ABCD-ReproNim: An ABCD Course on Reproducible Data Analyses

ABCD: Introduction to Biospecimens in the ABCD Study®

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DEVELOPING LAB

Learning Objectives of this Lecture

ABCD-ReproNim

- Describe the range of biospecimens in the ABCD Study®
- Describe the rationale for collecting each biospecimen in the ABCD Study®
- Summarize the methods of collection & storage for each biospecimen in the ABCD Study®
- Leverage salivary hormones to illustrate complexity of considerations for utilizing biospecimens in your statistical analyses
- Some general Do's and Don'ts when analyzing biospecimen data

Overview of biospecimens in ABCD: Baseline – Year 10?

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Week 6

Biospecimen Samples.

Sample Type	Purpose	Baseline 9–10 yrs #/participant	1 Year Follow-Up 10–11 yrs #/participant	2 Year Follow-Up 11-12 yrs	. . .
Screening for Alcohol & Drugs					
Saliva (onsite Dräger)*	Recent Substance Use	1	1	**1**	
Breath (onsite Breathalyzer)*	Recent Alcohol Use	1	1	**1**	
Hair (Psychemedics[a])**	Substance Use	1	1	**1**	
Urine (NicAlert)**	Recent Tobacco Use	0	1	**1**	
Pubertal Hormones					
Saliva (Salimetrics[b])	Pubertal Hormones	1	1	**1**	
Genomics/Epigenetics					
Saliva (RUCDR[c])	Genetics	1	0		
Blood (RUCDR[c]) (saliva if refuse blood)	Genetics	0***	0	**1**	
Timeline of Exposures					
Baby teeth (Dr. Arora – Mt. Sinai[d])	Environmental Exposures	1	1	**1**	

Uban et al., 2018 *DCN*

Methods of collection: frequency & timing

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Week 6

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1x/person/yr

1x/person ever*

Uban et al., 2018 *DCN*

Extra: Rationale & methods: Screening

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Week 6

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Urine (NicAlert)**	Recent Tobacco Use	0	1	1

- Do not want to assess participant while under influence of substances
- Collect biomarkers of history of use

Uban et al., 2018 *DCN*

Extra: Rationale & methods: Screening w/ saliva

ABCD-ReproNim

The Dräger DrugTest 5000 screening test.

Drug Type	Cut-off concentration	Detection time
Amphetamine	50 ng/mL	~20–50 h
Benzodiazepines	15 ng/mL	~12–24 h
Cannabis	5 ng/mL	~4–16 h
Cocaine	20 ng/mL	~5–12 h
MDMA	75 ng/mL	~24 h
Methadone	20 ng/mL	~15 h
Methamphetamine	35 ng/mL	~24 h

- ‘Positive or negative’ result displayed within 5-8 min’s.
- Sensitive to lower THC levels

Uban et al., 2018 *DCN*

Extra: Rationale & methods: Screening w/ breath

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- Breathalyzer for recent alcohol (BAL + time since last drink)
- Positive screens at baseline were exclusionary
- In year 1+, if positive screen, follow-up appointment scheduled to ensure no youth is tested under the influence.

Uban et al., 2018 *DCN*

Extra: Rationale & methods: Screening w/ hair

- ~10% at baseline
- ~3 month detection window
- Easy to store, still can assay hair with different shampoos or dyes
- Short hair is a limitation

parent drugs and metabolites: alcohol ethyl glucurolide (ETC), cannabis (11-Nor-9-carboxy-THC (THCCOOH) and cannabidiol (CBD)), methamphetamine and methylenedioxy-methamphetamine (MDMA), amphetamine, opiates (codeine morphone, hyrdomorph, oxycodone, hydrocodone), and cocaine/benzoylecgonine (BE).

https://issuu.com/surehire/docs/hair_collection_training_manual

Uban et al., 2018 *DCN*

Extra: Rationale & methods: Screening w/ urine

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- Begin Yr 1 for 10% of participants
- Measures cotinine (principal metabolite of nicotine)
- Sensitive to lower cotinine levels when urine is used
- Smoke exposure in past several days
- Positive screen for ‘tobacco user’: > 100 ng/mL cotinine

Uban et al., 2018 *DCN*

Introducing salivary hormones in ABCD

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Week 6

Biospecimen Samples.

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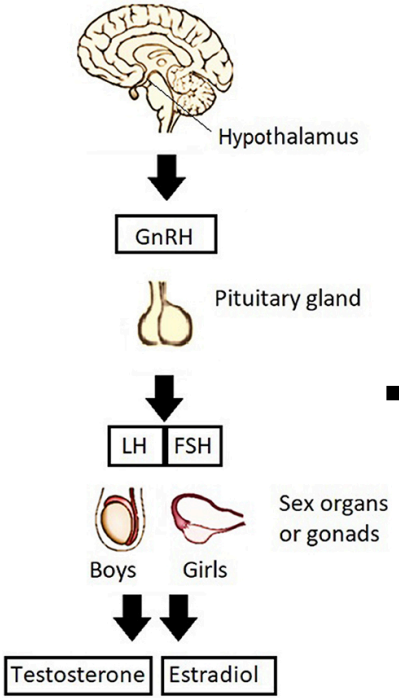
Uban et al., 2018 *DCN*

Introducing salivary hormones in ABCD: Rationale

ABCD-ReproNim



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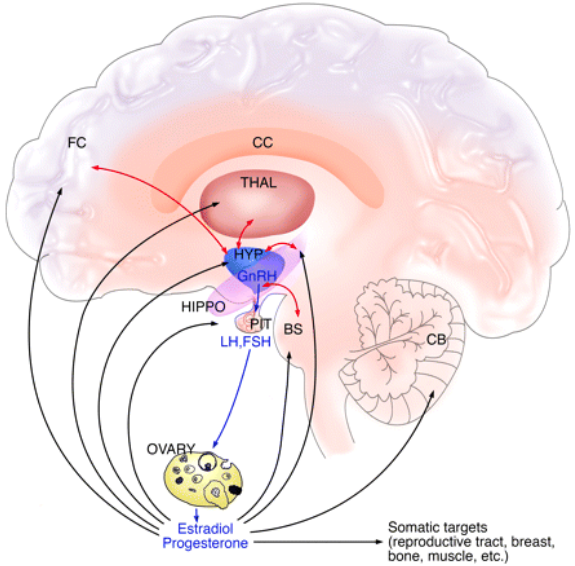

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Hormone monster

Barendse et al., 2020
Frontiers for Young Minds

Morrison et al., 2006
J. Neuroscience

Introducing salivary hormones in ABCD: Rationale

ABCD-ReproNim

Hormone monster

- Onset of puberty
- Duration of pubertal maturation
- Levels of hormones
- Patterns of hormones
- Sensitivity to hormones

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- pubertal maturation
  - body
  - brain
- mental health problems
- substance use problems
- behavioral problems

Uban et al., 2018 *DCN*
Herting & Uban et al., 2021 *Frontiers in Endocrinology*

Rationale & methods: Saliva for pubertal hormones

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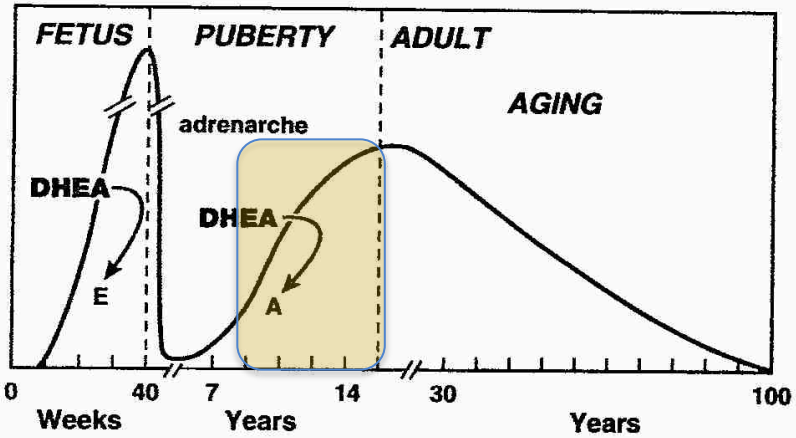
- All participants, 1x/yr, every yr, for 10 consecutive yrs.
- Passive drool
- Measures hormones (testosterone, DHEA, & estradiol in females at birth only).

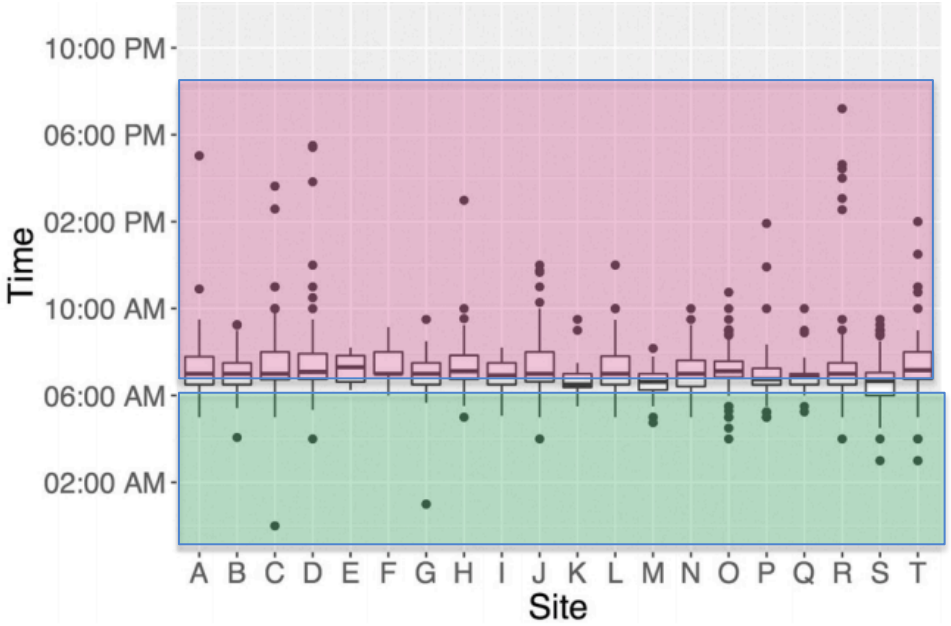


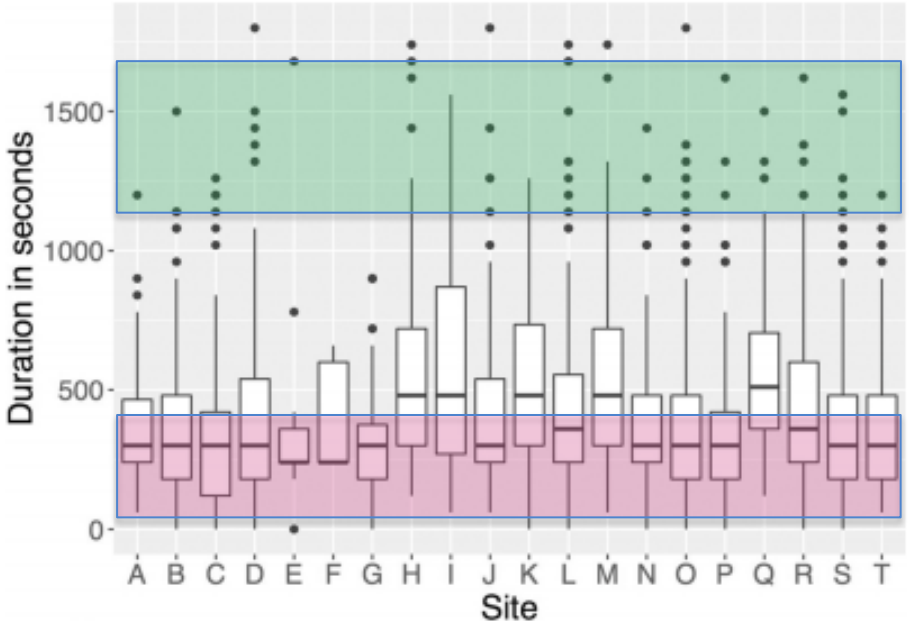
https://flipper.diff.org/app/pathways/info/2056

Uban et al., 2018 *DCN*
Herting & Uban et al., 2021 *Frontiers in Endocrinology*

Rationale & methods: hormones phase 1

ABCD-ReproNim





Uban et al., 2018 *DCN*

Rationale & methods: hormones phase 2

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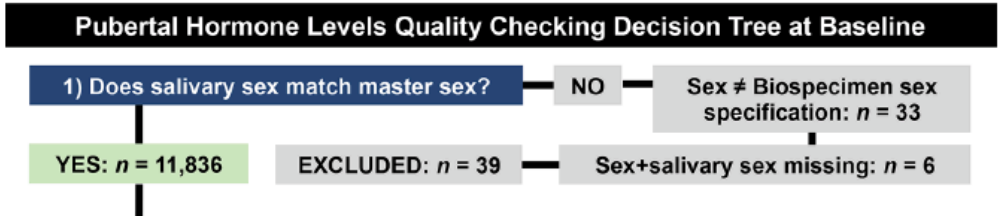

Herting & Uban et al., 2021 *Frontiers in Endocrinology*

Rationale & methods: hormones phase 2

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- Confounding variables

Hormone Levels	Males			Females		
	N	Mean ± SD	IQR	N	Mean ± SD	IQR
DHEA (pg/ml)	2,676	57.78 ± 43.78	50.04	2,430	76.87 ± 56.28	63.15
Testosterone (pg/ml)	2,622	32.80 ± 17.70	21.41	2,358	37.07 ± 18.37	22.94
Estradiol (pg/ml)	–	–	–	2,168	1.17 ± 0.52	0.69
Covariates	**N**	**Mean ± SD**	**IQR**	**N**	**Mean ± SD**	**IQR**
Caffeine in past 12 hours (N)	2,376	Yes = 161/No = 2,210	–	1,707	Yes = 95/No = 1,612	–
Physical activity in past 12 hours (N)	2,366	Yes = 318/No = 2,048	–	1,703	Yes = 216/No = 1,487	–
Time Since Midnight (minutes)	2,381	777.58 ± 181.73	313	1,712	776.53 ± 177.18	311
Collection Duration (minutes)	2,318	6.81 ± 5.44	6	1,676	7.49 ± 5.89	5
Time to Freeze (minutes)	2,335	2.69 ± 12.31	1	1,686	3.05 ± 14.38	1

- oral environment
- flow rate

Herting & Uban et al., 2021 *Frontiers in Endocrinology*

Rationale & methods: hormones phase 2

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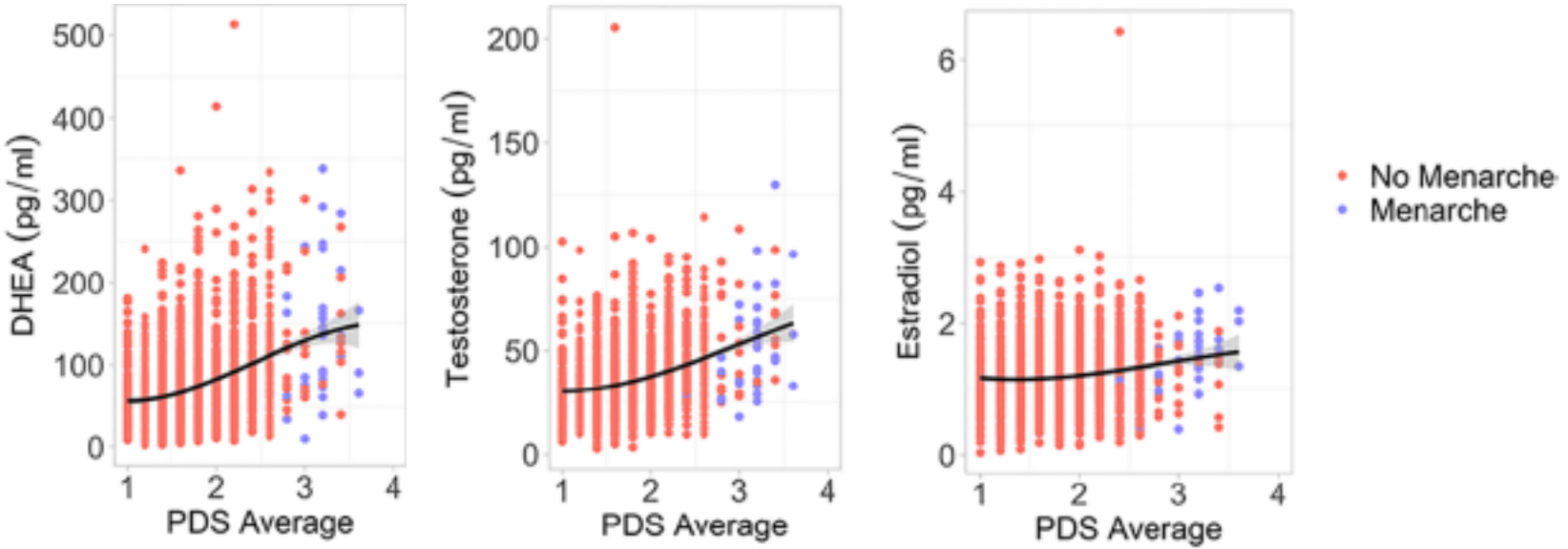
- Findings: females @ baseline



Herting & Uban et al., 2021 *Frontiers in Endocrinology*

Rationale & methods: hormones phase 3

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- How to use this data?

frontiers

Hormone Saliva Salimetric Scores (hsss01)		
Salimetrics hormone test mean (pg/mL)	hormone_scr_dhea_mean, hormone_scr_hse_mean, hormone_scr_ert_mean	dhea: all, hse (E2), female; ert (T): All
Salimetrics hormone test, repetitions 1 and 2 (pg/mL)**	hormone_scr_dhea_rep1, hormone_scr_hse_rep1, hormone_scr_ert_rep1	
Salimetrics hormone test below lower limit of sensitivity, replications 1 and 2**** (yes/no)	hormone_scr_dhea_rep1_II, hormone_scr_hse_rep1_II, hormone_scr_ert_rep1_II	
Salimetrics hormone quantity not sufficient, repetitions 1 and 2**** (yes/no)	hormone_scr_dhea_rep1_qns, hormone_scr_hse_rep1_qns, hormone_scr_ert_rep1_qns	
Salimetrics hormone test none detected, repetitions 1 and 2**** (yes/no)	hormone_scr_dhea_rep1_nd, hormone_scr_hse_rep1_nd, hormone_scr_ert_rep1_nd	

A researcher's guide to the measurement and modeling of puberty in the ABCD Study ® at baseline

Theresa W. Cheng[1*], Lucía Magis Weinberg[2], Victoria G. Williamson[1], Cecile D. Ladouceur[3], Sarah L. Whittle[4], Megan Herting[5], Kristina A. Uban[6], Michelle L. Byrne[7], Marjolein E. Barendse[1], Elizabeth A. Shirtcliff[8], Jennifer H. Pfeifer[1]

[1]University of Oregon, United States, [2]University of California, Berkeley, United States, [3]University of Pittsburgh, United States, [4]The University of Melbourne, Australia, [5]Keck School of Medicine, University of Southern California, United States, [6]University of California, Irvine, United States, [7]Monash University, Australia, [8]Iowa State University, United States

Submitted to Journal:
Frontiers in Endocrinology

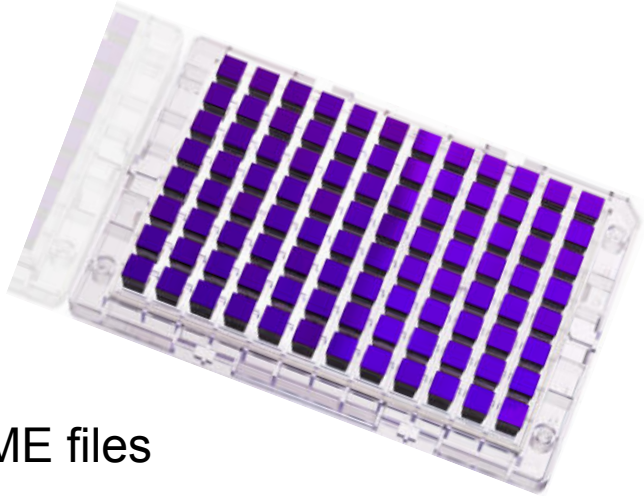
Specialty Section:
Pediatric Endocrinology

Uban et al., 2018 *DCN* Herting & Uban et al., 2021 *Frontiers in Endocrinology* Chen et al., 2021 *Under revision*

Rationale & methods: Genetics w/ saliva & blood

ABCD-ReproNim

- Some saliva @ baseline
- Blood @ Yr 2 for 100% of participants
- Smokescreen genotyping array, epigenetics coming
- Details in 3.0 release notes & accompanying README files



Methodology article | Open Access | Published: 27 February 2016

Smokescreen: a targeted genotyping array for addiction research

James W. Baurley, Christopher K. Edlund, Carissa I. Pardamean, David V. Conti & Andrew W. Bergen

BMC Genomics **17**, Article number: 145 (2016) | Cite this article

› Hypertension. 2020 Jan;75(1):59-70. doi: 10.1161/HYPERTENSIONAHA.118.12292. Epub 2019 Dec 2.

Influence of Dietary Approaches to Stop Hypertension–Type Diet, Known Genetic Variants and Their Interplay on Blood Pressure in Early Childhood: ABCD Study

Mohammad Hadi Zafarmand [1 2], Marit Spanjer [1], Mary Nicolaou [1], Hanneke A H Wijnhoven [3], Barbera D C van Schaik [4], Andre G Uitterlinden [5 6], Harold Snieder [7], Tanja G M Vrijkotte [1]

Affiliations + expand

PMID: 31786974 DOI: 10.1161/HYPERTENSIONAHA.118.12292

Rationale & methods: Exposures w/ baby teeth

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- On-going collection from all participants Uban et al., 2018 *DCN*
- Sub-study (n=500) sent to Manish Arora's lab NIH grant – Elizabeth Sowell
- 2nd trimester *in utero* through time of shed tooth
- Weekly averages of Pb and Mn

Tooykrub/shutterstock, Ocskay Bence/shutterstock

ABCD-ReproNim

On-going sub-studies that collect new specimens or analyze biobanked specimens

Blood Sample Collection

939 Shared Subjects

DESCRIPTION
N/A

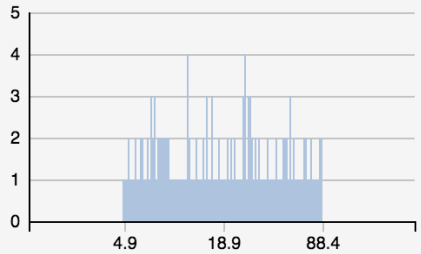
SHORT NAME
bsc01

DATA TYPE
Clinical Assessments

CATEGORY
Summary

Add Data Structure | Create Element Filter

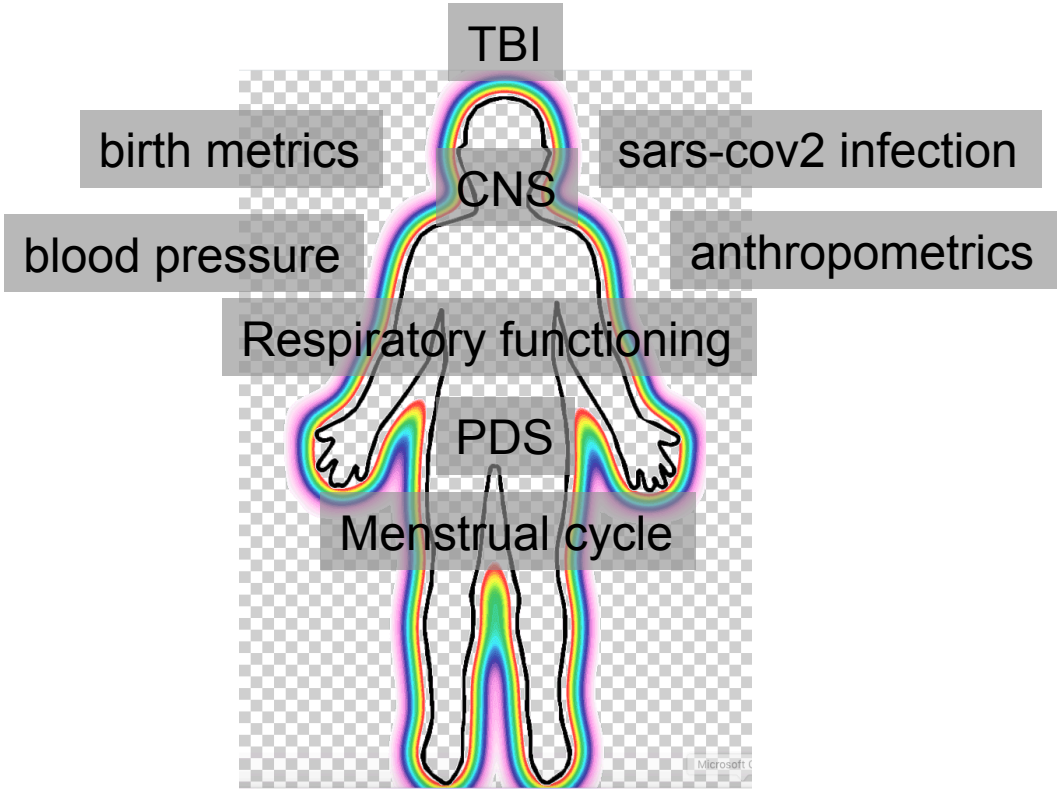
DISTRIBUTION FOR BSC01 / ACTH



Other ‘biomarkers’ in ABCD

ABCD-ReproNim

- Biological specimens
- Physiological measures



Some general Do's and Don'ts

- Do . . .

  Plot out all individual data for biomarkers and collection variables to identify physiologically or improbable values

  Publish decision trees and scripts

  Read all previously published articles with biospecimen

  Work with expert on biospecimen data

  Consider sociodemographic factors, sample bias, and methods

  Report effect sizes

- Don't . . . Be scared! You can do it – create your dream team!

Acknowledgements

Elizabeth Sowell, CHLA, USC
Doug Granger, UCI, IISBR, Salimetrics
Eric Kan, CHLA
Megan Herting, USC
Stefanie Bodison, USC
Marybel Gonzalez, UCSD

UCI Developing Brain Laboratory members:
Vida Rebello
Hawa Mariko
Minhaz Mohsin
Babette Steigelmann
Leila Nazarazi
Christian Black
Claudia Chavez
Nneoma Uba
Salma Nazarazi
Jamie Atienza
Savannah Tan
Hania Alim

ABCD ReproNim team:
Angie Laird
David Kennedy
Satra Ghosh
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IISBR at UCI colleagues
Hillary Piccerillo
Elizabeth Thomas
Jenna Riis
Michael Hoyt
Kate Kuhlman
Alyson Zalta
Ilona Yim