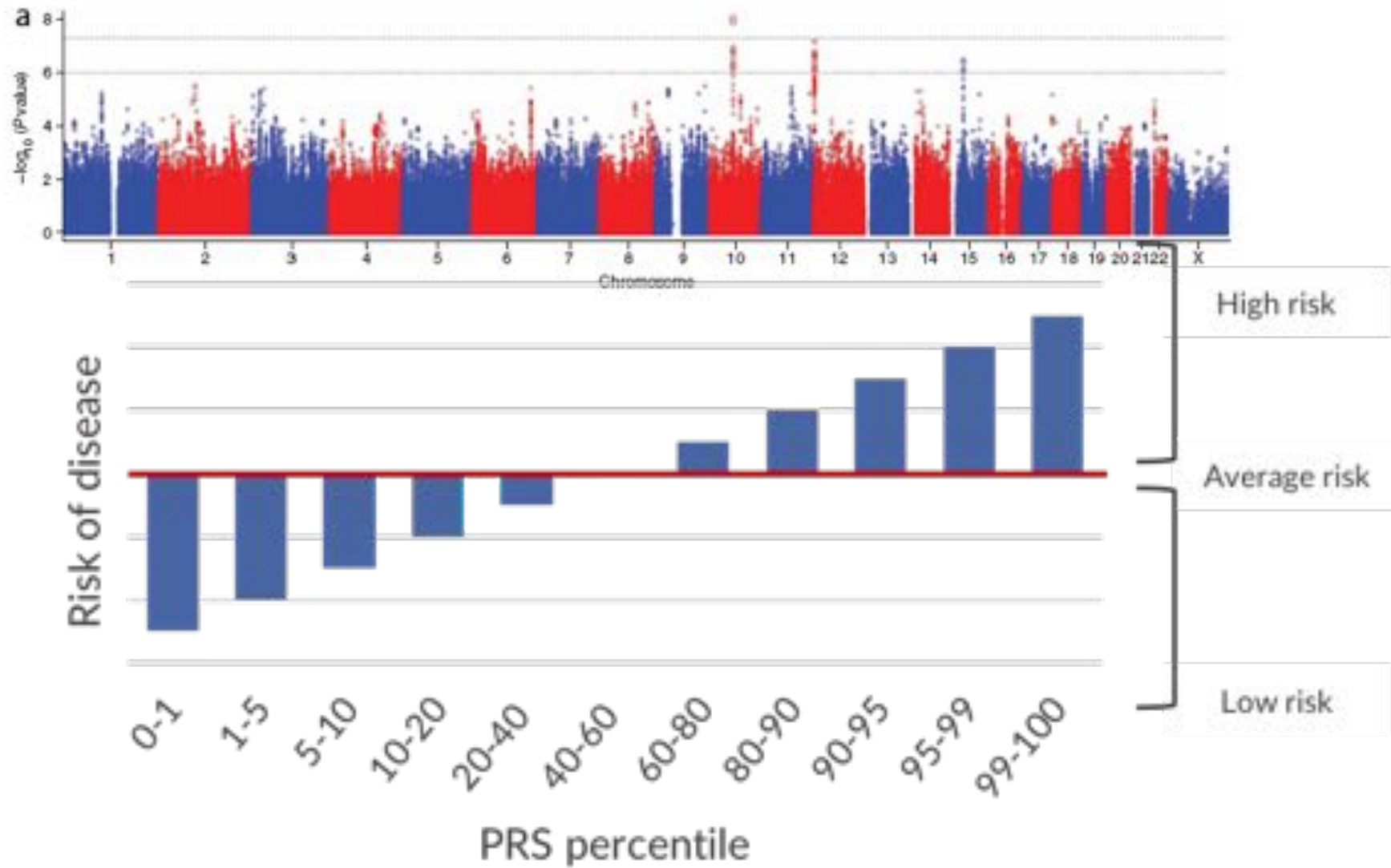


# From biology to new treatments

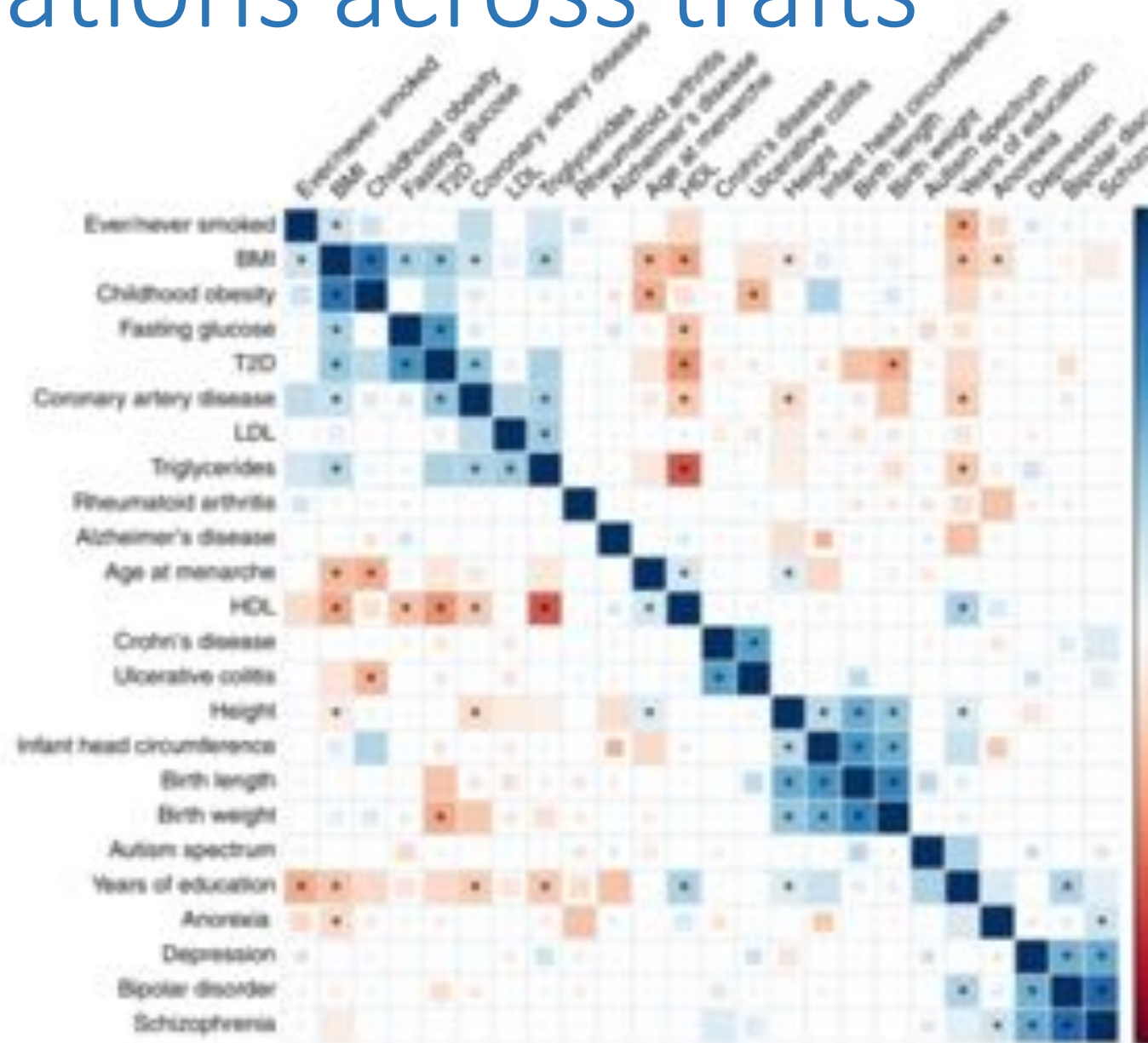
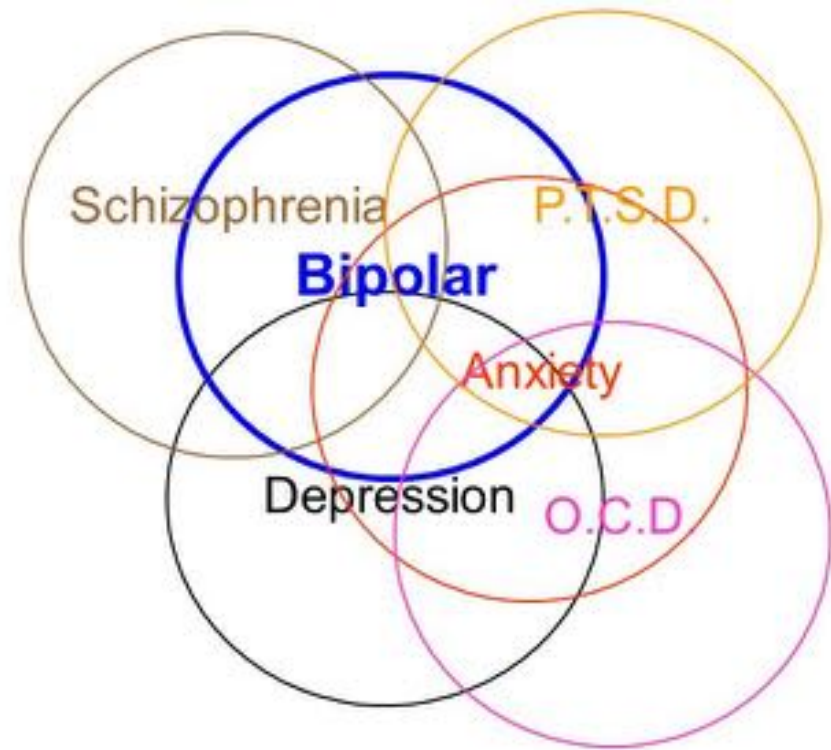


- Repurposing
- New drug target

# Polygenic risk scores



# Genetic correlations across traits





# The gifts of psychiatric genetics

- Improved biological understanding of mental disorders
- New ideas for better treatments
- Clearer view of relationships between disorders
- Estimation of individual biological risks
- Destigmatisation





# Comparative heritability of mental disorders

<b>Heritability</b>	<b>Mental disorders</b>	<b>Other Important Familial Traits</b>
20-40%	Anxiety disorders Depression Bulimia	Heart attacks Blood pressure
40-60%	Alcohol and drug dependence	IQ Plasma cholesterol Adult-onset diabetes
60-80%	Schizophrenia Bipolar Illness	Weight
80-100%	- -	Height

*Kendler (2003)*

“The PGC is the largest consortium and the largest biological experiment in the history of psychiatry”



Patrick Sullivan  
MD, FRANZCP

Psychiatric Genomics Consortium

## PGC Workgroups

Alzheimer's Workgroup	Attention Deficit Hyperactivity Disorders	Anxiety Workgroup	Autism Spectrum Disorders	Bipolar Disorders
Copy Number Variation Group	Cross-Disorder Group	Eating Disorders	Major Depressive Disorders	OCD & Tourettes Syndrome
Pathway Analysis Group	Post Traumatic Stress Disorders	Schizophrenia	Substance Use Disorders	