

**CAB Conference Call
September 26, 2019
12:00 EST
Meeting Minutes**

Participants:

Andrea	Jacobi Medical Center
Anisa	Harvard University
Antionette	University of Miami
Carol	Bronx-Lebanon Hospital Center
Claire	Harvard University
Delia	University of Miami
Exzavia	Children's Diagnostic and Treatment Center
Falon	University of Colorado, Denver
Gena	University of Miami
George	Harvard University
Jarmel	University of Illinois, Chicago
Jennifer	University of Colorado, Denver
Julie	Westat
Kamil	San Juan Hospital
Kimbrae	Texas Children's Hospital
Kylie	Texas Children's Hospital
Latonia	University of Illinois, Chicago
Lesley	Texas Children's Hospital
Megan	Westat
Morten	Bronx-Lebanon Hospital Center
Raiko	University of Colorado, Denver
Russ	Tulane University
Shannon	University of Alabama, Birmingham
Stephanie M.	University of California, San Diego
Theresa	Texas Children's Hospital
Tracey	University of Illinois, Chicago

• **APPROVAL OF MINUTES**

The minutes from the August 28, 2019 call were approved with no changes.

• **PHACS FALL 2019 NETWORK MEETING – Q & A**

George Seage, and **Russ Van Dyke** reviewed the CAB's questions from the PHACS Fall 2019 Network Meeting. Questions and answers included the following:

TRACK II Program and Families Living with HIV - Deb Murphy & Lisa Armistead

- **Does PHACS plan to work with Deb and Lisa to incorporate TRACK II into PHACS in some way?**

PHACS researchers are interested in creating a program like TRACK II in PHACS. **Deb** and **Lisa** were interested in working with PHACS in the future. PHACS hopes to consider doing a program with PHACS IV (the next round of PHACS funding). Researchers may be interested in trying out a program at a few sites first to see how it is received.

Latebreakers (part 1)

Trajectories of Bone Mineral Density Over Time in Children Living with Perinatally-Acquired HIV - Linda DiMeglio

- **What is the significance of looking at youth at or after Tanner Stage 5?**

As children age, their bones become harder and stronger. After the maximum is reached, bone density gets less and less over time. It is better for a person to reach the maximum later than earlier. The later the maximum is reached, the better the bones will hold up over time. Tanner Stage 5 means that a person has fully matured sexually. Looking at bone density at Tanner Stage 5 or later means that the person is close to maximum bone density.

- **At what age is typically the time of peak bone accrual?**

Peak bone accrual is around 20 years of age.

- **The presentation mentioned the limitation of the DXA scans being only 2-dimensional. Are there plans within PHACS to study bone mineral density using another type of scan?**

The DXA scan is similar to an x-ray scan. It looks at a 3D body projected on a flat screen. Researchers can study bone mineral density in 3D using CT scans. The advantage of using DXA scans is because there is much lower x-ray exposure.

Prediction of Bone Mineral Density with Polygenic Risk Scores Among HIV Infected/Uninfected Participants aged 7 – 12 – Sean Brummel

- **As a reminder, what is whole genome sequencing?**

This means researchers mapped out the genes of these participants. This allows researchers to understand the details of these participants' DNA. These studies were only done on participants who signed an informed consent form for genetic studies. Analyzing the data is complicated because there are many places where genetic changes can occur. PHACS is interested in using this information to see how the genes of participants in PHACS influence health outcomes.

- **Is PHACS going to consider using Dr. Brummel's model to study whether other health outcomes can be predicted using genomic data?**

Yes. PHACS hopes to use the model to look at the genetic data for participants in PHACS and look at many other health outcomes including heart health.

Latebreakers (part 2)

FGF-21 and GDF-15 on Mitochondrial Dysfunction – Mariana Gerschenson

- **What is mitochondrial disease/dysfunction (MD)?**

Mitochondria are the powerhouse of cells. They work to make energy. MD occurs when the mitochondria do not work as well as they should due to another disease or condition. This means that cells in people with MD might not be getting enough energy.

- **FGF 21 and GDF 15 were noted as "biomarkers." What exactly are biomarkers and why do we study them?**

Biomarkers refer to something that can be measured, usually in a laboratory test. Biomarkers are used to show signs of abnormal processes or diseases. Biomarkers may be used to see how

well the body responds to a treatment. They tell researchers something about how the body is working.

- **Dr. Gerschenson explained that this study suggested that in the future we may be able to use FGF 21 and GDF 15 to diagnose and treat children living with HIV to screen for MD. How would this be done? Would you have to compare levels of these substances in the individual child over time or would you compare them to a standard set of values?**

Researchers found that FGF 21 and GDF 15 are biomarkers that can show whether the mitochondria are working well. This is good news because tests for mitochondrial function are very expensive and complicated. Tests looking for FGF 21 and GDF 15 may be done using a simple blood test. This is much more ideal for screening tests. In the past, we've seen that some antiretroviral drugs had bad effects on mitochondria. This is why PHACS continues to research mitochondria.

Social Support and Viral Suppression - Kathy Tassiopoulos

- **Are site staff alerted if a participant scores particularly low on their social support evaluations so that they can intervene if necessary?**

The surveys are confidential. Participants answer the questions privately in clinic or at home. PHACS does not release any information from the surveys to site staff. This is because some of the questions are sensitive (questions about sexual behavior, sexually transmitted infections (STIs), and substance use).

- **Did PHACS develop the questions on the evaluations or did another group (i.e., NIH)?**

The questions were selected from the NIH Toolbox.

- **Are there measures taken to try to ensure that the participant answers the evaluations truthfully?**

There are questions in the surveys that are included to try to make sure that people are answering the questions truthfully. Some of the questions are asked over and over. The survey asks some of the same questions every year. Researchers can compare survey answers to confirm whether someone is answering truthfully.

- **Is PHACS interested in doing this kind of study on the women enrolled in the Women's Health supplement?**

PHACS is interested in studying social support in women. Some research suggests that women with social support may have better health outcomes.

STI Data from AMP/AMP Up - Barbara Moscicki

- **In the AMP and AMP Up data, far more females (218) than males (90) reported ever testing positive for an STI. Is there any interest in looking more into why this might be?**

PHACS is interested in studying reasons why more females than males reported testing positive for an STI. Part of the reason is because there are more women than men enrolled in PHACS. There may also be some testing bias because women may be receiving gynecological care. This means they may be getting more routine STI testing than men.

- **Is this study still in the capsule stage?**

The study is still in the capsule stage.

- **Will more PHACS researchers be able to use this data to study other STI-related factors or outcomes?**

PHACS researchers hope to use this data to study other STI-related factors or outcomes. The samples were tested in batches. Many PHACS researchers think it is important to research STIs as well as condom use.

Future Directions – I - Metabolic Syndrome – Stephanie Shiao

- **Dr. Shiao talked a lot about how the definition of metabolic syndrome has changed over time. Why might this have changed so much?**

Metabolic syndrome is a relatively new concept. The definition has been refined over time as researchers learn more about it.

- **What is lipodystrophy?**

Lipodystrophy is an abnormality in where the body fat is distributed. In the past, some antiretroviral drugs caused a loss of body fat in the extremities and in the face. Currently, research is showing some antiretroviral drugs cause an increase in body fat. Too much fat in the middle section of the body can be a sign of metabolic problems. PHACS is currently researching lipodystrophy.

Childhood Obesity and Diabetes – Linda DiMeglio

- **It was noted that Stavudine use was associated with lower extremity fat and higher trunk fat and trunk to extremity fat ratio. Were any other individual ARVs studies for body fat differences?**

Stavudine is the first antiretroviral drug to cause extreme lipodystrophy.

- **What is insulin resistance and why does it matter?**

Insulin resistance is also known as pre-diabetes. It means the body cannot regulate insulin as well as it could. If it progresses, it can turn into diabetes. Researchers want to study insulin resistance to find ways to prevent diabetes by learning what causes it.

- **What are examples of “metabolic outcomes”?**

Metabolic outcomes may include diabetes and coronary artery disease.

- **It was noted that insulin resistance IR was more likely to disappear in AMP participants who were male, had lower BMI, trend toward resolution with current lopinavir/ritonavir. Why might insulin resistance “disappear”?**

Exercise and weight lose can decrease insulin resistance. Body fat is a big factor in determining insulin resistance. Changes in medications may also play a role. Insulin resistance may not necessarily “disappear” but a person’s tendency to develop diabetes may disappear.

- **If a child is noted to be insulin resistant, does that automatically mean that they will have diabetes when they’re older?**

No, but it means that the child will very likely develop diabetes later in life.

- **Are the researchers interested in looking at specific ARVs and whether they are associated with type 2 diabetes?**

PHACS is interested in looking into certain antiretroviral drugs and their associations with early metabolic syndrome. This is an area that is becoming important as people living with HIV live longer. Researchers want to look at how these factors can influence health in the future.

Women's Health WG - Joint Interactive Panel Session - Understanding Challenges of the Care Continuum – Voices from PHACS

- **Is PHACS going to be studying transitions in the women's health supplement?**

PHACS hopes to study transitions in women. Researchers are interested in studying transitions from pregnancy to postpartum and transitions from obstetric care to adult HIV care. Every transition presents a possible risk of gaps in care.

Interactive HECC Session

- **What next steps is PHACS making toward incorporating person first language?**

PHACS plans to work with the HECC on the next steps. PHACS researchers hope to incorporate more person first language into presentations and manuscripts.

Substance Use Project - Sharon Nichols

- **Why is it important to study predictors of substance use in PHACS?**

It is important to monitor substance use. By looking at predictors of substance use, researchers can look at whether someone might be at risk for substance abuse. This is particularly important due to the opioid epidemic. PHACS also plans to start asking questions about vape use.

- **Were parents present during the AMP ACASI interviews?**

No, the ACASI interviews are done in private.

- **What does it mean that better cognitive functioning does not mean the youth has lower risk for substance use?**

There may be a variety of explanations for this. PHACS hopes to continue to study substance abuse and cognitive function.

- **Is substance use studied in SMARTT? In the SMARTT Young Adult Cohort?**

Yes, substance use is studied in the surveys in SMARTT and the SMARTT Young Adult Cohort.

ARV Exposure and 5yo ND/Language Outcomes - TJ Yao

- **What is neurodevelopmental dysfunction?**

Neurodevelopment reflects growth in the brain over time.

- **What are concomitant signals of language, behavioral and/or cognitive dysfunction?**

It can refer to how a child learns to do basic processes like learning to roll over, walk, and talk. Researchers use landmarks to look at how a child is doing compared to others. This means researchers may look at what age a child started sitting up, walking, or talking. Neurodevelopmental dysfunction is when a child has trouble meeting the landmarks. Cognitive development includes learning to do math, learning to read, and problem solving. PHACS looks at all of these landmarks and signals to see how a child is developing. Measuring language is a

cross cutting measure of how a child is developing. This is because language is actually a very complicated process.

- **What is bilirubin and why was it studied?**

Bilirubin is a yellow pigment that occurs normally when part of your red blood cells break down. Past research has shown that elevated bilirubin is seen in babies whose mothers took atazanavir during pregnancy. Elevated bilirubin may potentially cause bad health outcomes.

Quantitative Antibody and Proviral Burden – Katherine Luzuriaga

- **What was the overall takeaway from this study?**

This presentation was related to HIV cure research. There is a lot of interest in whether HIV can be cured. HIV can be treated very well. The problem with curing HIV is that it embeds itself in the DNA. Proviral burden is the amount of virus that is in the DNA. Researchers have been looking at ways of removing the virus from the DNA. Researchers are looking at whether a simple test can be done to see how much virus is in the DNA. Dr. Luzuriaga found that a routine antibody test can give an idea of how much virus is in the DNA. There are more complicated and expensive tests that can show researchers exactly how much virus is in the DNA. The antibody test is more of a tool.

Opioid, Marijuana, and Substance Use During Pregnancy and Postpartum - Lynn Yee

- **Did they specifically study marijuana use in states where use has been legalized?**

Yes, PHACS collects data on marijuana use on participants at all PHACS sites.

- **Is PHACS going to continue to study opioid use?**

Yes, PHACS will continue to study opioid use.

NICHD Strategic Planning Priorities

- **Where does PHACS fit in to NICHD's planning priorities?**

PHACS is preparing for the next round of funding (PHACS IV). The PHACS team is waiting for the official request for proposal for PHACS IV. The structure may change, but the research priorities will stay the same.

- **What can the CAB do to support the priorities?**

Researchers encourage the CAB to continue to provide feedback. NICHD takes CAB feedback very seriously. The CAB has a unique perspective on HIV research because of the impact HIV has on participants and their families.

ARV and Neural Tube Defects Update

- **As a reminder, what are neural tube defects?**

Neural tube defects occur when the spinal cord and covering do not close properly while the baby is in the womb. Babies with neural tube defects can be born with parts of the spine outside of the body. This can result in problems in the legs and sometimes paralysis of the lower body. They occur relatively uncommonly.

- **What was the overall takeaway from this study?**

A study was done in Botswana that looked at dolutegravir use in a small group of pregnant women. Researchers found an increased rate of neural tube defects. This raised a lot of concern

about dolutegravir use during pregnancy. More studies have been done using a larger sample size. Researchers are now seeing that in a larger sample, the rate of neural tube defects was not as high. This is good news.

Other Questions/Comments

- **Given the discussion about undetectable = untransmittable (U=U) at the CAB Retreat, do you think PHACS might be interested in researching U=U? What might you like to study about it?**

PHACS researchers want to ask participants about U=U in the PHACS surveys. This is a big initiative of the NIH and CDC. We want to encourage people to maintain suppressed viral load at undetectable levels. Research has shown that this reduces and eliminates the ability to transmit HIV sexually. We want to know whether the U=U concept is more well-known at some sites than others. It may be helpful for the CAB to consider talking about U=U in the PHACS CAB newsletter.

- **We talked about placenta research at other meetings, but not this meeting. Is PHACS still pursuing the possibility of placenta research?**

PHACS is still interested in placenta research. Placenta research will hopefully be pursued in PHACS IV.

NOTE: The next CAB call will be on Thursday, October 24, 2019 at 12:00 pm EST.