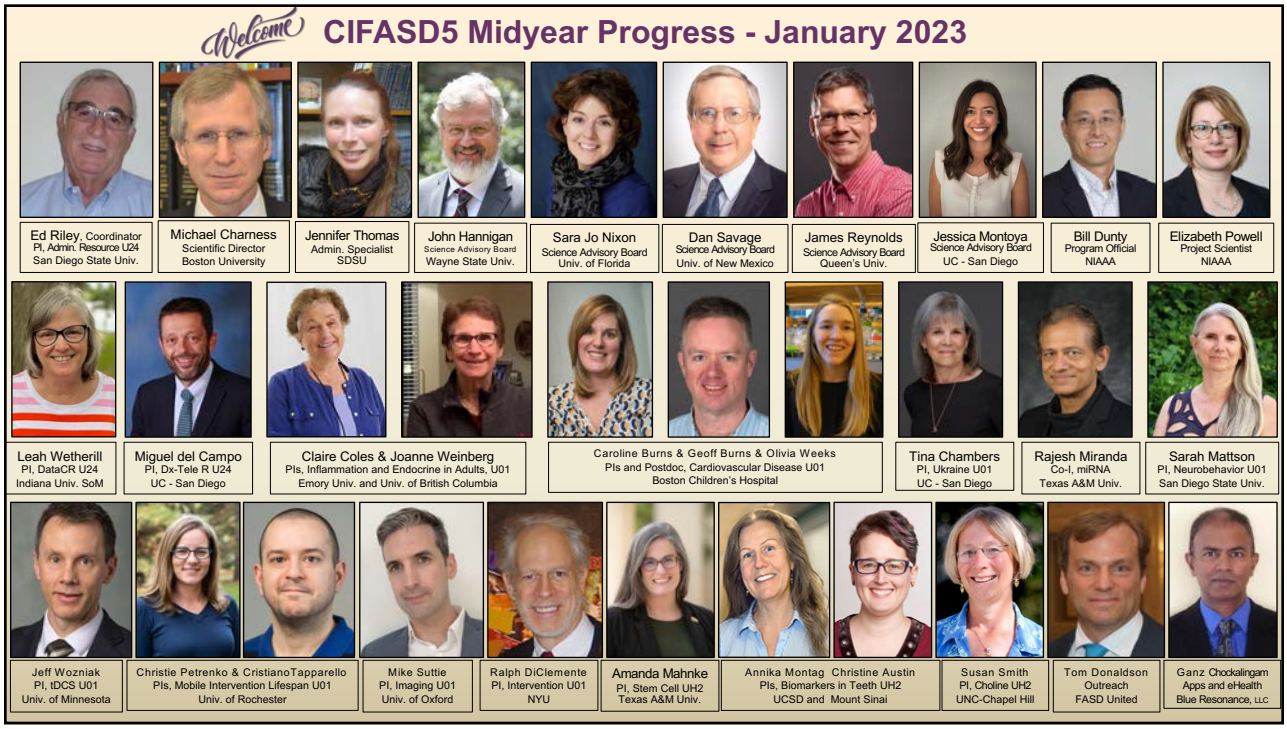
CIFASD5 Year 1
Midyear Project Progress Meeting
PPT Presentations
January 25 and February 22, 2023



CIFASD5 Project Composition

- **U24:** Administrative Resource (AdminR) of the CIFASD - Edward Riley (SDSU)
- **U24:** Diagnostic-Telemedicine Resource (DTR) - Miguel del Campo (UCSD)
- **U24**: Data Coordination Resource (DCR) - Leah Wetherill (IUSM)
- **U01:** Cardiovascular Disease in FASD - Caroline Burns and Geoff Burns (BCH)
- **U01:** Whole Body Effects of PAE Across the Life Span: Early Markers of and Clinical Interventions for Children and Adolescents in Ukraine - Christina Chambers (UCSD)
- **U01:** A Multisite Study of PAE: Effects of Inflammation and Endocrine Dysfunction in Adulthood - Claire Coles and Joanne Weinberg (Emory and UBC)
- **U01:** Designing a Hybrid Intervention Strategy to Reduce Alcohol Exposed Pregnancies - Ralph DiClemente (NYU)
- **U01:** Assessment of FASD Using Novel Web-Based Tools - Sarah Mattson (SDSU)
- **U01:** Leveraging Technology to Increase Quality of Life for FASD Across the Lifespan - Christie Petrenko and Cristiano Tapparello (UR)
- **U01:** Defining Translational Approaches for the Image-based Detection of PAE - Michael Suttie (Oxford)
- **U01:** tDCS and Cognitive Training in FASD - Jeffrey Wozniak (UMN)
- **UH2:** Lifelong Impact of PAE on Stem Cell Dynamics and Cellular Aging - Amanda Mahnke (TAMU)

Continuing UH2s

- Previously funded during CIFASD4 via a separate RFA
  - **UH2:** Mobile Health tools to promote health in adults with FASD – Christie Petrenko and Cristiano Tapparello (UR)
  - **UH2:** Choline Polymorphisms in FASD – Susan Smith (UNC)
  - **UH2:** Development of biomarkers in deciduous teeth of children with FASD that predict neurobehavioral performance – Annika Montag (UCSD) and Christine Austin (Mount Sinai)

CIFASD5 Consortium Structure

ADMINISTRATIVE RESOURCE (AdminR)

PI, Coordinator:	Edward Riley, SDSU
Scientific Director:	Michael Charness, Harvard
Admin. Specialist:	Jennifer Thomas, SDSU
Admin. Coordinator:	Jill Vander Velde, SDSU

SCIENCE ADVISORY BOARD

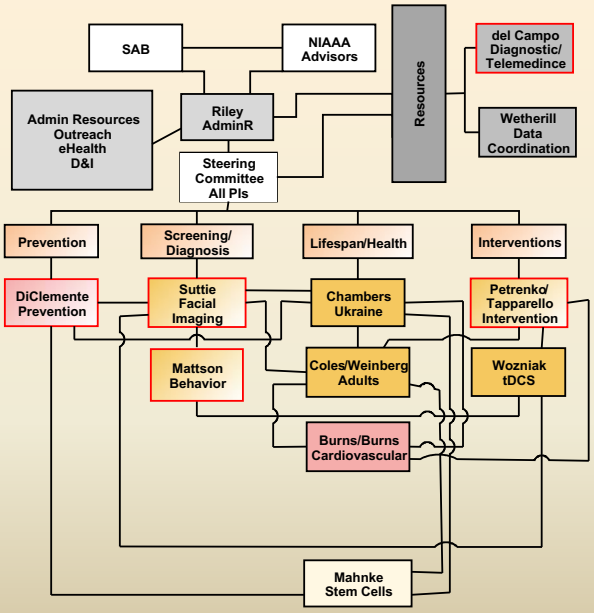
John Hannigan
Jessica Montoya
Sara Jo Nixon
James Reynolds
Daniel Savage

NIAAA ADVISORS

Elizabeth Powell, Project Scientist
Bill Dunty, Program Official

STEERING COMMITTEE
Chaired by Charness and Riley

U01 PIs	**U24 PIs**
C. Burns*/G. Burns*	M. del Campo
C. Chambers	L. Wetherill
C. Coles*/J. Weinberg*	**UH2 PIs**
R. DiClemente	A. Mahnke
S. Mattson	
C. Petrenko*^/C. Tapparello*^	A. Montag*^/ C. Austin*^
M. Suttie	S. Smith^
J. Wozniak	^ CIFASD4 UH2 PIs
* Multiple PI project	



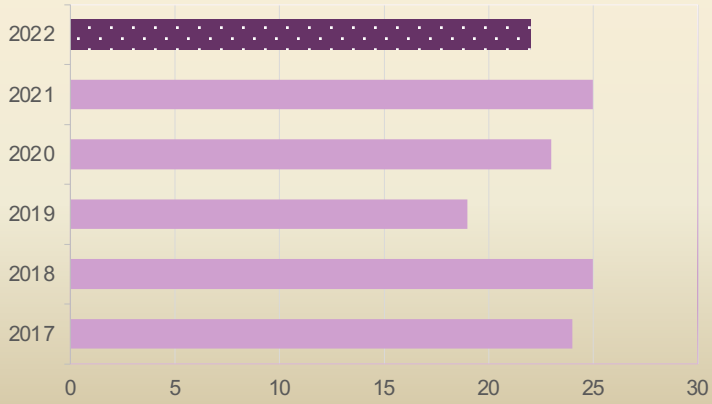
Overall CIFASD Goals

The **overall goals of CIFASD** aim to further refine definitive characteristics of fetal alcohol spectrum disorders (FASD) across the lifespan based on biological, physical, neurological, and/or behavioral assessment by:

- Improving screening, case recognition and diagnosis of FASD
- Assessing impact of having an FASD across the lifespan
- Identifying factors that impart greater risk/resiliency to FASD
- Developing intervention and prevention strategies for FASD
- Employing eHealth technologies so that our research and its applications can be more broadly disseminated

Publication Productivity of CIFASD

Publications citing **CIFASD** funding per PubMed
2017 to present = 138
2022 = 22



Total PubMed
CIFASD Publications = **347**

CIFASD investigators make significant contributions in high impact journals, such as:

- ***Lancet – Neurology***
- ***Nature***
- ***Trends in Cognitive Sciences***
- ***Journal of Neuroscience Development***
- ***Journal of Pediatrics***
- ***Proceedings of the National Academy of Sciences***

Publications Citing CIFASD Grants

August 2022 – Present n= 9

- Wedderburn CJ, Ringshaw JE, Donald KA, Joshi SH, Subramoney S, Fouche JP, Stadler JAM, Barnett W, Rehman AM, Hoffman N, Roos A, Narr KL, Zar HJ, Stein DJ. Association of Maternal and Child Anemia With Brain Structure in Early Life in South Africa. *JAMA Netw Open*. 2022 Dec 1;5(12):e2244772. PMCID: PMC9719049.
- Bandoli G, Coles C, Kable J, Jones KL, Delker E, Wertelecki W, Yevtushok L, Zymak-Zakutnya N, Granovska I, Plotka L, Chambers C; CIFASD. Alcohol-related dysmorphic features as predictors of neurodevelopmental delay in infants and preschool-aged children: Results from a birth cohort in Ukraine. *Alcohol Clin Exp Res*. 2022 Dec;46(12):2236-2244.
- Aguilar-Rivera M, Kable JA, Yevtushok L, Kulikovsky Y, Zymak-Zakutnya N, Dubchak I, Akhmedzhanova D, Wertelecki W, Chambers C, Coleman TP. Wireless Heart Sensor for Capturing Cardiac Orienting Response for Prediction of Neurodevelopmental Delay in Infants. *Sensors (Basel)*. 2022 Nov 25;22(23):9140. PMCID: PMC9739526.
- Fish EW, Mendoza-Romero HN, Love CA, Dragicevich CJ, Cannizzo MD, Boschen KE, Hepperla A, Simon JM, Parnell SE. The pro-apoptotic Bax gene modifies susceptibility to craniofacial dysmorphology following gastrulation-stage alcohol exposure. *Birth Defects Res*. 2022 Nov 15;114(19):1229-1243.
- Everson JL, Tseng YC, Eberhart JK. High-throughput detection of craniofacial defects in fluorescent zebrafish. *Birth Defects Res.* 2022 Nov 11.
- Borrego-Soto G, Eberhart JK. Embryonic Nicotine Exposure Disrupts Adult Social Behavior and Craniofacial Development in Zebrafish. *Toxics.* 2022 Oct 15;10(10):612. PMCID: PMC9611253.
- Boschen KE, Steensen MC, Simon JM, Parnell SE. Short-term transcriptomic changes in the mouse neural tube induced by an acute alcohol exposure. *Alcohol.* 2022 Oct 4:S0741-8329(22)00088-X.
- Ritfeld GJ, Kable JA, Holton JE, Coles CD. Effectiveness of Psychotropic Medications in Children with Prenatal Alcohol and Drug Exposures: A Case Series and Model of Care. *Child Psychiatry Hum Dev.* 2022 Oct 1.
- Montag AC, Chambers CD, Jones KL, Dassanayake PS, Andra SS, Petrick LM, Arora M, Austin C; Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD). Prenatal alcohol exposure can be determined from baby teeth: Proof of concept. *Birth Defects Res.* 2022 Aug 15;114(14):797-804. PMCID: PMC9378437.

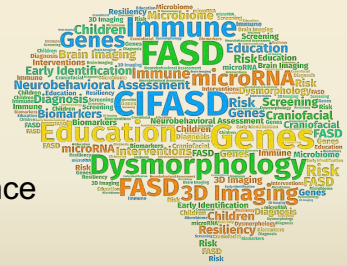
Publications Citing CIFASD Grants

Upcoming Publication

- Popova, S., Charness, M., Burd, L., Crawford, A., Hoyme, H., Mukherjee, R., Riley, E., Elliott, E. Fetal alcohol spectrum disorders. *Nature Reviews Disease Primers*, In press
  - Impact Factor 65.04 4th Highest journal IF in the medical field.

Specific Aims of the AdminR

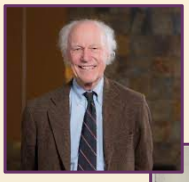
- Provide scientific and administrative direction, leadership, and oversight to the consortium
- Facilitate communication among the various projects and the dissemination of results.
- Assist with data management strategies
- Provide annual evaluations of progress
- Provide outreach, eHealth, and implementation assistance
  - FASD United
  - Blue Resonance, LLC
  - UCSD Altman Clinical and Translational Research Institute



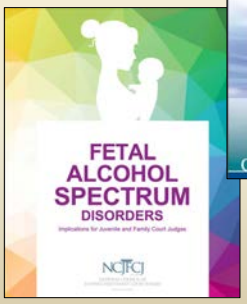
NIAAA$_{DA}$ Introduction and Q&A Session

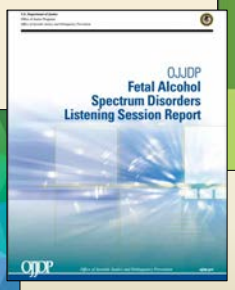
- **NIAAA:** Elizabeth Powell and Dan Falk
- **NIMH Data Archive:** Taameem Almaliki, Dan Janes, and Tracy King
- **DCR:** Leah Wetherill, Chris Hobbick, Cathy Wyss, and Peishan Zou
- **Sept. 6, 2022 Agenda:**
  - General NIAAA$_{DA}$ Introduction
  - CIFASD5 Workflow
    - Data Coordination Resource (DCR)
    - CIFASD investigators
    - NIAAA$_{DA}$
  - GUIDs
  - Q&A

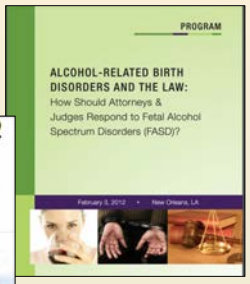
Invited Guests – Monthly Meetings



- FASD and the Criminal Justice System, Kenneth Lyons Jones

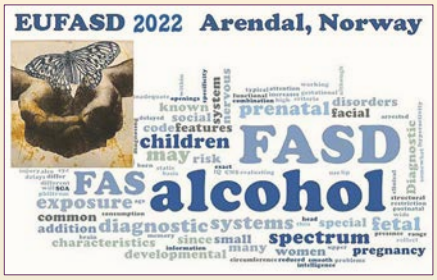






Invited Guests – Monthly Meetings

CIFASD Visibility



EUROPEAN FASD ALLIANCE

EUFASD

September 11 - 14, 2022
Arendal, Norway

Using technology to move forward on the recognition and treatment of FASD

Plenary session 6: ***CIFASD-symposium: Using technology to move forward on the recognition and treatment of FASD.*** *Session chair: Raja Mukherjee*

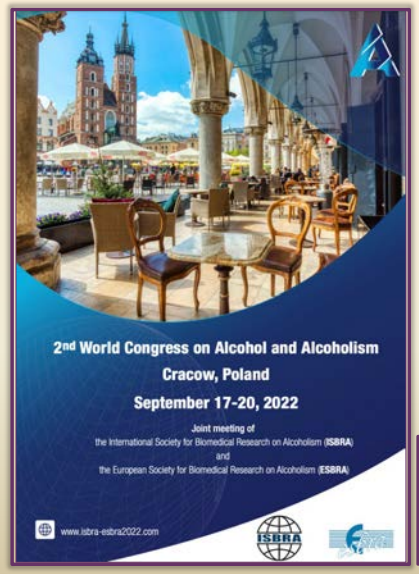
13.30 - 13.45: **Ed Riley**: *A smartphone app for the assessment of the sentinel facial features of FASD.*

13.45 - 14.00: **Michael Suttie**: *Automated, Accurate, and Objective Methods for the Identification of Facial Dysmorphism in FASD.*

14.00 - 14.15: **Sarah N. Mattson**: *Two web-based tools are effective in screening for FASD.*

14.15 - 14.30: **Christie L.M. Petrenko**: *Developing innovative mobile health interventions to increase access to care for people with FASD across the lifespan.*

CIFASD Visibility



Alcoholism and Stress: A Framework for Future Treatment Strategies
Volterra, Italy - May 2023

Graded regional cerebellar volume deficits in adolescents and adults with Fetal Alcohol Effect and Fetal Alcohol Syndrome

- Edward Riley

CIFASD Visibility

Research Society on Alcohol

46th Annual RSA Scientific Meeting

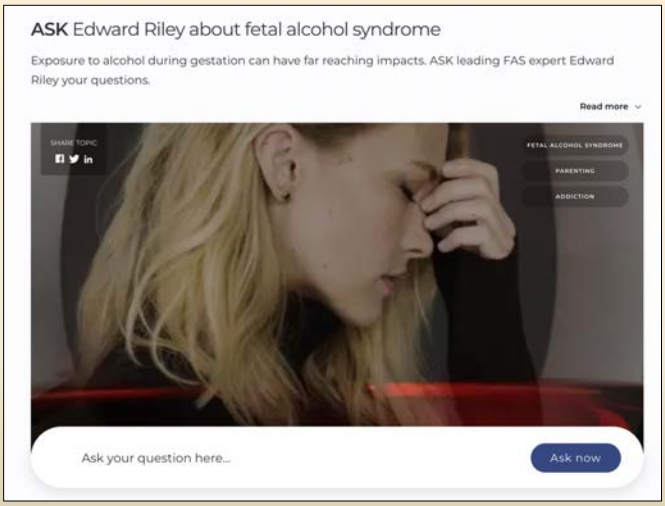
June 24-28, 2023
Bellevue, Washington

CIFASD Translational Research on FASD

- Olivia Weeks, Congenital heart defects and adult cardiovascular dysfunction in a zebrafish model of fetal alcohol spectrum disorders
- Susan Smith, Polymorphisms in choline transporter SLC44A1 are associated with reduced cognitive performance in those who experience heavy prenatal alcohol exposure
- Blake Gimbel (Wozniak lab), Atypical neurodevelopmental trajectories following prenatal alcohol exposure: Further evidence from cortical, subcortical, and white matter diffusion MRI paradigms
- Edward Riley, A smartphone app for the assessment of the sentinel facial features of FASD

CIFASD Outreach and Education

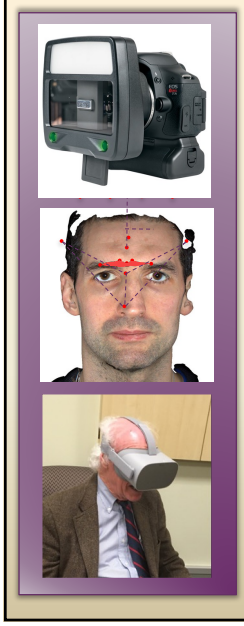
Psychwire

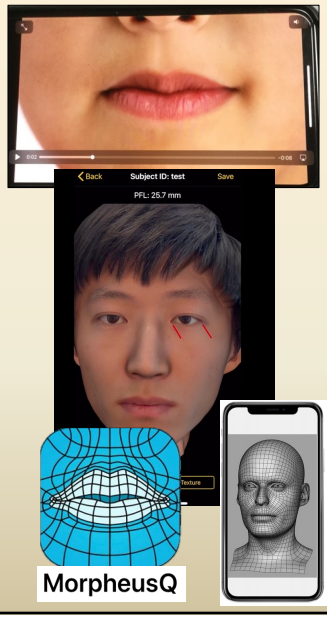


Science Advisory Board (SAB) Members

- Continuing members John Hannigan (Chair), Sara Jo Nixon, Dan Savage, and James Reynolds; New member Jessica Montoya
- SAB members presented on their research during the September and October monthly meetings
- Annual SAB Evaluations will be completed following the this meeting utilizing the progress reports and presentations
- Evaluations will be distributed to AdvisoryC members and Project PIs by the Consortium Coordinator

Blue Resonance, LLC





MorpheusQ

FASD-Tree

BRAIN-online

FASD United

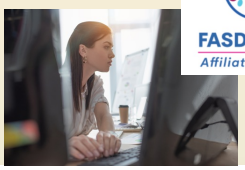
facebook

FASD United
February 11 at 11:00 AM ·

FMF (Families Moving Forward) is looking to recruit a total of 300 parents/caregivers of children with FASD or prenatal alcohol exposure.
Do I qualify?
-have a child (ages 3 to 12)
-live in the US
-have an iOS device (iphone or ipad). ... See more

FASD United
THE NATIONAL VOICE ON FETAL ALCOHOL SPECTRUM DISORDERS
Weekly Roundup

FASD United
Affiliate Network



twitter

BRAIN-Online FASD Screening Tool

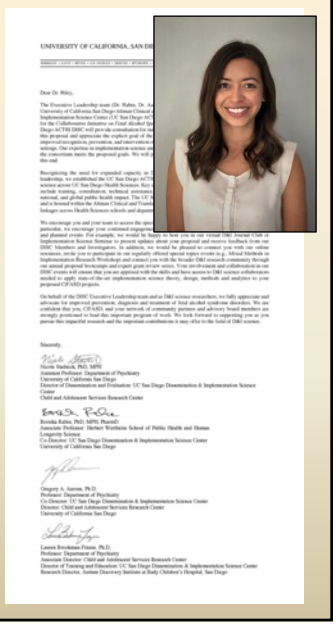
BRAIN-online is a new web-based screening tool that assesses cognitive and behavioral features known to be associated with FASD. If you think that you or someone you care for may have FASD, BRAIN-online can act as the first step in connecting to a diagnosis.

TAKE THE TEST

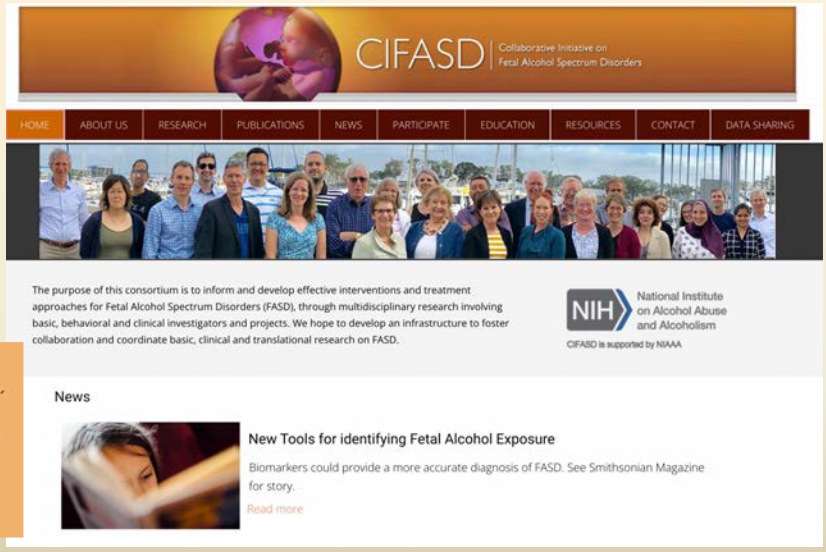
INDIANA ALLIANCE
On Prenatal Substance Exposure

Dissemination and Implementation

- San Diego Altman Clinical and Translational Research Institute - Dissemination and Implementation Science Center (UC San Diego ACTRI DISC)
- Added Jessica Montoya from ACTRI DISC to our SAB
- Beyond consulting services to each project, the ACTRI DISC provides:
  - training, consultation, technical assistance, and mentoring to advance D&I science for local, national, and global public health impact.
  - Proposal Boot Camp
  - Online Resources
  - Seminars, and special topic events



CIFASD.org > News

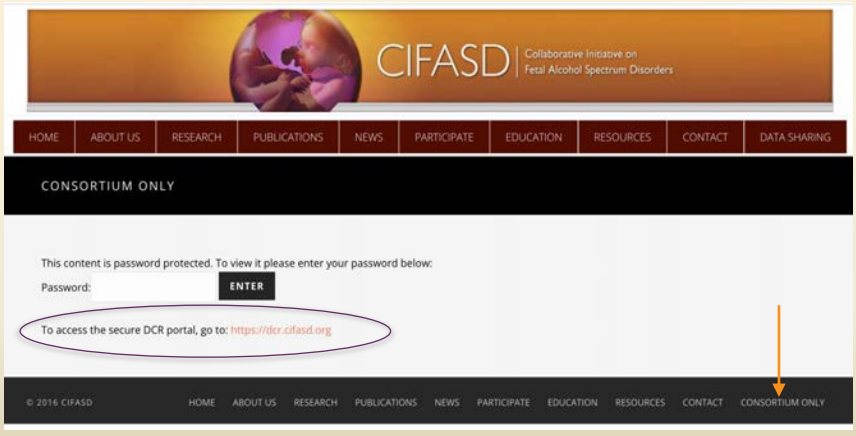


CIFASD.org > Research > CIFADS5

RESEARCH PROJECTS AND COMPONENTS

- Administrative Resource of the CIFASD (Edward Riley, PI)
- FASD Diagnostic Telemedicine Resource (Miguel del Campo, PI)
- CIFASD Data Coordination Resource (Leah Wetherill, PI)
- Cardiovascular Disease in Fetal Alcohol Spectrum Disorder (Caroline Burns and Geoff Burns, MPIs)
- Whole body Effects of PAE across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents (Christina Chambers, PI)
- A Multisite Study of Prenatal Alcohol Exposure: Inflammation and Endocrine Dysfunction in Adulthood (Claire Coles and Joanne Weinberg, MPIs)
- Designing a Hybrid Intervention Strategy to Reduce Alcohol Exposed Pregnancies (Ralph DiClemente, PI)
- Assessment of Fetal Alcohol Spectrum Disorders (FASD) Using Novel Web-Based Tools (Sarah Mattson, PI)
- Leveraging Technology to Increase Quality of Life for FASD across the Lifespan (Christie L. McGee Petrenko and Cristiano Tapparello, MPIs)
- Defining Translational Approaches for the Image-Based Detection of Prenatal Alcohol Exposure (Michael Suttie, PI)
- tDCS and Cognitive Training as a Neurodevelopmental Intervention in FASD (Jeff Wozniak, PI)
- Lifelong Impact of PAE on Stem Cell Dynamics and Cellular Aging (Amanda Mahnke, PI)
- Biomarkers in Children with FASD that Predict Neurobehavioral Performance (Annika Montag and Christine Austin, MPIs)
- Mobile Health Tools to Promote Health in Adults With FASD (Christie L. McGee Petrenko and Cristiano Tapparello, MPIs)
- Choline Polymorphisms in FASD (Susan M. Smith, PI)

CIFASD.org > Consortium Only > DCR Portal



CIFASD Publications Policy

CIFASD Publication Process

Policies and forms are housed within the secure section of the CIFASD website.

Concept Proposal
Complete the online
Concept Proposal Form

CIFASD Investigators
Review Concept Proposal:
Provide comments, indicate interest, define proposed contribution

Review Comments/ Respond to CIFASD Investigators

Analyses Proceed/ Manuscript Prepared
Provide updates to CIFASD ~ every 6 months to ensure progress

Prior to Submission
Complete the online
Manuscript Submission Template Form

Post-Acceptance
Complete the online
Post-Acceptance Form

Ensure Compliance
NIH Public Access Policy

Special Thanks to:

Bill Dunty

Elizabeth Powell

Science Advisory Board

Michael Charness

Jennifer Thomas

Jill Vander Velde

Publications Policy and Data Sharing Committees

Thank You

National Institute on Alcohol Abuse and Alcoholism

Tom Donaldson, FASD United
CIFASD Outreach, AdminR subaward

FASD United Objectives

- Increase recognition, support, and services for the FASD community
- Educate practitioners, policymakers and the public
- Advocate for legislation and policy change
- Expand the FASD network

CIFASD Outreach Aims

- Disseminate published findings
  - Presentations, trainings, and briefings
  - Website, eNewsletter, social media
  - Affiliates and partners
- Assist with study participant recruitment
- Highlight scientists and their research
- Serve as a liaison between scientists and the FASD community and FASD United partners

Recent Activities

CIFASD members presented at a September 21, 2022, workshop to kick off a Department of Defense project at the Uniformed Services University, Center for health Services Research to investigate FASD in the military health system

- Christie Petrenko, PhD
- Jeff Wozniak, PhD
- Bill Dunty, PhD

- Policymaker briefings
  - Investigators participated in 17 virtual meetings
- CIFASD featured in FASD United media channels

FASD United Weekly Roundup | PAE FAQs | FASD FAQs

Planned Activities

- Organize the participation of CIFASD investigators at a September, Washington, D.C., one-day conference and separate congressional briefing co-hosted by FASD United.
- Work with Sarah Mattson, PhD, to promote and place her BRAIN-Online FASD Screening Tool on fasdunited.org and FASD United affiliate websites.
- Develop an infographic, slide presentation, and a page on fasdunited.org (linked to cifasd.org) for lay audiences describing scientific aims and the significance of research for individuals living with FASD and systems of care.

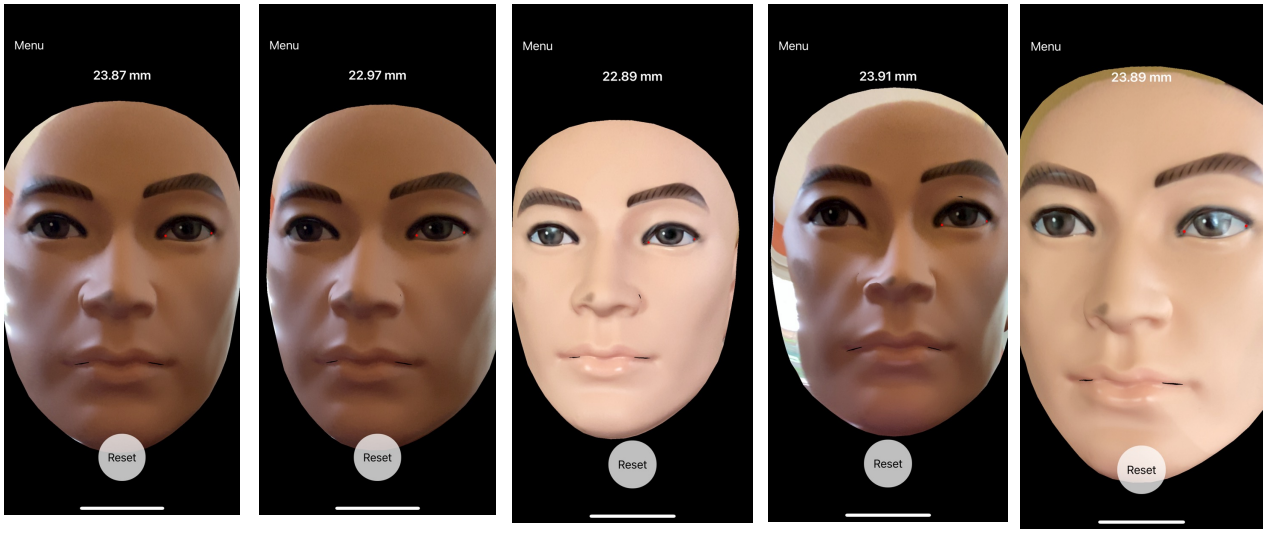
E-Health Applications

Ganz Chockalingam
Blue Resonance, LLC

MORPHEUSQ

Easier way to measure PFL

How accurate?



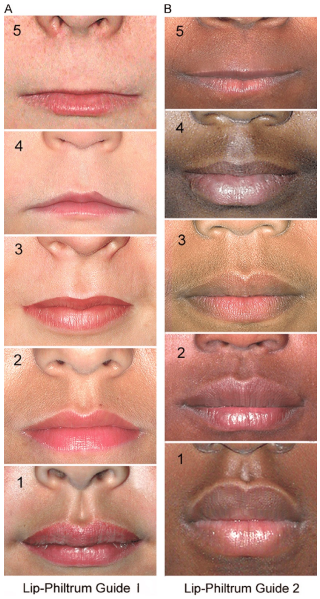
CALIPERS: 23.85 MM

N=10 MEAN : 23.625 SD : 0.404

MORPHEUSQ

Support for Age/Sex/Race

Current Guide



Lip-Philtrum Guide 1 Lip-Philtrum Guide 2

Age/Race/Sex/Ethnicity

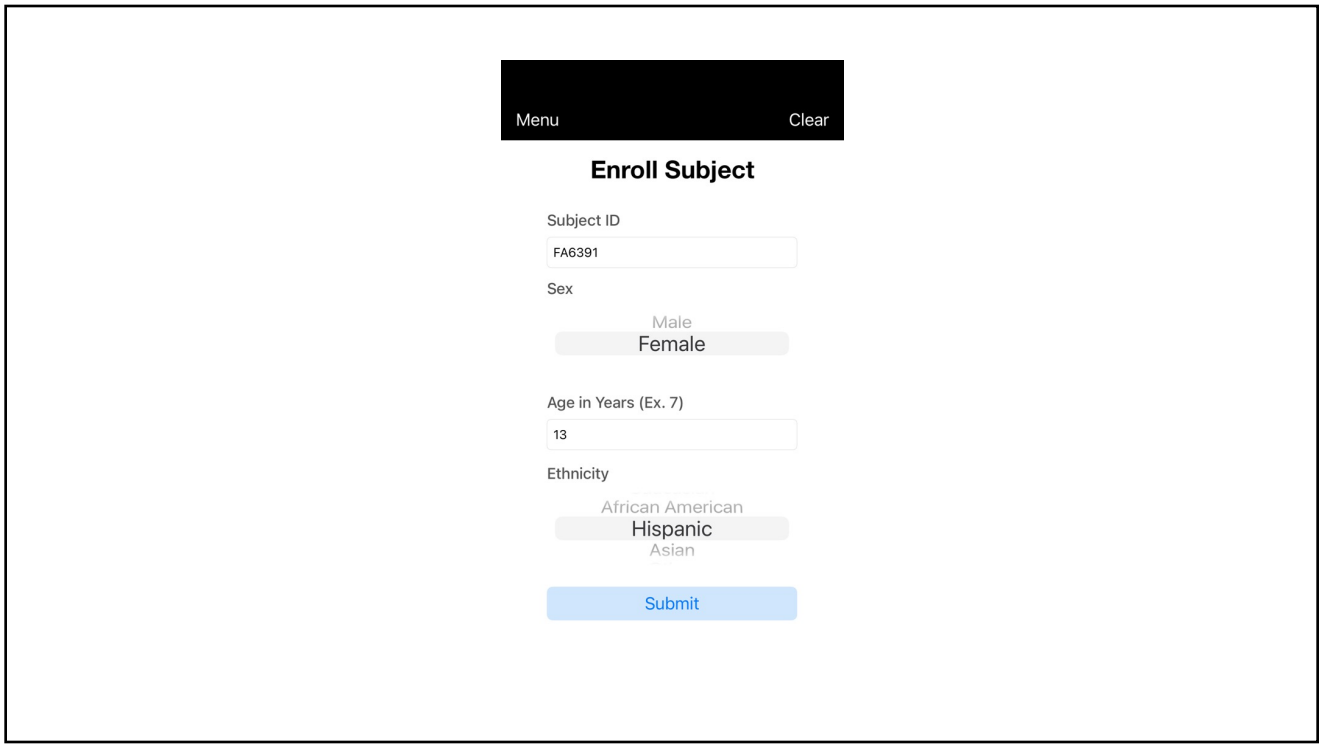
1. **Support for Age groups**
   3-7 Yrs
   7-14 Yrs
   14-21 Yrs

2. **Race:**
   Caucasian
   African American
   Hispanic
   Asian

3. **Male/Female**

4x3x2 = 24 Subjects

Front & Lateral View = 48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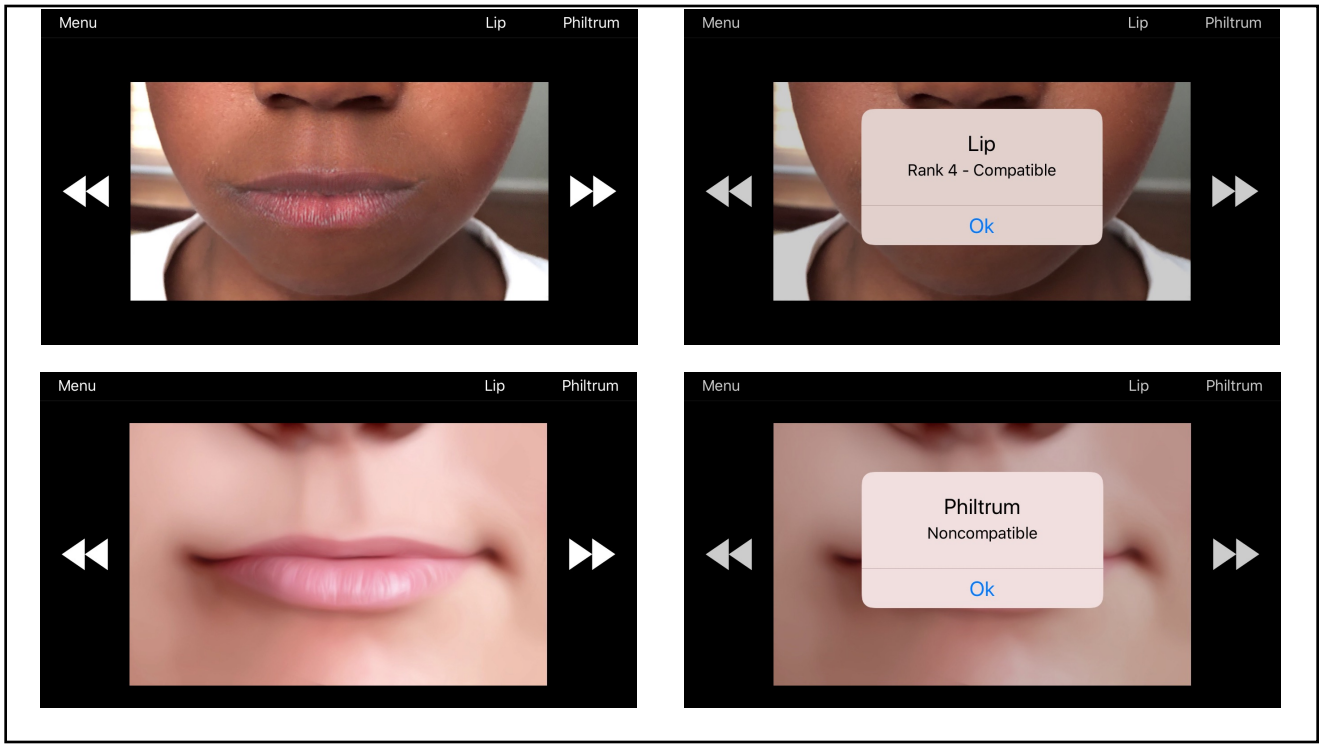
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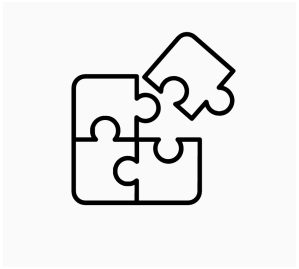


BRAIN
(Sarah Mattson)

E-Tree
(Sarah Mattson)

U24 Diagnostic Telemedicine resource (DTR)

Miguel del Campo, MD, PHD
Kenneth L. Jones, MD
CIFASD dysmorphology core
Institute for fetal alcohol spectrum disorders discovery (IFASDD)
University of California San Diego

Aims

1. Training of examiners
2. Exam with standard techniques, Morpheus Q and 3D photos
3. Screening In Alaska

Accomplishments

Several trainings initiated
IRB for physical exams/photos at UCSD/Rady Completed
Recruitment for Aim 2 running

IRB for Alaska in discussion/process
Cultural sensitivity courses completed

SOP manuals
Training and physical exams
Screening in Alaska

Specific Aim 1

- The primary aim of the Diagnostic-Telemedicine Resource (DTR) is to ensure that participants recruited in CIFASD5 projects receive a standardized, comprehensive evaluation of the physical features diagnostic of FASD. To maximize CIFASD5-wide diagnostic efficiency and consistency, and to increase diagnostic capacity, **we will use telemedicine to complement in-person training of local health care providers** who will perform the majority of the evaluations at CIFASD sites. The DTR will ensure the fidelity of these exams using the telemedicine approaches previously developed and validated in CIFASD

Accomplishments:

U01 Jeff Wozniak Minnesota. 7 trainees first session
U01 Sarah Mattson 3 trainees first session
SOP: Two initial training sessions without subjects
Telemedicine exam of at least 2 subjects
Proctoring 2 exams and re-training after 10 subjects
Discuss in person proctoring

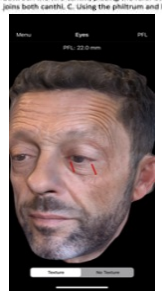
Specific Aim 2

The DTR will test three novel eHealth tools that would provide accessible, scalable, low-cost solutions to screening and diagnosis for FASD, and compare each of these to the standard in-person **dysmorphology examination by experts** used in all previous iterations of CIFASD1-4. In Aim 2, we will: 1) **determine the accuracy of MorpheusQ** in detection of the cardinal facial features of FASD compared to the gold standard in-person expert exam; 2) in collaboration with CIFASD5 Investigator Suttie's U01 project, determine **the accuracy of 3D facial signatures compared to the gold standard in-person expert exam.** Under Aim 2, we will also work with CIFASD5 Investigator Mattson's U01 project to evaluate the effectiveness of these and other eHealth tools (FASD-Tree and Brain-online) utilized in combination to support diagnosis of the full range of FASD classifications.

28 cases (50/year)
30 cases preliminary data

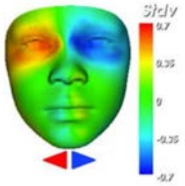
28 cases (50/year) with full physical examination/Morpheus Q for Sarah Mattson U01 FASD tree

Figure 4. A and B. Correct measurement of the palpebral fissures with a hard ruler measuring between the two canthi, placing the ruler at the right angle of the face, parallel to the line that joins both canthi. C. Using the philtrum and lip guide and looking with a 45 degree angle.



PFL rotational scan
17 cases (50/year)
30 cases preliminary data

PFL frontal scan scan
28 cases (50/year)
30 cases preliminary data



A

Working with IRB on storage and transmission of images

Specific Aim 3

- A major advantage of telemedicine is that it removes geographical barriers to screening and diagnosis. In Aim 3, we will demonstrate integration of the CIFASD5 DTR findings from Aims 1 and 2 into a real-world setting. In isolated communities in Alaska that are highly-impacted by prenatal alcohol, **we will train providers via telemedicine and test the application of our eHealth tools to improve access to accurate diagnosis.**

Years 1-2. 30 cases per year in FASD diagnostic centers. No recruitment yet

Accomplishments:
Meetings with FASD diagnostic groups coordinator of Dept of Health (Hope Finkelstein)
Collaboration of anthropologist Travis Hedwig
Discussing IRB
Discussing collaborating IRB
2 courses on cultural sensitivity
SOP manual for the comprehensive screening process
1st year. Obtain IRB approval
Initiate/complete recruitment

For other U01

- Schedule trainings
- Include in IRB remote or in person supervision of physical examinations
- Feedback to finalize SOP manuals
- Thanks for support Administrative core Ed Riley Alaska

In San Diego

systematic screening of the child welfare population

systematic screening of the juvenile justice population

- Questions?

Data Coordination Resource (DCR)
Leah Wetherill

Abigail Erickson, BS, CCRP

SCHOOL OF MEDICINE

Aim 1: Informed Consent

PI Last Name	Project	IRB Information / Status	DCR Review Status	Data Sharing language approved by DCR?
Del Campo	Diagnostic telemedicine	IRB approval received	Complete	Yes
Wozniak	Transcranial direct current stimulation (tDCS) and cognitive training in FASD	IRB approval received	Complete	Yes
Coles Weinberg	Multisite study of PAE: Effects of inflammation and endocrine dysfunction in adulthood	IRB approval received	Complete	Yes
Chambers	Whole body effects of PAE across the lifespan: Early markers of & clinical interventions for children and adolescents in Ukraine	IRB approval received	Complete	Yes
Mattson	Assessment of FASD Using Novel Web-Based Tools	Amendment under review with IRB	In progress	Under review
DiClemente	Designing a hybrid intervention strategy to reduce alcohol exposed pregnancies	ICF language not reviewed yet as alternative site approval is still in progress	In progress	Not yet - PI knows to work with DCR on data sharing language in ICF
Montag Austin	Teeth (Tooth Fairy)	Amendment under IRB review; DCR is not responsible for uploading this CIFASD4 data	In progress	Yes - DCR reviewed data sharing language as requested by Montag. Was not necessary since UH2 was part of CIFASD4
Wetherill	Data Coordination Resource	No ICF needed. Submitted to IRB as new protocol on 2/7/2023.	In progress	Not applicable - will not consent subjects.
Burns Burns (Weeks)	Cardiovascular Disease in FASD	No ICF needed, but Weeks is in the process of figuring out if they need to update their IRB submission to indicate sharing of data with CIFASD and NDA	n/a	Not applicable; IRB exempt status
Mahnke	Lifelong impact of PAE on stem cell dynamics and cellular aging	Study will not consent subjects	n/a	Not applicable; IRB exempt status
Smith	Choline Polymorphisms in FASD	Not recruiting participants	n/a	Not applicable
Petrenko Tapparello	Leveraging technology to increase quality of life for FASD across the lifespan	Not needed - not data sharing in first phase of project	n/a	Not applicable; IRB exempt status
Suttie	Defining translational approaches for the image-based detection of PAE	Not directly recruiting subjects; No ICF needed	n/a	Not applicable; IRB exempt status

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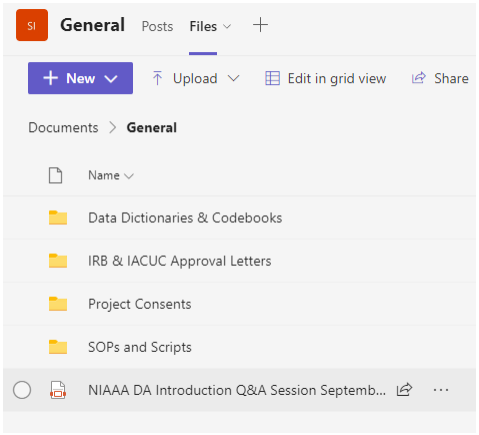
Aim 1: GUIDs



- Ready to assign GUIDS
  - Wozniak
  - Mattson
- Obtained pseudoGUIDS
  - Weeks/Burns
  - Mattson

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Aim 1: Data Dictionaries & Structures
(Data Collection Profile)

- DCR responsible for 9 projects
- 7 projects provided list of Data Structures (assessments, questionnaires, tools, etc.)
- Structure → Data dictionary
- 92 Data Structures
  - 46 exist in the NDA
    - 15 are finalized and uploaded to Data Expected at NDA
  - Requested Data Curator to create remaining 46 structures

Data Collection Instrument	in NDA	# projs collecting	# subjects
NDAR Required Subject Definition		10	1916
Will Collect 3D Images		9	830
3D Image Analysis		1	0
AB Game		1	0
Adult Health Survey		3	360
Adverse Childhood Experiences (ACEs)	1	4	170
Alcohol and Drug Use Disorders Identification Test (AUDIT)	1	4	360
Alcohol Timeline Followback Method Assessment	1	1	0
Autoimmune Survey (Cananda) and Chronic Health Supplement (Atlanta & Seattle)		3	360
BRIEF Cope	1	3	360
Barriers to Healthcare Checklist	1	1	0
BASC-III Parent Rating Scale	1	2	1120
Basic Psychological Need Satisfaction and Frustration scale	1	1	0
Bayley-II Scales of Infant Development	1	1	0
Bayley-III Scales	1	1	0

Aims 1+2: Create DCR & Upload to NDA

Data Expected	Targeted Enrollment	Initial Submission	Subjects Submitted	Status
Delis-Kaplan Executive Function System (D-KEFS)	470	04/01/2023	0	Approved
Behavior Assessment System for Children (BASC)	70	04/01/2023	0	Approved
Spence Childrens Anxiety Scale	20	04/01/2023	0	Approved
Wechsler Intelligence Scale for Children	70	04/01/2023	0	Approved
Substance Use Survey	360	04/01/2023	0	Approved
Symptom Checklist-90-Revised	360	04/01/2023	0	Approved
Beck Depression Inventory	120	04/01/2023	0	Approved
Beck Anxiety Inventory	120	04/01/2023	0	Approved
The Penn State Worry Questionnaire	120	04/01/2023	0	Approved
Flanker Task	70	04/01/2023	0	Approved
Brief_COPE	360	04/01/2023	0	Approved
Autism Spectrum Disorder (ASD) related basic information	360	04/01/2023	0	Approved
Maastricht Assessment of Coping Strategies	360	04/01/2023	0	Approved
Child Eating Behavior Questionnaire (CEBQ)	20	04/01/2023	0	Approved
Oral Symbol Digit Test	70	04/01/2023	0	Approved
ACEs	150	04/01/2023	0	Requested
3D Image Data	1	04/01/2023	0	Requested

Aim 1: Overview

PI	ICF DCR Approval	ICF IRB Approval	Data Collection Profile	Data Dictionaries Started	Data Dictionaries & Upload Template(s) Finalized	Data Received?	GUID Access	Enrolled	Target Enrollment
Wozniak	✓	✓	✓	✓	✓	✓	✓		70
Suttie	N/A	N/A	✓	✓	✓	✓	N/A		?
Burns, Burns, & Weeks	N/A	N/A	✓	✓	waiting on irb approval of date masking	✓	Pseudo-GUIDs	416	416
Mahnke	N/A	N/A	✓	✓	✓		N/A		36
Mattson	✓	Approval received, not implemented	✓	✓	waiting on Matthew to link data elements to NDA elements		✓		1050
Coles (Emory + UW)	✓	✓	✓	✓	waiting on data dictionaries.				120
del Campo	✓	✓	In Progess	✓					?
Weinberg (Canada)	✓	In Progress	✓		waiting on data dictionaries.				120
Chambers (Pilot)	✓	✓	✓	waiting on DD's & approval on exsiting NDA structures					20
DiClemente									?
Petrenko & Tapparello	N/A	N/A	N/A	N/A	N/A	N/A	N/A		?

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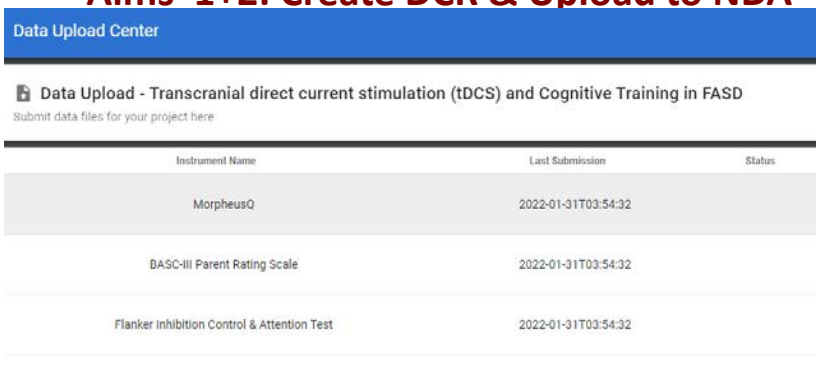
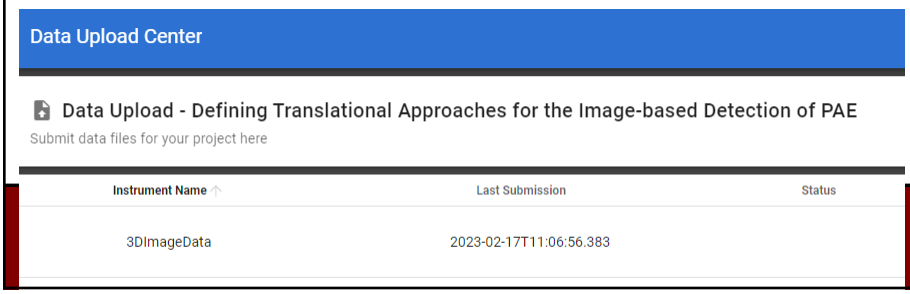
Aims 1+2: Create DCR & Upload to NDA





Aims 1+2: Create DCR & Upload to NDA

DCR

- Project data from
  - Wozniak
  - Suttie
  - Weeks
- Testing portal for issues, errors, feedback to investigator
- Portal fully functional by February 28

NDA UPLOAD

- Upload test data to NDA by March 13
- Resolves errors, issues
- Upload first data package to NDA by April 1

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Aim 4: Archived CIFASD 4 Data

PI	project	DD	Data File	last upload	genetic data	cytokine	photo	dysmorph	# unique IDs	mult visits?	final
Wozniak	Neurobehavior - Wozniak*	1	1	2/15/2023	1		1	1	96	1	1
Petrenko Tapparello	Feasibility Trial	1	1	2/15/2023	1		1		105	1	1
Petrenko Tapparello	FMF Connect RCT	1	1	2/15/2023	1		1		129	1	1
Coles	Adults	1	1	2/13/2023	1	1	1	1	382	1	1
Wozniak	Neuroimaging - Wozniak*	1	1	2/13/2023	1		1	1	96	1	1
Blanchard Mooney	Microbiome	1	1	12/1/2021							1
Hashimoto-Torii	Biomarkers	1	1	7/15/2021							1
Foroud	Human Genetics	1	1	6/8/2022	1		1				
Jones	Dysmorphology	1	1	5/2/2022							
Mattson	FASD-Tree	1	1	4/1/2022							
Eberhart	Zebrafish Genetics	1	1	12/15/2021							
Weinberg	Immune	1	1	12/2/2021	1		1				
Parnell	Mouse Genetics	1	1	12/1/2021							
Mattson	Demographics	1	1	7/16/2021							
Mattson	Neurobehavior - Mattson	1	1	4/1/2021							
Suttie	Neonatal		1	3/23/2021							
Suttie	2D and 3D images	1		0							
Weinberg/Chambers	Cytokine			0							
Chambers	Ukraine			0							
Montag	Tooth fairy	1	1	12/14/2022					2		N/A

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Impact of Prenatal Alcohol Exposure on Lifelong Heart Health

Caroline Burns, Geoff Burns, and Olivia Weeks

Aim 1.

HUMANS

Determine Incidence of Cardiovascular Diseases in Patients with FASDs.

- Congenital heart defect
- Myocardial infarction
- Cardiomyopathy
- Hypertension
- Cerebrovascular accident

Aims 2 and 3.

ZEBRAFISH

Identify Mechanisms of Congenital Heart Defects in Zebrafish with Embryonic Alcohol Exposure (EAE).

Assess Lifelong Cardiomyopathy and Heart Failure Risk in Zebrafish with Embryonic Alcohol Exposure (EAE).

AIM 1

HUMANS

Determine the Incidence of Cardiovascular Diseases in a Retrospective Clinic Cohort Study of Patients with FASDs

IRB Approval: **Completed** ✓

Subject Recruitment: **Completed** ✓
206 males (50% CTRL, 50% FASDs)
209 females (50% CTRL, 50% FASDs)

Data Dictionary (DD): **Nearly Completed**
- Returned initial data on all 417 patients through the DD platform

Major Research Accomplishments:

1. Completed data collection of most cardiometabolic and cardiac parameters.
2. Initiated in-depth collection of cardiac diagnoses from patient records.

Future Goals:

1. Finish data collection of patient echocardiography results.
2. Perform preliminary analysis and age adjustment for all data parameters.

Interactions:
- Work with Tina Chambers to evaluate CHDs and heart murmur incidence in the Ukraine cohort.

AIM 2

ZEBRAFISH

Identify Mechanisms of Congenital Heart Defects in Zebrafish with Embryonic Alcohol Exposure

IACUC Approval: Completed ✓

Major Research Accomplishments:

1. Performed in-depth characterization of congenital cardiac abnormalities arising from EtOH in zebrafish.
2. Identified the PDGF and PI3K pathways as likely molecular mediators of EtOH-induced cardiomyocyte migration defects and congenital heart defects.

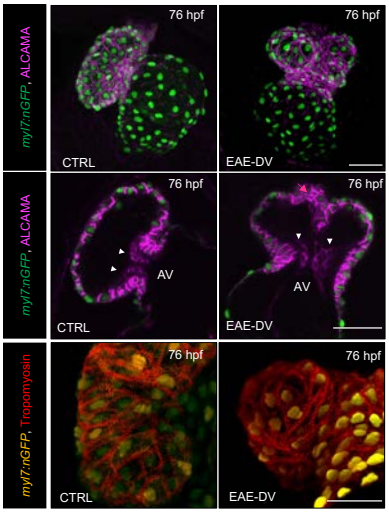
Future Goals:

1. Sorting and RNA sequencing of migrating cardiomyocytes during early cardiac development following EtOH exposure to identify novel molecular mediators of congenital heart defect phenotypes.

2. Further characterize of the impacts of EtOH on *pdgfra* and PI3K signaling.

Interactions:

- Work with Tina Chambers to determine overlap between RNA seq hits and GWAS data.



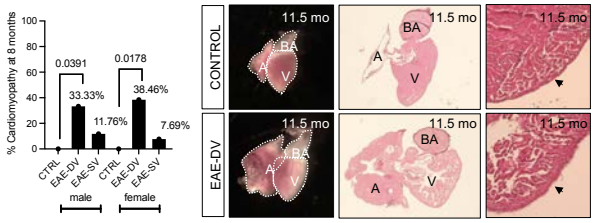
AIM 3

ZEBRAFISH

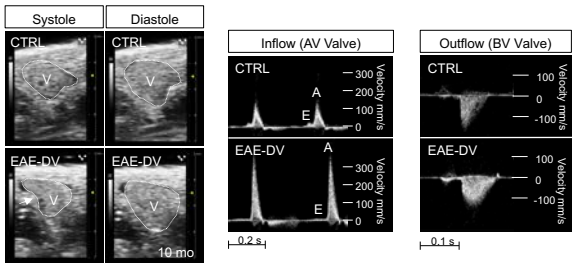
Assess Cardiomyopathy Risk in Adult Zebrafish with Prior Embryonic Alcohol Exposure

Major Research Accomplishments:

1. Demonstrated that EAE zebrafish develop features of cardiomyopathy during adulthood.



2. Developed echocardiography as a tool and used it to define functional changes in the adult EAE heart, which appear to result from increased atrial pressure and diastolic dysfunction.



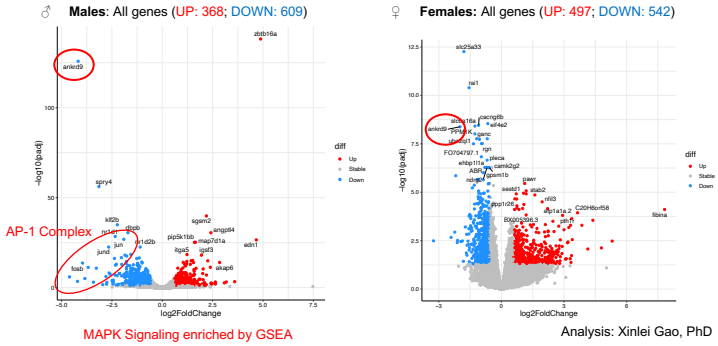
AIM 3

ZEBRAFISH

Assess Cardiomyopathy Risk in Zebrafish with Embryonic Alcohol Exposure

Major Research Accomplishments:

3. Performed RNA sequencing on adult CTRL and EAE ventricles and identified novel genes that define and potentially explain some features of heart failure.



MAPK Signaling enriched by GSEA

Analysis: Xinlei Gao, PhD

Future Goals:

1. Validate RNA sequencing results through qRT-PCR and IHC.
2. Attempt a pharmacological or genetic rescue, if pathways allow.
3. Submit a manuscript for publication.

Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Christina Chambers, Rajesh Miranda, Claire Coles, Julie Kable, Amanda Mahnke, Gretchen Bandoli, Wladimir Wertelecki, Lyuba Yevtushok, Natalya Zymak-Zakutnya

Collaborative Initiative on Fetal Alcohol Spectrum Disorders
January 25, 2023

UC San Diego School of Medicine

CIFASD5 Aims

UC San Diego School of Medicine

Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Aim 1: Compare the prevalence and characteristics of subclinical and clinical signs/symptoms of current and developing metabolic and other chronic diseases and contributing factors in 180 PAE children/adolescents age-matched to 120 children/adolescents with no/minimal PAE.

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Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Aim 2: Using the same sample from Aim 1, compare findings on experimental measures of microvasculature, premature aging, inflammation and altered miRNA expression.

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Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Aim 3: Collaborate with and support other projects in the Consortium.
3.a. Provide core facility resources in the Miranda laboratory to assay blood samples and interpret findings across the Consortium for miRNA expression and telomere length for the Coles/Weinberg and DiClementi/Capasso U01s
3.b. Collaborate with U01 Investigators Burns/Weeks and Coles/Weinberg on interpretation of findings regarding PAE-related metabolic/cardiovascular disease and manifestations of co-morbidities in adults with FASD.
3.c. Provide 3D images and related clinical data for children/adolescents with and without PAE to the Suttie U01
.

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Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Progress on Aims 1-3 - US

1. Revised U.S. pilot to perform at only one site - UCSD
2. Obtained IRB approval for pilot
3. Adapted adult health questionnaire for child
4. Ordered equipment (nail fold capillary measure)
5. Made arrangements for clinical sampling in general pediatrics
6. Developing data dictionaries for instruments
7. RA identifying participants from FASD Registry now
8. Bi-weekly meetings with del Campo and Mattson to coordinate efforts

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Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Progress on Aims 1-3 - Ukraine

1. Study psychologist at Rivne site has started recontacting prior study participant families; 20 in exposed group located so far; will continue and then move to unexposed group
2. Both sites have a pediatrician assigned to identifying community participants with FAS; no shortage
3. Translation of study instruments in progress
4. Weekly meetings to assess situation

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Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

XO

- WGS of mother/child pairs completed last year; analysis of data in progress
- 1st wave focused on collaboration with Susan Smith
- Shared Weeks/Burns preliminary findings to explore in this data set

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Whole Body Effects of PAE Across the Life Span: Early Markers of & Clinical Interventions for Children and Adolescents in Ukraine

Plans for remainder of Year 1

1. Initiate pilot to be completed by end of 2023
2. Complete preparations in Ukraine
3. Explore further collaboration with Ukraine Newborn Register on incidence and type of heart defects in population-based data source
4. Begin receiving biospecimens from pilot, Coles/Weinberg and DiClemente

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miRNA assessment – CIFASD4 samples

- Child samples – 77 samples analyzed, 5 excluded for hemolysis by
  - Preliminary assessment presented at RSA2022

	Neurodevelopment		
	Normal	Delayed	Unknown
no/low PAE	15	18	
PAE	11	27	1

- Maternal samples – previously published data from 93 subjects
  - Finished assaying an additional 30 subjects
- Maternal/child dyads – now have 56 matched maternal/child dyads

	Neurodevelopment		
	Normal	Delayed	Unknown
no/low PAE	11	13	
PAE	9	22	1

miRNA/Cytokine overlap

- Maternal: 99 samples with miRNA and cytokines
- Child: 77 samples with miRNA and cytokines
- Maternal/Child dyads: 46 dyads with both miRNA and cytokines

	Neurodevelopment	
	Normal	Delayed
no/low PAE	9	10
PAE	8	19

Analysis Timeline

- Child miRNA analysis – Spring 2023
- Cytokine dyad analysis (collaboration with Weinberg/Bodnar/Raineki) – Spring 2023
- miRNA dyad analysis – Summer/Fall 2023
- miRNA/Cytokine analyses – Summer/Fall 2023

A Multisite Study of Prenatal Alcohol Exposure: Effects of Inflammation and Endocrine Dysfunction in Adulthood

NIH/NIAAA #: U01AA026108

Claire D. Coles, PhD
Joanne Weinberg, PhD
and
Susan Stoner, PhD
Tamara Bodnar, PhD
Charlis Raineki, PhD
Brock University, Ontario

Sites

Emory University School of Medicine
Atlanta, GA

University of British Columbia
Vancouver, BC

University of Washington
Seattle, Washington

Specific Aims:

In Middle-Aged Adults with PAE, in comparison to SES controls and Older Contrast groups, evaluate the following:

- *The role of immune and endocrine dysregulation in physical and mental health within the individual's social context (examining both negative and positive influences).*
- *The impact of PAE as well as immune and endocrine status on neurocognitive performance and markers of early on-set functional deficits within the social context.*

Accomplished since August 2022:

- Semi-monthly meetings are on-going.
- Developed Multisite Team Organization and Activities
  - *Allowing smooth coordination of activities among sites and investigators.*
- IRB
  - *Requirement for single site Human Subject approval (sIRB) was a process of 6 months. UWA agreed to act as the approving agency and then coordinated with Emory.*
  - *Following that Canadian Clinical Ethics Review Board (CREB) applicants submitted with adjustments for Canadian protocols and requested revisions completed. Awaiting final approval, February 28th.*

- Refined instrument battery & developed data collection protocols
- Data collection, storage, and sharing.
  - *Collaborated with Indiana Data Repository to create instruments consistent with their requirements and those of NIMH Data Archives.*
  - *Developed data collection and storage instruments in REDCap and Qualtrics.*
  - *Data dictionaries completed*

- Identified Participant pools to facilitate recruitment.
  Recruitment & Data Collection to begin in March/April 2023.

  - Atlanta. 90 from CIFASD4 Registry and Longitudinal Cohort. 30 Older adults to be recruited from EUSM Department of Neurology's Health Aging Cohort.
  - Seattle. 90 from Registry of FASD/control participants and will recruit community sample of 30 older adults.
  - Canada. 90 FASD/Controls from community clinics plus 30 older adults in collaboration with colleagues at Brock University.

Interaction with other CIFASD5 Investigators

Rajesh Miranda, PhD, Texas A & M ,is a collaborator and will be analyzing cRNAseq from Canadian samples.

Michael Suttie, PhD, University of Oxford, will be receiving 3-D images of Adults for data analysis.

Leah Wetherill, PhD, Indiana University, is collaborating for data sharing.

Miguel Del Campo, MD, UCSD, will provide oversight of dysmorphology exams.

Amanda Mahnke, PhD, will receive peripheral blood cells for generation into human induced pluripotent stem cells (UH2 project).

Designing a Hybrid Intervention Strategy to Reduce Alcohol Exposed Pregnancies

PI: RALPH DICLEMENTE, PHD

SITE PI: ANGELA STOTTS, PHD

Russia

Houston

UT Health Science Center at Houston

In the Texas Medical Center

McGovern Medical School
- Family and Community Medicine
- Obstetrics, Gynecology, and Reproductive Medicine

Aims & Hypotheses

The web-based behavioral intervention combined with motivational counseling delivered in a prenatal clinic will:

1. Reduce drinking in a predominantly minority population of people who are pregnant and drinking. Outcome: Negative PEth test in the 2nd and 3rd trimester

2. Reduce adverse birth outcomes.

Design: 2-group RCT, control = Usual Care

Two large prenatal clinics:

UT Physicians Obstetrics and Gynecology Continuity Clinic

LBJ Hospital Prenatal Clinic

Progress to date

Met multiple times with NIAAA program officers.

Rewrote the grant application based on Houston as the site.

Received IRB approval from the UTHouston Committee for the Protection of Human Subjects.

NYU relying on the UT IRB.

Waiting on the NOA.

Houston: Interviewing for staff and establishing screening protocol for the OB clinics

NYU: Gathering measures and modifying the intervention

U01: Assessment of Fetal Alcohol Spectrum Disorders (FASD) Using Novel Web-Based Tools

Sarah Mattson, Ph.D.
San Diego State University

Aim of Project

- ★ **To improve the detection of fetal alcohol spectrum disorders (FASD).**
  - To achieve this aim, we will deploy web-based tools which aid in the screening and evaluation of FASD.
    - FASD-Tree
    - Brief Assessment of Individual Neurobehavior – online version (BRAIN-online).

Primary Tools

FASD-Tree is a web-based screening tool that records physical and behavioral data and outputs a dichotomous result (affected/not affected) and a continuous risk score (0-5) indicating the presence and degree of alcohol-related effects.

BRAIN-online is a cognitive test administered on a home computer that measures fine-motor speed, reaction time, response inhibition/impulsivity, attention, problem-solving, memory, processing speed, spatial working memory, and set-shifting.

IRB Status

- ★ Mostly approved
  - Some amendments still needed related to expanding/changing project details

C5 Accomplishments: BRAIN-online

- ★ Continuing to collect data with BRAIN-online in San Diego
  - 12 subjects tested
- ★ Initiated the “public study” in which BRAIN-online was made available to the public through the Indiana Alliance (Indiana Affiliate of FASD United)
  - 6 adult subjects tested
  - 2 child subjects tested
- ★ We are hoping to add more FASD United Affiliates to the public study
- ★ Assisting D.r Wozniak with including BRAIN-online in his U01 project
- ★ Developed a feedback report for use with BRAIN-online for those who request feedback (7 of 8 so far)

C5 Accomplishments: FASD-Tree

- ★ Working on adding improvements to FASD-Tree including:
  - Adding the full dysmorphology form,
  - Allowing storage and download of BRAIN-online and MQ data with FASD-Tree data
  - Adding/Fixing percentiles
  - Correcting field names
  - Allowing for repeated participation
- ★ Completed the ARND algorithm and feedback mechanism. Hoping to incorporate this algorithm into FASD-Tree

C5 Accomplishments: Other Measures

- ★ Facial Imaging
  - MorpheusQ: 13 Subjects (currently on hold) [Riley/Del Campo]
  - 3D Images (Canfield): 24 Subjects [Suttie]
- ★ Dysmorphology: We've had 1 training meeting with Dr. Del Campo to train for dysmorphology evaluations. A second meeting is planned for early 2023
- ★ Neuropsychological Testing with C5 battery: 20 subjects
- ★ Canada: Presenting to Canadian clinics in April

C5 Accomplishments: Recruitment Summary

	Total	C5	Public Study	Young Adults
Referrals	–	28	–	–
FASD-Tree	361	17	–	–
BRAIN-online	262	12	8	906
NP Testing	–	20	–	–

Accomplishments: Papers

1. Mattson, S.N., Jones, K.L., Chockalingam, G., Wozniak, J.R., Hyland, M.T., Courchesne, N.S., Del Campo, M., Riley, E.P., & the CIFASD. (2023). Validation of the FASD-Tree as a screening tool for fetal alcohol spectrum disorders. Alcoholism: Clinical and Experimental Research, 46 (1): 52-65. Published online 2021 Dec 2. doi: 10.1111/acer.14987. PMCID: PMC8799504

2. Hyland, M.T., Courchesne-Krak, N.S., Bernes, G.A., Wozniak, J.R., Jones, K.L., Del Campo, M., Riley, E.P., Mattson, S.N., & the CIFASD. Results of an FASD screening tool are associated with neuropsychological and behavioral measures. Submitted 12/14/2022

Accomplishments: RSA Abstracts

Veziris, C. R., Hyland, M.T., Kable, J.A,. Wozniak, J.R., Coles, C.D., May, P.A., Kalberg, W.O., Sowell, E.R., Riley, E.P., Mattson, S.N., & the CIFASD. Validation of the ND-PAE diagnosis in children with heavy prenatal alcohol exposure.

Estrada, C.S., Veziris, C.R. Hyland, M.T., Brucks, B. Mattson, S.N., & the CIFASD. Is there a relationship between covid-19 related stress and alcohol use in college students?

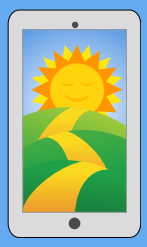
Felicicchia, R.J., Hyland, M.T., Roesch, S.C. & Mattson, S.N. Differences in the family environment in children with and without prenatal alcohol exposure.

Felicicchia, R.J., Hyland, M.T., Roesch, S.C. & Mattson, S.N. Two unique profiles of family environment exist among families of children with prenatal alcohol exposure.

Mattson, S.N., Veziris, C. R., Hyland, M.T., Kable, J.A,. Wozniak, J.R., Coles, C.D., May, P.A., Kalberg, W.O., Sowell, E.R., Riley, E.P., & the CIFASD. Evaluation of proposed criteria for ND-PAE in a large sample of individuals with heavy prenatal alcohol exposure.

Plans for the Rest of Y1 (Aspirational)

- ★ Continue data collection
- ★ Expand Public Project to include additional FASD United affiliates
- ★ Set up data collection/feedback in Canada (in collaboration with Dr. Cook)
- ★ Continue to assist Dr. Del Campo in setting up the Alaska site
- ★ Finalize updates on FASD-Tree
- ★ Integration of FASD-Tree and BRAIN-online
- ★ Methods paper on BRAIN-online



Leveraging Technology to Increase Quality of Life for FASD Across the Lifespan

Christie L. M. Petrenko, Ph.D. & Cristiano Tapparello, Ph.D.

Mt. HOPE family center

UNIVERSITY of ROCHESTER

Families Moving Forward CONNECT

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Antique Lutke
ALC / Self-Advocate

Katrina Griffin
ALC / Self-Advocate

Maggie May
ALC / Self-Advocate

Emily Hargrove
ALC / Self-Advocate

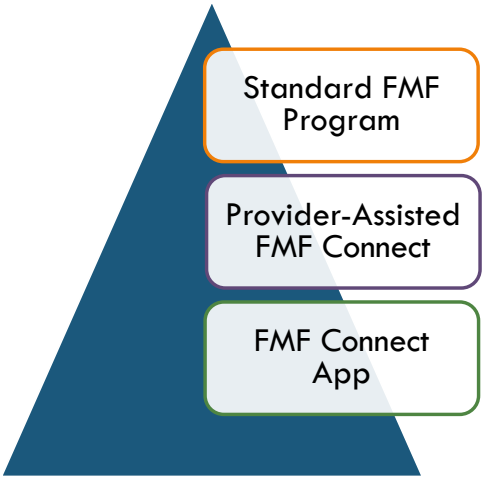
Families Moving Forward CONNECT

CIFASD5 Aims

- **Aim 1**: Provider-Assisted FMF Connect (Mental Health Providers - Child)
  - *Formative:* use focus groups and implementation mapping to design "Provider-Assisted FMF Connect" and implementation packages (Year 1)
  - 3-parallel arm RCT with 250 mental health providers (Years 2-5)
- **Aim 2**: My Health Coach app (Adults with FASD) – from UH2
  - 2-parallel arm RCT with 120 adults with FASD (Years 2-3)
- **Aim 3**: Determined App system (Teens with FASD and Caregivers)
  - Use focus groups and advisory board input to design Determined app system (Years 3-4)
  - Usability testing with 10 teens and caregivers (Year 5)

3

CHILDHOOD: BUILDING A CONTINUUM OF CARE



Families Moving Forward Program

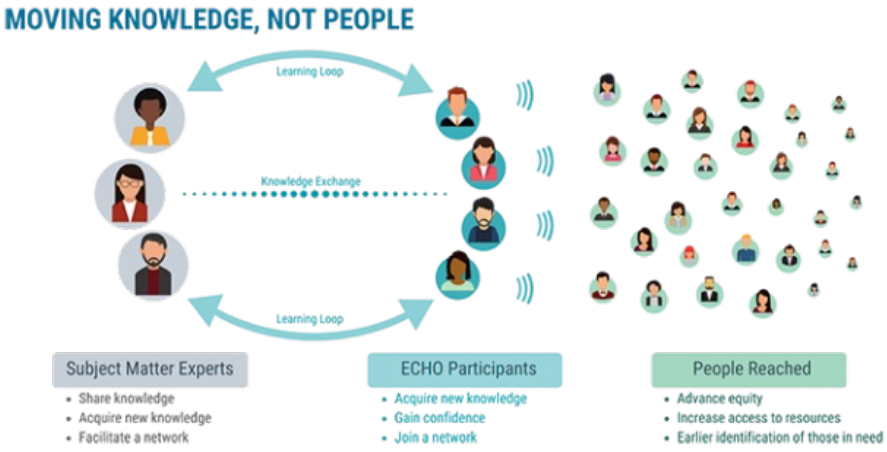
1:1 Program with therapist
In home, clinic, or telehealth
7-9 months
Therapists – 40+ hrs training

THIS PROJECT ☺

Families Moving Forward CONNECT

Self-directed app to be used by caregivers

PROJECT ECHO©
(EXTENSION OF COMMUNITY HEALTHCARE OUTCOMES)



Families Moving Forward CONNECT

Provider-Assisted FMF Connect

- Established weekly working group to develop intervention / training materials
- Recruited applicants for Parent Hub Team member; group interview / focus group
- Established monthly full Hub Team meeting

6

Mental Health Provider Focus Groups

- 2 rounds of focus groups
  - 1st round (fall 2022) to determine acceptability, inform design
  - 2nd round (spring 2023) refine materials and implementation plan
- 62 providers screened eligible to date
- Four 1st round groups completed (n=28)

7

Initial Focus Group Preliminary Themes

- Concept of Provider-Assisted FMF Connect is acceptable
- Providers want flexibility in how would use FMF Connect app with caregivers
- Both tele-mentoring and self-directed training were acceptable; individual preferences and logistical considerations
- Identification of motivators and barriers

8

Intervention Material Development Progress

- Introductory webinar (recruitment tool) created and piloted with NSAW Maine with high ratings
- ECHO didactic training materials for 5 sessions (of 12) under development
- Will then derive self-directed trainings and implementation materials – Aiming ~April 2023

9

Other Updates

- IRB for Aim 1 focus groups approved 05/11/2022
- CIFASD5 projects supported recruitment for provider focus groups

10

Families Moving Forward CONNECT

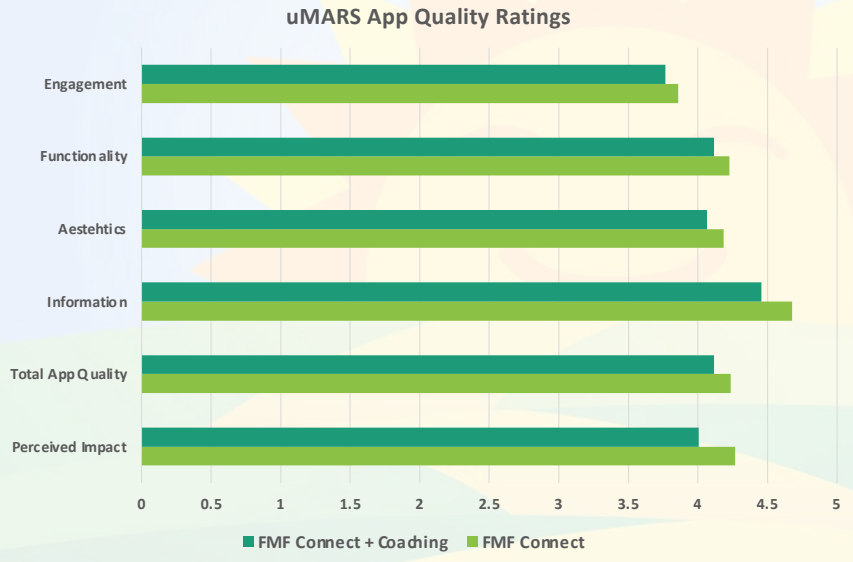
CIFASD4 Aim 3 RCT – New Findings!

Group	Total Assigned	T1 Complete	Received App	Installed App	T2 Complete	T3 Complete
FMF + Coaching	43	41	41	39	30	30
FMF Alone	43	39	39	35	28	22
Wailtlist	42	39	--	–	32	30
TOTALS	128	119	80	74	90 of 119	82 of 119
Percentage of Total	-	93%		93%	76%	69%

11

Families Moving Forward CONNECT

CIFASD4 Aim 3 RCT – New Findings!

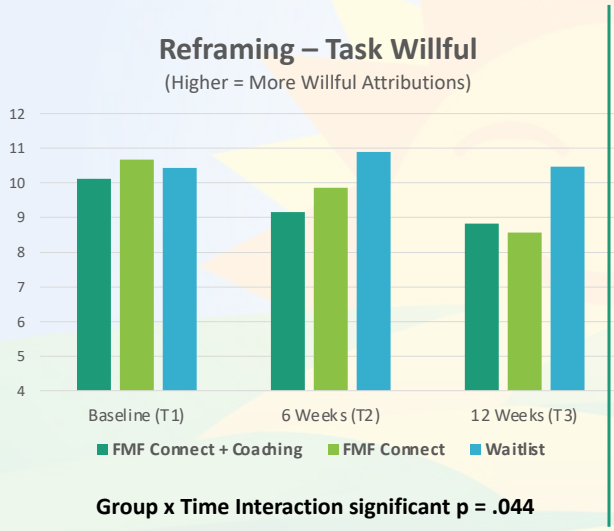


Families continue to report high ratings of app quality and satisfaction

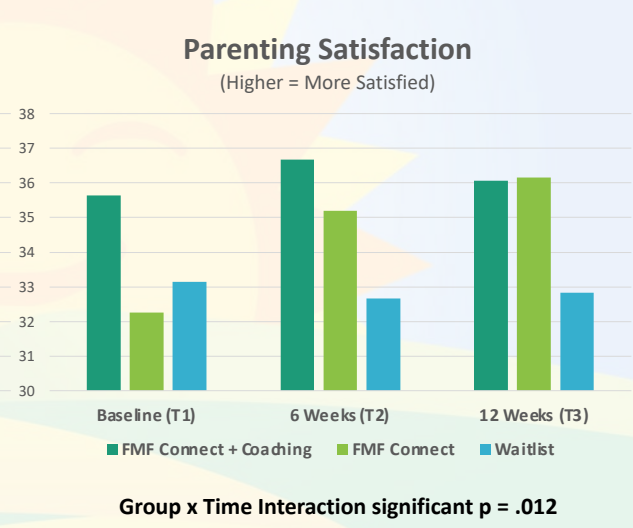
12

Families Moving Forward CONNECT

CIFASD4 Aim 3 RCT – New Findings!



Group x Time Interaction significant p = .044



Group x Time Interaction significant p = .012

13

14

NIH National Institute on Alcohol Abuse and Alcoholism
NIH...Turning Discovery Into Health®

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Defining Translational Approaches for the Image-based Detection of Prenatal Alcohol Exposure

CIFASD5 2023

Michael Suttie

CIFASD | Collaborative Initiative on Fetal Alcohol Spectrum Disorders

Nuffield Department of Women's and Reproductive Health, University of Oxford

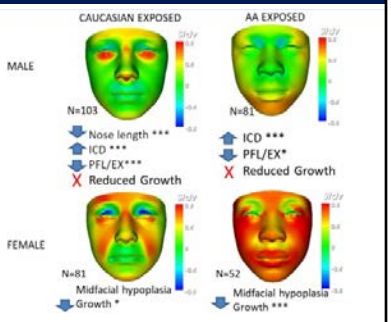
UNIVERSITY OF OXFORD

Aim 1 **Identifying factors secondary to alcohol that may influence outcomes**.

- Primary investigating sexual dimorphism and co-exposures on facial dysmorphism

Aim 2. **Investigating facial dysmorphism using 3D imaging**

- Age-specific FASD associated facial dysmorphism
  - **Neonates** to **adults**
- Assessing impact of intervention during pregnancy designed to reduced consumption



Aim 3 **Clinical Translation**

- Develop fully **automated** 3D facial analysis using machine learning suitable for clinical deployment.
- Develop novel **multi-modal** deep learning architecture combining **face and neurocognitive assessment**
- eHealth App-Based Integration: Providing facial analysis access to apps to facilitate both clinical and research goals
- **Software distribution**. We will generate general-purpose face analysis software for facial analyses and clinical deployment

Nuffield Department of Women's and Reproductive Health, University of Oxford

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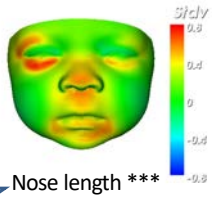
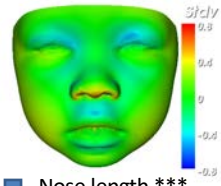
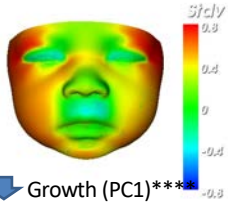
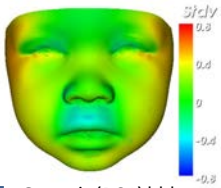
IRB

Nuffield Department of Women's and Reproductive Health, University of Oxford

UNIVERSITY OF OXFORD

Facial Morphology of Concurrent Prenatal Alcohol and Smoke Exposure using 3D Imaging

	PASS 1M	PASS 1Y
MALE	 Nose length *** ICD ***	 Nose length *** ICD ***
FEMALE	 Growth (PC1)*** ICD***	 Growth (PC1)***

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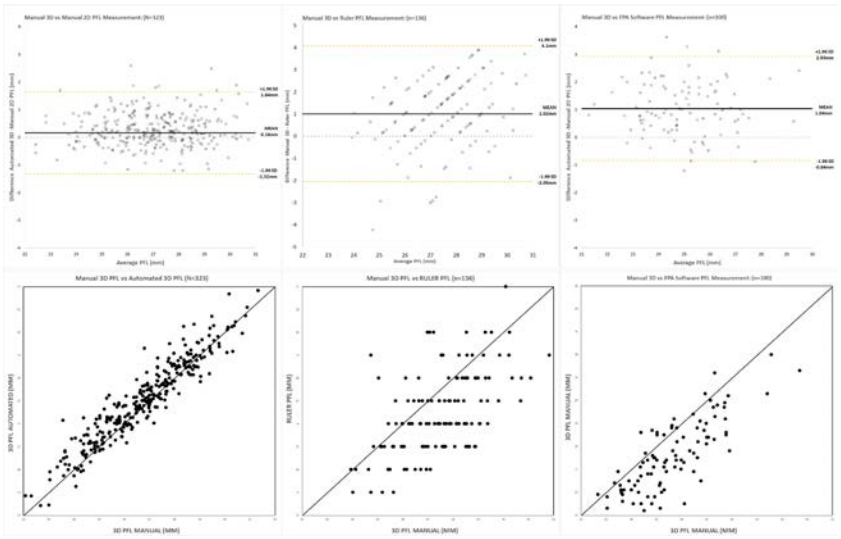
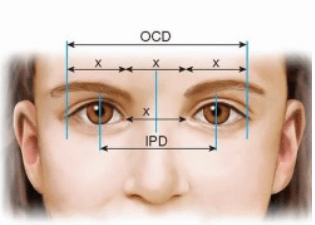
Ocular Measurements in FASD – An automated method for detection





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Outputs

EUFASD 2022 – Arendal, Norway
Plenary talk CIFASD session

FASD in the UK: Building on 20 years of progress – Manchester, UK
Plenary talk
3D imaging workshop

RSA 2023 Submission accepted:
MACHINE LEARNING APPROACHES IN THE IDENTIFICATION OF INDIVIDUALS WITH FETAL ALCOHOL SPECTRUM DISORDERS
Dr Gretchen Bandoli

Alcoholism and Alcohol-related disorders
BOOK CHAPTER:

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Major goal(s) to complete by end of year 1

Paper submissions:

- **Imaging-Based Ocular Measurements for the Assessment of Fetal Alcohol Spectrum Disorder**
  Final draft for immanent submission to ACER
- **Facial Morphology of Concurrent Prenatal Alcohol and Smoke Exposure using 3D Imaging**
  Contribution to Frontiers in Neuroscience Research Topic on "Perspectives and Recent Advances in Fetal Alcohol Spectrum Disorders Research"

New Starter:

- **Dr Yan Xia** - Specialist in 3D imaging, deep learning and AI for medical image analysis

Progress with clinical tools, FaceScreen server development

Develop multi-modal deep learning methods for 3D face-neurocognitive assessment

Set up HIPAAA compliant server – Internal clinical translation theme BDI

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iPhone Scanning

bellus3D

EM3D APP

FUEL3D SHAPING FUTURES

CIFASD Collaborations

- Dr Sarah Mattson – 3D Face <-> Neurocognitive assessment tools
- Dr Miguel del Campo – Clinical validation, image data/dysmorphology
- Dr Ralph DiClemente – Intervention assessment
- Dr Leah Wetherill – Data Coordination Resource

- Dr Jeff Wozniak, Dr Claire Coles, Dr Joanne Weinberg, Dr Christie Petrenko, Dr Tina Chambers

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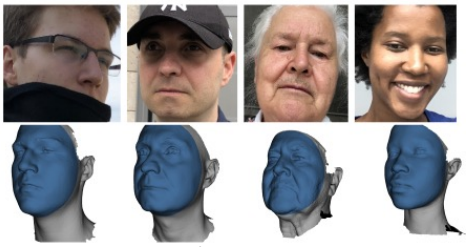
'External' Collaboration

3D from 2D

- Dr Tinashe Mutsvangwa
  University of Cape Town
- Prof Bernhard Egger
  Friedrich-Alexander-Universität Erlangen-Nürnberg, FAU



Sanyal et al. RingNet: Learning to Regress 3D Face Shape and Expression from an Image without 3D Supervision, CVPR 2019
Feng et al. Learning an Animatable Detailed 3D Face Model from In-The-Wild Images, SIGGRAPH 2021

Dr Raja Mukherjee
Dr Neil Aton

TDCS and Cognitive Training in FASD

JEFFREY R. WOZNIAK, PH.D., L.P.
UNIVERSITY OF MINNESOTA

Aims

1. Evaluate 5 sessions of active TDCS vs. sham with Cognitive Training;
   Active → Improved sustained attention and ADHD symptoms compared to sham

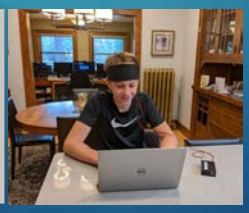
2. Quantify dose-response by comparing 10 active to 5 active sessions of TDCS
   10 → Improved sustained attention and ADHD symptoms compared to 5 sessions

3. Establish durability of benefits
   At two months, improvements will be sustained and 10 sessions > 5 sessions

4. Using fMRI, measure changes in brain connectivity in limbic and salience networks

Progress

- Initial IRB approval: 6/10/2022
- Modifications approved: 0/15/2022
- New modification submitted 1/6/2023 (following another study's status change)
- Ancillary review by drug/device regulatory review (approved 1/23/2023)
  - Abbreviated Investigational New Device (IDE) status confirmed (1/23/2023)
  - Local IRB is surrogate overseer of the IDE
  - Devices are non-significant risk (NSR)



FDA

National Archives and Records Administration

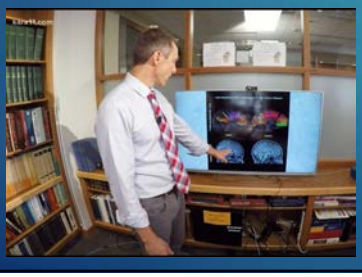
code of federal regulations

Progress

- First participant enrolled 11/10/2022
  - Completed 4 sessions
  - 9 year old; Could not tolerate the stimulation / significant behavioral challenges
- One participant ineligible (benign rolandic epilepsy)
- Two additional participants waiting enrollment (pending IRB/HIPCO approvals)
  - 11 year old female
  - 14 year old male

Progress

- MRI scan
  - Two Visit-1 MRI scans complete
  - Data acquired, processed, and passed quality control
  - fMRI – functional connectivity
  - Diffusion – Neurite Orientation and Dispersion Index



NODDI

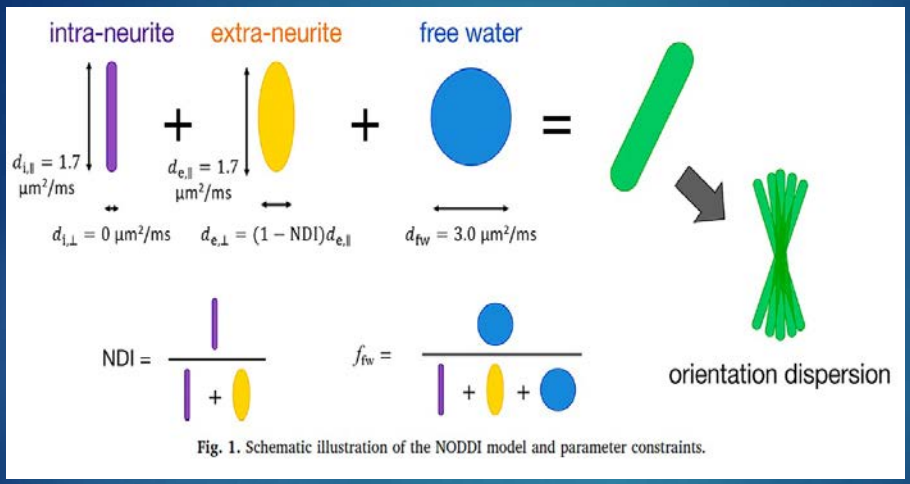


Fig. 1. Schematic illustration of the NODDI model and parameter constraints.

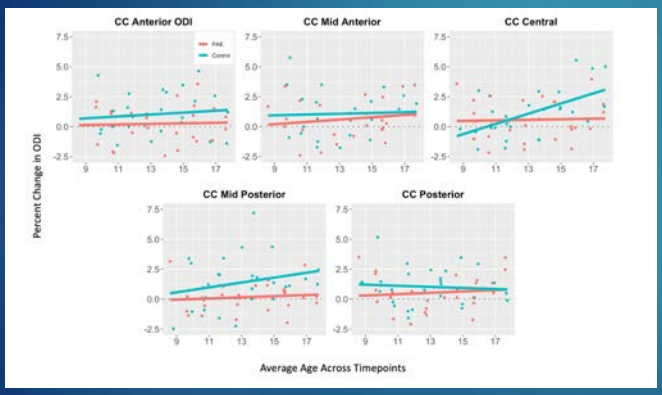
Values range from 0 to 1
1 = neurites densely packed
0 = low neurite density

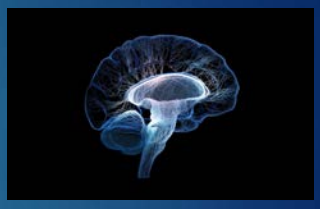
Interactions

- **Miguel del Campo, UCSD** – Currently training clinicians, a post-doc, and coordinators at UMN to conduct dysmorphology exams
  - Next session: January 27, 2023
- **Sarah Mattson, SDSU** – BRAIN online will be administered to participants
- **Mike Suttie, Oxford** – We will collect and share 3D facial images
  - Canfield system
- **Leah Wetherill, Indiana U.** – Perhaps 85% of data dictionary built, but needs fine-tuning

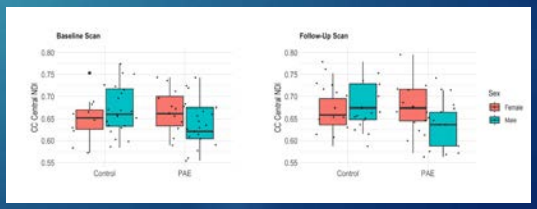
CIFASD Manuscripts in progress

- *Atypical developmental trajectories of white matter microstructure in prenatal alcohol exposure: Preliminary evidence from neurite orientation dispersion and density imaging (NODDI)*



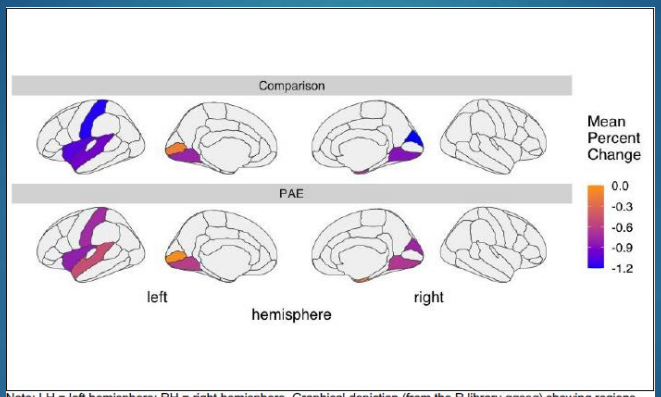


Frontiers in Neuroscience (Special issue)

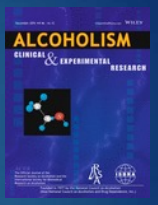


CIFASD Manuscripts in progress

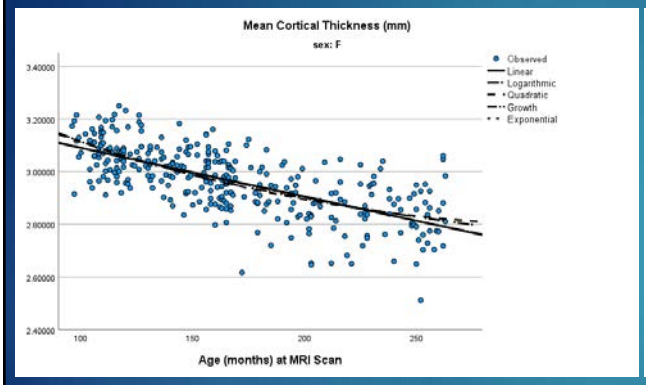
- *Delayed cortical thinning in children and adolescents with prenatal alcohol exposure*

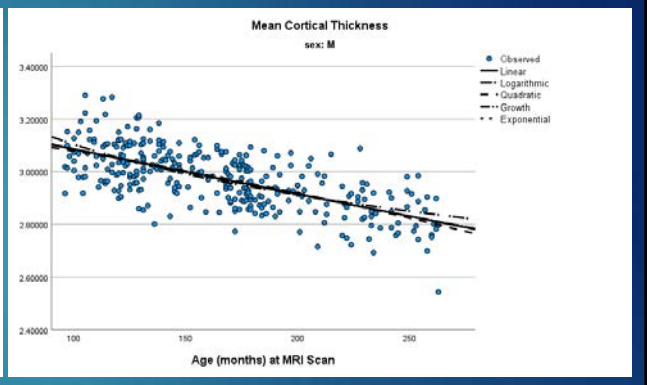


Note: LH = left hemisphere; RH = right hemisphere. Graphical depiction (from the R library *ggseg*) showing regions with significant differences (uncorrected for multiple comparisons) in mean symmetrized percent change in cortical thickness by diagnostic group. PAE participants demonstrated significantly less negative percent change in cortical thickness (i.e., less cortical thinning) across time than Comparison participants in LH postcentral, LH superiortemporal, RH entorhinal, LH lingual, RH lingual, LH pericalcarine, RH cuneus, and LH insular cortices.



Alcoholism: Clinical & Experimental Research (under revision)






Thank You!
NIH
National Institute
on Alcohol Abuse
and Alcoholism
MASONIC INSTITUTE FOR
THE DEVELOPING BRAIN
CIFASD
Collaborative Initiative on
Fetal Alcohol Spectrum Disorders

Lifelong impact of PAE on stem cell dynamics and cellular aging

UH2AA030186

AMANDA H. MAHNKE, PH.D.
ACES ASSISTANT PROFESSOR
TEXAS A&M UNIVERSITY SCHOOL OF MEDICINE
FEBRUARY 22, 2023

Specific Aims

Aim 1 - Does PAE diminish stem cell function across the lifespan?

A) Create human-induced pluripotent stem cells (hiPSCs) from peripheral blood mononuclear cells obtained from diverse age CIFASD cohorts
- Neonate – DiClemente; Child/Adolescent – Chambers; Adult – Coles/Weinberg

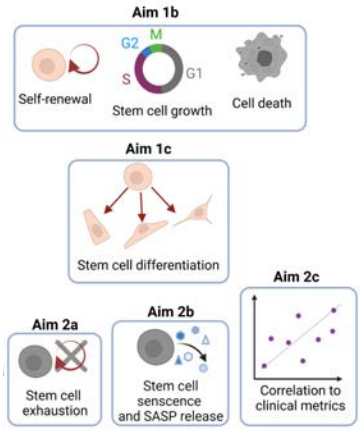
B) Assess hiPSCs for growth, renewal, differentiation

Aim 2 - Does PAE induce or exacerbate stem cell aging?

A) Assess metrics of stem cell exhaustion

B) Assess stem cell senescence and the production/release of senescence-associated secretory phenotype (SASP) molecules

C) Correlate changes in stem cell biology to clinical metrics

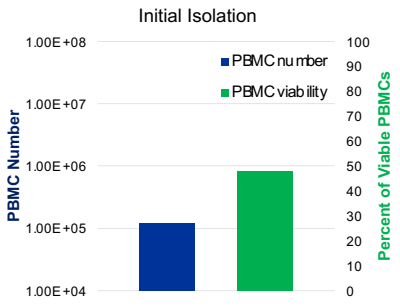


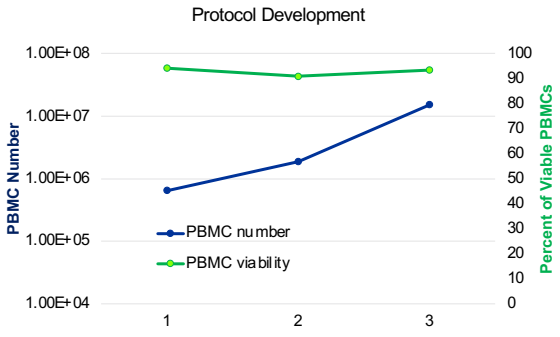
Progress so far

- IRB and IBC approval (IRB as exempt)
- Personnel hiring
- Work with Data Coordination Resource (Wetherill U24) - data dictionary created and approved
- Worked with Canadian Adult Cohort (Coles/Weinberg) to include appropriate consent language for this project
- SOP development
- Assay design

Progress so far

- SOP development
  - Refining PBMC isolation protocol with commercially available blood samples
  - Working with Drs. Bodnar and Raineki (Coles/Weinberg U01) to test PBMC isolation protocol





Progress so far

- Designing qPCR primers for senescence and SASP markers

Gene Target	Role	Designed	qPCR	Sequenced	Status
IL-6	SASP	Yes	Yes	Yes	Validated ✓
VEGFA	SASP	Yes	Yes	Yes	Validated ✓
CXCL8	SASP	Yes	Yes	Yes	Validated ✓
IL-1A	SASP	Yes	No	—	Reassess
VEGFC	SASP	Yes	No	—	Reassess
GLB1	Senescence	Yes	Yes	In progress	
p16INK4A/CDKN2A	Senescence	Yes	Yes	In progress	
p14ARF/CDKN2A	Senescence	Yes	Yes	In progress	
p21/CDKN1A	Senescence	Yes	Yes	In progress	
IL-7	SASP	Yes	In progress	—	
IL-8	SASP	Yes	In progress	—	
CSF2(GM-CSF)	SASP	Yes	In progress	—	
LMNB1	Senescence	Yes	In progress	—	
TP53	Senescence	Yes	In progress	—	
NOTCH1	Senescence	Yes	In progress	—	

Anticipated progress by end of Yr 1

- Create hiPSCs from PBMCs derived from commercially available blood (donors aged 36-44)
  - Create hiPSC induction protocol
- Using isolated PBMCs and hiPSCs created from commercially available blood
  - Assess staining, flow cytometry, and other proposed techniques
  - Create standard protocols for proposed assays
- First set of sample collection underway (Adults, Vancouver)
- Continued discussions with other cohort collaborators for samples

Development of biomarkers in deciduous teeth of children with FASD that predict neurobehavioral performance

1 UH2 AA029062-01

PIs: Annika Montag & Christine Austin

CIFASD4 2023 Progress Meeting

UC San Diego School of Medicine

Rady Children's Hospital San Diego

Icahn School of Medicine at Mount Sinai

Specific Aims

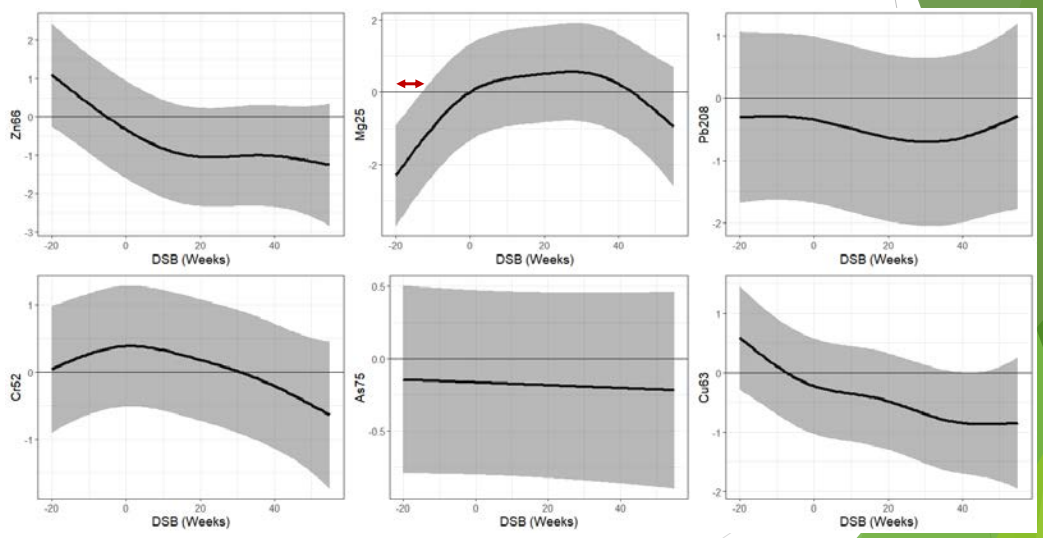
Aim 1. Determine the sensitivity and specificity of direct and indirect biomarkers of PAE in deciduous teeth of 25 children with FASD and 25 children with known absence of PAE.

Aim 2. Assess associations among magnitude and gestational timing of PAE identified in the deciduous teeth of 25 children with FASD and 25 children with known absence of PAE and neurobehavioral deficits.

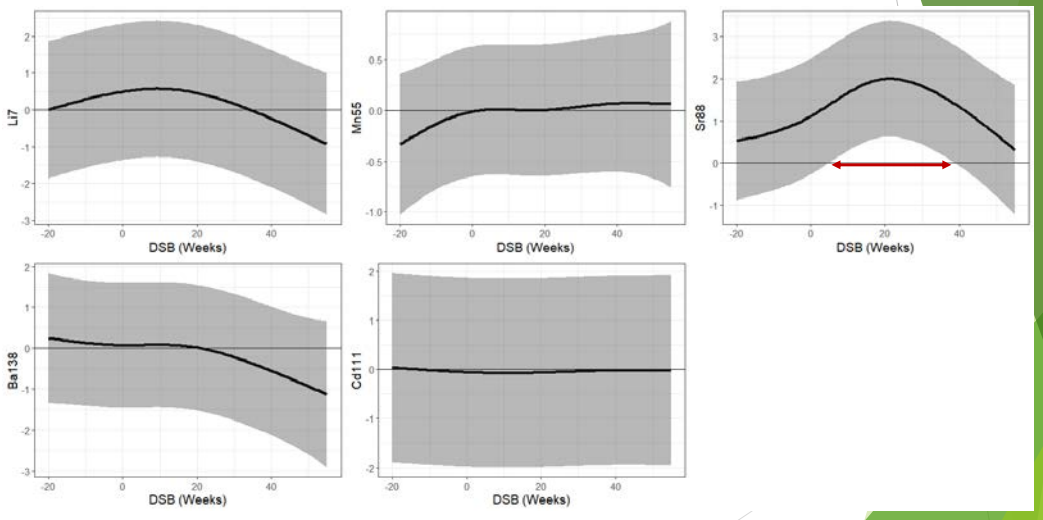
Aim 3. Explore the interaction between PAE and exposures to neurotoxic and nutritive metals during prenatal and early life.

Aim 4. Explore potential biomarkers of co-exposures including cannabis, tobacco, and opioids.

Aim 3: Metals Analysis



Aim 3: Metals Analysis



Aim 1: EtG and EtS Biomarkers

	2nd Trimester		3rd Trimester		Postnatal	
Donor	EtG (pg/mg tooth)	EtS (pg/mg tooth)	EtG (pg/mg tooth)	EtS (pg/mg tooth)	EtG (pg/mg tooth)	EtS (pg/mg tooth)
Cntrl 1	-	-	0.00	0.00	0.00	0.00
Cntrl 2	0.00	28.16	0.00	11.62	0.00	0.00
Cntrl 3	-	-	0.00	85.39	0.00	0.00
Cntrl 4	164.29	0.00	0.00	0.00	0.00	0.00
Case 1	66.89	0.00	84.52	0.00	159.63	12.18
Case 2	73.20	0.00	31.12	0.00	8.45	0.00
Case 3	0.00	230.49	0.00	55.88	0.00	43.73
Case 4	0.00	21.09	0.00	0.00	0.00	0.00
Case 5	-	-	0.00	16.96	0.00	0.00
Case 6	0.00	87.01	0.00	12.35	0.00	3.91

My Health Coach:

Mobile Health Tools to Promote Health in Adults with Fetal Alcohol Spectrum Disorder

CHRISTIE L. M. PETRENKO, PH.D.
CRISTIANO TAPPARELLO, PH.D

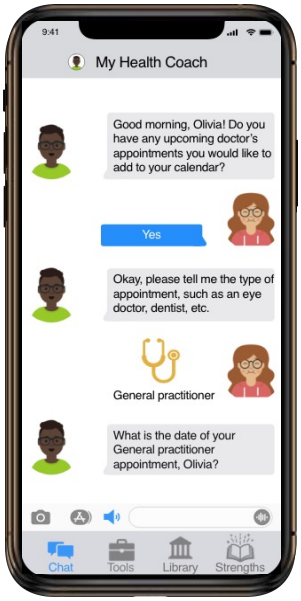
UH2 AA029050
February 2023

PARTNERSHIP WITH THE ADULT LEADERSHIP COMMITTEE OF FASD CHANGEMAKERS

AIMS

1) Development of "My Health Coach" app
- Identify & refine functionalities through focus groups and survey methods.
- Develop an iOS prototype for testing

2) Feasibility Study



PROGRESS

- 15 Advisory board meetings
- Completed development of interactive prototype design
- Completed focus group data collection (Aim 1)
- Completed Survey data collection in progress (Aim 1)

FOCUS GROUP & SURVEY RESULTS

MANUSCRIPT IN PREPARATION

Global impressions overwhelmingly positive

All app features shown were acceptable to participants

App looked easy to use, and seen as condition management and advocacy tool

Recommendations: Accessibility Accountability, Expanded app features and design

COMMUNITY ADVISORY BOARD BEST PRACTICES

MANUSCRIPT IN PREPARATION

Through 2 rounds of interviews and 1survey, we have found:

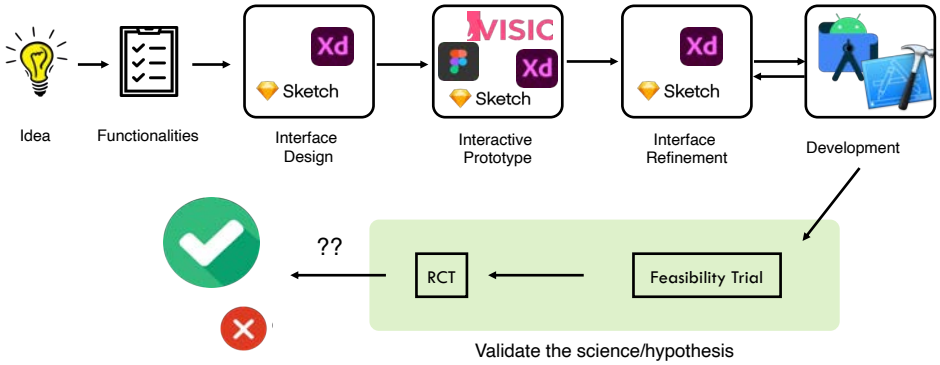
ALC members have experienced identified benefits of community-based participatory research (Israel, 1998)

Identified facilitators and barriers to partnering with research teams as self-advocates

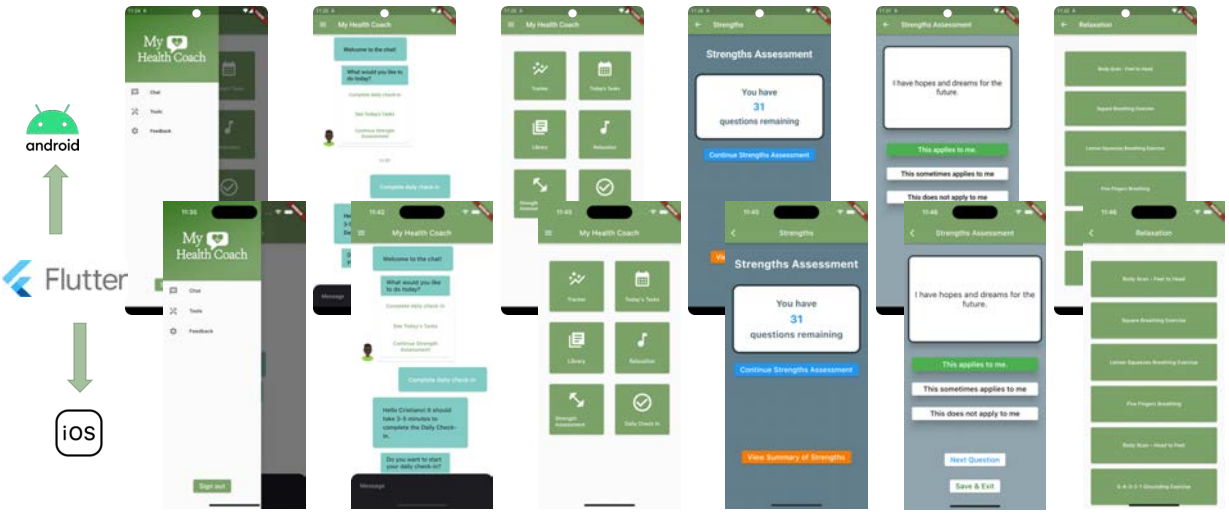
Identified ways in which partnership has strengthened the project

Co-creating a toolkit for future partnerships

APP DEVELOPMENT



APP DEVELOPMENT



FEASIBILITY TRIAL PREPARATION

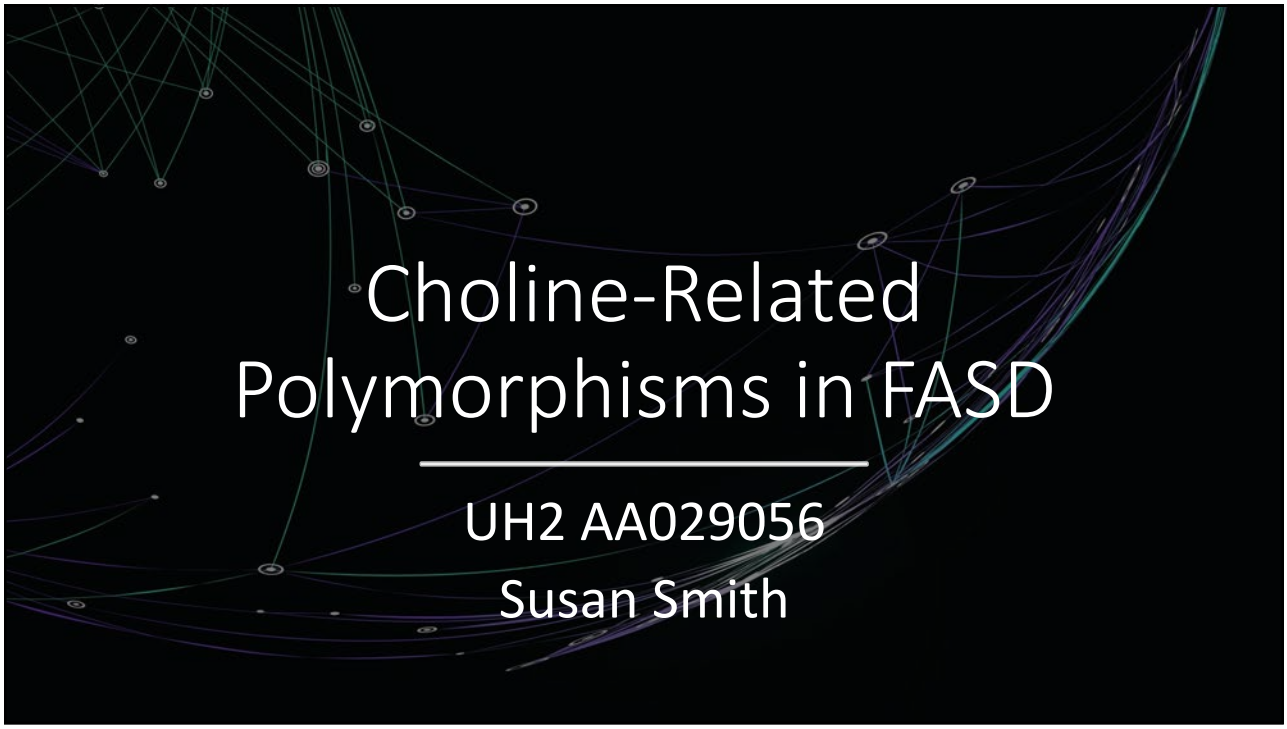
Developed iOS and Android prototype

Content developed:
- 75 daily messages
- 11 factsheets
- 42-item strengths assessment

Measurement battery reviewed with advisory board and adapted – programmed on REDCap

ClinicalTrials.gov registration

IRB approval pending since December 2022 due to app security review
- Recruitment will launch as soon as IRB is approved



Choline-Related Polymorphisms in FASD

UH2 AA029056

Susan Smith

Aim 2 Hypothesis: Polymorphisms that increase choline/1C needs are associated w/ worsened cognitive outcomes in those with heavy PAE

- Completed analysis of CIFASD2/3
- 260 Control, 254 Alcohol-exposed (544 total)
- No choline supplements (dietary only)
- Association analysis:
  - 114 SNPs x 799 Behavioral Endpoints

Cognitive Measures are Associated with *SLC44A1* (rs3199966, S644A) in Those with Heavy PAE

Cognitive Measurement	ADD Model	ADD x PAE
	Padj	Padj
DAS-II **General Cognitive Abilities**, Percentile	0.03056	0.01447
DAS-II General Cognitive Abilities, Mean Total Score	0.03056	0.01160
DAS-II **Nonverbal Reasoning Cluster**, Percentile	0.03898	0.01553
DAS-II **Recall of Designs**, Age Equivalent	0.03343	0.02038
DAS-II Recall of Designs, Percentile	0.03056	0.02005
DAS-II Recall of Designs, Total Score	0.03056	0.02038
DAS-II **Sequential and Quantitative Reasoning**, Ability Score	0.03056	0.01160
DAS-II Sequential and Quantitative Reasoning, Age Equivalent	0.04810	0.01131
DAS-II Sequential and Quantitative Reasoning, Percentile	0.03056	0.01131
DAS-II Sequential and Quantitative Reasoning, Total Score	0.03056	0.01131
VABSIIP **Internalizing V-score**	0.03056	0.01160

Next Steps…

- Finish manuscript draft and circulate to co-authors
- Complete association analysis for SLC44A1 in Ukrainian / OmniNet
- Submit R01 for Feb 5 to explore additional 1C-related genes
- Functional cell studies