XVII Congreso Colombiano y
XI Congreso Internacional de Genética Humana

Avances en la genética y sus aplicaciones en la era de las ómicas

Junio 14 al 16 de 2023 Fórum UPB Medellín - Colombia

Análisis Ómicos y Trastornos Neuropsiquiátricos

Diego A. Forero, MD, PhD
Investigador Líder e Investigador Sénior
Facultad de Ciencias de la Salud y del Deporte, Fundación Universitaria del Área Andina

Organizan:

MD: Universidad Nacional de Colombia (2003)
PhD in Biomedical Sciences: University of Antwerp, Belgium (2009)

Neurosciences Research Group, Universidad Nacional de Colombia, Colombia
Applied Molecular Genomics Group, University of Antwerp, Belgium
Laboratory of Developmental Genetics, Catholic University of Leuven, Belgium
Unit of Animal Genomics, University of Liege, Belgium
Laboratory of NeuroPsychiatric Genetics, UAN, Colombia
PhD Program in Health Sciences, UAN, Colombia
School of Health and Sports Sciences, Fundación Universitaria del Área Andina

AREANDINA
Fundación Universitaria del Área Andina

KATHOLIEKE UNIVERSITEIT LEUVEN

VIB

Universiteit Antwerpen

ULg
UNIVERSITÉ de Liège

Author of 114 Articles and 8 Chapters in International Scientific Journals and Books

Cumulative Impact Factor: 470.328, H index: 36

Peer Reviewer for 122 International Scientific Journals

-Editor, BMC Research Notes (Q2).
-Editor, PLOS One (Q1).

-Editorial Board Member, Personalized Medicine (Q3).

-Review Editor, Frontiers in Neurology (Q2).

- Editorial Board Member, American Journal of Genetics (Q1).

- Editorial Board Member, Oxford Open Digital Health

Plan Decenal de Salud Pública, 2012-2021

Tabla 13. Veinte primeras causas según AVISAS (por 1.000 personas) en ambos sexos de todas las edades

1 Cardiopatía hipertensiva
2 Depresión mayor unipolar
3 Caries dental
4 Asfixia y trauma al nacer
5 Agresiones
6 Bajo peso al nacer
7 Enfermedad pulmonar obstructiva crónica
8 Asma
9 Glaucoma
11 Trastornos Bipolares
13 Edentulismo
14 Cirrosis Hepática
15 Enfermedad cerebrovascular
16 Infecciones de vías respiratorias inferiores
17 Esquizofrenia
18 Otras afecciones perinatales
19 Epilepsia
20 Otras lesiones no intencionales

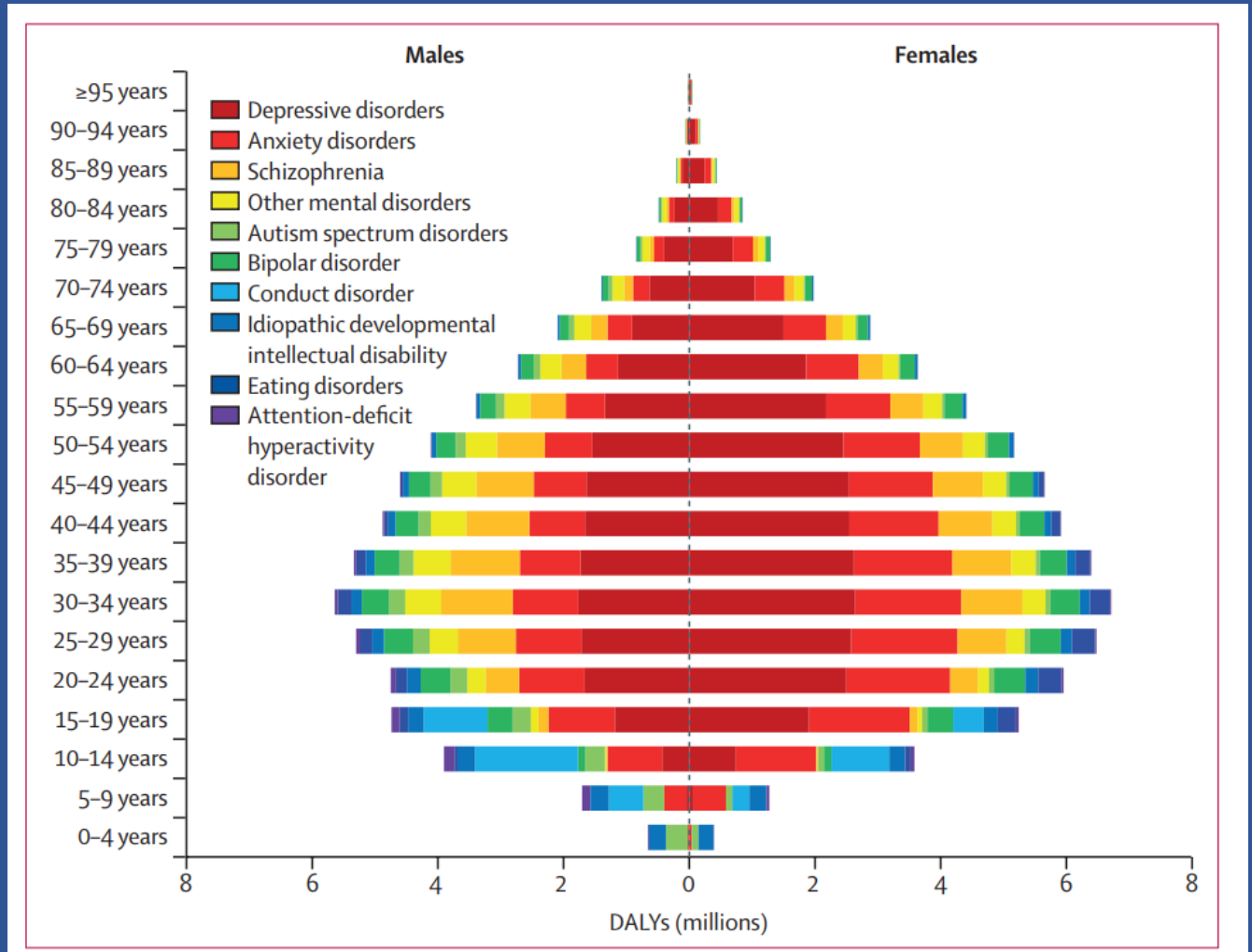


Figure 1: **Global DALYs by mental disorder, sex, and age, 2019**
DALYs=disability-adjusted life-years.

GBD 2019 Mental Disorders Collaborators. **Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019**. Lancet Psychiatry . 2022 Feb;9(2):137-150.

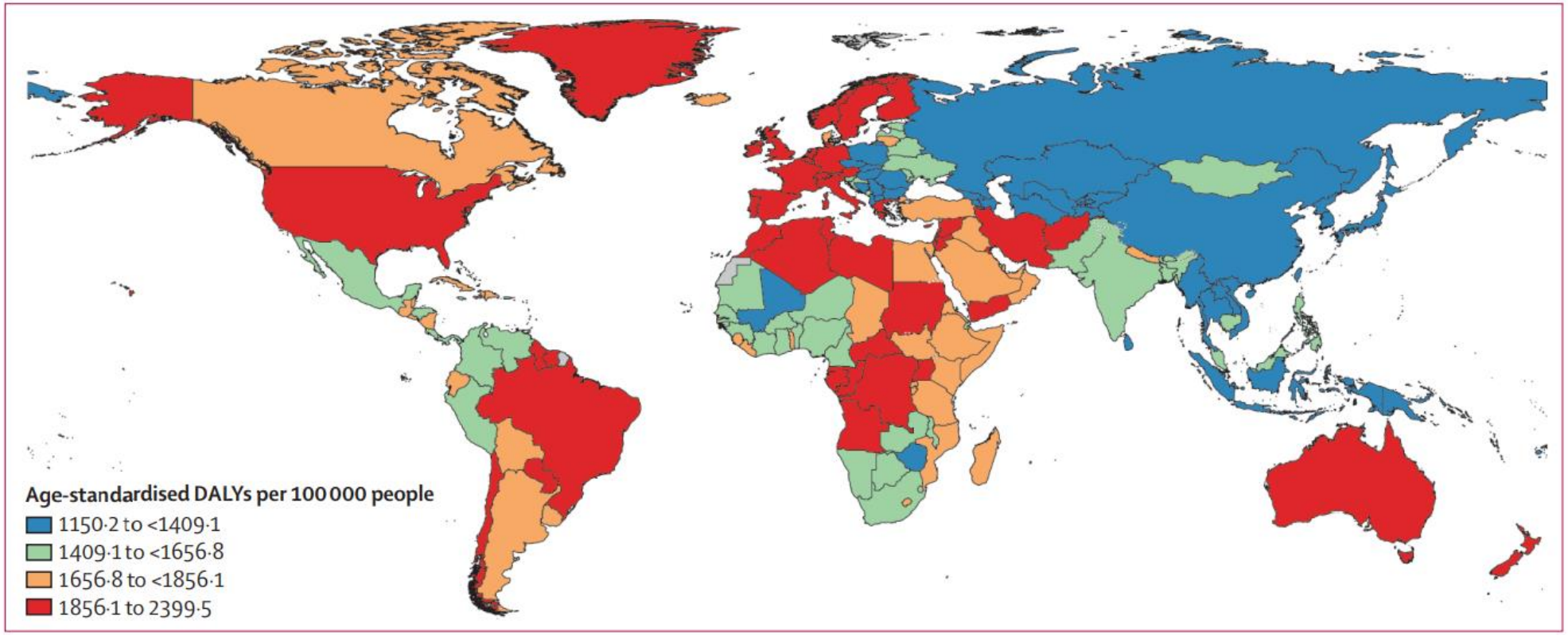


Figure 3: **Age-standardised DALYs per 100 000 attributable to mental disorders, 2019**
DALYs=disability-adjusted life-years.

GBD 2019 Mental Disorders Collaborators. **Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019**. Lancet Psychiatry . 2022 Feb;9(2):137-150.

Table 2. Twelve-Month Prevalence of World Mental Health Composite International Diagnostic Interview/*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition**

Country	% (95% Confidence Interval)				
	Anxiety	Mood	Impulse-Control	Substance	Any
Americas					
Colombia	10.0 (8.4-11.7)	6.8 (6.0-7.7)	3.9 (3.2-4.7)	2.8 (2.0-3.7)	17.8 (16.1-19.5)
Mexico	6.8 (5.6-7.9)†	4.8 (4.0-5.6)	1.3 (0.9-1.8)‖	2.5 (1.8-3.3)	12.2 (10.5-13.80)
United States	18.2 (16.9-19.5)	9.6 (8.8-10.4)	6.8 (5.9-7.8)	3.8 (3.2-4.5)	26.4 (24.7-28.0)
Europe					
Belgium	6.9 (4.5-9.4)	6.2 (4.8-7.6)§	1.0 (0.3-1.8)‖	1.2 (0.6-1.9)‡‡	12.0 (9.6-14.3)
France	12.0 (9.8-14.2)	8.5 (6.4-10.6)§	1.4 (0.7-2.0)‖	0.7 (0.3-1.2)‡‡	18.4 (15.3-21.5)
Germany	6.2 (4.7-7.6)	3.6 (2.8-4.3)§	0.3 (0.1-0.6)‖	1.1 (0.4-1.7)‡‡	9.1 (7.3-10.8)
Italy	5.8 (4.5-7.1)	3.8 (3.1-4.5)§	0.3 (0.1-0.5)‖	0.1 (0.0-0.2)‡‡	8.2 (6.7-9.7)
Netherlands	8.8 (6.6-11.0)	6.9 (4.1-9.7)§	1.3 (0.4-2.2)‖	3.0 (0.7-5.2)‡‡	14.9 (12.2-17.6)
Spain	5.9 (4.5-7.3)	4.9 (4.0-5.8)§	0.5 (0.2-0.8)‖	0.3 (0.0-0.5)‡‡	9.2 (7.8-10.6)
Ukraine	7.1 (5.6-8.6)†‡	9.1 (7.3-10.9)§	3.2 (2.4-4.0)¶#**	6.4 (4.8-8.1)‡‡	20.5 (17.7-23.2)
Middle East and Africa					
Lebanon	11.2 (8.9-13.5)	6.6 (4.9-8.2)	1.7 (0.8-2.6)¶**	1.3 (0.0-2.8)	16.9 (13.6-20.2)
Nigeria	3.3 (2.4-4.2)	0.8 (0.5-1.0)	0.0 (0.0-0.1)¶#**	0.8 (0.3-1.2)	4.7 (3.6-5.8)
Asia					
Japan	5.3 (3.5-7.0)†	3.1 (2.2-4.1)	1.0 (0.4-1.5)¶#**††	1.7 (0.3-3.0)	8.8 (6.4-11.2)
People's Republic of China					
Beijing	3.2 (1.8-4.6)†	2.5 (1.5-3.4)	2.6 (1.3-3.9)¶#**	2.6 (1.2-3.9)	9.1 (6.0-12.1)
Shanghai	2.4 (0.9-3.9)†	1.7 (0.6-2.9)	0.7 (0.4-1.1)¶#**	0.5 (0.3-0.6)	4.3 (2.7-5.9)

Demyttenaere K, Bruffaerts R, Posada-Villa J, Gasquet I, Kovess V, Lepine JP, Angermeyer MC, Bernert S, de Girolamo G, Morosini P, Polidori G, Kikkawa T, Kawakami N, Ono Y, Takeshima T, Uda H, Karam EG, Fayyad JA, Karam AN, Mneimneh ZN, Medina-Mora ME, Borges G, Lara C, de Graaf R, Ormel J, Gureje O, Shen Y, Huang Y, Zhang M, Alonso J, Haro JM, Vilagut G, Bromet EJ, Gluzman S, Webb C, Kessler RC, Merikangas KR, Anthony JC, Von Korff MR, Wang PS, Brugha TS, Aguilar-Gaxiola S, Lee S, Heeringa S, Pennell BE, Zaslavsky AM, Ustun TB, Chatterji S; WHO World Mental Health Survey Consortium. **Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys.** JAMA. 2004 Jun 2;291(21):2581-90.

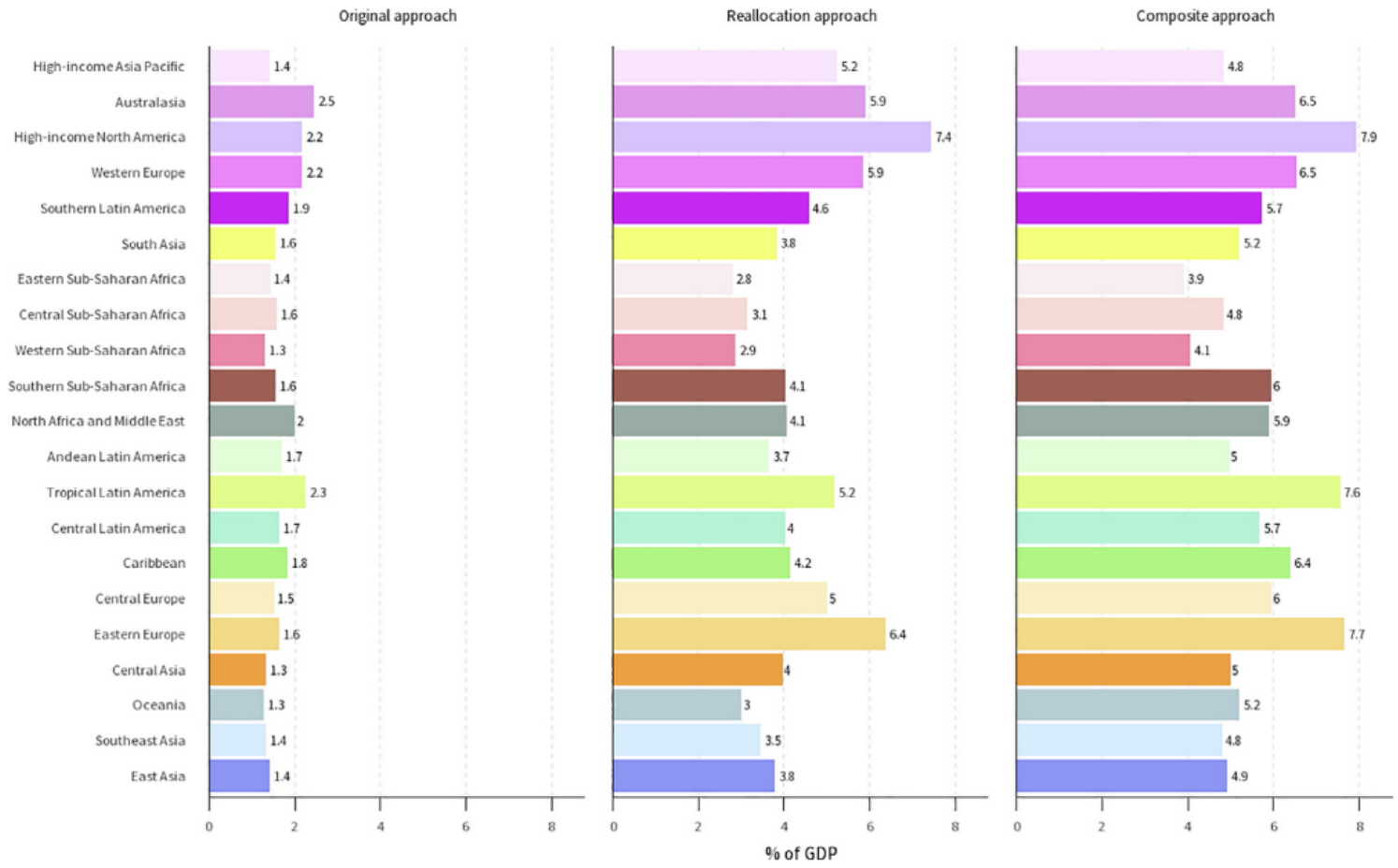


Figure 2. Economic burden of mental disorders, as a percent of GDP. The economic value is determined by using GDP per capita (USD 2019) as the value of a DALY. Values are aggregated by GBD region. GDP: gross domestic product; USD: United States dollar; DALY: disability-adjusted life year; GBD: Global Burden of Disease.

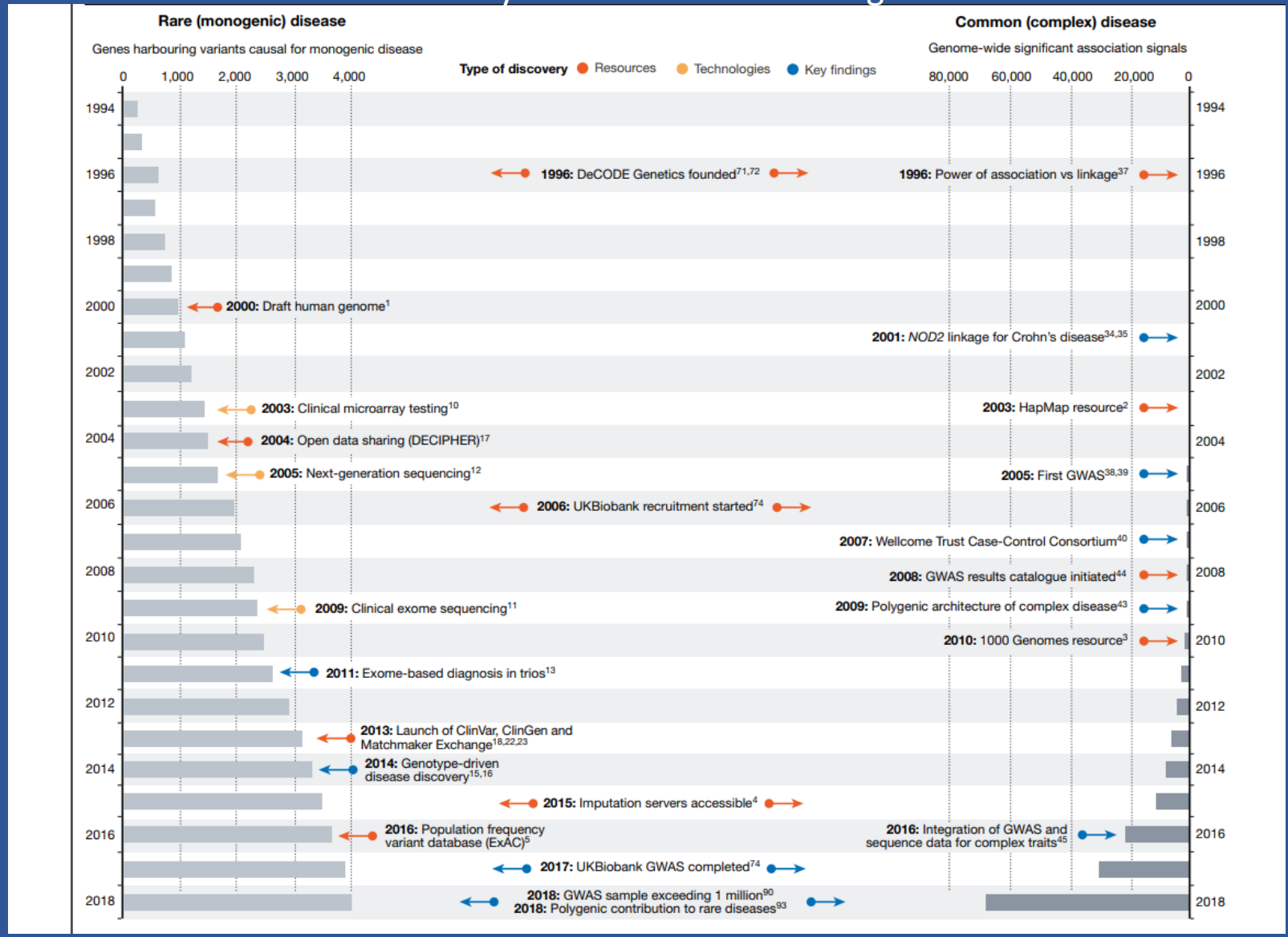
Arias D, Saxena S, Verguet S. **Quantifying the global burden of mental disorders and their economic value**. EClinicalMedicine. 2022 Sep 28;54:101675.

Table 1 Heritability and genetic correlation estimates for selected psychiatric disorders

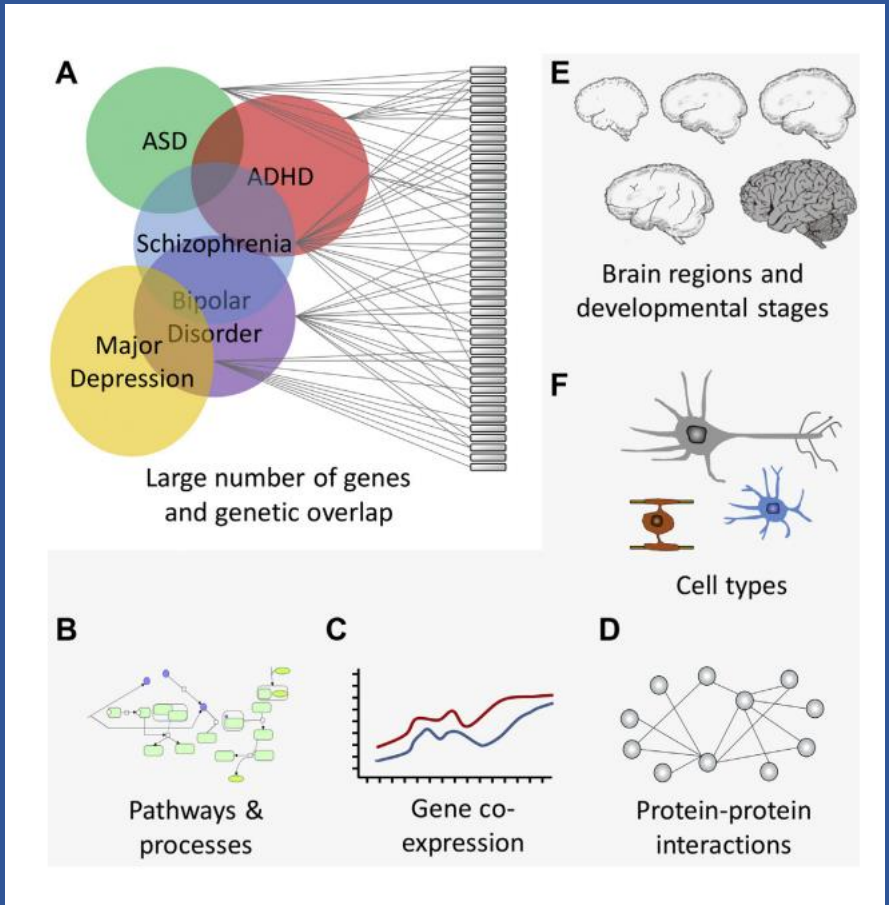
Disorder	ASD	ADHD	SCZ	BD	MDD	AN	OCD	PTSD
ASD	0.24 (0.19-0.30) 0.74 (0.70-0.87)[¢]	0.08 (-0.11-0.27)	0.21 (0.09-0.32)	0.10 (-0.03-0.23)	0.16 (0.04-0.27)	0.03 (-0.16-0.23)	0.00 (-0.21-0.21)	0.04 (-0.34-0.41)
ADHD	.87 (0.77-1.0)*	0.10 (0.08-0.12) 0.79 (0.61-0.88)*	0.22 (0.13-0.31)	0.26 (0.15-0.38)	0.52 (0.41-0.63)	-0.21 (-0.42- -0.00)	-0.07 (-0.25-0.12)	0.45 (0.11-0.78)
SCZ	N/A	N/A	0.26 (0.24-0.28) 0.77 (0.67-0.87)[¥]	0.68 (0.64-0.72)	0.34 (0.30-0.40)	0.22 (0.11-0.32)	0.33 (0.21-0.44)	0.15 (-0.03-0.32)
BD	0.24 (0.24-0.29)[&]	0.33 (0.32-0.39)[&]	0.68 (0.67-0.73)[!]	0.21 (0.19-0.22) 0.68 (0.64-0.72)[¥]	0.35 (0.28-0.41)	0.19 (0.08-0.30)	0.31 (0.18-0.44)	0.10 (-0.11-0.25)
MDD	N/A	N/A	N/A	0.65 (0.58-0.75)[$]	0.11 (0.10-0.12) 0.45 (035-0.55)¥	0.20 (0.03-0.30)	0.23 (0.11-0.35)	0.52 (0.23-0.81)
AN	N/A	N/A	N/A	N/A	N/A	0.17 (0.12-0.22) 0.57 (0.0-0.81)[¶]	0.52 (0.29-0.75)	-0.02 (-0.39-0.36)
OCD	N/A	0.63 (0.39-0.87)[%]	N/A	N/A	N/A	0.52 (0.26-0.81)[@]	0.26 (0.20-0.33) 0.45 (0.30-0.60)¥	0.28 (-0.08-0.64)
PTSD	N/A	N/A	N/A	N/A	1.0[§]	N/A	N/A	0.15 (0.03-0.30) 0.38 (0.25-0.52)[v]

Smoller JW, Andreassen OA, Edenberg HJ, Faraone SV, Glatt SJ, Kendler KS. **Psychiatric genetics and the structure of psychopathology.** Mol Psychiatry. 2019 Mar;24(3):409-420.

Growth in the discovery of disease-associated genetic variation



Claussnitzer M, Cho JH, Collins R, Cox NJ, Dermitzakis ET, Hurles ME, Kathiresan S, Kenny EE, Lindgren CM, MacArthur DG, North KN, Plon SE, Rehm HL, Risch N, Rotimi CN, Shendure J, Soranzo N, McCarthy MI. **A brief history of human disease genetics**. Nature. 2020 Jan;577(7789):179-189.

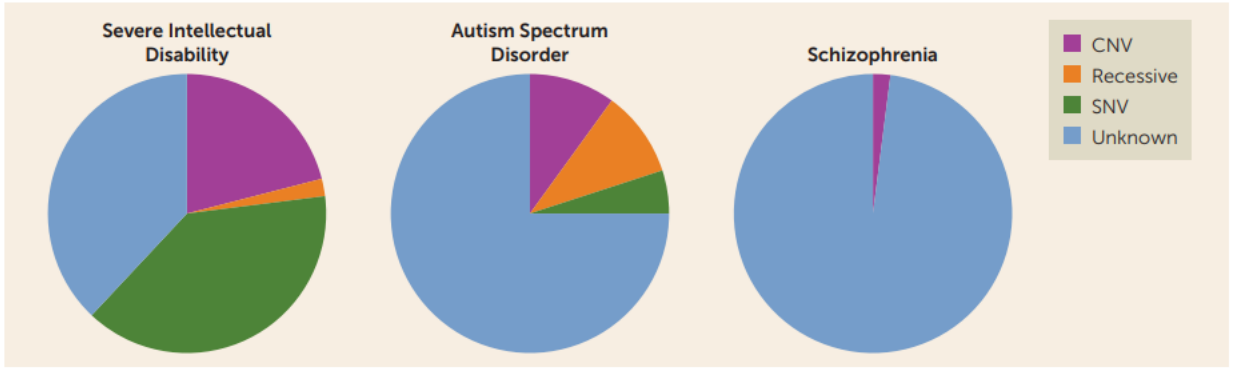


Systems biology approaches to study the complex genetics of psychiatric disorders

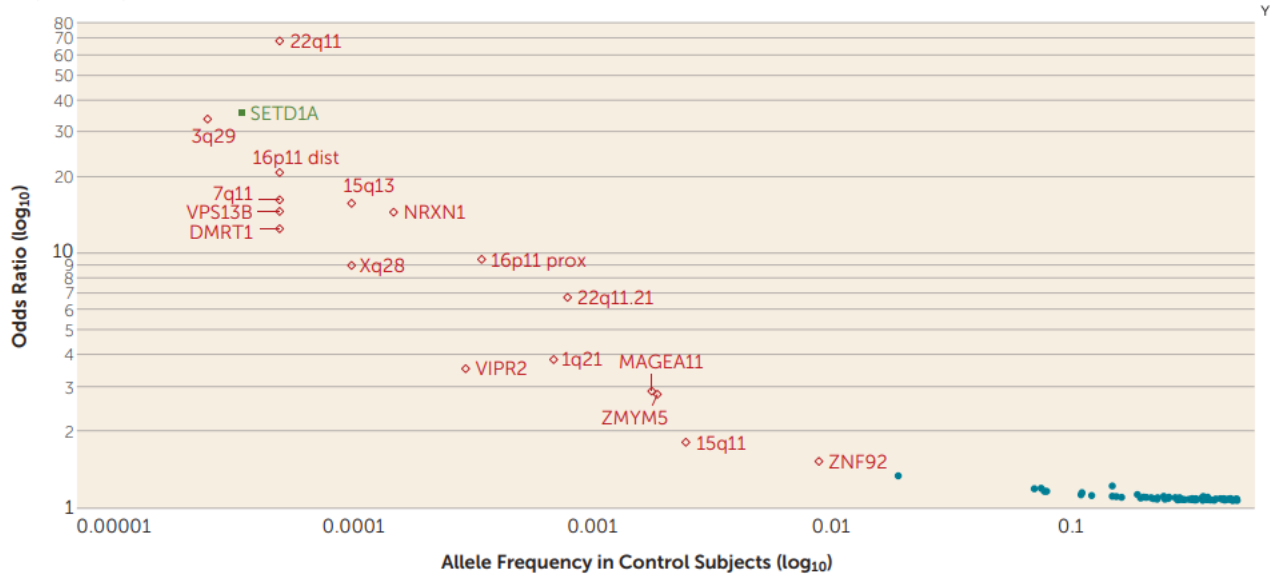
Shohat S, Amelan A, Shifman S.
Convergence and Divergence in the Genetics of Psychiatric Disorders From Pathways to Developmental Stages.
Biol Psychiatry. 2021 Jan 1;89(1):32-40.

FIGURE 2. Types of Genetic Variants Empirically Associated With Severe Psychiatric Disorders

A. Genetic causes of severe psychiatric disorders[a]

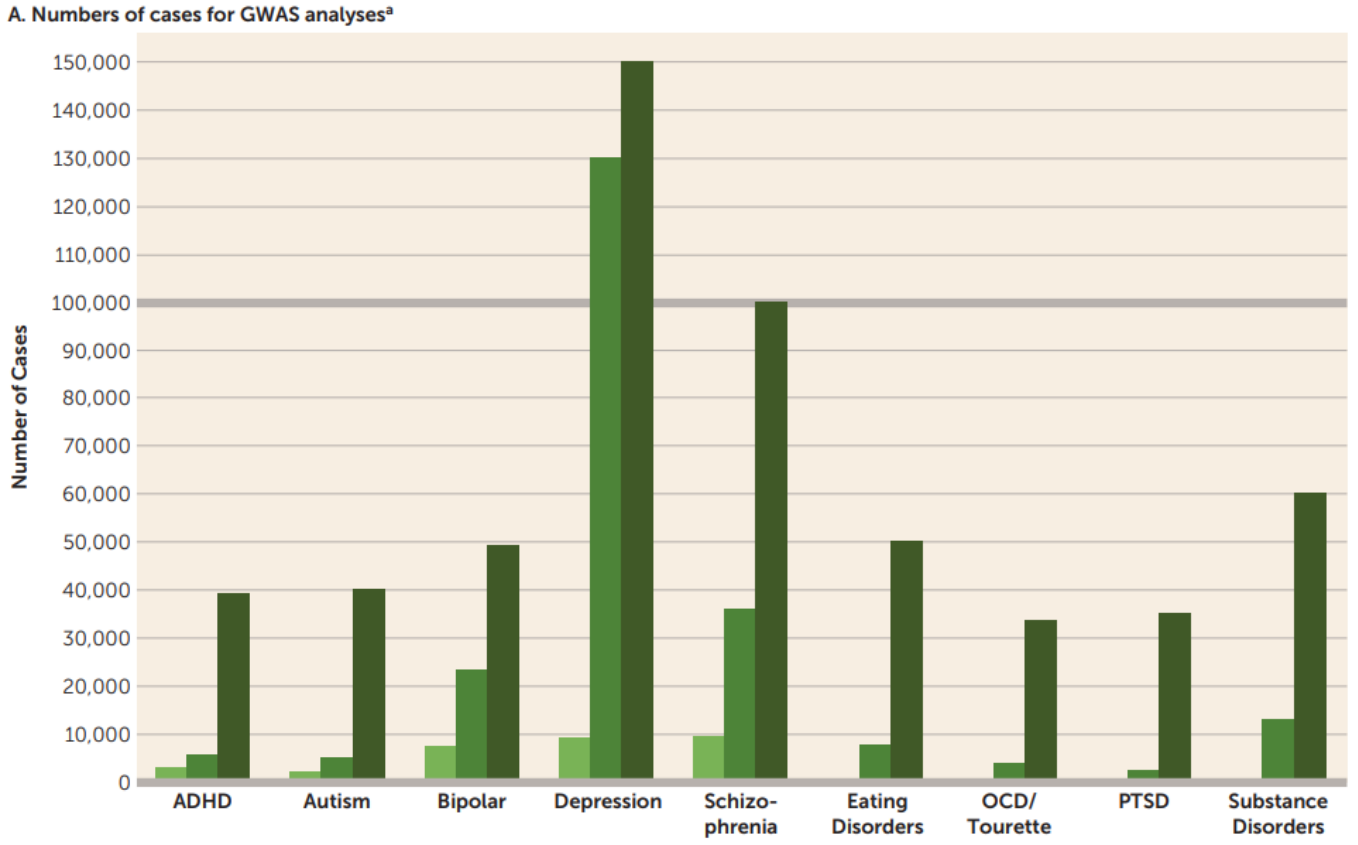


B. Significant genetic associations for schizophrenia[b]



Sullivan PF, Agrawal A, Bulik CM, Andreassen OA, Børglum AD, Breen G, Cichon S, Edenberg HJ, Faraone SV, Gelernter J, Mathews CA, Nievergelt CM, Smoller JW, O'Donovan MC; Psychiatric Genomics Consortium. **Psychiatric Genomics: An Update and an Agenda.** Am J Psychiatry. 2018 Jan 1;175(1):15-27.

FIGURE 4. GWAS Sample Sizes and Rates of Discovery in Psychiatric Genomics Consortium (PGC) Studies



Sullivan PF, Agrawal A, Bulik CM, Andreassen OA, Børglum AD, Breen G, Cichon S, Edenberg HJ, Faraone SV, Gelernter J, Mathews CA, Nievergelt CM, Smoller JW, O'Donovan MC; Psychiatric Genomics Consortium. **Psychiatric Genomics: An Update and an Agenda.** Am J Psychiatry. 2018 Jan 1;175(1):15-27.

Background of the Psychiatric Genomics Consortium (PGC)

A. BACKGROUND

General Information

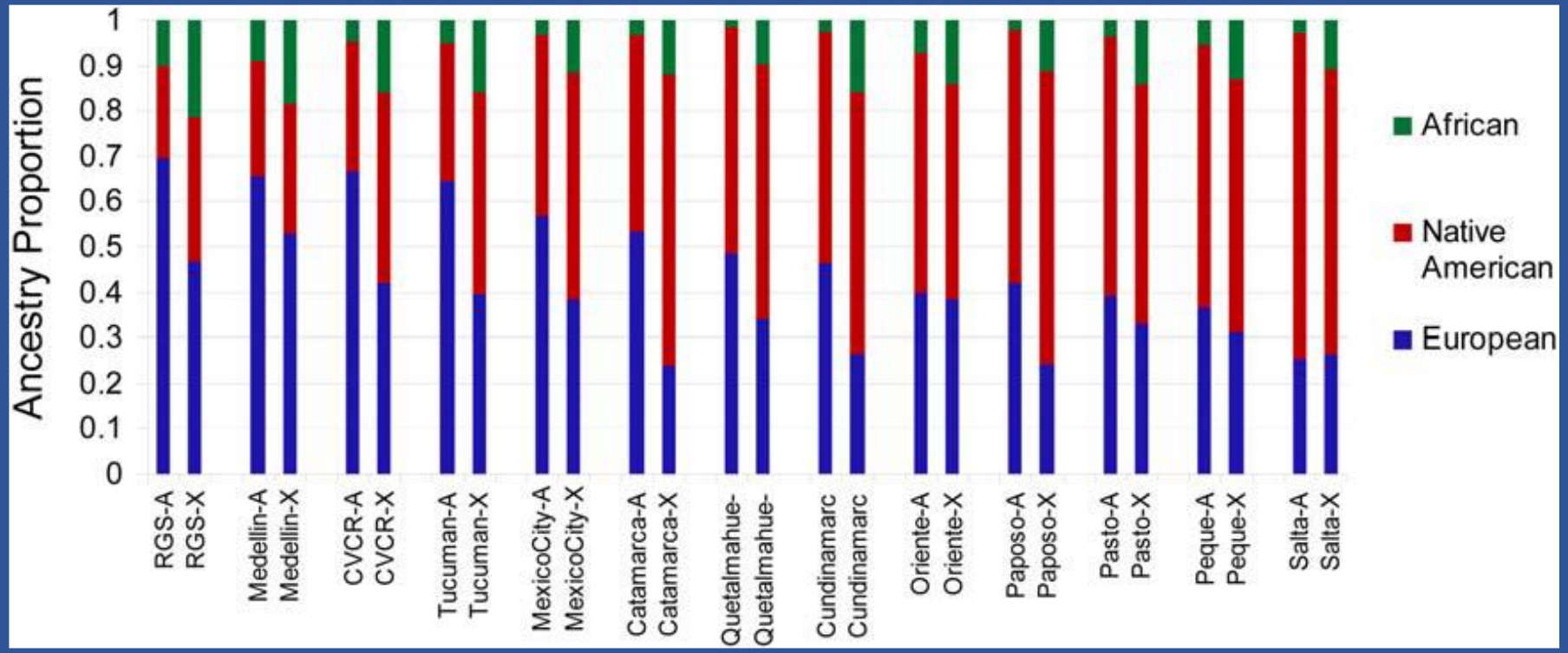
- The PGC has been in continuous existence from 2007 to the present.
- The international membership includes over 800 scientists from 40 countries.
- The nine PGC working groups study attention deficit hyperactivity disorder, autism, bipolar disorder, eating disorders, major depressive disorder, obsessive-compulsive disorder/Tourette syndrome, posttraumatic stress disorder, schizophrenia, and substance use disorders. Provisional groups for anxiety disorders and Alzheimer's disease were added in 2016.
- Current goals are to obtain genome-wide association data on 100,000 cases for each disorder.
- The PGC includes groups focused on cross-disorder analysis, copy number variation, statistical analysis, and pathway analysis.
- The PGC has published 24 main papers and 51 secondary analysis papers (see Table S2 in the data supplement accompanying the online version of this article). At least 141 papers have made use of PGC results.

PGC Core Principles

- Given the human, medical, and societal impact of psychiatric disorders, the PGC is passionate about rapid progress, and it is a world leader in data and results sharing.
- The PGC is characterized by open, inclusive, participatory, and democratic science.
- Core PGC activities are commercially "pre-competitive": identifying the genomic results is a public good and part of the fundamental characterization of these psychiatric disorders.
- The PGC is committed to producing robust, replicable, and secure findings. Its work is based on rigorous methodology, a strong empirical focus, and healthy questioning of prior knowledge and assumptions.
- The PGC has a "mega-analysis" framework: members share raw genotype data so that all samples can be processed using a uniform quality control, imputation, and analysis pipeline.

Sullivan PF, Agrawal A, Bulik CM, Andreassen OA, Børglum AD, Breen G, Cichon S, Edenberg HJ, Faraone SV, Gelernter J, Mathews CA, Nievergelt CM, Smoller JW, O'Donovan MC; Psychiatric Genomics Consortium. **Psychiatric Genomics: An Update and an Agenda.** Am J Psychiatry. 2018 Jan 1;175(1):15-27.

Latin American populations



Wang S, et al. Geographic patterns of genome admixture in Latin American Mestizos. PLoS Genet. 2008 Mar 21;4(3):e1000037.

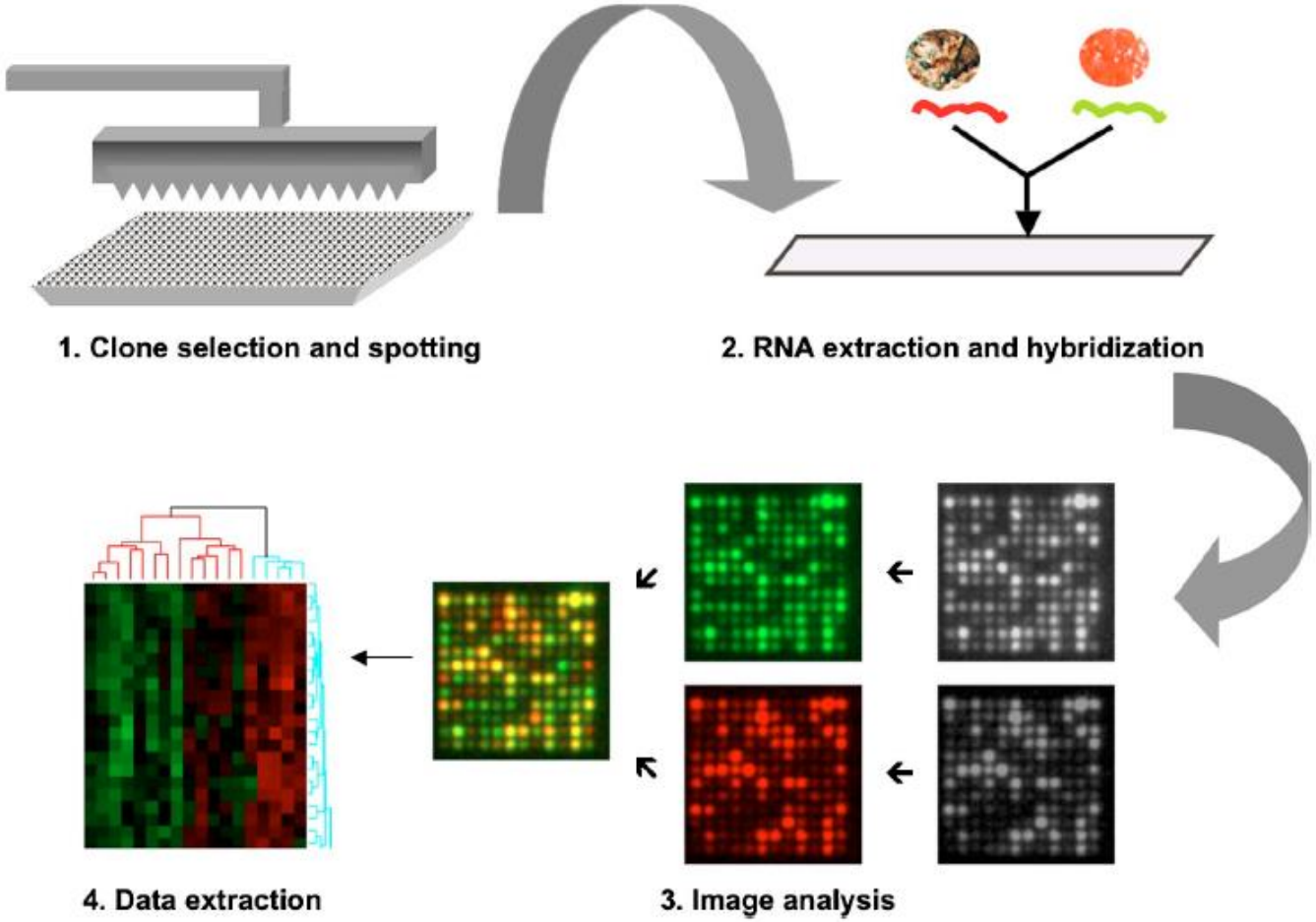
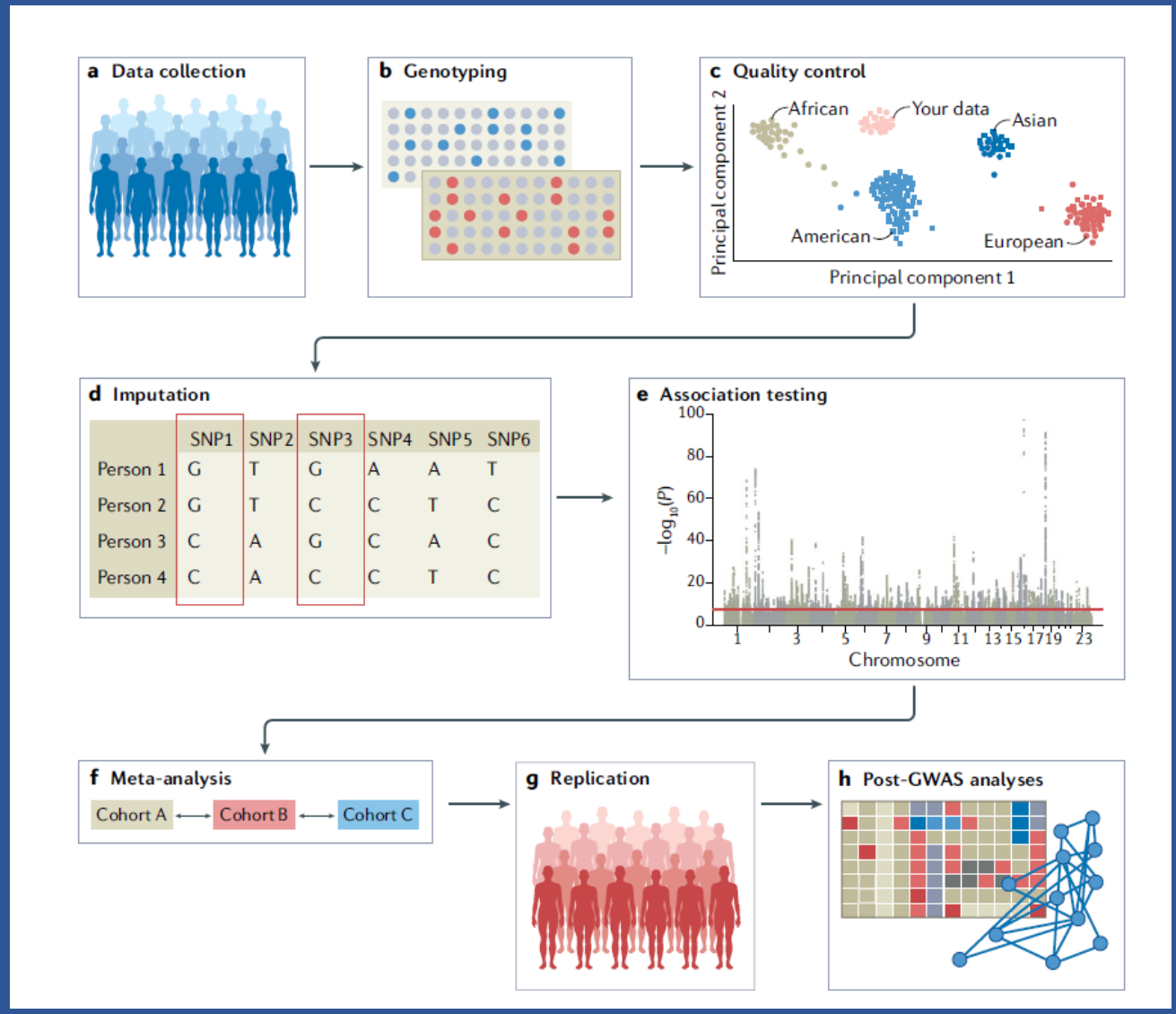


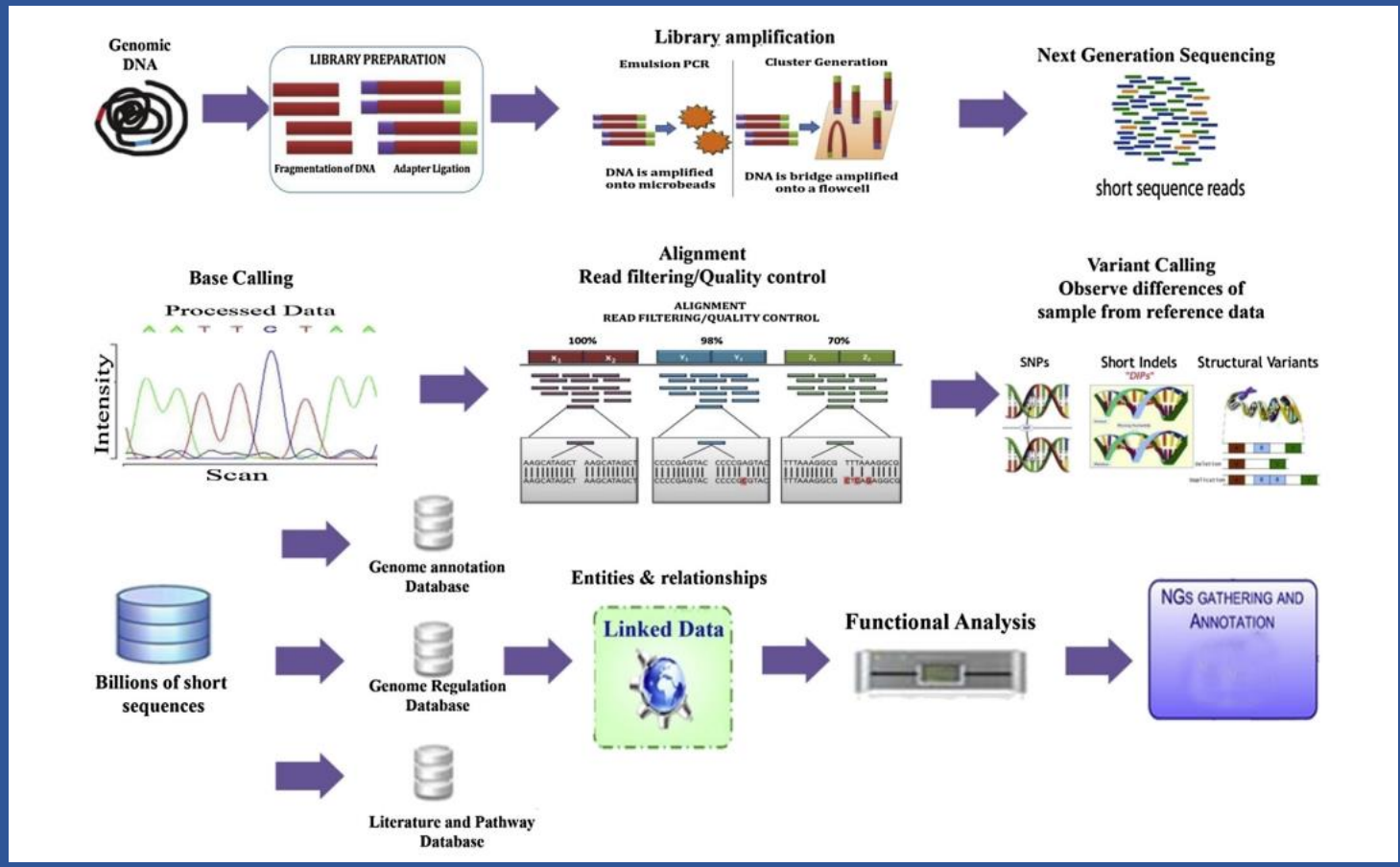
Fig. 1. Microarray technology: From bedside to bench and back again. (1) Clones or oligonucleotides are selected and robotically spotted onto a glass slide or nylon filter. (2) RNA is extracted from cells or tissues of interest and labeled either with cy3 or cy5 (glass slides) or with P^{33} (nylon filters) and hybridized. (3) Images are analyzed using programs such as ArrayPro or IPLAB. (4) Data is clustered and information extracted using bioinformatics.

Weeraratna AT, Nagel JE, de Mello-Coelho V, Taub DD. **Gene expression profiling: from microarrays to medicine**. J Clin Immunol. 2004 May;24(3):213-24.



Overview of steps for conducting GWAS

Uffelmann E, Huang QQ, Munung NS, de Vries J, Okada Y, Martin AR, Martin HC, Lappalainen T, Posthuma D.
Genome-wide association studies.
Nature Reviews Methods Primers. 2021 Aug 26;1(1):1-21.



Next-Generation Sequencing methodology.

Nayarisseri A, Yadav M, Bhatia M, Pandey A, Elkunchwar A, Paul N, Sharma D, Kumar G.
Impact of Next-Generation Whole-Exome sequencing in molecular diagnostics.
Drug Invention Today. 2013 Dec 1;5(4):327-34.

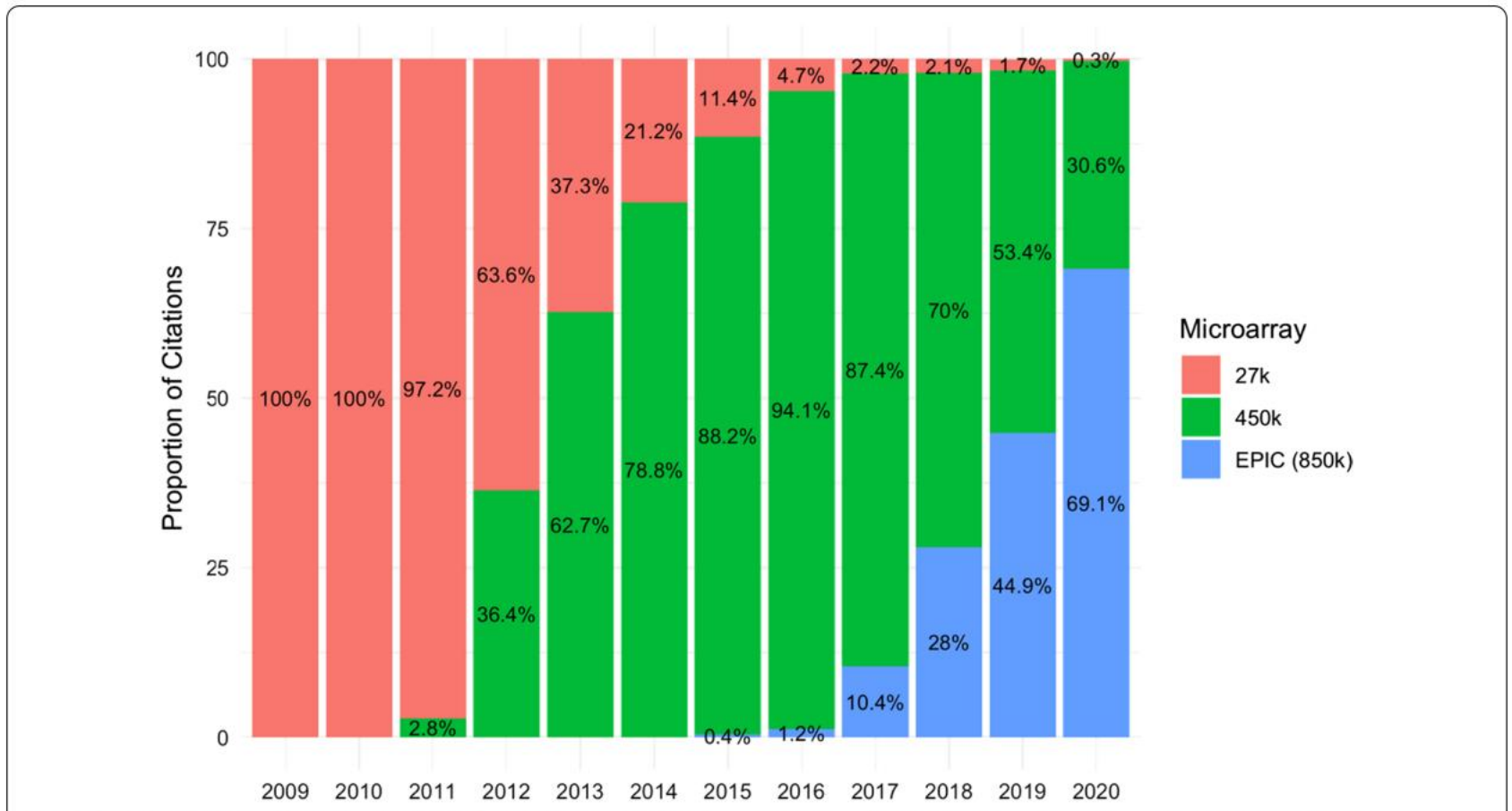


Fig. 1 Popularity of methylation microarrays. The proportion of EWASes deposited on GEO (NCBI) each year, by array type. Abbreviations: EWAS = Epigenome-wide association study, GEO = Gene Expression Omnibus, NCBI = National Center for Biotechnology Information

Campagna MP, Xavier A, Lechner-Scott J, Maltby V, Scott RJ, Butzkueven H, Jokubaitis VG, Lea RA.
Epigenome-wide association studies: current knowledge, strategies and recommendations.
Clin Epigenetics. 2021 Dec 4;13(1):214.

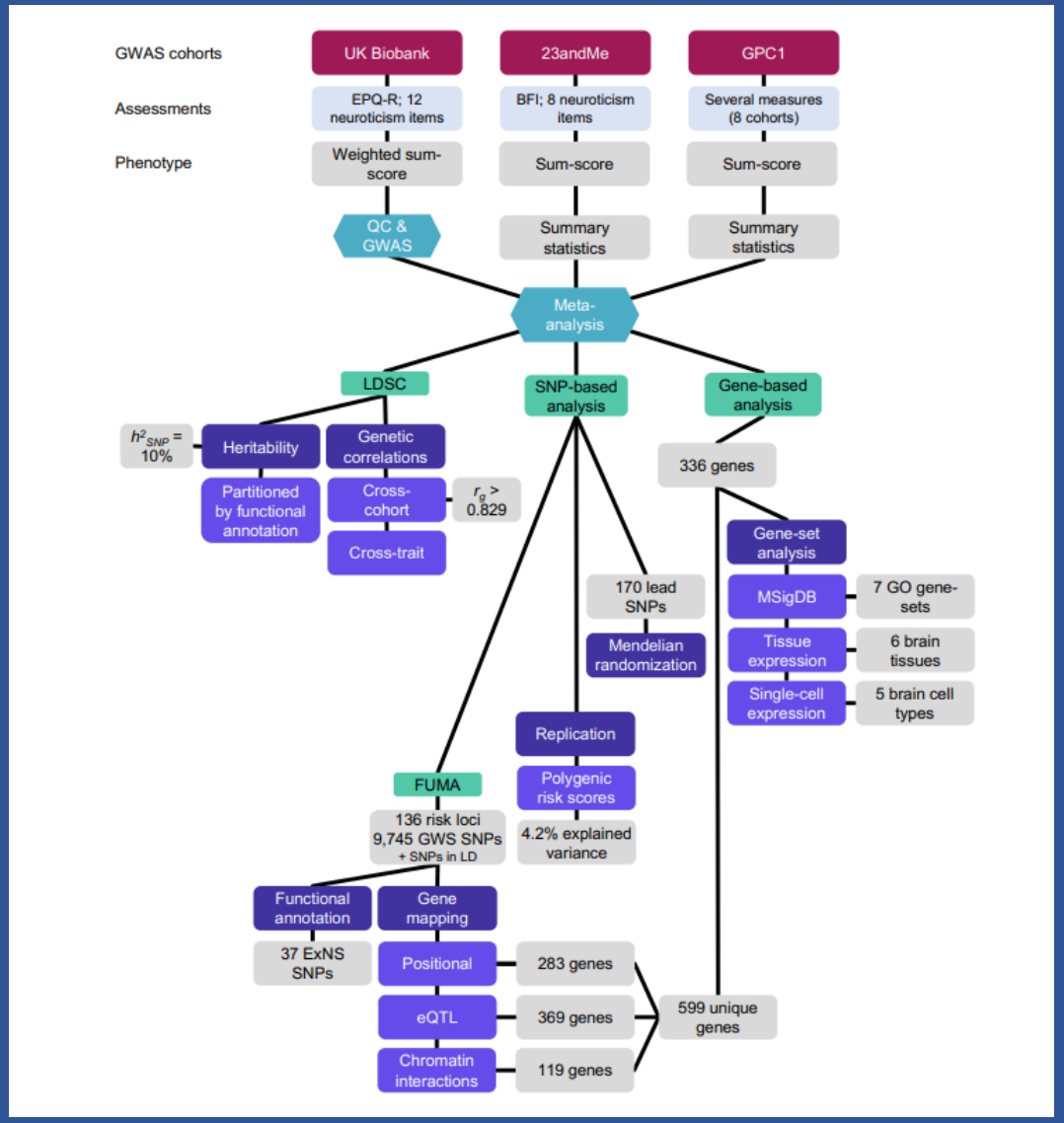
Table 1 | Demographics of European ancestry samples for different phenotype definitions

Cohort	Case	Control	Total (% female)
MVP-MDD	83,810	166,405	250,215 (7)
MVP SR Depression	55,228	155,103	210,331 (7)
23andMe self-reported diagnosis of depression	75,607	231,747	307,354 (48)
PGC + UKB broad depression	170,756	329,443	500,199 (54)
FinnGen mood (affective) disorders	10,418	86,081	96,499
MDD-META (MVP MDD + 23andMe + UKB/PGC + FinnGen)	**340,591**	**813,676**	**1,154,267**
SR Depression meta (MVP SR Depression + 23andMe + UKB/PGC + FinnGen)	**312,009**	**802,374**	**1,114,383**
MVP PHQ-2	175,553 (8)		
UKB PHQ-2	111,268 (54)		
PHQ-2 meta (MVP PHQ2 + UKB PHQ2)	**286,821**		

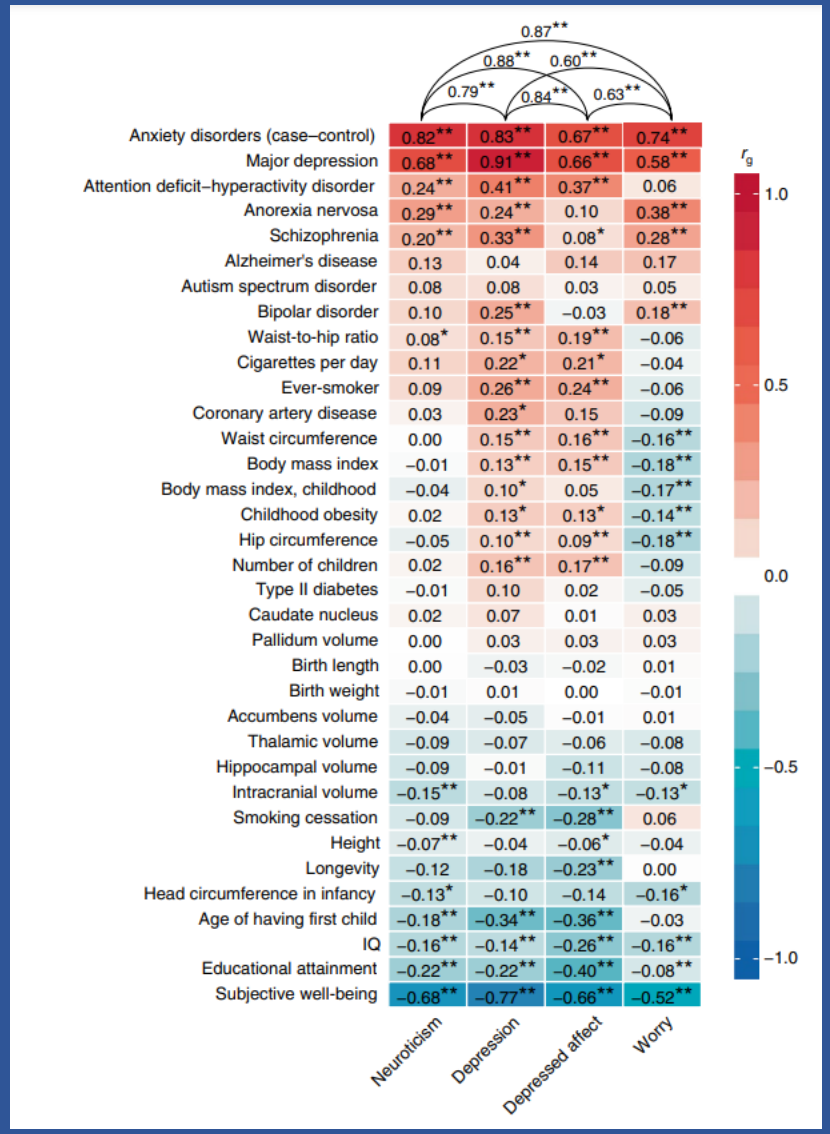
Levey DF, Stein MB, Wendt FR, Pathak GA, Zhou H, Aslan M, Quaden R, Harrington KM, Nuñez YZ, Overstreet C, Radhakrishnan K, Sanacora G, McIntosh AM, Shi J, Shringarpure SS; 23andMe Research Team; Million Veteran Program; Concato J, Polimanti R, Gelernter J**. Bi-ancestral depression GWAS in the Million Veteran Program and meta-analysis in >1.2 million individuals highlight new therapeutic directions**. Nat Neurosci. 2021 Jul;24(7):954-963.

Tissue-based gene association study (TWAS) and fine mapping.

Levey DF, Stein MB, Wendt FR, Pathak GA, Zhou H, Aslan M, Quaden R, Harrington KM, Nuñez YZ, Overstreet C, Radhakrishnan K, Sanacora G, McIntosh AM, Shi J, Shringarpure SS; 23andMe Research Team; Million Veteran Program; Concato J, Polimanti R, Gelernter J**. Bi-ancestral depression GWAS in the Million Veteran Program and meta-analysis in >1.2 million individuals highlight new therapeutic directions**. Nat Neurosci. 2021 Jul;24(7):954-963.



Nagel M, Jansen PR, Stringer S, Watanabe K, de Leeuw CA, Bryois J, Savage JE, Hammerschlag AR, Skene NG, Muñoz-Manchado AB; 23andMe Research Team; White T, Tiemeier H, Linnarsson S, Hjerling-Leffler J, Polderman TJC, Sullivan PF, van der Sluis S, Posthuma D. **Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways**. Nat Genet. 2018 Jul;50(7):920-927.



Nagel M, Jansen PR, Stringer S, Watanabe K, de Leeuw CA, Bryois J, Savage JE, Hammerschlag AR, Skene NG, Muñoz-Manchado AB; 23andMe Research Team; White T, Tiemeier H, Linnarsson S, Hjerling-Leffler J, Polderman TJC, Sullivan PF, van der Sluis S, Posthuma D. **Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways**. Nat Genet. 2018 Jul;50(7):920-927.

Forero DA, Lopez-Leon S, González-Giraldo Y, Bagos PG.
Ten simple rules for carrying out and writing meta-analyses.
PLoS Computational Biology (Q1) 2019 May 16;15(5):e1006922.

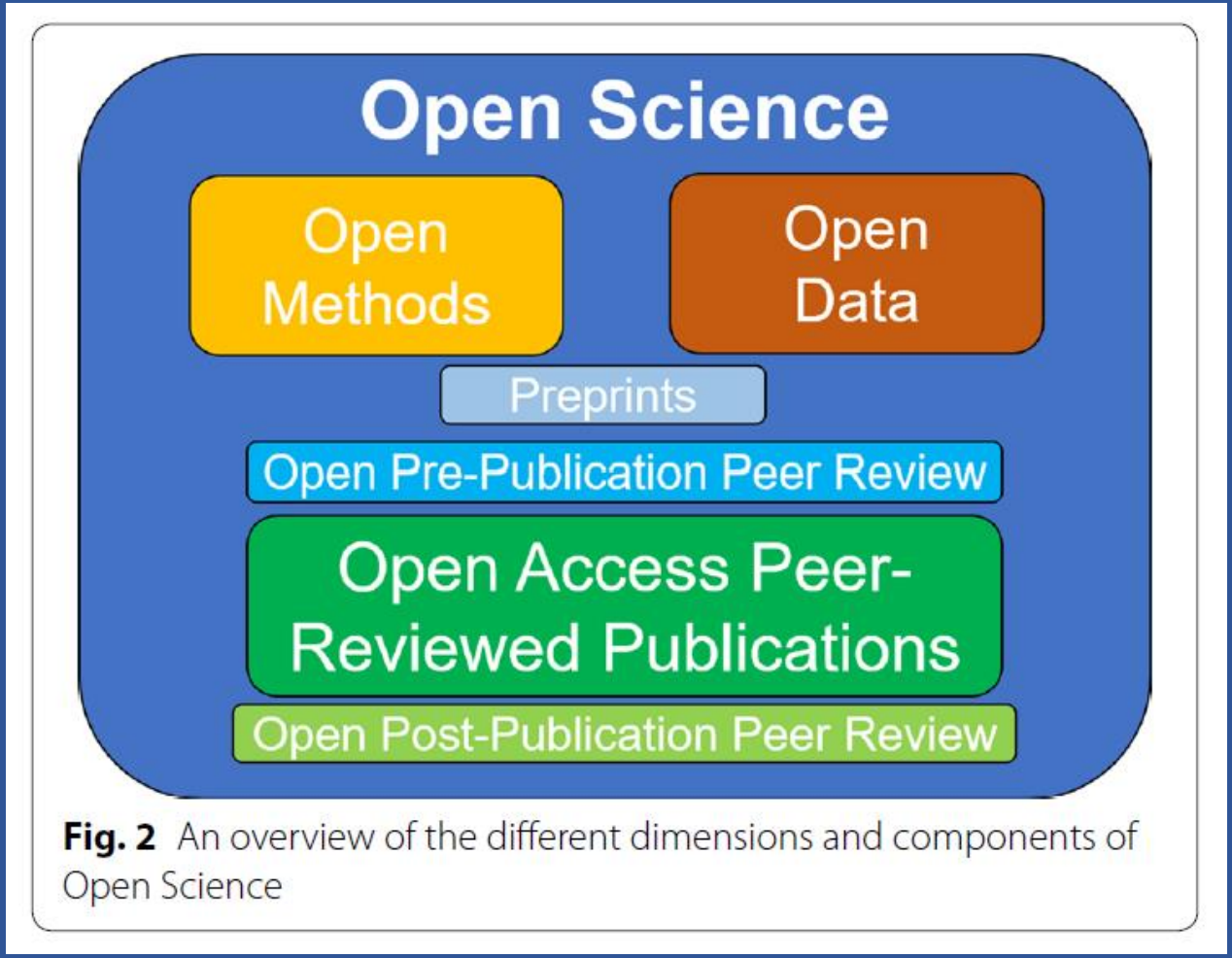


Fig. 2 An overview of the different dimensions and components of Open Science

Forero DA, Lopez-Leon S, Perry G. **A brief guide to the science and art of writing manuscripts in biomedicine**. J Transl Med. 2020 Nov 10;18(1):425.

Forero *et al. BMC Res Notes* (2021) 14:405
https://doi.org/10.1186/s13104-021-05817-z

BMC Research Notes

COMMENTARY Open Access

The importance of adherence to international standards for depositing open data in public repositories

Diego A. Forero[1,2*], Walter H. Curioso[3] and George P. Patrinos[4,5,6]

Forero DA, Curioso WH, Patrinos GP. **The importance of adherence to international standards for depositing open data in public repositories.** *BMC Res Notes. 2021 Nov 2;14(1):405.*

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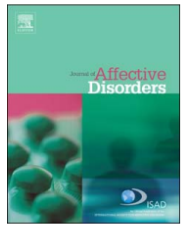


Research paper

A comprehensive regional analysis of genome-wide expression profiles for major depressive disorder

Diego A. Forero[a,*], Gina P. Guio-Vega[a], Yeimy González-Giraldo[b]

[a] Laboratory of NeuroPsychiatric Genetics, Biomedical Sciences Research Group, School of Medicine, Universidad Antonio Nariño, Bogotá, Colombia
[b] Departamento de Nutrición y Bioquímica, Facultad de Ciencias, Pontificia Universidad Javeriana, Bogotá, Colombia

Table 1
Overview of details for original studies included in a meta-analysis of GWES for MDD.

Paper	PMID	Record	Region	Platform	# probes	# samples Ca/Co
–	–	AltarC[a]	PFC	HG-U133A	22,283	11/29
–	–	AltarB[a]	PFC	Ag-Human 1	12,811	11/10
Belzeaux et al., 2012	23149449	GSE38206	Blood	SurePrint G3 v3	26,083	9/9
Chang et al., 2014	24608543	GSE54565	ACC	HG-U133 Plus 2.0	54,675	16/16
Chang et al., 2014	24608543	GSE54566	Amy	HG-U133 Plus 2.0	54,675	14/14
Chang et al., 2014	24608543	GSE54562	ACC	HumanHT-12 v3.0	49,576	10/10
Chang et al., 2014	24608543	GSE54563	ACC	HumanHT-12 v3.0	49,576	25/25
Chang et al., 2014	24608543	GSE54564	Amy	HumanHT-12 v3.0	49,576	21/21
Chang et al., 2014	24608543	GSE54571	ACC	HG-U133 Plus 2.0	54,675	13/13
Chang et al., 2014	24608543	GSE54572	ACC	HG-U133 Plus 2.0	54,675	12/12
Chang et al., 2014	24608543	GSE54568	PFC	HG-U133 Plus 2.0	54,675	15/15
Chang et al., 2014	24608543	GSE54567	PFC	HG-U133 Plus 2.0	54,675	14/14
Chang et al., 2014	24608543	GSE54575	PFC	HG-U133A	22,283	12/12
Chang et al., 2014	24608543	GSE54570	PFC	HG-U133A	22,283	13/13
–	–	Feinberg[a]	Cerebellum	HG-U95Av2	12,625	26/28
Iwamoto et al., 2004	14743183	GSE12654	PFC	HG-U95Av2	12,625	12/14
–	–	GSE53987	PFC	HG-U133 Plus 2.0	54,675	17/19
Liu et al., 2014	24676134	GSE52790	Blood	HG-Glue	39,224	10/12
Miyata et al., 2016	26926397	GSE76826	Blood	SurePrint G3 v2	24,128	10/12
Savitz et al., 2013	23064081	GSE39653	Blood	HumanHT-12 v4.0	48,107	22/23
–	–	SklarA[a]	PFC	HG-U95Av2	12,625	11/12
–	–	SklarB[a]	Cerebellum	HG-U95Av2	12,625	13/10
Spijker et al., 2010	20471630	GSE19738	Blood	HG-G4112A	41,073	33/34
–	–	GSE32280	Blood	HG-U133 Plus 2.0	54,675	8/8

Abbreviations: Amy: Amygdala; PFC: Prefrontal cortex; ACC: Anterior Cingulate Cortex; HG-U133 Plus 2.0: GeneChip Human Genome U133 Plus 2.0 Array (Affymetrix); HG-U133A: GeneChip Human Genome U133A Array (Affymetrix); HG-U95Av2: GeneChip Human Genome U95 Version 2 Array (Affymetrix); HumanHT-12 v3.0: HumanHT-12 v3.0 Gene Expression BeadChip (Illumina); SurePrint G3 v3: SurePrint G3 Human GE v3 8 × 60 K Microarray (Agilent); SurePrint G3 v2: SurePrint G3 Human GE v2 8 × 60 K Microarray (Agilent); HumanHT-12 v4.0: HumanHT-12 v4.0 Gene Expression BeadChip (Illumina); HG-G4112A Whole Human Genome Oligo Microarray G4112A (Agilent); HG-G4112A: Whole Human Genome Oligo Microarray G4112A (Agilent); Ag-Human 1: Human 1 cDNA microarray (Agilent); HG-Glue: Glue Grant Human Transcriptome Array (Affymetrix).

[a] Datasets from Stanley Medical Research Institute Online Genomics Database.

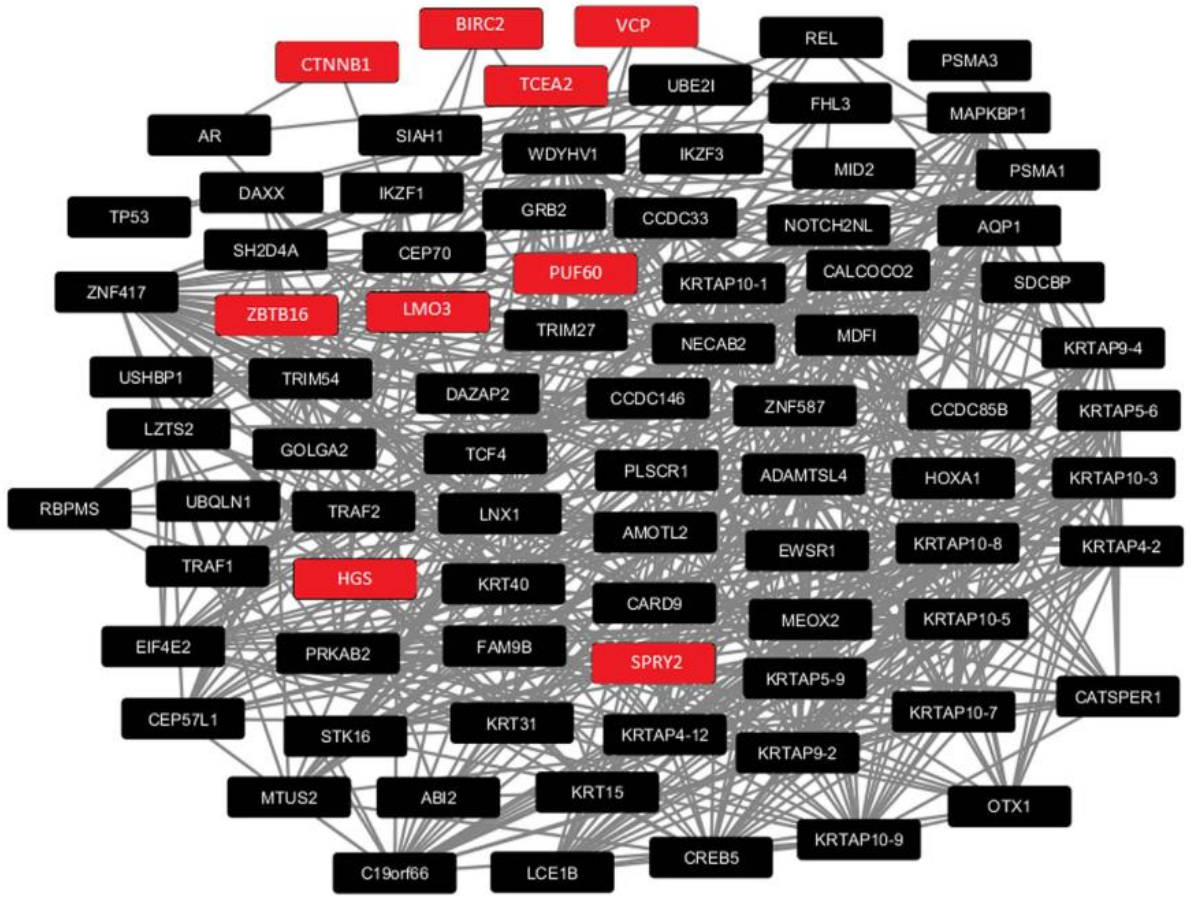


Fig. 1. Protein-protein interaction network for differentially expressed genes derived from a meta-analysis of GWES for prefrontal cortex of patients with major depressive disorder. A highly connected module is shown and DE genes are highlighted in red. Abbreviations: BIRC2: baculoviral IAP repeat-containing 2; CTNNB1: catenin (cadherin-associated protein), beta 1 88 kDa; HGS: hepatocyte growth factor-regulated tyrosine kinase substrate; LMO3: LIM domain only 3 (rhombotin-like 2); PUF60: poly-U binding splicing factor 60KDa; SPRY2: sprouty homolog 2 (Drosophila); TCEA2: transcription elongation factor A (SII), 2; VCP: valosin-containing protein; ZBTB16: zinc finger and BTB domain containing 16.

Cellular and Molecular Neurobiology
https://doi.org/10.1007/s10571-020-00927-x

ORIGINAL RESEARCH

Functional Genomics of Epileptogenesis in Animal Models and Humans

Diego A. Forero[1,2]

Received: 3 December 2019 / Accepted: 20 July 2020

Table 1 Details of GWES included

Organism	Author	NCBI GEO	Design	Platform	PMID
Human	Helbig (2008)	GSE7486	Lymphoblastoid cell lines from patients with idiopathic absence epilepsies	Affymetrix Human Genome U133 Plus 2.0 Array	18435749
Mouse	Kalozoumi (2018)	GSE88992	Hippocampi from mice treated with kainate	Affymetrix Mouse Genome 430 2.0 Array	30114263
Mouse	Losing (2017)	GSE100202	Hippocampi from mice treated with pilocarpine	Affymetrix Mouse Gene 1.0 ST Array	28716058
Mouse	Kedmi (2007)	GSE6614	Brains from mice with nicotine-induced seizures	Affymetrix Murine Genome U74A Version 2 Array	17456735
Rat	Wilson (2005)	GSE1834	Hippocampi from rats treated with kainate	Affymetrix Rat Genome U34 Array	15800381
Rat	Okamoto (2010)	GSE14763	Hippocampi from rats treated with pilocarpine	GE Healthcare/Amersham Biosciences CodeLink™ Rat Whole Genome Bioarray	20377889
Rat	McClelland (2014)	GSE22894	CA1 from rats treated with kainate	Illumina ratRef-12 v1.0 expression beadchip	25117540
Zebrafish	Grone and Baraban 2015	GSE43312	Larvae from Scn1a mutant zebrafish	Agilent-026437 D. rerio Oligo Microarray V3	(–)
Drosophila	Singh (2011)	GSE10988	Heads from drosophila treated with levetiracetam and Pentylenetetrazole	CDMC_Drosophila_12k1	21503142

PMID PubMed identifier, *NCBI GEO* NCBI GEO database identifier

Table 2 Main candidate genes

Gene	Evidence	Gene	Evidence	Gene	Evidence	Gene	Evidence
ADCY7	Mm-GW	*FUS*	Mm-GW	*LXN*	Hs-Mm-Rn	*S100A4*	Mm-Rn-Dr
ANXA5	Mm-Rn-Dr	*GABRA2*	Mm-GW	*MAPK6*	Mm-Rn-Dr	*SCN1A*	Mm-GW
ATP1B2	Hs-Mm-Dr-Dm	*GALNT3*	Mm-GW	*MCM6*	Hs-Mm-Rn	*SCN3A*	Mm-GW
ATP2B2	Mm-Rn-Dr	*GATM*	Hs-Mm-Rn	*MRPL10*	Hs-Dr-GW	*SEC61A1*	Mm-Rn-Dr
ATXN1	Mm-GW	*GJA1*	GW-Mm-Dr	*MYC*	Mm-Rn-Dr	*SEC61B*	Hs-Mm-Rn-Dr
BCKDK	GW-Mm-Dr	*GLS*	Hs-Dr-GW	*MYO5B*	Mm-Rn-Dr	*SERPINE1*	Mm-Rn-Dr
BOK	Mm-Rn-Dr	*GNAQ*	Hs-Mm-Dm	*NAB1*	Hs-Mm-GW	*SMAD1*	Hs-Mm-Rn
BRD7	Mm-GW	*GPD1*	Hs-Mm-Dm	*NDUFS2*	Hs-Mm-Dm	*SOX11*	Mm-Rn-Dr
CADPS	Hs-Mm-Rn	*GRIK1*	Mm-GW	*NFE2L1*	Mm-GW	*STAM2*	Hs-Mm-Dm
CALM2	Mm-Rn-Dr	*GRIN1*	Hs-Mm-Rn	*NINJ1*	Hs-Mm-Rn	*STAT3*	Hs-Mm-Rn
CAPZA2	Hs-Mm-Rn	*GTPBP1*	Hs-Mm-Dr-Dm	*NOL6*	Hs-Dr-Dm	*STX1B*	Mm-GW
CBX1	GW-Mm-Dr	*HAND2*	Hs-Mm-Dr-Dm	*NPEPPS*	Mm-GW	*SUMO3*	Hs-Dr-Dm
CCL2	Mm-Rn-Dr	*HEATR3*	GW-Dr	*NTRK2*	Hs-Mm-Rn	*TBX21*	GW-Dr
CDO1	Hs-Mm-Rn	*HK2*	Mm-Rn-Dr	*OLFM1*	Hs-Mm-Rn-Dr	*THRA*	Mm-Rn-Dr
CLIC4	Hs-Mm-Dr-Dm	*HOXB5*	GW-Dr	*P4HB*	Hs-Mm-Rn-Dr	*TMPO*	Hs-Mm-Rn-Dr
CPD	Hs-Mm-Dm	*HOXB9*	Mm-GW	*PENK*	Hs-Mm-Rn	*TPM2*	Hs-Mm-Dm
CYP7B1	Hs-Mm-Rn	*INPP1*	Mm-GW	*PHKG2*	Mm-GW	*TPM3*	Hs-Mm-Dr-Dm
DGKA	Mm-Rn-Dr	*ITGAX*	Mm-GW	*PLCD1*	Mm-Rn-Dr	*TPM4*	Hs-Mm-Dr-Dm
EEF2K	Mm-Rn-Dr	*ITGB1*	Mm-Rn-Dr	*PNPO*	Mm-GW	*TPSB2*	Hs-Dr-Dm
F3	Mm-Rn-Dr	*ITSN2*	GW-Dr	*PPP3CA*	Hs-Mm-Rn	*USP21*	Hs-Mm-Dm
FAM173A	Hs-Mm-Dm	*KCNAB1*	Mm-GW	*PTGFRN*	Hs-Mm-Rn	*VIM*	Hs-Mm-Rn-Dr
FBRS	Mm-GW	*KCNC1*	Hs-Mm-Rn	*PTPN1*	Hs-Mm-Rn	*VKORC1*	Mm-GW
FBXL19	GW-Dr	*KPNB1*	Mm-GW	*PTPN2*	Hs-Mm-Rn	*VSNL1*	Hs-Mm-Rn
FKBP1B	Mm-GW	*LOXL1*	Hs-Mm-Rn	*PTPRF*	Hs-Mm-Rn-Dr	*XPO7*	Hs-Mm-Rn

Hs GWES in humans, *Mm* meta-analysis of GWES in mice, *Rn* convergence of GWES in rats, *Dm* GWES in fruit flies, *Dr* GWES in zebrafish, *GW* GWAS in humans

Journal of Molecular Neuroscience (2020) 70:1887–1893
https://doi.org/10.1007/s12031-020-01585-w

Integrative In Silico Analysis of Genome-Wide DNA Methylation Profiles in Schizophrenia

Diego A. Forero [1] · Yeimy González-Giraldo [2]

Received: 6 January 2020 / Accepted: 13 May 2020 / Published online: 26 May 2020

Table 1 Details of EWAS included

Author, year	NCBI GEO	Tissue	Sample size	Platform	PMID
Wockner, 2014	GSE61107	Frontal cortex	24 SZ and 24 controls	Illumina Infinium Human Methylation 450 Beadchip (GPL13534)	24,399,042
Chen, 2014	GSE38873	Cerebellum	46 SZ and 47 controls	Human Methylation 27 BeadChips (GPL8490)	25,243,493
Viana, 2017C	GSE89702	Cerebellum	16 SZ and 17 controls	Illumina Infinium Human Methylation 450 Beadchip (GPL13534)	28,011,714
Viana, 2017H	GSE89703	Hippocampus	14 SZ and 13 controls	Illumina Infinium Human Methylation 450 Beadchip (GPL13534)	28,011,714
Abdolmaleky, 2018	GSE120341	Prefrontal cortex	3 SZ and 4 controls	Human Methylation 27 BeadChips (GPL8490)	30,468,562

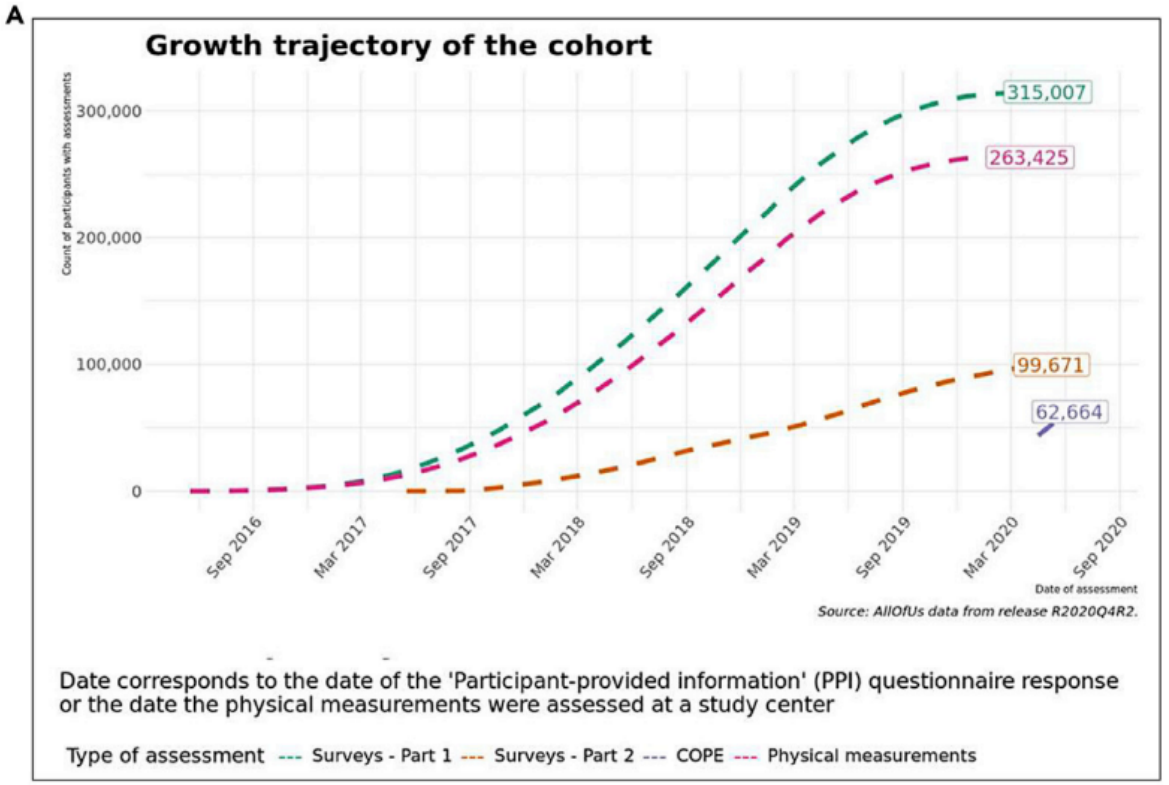


Figure 1. Overview of data types included in the beta-release curated data repository

(A) Growth trajectory of participant data types after enrollment. Survey part 1 (green) includes "the Basics," "Lifestyle," and "Overall Health" surveys; survey part 2 (pink) includes "Personal Medical History," "Health Care Access and Utilization," and "Family Medical History." Physical measurement accrual is shown in red, and the COVID-19 Participant Experience (COPE) survey is shown in purple. Note that the flattening is artificial due to the random date shift introduced to protect participant privacy. (B) Historical availability of participants' electronic health record (EHR), survey, and device data.

RESULTS

Ramirez AH, Sulieman L, Schlueter DJ, Halvorson A, Qian J, Ratsimbazafy F, Loperena R, Mayo K, Basford M, Deflaux N, Muthuraman KN, Natarajan K, Kho A, Xu H, Wilkins C, Anton-Culver H, Boerwinkle E, Cicek M, Clark CR, Cohn E, Ohno-Machado L, Schully SD, Ahmedani BK, Argos M, Cronin RM, O'Donnell C, Fouad M, Goldstein DB, Greenland P, Hebbring SJ, Karlson EW, Khatri P, Korf B, Smoller JW, Sodeke S, Wilbanks J, Hentges J, Mockrin S, Lunt C, Devaney SA, Gebo K, Denny JC, Carroll RJ, Glazer D, Harris PA, Hripcsak G, Philippakis A, Roden DM; All of Us Research Program. **The All of Us Research Program: Data quality, utility, and diversity**. Patterns (N Y). 2022 Aug 12;3(8):100570.

Extended Data Table 3 | Counts and proportions of self-reported ethnic groups among 488,377 genotyped UK Biobank participants

Ethnic group	Self-reported ethnic background	Count of genotyped UK Biobank participants	
White			460,186 (94.23%)
	British	431,059 (88.26%)	
	Any other white background	15,821 (3.24%)	
	Irish	12,760 (2.61%)	
	White	546 (0.11%)	
Asian or Asian British			9,474 (1.94%)
	Indian	5,716 (1.17%)	
	Pakistani	1,748 (0.36%)	
	Any other Asian background	1,747 (0.36%)	
	Bangladeshi	221 (0.05%)	
	Asian or Asian British	42 (0.01%)	
Black or Black British			7,649 (1.57%)
	Caribbean	4,299 (0.88%)	
	African	3,206 (0.66%)	
	Any other Black background	118 (0.02%)	
	Black or Black British	26 (0.01%)	
Chinese			1,504 (0.31%)
	Chinese	1,504 (0.31%)	
Mixed			2,843 (0.58%)
	Any other mixed background	996 (0.2%)	
	White and Asian	802 (0.16%)	
	White and Black Caribbean	597 (0.12%)	
	White and Black African	402 (0.08%)	
	Mixed	46 (0.01%)	
Other/Unknown			6,721 (1.38%)
	Other ethnic group	4,357 (0.89%)	
	Not stated	2,364 (0.48%)	

Bycroft C, Freeman C, Petkova D, Band G, Elliott LT, Sharp K, Motyer A, Vukcevic D, Delaneau O, O'Connell J, Cortes A, Welsh S, Young A, Effingham M, McVean G, Leslie S, Allen N, Donnelly P, Marchini J. **The UK Biobank resource with deep phenotyping and genomic data**. Nature. 2018 Oct;562(7726):203-209.

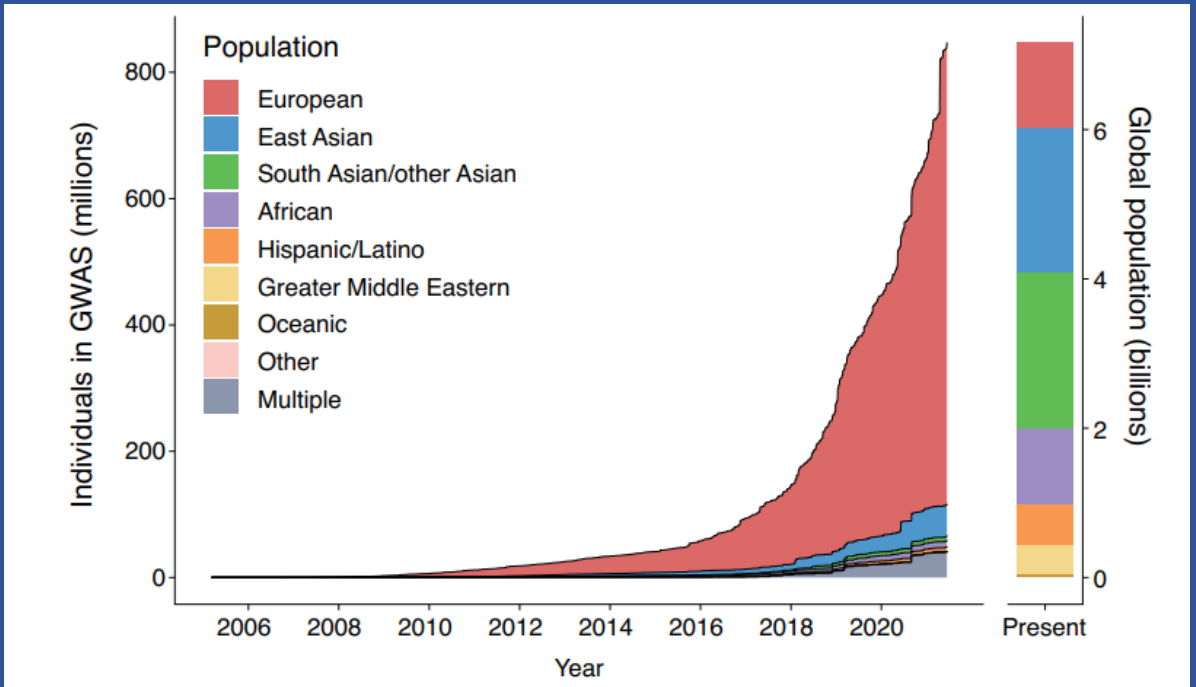


Fig. 1 | The proportion of samples from individuals cumulatively reported by the GWAS Catalog[1] as of 8 July 2021.

Fatumo S, Chikowore T, Choudhury A, Ayub M, Martin AR, Kuchenbaecker K. **A roadmap to increase diversity in genomic studies.** Nat Med. 2022 Feb;28(2):243-250.

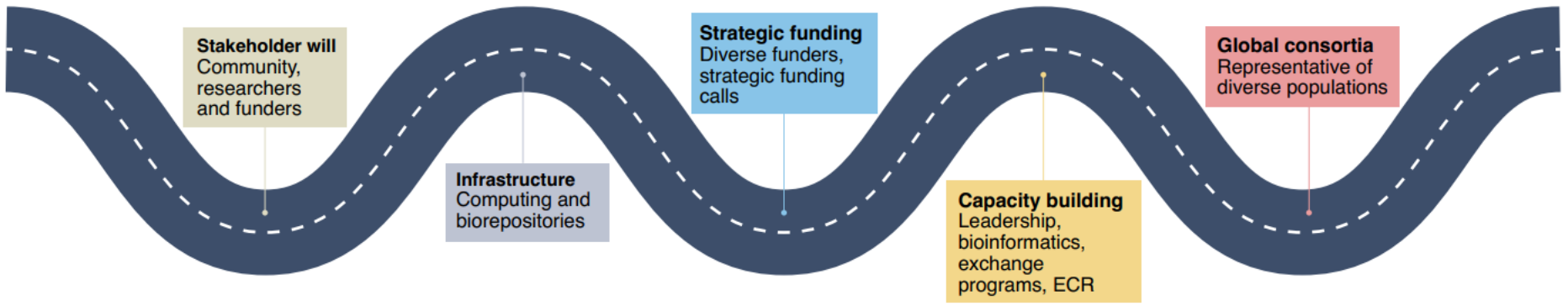


Fig. 3 | Roadmap showing the key pillars for setting up and sustaining diverse global genomic studies. ECR, early career researcher.

Fatumo S, Chikowore T, Choudhury A, Ayub M, Martin AR, Kuchenbaecker K. **A roadmap to increase diversity in genomic studies.** Nat Med. 2022 Feb;28(2):243-250.

LAGC

Latin American Genomics Consortium

latinamericangenomicsconsortium.org

The Drug Development Process: It's Long, Expensive and Risky

	Target to Hit	Hit to Lead	Lead Optim	Non-Clinical	Phase 1	Phase 2	Phase 3	Sub to Launch
# per Launch	24.3	19.4	14.6	12.4	8.6	4.6	1.6	1.1
P(TS)	80%	75%	85%	69%	54%	34%	70%	91%
Cycle time (yrs)	1.0	1.5	2.0	1.0	1.5	2.5	2.5	1.5
Cost/launch ($mil)	$94	$166	$414	$150	$273	$319	$314	$48
P(TS)AD[1]					28%	8%	1.8%	100%

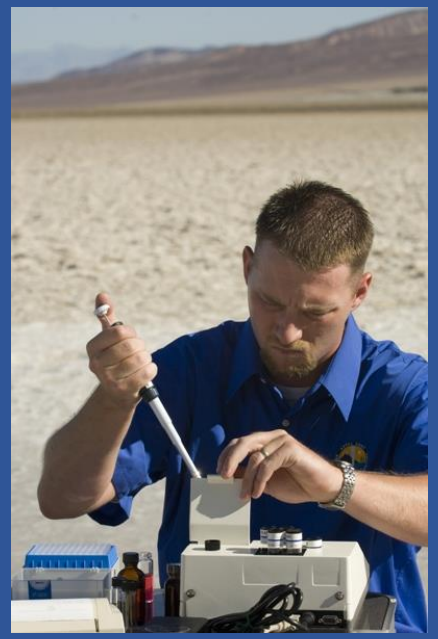
Adapted from: SM Paul et al. Nature Reviews: Drug Discovery, 2010.
Costs are capitalized based on 11% cost of capital and in 2010 dollars.

[1]Adapted from: JA Cummings et al. Alz Res & Therapy, 2014.

Fig. 1. A diagram of the stages of drug discovery and development with estimates of cost and duration. Adapted from [3] and [4].

Mohs RC, Greig NH. **Drug discovery and development: Role of basic biological research.** Alzheimers Dement (N Y). 2017 Nov 11;3(4):651-657.

From Data Generation to Data Analysis



Mitropoulos K, Al Jaibeji H, **Forero DA**, Laissue P, Wonkam A, Lopez-Correa C, Mohamed Z, Chantratita W, Lee MT, Llerena A, Brand A, Ali BR, Patrinos GP. **Success stories in genomic medicine from resource-limited countries**. Hum Genomics. 2015 Jun 18;9:11.

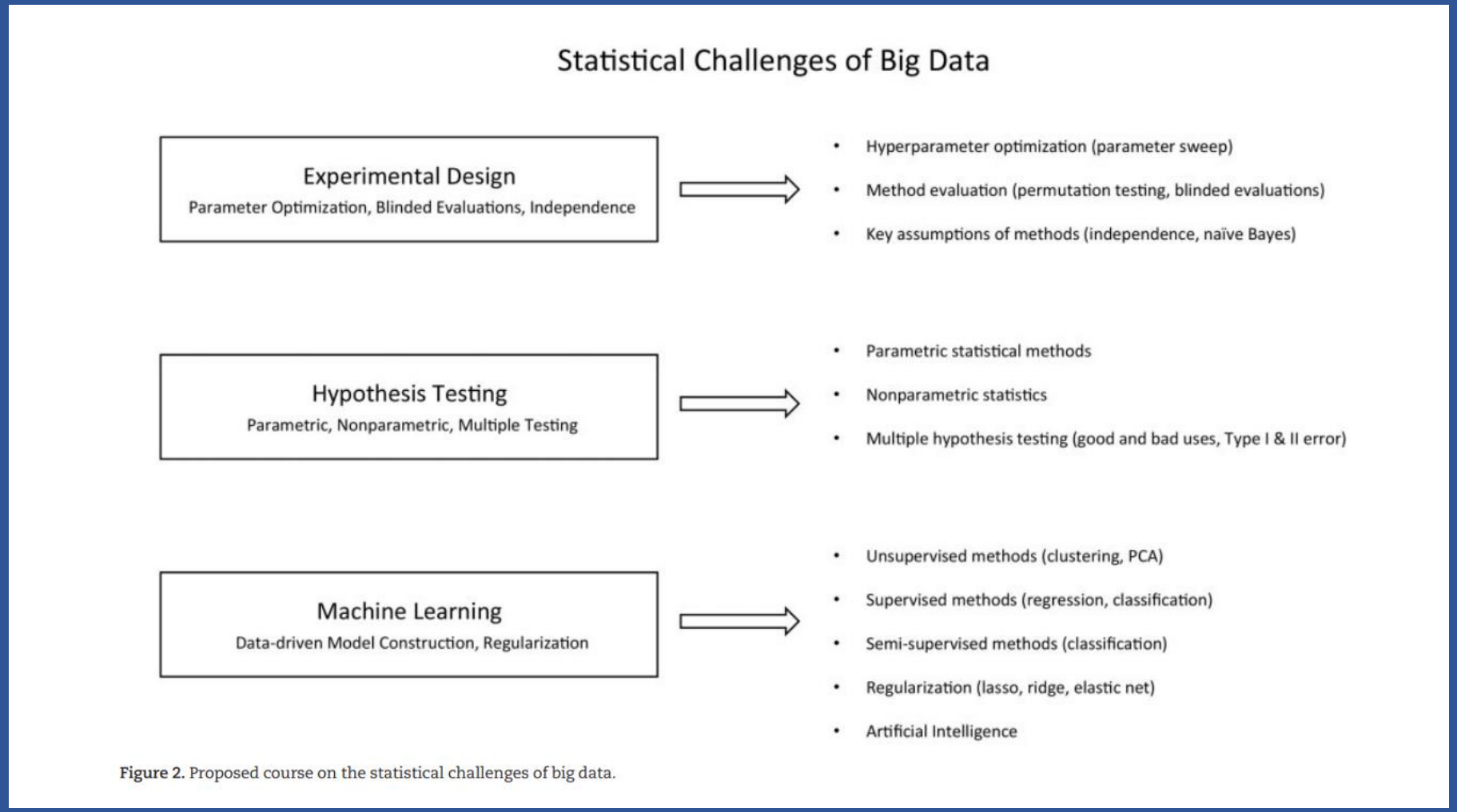


Figure 2. Proposed course on the statistical challenges of big data.

Greene AC, Giffin KA, Greene CS, Moore JH. **Adapting bioinformatics curricula for big data**. Brief Bioinform. 2016 Jan;17(1):43-50.

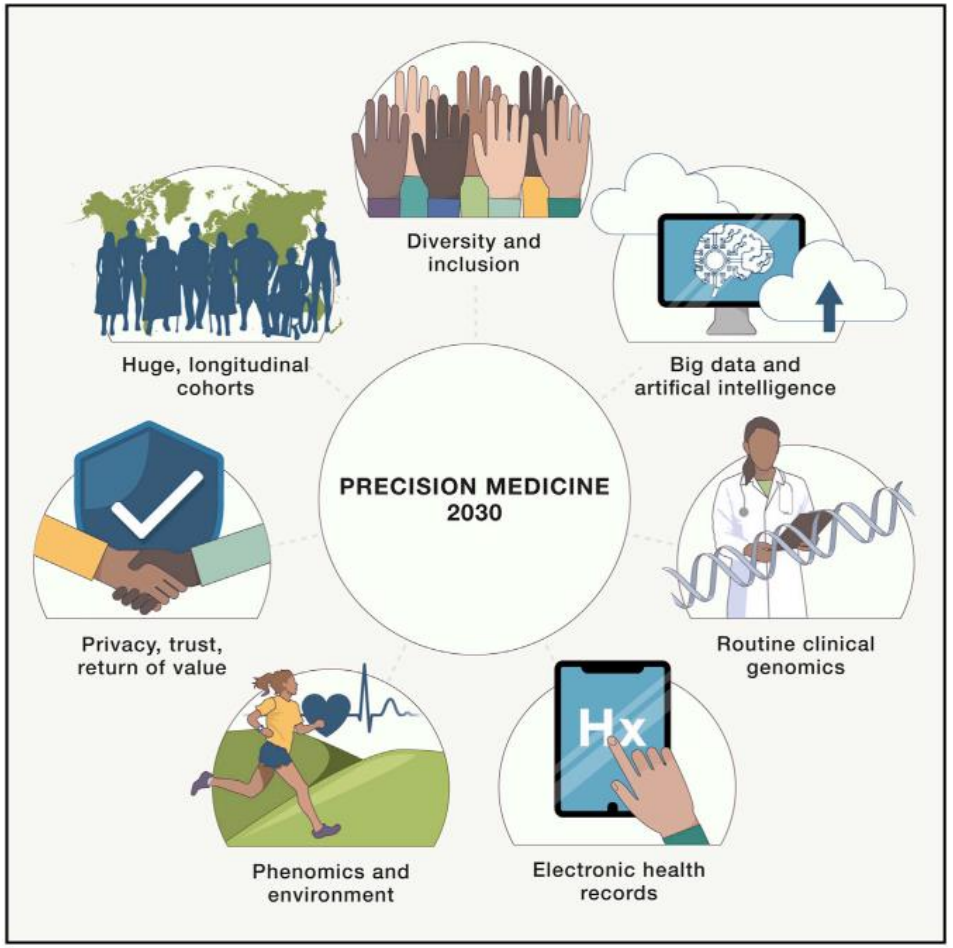
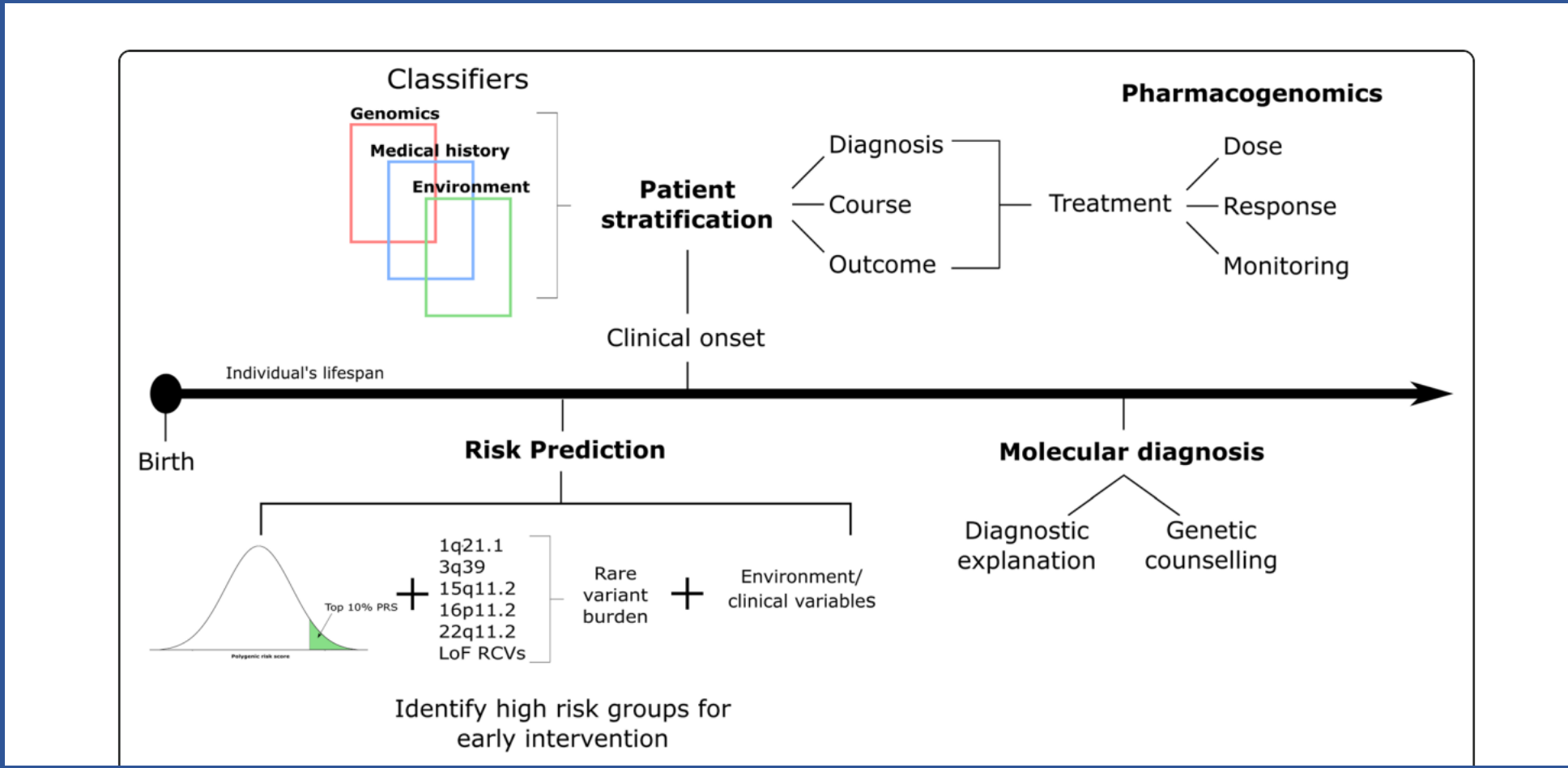


Figure 1. Seven opportunities for precision medicine by 2030

Denny JC, Collins FS. **Precision medicine in 2030-seven ways to transform healthcare.** Cell. 2021 Mar 18;184(6):1415-1419.

Illustration of what precision psychiatry might look like



Rees E, Owen MJ. **Translating insights from neuropsychiatric genetics and genomics for precision psychiatry.** Genome Med. 2020 Apr 29;12(1):43.

“A consolidation of the collaborations between groups from different LMICs would lead to additional advantages, such as establishment of **international research consortia** that could lead to studies with larger samples sizes. **Advances in genomics of NPDs will benefit the entire humanity** rather than one or other population group.”

Forero DA, Vélez-van-Meerbeke A, Deshpande SN, **Nicolini H**, Perry G. **Neuropsychiatric genetics in developing countries: Current challenges**. World J Psychiatry. 2014 Dec 22;4(4):69-71.

There are several opportunities for the strengthening of research in genomics of neuropsychiatric disorders in Latin America. There is the need for the **consolidation of international and interinstitutional consortia** (promoting public/private partnerships) in the region, to facilitate the sharing of resources and to achieve the large sample sizes currently needed in the field, from the perspective of open science. In this context, the **Latin American Genomics Consortium (LAGC) has been recently created as a major and inclusive initiative** in the region.

Forero DA. **Genomics of psychiatric disorders: Regional challenges and opportunities**. Biomédica. 2023 Mar 30;43(1):5-7.

As genomics involves expensive high-throughput platforms, adequate **local funding for those analysis is key**, highlighting the importance of having **research in mental health as a priority from the governments.** Longitudinal studies, such as cohorts, will benefit from increased funding. **In the context of the need of novel treatment strategies, it is well known that biomedical sciences are fundamental for the drug discovery processes,** which require years and large budgets.

Forero DA. Genomics of psychiatric disorders: Regional challenges and opportunities. Biomédica. 2023 Mar 30;43(1):5-7.

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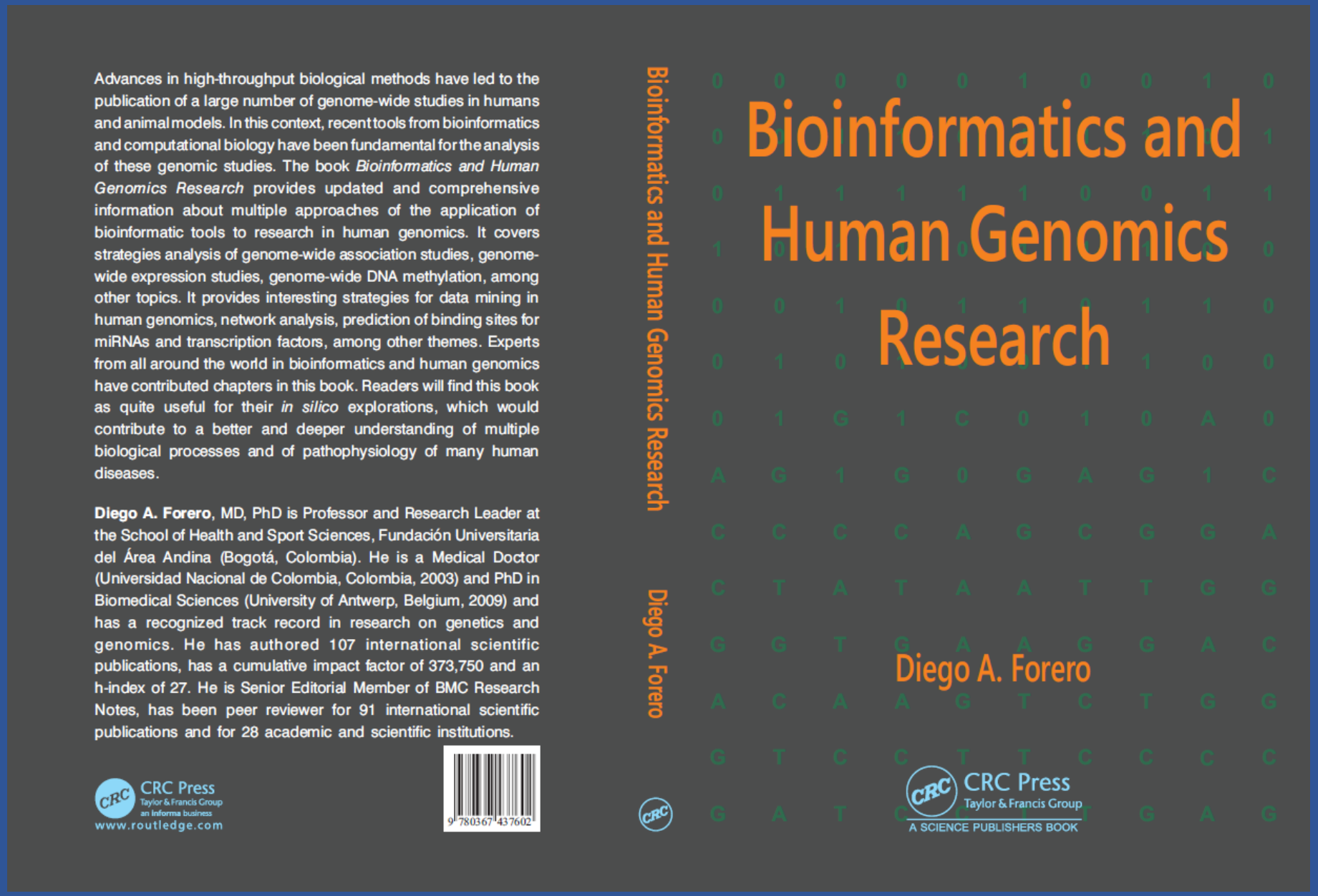

https://www.taylorfrancis.com/books/edit/10.1201/9781003005926/bioinformatics-human-genomics-research-diego-forero

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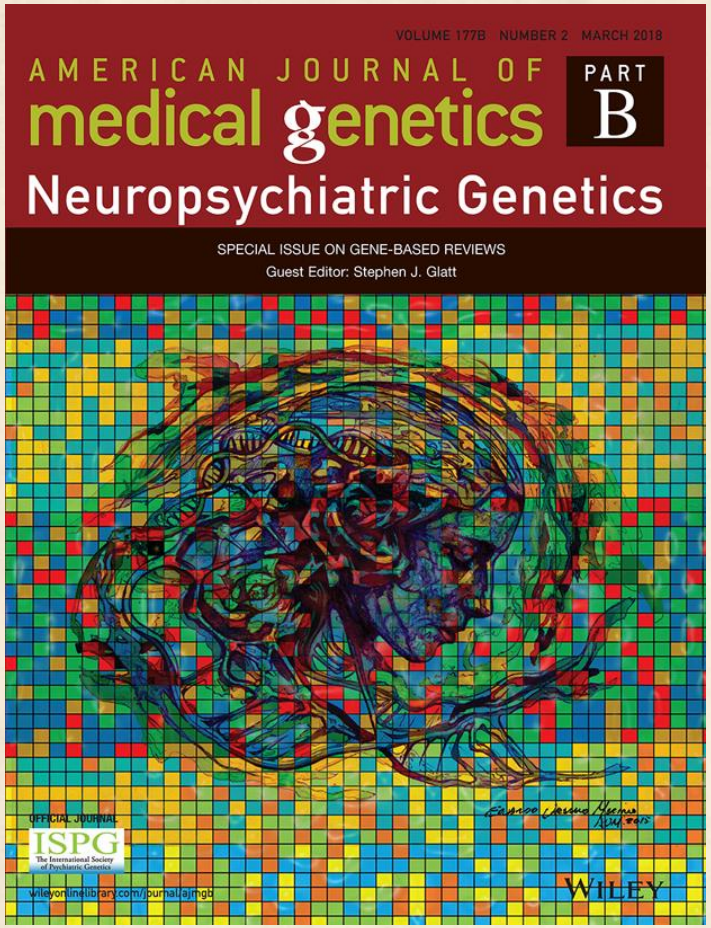

Diego A. Forero, MD, PhD

Gracias

dforero41@areandina.edu.co

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