CAB Conference Call
April 25, 2019
12:00 EST
Meeting Minutes

Participants:

Alex	FSTRF
Andrea	Jacobi Medical Center
Andrew	University of Colorado, Denver
Anisa	Harvard University
Brandon	University of Florida, Jacksonville
Carol	Bronx-Lebanon Hospital Center
Claire	Harvard University
Ellen	Ann & Robert Lurie Children's Hospital
Exzavia	Children's Diagnostic and Treatment Center
George	Harvard University
Jennifer	University of Colorado, Denver
Joel	University of Puerto Rico
Juanita	Tulane University
Julie	University of Alabama, Birmingham
Julie	Westat
Kimbrae	Texas Children's Hospital
Kylie	Texas Children's Hospital
Latonia	University of Illinois, Chicago
Lesley	Texas Children's Hospital
Liz	Harvard University
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
Stephanie S.	University of Miami
Theresa	Texas Children's Hospital
Tracy	University of Illinois, Chicago
Trinise	Tulane University

• APPROVAL OF MINUTES

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

• CAB CHAIR AND VICE CHAIR ELECTIONS

Megan talked about the CAB Chair and Vice Chair Nominations. Several CAB members nominated themselves or others for the CAB Chair or Vice Chair positions. New CAB Chairs will be announced during the May CAB conference call.

Megan talked about the voting process. **Megan** will send out a link to an anonymous online ballot. CAB members can vote through the online ballot or by email. Only active PHACS CAB members should vote for the new Chairs. CAB members should vote only once.

- **SPRING 2019 LEADERSHIP RETREAT**

Stephanie talked about the Spring 2019 Leadership Retreat. The retreat was held on on April 8-9, 2019 in Potomac, Maryland. The retreat focused on the future of PHACS. There were many presentations focused on specific research topics. Based on feedback from the CAB, **Stephanie** and **Brandon** chose several presentations for the PHACS Leadership to review with the CAB.

Dr. George Seage talked about the presentations on data collection. The first speaker was **Dr. Eric Engels**. **Dr. Engels** is an investigator at the National Cancer Institute (NCI). Each state has an HIV and a cancer tumor registry. A registry is like a database of medical events. The NCI did a study using data from eleven states. The NCI compared the HIV and tumor registries in those states. The NCI compared the registries to look at people who had HIV, as well as a tumor or cancer. These findings help researchers learn about what types of cancer people living with HIV may have.

In the past before Highly Active Antiretroviral Therapy (HAART), there were high rates of Kaposi sarcoma (cancer of the blood vessels). There were also high rates of types of lymphoma (cancer of the lymph nodes). After people started using HAART, rates of cancers went down. Some cancer rates are still higher in people living with HIV compared to people not living with HIV. However, the rates of solid tumor cancers such as lung, breast, and/or kidney are not higher in people living with HIV.

It is important to continue to follow people with living with HIV. More research is needed on cancer in people living with HIV. Many cancers form in older people. More research is needed over time to determine whether cancer rates are truly higher in people living with HIV.

Kim asked about other factors associated with cancer. **Dr. Seage** talked about the tumor registry. Cancers from all people are included in the registry. This includes cancers associated with all types of factors not just HIV.

Dr. Seage talked about **Dr. Kunjal Patel's** presentation. **Dr. Patel** talked about developing better ways to study HIV complications. Complications may include cancer and birth defects. **Dr. Patel** talked about looking at the Medicaid database. Many women in SMARTT get their healthcare financing through Medicaid. That data can be accessed by researchers. However, there are no names in the database. The Medicaid database uses codes. There are codes that identify certain HIV tests and antiretroviral medications. These tests and medications are unique to people living with HIV. Even though the database will not reveal a person's name, researchers can look specifically for these codes to find data on people living with HIV. Some of the codes can help find people born with HIV.

The Medicaid database is not really set up for research. It is primarily set up to house provider reimbursement information. **Dr. Patel** is trying to match the Medicaid data with the Centers for Disease Control (CDC) data. This will help researchers look more closely at complications in a larger number of people. The Medicaid database has about 80,000,000 people. The PHACS dataset has only about 4,000 people. By looking at such a large database, researchers can look to see if there were any trends in complications or diseases that were not seen in PHACS.

There are some disadvantages of using the Medicaid database. The database is old. The most recent version is through 2013. This is a problem because it does not show newer medications. Additionally, the database only shows diagnoses, medications, and hospitalizations. It does not show the wide range of clinical information collected in PHACS.

Theresa talked about the Ryan White Title IV, Part D and HIV medication databases. **Dr. Seage** explained that researchers are interested in continuing to compare data in different databases. It is helpful to reference national databases. Databases that vary by state can be difficult to compare.

Dr. Ellen Chadwick talked about the retreat presentations that focused on placenta research. There were four presentations. **Dr. David Weinberg** is the head of the National Institutes of Health (NIH) Human Placenta Project (HPP). **Dr. Weinberg** gave an overview of the function of the placenta. The function of the placenta is to transfer nutrients, oxygen, and water from mother to fetus. It also functions

to remove waste from the fetus. It acts as a filter. Understanding the health of the placenta may help researchers understand some of the outcomes of the fetus. Outcomes may include birth weight, and premature birth.

The HPP has done many studies on the placenta. Studies have included ultrasounds during pregnancy. The ultrasounds were used to study the placenta. Other studies used magnetic resonance imaging (MRI). These studies looked at the structure of the placenta. Some studies looked at the placenta under the microscope after the placenta was delivered. These microscopic studies looked at the chemical and genetic makeup of the placenta.

Understanding the placenta better will help guide interactions between the placenta, mother, and fetus. These studies also helped researchers look at possible effects of exposures from the environment or medications. PHACS might be a great study for future placenta research.

Dr. Jack Moye from NICHD and **Dr. George Seage** also presented on the placenta at the retreat. They talked about current placenta studies supported by NICHD.

One placenta study supported by NICHD was the National Children's Vanguard Pilot Study. This study looked at on the origins of health and disease starting from pregnancy. The study looked at environmental exposures to the fetus during pregnancy. Environmental exposures may include air pollution, substance use, and/or medication use. From that study, a protocol was created on how to best to collect and store placenta specimens. This helped inform future placenta research. The study determined that for genetic studies, the placenta must be studied within four hours of birth.

The Zika in Infants and Pregnancy Study (ZIP) looked at outcomes of Zika infection in pregnant mothers in South and Central America. The study has enrolled almost 6,500 women so far. They hope to study the placentas in all the women whose blood tests show they were exposed to Zika. They also hope to study 1/10 of the women whose blood tests showed that they were never exposed to Zika.

The HIV and Zika in Infants and Pregnancy Study (HIV ZIP) is being led by **Dr. George Seage.** It is similar to ZIP. The study will compare women living with HIV and women living without HIV in sites that are supported by NICHD. These sites are in Brazil, Puerto Rico, Florida, and New York. Five of the sites in the study are PHACS sites. This study has enrolled women who were at risk of acquiring Zika. They were considered at risk if they traveled to areas where Zika was common. They were also at risk if they had any local exposures or exposures through sexual contact. The first phase of the study looked to enroll women and study their babies for birth defects and health outcomes.

If the first phase of HIV ZIP was successful, enrollment would be expanded. At the time of the retreat, about 200 women had been enrolled. The HIV ZIP study found that only 6 of the 200 mothers were exposed to Zika. They needed 20 women in order to expand the study. At this time, the study will continue to look at the women enrolled, but not expand to a larger study. About 174 births were included in the study. Many women donated their placentas for the study. It shows how hard the sites were working to collect placentas for the study. The 1-year follow up study visits are currently ongoing. The study expects to complete all births by June 2019. There will be another year of follow up before results will be studied.

The last placenta presentation was by **Dr. John Sled. Dr. Sled** performs ultrasounds on the flow of blood. He looks at the umbilical blood vessels of the placenta. These blood vessels connect the placenta to the baby. These studies help researchers understand the growth of the placenta. They also help researchers understand the impact on the growth of the fetus. He was interested in any differences in these growth findings with exposures to antiretroviral medications.

Dr. Sled first studied mice. Some of the mice were given antiretroviral medications. Some of the mice were not given any medications. He used ultrasounds to look at both sets of mice. He looked at the placentas after the mouse litters were born. He found that antiretroviral medications were associated with a somewhat lower weight of the fetus and the placenta. There were also some changes in the blood flow patterns. When the placentas were delivered, there were smaller blood cells in the placentas of the mice who were given antiretroviral medications. However, there were more blood vessels even though they were smaller.

Dr. Sled wanted to carry out the ultrasound study in humans. He did a small pilot study in women. Some women in the study were living with HIV. Some women in the study were not living with HIV. He did six ultrasounds of the umbilical blood vessels throughout pregnancy. He also looked at the size and shape of the blood vessels in the placenta after the baby was delivered. He found he could measure blood flow patterns in the umbilical blood vessels in human women. Some of the changes in the blood flow patterns may be related to changes in the placenta. **Dr. Sled** hopes to study a larger number of women in order to make any conclusions.

The placenta presentations showed that the placenta may be able to provide important information about health outcomes for the fetus before and after delivery. Researchers hope to study the placenta to come up with ways to promote good health in mothers and babies during pregnancy.

Dr. Russ Van Dyke talked about three latebreaker presentations about genetics. Latebreaker presentations are recent studies done in PHACS. Many health outcomes can be influenced by genetics. In the past, researchers thought that one change might produce one single effect in a person. Researchers have now found that genetics are much more complicated. In general, many genetic changes all together contribute to health outcomes. Researchers are interested in learning why a person has a particular outcome. Genetics may play a role.

The first presentation was by **Dr. Sean Brummel. Dr. Brummel** is a statistician at the PHACS Data and Operations Center (DOC) at Harvard University. Several years ago, PHACS performed whole genome sequencing on most participants in AMP. 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.

Dr. Brummel looked at bone mineral density and genetic health. He looked at data from Dual-energy X-ray absorptiometry (DEXA) scans on PHACS participants. The DEXA scans measure total body bone mineral density. He looked at whether there were genetic changes that would predict bone mineral density. He also looked at how that might influence changes in other outcomes. Other outcomes included how well a person responds to antiretroviral medications, and how the body responds to HIV infection.

Dr. Brummel found over 3,000 possible gene changes that have been identified as possibly related to changes in bone mineral density. He developed a model. The model looked at a particular pattern of changes in genes associated with bone mineral density. He used the model to create a score for each participant. The score helped predict each participant's total body mineral density. The model was better at predicting total body density than the density of the spine. This may help researchers predict what a participant's total bone mineral density might be by looking at their genes. Researchers may be able to look at how other factors in genes may be related to bone mineral density.

Dr. Carmen Marsit's presentation focused on epigenetics. **Dr. Marsit** is a Professor at Emory University. Epigenetics are genetic changes that change in a person over time. They can change with aging or environmental exposures. These changes can occur during a lifetime. The changes that occur can be used to figure out the age of a person. It's a way of looking at aging from a biological point of view. Epigenetics help researchers determine the DNA age of a person.

Dr. Marsit found that genetic aging may be faster in people living with HIV. He found that HIV infection may be related to faster aging based on epigenetic changes in DNA. In addition, increased viral load was associated with increased aging. This means DNA in people with high viral loads may age faster. Lower CD4 counts were associated with increased aging. This means DNA in people with low CD4 counts may age faster. The third line of antiretroviral treatment was also associated with increased aging. This means DNA in people who failed their first two lines of antiretroviral treatment may age faster. This means that uncontrolled HIV may be responsible for faster genetic aging. Researchers want to continue to study HIV, epigenetics, and aging. Researchers needs to continue to follow participants to see how the epigenetic changes occur over time.

The third presentation on genetics was by **Dr. Mitchell Machiela. Dr. Machiela** is an investigator at NCI. **Dr. Machiela** talked about genetics and zidovudine (ZDV) use during pregnancy in babies. He

looked at white blood cells collected from babies at birth. He look at the DNA in the cells. He compared babies exposed to ZDV and babies not exposed to ZDV. He looked at telomeres. Telomeres are expansions at the end of DNA. As a person ages, the telomeres get shorter. He found that babies exposed to ZDV in utero had longer telomeres. Babies who had mothers with higher viral loads had shorter telomeres. This may mean that treating a mother with ZDV during pregnancy may help babies develop longer telomeres. Researchers need to study more about the outcomes of being born with longer telomeres.

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