# ESSGN

*European Social Science Genetics Network*

**Stephanie von Hinke and Titus Galama**

What do you see in this logo?

# ESSGN

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# First, some housekeeping

- **Monday (organized)**
  Birraria La Corte. Campo San Polo, 2168 at 19:30
  Fixed menu
- **Tuesday -- nothing organized (on your own)**
- **Wednesday (organized, [official] meeting dinner)**
  Hyatt Restaurant at Murano at 19:30.
  Private boat from San Servolo to Murano Island.
  4 course menu
- **Thursday**
  Self-organized aperitivo at the fish market next to Rialto Bridge. Venetian tapas in informal setting (request reimbursement from your University)
- **Friday -- nothing organized (on your own)**

# What you will learn in this presentation

- What ESSGN is / who we are
- What your training looks like / how it is structured
- Why social-science genetics is cool, important and what we can do now
- Basic recent history, GWAS and PGIs
- A few examples of gene-by-environment interplay studies (if we have time)

# Outline

- Introduction to ESSGN
- ESSGN structure, goals and projects
- Motivation
- Social-science genetics
  i. introduction
  ii. genetics primer
  iii. genome-wide association studies
  iv. polygenic indices
  v. gene-by-environment (GxE) interplay
- Concluding remarks

# Eight universities …

VU VRIJE UNIVERSITEIT AMSTERDAM

UNIVERSITÄT BIELEFELD

ERASMUS UNIVERSITEIT ROTTERDAM

ALMA MATER STUDIORUM UNIVERSITÀ DI BOLOGNA

UiO : University of Oslo

UPPSALA UNIVERSITET

University of BRISTOL

UNIVERSITY OF OXFORD

# … connecting many researchers (only leads shown)

| Project leaders | | | | |
|---|---|---|---|---|
| **Institute** | **Project leader** | | **Email address** | |
| VU | Titus Galama | Abdel Abdellaoui | t.j.galama@vu.nl | a.abdellaoui@amsterdamumc.nl |
| EUR | Hans van Kippersluis | Niels Rietveld | hvankippersluis@ese.eur.nl | nrietveld@ese.eur.nl |
| U of Bielefeld | Felix Tropf | Martin Diewald | fctropf@gmail.com | martin.diewald@uni-bielefeld.de |
| U of Bologna | Pietro Biroli | Nicola Barban | pietro.biroli@unibo.it | n.barban@unibo.it |
| U of Oslo | Eivind Ystrom | Alexandra Havdahl | eivind.ystrom@psykologi.uio.no | alexandra.havdahl@psykologi.uio.no |
| U of Uppsala | Rafael Ahlskog | Sven Oskarsson | rafael.ahlskog@statsvet.uu.se | Sven.Oskarsson@statsvet.uu.se |
| U of Bristol | Stephanie von Hinke | Paul Hufe | s.vonhinke@bristol.ac.uk | paul.hufe@bristol.ac.uk |
| U of Oxford | Melinda Mills | Augustine Kong | melinda.mills@sociology.ox.ac.uk | augustine.kong@bdi.ox.ac.uk |

# Seven non-academic partners

Government Office for Science

KONINKLIJKE NEDERLANDSE AKADEMIE VAN WETENSCHAPPEN

RAND EUROPE

The Health Foundation

prometeia

Centre international de Recherche sur le Cancer

Organisation mondiale de la Santé

CENTERDATA research institute

# … providing policy, health and other experiences (only leads shown)

| Associate Partners | | |
|---|---|---|
| **Institute** | **Name** | **Email address** |
| GO Science | Tom Wells | tom.wells@go-science.gov.uk |
| Prometeia | Michele Leoncelli | michele.leoncelli@prometeia.com |
| IARC | Isabelle Soerjomataram | soerjomatarami@iarc.who.int |
| RAND | Stijn Hoorens | hoorens@randeurope.org |
| Health Foundation | Toby Watt | toby.watt@health.org.uk |
| CentERdata | Marcel Das / Tom Emery | marcel.das@centerdata.nl |
| NIDI | Govert Bijwaard | bijwaard@nidi.nl |

# Thirteen DCs …

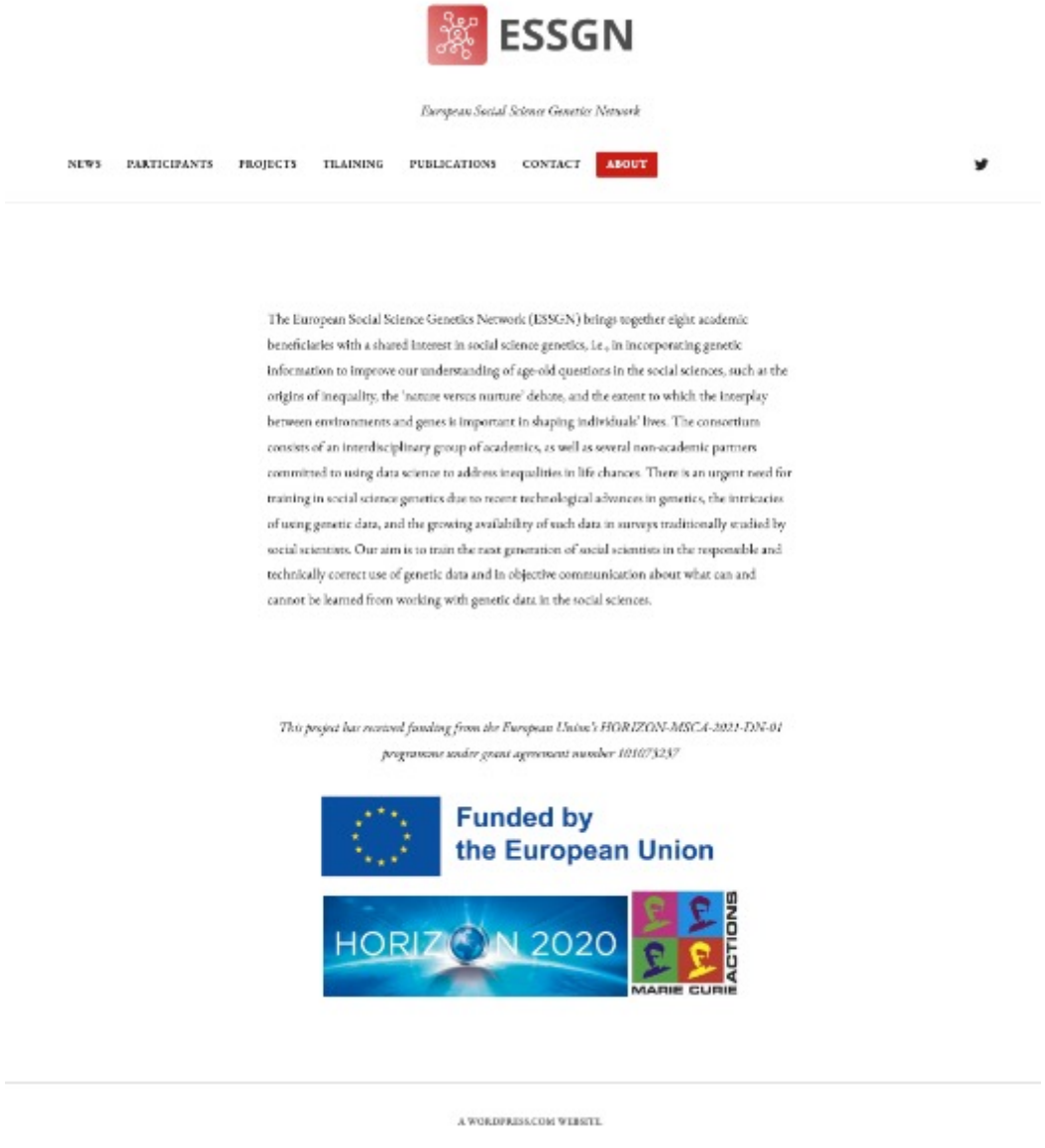
| Doctoral candidates | | | |
|---|---|---|---|
| **DCs** | **Name** | **E-mail address** | **Institute** |
| DC1 | Tim Wienand | tim-wienand@gmx.de | EUR |
| DC2 | Xinmiao Zhang | xinmiaozh@gmail.com | EUR |
| DC3 | Qiyuan Peng | pengqiyuan1128@gmail.com | U of Oslo |
| DC4 | tbd | | VU |
| DC5 | Sergio Ordonez-Beltran | sergio-daniel.ordonez-beltran@etu.univ-amu.fr | U of Bristol |
| DC6 | Nadia Harerimana | nadia.harerimana@uni-bielefeld.de | U of Bielefeld |
| DC7 | Lyydia Alajääskö | lyydia.alajaasko@gmail.com | VU |
| DC8 | Rossella de Sabbata | rosselladesabbata@gmail.com | U of Bristol |
| DC9 | Vincent Straub | vincejstraub@gmail.com; vincent.straub@seh.ox.ac.uk | U of Oxford |
| DC10 | Mar Talens Martin-Borregon | mar.talensmb@gmail.com | U of Bologna |
| DC11 | Tomeu Lopez-Nieto Veitch | tomeu.lnv@gmail.com | U of Bologna |
| DC12 | Ralph Porneso | ralphporneso@gmail.com | U of Oslo |
| DC13 | Asya Bülbül | asiabulbul@gmail.com | U of Uppsala |

# … and several affiliated DCs / postdocs

| Affiliated ESSGN PhDs / Postdocs | | | |
|---|---|---|---|
| **Institute** | **Name** | **Email address** | **Supervisor** |
| U of Bologna | Giorgia Mezzetti | | Pietro Biroli |
| U of Oxford | Robert Campbell | h.campbell.robert@gmail.com | Melinda Mills |
| U of Bielefeld | Yixuan Liu | yixuan.liu@uni-bielefeld.de | Martin Diewald |
| U of Oslo | Meseret Mamo | | Alexandra Havdahl |
| U of Oslo | Stian Valand | | Alexandra Havdahl |
| U of Oslo | tbd | | Alexandra Havdahl |
| U of Uppsala | Qinya Feng | qinya.feng@statsvet.uu.se | Sven Oskarsson/Rafael Ahlskog |
| U of Uppsala | Oskar Pettersson | oskar.pettersson@statsvet.uu.se | Sven Oskarsson/Rafael Ahlskog |
| EUR | Tilbe Atav | | Niels Rietveld |
| U of Oslo | Qi Qin | qi.qin@psykologi.uio.no | Eivind Ystrom |
| U of Oslo | Joakim Coleman Ebeltoft | j.c.ebeltoft@psykologi.uio.no | Eivind Ystrom |
| U of Oslo | to be hired | | Eivind Ystrom |
| VU | David van den Berg | | Abdel Abdellaoui |
| VU | Marina Aguilar Palma | m.aguiar.palma@vu.nl | Titus Galama |
| VU | Nursena Aksunger | n.aksunger@vu.nl | Titus Galama |

# Website is up, but needs more content (Rafael)

## www.essgn.org



# Tabs for news, participants etc. and X (Twitter)

ESSGN

*European Social Science Genetics Network*

NEWS PARTICIPANTS PROJECTS TRAINING PUBLICATIONS CONTACT ABOUT

The European Social Science Genetics Network (ESSGN) brings together eight academic beneficiaries with a shared interest in social science genetics, i.e., in incorporating genetic information to improve our understanding of age-old questions in the social sciences, such as the origins of inequality, the 'nature versus nurture' debate, and the extent to which the interplay between environments and genes is important in shaping individuals' lives. The consortium consists of an interdisciplinary group of academics, as well as several non-academic partners committed to using data science to address inequalities in life chances. There is an urgent need for

# Horizon Europe

THE NEXT EU RESEARCH & INNOVATION PROGRAMME (2021–2027)

#HorizonEU

Research and Innovation

MARIE CURIE ACTIONS

Funded by the European Union

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# Management

## Kim Zandvliet

## Stephanie von Hinke and Titus Galama

# Additional support for DCs from other researchers / postdocs

| Participating organisation | Country | Beneficiary/AP | No. of PhDs | PI/Co-Is |
|---|---|---|---|---|
| **VU University Amsterdam** | NL | Beneficiary | 2 PhDs | Titus Galama<br>Andries Marees<br>Karin Verweij<br>Abdel Abdellaoui<br>Aysu Okbay |
| **Erasmus University Rotterdam** | NL | Beneficiary | 2 PhDs | Hans van Kippersluis<br>Niels Rietveld<br>Janine Felix<br>Dilnoza Muslimova<br>Tilbe Atav |
| **University of Bielefeld** | DE | Beneficiary | 1 PhD | Felix Tropf<br>Martin Diewald |
| **University of Bologna** | IT | Beneficiary | 2 PhDs | Nicola Barban<br>Pietro Biroli |
| **University of Oslo** | NO | Beneficiary | 2 PhDs | Alexandra Havdahl<br>Eivind Ystrom |
| **University of Uppsala** | SE | Beneficiary | 1 PhD | Sven Oskarsson<br>Rafael Ahlskog |
| **University of Bristol** | UK | Associated Partner | 2 PhDs | Stephanie von Hinke<br>Paul Hufe<br>Emil Sorensen<br>Nicolai Vitt<br>Neil Davies |
| **University of Oxford** | UK | Associated Partner | 1 PhD | Melinda Mills<br>Augustine Kong<br>Evelina Akimova<br>Xuejie Ding |

# Overarching question and research objectives

**To what extent do inequalities in life chances arise from genetic variation, environmental factors, and their interplay, and what can we do about it?**

**Research Objective 1:**

***To what extent do nature and nurture contribute to equality of opportunity and intergenerational mobility?***

**DC 1-3**

**Research Objective 2:**

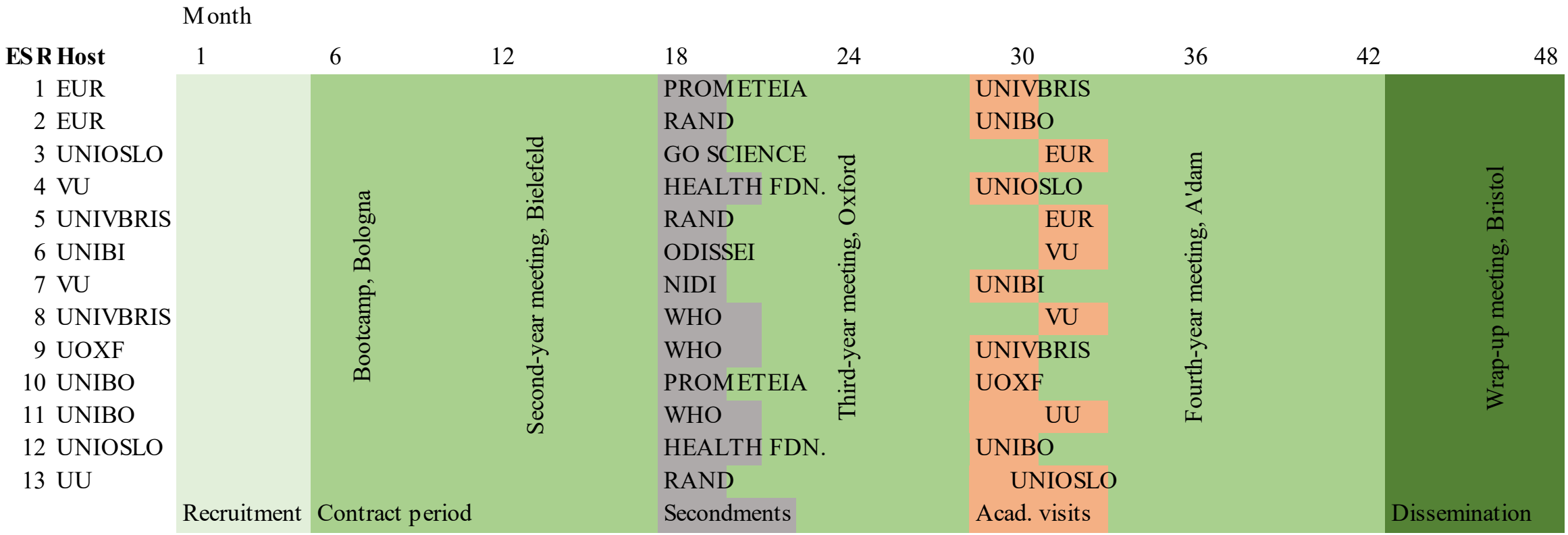
***How important is the nature-nurture interplay in causally shaping life chances?***

**DC 4-13**

| 13 doctoral projects | 13 research questions | 13 approaches | |
|---|---|---|---|
| **To what extent do nature and nurture contribute to equality of opportunity and inter-generational mobility?** | | | |
| Heritability and fairness | To what extent does society perceive genetic inequalities as fair and socially acceptable? | Use genetic & socioeconomic data to separate circumstances from effort. Survey citizens, and test changes in perceptions regarding equality of opportunity based on new data. | **DC1: Tim Wienand (EUR)** |
| The origins of intergenerational persistence | Why do wealthy parents have wealthy children? | Use data on multiple generations to assess extent to which intergenerational persistence of, e.g., education and wealth, have environmental and genetic origins. | **DC2: Zinmiau Zhang (EUR)** |
| Causal intergenerational persistence | Can strong intergenerational transmission of education be attributed to genetics or SES? | Use genetic data from parents and their children, to quantify the direct and indirect genetic effects of mothers and fathers on offspring educational achievement. | **DC3: Qiyuan Peng (Oslo)** |
| **How important is the nature-nurture interplay in causally shaping life chances?** | | | |
| Causal G×E interplay for SES and health | What explains the large disparities in health between SES groups? | Use genetic, socioeconomic, & administrative microdata of the entire Dutch population on health and SES to estimate causal genetic and environmental effects in G×E interplay. | **DC4: tbd (VU)** |
| Dynamic complementarities in human capital | Do students with low genetic propensity for education benefit more from teacher quality? | Match data on school quality to genotyped parent-child trios in UK and Norwegian datasets to explore teacher effects on life chances by the genetic propensity of students | **DC5: Sergio Ordonez-Beltran (Bristol)** |
| Regional heterogeneity in genetic effects | What explains the missing heritability puzzle? | Genetic discovery studies do not explain as much genetic variation as twin studies. Explore whether specific measures of regional environments in the UK explain the gap. | **DC6: Nadia Harerimana (Bielefeld)** |
| Genetic variation as a driver of 'brain drain' | Can selective migration based on socio-economic potential explain growing inequality? | Explore whether selective migration (brain drain / gain) based on individual's genetic propensity to education contributes to growing socioeconomic inequalities in the UK. | **DC7: Lyydia Alajääskö (VU)** |

| | | | |
|---|---|---|---|
| The role of genetics in the developmental origins | Can genetic predisposition moderate detrimental effects of early life circumstances in older age? | Explore long-term effects of early life circumstances, such as prenatal pollution exposure, on socioeconomic and health outcomes in later life and how this varies by genetics. | **DC8: Rossella de Sabbata (Bristol)** |
| The role of genetics in the transition to early adulthood | Can genetic predisposition moderate detrimental effects of early life circumstances in adolescence? | Explore intermediate-term effects of family and socioeconomic circumstance and genetics on externalizing behaviour and socioeconomic outcomes in adolescence. | **DC9: Vincent Straub (Oxford)** |
| Epigenetic aging and G×E | Do family formation decisions, and socioeconomic shocks (such as job loss) affect epigenetic ageing? | Combine epigenetic markers from surveys with polygenic scores derived from genotyped data to investigate how G×E interplay affects epigenetic ("gene-expression") ageing. | **DC10: Mar Talens Martin-Borregon (Bologna)** |
| Estimation of treatment effects | Can genetic data provide a biological foundation for observed heterogeneity in individuals' choices? | Leverage genetic data 1) in structural models of human capital formation to obtain insight into the deep parameters of the model and 2) to model selection into treatment. | **DC11: Tomeu Lopez-Nieto Veitch (Bologna)** |
| Heterogeneity in social mobility | To what extent are both direct and indirect genetic effects fixed or heterogenous across environments? | Combine genotyped trios and pedigree data to estimate population average direct and parental indirect genetic effects and how they vary by environment. | **DC12: Ralph Porneso (Oslo)** |
| G×E in political and prosocial attitudes and behaviour | How are political and prosocial attitudes and behaviour shaped by genetic and environmental factors? | Investigate how political and prosocial attitudes and behaviour are shaped by the complex interplay between genetic and environmental factors. | **DC13: Asya Bülbül (Uppsala)** |

# Exchanges with non-academic partners, meetings and annual conferences



# Training

1. **Local institutional networks**
   - **Main supervisor(s)**
   - **Mentored by senior post-doc / junior faculty if possible (DT to set up)**

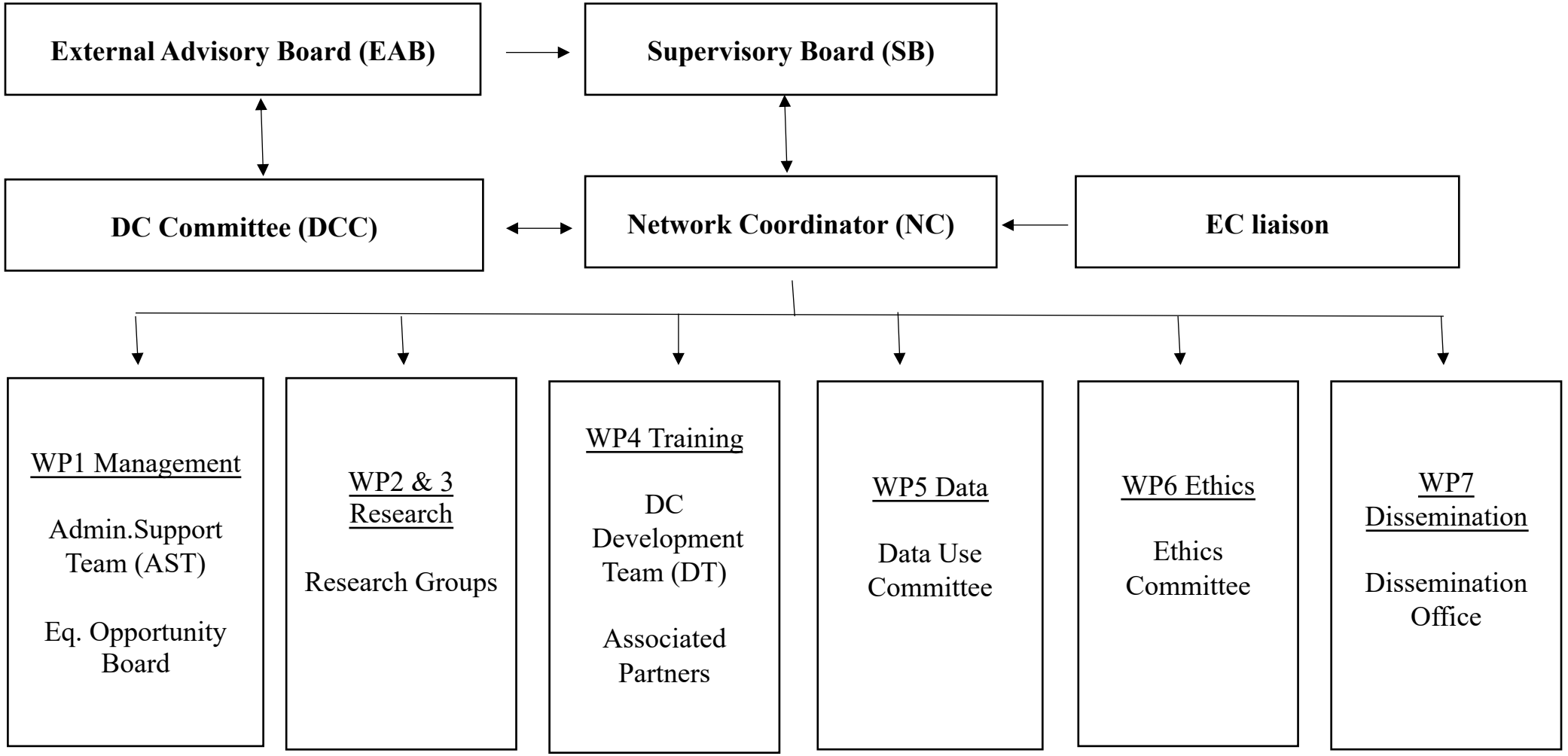
2. **Cross institutional networks**
   - **Co-supervision by at least 1 other researcher from a *different* University within the Consortium**
   - **External mentor (DT to set up)**

3. **Whole network teaching**
   - **All supervisors will contribute**
   - **Material shared across all Universities**

# Co-supervision by at least 1 other researcher from a *different* University within the Consortium

| | Co-supervision by supervisor at: |
|---|---|
| DC1: Tim Wienand (EUR) | University of Bristol |
| DC2: Zinmiau Zhang (EUR) | University of Bologna |
| DC3: Qiyuan Peng (Oslo) | Erasmus University Rotterdam |
| DC4: tbc (VU) | University of Oslo |
| DC5: Sergio Ordonez-Beltran (Bristol) | Erasmus University Rotterdam |
| DC6: Nadia Harerimana (Bielefeld) | VU University Amsterdam |
| DC7: Lyydia Alajääskö (VU) | University of Bielefeld |
| DC8: Rossella de Sabbata (Bristol) | VU University Amsterdam |
| DC9: Vincent Straub (Oxford) | University of Bristol |
| DC10: Mar Talens Martin-Borregon (Bologna) | University of Oxford |
| DC11: Tomeu Lopez-Nieto Veitch (Bologna) | University of Uppsala |
| DC12: Ralph Porneso (Oslo) | University of Bologna |
| DC13: Asya Bülbül (Uppsala) | University of Oslo |

# Structure




External Advisory Board: Paige Harden, Kathleen Mullen Harris, Dan Benjamin, Michelle Meyer, TBD non academic

# Be aware, ESSGN DCs, you have meetings on Wednesday

| Committee | Time |
| --- | --- |
| DC Committee | 9.00-9.30 |
| Supervisory Board | 9.30-11.00 |
| **Parallel Session** | |
| DC Development Team | 11.15-12.15 |
| Data Use Committee | 11.15-12.15 |
| Ethics Committee | 11.15-12.15 |

# DC committee needs to elect a chair (anybody?)

| Committee | Time |
| --- | --- |
| DC Committee | 9.00-9.30 |
| Supervisory Board | 9.30-11.00 |

| Parallel Session | |
| --- | --- |
| DC Development Team | 11.15-12.15 |
| Data Use Committee | 11.15-12.15 |
| Ethics Committee | 11.15-12.15 |

# Supervisory Board (SB)

| Supervisory Board | | |
|---|---|---|
| **Institute** | **Name** | **Email address** |
| VU | Titus Galama | t.j.galama@vu.nl |
| EUR | Hans van Kippersluis | hvankippersluis@ese.eur.nl |
| U of Bielefeld | Felix Tropf | fctropf@gmail.com |
| U of Bologna | Pietro Biroli | pietro.biroli@unibo.it |
| U of Oslo | Eivind Ystrom (Alexandra) | eivind.ystrom@psykologi.uio.no |
| U of Uppsala | Rafael Ahlskog | rafael.ahlskog@statsvet.uu.se |
| U of Bristol | Stephanie von Hinke | s.vonhinke@bristol.ac.uk |
| U of Oxford | Melinda Mills | melinda.mills@sociology.ox.ac.uk |
| EUR | Xinmiao Zhang (DC) | xinmiaozh@gmail.com |
| U of Oslo | Ralph Porneso (DC) | ralphporneso@gmail.com |

- **Main decision-making body of ESSGN**
- **Composed of one representative from each beneficiary and two DC representatives**
- **Will supervise network activities and ensure adherence to the consortium agreement**

# External Advisory Board (EAB)

| External Advisory Board | | |
|---|---|---|
| **Affiliation** | **Name** | **Email address** |
| University of Texas | Paige Harden | harden@utexas.edu |
| Geisinger | Michelle Meyer | mmeyer@geisinger.edu |
| UCLA | Daniel Benjamin | daniel.benjamin@gmail.com; daniel.benjamin@anderson.ucla.edu |
| UNC | Kathleen Mullen | kathie_harris@unc.edu |
| | Tbd – non academic | |

- **Provides an independent, authoritative assessment of the progress of ESSGN**
- **External monitor**
- **Provide strategic advice to stakeholders**

# DC Committee (DCC)

| Doctoral candidates | | | |
|---|---|---|---|
| **DCs** | **Name** | **E-mail address** | **Institute** |
| DC1 | Tim Wienand | tim-wienand@gmx.de | EUR |
| DC2 | Xinmiao Zhang | xinmiaozh@gmail.com | EUR |
| DC3 | Qiyuan Peng | pengqiyuan1128@gmail.com | U of Oslo |
| DC4 | tbd | | VU |
| DC5 | Sergio Ordonez-Beltran | sergio-daniel.ordonez-beltran@etu.univ-amu.fr | U of Bristol |
| DC6 | Nadia Harerimana | nadia.harerimana@mssm.edu | U of Bielefeld |
| DC7 | Lyydia Alajääskö | lyydia.alajaasko@gmail.com | VU |
| DC8 | Rossella de Sabbata | rosselladesabbata@gmail.com | U of Bristol |
| DC9 | Vincent Straub | vincejstraub@gmail.com | U of Oxford |
| DC10 | Mar Talens Martin-Borregon | mar.talensmb@gmail.com | U of Bologna |
| DC11 | Tomeu Lopez-Nieto Veitch | tomeu.lnv@gmail.com | U of Bologna |
| DC12 | Ralph Porneso | ralphporneso@gmail.com | U of Oslo |
| DC13 | Asya Bülbül | asiabulbul@gmail.com | U of Uppsala |

- **The DC chair will be elected by you (on Weds)**
- **Chair will rotate annually**
- **Report to DC Development Team**
- **Meet in person at network meetings (more frequently if required)**

# Administrative Support Team

| Administrative Support Team | | |
|---|---|---|
| **Affiliation** | **Name** | **Email address** |
| VU | Project manager - Kim Zandvliet | k.zandvliet-oerlemans@vu.nl |
| VU | Project control - Imane Batou | i.batou@vu.nl |
| | Legal | |
| VU | Research Office (Data steward, grant advisor) | Researchoffice.sbe@vu.nl |

- **The team will support the coordinators in the day-to-day management and communication**
- **Liaise with funding authority concerning reporting, financial, legal and risk management**

# Equal Opportunity Board

| Equal Opportunity Board | | |
|---|---|---|
| **Affiliation** | **Name** | **Email address** |
| VU | Titus Galama | t.j.galama@vu.nl |
| U of Bristol | Stephanie von Hinke | s.vonhinke@bristol.ac.uk |
| VU | Kim Zandvliet | k.zandvliet-oerlemans@vu.nl |

- **In case of any grievances regarding equal opportunities**
- **Promoting gender equality on committees**

# DC Development Team (DT)

| DC Development Team | | |
|---|---|---|
| **Affiliation** | **Name** | **Email address** |
| EUR | Supervisor 1 – Hans van Kippersluis | hvankippersluis@ese.eur.nl |
| VU | Supervisor 2 – Abdel Abdellaoui | a.abdellaoui@amsterdamumc.nl |
| U of Bristol | Nicolai Vitt (Postdoc) | nicolai.vitt@bristol.ac.uk |
| EUR | Dilnoza Muslimova (Postdoc) | muslimova@ese.eur.nl |
| U of Uppsala | Asya Bülbül (DC) (rotate annually) | asiabulbul@gmail.com |
| U of Oslo | Qiyuan Peng (DC) (rotate annually) | pengqiyuan1128@gmail.com |

- **Assess progress in research and career development by reviewing each DC's Personal Career Development Plan**
- **Organise mentoring to provide advice to DCs and supervisors**
- **Coordinate task-related, generic and transferable skills at annual workshops**

# Data Use Committee

| Data Use Committee | | |
|---|---|---|
| **Affiliation** | **Name** | **Email address** |
| UBIEL | WP 3 Lead Martin Diewald | martin.diewald@uni-bielefeld.de |
| U of Bologna | Nicola Barban | n.barban@unibo.it |
| U of Oxford | Vincent Straub (DC) | vincent.straub@seh.ox.ac.uk |
| VU | Lyydia Alajääskö (DC) | lyydia.alajaasko@gmail.com |
| U of Bristol | Sergio Ordonez-Beltran (DC) | sergio-daniel.ordonez-beltran@etu.univ-amu.fr |

- **Ensure setting up necessary infrastructure**
- **Formulate Data Management Plan**
- **Each University remains responsible for liaising with own IT departments regarding security protocols and safe data storage**

# Ethics Committee

| Ethics Committee | | |
|---|---|---|
| **Affiliation** | **Name** | **Email address** |
| VU | Aysu Okbay | aysuokbay@gmail.com |
| EUR | Niels Rietveld | nrietveld@ese.eur.nl |
| U of Oslo | Qiyuan Peng (DC) | pengqiyuan1128@gmail.com |
| EUR | Tim Wienand (DC) | tim-wienand@gmx.de |
| U of Bologna | Tomeu Lopez-Nieto Veitch (DC) | tomeu.lnv@gmail.com |

- **Advise on ethical matters, in particular to those relating to the use of genetic data**
- **Meet in person at joint meetings (more if necessary)**

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Questions?

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# Health disparities between SES groups are large …

- Substantial inequalities in health exist across a multitude of indicators of socioeconomic status (SES)
  i. education, income, wealth, minority status

- … and across multiple indicators of health
  i. subjective measures of health
  ii. objective measures: onset of chronic diseases, disability and mortality (e.g., Adler et al. 1994, Marmot et al. 1991, Smith 1999)

# … and they start very early in life

- Substantial inequalities in health exist across a multitude of indicators of socioeconomic status (SES)
  i. education, income, wealth, minority status

- … and across multiple indicators of health
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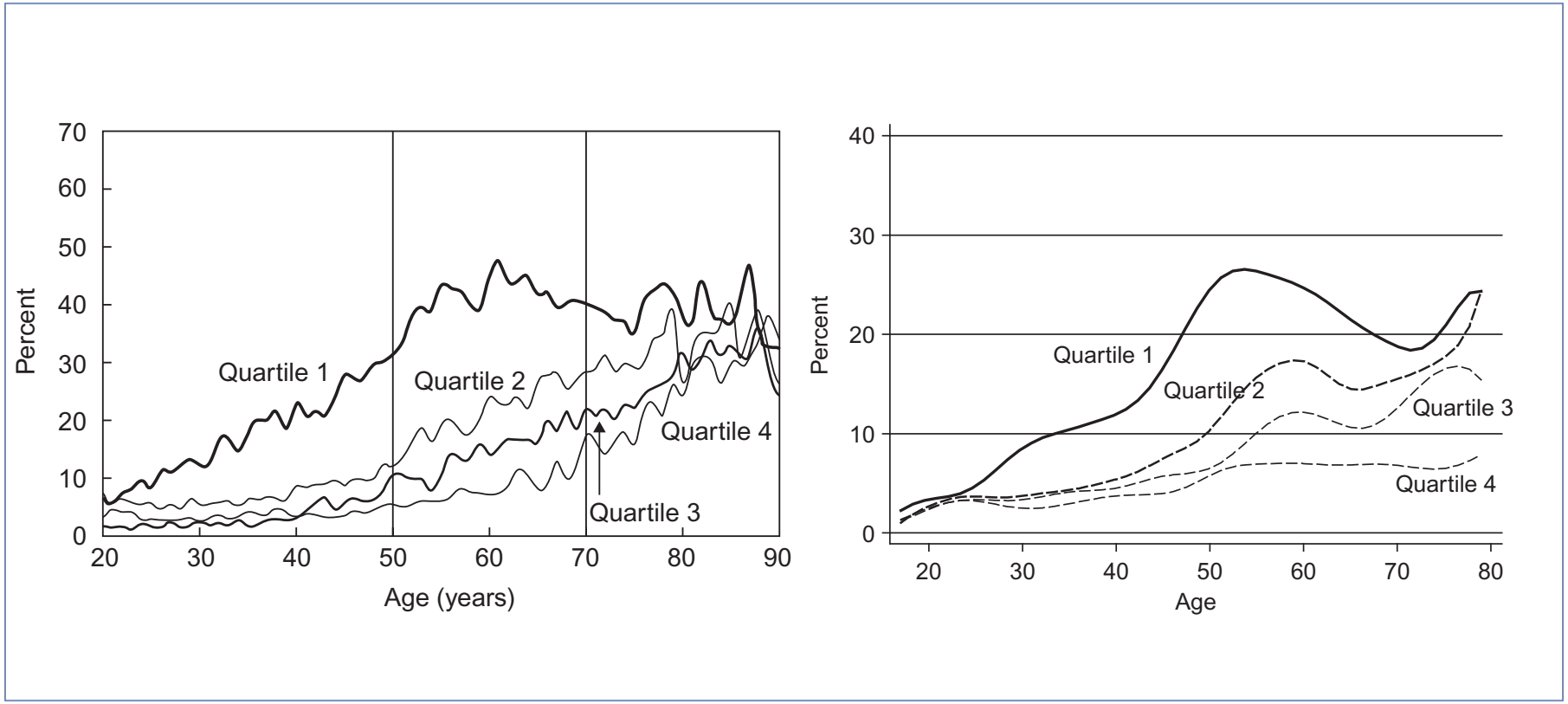
**How early?**

# … and they start very early in life

- Substantial inequalities in health exist across a multitude of indicators of socioeconomic status (SES)
  i. education, income, wealth, minority status

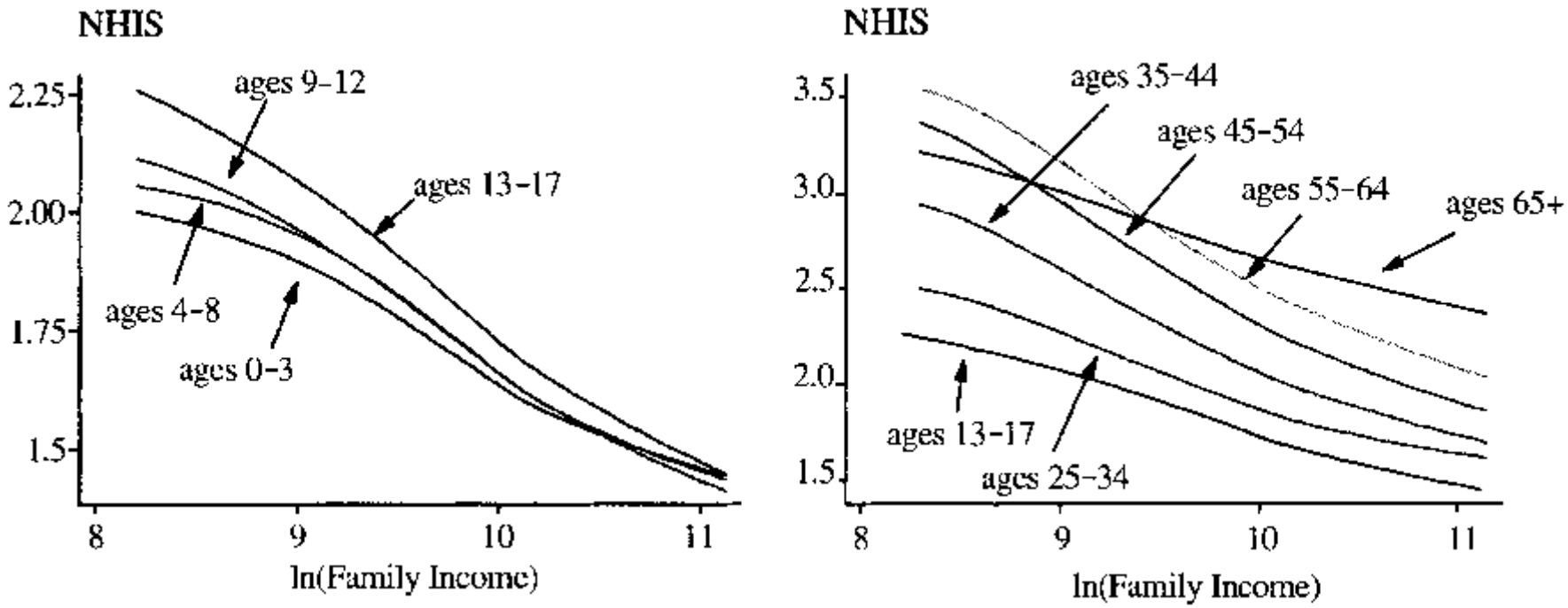
- … and across multiple indicators of health
  i. subjective measures of health
  ii. objective measures: onset of chronic diseases, disability and mortality (e.g., Adler et al. 1994, Marmot et al. 1991, Smith 1999)
- **Differences in health start early, become more pronounced as children age, and widen until about age 60 when differences in health appear to narrow (Case et al. 2002)**

# Percentage reporting fair/poor health by specific household-income quartile




Percentage Reporting Fair or Poor Health (bottom two categories of Self-Reported Health) by Age-Specific Household Income Quartiles. Left: US National Health Interview Surveys, 1991--1996, taken from Smith (2004); Right: Dutch CBS Health Interview Surveys, 1983—2000, taken from Galama & Van Kippersluis (2013), Health and Inequality: Research on Economic Inequality, 21, p.263

# They start very early in life




Self-reported health status (1=excellent, 5=poor) for children (LHS) and adults (RHS) from the National Health Interview Survey. College-age adults (ages 18-24) not included due to concerns about representativeness of this sample, and because it is unclear whether these respondents report their current incomes or that of the families in which they were raised. Figure taken from Case, Lubotsky & Paxson (2002).

# This is true also for human capital (cog skills)

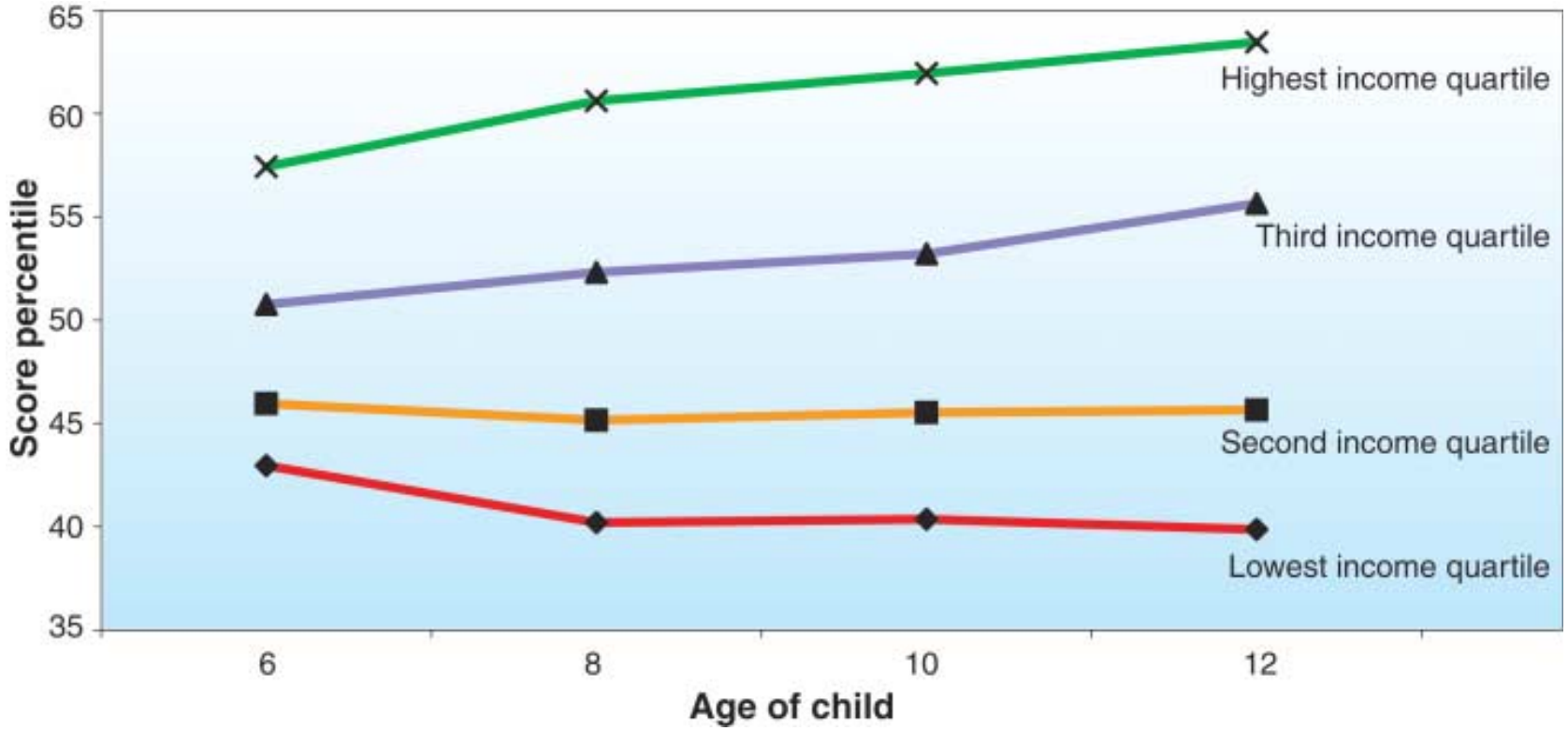



**Fig. 1.** Average percentile rank on Peabody Individual Achievement Test–Math score by age and income quartile. Income quartiles are computed from average family income between the ages of 6 and 10. Adapted from (*3*) with permission from MIT Press.

Heckman, J. J. (2006). Science, 312(5782), 1900-1902.
Heckman, J. J. (2007). Proceedings of the national Academy of Sciences, 104(33), 13250-13255.

# Relative importance of determinants not known


**What do you think are the most important factors?**

# Relative importance of determinants not known

- **Some claim**
  - **40% of early deaths are due to behavior**
  - **30% are due to genetic predispositions**
  - **15% are due to social circumstances**
  - **10% are due to shortfalls in medical care, and**
  - **5% are due to environmental exposures (McGinnis et al. 2002)**
- **These domains, however, interact, suggesting this simple division is not as clear cut**
  i. **genes may predispose individuals to certain unhealthy behaviors and health conditions**
  ii. **but extent to which genes are expressed depends on environmental exposures (Gluckman & Hanson 2006, Rutter 2006)**
  iii. **fetal environment can become biologically embedded in the body (Gluckman & Hanson 2006)**
- **There is a need to disentangle biological pathways vs. behavioral responses (Heckman 2012, Conti 2013)**

McGinnis, et al. (2002) [cited in Heckman (2012)]

# Eighty-five percent of early deaths due to

**Behavior**

**Socioeconomic circumstances**

**Genetics**

McGinnis, et al. (2002) [cited in Heckman (2012)]

## Nature

## Nurture

## Family background and behavior

# Outline

- Introduction to ESSGN
- ESSGN structure, goals and projects
- Motivation
- Social-science genetics
    i. introduction
    ii. genetics primer
    iii. genome-wide association studies
    iv. polygenic indices
    v. gene-by-environment (GxE) interplay
- Concluding remarks

# Eighty-five percent of early deaths due to

**Behavior**

**Socioeconomic circumstances**

**Genetics**

McGinnis, et al. (2002) [cited in Heckman (2012)]

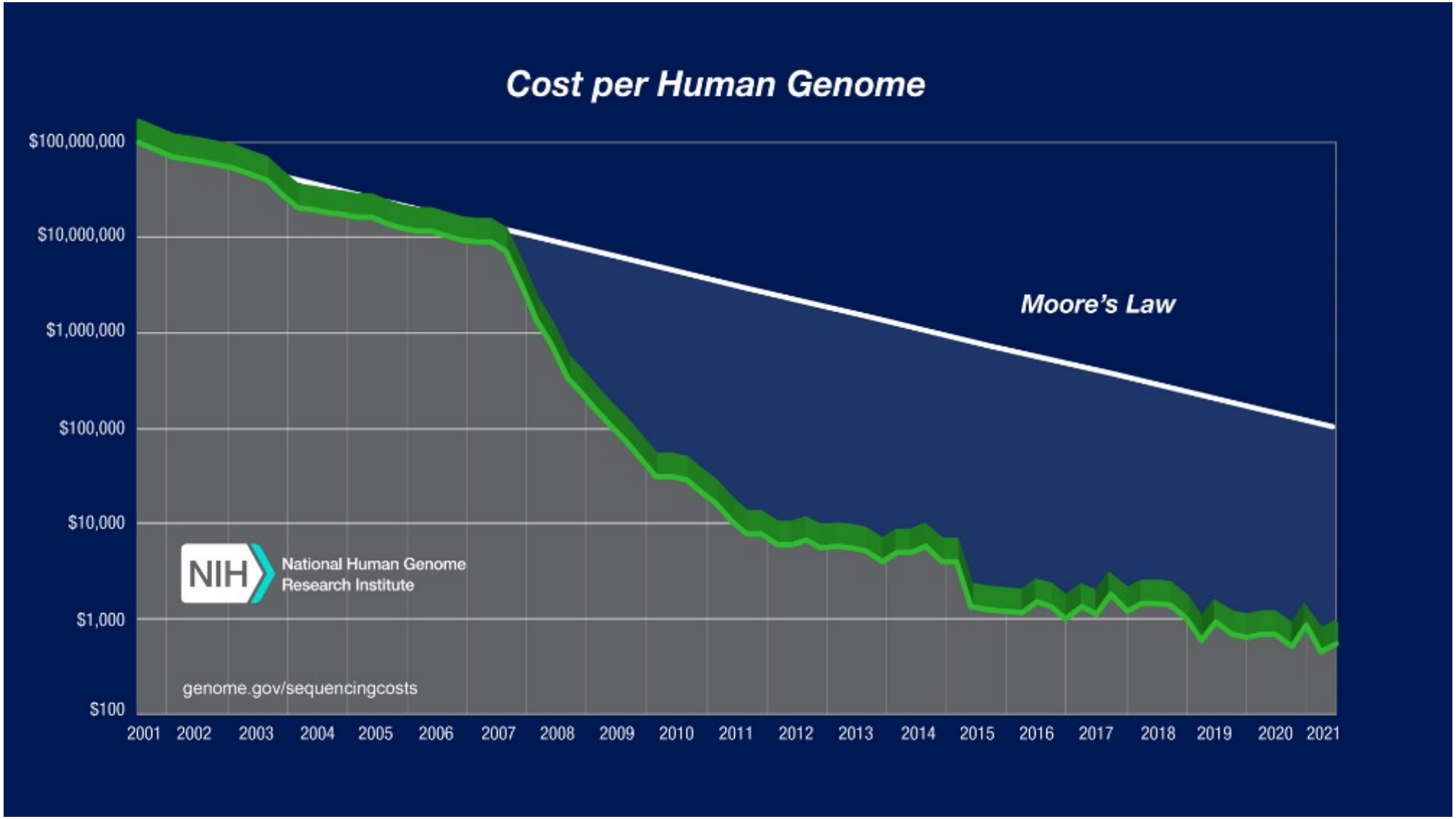
# What is social-science genetics?

- **New field at the intersection of the social-sciences and genetics that seeks to:**
  i. **uncover genetic variants related to social, economic and health traits**
  ii. **use the resulting findings to improve our understanding of socio-economic and health outcomes, choices and behaviors**
- **Examples of social/socio-economic traits and outcomes:**
  i. **economic preferences (e.g., risk, time)**
  ii. **health and human capital (e.g., obesity, education, cognition, subjective wellbeing, smoking, drinking, mental health, ADHD)**
  iii. **income, social deprivation, education**
- **Interdisciplinary field**
- **Europe has significant strengths in this area → ESSGN**

# Why now?

**Press conference, June 26th, 2000**
**Completion of the first “rough draft” of the human genome**

# Costs rapidly falling

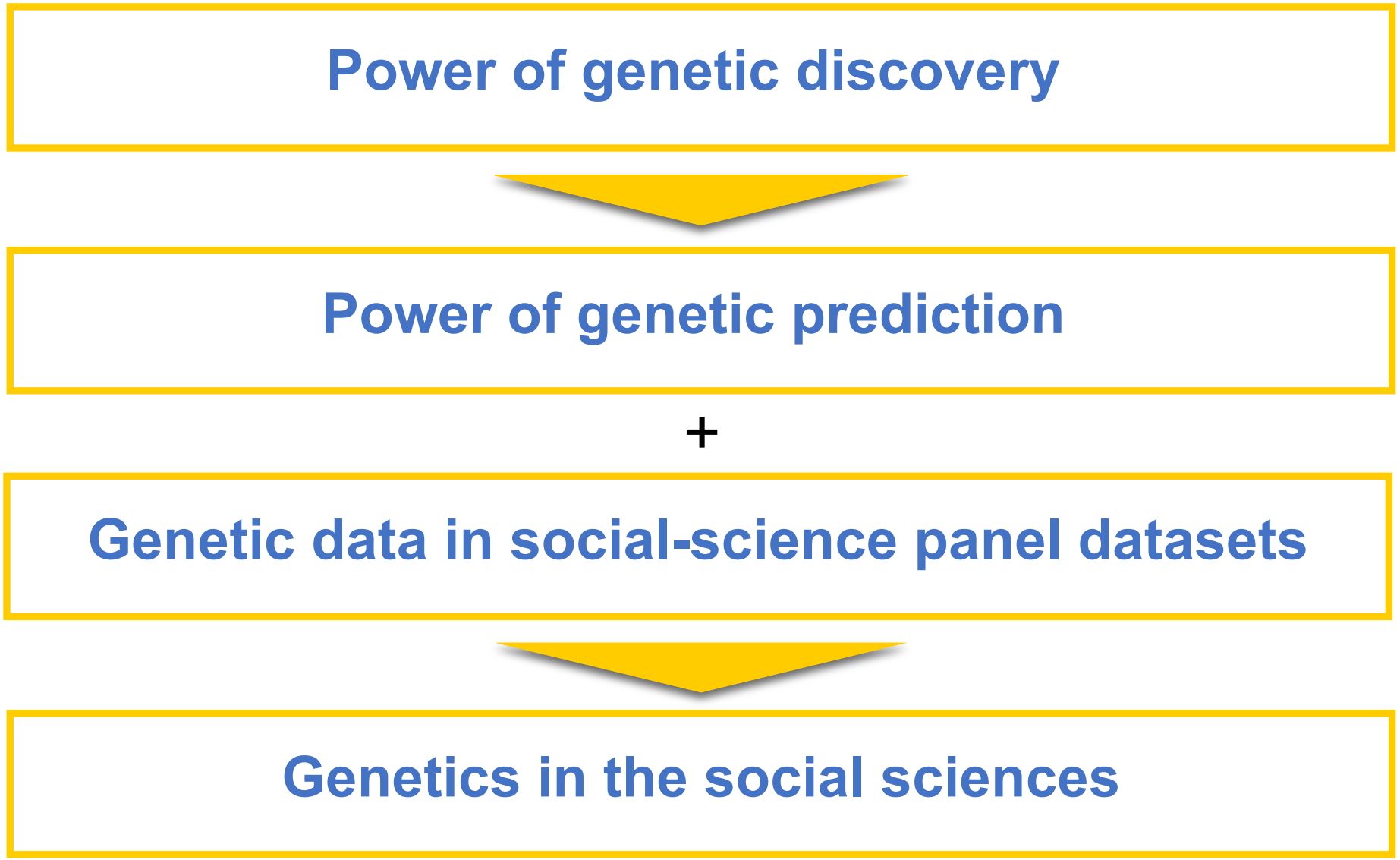


# Genetic data is both valuable and cheap

- **Conditional on the genotypes of the parents, the genotype of the offspring is the result of a perfectly randomized lottery draw**
  i. **natural experiment**
  ii. **genotype remains (almost entirely) constant throughout life and affects a broad range of phenotypes**
- **Nowadays, it is possible to collect high-accuracy measures of an individual's genome at reasonable cost**
  i. **sequencing (all ~3 billion genetic variants) ~ 600$ p.p.**
  ii. **common genetic variants (~2 million SNPs) ~ 50$ p.p.**
  iii. **customized sub-sets of common genetic variants p.p. (e.g. metabo-chip ~200,000 SNPs) ~ 20$ p.p.**
- **Rapid decrease in genotyping costs continues**

Courtesy Philipp Koellinger

# Revolution in genetic discovery and prediction



# Large panel datasets have released genetic data

# ... and, very large ones currently in the field

# Why study genetics?

- Human behavior and achievement are heritable
- DNA is special
  i. immutable
  ii. determined at conception (it comes before everything else)
- Genetic discoveries can provide clues to causal pathways, biology, and guide interventions
- There is a need to integrate behaviors, socioeconomic environments / conditions and biology to understand human capital and health formation and disparities therein (Heckman 2012, Conti 2013)

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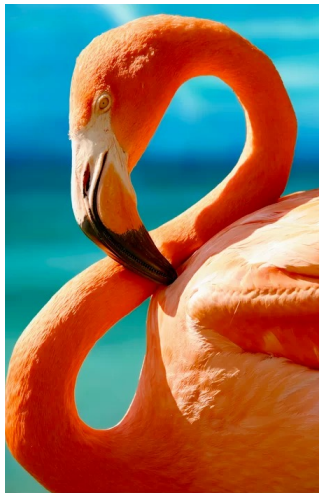
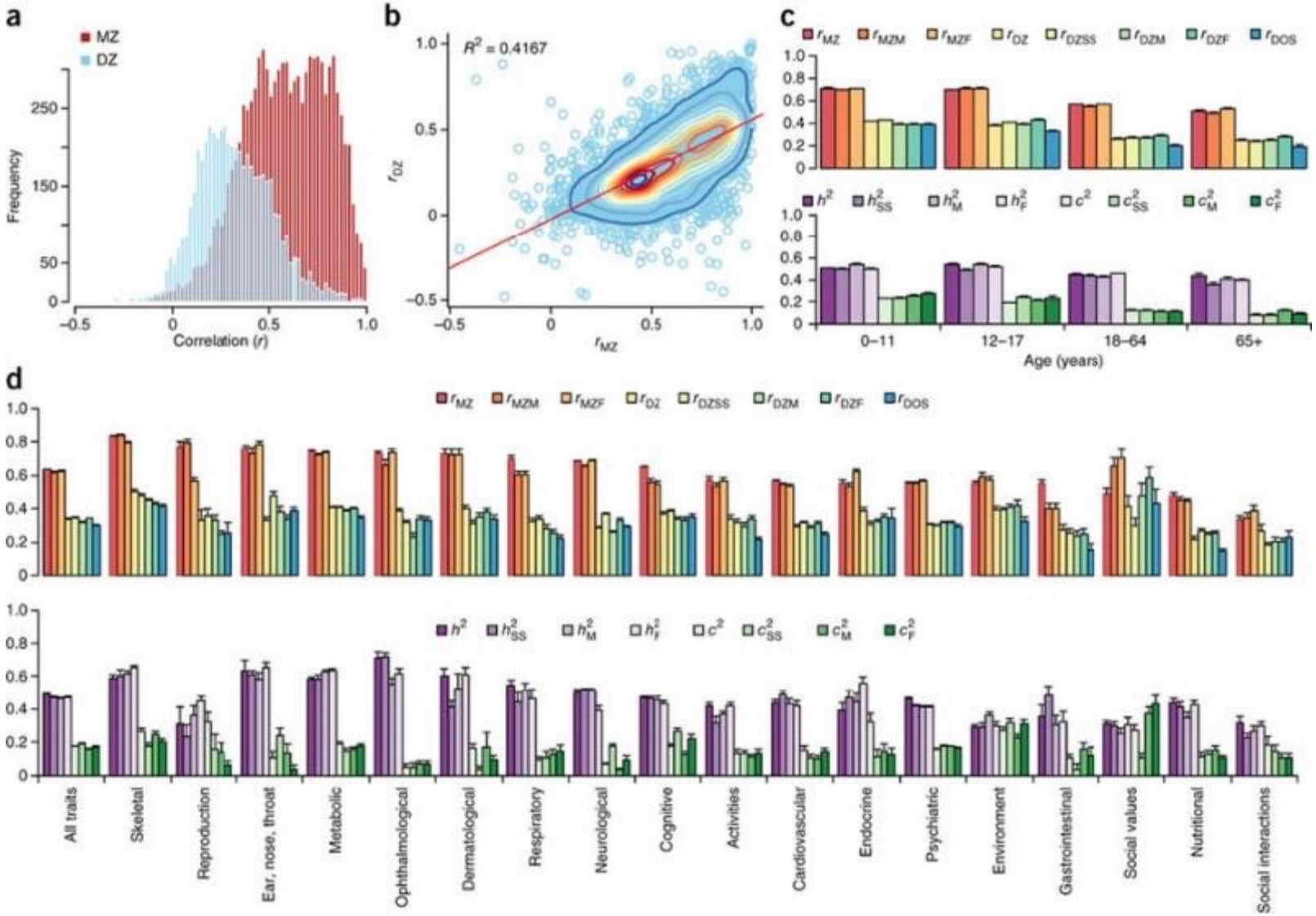
# Heritability

- **Heritability: the proportion of observed differences in a trait among individuals of a population that is due to genetic differences among these individuals**
  - **i. does not imply determinism or absence of choice**
  - **ii. puts no upper bound on the potential effect of the environment, even if $h^2$=100%**
  - **iii. not a natural constant**
  - **iv. differences across time and environments**



Courtesy Philipp Koellinger

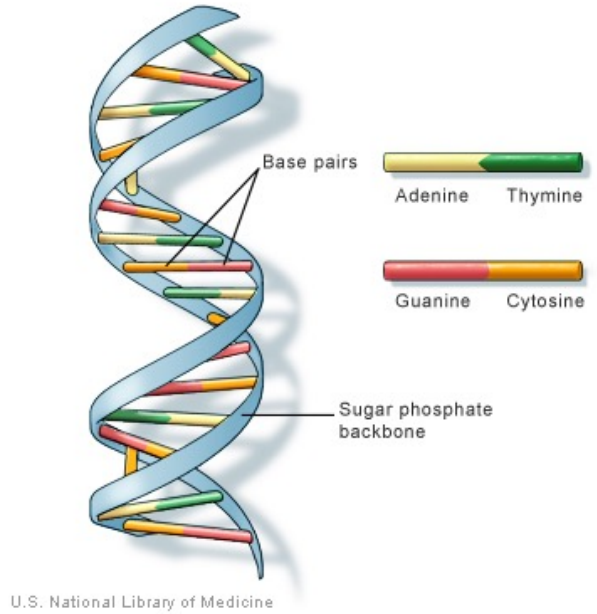
# Virtually all human traits are heritable




Polderman et al. (2015), Nature Genetics

# Genetics for social scientists

- **Four nucleotides are building blocks of DNA**
  i. **A (adenine), C (cytosine), G (guanine), T (thymine)**
- **Human genome ~3.1 billion pairs (one from mother, one from father) of nucleotides on 23 chromosomes**
- **Unrelated humans have >99% of their genomes in common**
- **A locus at which nucleotides vary is called a Single Nucleotide Polymorphism (SNP)**




Courtesy Pietro Biroli

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# Candidate gene studies (theoretical testing)

## Most Reported Genetic Associations With General Intelligence Are Probably False Positives

Christopher F. Chabris[1], Benjamin M. Hebert[2], Daniel J. Benjamin[3], Jonathan Beauchamp[2], David Cesarini[4], Matthijs van der Loos[5], Magnus Johannesson[6], Patrik K. E. Magnusson[7], Paul Lichtenstein[7], Craig S. Atwood[8], Jeremy Freese[9], Taissa S. Hauser[10], Robert M. Hauser[10], Nicholas Christakis[11,12], and David Laibson[2]

Psychological Science
23(11) 1314–1323

DOI: 10.1177/095679
http://pss.sagepub.com
SAGE

# Candidate gene studies (theoretical testing)

Behav Genet (2012) 42:1–2
DOI 10.1007/s10519-011-9504-z

BRIEF COMMUNICATION

## Editorial Policy on Candidate Gene Association and Candidate Gene-by-Environment Interaction Studies of Complex Traits

John K. Hewitt

# Candidate gene studies (theoretical testing)

The literature on candidate gene associations is full of reports that have not stood up to rigorous replication. This is the case both for straightforward main effects and for candidate gene-by-environment interactions (Duncan and Keller 2011). As a result, the psychiatric and behavior genetics literature has become confusing and it now seems likely that many of the published findings of the last decade are wrong or misleading and have not contributed to real advances in knowledge. The reasons for this are complex, but include the likelihood that effect sizes of individual polymorphisms are small, that studies have therefore been underpowered, and that multiple hypotheses and methods of analysis have been explored; these conditions will result in an unacceptably high proportion of false findings (Ioannidis 2005).

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# Genetic discovery studies (GWAS)

**Genome-wide association studies (GWAS)**

- **A-theoretical testing of all $K \ll J$ SNPs measured on the chip ($K \approx$ 0.5-2.5 million) or imputed ($K \approx$ 9 million).**
- **Genome-wide significance: p = 5 x $10^{-8}$**
- **Frequentist justification: Bonferroni correction for ~1 million effectively independent loci in Europeans**
- **Bayesian justification: Need stringent significance threshold given low prior for any specific locus**
- **Causal model:**

$$\tilde{y}_i = \sum_{k=1}^{K} \beta_k x_{ik} + \mathbf{z}_i' \boldsymbol{\gamma} + \eta_i.$$

Courtesy Dan Benjamin

# The dimensionality problem

**Cannot estimate this regression:**

$$\tilde{y}_i = \sum_{k=1}^{K} \beta_k x_{ik} + \boldsymbol{z}_i' \boldsymbol{\gamma} + \eta_i$$

**unless $N > K + |\gamma| \approx 9$ million!**

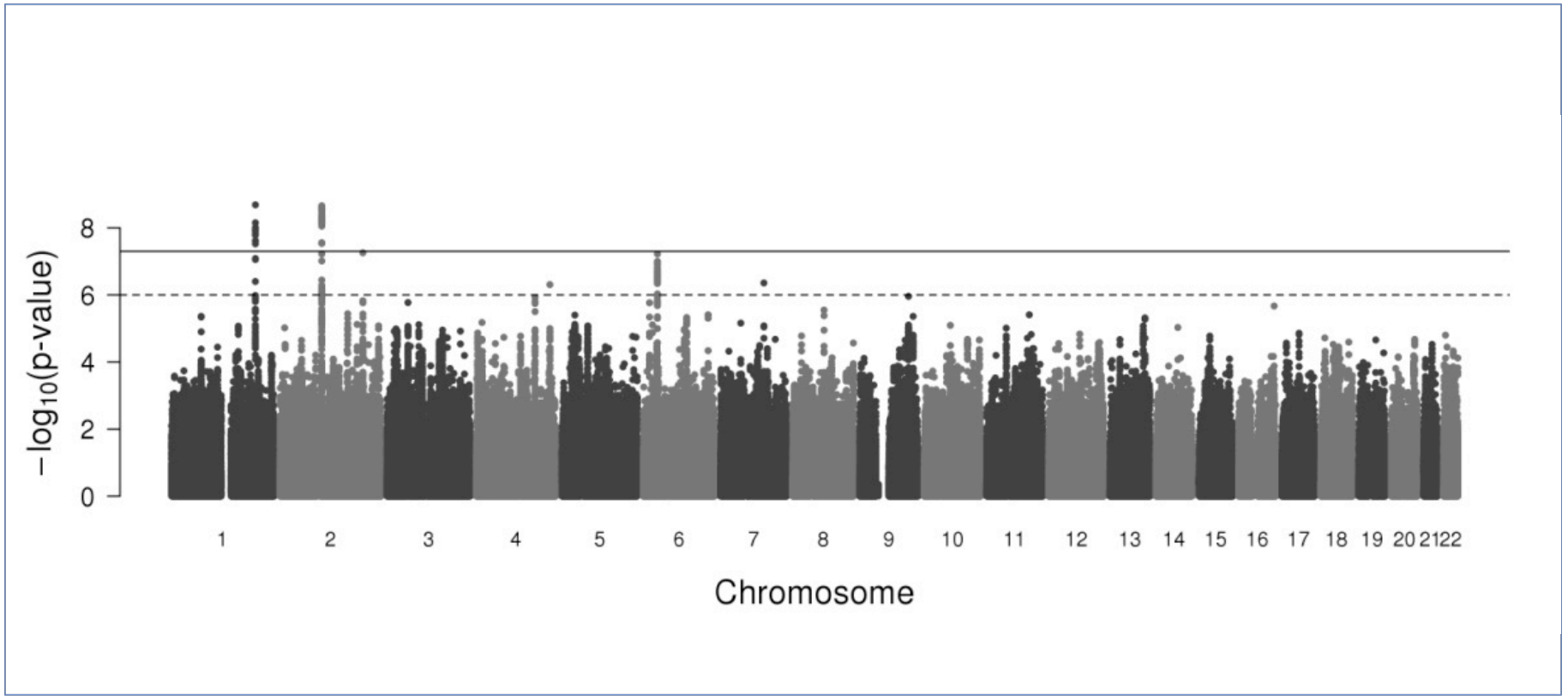
**Standard solution: estimate univariate regressions:**

$$\tilde{y}_i = \beta_k^{GWAS} x_{ik} + \boldsymbol{z}_i' \boldsymbol{\gamma}_k + \epsilon_{ik}.$$

**Abdel, Aysu, will discuss GWAS in much more detail**

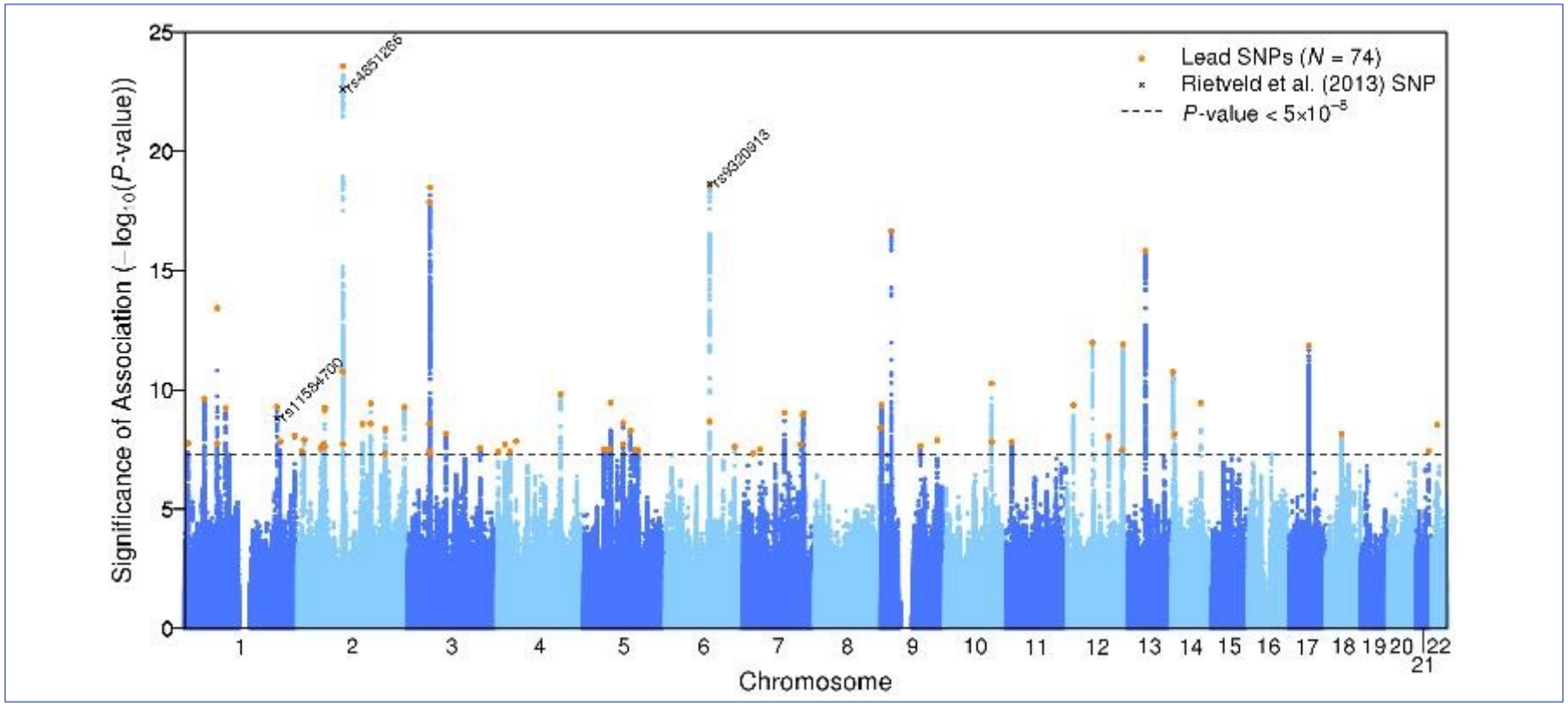
Courtesy Dan Benjamin

# EA1 (3 genome-wide SNPs) – Manhattan plot



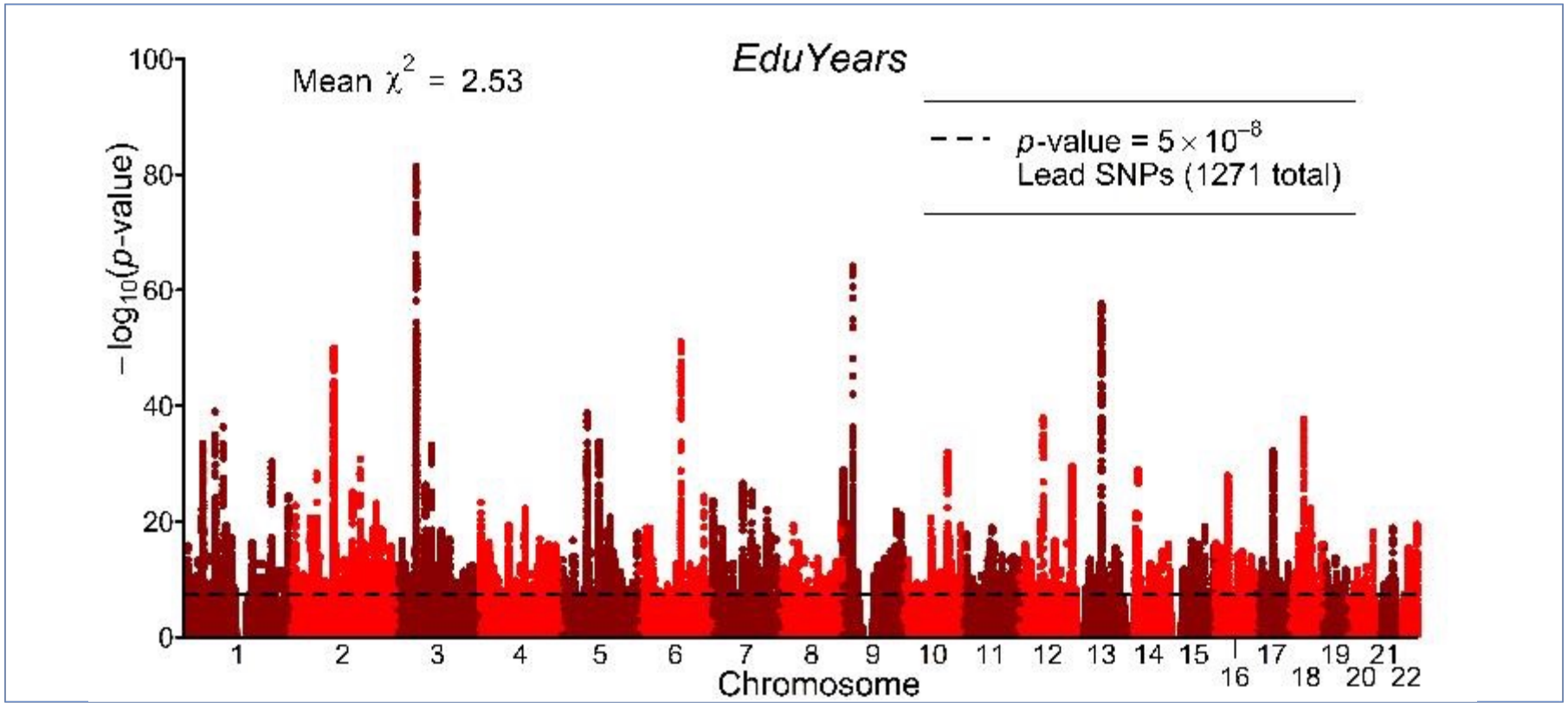

Rietveld et al. (2013, Science)
Discovery: N = 101,069 individuals (41 datasets)
Replication: N = 25,490 individuals (12 datasets)

# EA2 (74 genome-wide SNPs)



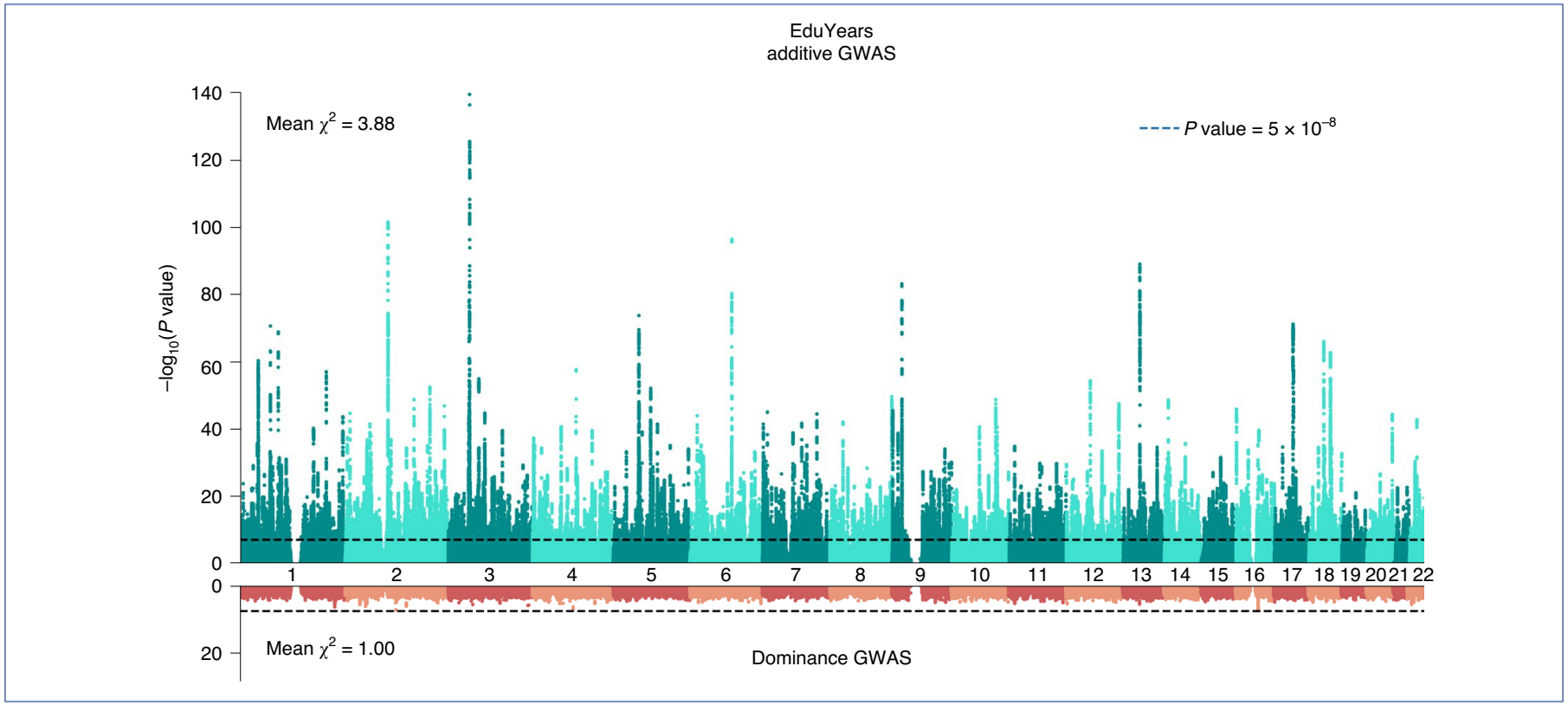

Okbay et al. (2016, Nature)
Discovery: N = 293,723 individuals (63 datasets)
Replication: N = 111,349 individuals (UK Biobank 1st release)

# EA3 (1,271 genome-wide SNPs)




Lee et al. (2018, Nature Genetics)
Discovery: N = 1,131,881 individuals (70 datasets)
Replication: Okbay et al. (N = 405,073) in new data (N = 726,808), and vice-versa.

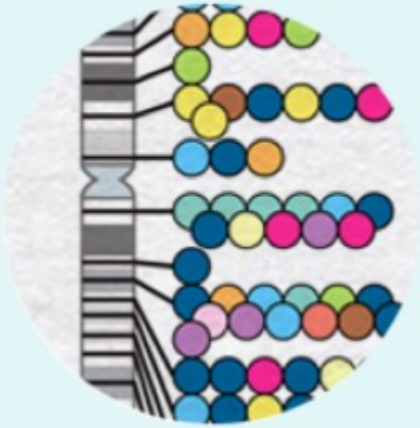
# EA4 (3,952 genome-wide SNPs)




Okbay et al. (2022, Nature Genetics)
Discovery: N = 3,037,499 individuals (69 cohorts + UKB + 23andMe)

# GWAS Catalog

## GWAS Catalog

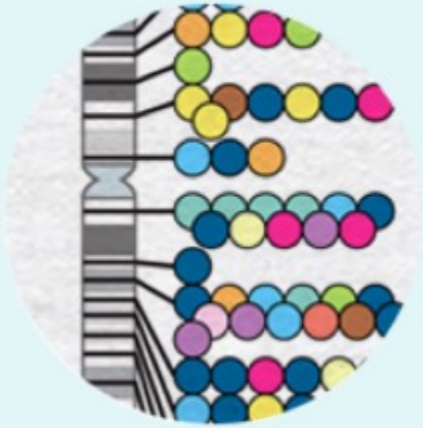


The NHGRI-EBI Catalog of published GWAS studies provides a publicly available curated resource of SNP-trait associations and summary statistics

www.ebi.ac.uk/gwas

# Explosion of GWAS

## GWAS Catalog



As of September 2019 the GWAS Catalog contains more than 157,000 associations from 4220 publications

This slideshow demonstrates the increasing number of associations from 2005-2019

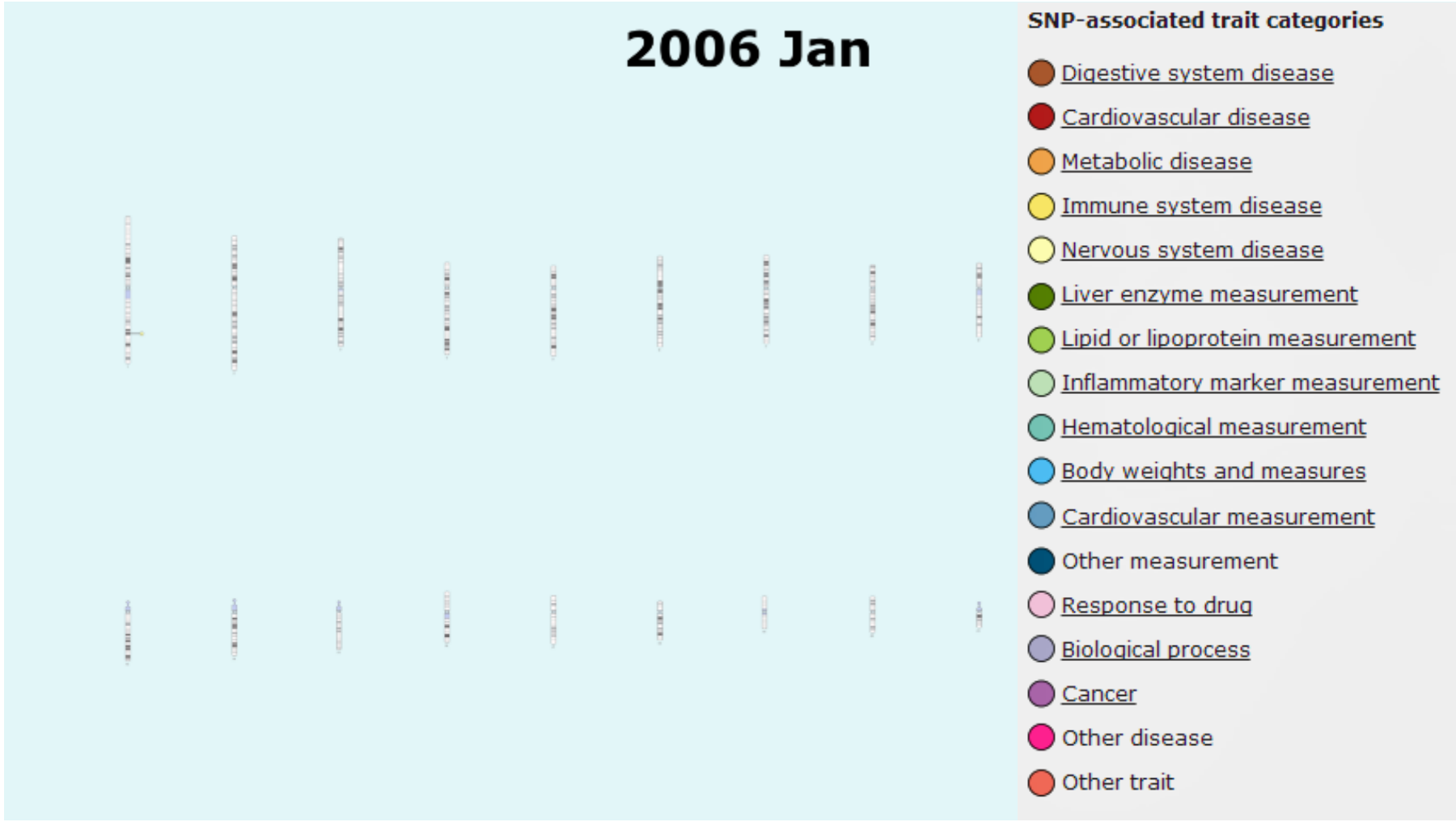
Each dot represents a SNP-Trait association (p<5e-8), each colour represents a different trait category

*Buniello A, MacArthur JAL, Cerezo M, Harris LW, Hayhurst J, Malangone C, McMahon A, Morales J, Mountjoy E, Sollis E, Suveges D, Vrousgou O, Whetzel PL, Amode R, Guillen JA, Riat HS, Trevanion SJ, Hall P, Junkins H, Flicek P, Burdett T, Hindorff LA, Cunningham F and Parkinson H.*

**The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays and summary statistics 2019.**

Nucleic Acids Research, 2019, Vol. 47 (Database issue): D1005-D1012.

# Each color indicates a trait category



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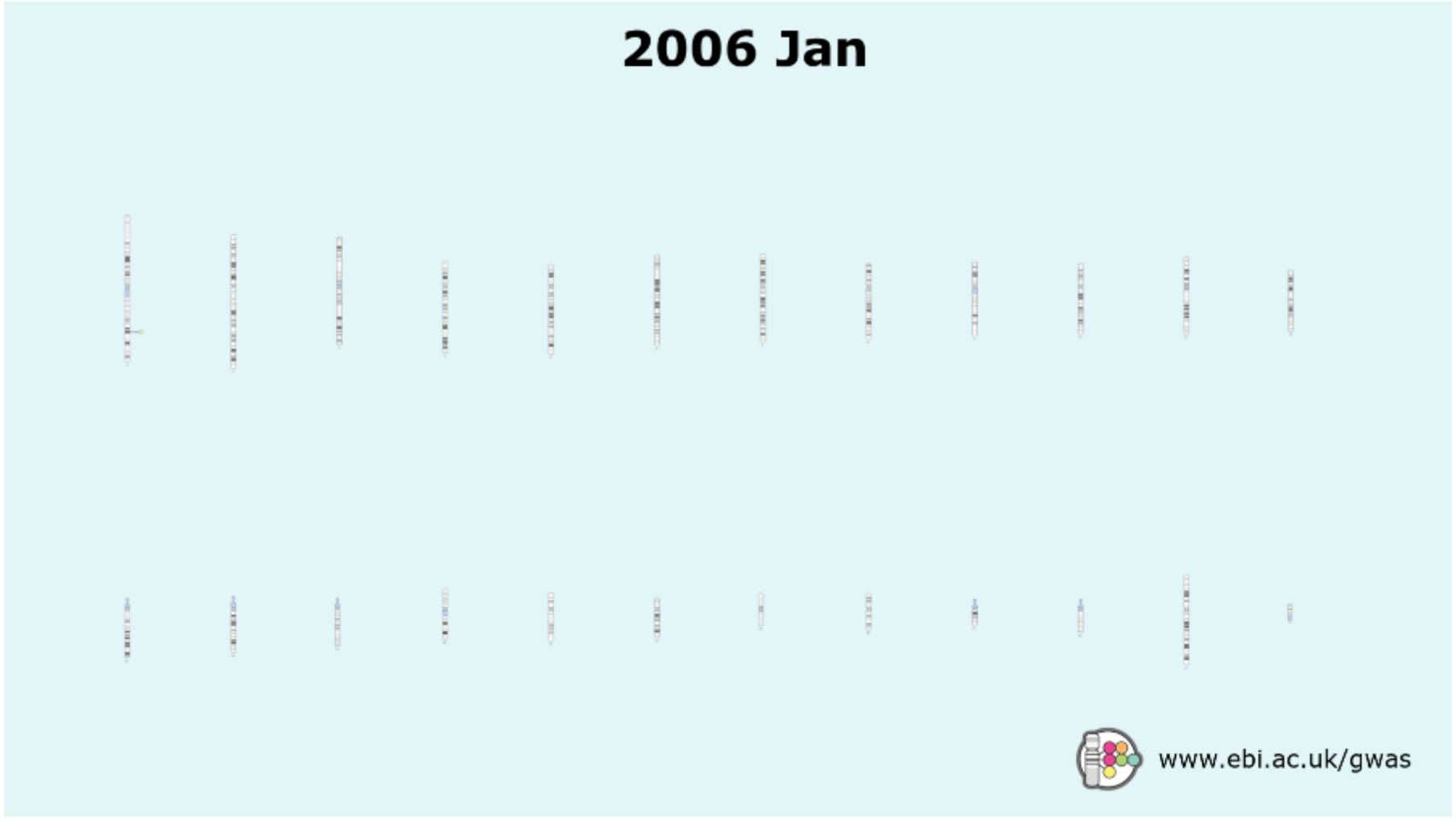

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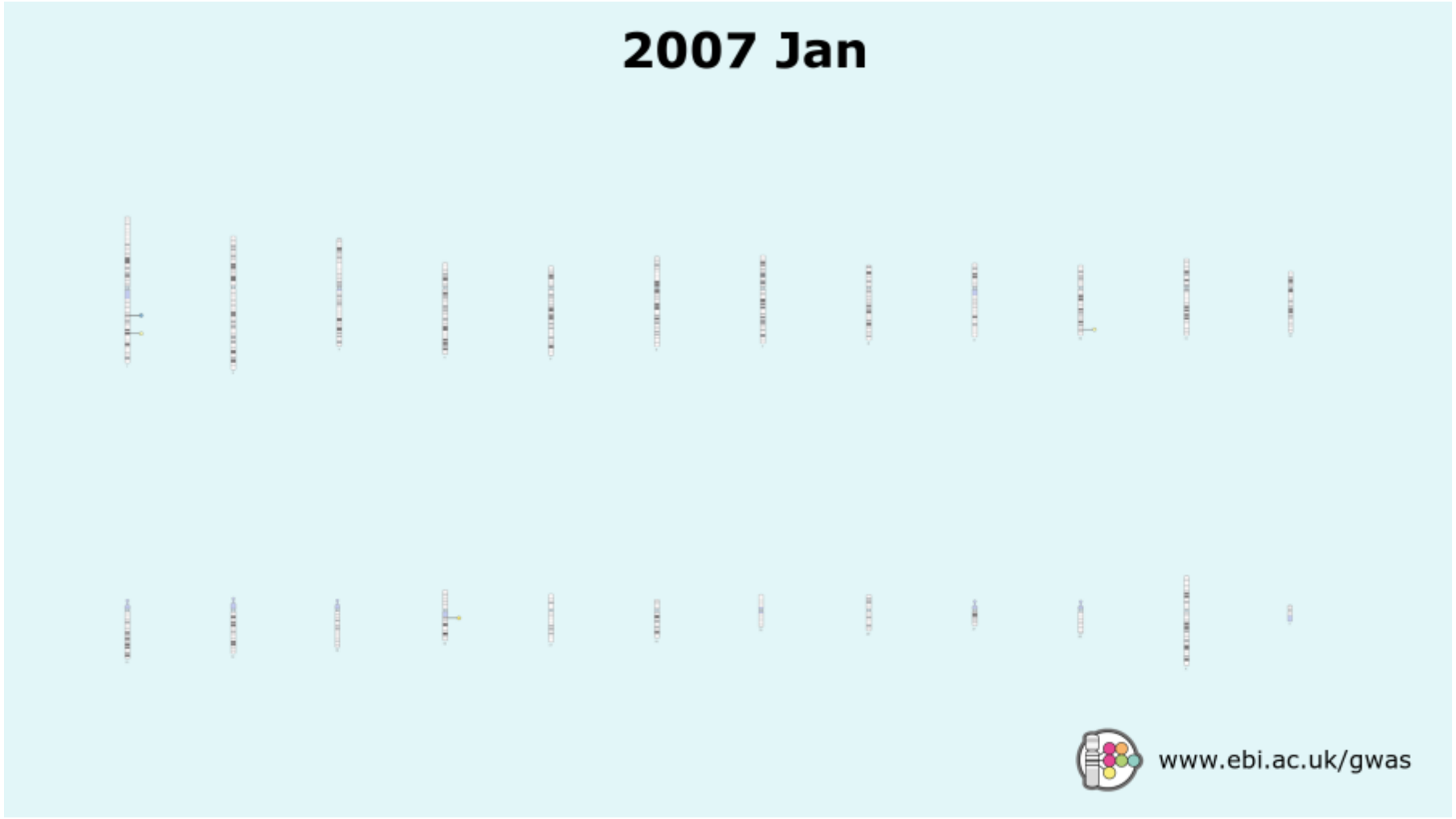

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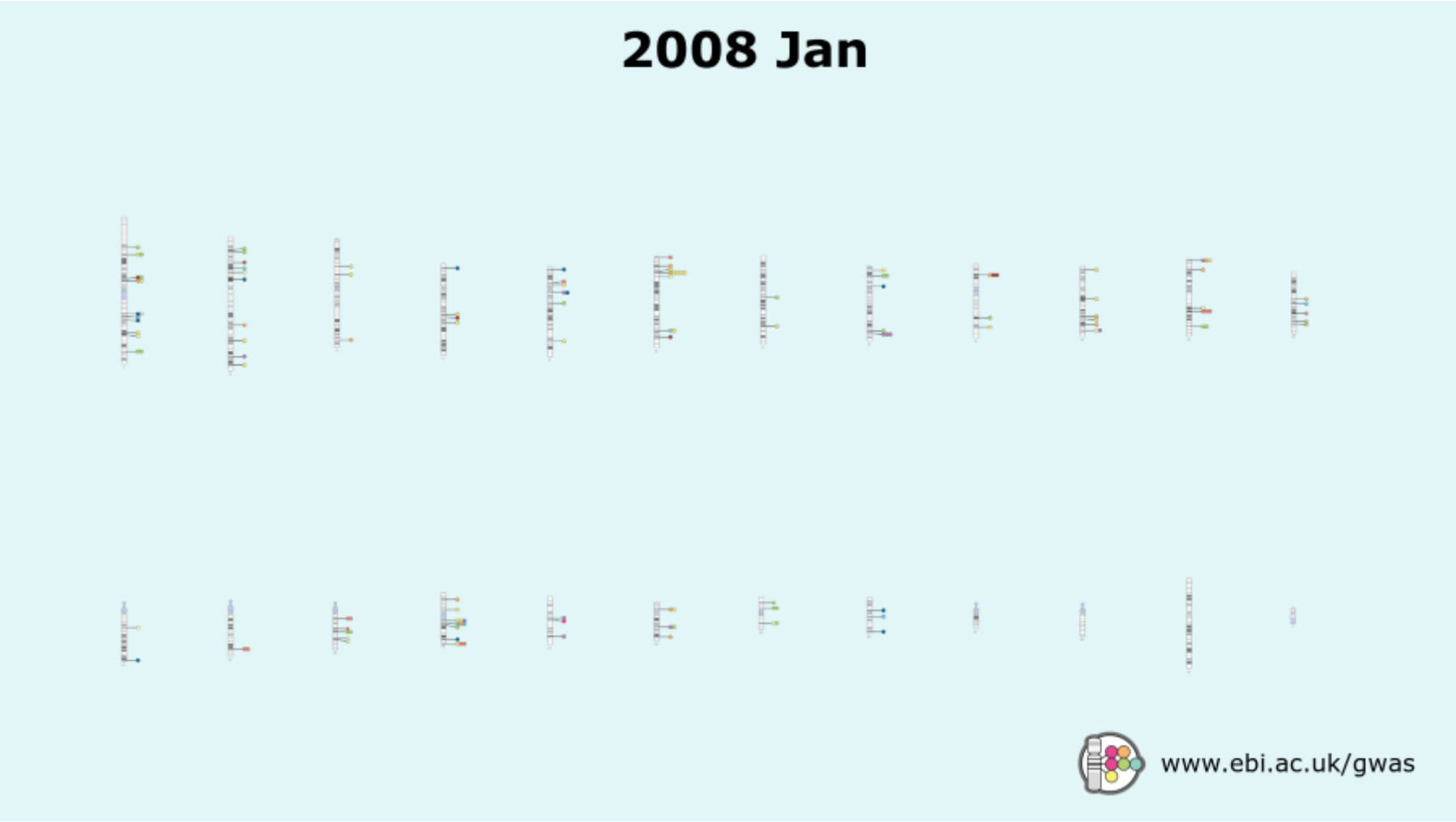

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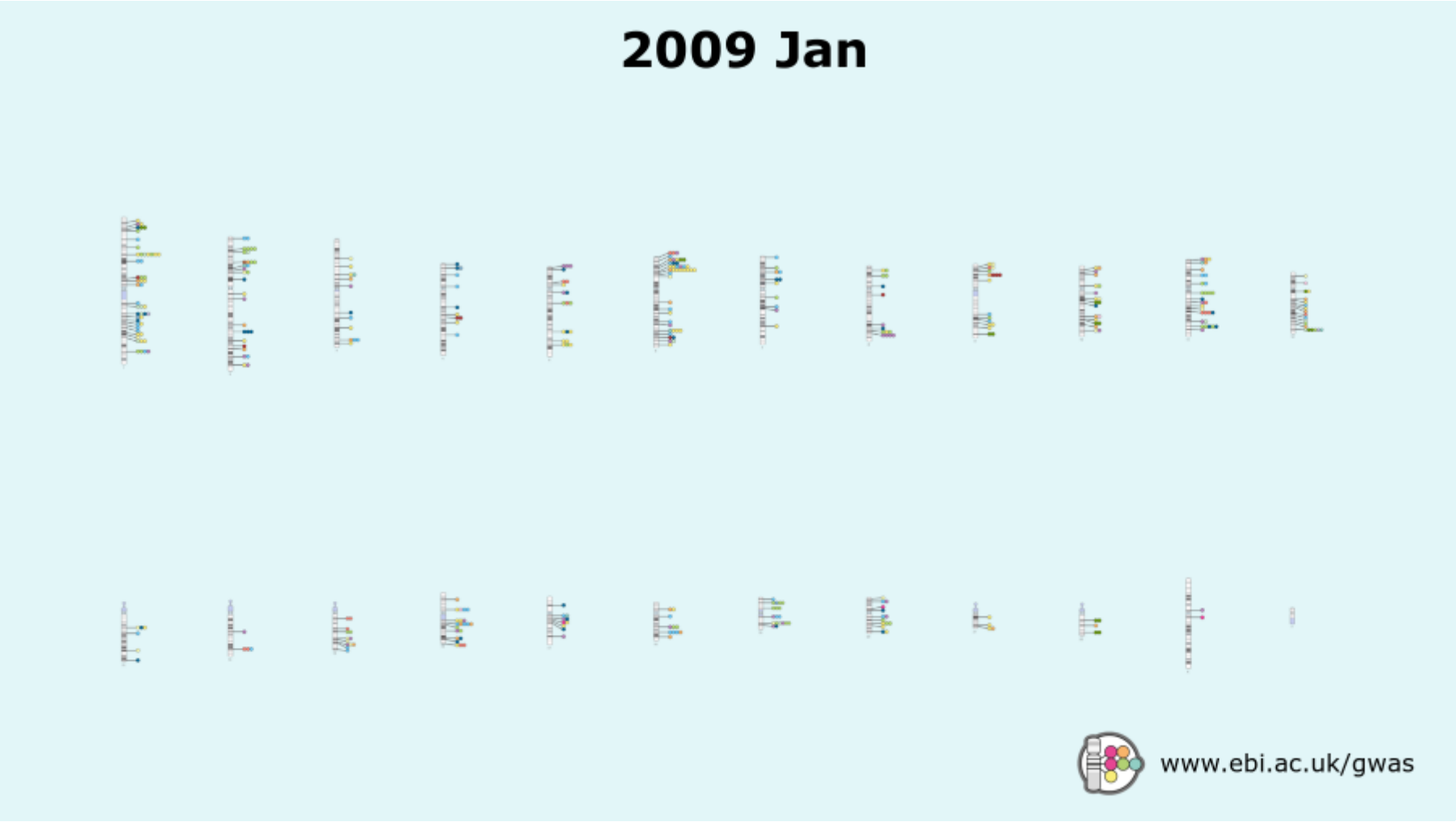

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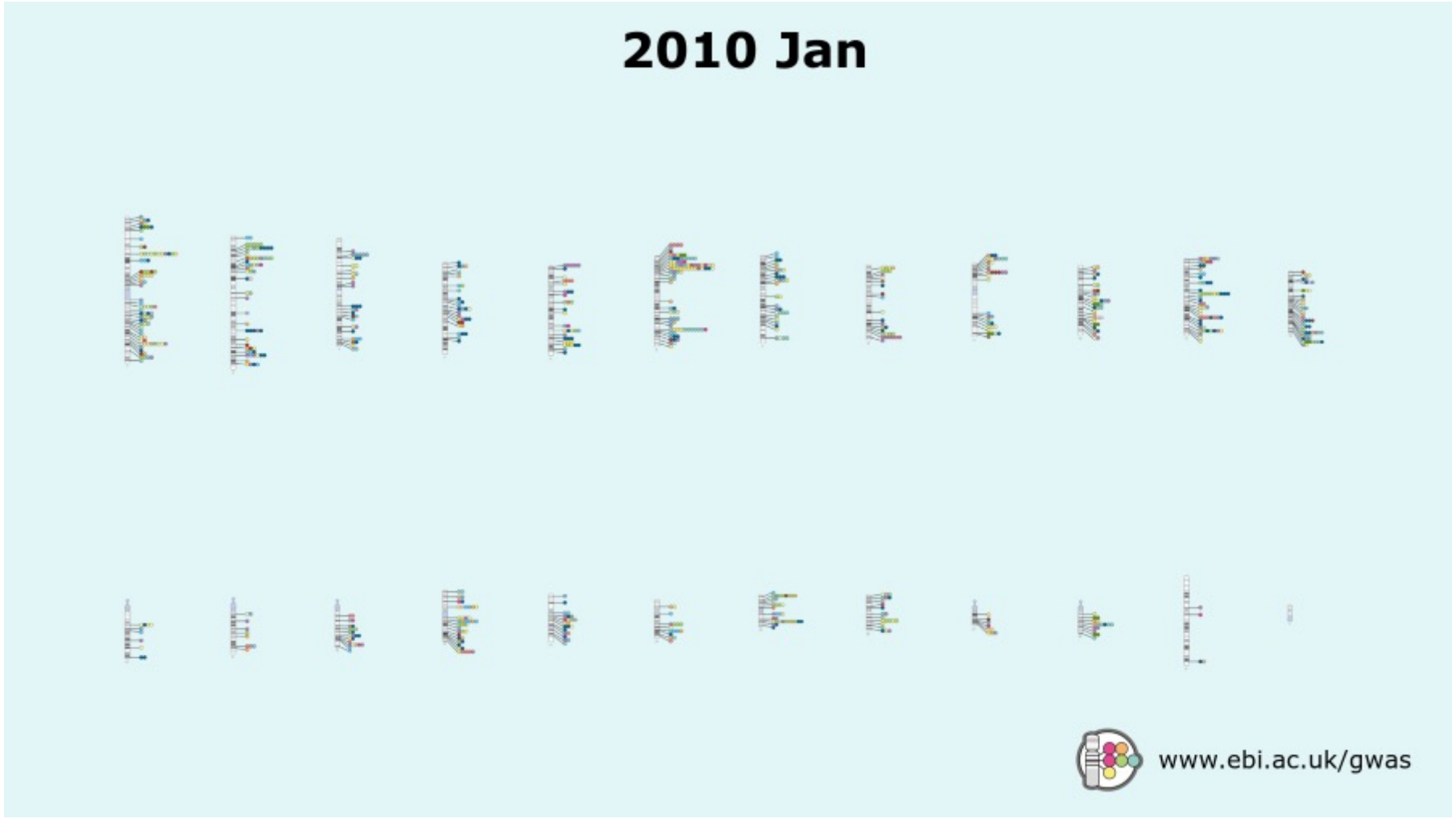

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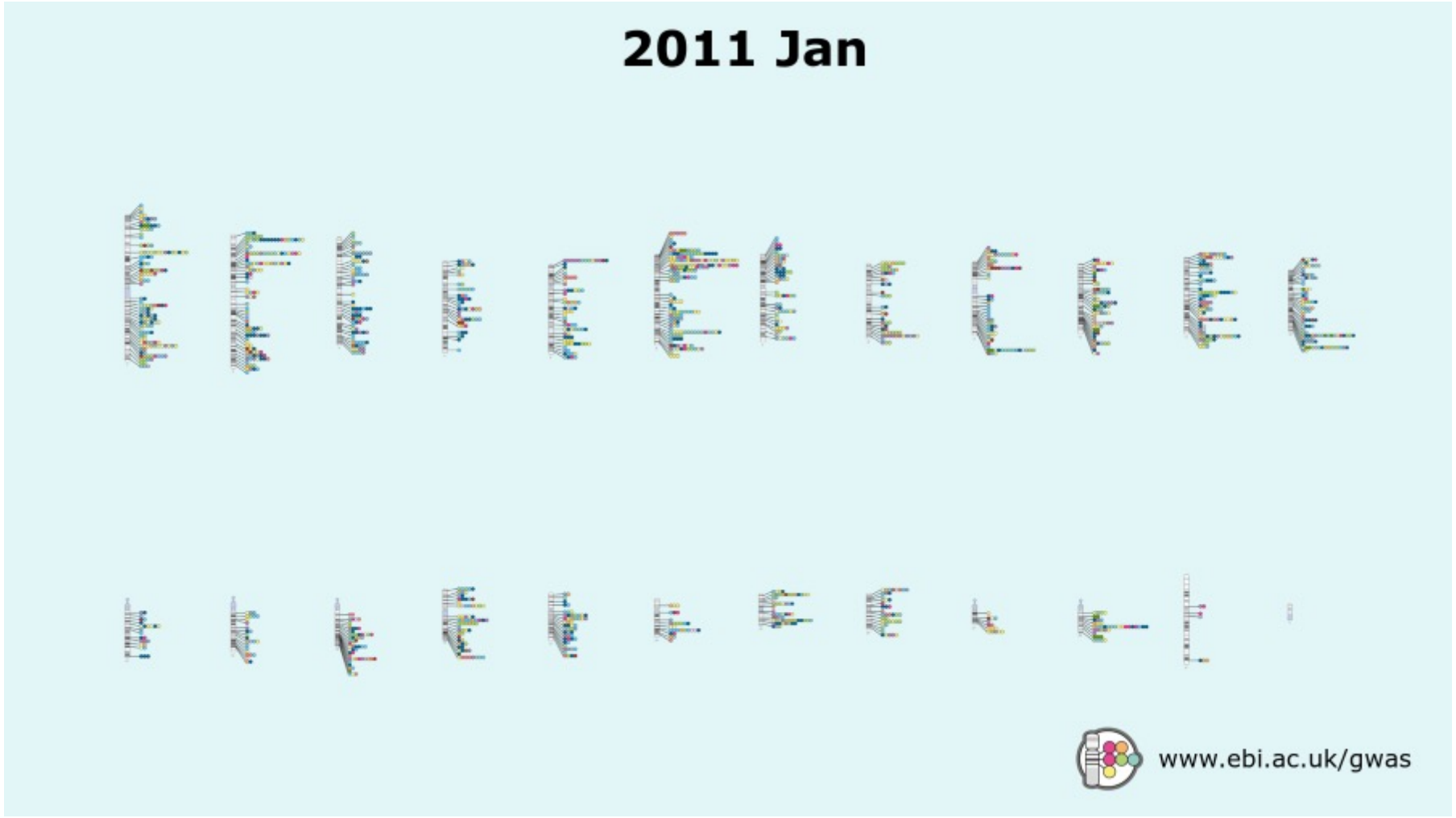

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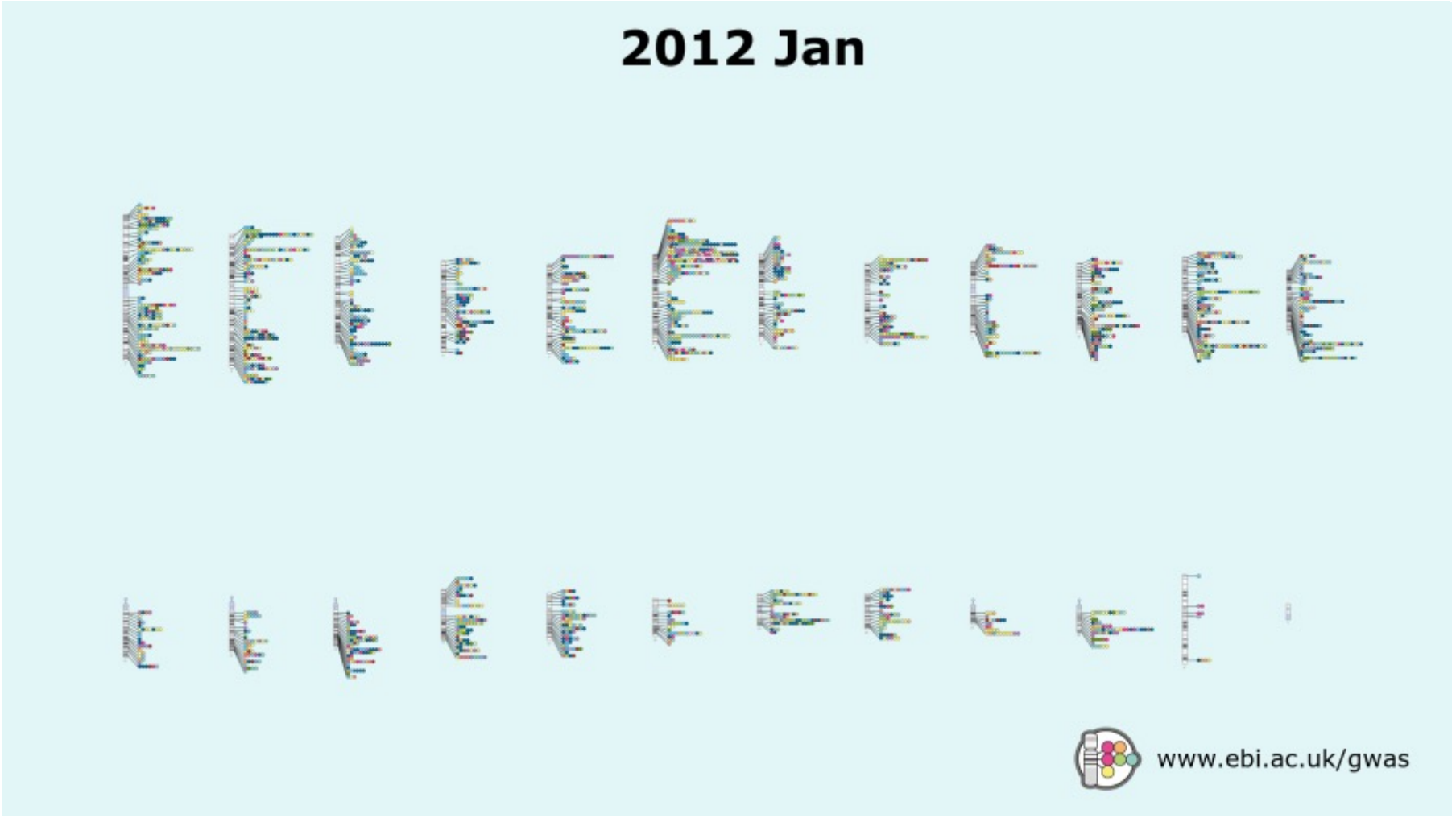

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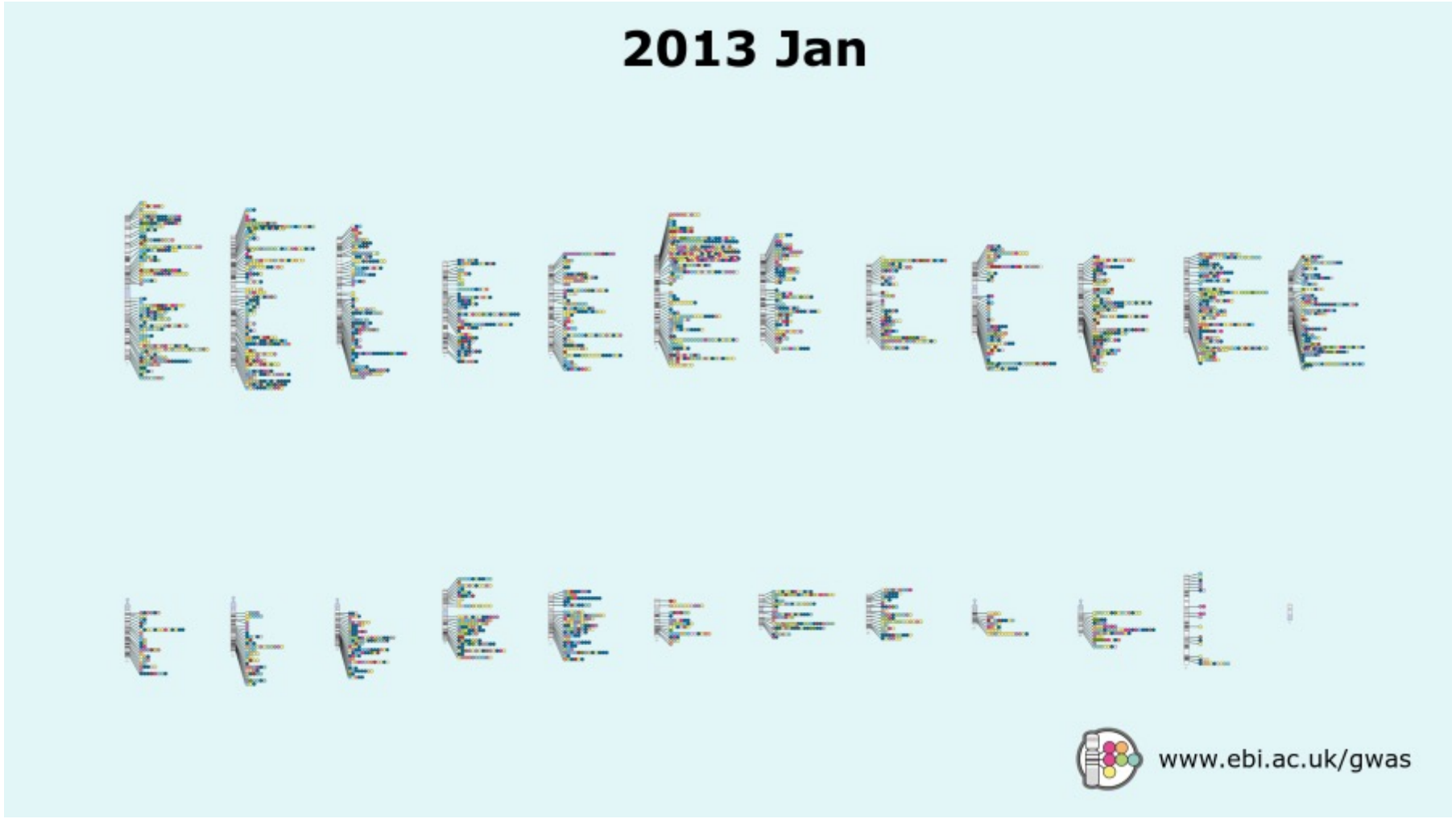

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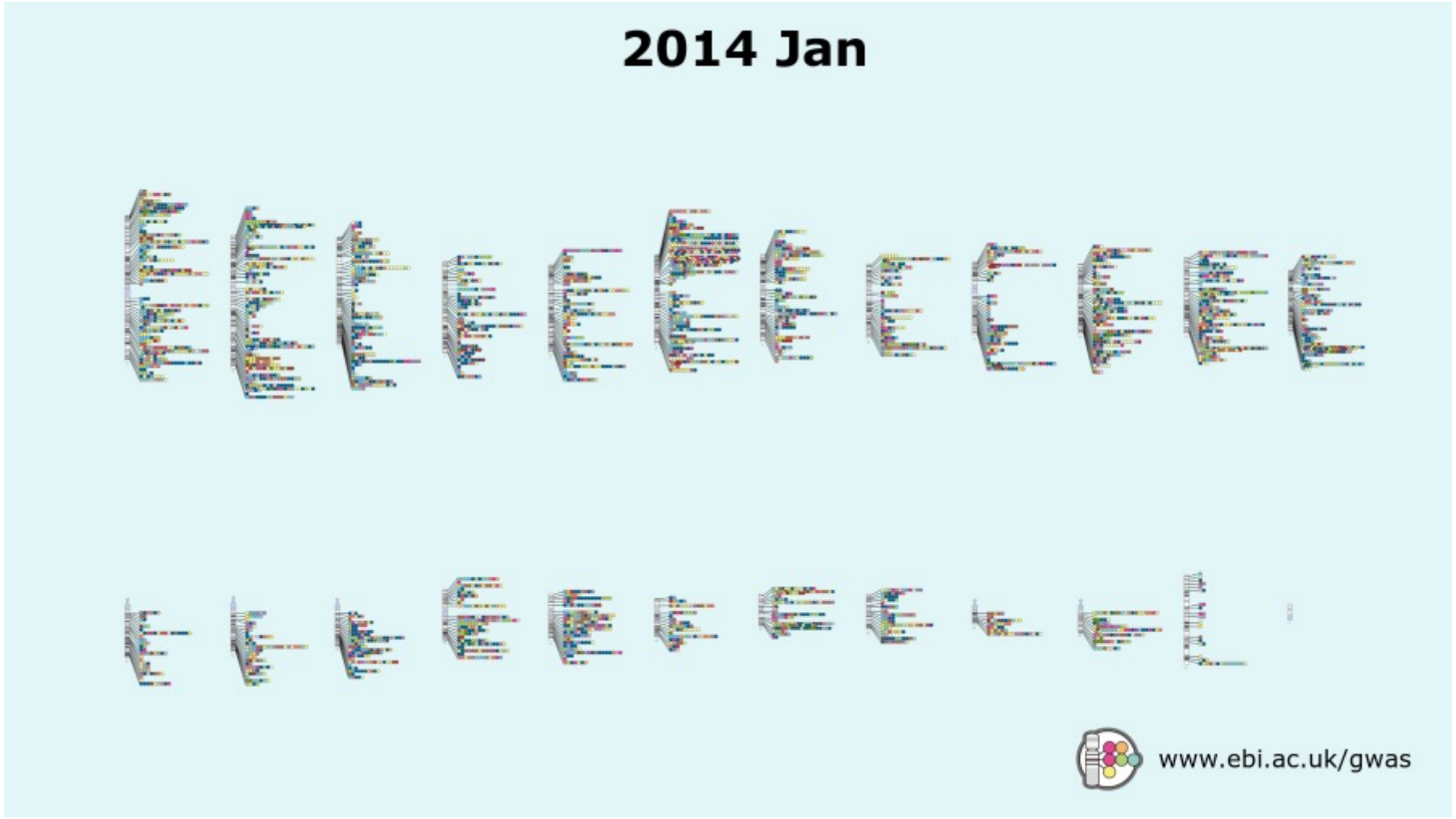

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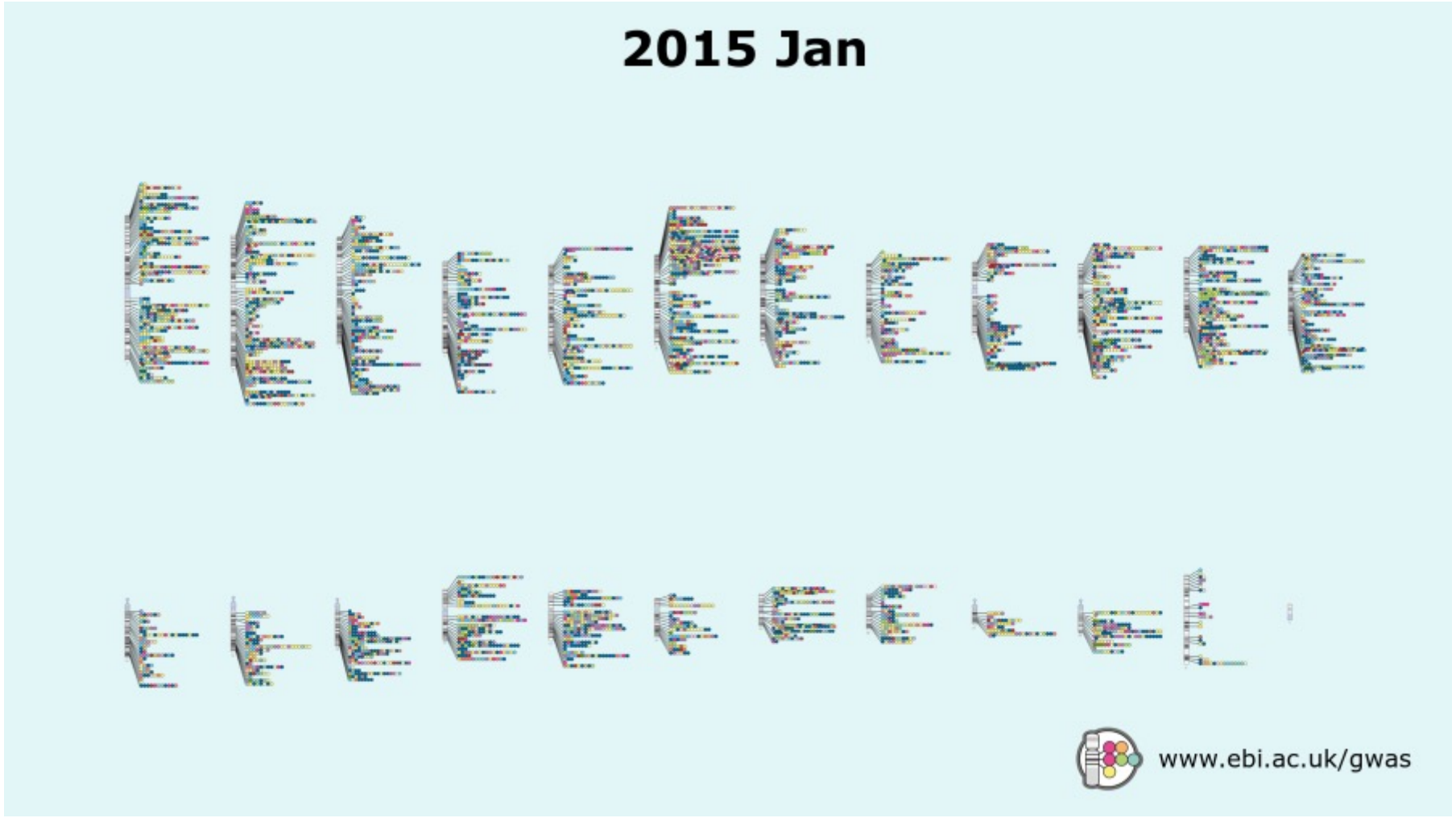

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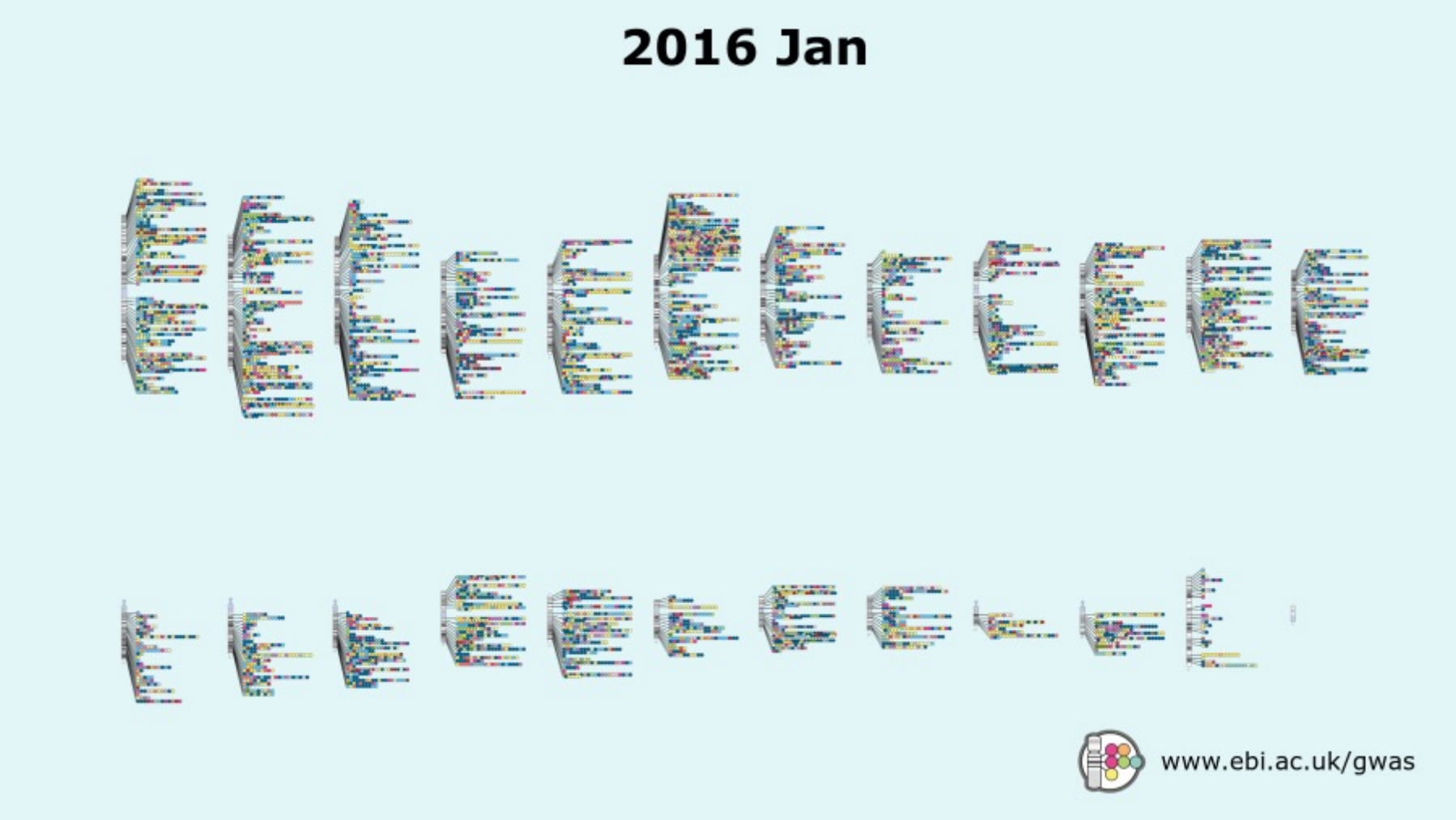

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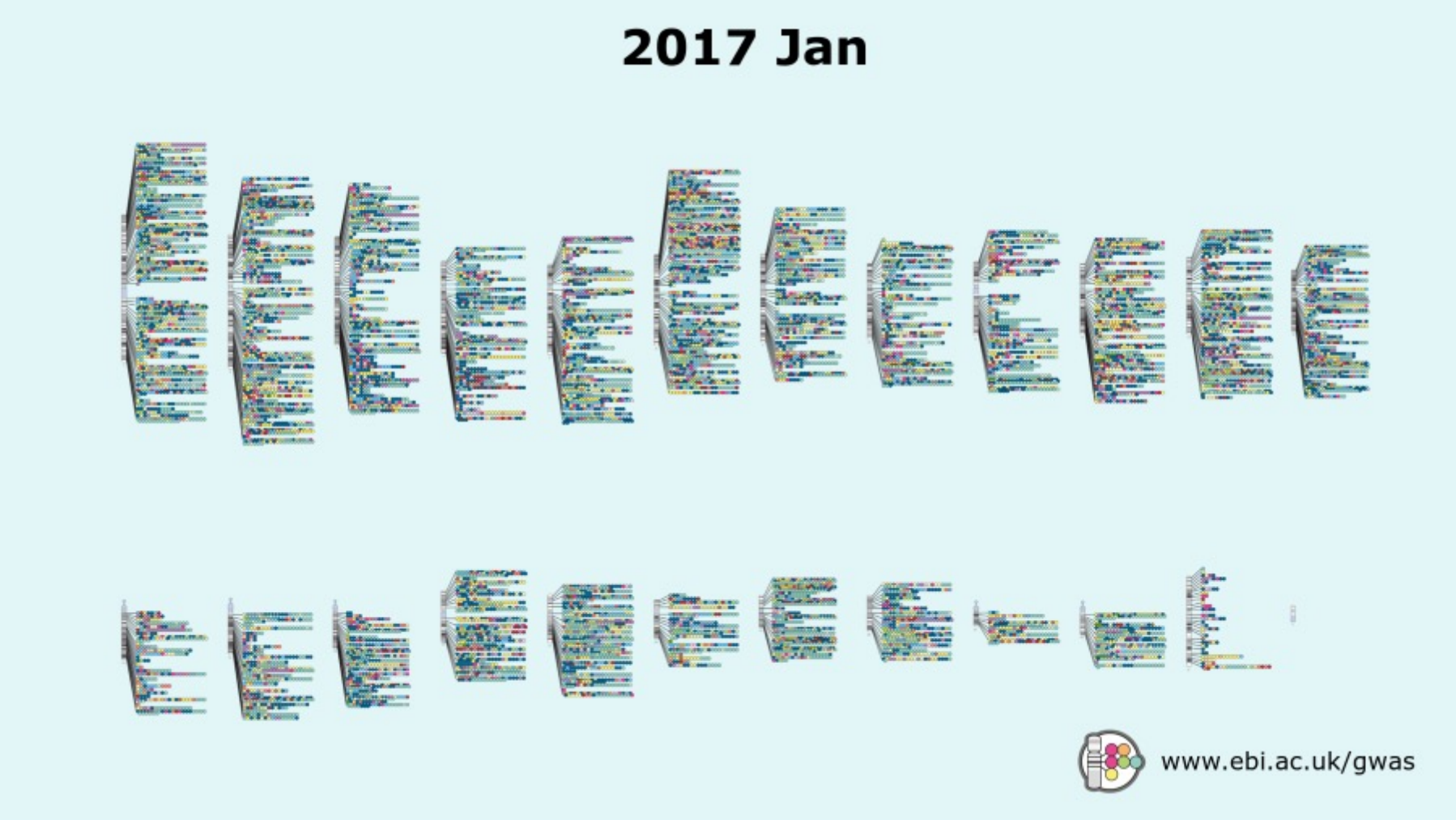

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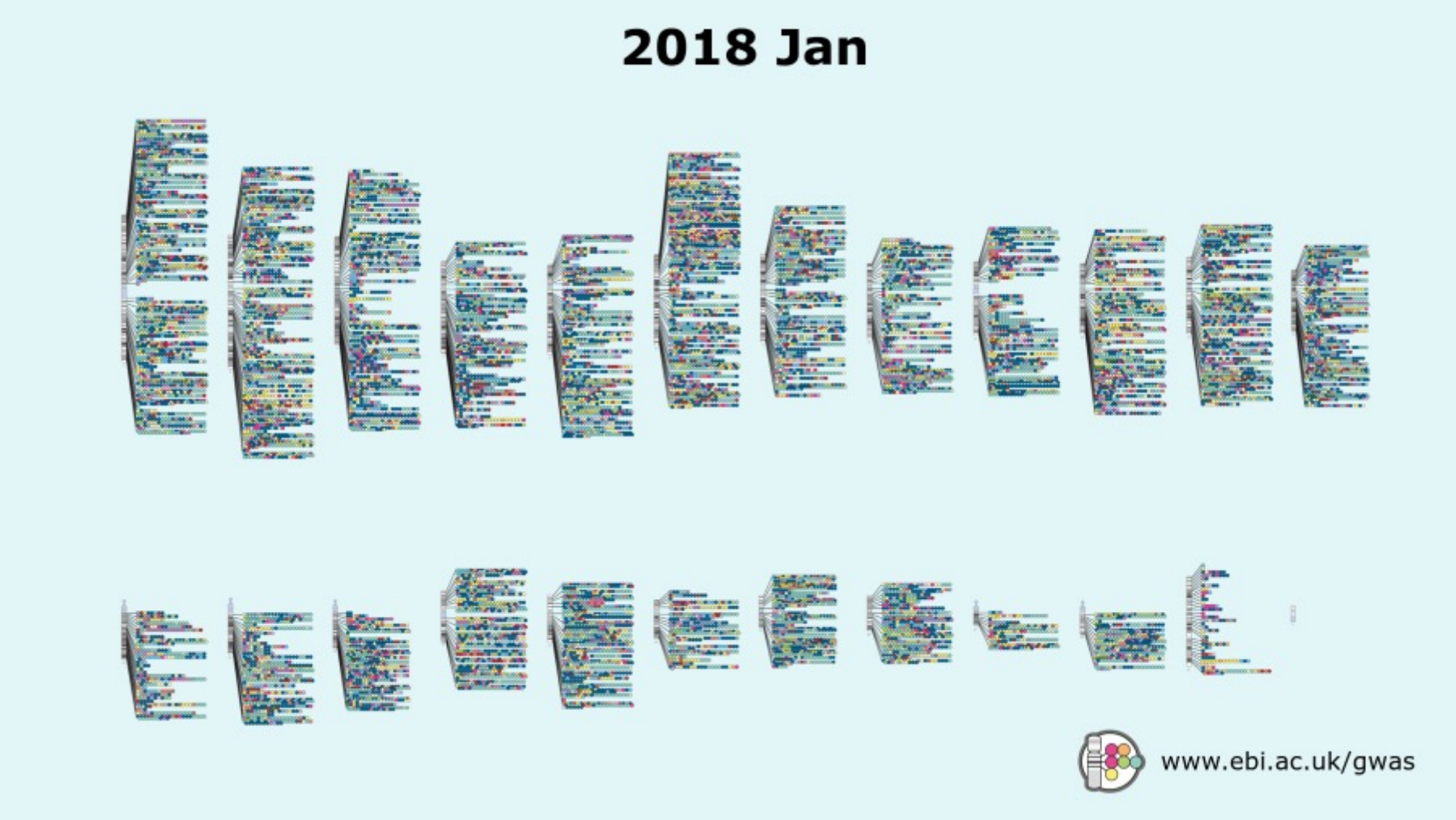

# GWAS Catalog

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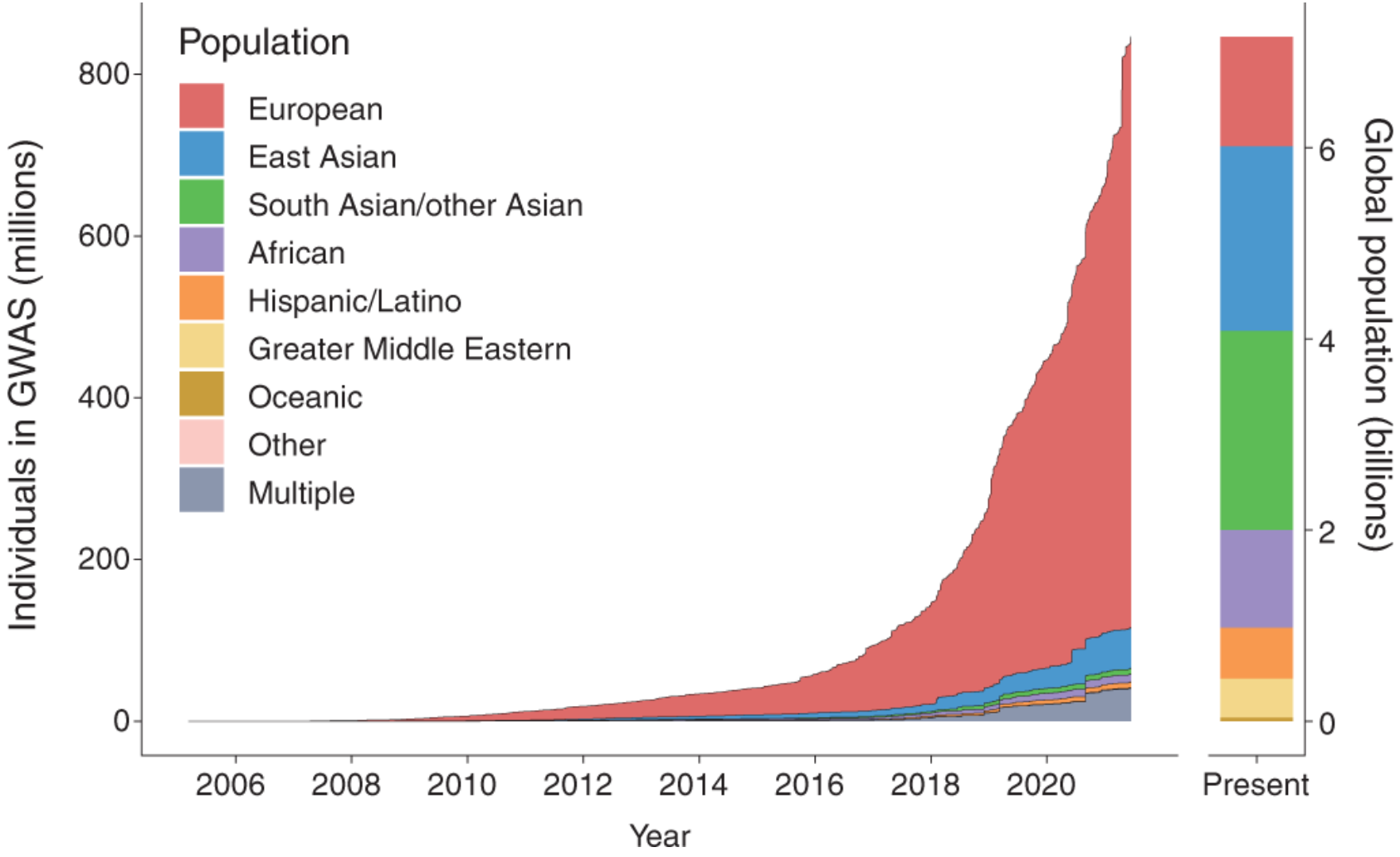
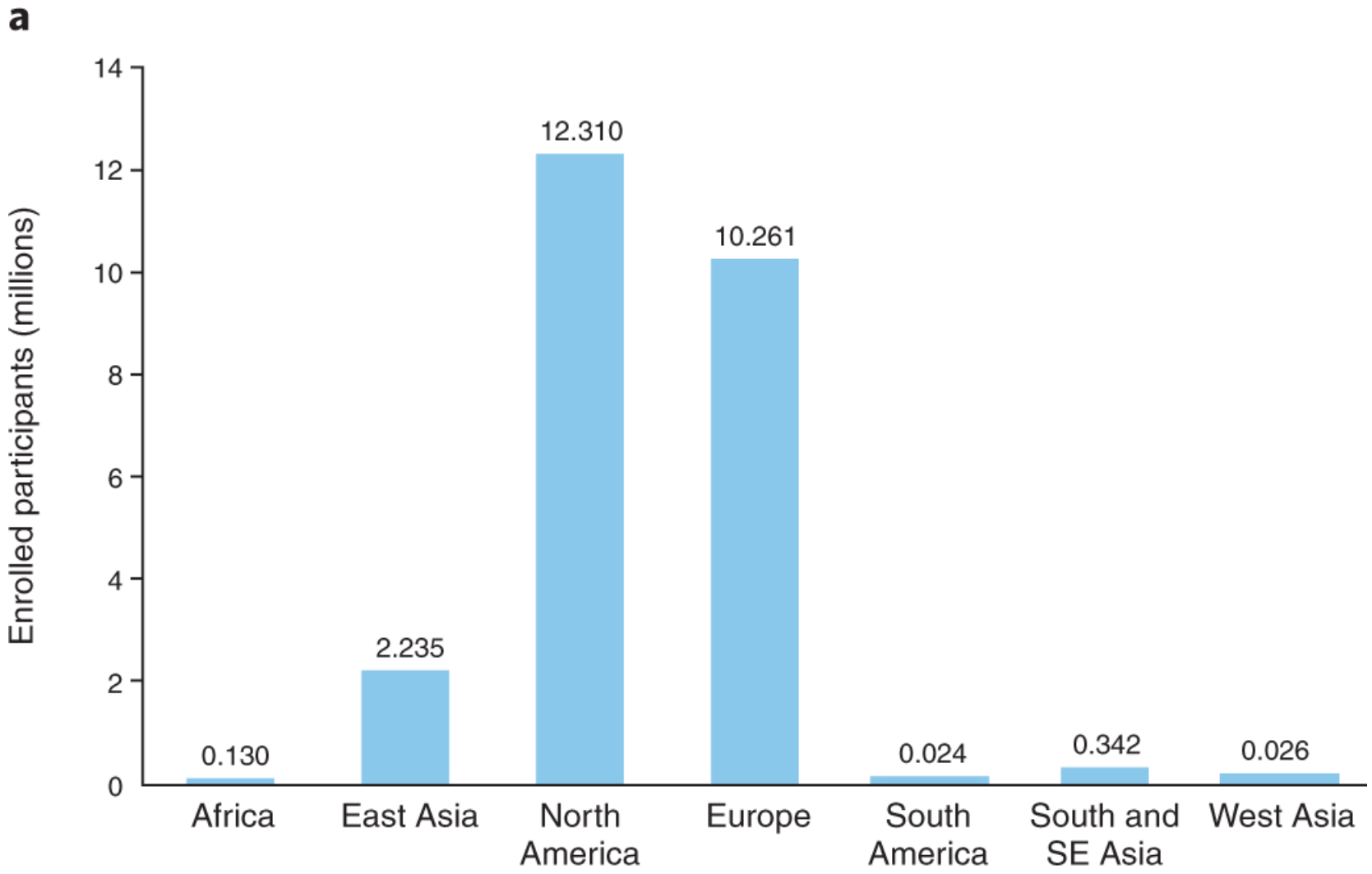
# GWAS are increasingly powerful




Martin et al. (2019) Nature Genetics; updated Fatumo et al. (2022) Nature Medicine

# ... but genetics has a HUGE diversity problem

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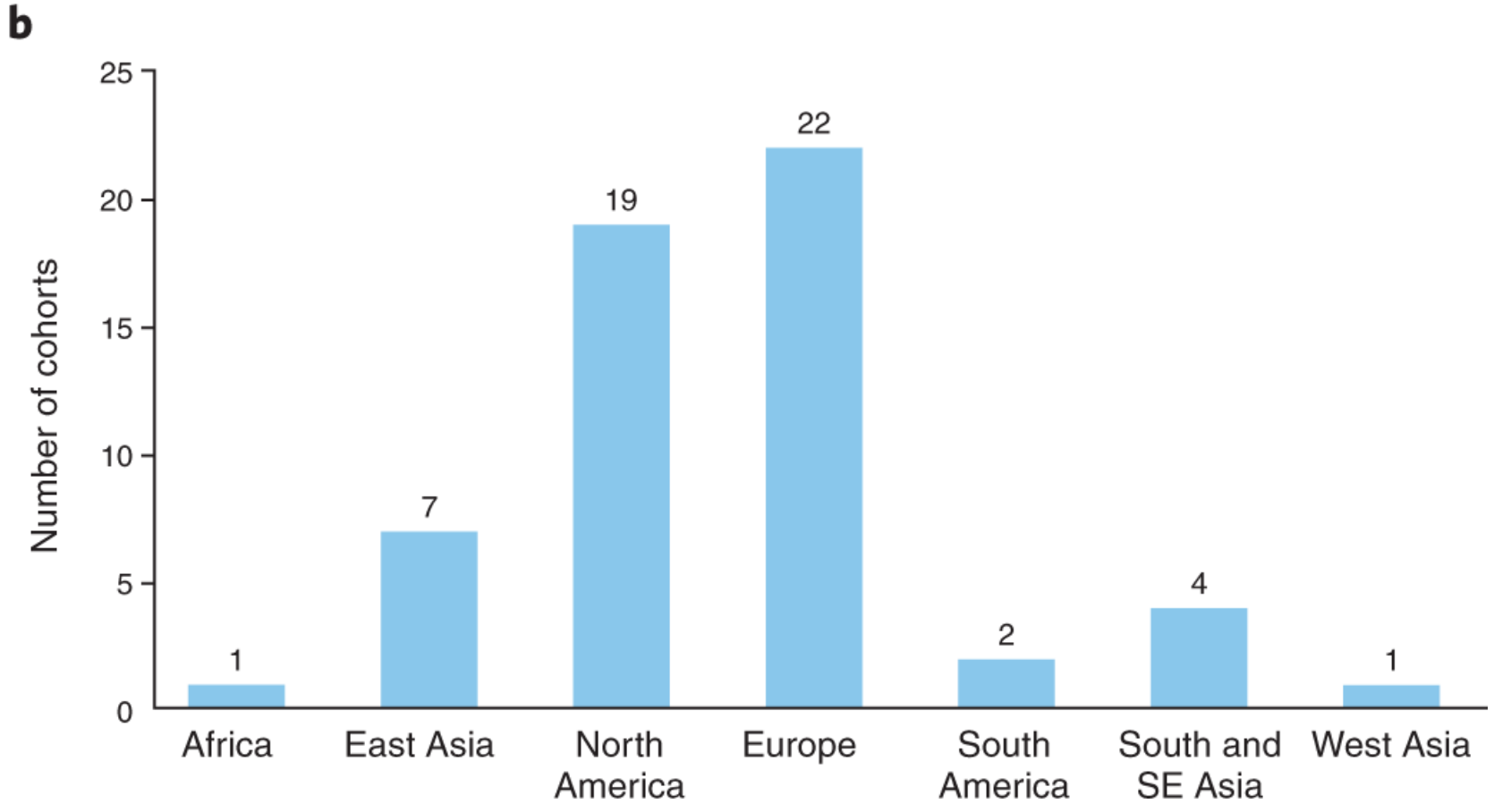


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# Polygenic Index (PGI)

**Summary measure of an individuals' 'genetic predisposition'**

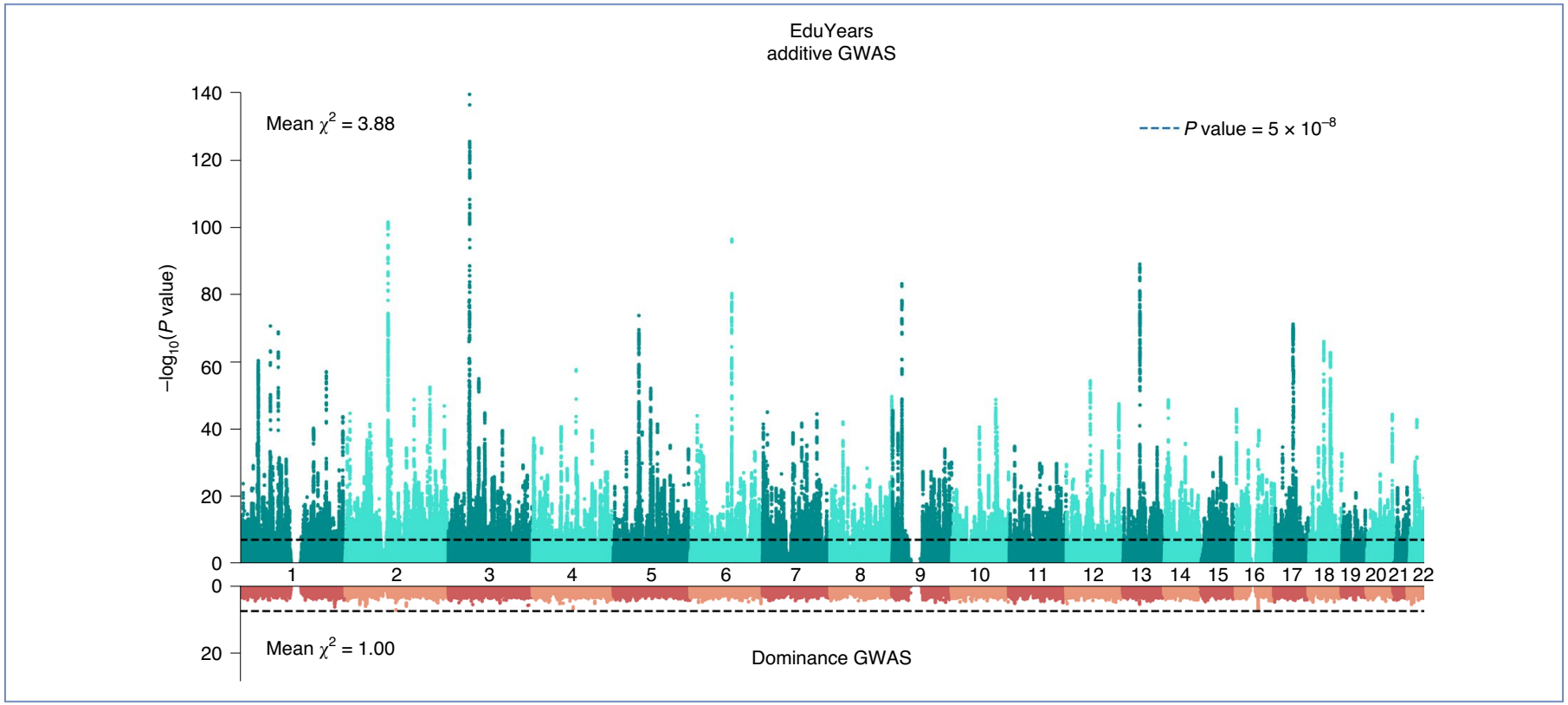
**Best linear genetic predictor**

**Does not mean it is solely biological or immutable**

**It captures environmental components**

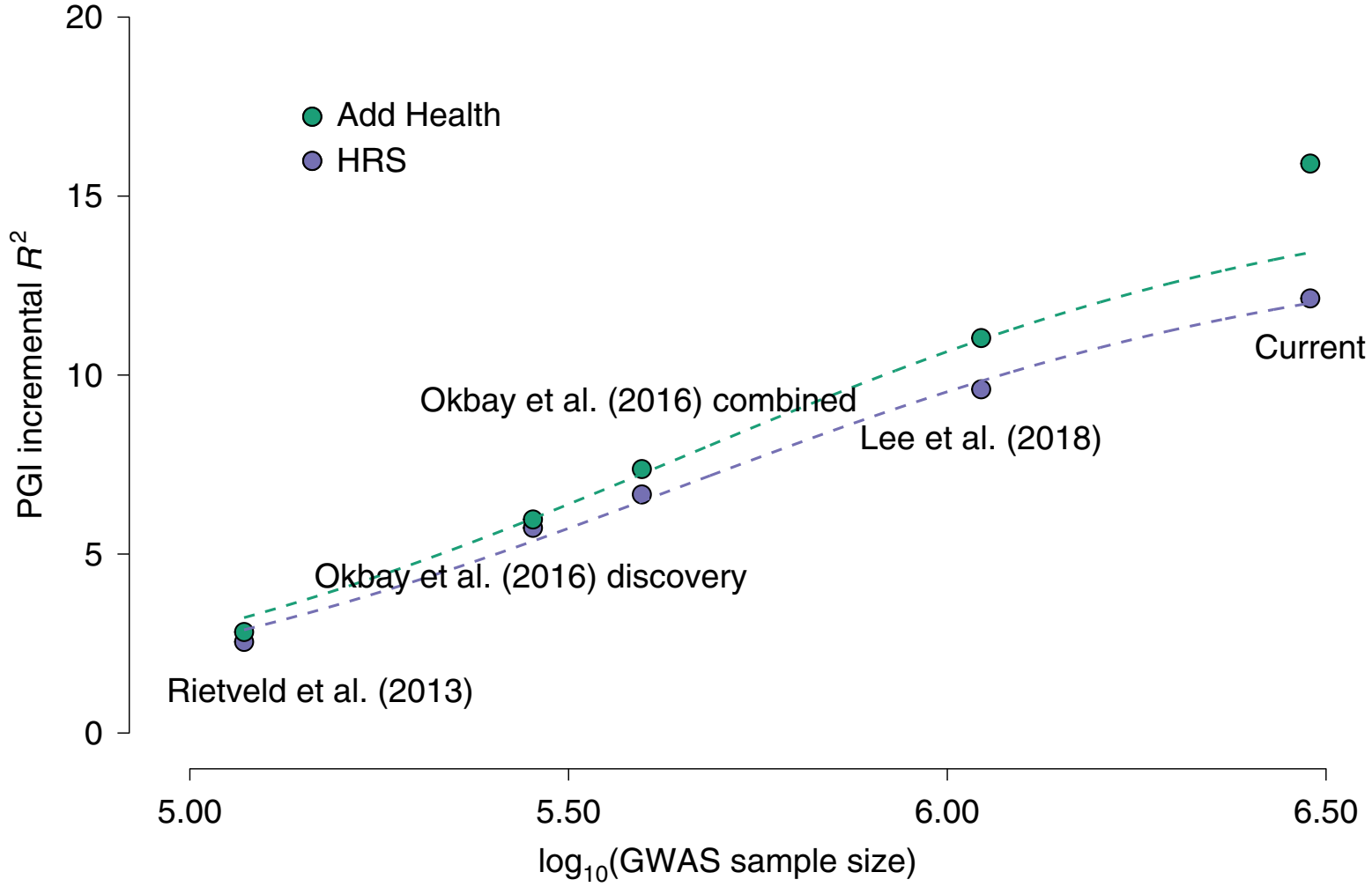
**Asyu Okbay will discuss these in much more detail**

# Think of it as the weighted sum over all SNP effects across the genome




Okbay et al. (2022, Nature Genetics)
Discovery: N = 3,037,499 individuals (69 cohorts + UKB + 23andMe)

# Polygenic indices (PGIs) explain growing share of the variation between individuals




Okbay et al. (2022, Nature Genetics)

# Outline

- Introduction to ESSGN
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# Can environments protect against genetic risk?

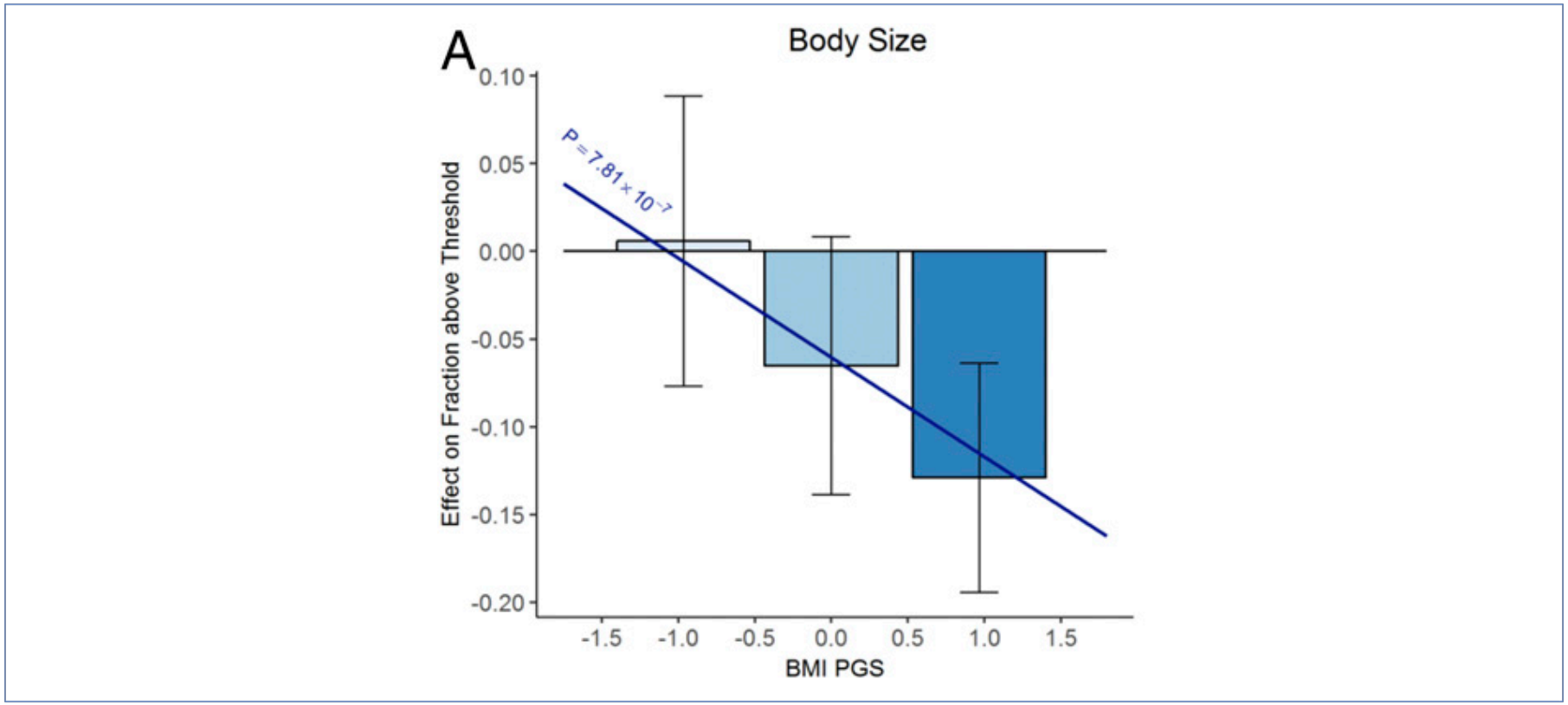
## Nature

## Nurture

**Interplay between G and E in behaviors / outcomes**
**(just one type of application; there are many others)**

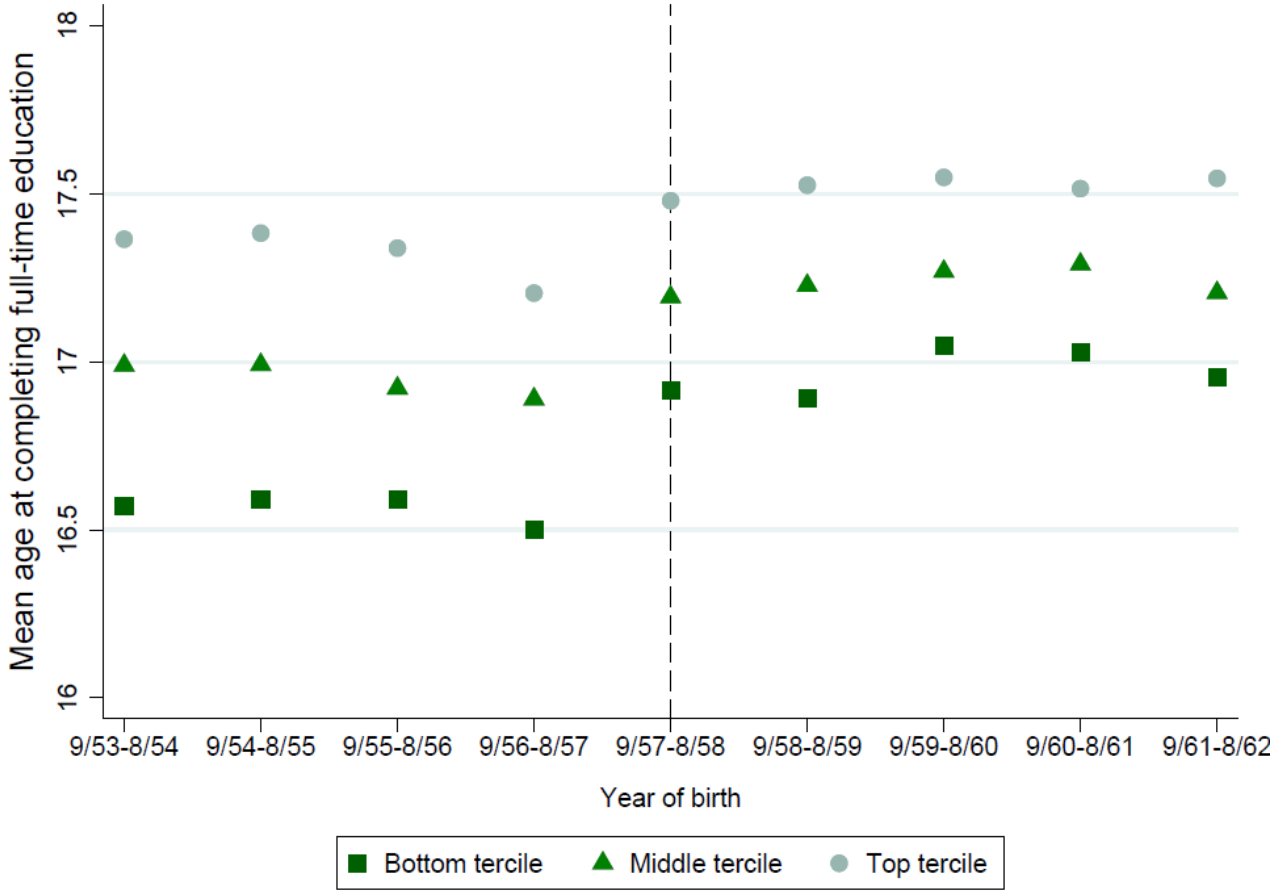
# G + E + GxE

# Barcellos, Carvalho and Turley (2018), PNAS



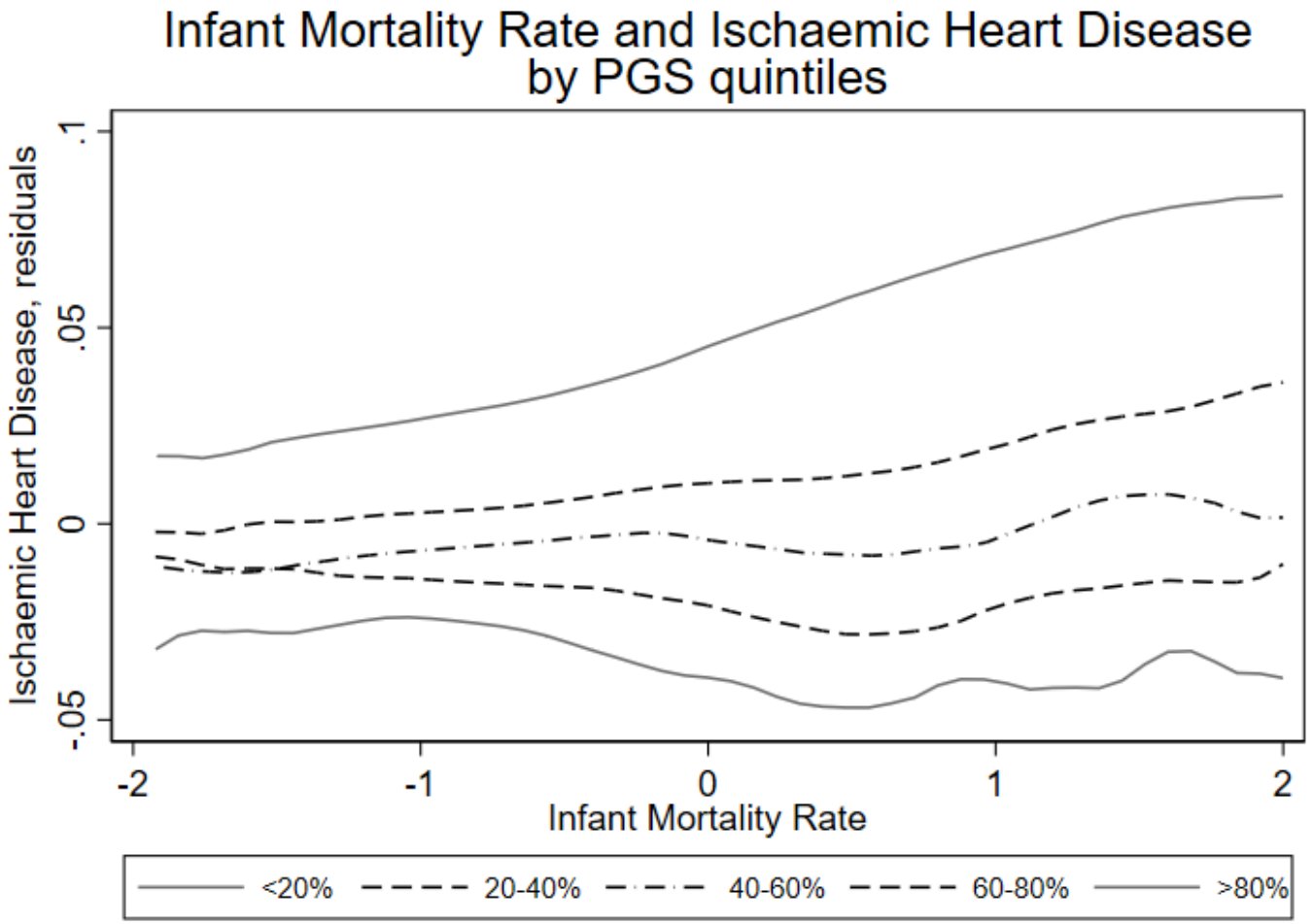

Terciles of BMI PGI and the 1972 ROSLA which raised school leaving age to age 16 years.

# Rietveld et al. (in progress)



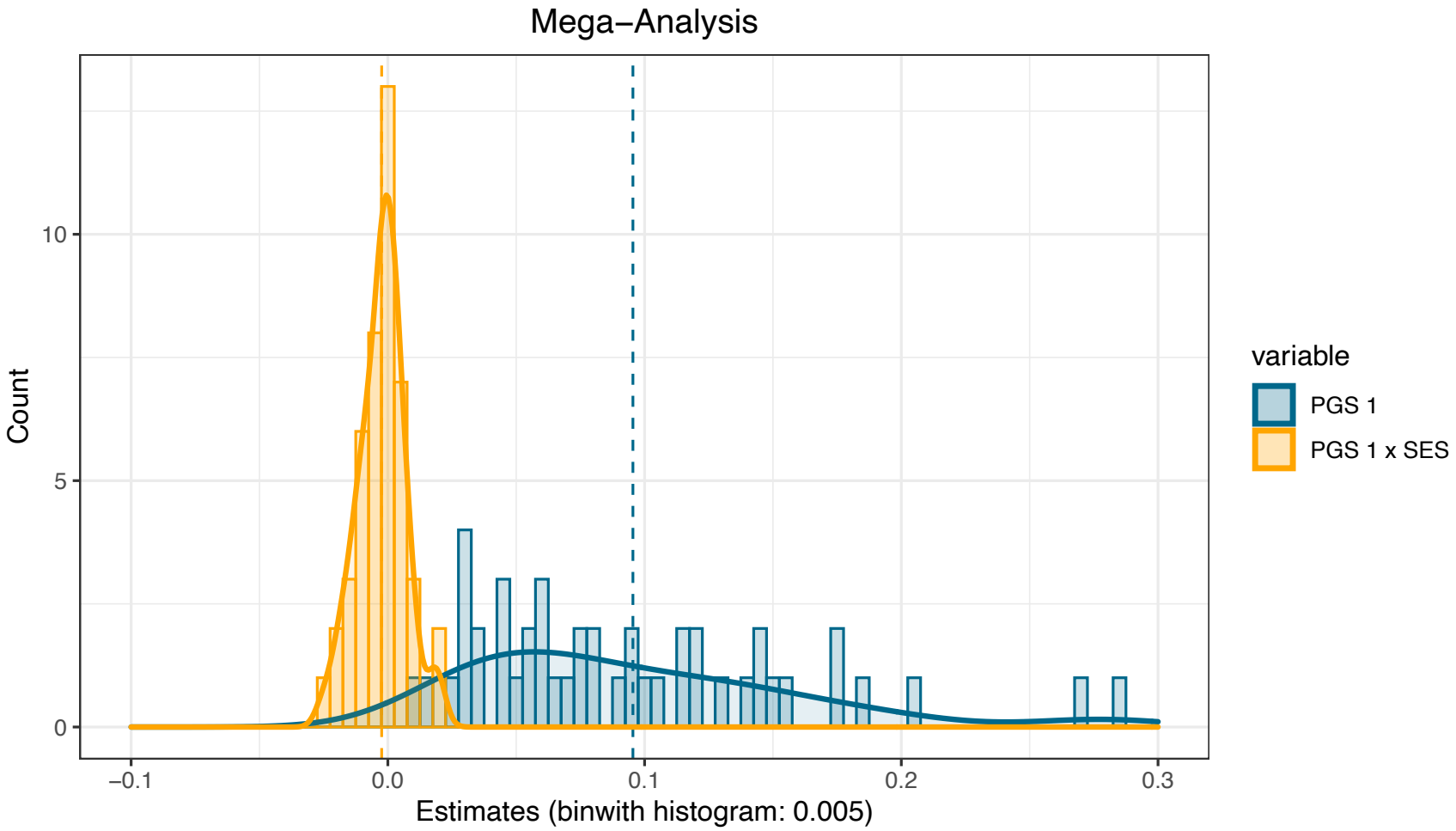

Terciles of EA PGS (EA4) and the 1972 ROSLA which raised school leaving age to age 16 years.

# Baker et al. (in progress)




Quintiles of IHD PGS by Infant Mortality Rate in the year and district of birth.

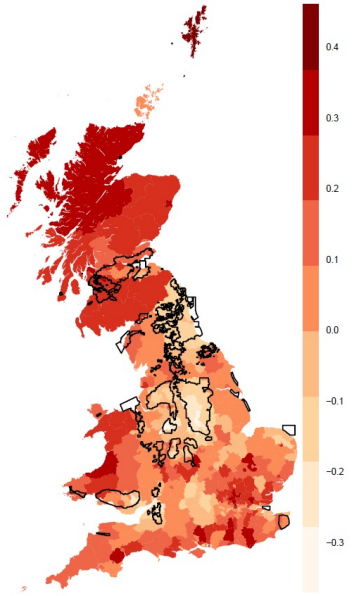
# Biroli et al. (in progress)



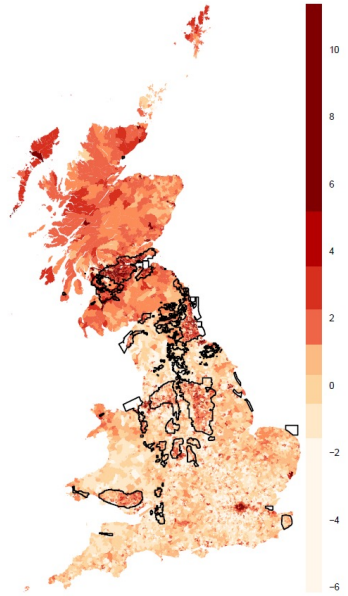

Meta analysis of PGI by childhood (parental) SES for 45 traits in three datasets

# Abdellaoui et al. (2019)

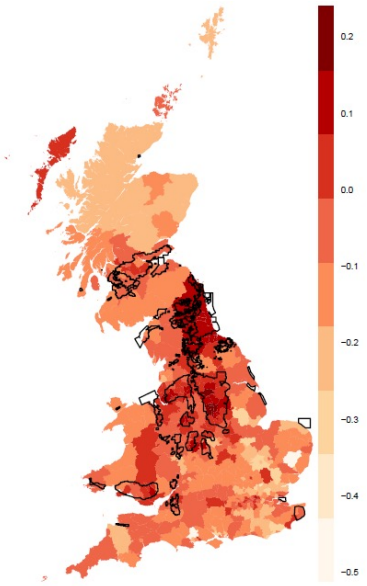
black lines = coal regions



Educational Attainment Polygenic Score

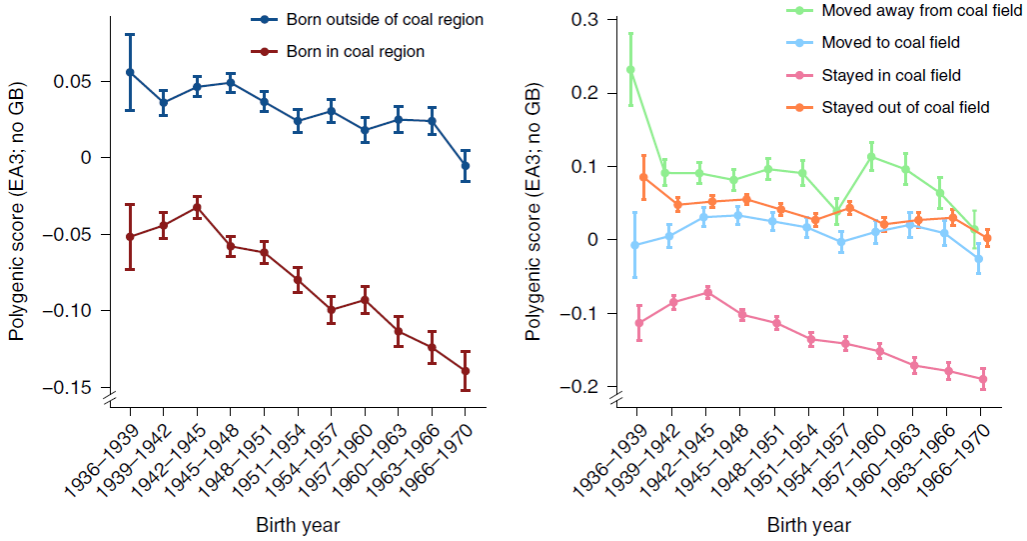


Townsend Index (measure of regional **SES**)



Overall Health

Educational Attainment Polygenic Score




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*]

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# How can results be used?

- **Clarify misunderstandings**
  i. Illustrate limits of a deterministic view of genetics
- **Inform debate on "fairness" of inequality**
  i. EOp framework considers "effort" to be rewarded
  ii. What does that mean with two lotteries of life (G and family)
- **Compensate for disadvantages**
  i. e.g., dyslexia
- **Help people make better decisions**
  i. e.g., retirement planning
- **Make better public policies**
  i. based on better understanding of the effects of policies
- **Improve public health**
  i. faster progress in genetic epidemiology by including social-scientific insights and variables
  ii. early intervention based on genetic risks
  iii. personalized medicine

Courtesy Philipp Koellinger

**Exciting young new field of inquiry at the intersection of several disciplines, using new technology. Much needs to be worked out but progress is immensely fast.**

# Thank You!

Nature

Nurture

Family background and behavior

# ESSGN

*European Social Science Genetics Network*