Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

Gaya J. Dowling, Ph.D.
Elizabeth Hoffman, Ph.D.
Kimberly LeBlanc, Ph.D.

May 11, 2021

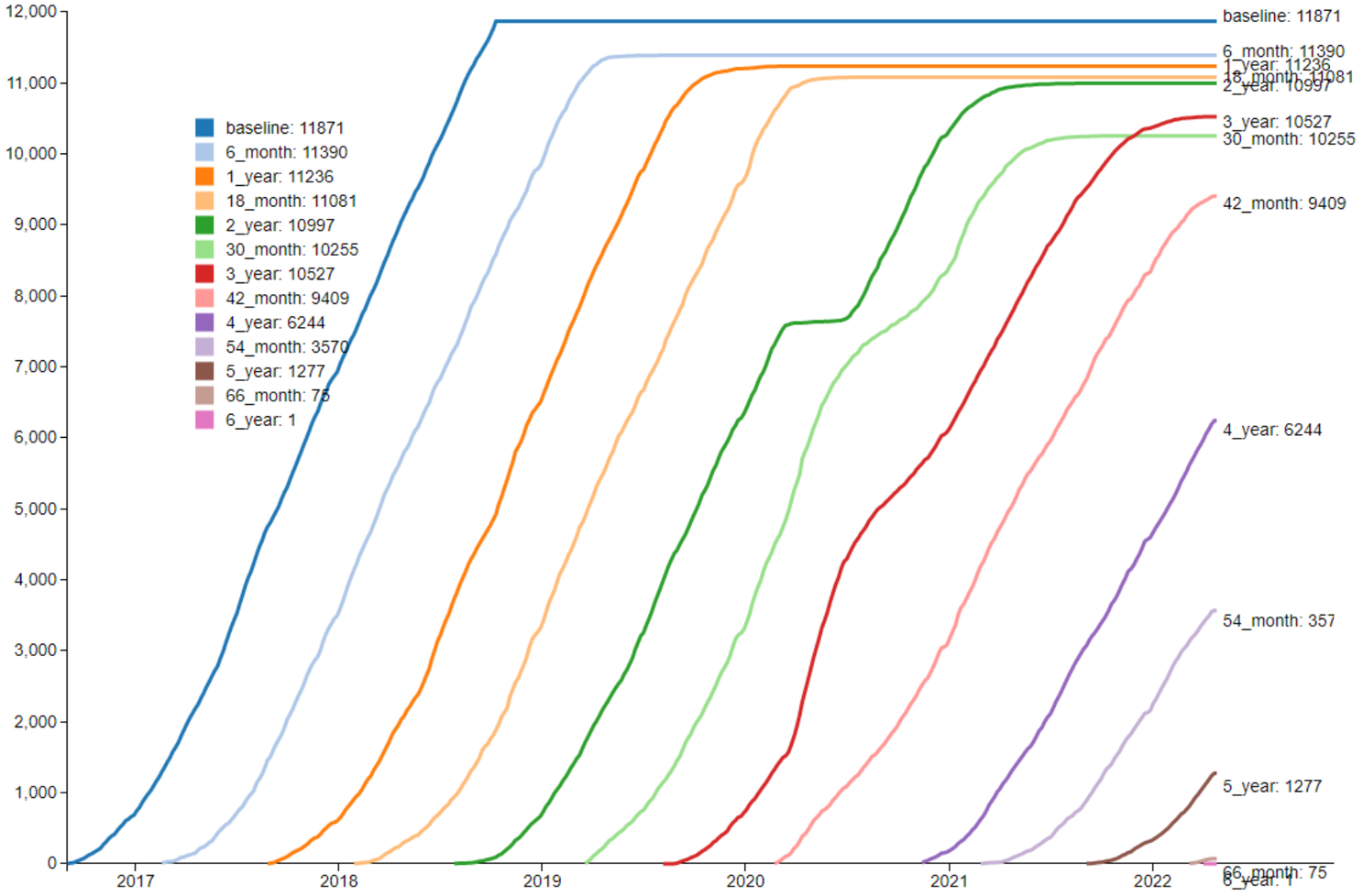
Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

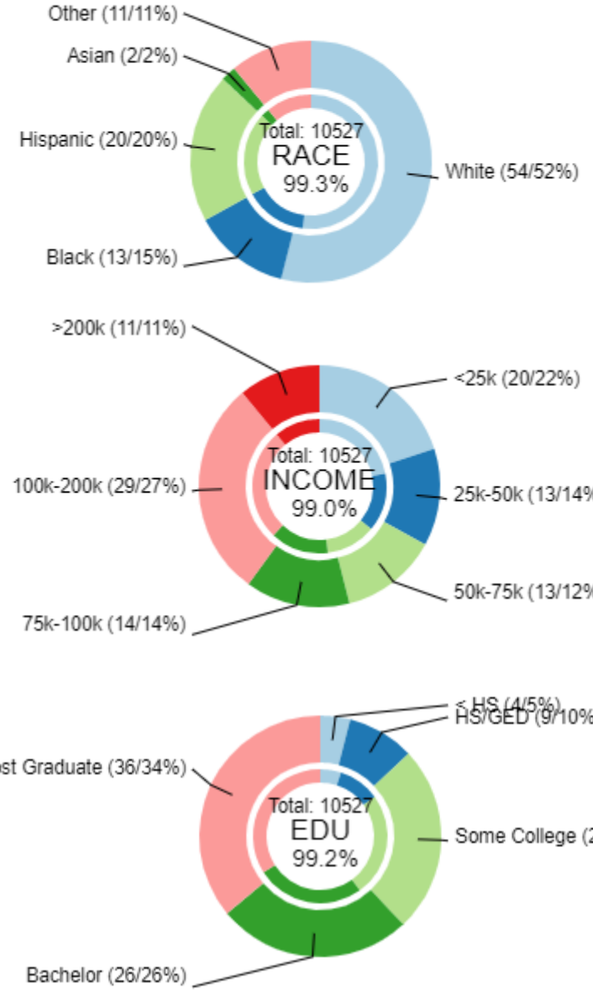
- **Retention and COVID-19 impacts**
- ABCD Justice, Equity, Diversity, and Inclusion (JEDI) Progress
- COVID-19 Data Collection
- Data Sharing and Use
- Recent findings

Retention

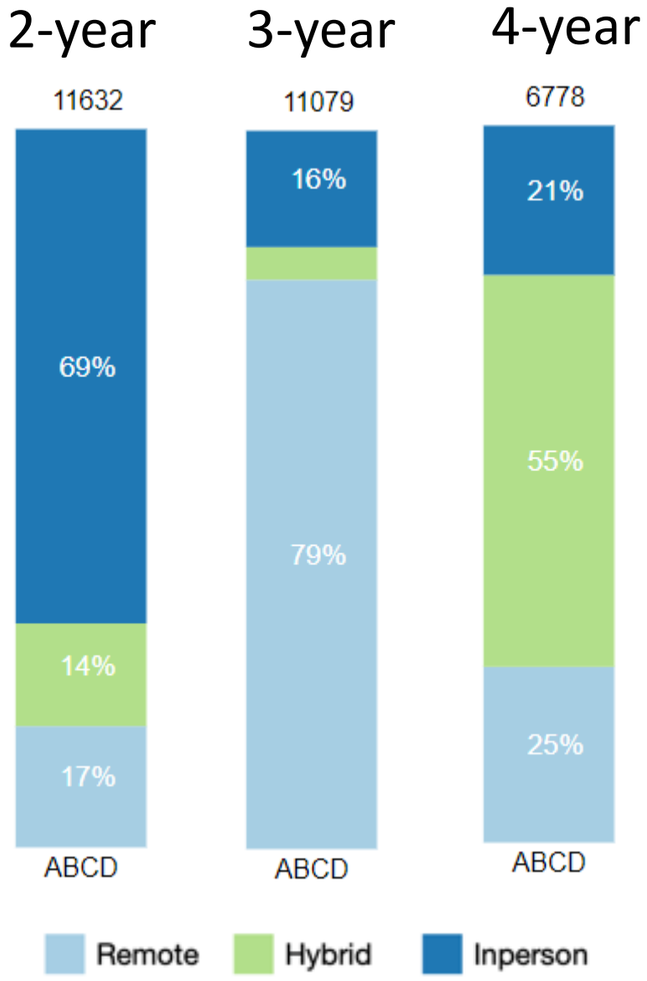
98.1%
Retained



3-year follow-up



Visit Type



Main reasons for Remote Assessments thus far are:

1. MRI contraindications (i.e., families likely to opt for remote assessments due to factors such as braces [and distance])
2. Families not willing to come into the testing center due to COVID concerns.

Questions under investigation:

- What is the impact of hybrid assessments on data quality?
- Is there differential participation in hybrid vs. in-person visits by race/ethnicity, SES?
    - Does this impact data completeness?

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

- Retention and COVID-19 impacts
- **ABCD Justice, Equity, Diversity, and Inclusion (JEDI) Progress**
- COVID-19 Data Collection
- Linked External Data
- Data Sharing and Use
- Recent findings

ABCD Justice, Equity, Diversity, Inclusion Initiative

Kara Bagot

Damien Fair

URM

Bonnie Nagel

Workgroups

Investigators **Trainees** **RAs** **Staff**

1. Diversity Sensitive Methods

2. Diversity in ABCD

3. Responsible use of ABCD diversity data

ABCD Justice, Equity, Diversity, Inclusion Initiative

Leadership and Decision-Making	Search for Associate Director for Equity, Diversity, and Inclusion in Coordinating Center
	Broaden Steering Committee Membership
Diversity-Sensitive Methods	Removed/changed wording of questions/scripts
	Training in culturally-sensitive hair collection
Scientific Workforce Diversity	Scientific Training in Addiction Research Techniques (START) Pilot Program for historically underrepresented/underserved scholars to increase access to the rich ABCD dataset by providing hands-on instruction and mentorship.
Responsible Data Use	Psychological Sciences Paper – Responsible Use of Open-Access Developmental Data: The ABCD Study

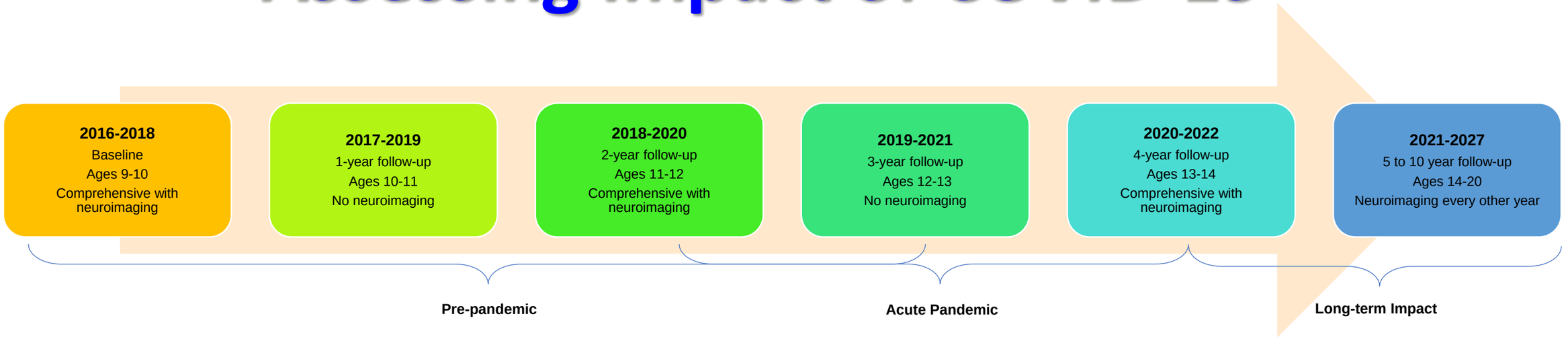
START

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

- Retention and COVID-19 impacts
- ABCD Justice, Equity, Diversity, and Inclusion (JEDI) Progress
- **COVID-19 Data Collection**
- Linked External Data
- Data Sharing and Use
- Recent findings

Assessing Impact of COVID-19



Design

- Questionnaires (May, June, Aug, Oct, Dec 2020) sent to all participants
- FitBit extension - Pre-post data on activity, sleep, heart rate
- Map variation in community impact to correlate with questionnaire data. Examples of existing datasets:
  - Prevalence relative to population density
  - Timing of implementation of state/local policies
  - Social distancing based on cell phone movement
  - Changes in unemployment

Domains covered in the ABCD COVID-19 questionnaire

	Youth	Parent
Family Situation: home composition, economic impact, food, illness, parent support	X	X
Youth's Schooling: quality, quantity, methods, and supervision	X	X
Youth's Routine: sleep and physical activity	X	X
Relationships: friends and family	X	
Attitudes & Adherence: COVID-19 public health directives	X	X
Mental Health & Stress: depression, anxiety, worry, post-traumatic stress	X	X
Substance Use: vaping of nicotine and cannabis, alcohol use, other intoxicant use	X	X
Screen Media Use: for school, socializing, other reasons	X	X
Media/News Exposure: to COVID-19	X	X
Youth's COVID-19 symptoms, diagnosis, and testing		X

Assessing Impact of COVID-19

Mental Health

Journal of Adolescent Health
Volume 70, Issue 3, March 2022, Pages 387-395

The Pandemic's Toll on Young Adolescents: Prevention and Intervention Targets to Preserve Their Mental Health

JAMA Psychiatry

Association of Social Determinants of Health and Vaccinations With Child Mental Health During the COVID-19 Pandemic in the US

Substance Use

Journal of Adolescent Health
Volume 69, Issue 3, September 2021, Pages 390-397

Early Adolescent Substance Use Before and During the COVID-19 Pandemic: A Longitudinal Survey in the ABCD Study Cohort

Marginalized Communities

JAMA Psychiatry

Multivariate, Transgenerational Associations of the COVID-19 Pandemic Across Minoritized and Marginalized Communities

frontiers in Public Health

Resilience to COVID-19: Socioeconomic Disadvantage Associated With Positive Caregiver–Youth Communication and Youth Preventative Actions

Physical Activity

Biological Psychiatry: Global Open Science

Longitudinal Impact of Childhood Adversity on Early Adolescent Mental Health During the COVID-19 Pandemic in the ABCD Study Cohort: Does Race or Ethnicity Moderate Findings?

BMC Public Health

Parent-adolescent agreement in reported moderate-to-vigorous intensity physical activity during the COVID-19 pandemic

Preventive Medicine Reports
Volume 25, February 2022, 101685

Moderate-to-vigorous intensity physical activity among adolescents in the USA during the COVID-19 pandemic

Screen Time

JAMA Pediatrics

Screen Time Use Among US Adolescents During the COVID-19 Pandemic
Findings From the Adolescent Brain Cognitive Development (ABCD) Study

ACADEMIC PEDIATRICS
The Official Journal of the Academic Pediatric Association

Parent-Adolescent Discrepancies in Adolescent Recreational Screen Time Reporting During the Coronavirus Disease 2019 Pandemic

Learning

frontiers in Education

Negative Impacts of Pandemic Induced At-Home Remote Learning Can Be Mitigated by Parental Involvement

Journal of Attention Disorders

Impact of COVID-19 on Youth With ADHD: Predictors and Moderators of Response to Pandemic Restrictions on Daily Life

Long COVID – Researching COVID to Enhance Recovery

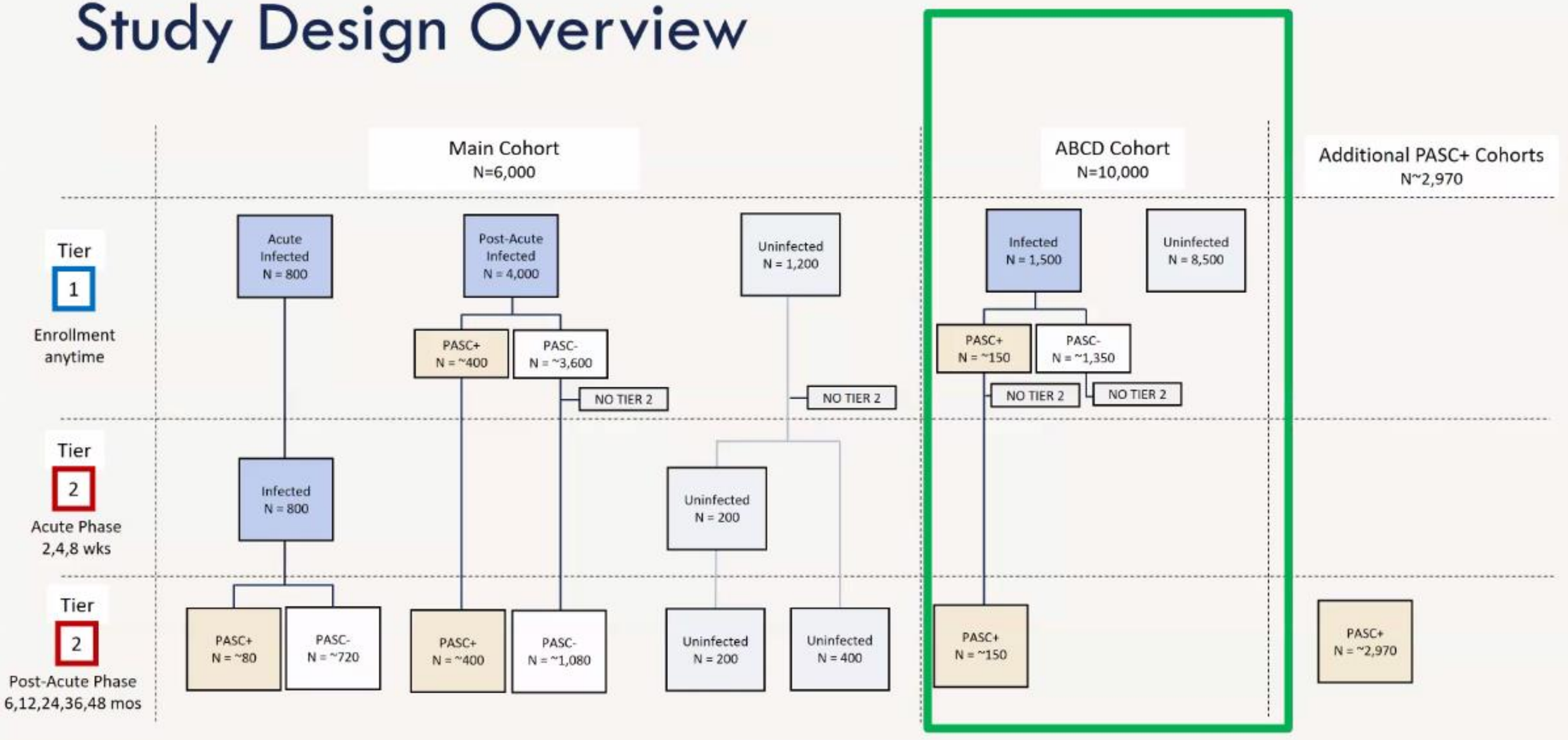
Pediatric Cohort Specific Aims

Aim 1. Characterize the incidence, prevalence, and long-term sequelae, including clinical and biological features, severity, and distinct sub-phenotypes, following SARS-CoV-2 infection (index date).

Aim 2. Characterize the clinical course and recovery of acute and post-acute sequelae over time and determine associated risk factors for Long COVID among SARS-CoV-2 infected individuals compared to uninfected individuals.

Aim 3. Define the pathophysiology and biologic mechanisms of post-acute sequelae, including direct and indirect causal effects of SARS-CoV-2 infection, and potential modifiers (e.g., sex, age and race/ethnicity).

Study Design Overview



RECOVER
Researching COVID to Enhance Recovery

ABCD (21 sites): 10 of these sites are the same as other main cohort sites (or in the same area)

Researching COVID to Enhance Recovery (RECOVER)

ABCD-RECOVER

With better characterized infection status, i.e., COVID antibody results; Long COVID symptom survey, the ABCD Study has potential to address:

- Prevalence of infection and Long COVID in adolescents, and within different communities and subgroups
- Pre-infection risk and resilience factors that modify the ‘infection-related’ outcomes.
- Isolate infection effects vs pre-pandemic and general pandemic impacts
- In-depth brain, cognitive, and mental health phenotyping
- Long-term outcomes given ABCD will follow cohort for another 6 years

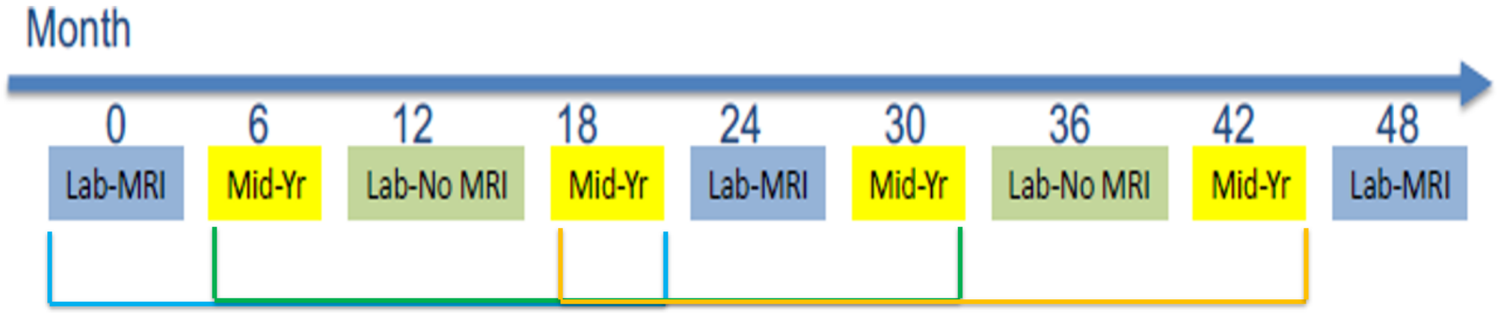
Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

- Retention and COVID-19 impacts
- ABCD Justice, Equity, Diversity, and Inclusion (JEDI) Progress
- COVID-19 Data Collection
- **Data Sharing and Use**
- Recent findings

ABCD Annual Data Releases

Curated data are released annually via the NIMH Data Archive (https://nda.nih.gov/abcd)



2019 Data Release 2.0
- Full cohort baseline (with imaging)
- Hurricane Irma substudy
- Fitbit data
- Interim:
  - 6-month
  - 18-month
  - 1-year

2020 Data Release 3.0
- Full cohort 1-year follow-up
- Full cohort 6-month follow-up
- Interim:
  - 18-month
  - 30-month
  - 2-year (imaging)

2021 Data Release 4.0
- Full cohort 2-year follow-up (with imaging)
- Full cohort 18-month follow-up
- Interim:
  - 30-month
  - 42-month
  - 3-year

AVAILABLE NOW

ABCD COVID-19 Supplemental Data Release is now available

This release consists of survey responses from ABCD families about the impact of the pandemic on their lives. Visit the NIMH Data Archive for more information.

Welcome to the NIMH Data Archive

https://nda.nih.gov/abcd

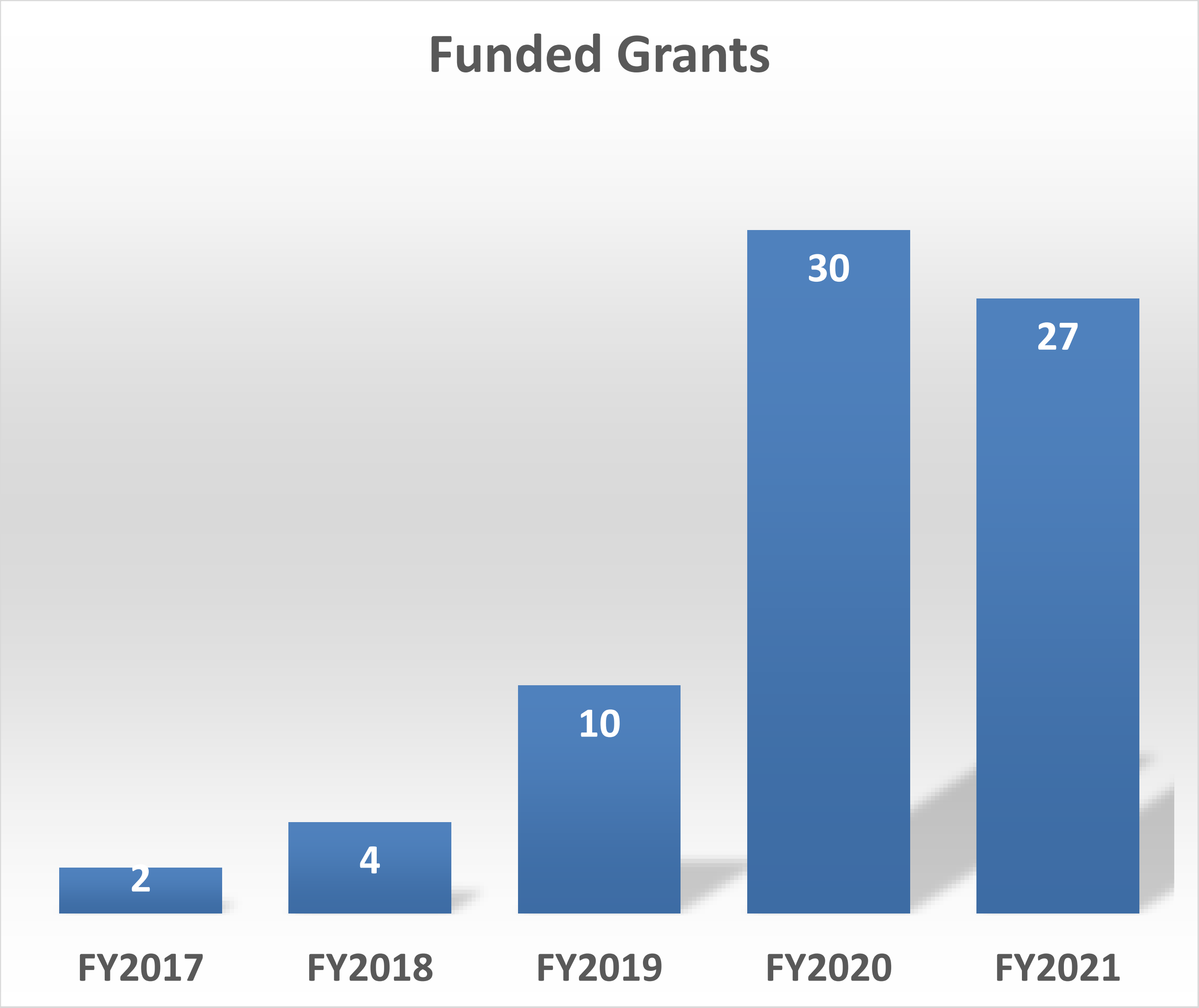
RFA-DA-22-037 – Accelerating the Pace of Drug Abuse Research Using Existing Data (R01 Clinical Trial Optional)

RFA-DA-22-038 – Accelerating the Pace of Drug Abuse Research Using Existing Data (R01 Clinical Trial Optional)

PAR-22-137 – Accelerating the Pace of Child Health Research Using Existing Data from the Adolescent Brain Cognitive Development (ABCD) Study (R01 Clinical Trial Not Allowed)

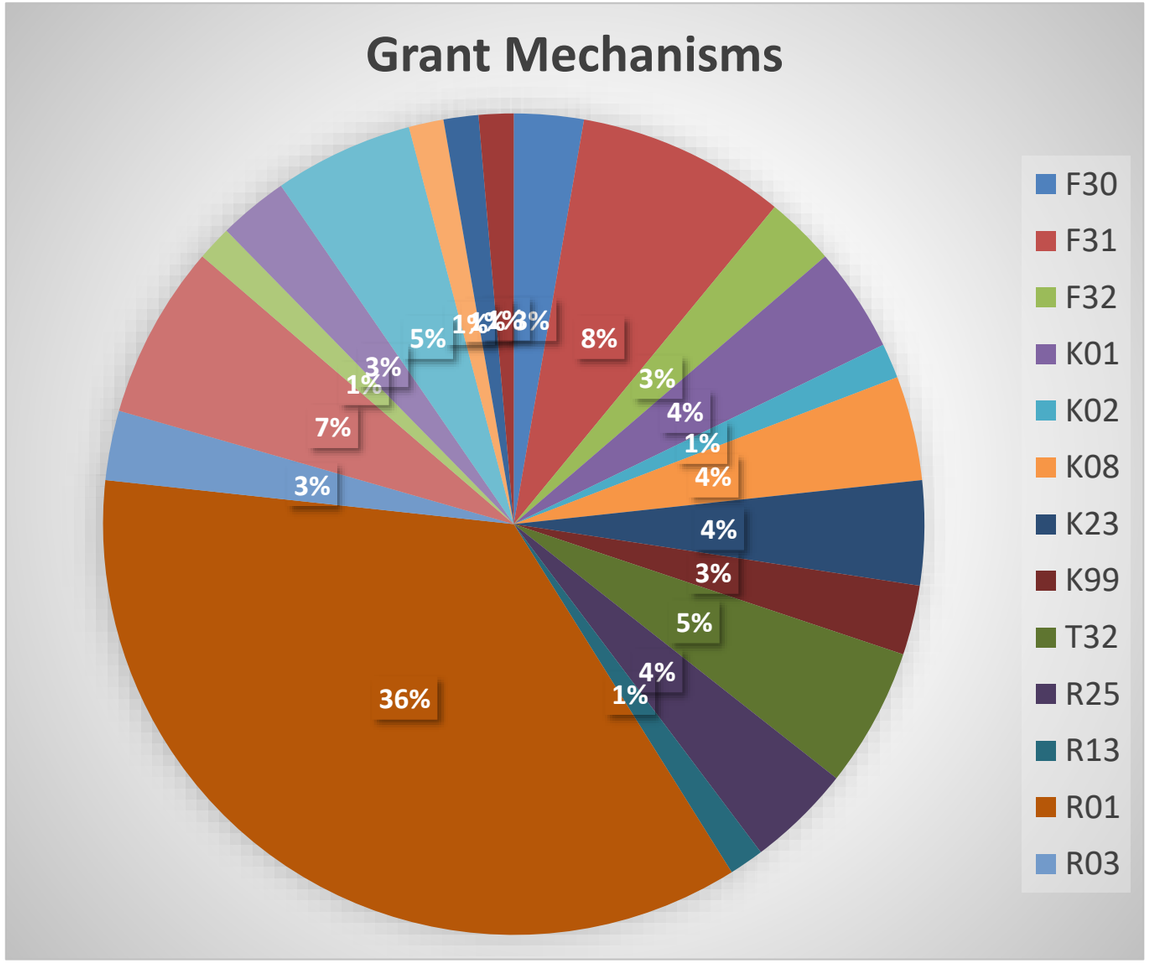
PAR-22-138 – Accelerating the Pace of Child Health Research Using Existing Data from the Adolescent Brain Cognitive Development (ABCD) Study (R21-Clinical Trial Not Allowed)

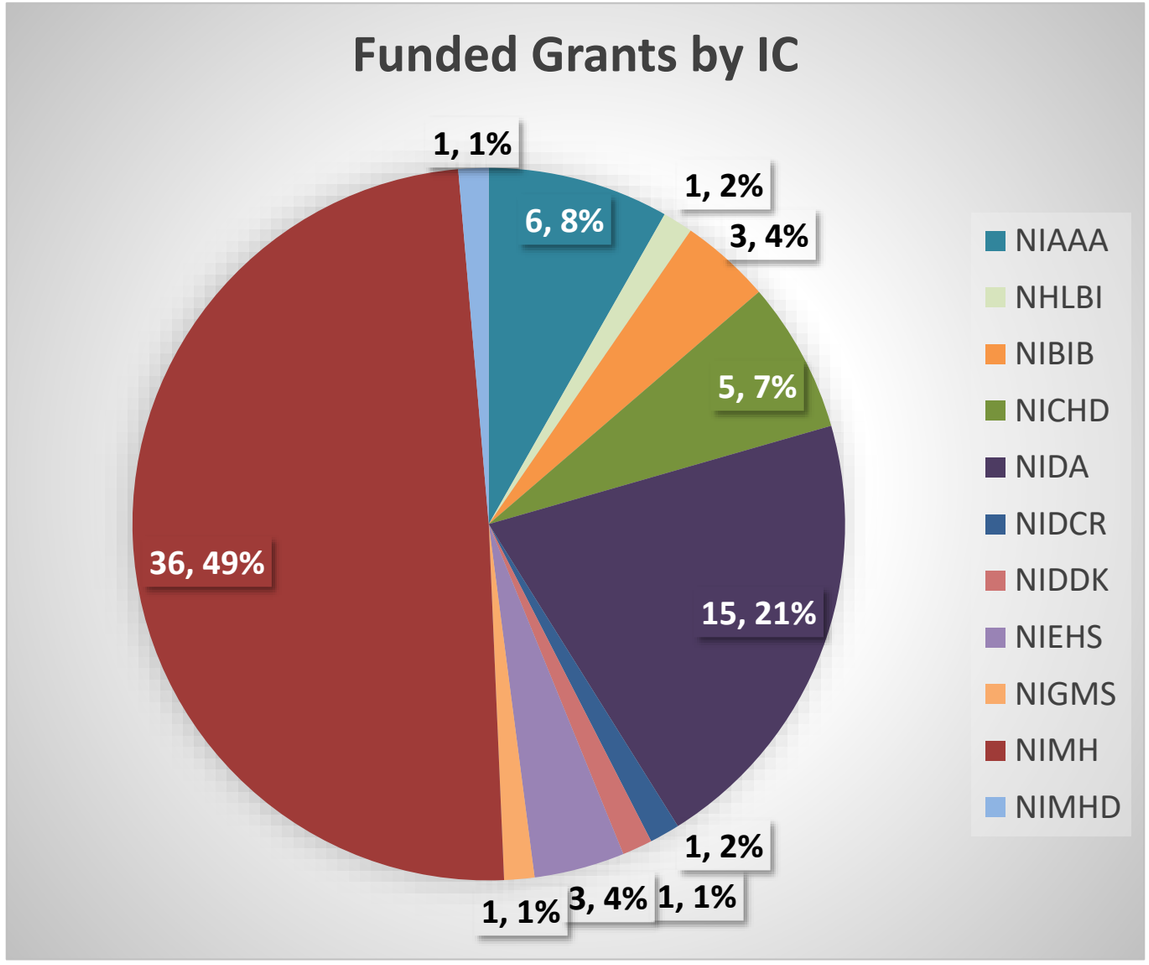
Funded Grants Leveraging ABCD Data



N=73 (as of December 2021)

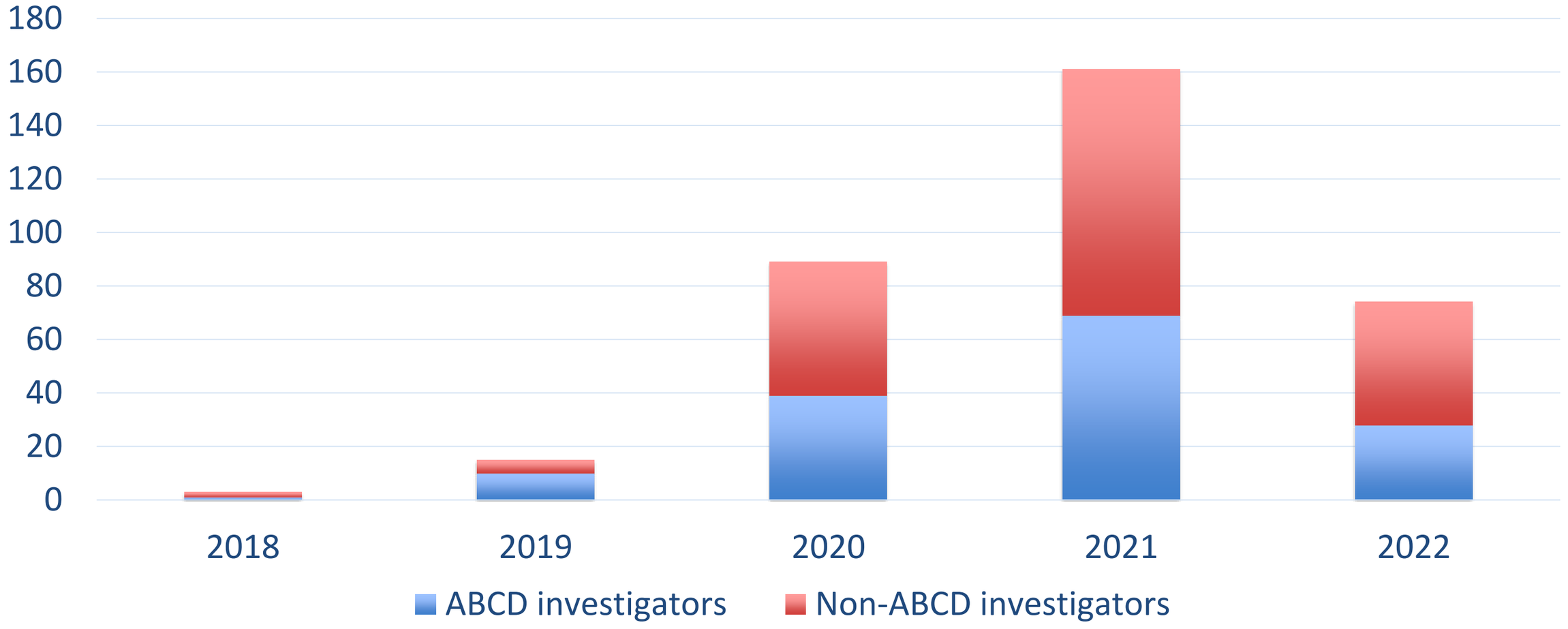
Funded Grants Leveraging ABCD Data





N=73

ABCD Publications



N=342 (as of 5/3/22)

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

ABCD Research Questions

Methodology/Tools Development

Additional Research Questions

Using ABCD Data with Other Datasets

Mechanistic Studies

Diagnostic/ Intervention Development

Policies/Practices

Reproducible brain-wide association studies require thousands of individuals

Marek et al. (2022), *Nature*

Cross-ethnicity/race generalization failure of behavioral prediction from resting-state functional connectivity

Li et al. (2022), *Science Advances*

Adolescent Brain Cognitive Development®

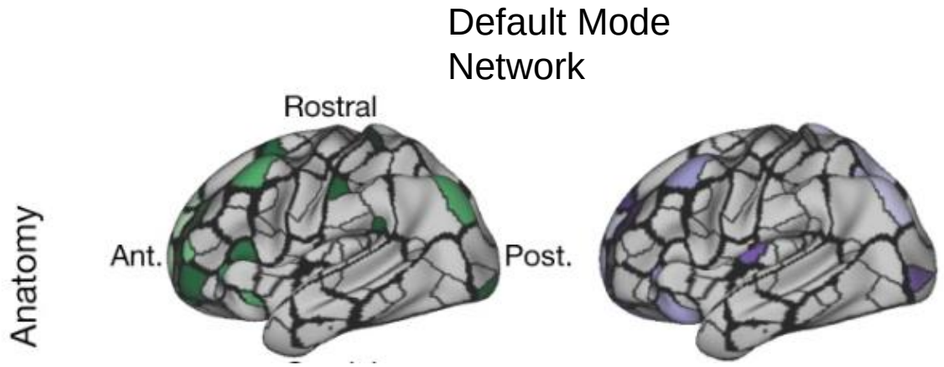
Teen Brains. Today's Science. Brighter Future.

Implications of Small Samples in Brain-Wide Association Studies (BWAS)

- Historical reliance on small sample sizes in neuroimaging studies may contribute to replication failures in Brain Wide Association Studies (linking individual variability in brain to variation in behavior)
- Previous BWAS studies in the 10s, 100s of participants have likely been underpowered with irreproducible and inflated associations
- Inflated associations are exacerbated by publication bias (biasing large effects)

Design & Analysis

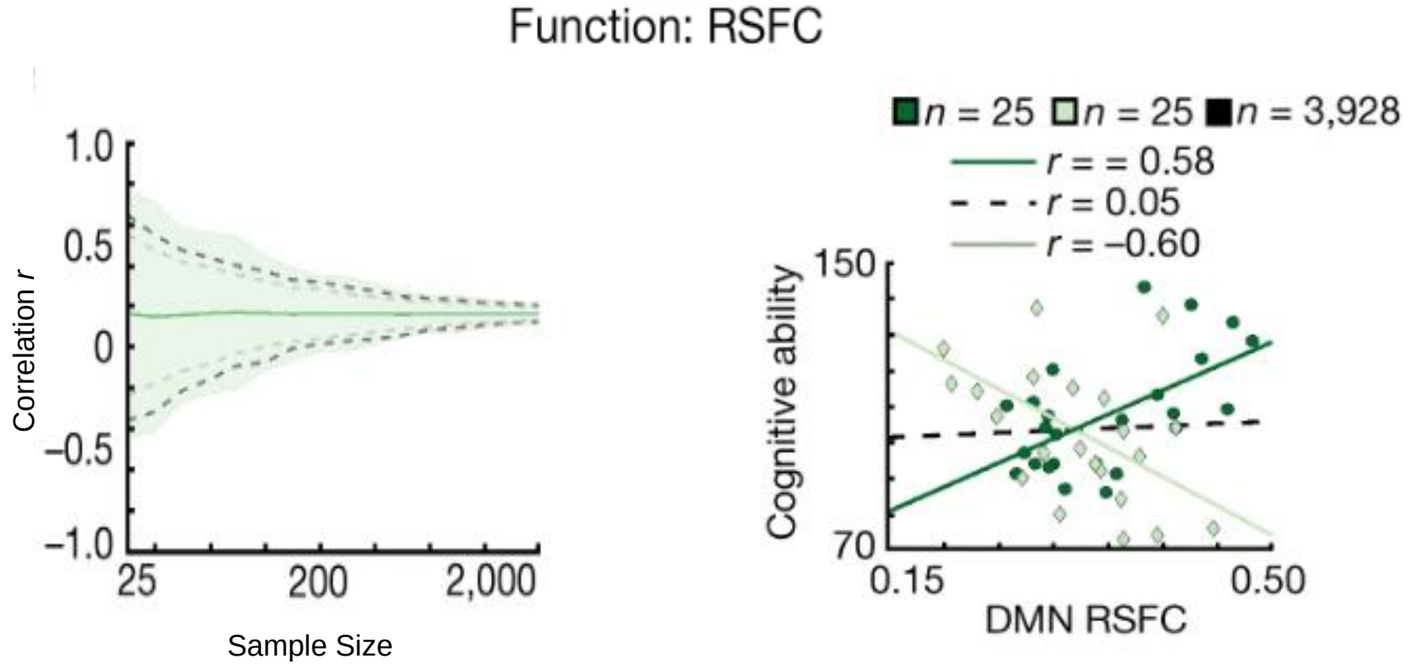
- ❑ 50,000 individuals from the ABCD Study®, UK Biobank, and Human Connectome Study (youth through adulthood)
- ❑ Began with ABCD and used HCP and UKB to verify univariate effect size distributions
- ❑ Examined associations between brain (cortical thickness; resting state functional connectivity) and behavioral phenotypes (cognitive ability; psychopathology)
- ❑ Performed billions of univariate and multivariate analyses to evaluate BWAS effect sizes and reproducibility as a function of sample size, from n = 25 to n = 32,572



Phenotypes
- NIH Toolbox measures
- Child Behavior Checklist subscales

Results

I. Less variability in effect sizes with increasing sample size in univariate BWAS



II. Stronger multivariate out-of-sample associations compared to univariate

III. Greater concordance between in-sample and out-of-sample replicates with larger Ns

Large sample sizes are needed for accurate estimation of effects in BWAS

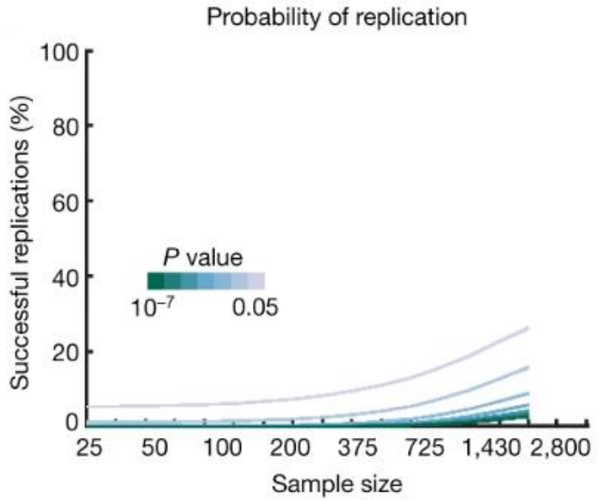
This does not mean that small n neuroimaging is not valuable for other paradigms (e.g., within-person designs)

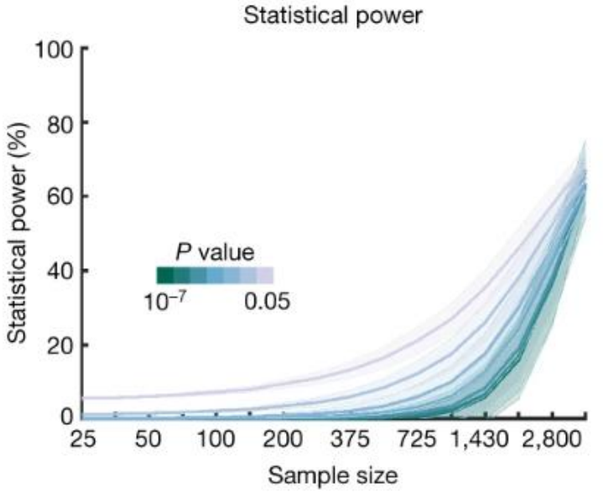
Nico Dosenbach
@ndosenbach

Title: This paper is about BWAS, replicability and sample sizes

Abstract:

1. Neuroimaging is great; lesion mapping structural MRI and classical task fMRI replicate well.
2. BWAS = associations between inter-individual differences in brain structure or function and complex cognitive or mental health phenotypes, has not been replicating as well
3. Hypothesis: Maybe BWAS needs larger samples than classical structural MRI/task fMRI
4. Used ~ 50K subs and found that BWAS only replicates well with samples in the thousands (hypothesis confirmed)
5. fMRI > structural MRI; NIH toolbox > CBCL; multivariate > univariate
6. Reminder: classical fMRI & lesion studies ≠ BWAS





Reproducible brain-wide association studies require thousands of individuals

Marek et al. (2022), *Nature*

Cross-ethnicity/race generalization failure of behavioral prediction from resting-state functional connectivity

Li et al. (2022), *Science Advances*

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

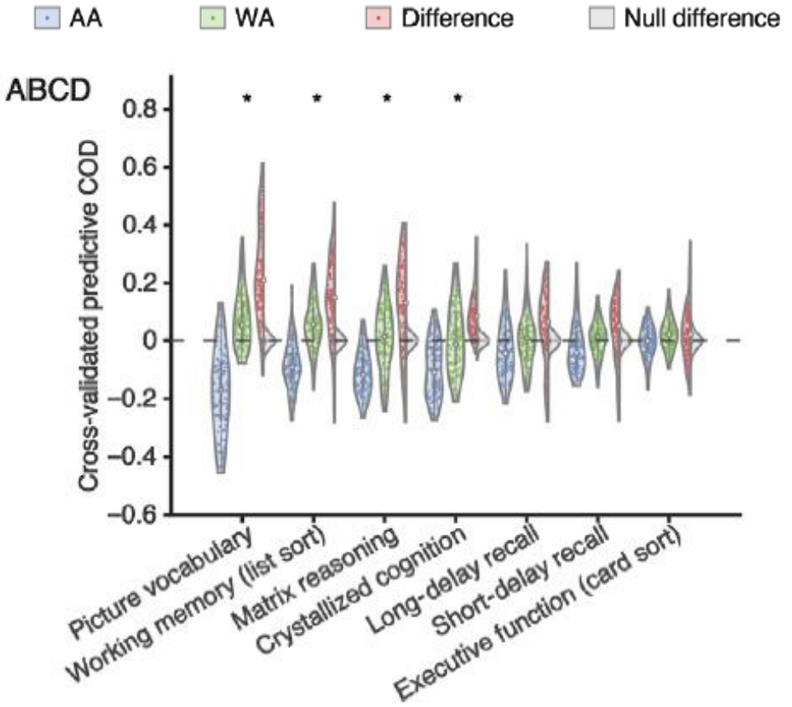
Cross-ethnicity/race generalization failure of behavioral prediction from resting-state functional connectivity

- Predictive models using machine learning are widely used in population neuroscience and precision medicine, but concerns have been raised about the validity of these approaches for specific populations.
- Li et al. investigated algorithmic fairness using data from the Human Connectome Project and the ABCD Study®.

Predictive models of behavioral phenotypes from resting-state functional connectivity (RSFC) data do not generalize across populations

Biases skew predictions of behavior from neuroimaging

- Matched AA and WA on demographics and behavioral performance
- Compared prediction accuracy between WA and AA, when models were trained on the entire sample. *This mimics the dominant approach currently taken in the field*
- In general, given equivalent actual scores on a particular measure, prediction errors in AA were larger than in WA
- For example, cognition (picture vocabulary, working memory, matrix reasoning, crystallized cognition) was more poorly predicted in AA than WA



Biases skew predictions of behavior from neuroimaging

- To obtain a more valid predictive model, training was performed separately on WA and AA using data from ABCD
- For the model trained on AA
  - 8/36 measures showed greater prediction accuracy for AA than WA
  - 19/36 measures still showed greater prediction accuracy for WA than AA

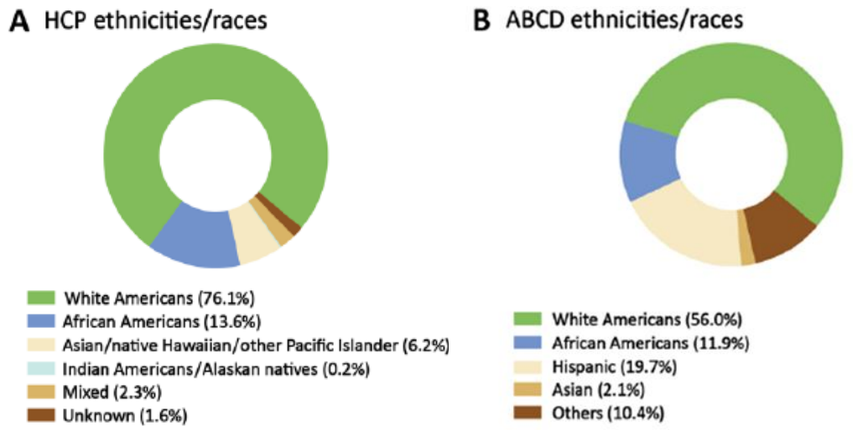
- In contrast, for the model trained only on WA, there was greater prediction accuracy in AA compared to WA for two measures

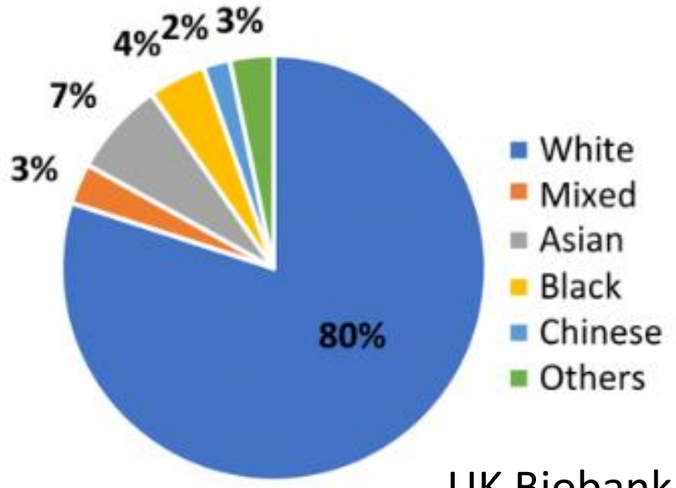
Training the model specifically on AA increased prediction accuracy but not completely.

Biases skew predictions of behavior from neuroimaging

- Biased prediction of behavior and neurocognition was observed when comparing predictive models for WA and AA using a standard training approach
- The difference between the two groups was partly related to the dominance of WA in the datasets
- We need more data from underrepresented groups in US and globally

Taken together, both papers demonstrate how ABCD can be used to expose limitations in widely adopted methodologies and analytic approaches and inform considerations for the future.





UK Biobank

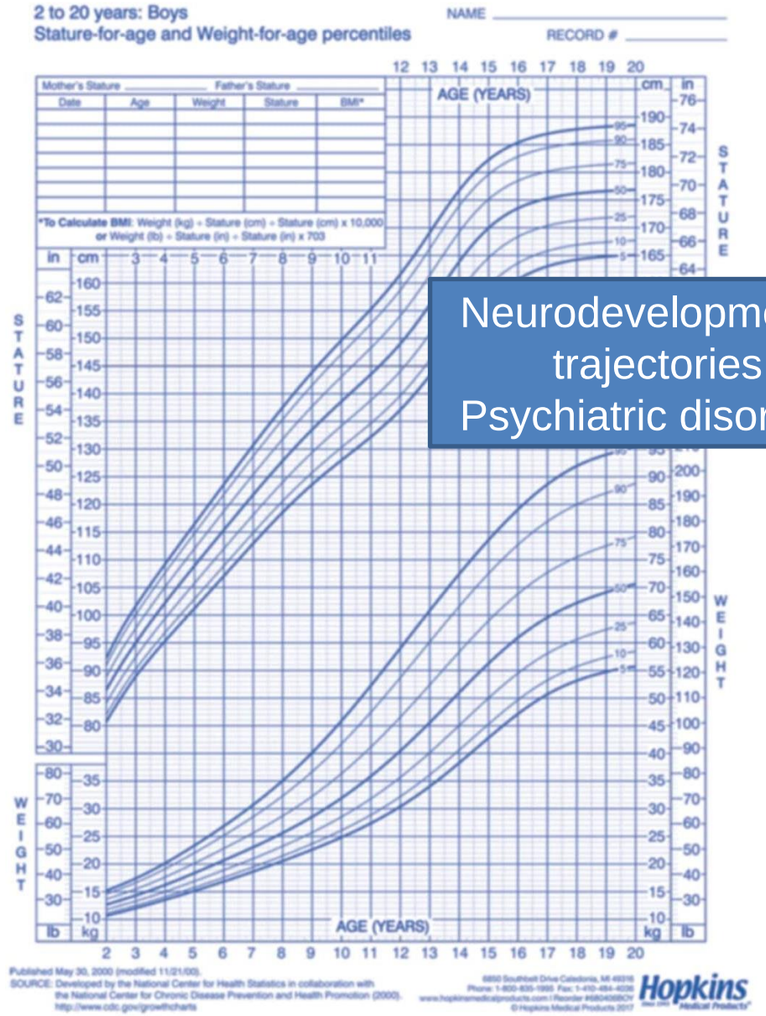
Brain charts for the human lifespan

R. A. I. Bethlehem et al. (2022) *Nature*

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

No reference standards currently exist for brain development

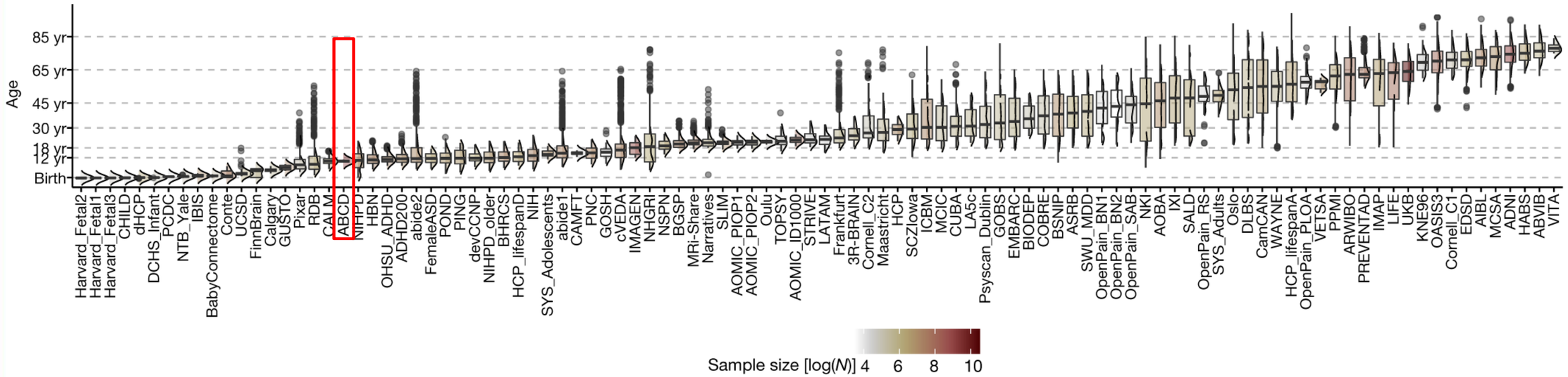


Neurodevelopmental trajectories
Psychiatric disorders

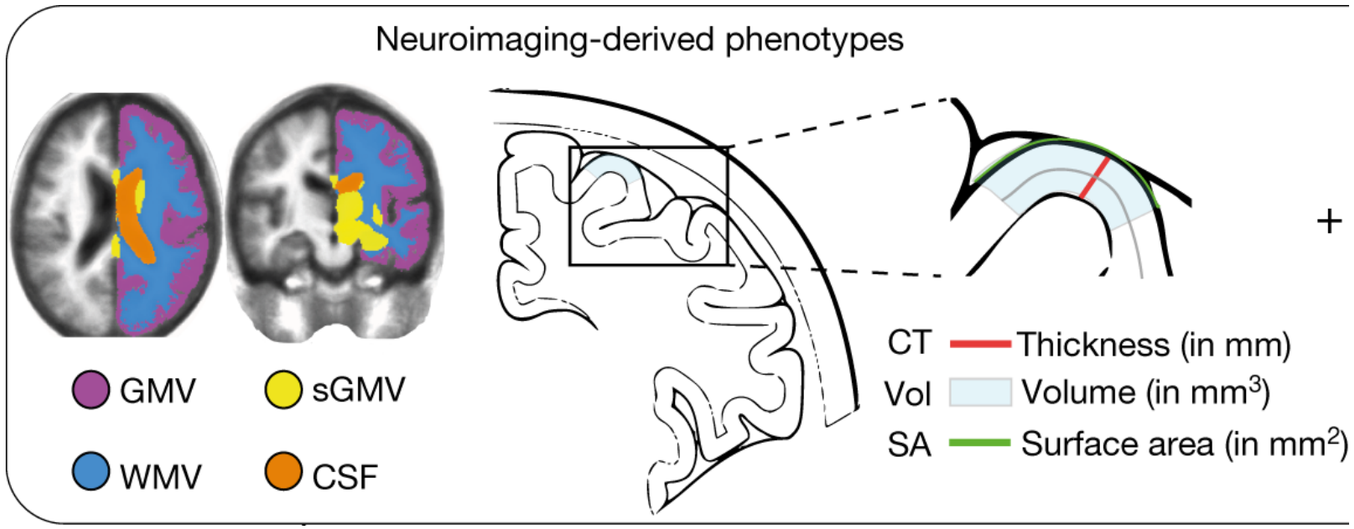
Neurodegenerative disorders

- Challenge: neuroimaging data is highly sensitive to variation in scanner platforms and sequences, data quality control, pre-processing and statistical analysis
- Large scale datasets (like ABCD) and recent advances in neuroimaging and statistics have now made it possible
- The ABCD Study aspired to contribute to neurodevelopmental trajectories from its inception

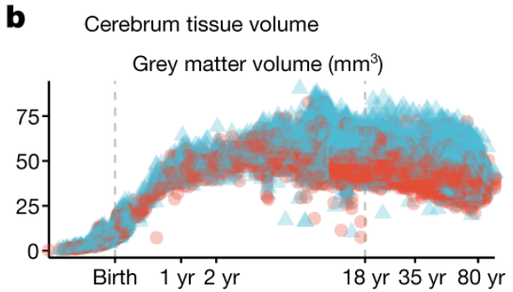
Mapping normative brain growth

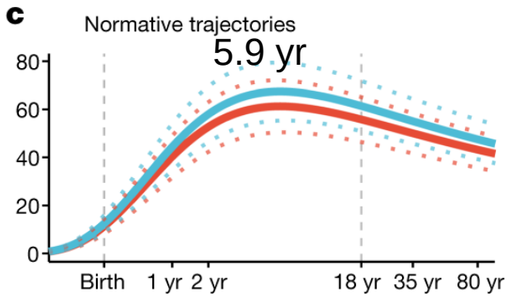


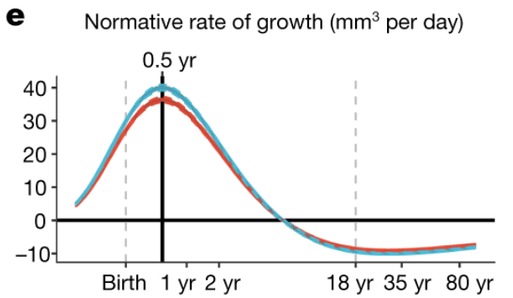
- 123,984 MRI scans, across more than 100 primary studies, from 101,457 human participants between 115 days post-conception to 100 years of age



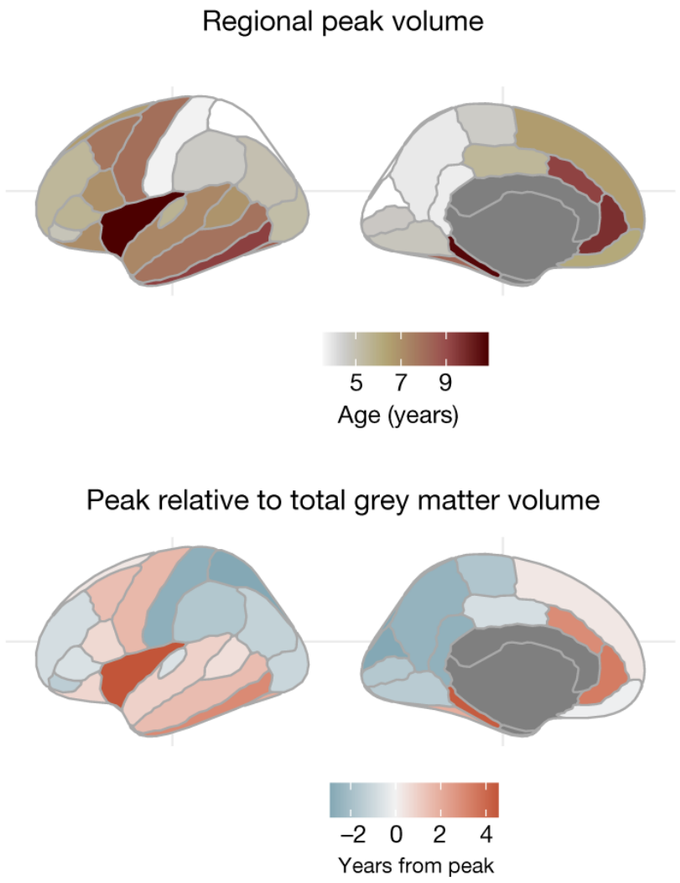
Human brain charts





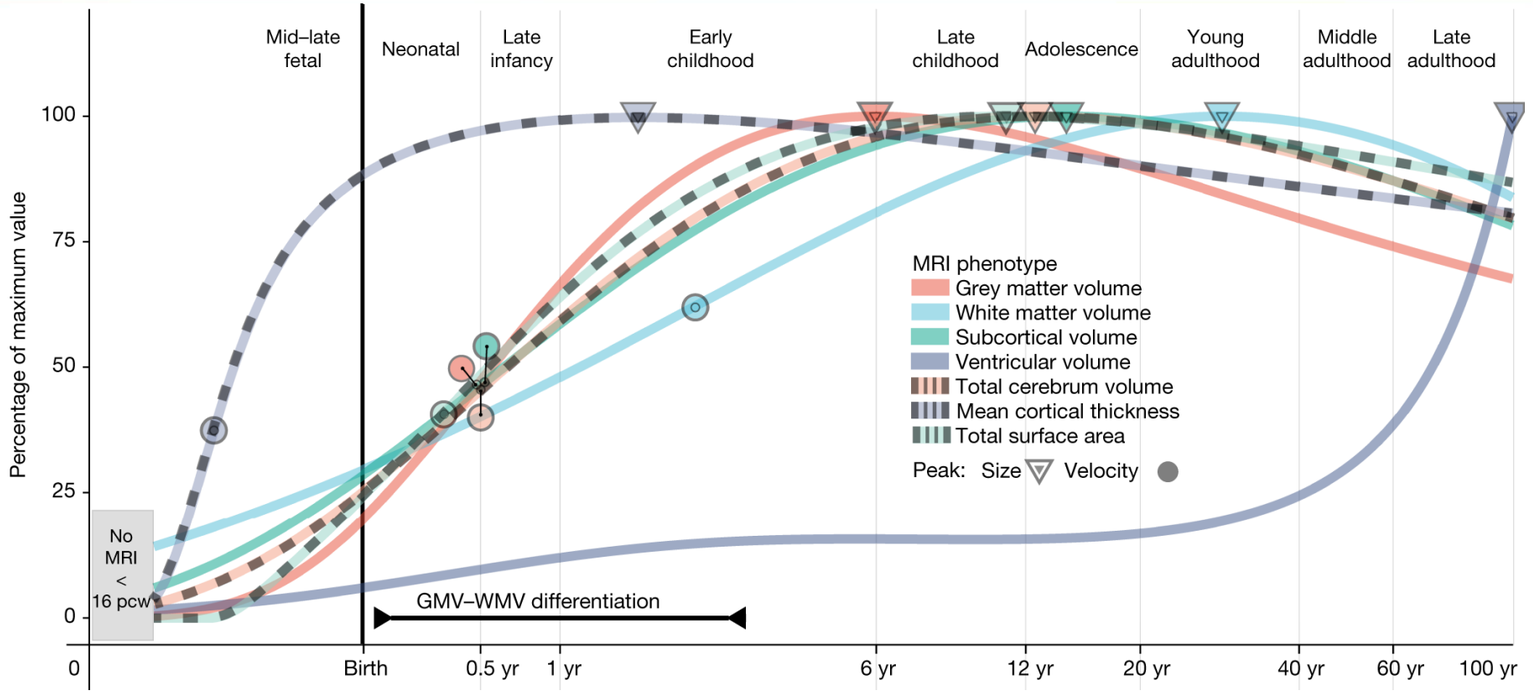


Regional phenotypes

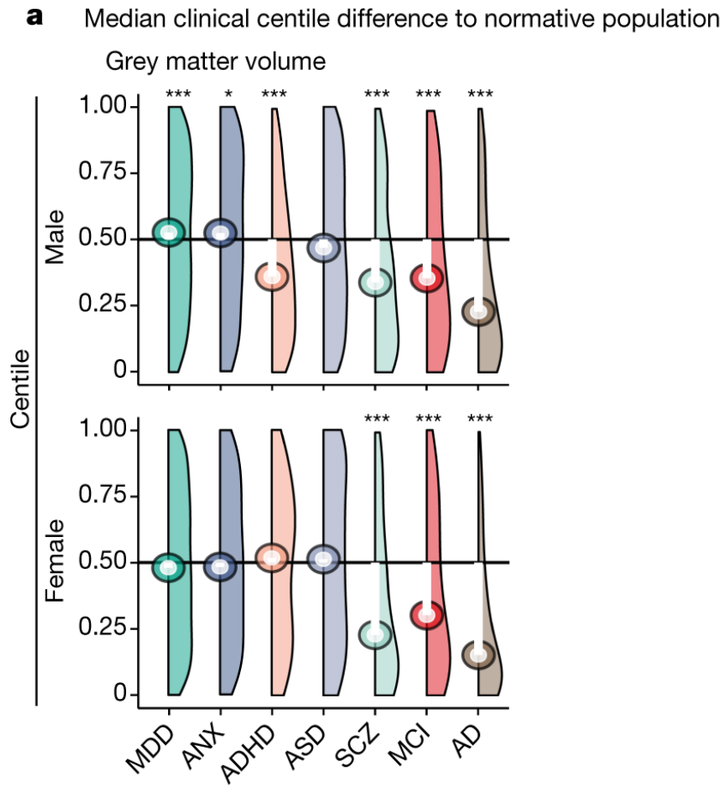


- Primary sensory regions reached peak volume earliest and showed faster post-peak declines
- Fronto-temporal association cortical areas peaked later and showed slower post-peak declines
- This spatial pattern recapitulated a gradient from sensory-to-association cortex that has been previously associated with multiple aspects of brain structure and function

Neurodevelopmental Milestones



Case–control differences of centile scores



- Largest deviations for Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI), and Schizophrenia (SCZ)
- Sex specific effects for SCZ (female) and ADHD (male)

Conclusions

- Proof of principle for:
  - Defining normative trajectories of sex-stratified, age-related change in multiple MRI-derived phenotypes across the lifespan
  - Quantifying neuroanatomical atypicality of brain scans collected across multiple clinical disorders
- Developed an interactive open resource to benchmark brain morphology from any current or future sample of MRI data: http://www.brainchart.io/
- Caveats:
  - Dataset is biased towards European and North American populations and European ancestry groups and higher SES individuals
  - Fetal, neonatal and mid-adulthood (30–40 years of age) groups were under-represented
  - Brain charts are not immediately suitable for clinical use or quantitative diagnosis
- *The present work shows that building normative charts to benchmark individual differences in brain structure is achievable at global scale and over the entire life-course*

Thank you to…

- 10 Federal partner agencies and their staff
- 21 research sites, coordinating center, data analysis informatics and resource center
- Hundreds of investigators and trainees
- **Even more research assistants and staff**
- **And nearly 12,000 participants and their families**

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

ABCDStudy.org

AdolescentBrain@mail.nih.gov