

**CAB Conference Call
October 25, 2018
12:00 EST
Meeting Minutes**

Participants:

Alex	FSTRF
Andrea	Jacobi Medical Center
Brandon	CAN Community Health
Carrie	University of Colorado, Denver
Claire	Harvard University
Ellen	Ann & Robert Lurie Children's Hospital of Chicago
Exzavia	Children's Diagnostic and Treatment Center
Fallon	University of Colorado, Denver
George	Harvard University
Jennifer	University of Colorado, Denver
Julie	University of Alabama, Birmingham
Julie	Westat
Kamil	San Juan Hospital
Kimbrae	Texas Children's Hospital
Kylie	Texas Children's Hospital
Latonia	University of Illinois, Chicago
Liz	Harvard University
Lourdes	San Juan Hospital
Megan	Westat
Michelle	Harvard University
Rosetta	Bronx-Lebanon Hospital Center
Russ	Tulane University
Shannon	University of Alabama, Birmingham
Stephanie	University of California, San Diego
Stephanie	University of Miami
Theresa	Texas Children's Hospital
Veronica	University of California, San Diego

• **APPROVAL OF MINUTES**

The minutes from the September 27, 2018 call were approved with no changes.

• **CAB UPDATES**

Megan Reznick talked about CAB updates. During the September CAB call, there were many interruptions. Many of the CAB ground rules were violated during the call. This left the CAB unable to have the Women's Health Working Group (WG) discussion. CAB members are encouraged to think about ways to hold each other accountable to the ground rules. CAB members can submit their ideas through the evaluation survey. Additionally, a make-up call has been scheduled with the Women's Health WG Leadership. The make-up call is tomorrow, October 26th at 12:00 PM EST.

Megan talked about CAB call improvements. **Megan** will now be using moderator functions on the CAB calls. This means that the moderator can manage mute, roll call, and connectivity.

Megan talked about the PHACS CAB Newsletter, January 2019 edition. The theme for the newsletter is the past, present, and future of PHACS. CAB members are encouraged to submit articles for the newsletter.

- **PHACS FALL 2018 NETWORK MEETING – Q & A**

Ellen Chadwick, Liz Salomon, George Seage, and Russ Van Dyke reviewed the CAB's questions from the PHACS Fall 2018 Network Meeting. Questions and answers included the following:

Sonia Hernandez-Diaz - Pharmaco-epidemiology/vigilance in pregnancy

- **What exactly 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 paralysis of the lower body.

- **Have we looked at neural tube defects in PHACS?**

Data on neural tube defects is collected in PHACS. Researchers have not yet analyzed any of the data. There don't appear to be many neural tube defects in PHACS.

- **Why did Dr. Hernandez-Diaz compare thalidomide with dolutegravir? What are the possible implications?**

Dr. Hernandez-Diaz talked about thalidomide as an example. Thalidomide was thought to be safe during pregnancy in the 1950s, but it caused birth defects. It is an example of drug safety in pregnancy.

- **It seems like much of the early HIV research studies take place in African countries. Why is that?**

There are many women and babies living with HIV in African countries. This means that researchers can do studies on a larger number of people than there are in other countries.

- **What was the overall take home message from this presentation?**

The more ways you can look at a problem, the better you can try to solve it. The more ways you can explore drug safety, the better you can tell if a drug is safe to use or not.

Rebecca Zash - Using Observational Data to Evaluate the Safety of ART in Pregnancy

- **Is dolutegravir being observed in PHACS/SMARTT?**

Yes, researchers record all antiretroviral drugs taken by mothers enrolled in PHACS.

- **Dr. Zash's presentation made me think about SMARTT. How long is PHACS planning to follow SMARTT mothers?**

In the Women's Supplement, women are followed for a couple years. PHACS is hoping to get additional funding to follow mothers even longer. In SMARTT, mothers are followed in relation to their children.

Caitlin Dugdale - Risks and benefits of dolutegravir-based ART for women of childbearing age living with HIV in South Africa

- **Why is there so much focus on dolutegravir right now?**

Some early studies in Botswana showed that there may be an increased risk of neural tube defects in babies exposed to dolutegravir. The risk was more than expected. Researchers are now doing more research to study the risk factors more closely.

- **Is Dr. Dugdale’s team continuing this research in South Africa?**

Dr. Dugdale used data from a population of women in South Africa. She used a computer program to help her analyze the data. She wanted to try to project what would happen if there were thousands more patients taking dolutegravir. She wanted to know if the risk of defects would be high. There may be ongoing studies in South Africa.

- **How can we translate the information from the South Africa studies to PHACS in the United States? Are we seeing the same effects or are there other factors to consider such as access to medical care, environmental factors, etc.? If so, then how is this data useful to us?**

It is important to look at all factors that can affect data in a study. PHACS researchers try to think about many factors when analyzing study data.

Claudia Crowell – Safety of In Utero Antiretroviral Exposure: Neurologic Outcomes in HIV-Exposed, Uninfected Children

- **Was there any data on how the children with seizures were developing? Is there any follow up data?**

The study did not have data on how the children with seizures were developing. However, children with seizures are being followed individually at their local sites.

- **What happens when research shows that a drug isn’t as safe as we thought for pregnant women anymore? Is there an official process for doctors to change the medications?**

Announcements on major study findings are sent out worldwide. As soon as any important signal is noticed, it’s important for the research community to be informed.

Kate Powis – Temporal Trends in ARV Use in Pregnancy, AIM 3 (predictors of preferred regimens)

- **Did this analysis account for factors such as health insurance? For example, perhaps a mother did not utilize the “preferred” regimen because that medication wasn’t covered by her health insurance?**

The study did not have data on the reasons for antiretroviral choices. Data was available on what drugs were used, but not why they were chosen. Information on health insurance was not known. Researchers are also interested in looking at sites within states with Medicaid expansion to look at whether Medicaid funding could have affected antiretroviral choices.

- **Were the PHACS sites in Puerto Rico included in this analysis?**

Yes, Puerto Rico was included.

- **Is this analysis continuing? Is there an expectation that “preferred” regimens will change in the future?**

Researchers are not collecting any new data for this analysis. That being said, preferred regimens are updated at least every year. Updates are based on new data. It is an ongoing process.

- **Are they planning to use these results to predict health outcomes for the children?**

No, not in this study. Long term outcomes for youth exposed to antiretrovirals are being studied in SMARTT.

- **Was alcohol or substance use factored into whether a mother would use a “preferred” regimen? Do we look at any data on alcohol and ARV interaction?**

Since the study did not explore the reasons behind the choices, there wasn't any data on whether alcohol use factored into decisions. Data on alcohol use is collected in PHACS for other studies.

Jennifer Jao - Neurodevelopmental Outcomes of Infants Born to Women with Perinatally vs. Non-Perinatally Acquired HIV in PHACS SMARTT

- **Were these results of PHIV mothers and their 1-year-olds compared to other women living with HIV in PHACS and their 1-year-olds?**

Yes, these two groups were compared in this study.

- **Was there a reason why mothers with twins were not included in the study?**

Twin development may vary. If differences are found between twins, it can be difficult to figure out where maternal exposure fits in.

- **Were any environmental factors included in this study?**

No, environmental factors were not included.

- **This presentation referenced the “Bayley” assessment. How does PHACS decide which assessments to use to study children?**

The Bayley assessments is the most widely used study instrument in clinical development and research in the United States. The Bayley has been used in HIV research for 30 years. PHACS chooses assessments that have been tested and validated.

Kunjai Patel – Outcomes of second-line antiretroviral therapy (ART) in HIV-infected children: a CIPHER analysis

- **What exactly is second-line ART?**

Second line ART is the second round of antiretroviral drugs that a person takes if the first round doesn't seem to be working anymore.

- **Was parental involvement and encouragement observed as a factor in whether a child would successfully start a second more effective treatment?**

Not, not in this analysis.

- **Did they collect any data on which specific medications or classes of medication failed?**

Yes, the study looked at specific medications and classes of medications.

- **Was failure ever due to the side effects of the medication?**

Side effects were not studied in this analysis.

- **Does “failure” mean “resistance”?**

Not necessarily. A viral load failure may have many different reasons. A person may not be taking their medication correctly. They could be vomiting their medication. It could also mean that a person has become resistant.

Sean Brummel – Cumulative measures of viral load burden in pediatric HIV research

- **What is viral load burden?**

Viral load burden is viral load over time. It is a look at all the viral loads in a specific time frame.

- **What was the take home message from this presentation?**

This presentation was looking at how to account for missing information. It also looked at how to relate missing information to specific findings.

Annette Sohn - GRADUATE: Harmonizing data around adolescent transitions and transfers in care

- **Is it expected that data from these studies will translate into transition to adult care in the United States?**

Researchers are still comparing data from these studies. It is not yet known if the findings will be the same in the United States.

Kathy Tassiopoulos - AMP Up early transition to adult care outcome

- **Was health insurance coverage included as a factor for transition?**

Health insurance was not studied in this analysis.

- **It was noted that age at transition was associated with satisfaction with adult care clinic and provider, but not with retention in care. Will you please explain this finding?**

This means that just because the young adult is satisfied with their transition doesn't mean that they will still want to go to the clinic. Just because they transitioned doesn't necessarily mean they will keep up with their visits.

- **Is PHACS currently doing anything to facilitate transition or are we just monitoring this data?**

PHACS is currently monitoring this data. All PHACS sites have very active transitions plans to help make the best transitions possible.

- **Do we have data on what programs for transition are offered at PHACS sites?**

Yes. Data on transition programs is being collected on an ongoing basis.

- **Was there data presented on health outcomes for young adults who had transitioned versus those who had not?**

This presentation focused on viral load before and after a transition. It did not compare that data between young adults who had transitioned versus those who had not.

- **Is PHACS going to be considering transition research for SMARTT adolescents aging into adulthood?**

Data on transition will be collected. PHACS collects data on transition programs at each site. Transition programs vary by site. This means comparing transition data between sites can be tricky.

- **Please describe DNA methylation.**

Parents pass traits on to their children through DNA. Sometimes, the DNA in our bodies is modified. DNA methylation is the process of modifying DNA. The DNA isn't changed, it's just modified. Epigenetics is the study of changes in people caused by modifications of their genes. Once the modifications occur, they can be passed on to children. These modifications can be caused by factors experienced in life. Perinatal HIV infection can cause some changes in the patterns of DNA. HIV infection can also change how certain genes are expressed. This means they can be either more or less expressed based on DNA methylation. HIV exposure or infection can create these modifications. These modifications can be passed on to children. This can potentially affect how they respond to infection. It can also affect how they experience side effects.

- **Since PHACS is looking into doing further DNA research, is DNA methylation something PHACS will be exploring?**

Yes, PHACS will look into studying DNA methylation. Carmen Marsit is working on an analysis in AMP and AMP Up.

Peter Torre - Words-in-Noise (WIN) Test Data in AMP Up Young Adults

- **Is the WIN test done in SMARTT?**

No. The WIN test is one of the NIH Toolbox assessments. The NIH Toolbox is given in AMP Up.

- **Will there be further research done in AMP Up using the WIN test?**

Yes. The assessments that are part of the NIH Toolbox are given during the AMP Up Entry, 3 Year, and 6 Year visits. In addition, there is a substudy in PHACS. In the substudy, researchers are looking to compare the WIN with the standard pure tone hearing test. Researchers want to compare the tests to see how the data can be used together.

Kathy Tassiopoulos - Mental health and cognitive function evaluations in AMP Up – Entry and Year 3

- **These results were taken from tests done at the entry visit and the Year 3 visit in AMP Up. Are there additional mental health and cognitive function tests at later years in AMP Up?**

These tests are also done during the AMP Up Entry, 3 Year, and 6 Year visits. If the AMP Up study continues, the tests may be done during later time points as well. Researchers are interested in looking at long term changes over time.

- **Are the PHACS researchers also looking at substance use among young adults in AMP Up? Are we comparing substance use with depression and social support scores? Is there every a scenario where AMP Up participants would need to re-take these questionnaires?**

Substance use is assessed in AMP Up. Data is collected every year. Sharon Nichols is currently doing an analysis looking at substance use and how it relates to behavioral issues and neurocognitive testing.

- **Are there any complaints from participants about the questionnaires being too long?**

Many of the AMP Up questionnaires come from the NIH Toolbox. There haven't been many complaints about the questionnaires being too long.

Michael Corley – Identifying immunoepigenetic biomarkers of cardiac toxicity in perinatally HIV-infected adolescents and young adults

- **What was the take home message from this presentation?**

This presentation showed that children living with HIV were showing changes in epigenetic patterns. Michael Corley will be re-doing these analyses in the new cardiac echocardiogram substudy. Participating sites will be repeating cardiac echocardiograms. A cardiac echocardiogram is an ultrasound of the heart. The new analyses will look at heart function over time. Researchers will look at long term changes in how the heart functions. They will also look at some of the epigenetic changes and how those relate to how well the heart works.

Peter Torre - Auditory Research in Children with HIV (ARCH): Cape Town; ND/Neuroimaging (ages 11-12)

- **Is PHACS going to start doing this neuroimaging and direct measures of auditory function to look at children’s auditory systems?**

PHACS previously conducted a neuroimaging study. This study was done in Chicago. About 40 participants had neuroimaging tests done. About 36 out of the 40 participants also had hearing testing done within two years of their neuroimaging scan. PHACS researchers plan to compare the results of these two tests. This is a pilot study because it involves a small number of people.

Other

- **Regarding questionnaires about patient health – are caregiver questionnaires in PHACS translated into Creole? How does PHACS decide whether to translate the questionnaires into a certain language?**

Most caregiver questionnaires are in Spanish. PHACS does not directly translate any questionnaires. PHACS can only use a questionnaire if the company who makes the questionnaire has made it available in other languages. This is because PHACS only uses assessments that are tested and validated. Validating tests helps make sure they’re reliable. This helps researchers be able to compare results from different languages in a standard way.

- **Many of the studies presented that took place in Africa revealed some really high mortality rates. This felt very alarming. Are we seeing mortality rates like this for mothers and children in the United States?**

The mortality rate in PHACS is very low.

- **Have any sites considered involving parents in young adult transition plans?**

PHACS is not collecting data on parents involved in transition plans. That being said, parent involvement is often very helpful. It varies by young adult and by site.

- **How does PHACS decide on which areas of health to study in children?**

The Working Groups (WGs) were created to study specific areas of health. CAB members are encouraged to participate in the PHACS WGs.

NOTE: The next CAB call will be on Thursday, November 29, 2018 at 12:00 pm EST.