CAB Conference Call
May 24, 2018
12:00 EST
Meeting Minutes

Participants:

Andrea	Jacobi Medical Center
Brandon	University of Florida, Jacksonville
Camille	San Juan Hospital
Delia	University of Miami
Ellen	Ann & Robert Lurie Children's Hospital of Chicago
Exzavia	Children's Diagnostic and Treatment Center
Gena	University of Miami
Jeanie	University of Southern California
Jennifer	Colorado
Jennifer	San Juan Hospital
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
Leslie	Texas Children's Hospital
Liz	Harvard University
Lourdes	San Juan Hospital
Marilyn	Bronx-Lebanon Hospital Center
Megan	Westat
Paolin	University of Colorado, Denver
Raiko	University of Colorado, Denver
Russ	Tulane University
Shannon	University of Alabama, Birmingham
Stephanie	University of California, San Diego
Stephanie	University of Miami
Trinise	Tulane University
Veronica	University of California, San Diego
Zena	University of Miami

• APPROVAL OF MINUTES

The minutes from the April 26, 2018 call were approved with no changes.

• SPRING 2018 LEADERSHIP RETREAT REVIEW

Dr. Ellen Chadwick talked about the Spring 2018 Leadership Retreat.

The MACS and WIHS Combined Cohort Study
On the first day the PHACS Leadership talked about collaboration. A guest speaker talked about the Multi Center AIDS Cohort Study (MACS). He also talked about the Women's Interagency Health Study (WIHS). Previously, MACS focused on men. WIHS focused on women. Both studies followed study participants over time. As of this year, there will be a combined effort to combine these two studies. Researchers will study long-term complications between the two cohorts. Long-term complications may include heart disease, lung disease, blood systems, inflammation, sleep, substance use, aging, menopause, menstrual patterns, cancer, and viral load and the effect of antiretroviral (ARV) treatment over time. Researchers will also look at societal issue such as support, stigma, and discrimination. The

MACS and WIHS groups are in the process of putting in an application to NIH to move forward as a combined study.

Additional Maternal Data Collection for SMARTT Dynamic Cohort Biological Mothers
Dr. Chadwick talked about additional maternal data collection for SMARTT dynamic cohort biological mothers. PHACS was granted a supplement to study the health of biological mothers of children in the SMARTT Dynamic Cohort. The study is enrolling mothers of SMARTT Dynamic Cohort participants before birth and up until children reach four years of age. Researchers will be looking at mothers' health in this study. The purpose of the study is to look at the health of young women living with HIV who are of reproductive age. The research team will look at pregnancy outcomes such as blood pressure during pregnancy and viral response during pregnancy. They will also study illnesses in pregnancy and retention in health care. The study will be open to enrollment over approximately two years. PHACS researchers also applied for a grant for a follow up study to study these mothers, but the NIH decided not to award the grant at this time. PHACS researchers plan to reapply for the grant to conduct a larger study looking at mothers' health over a long period of time.

Updates on Studies in Progress: Cardiac and Pulmonary Imaging Studies
Dr. Chadwick talked about the studies in progress. Many years ago before ARV medications were widely available, many people living with HIV developed heart failure or other heart and lung complications. Now, better ARV medications are available and heart disease in young people living with HIV is very uncommon. In these studies, researchers will be doing Magnetic Resonance Imaging (MRIs) of the heart. Using the MRI, researchers will look for any evidence of heart problems. These studies will be done at Boston Children's Hospital. This study is a pilot study, which means they will be looking at data for only a small number of people. If the pilot study's findings look promising it may later be expanded to a larger number of people.

Oral Health Follow Up Study
The oral health research team is launching a follow up study to the initial Oral Health Substudy. This study will involve youth in AMP. The initial study found a higher number of cavities in teeth and inflammation of gum in youth in AMP. Average numbers of cavities and inflammation were high for both youth born with HIV and HIV exposed but uninfected (HEU). The follow up study will look at oral health data over time. Researchers will assess the risk of cavities, tooth quality, and gum disease in youth in AMP and look for reasons for the large numbers of cavities in these youth.

HPV Substudy
The HPV substudy will recruit young women who were born with HIV and who have received the Human Papilloma Virus (HPV) vaccine. Our data suggests that the HPV vaccine does not seem to work as well in protecting against cervical disease in young women born with HIV as those without HIV. The HPV substudy is being done to see if vaccine failure is causing the higher rate of HPV, which could suggest better ways to give the HPV vaccine, such as giving it at an earlier age or giving additional doses of the vaccine, in order to prevent cervical disease due to HPV. In the HPV Substudy, researchers will do pelvic exams to look for abnormalities of the cervix due to HPV. Biopsies of any abnormalities will be taken to see whether there are changes that could eventually lead to cancer or cervical disease.

Temporal Antiretroviral Prescribing Trends for Pregnant Women Living with HIV
This study is looking at the patterns of ARVs that were prescribed to women living with HIV during pregnancy. The research team has looked at data from 2008-2017. Researchers are describing what ARVs were prescribed compared to what ARVs were "recommended" by guidelines at the time. Researchers want to know if women were receiving the ARVs that were considered to be recommended or if they were receiving other ARVs that may not have necessarily been on the "recommended" list. The reason someone may not have received ARVs that were on the recommended list is because they might have been receiving newer ARVs that had not yet been repeatedly tested in women living with HIV during pregnancy. The reason could also be because a woman's virus was more resistant to some of the older ARVs. Researchers were specifically looking at how often women were treated with the recommended ARVs. Researchers found that women who had never been pregnant before or who just started ARVs during pregnancy were more likely to be prescribed "recommended" ARVs. Women who had been on ARVs for many years were less likely to be prescribed "recommended" ARVs.

Repeat Pregnancies in SMARTT

Another study was being done to look at changes in viral load (VL) and CD4 counts, and ARV medications in pregnancy between the first pregnancy and subsequent pregnancies in mothers in SMARTT. Many of the mothers had suppressed VLs during pregnancy, but frequently after pregnancy the VL would rebound into the detectable range. During a second pregnancy, the VL fell again and was slightly lower at the end of the second pregnancy than it was after the first pregnancy. This study sends a message that more should be done to make sure mothers can keep their VL undetectable between pregnancies. Researchers in this study also looked at the frequency of babies delivered preterm. Previous studies have suggested that preterm deliveries may be associated with the protease inhibitor ARVs. The study suggests that mothers who were using protease inhibitor ARVs in sequential pregnancies were slightly more likely to have a preterm birth than women who had taken a protease inhibitor ARV during their first pregnancy and switched to a different type of ARV for the second pregnancy.

SMARTT Hospitalizations
Researchers in this study looking at rates of hospitalization in youth in SMARTT compared to children in the US who were not born with or exposed to HIV. Similar studies were done in low income countries. In those studies, researchers found that HEU youth have higher rates of infections than HIV unexposed youth. However, there are often more challenges to stay healthy in low income countries. In this study, researchers looked at youth in SMARTT in the first two years of life. The study suggests that youth in SMARTT had almost twice the rate of hospitalization and infection-related hospitalization in the first two years of life. These findings were similar to the findings in low income countries. Researchers want to investigate why it is slightly more likely for youth in SMARTT to be hospitalized with infections than HIV unexposed youth.

ARV Use and Cardiac Echocardiogram Results in AMP
An echocardiogram is an ultrasound of the heart. In this study, researchers used echocardiograms to look at possible heart problems in youth in AMP. Researchers wanted to learn whether heart problems may be related to specific ARV medications. Research from this study suggested that it is hard to relate heart problems to specific ARV medications. This is because many ARV medications are taken together. The research suggested that youth taking a protease inhibitor had better heart function that those taking other ARVs. Zidovudine was linked to a minor negative affect on heart function. The results did not imply that the negative effects caused a problem with how well the heart works. It just showed up as something that could be seen on the echocardiogram. Overall, the research suggested that heart function was very good where ARVs are readily available.

Postpartum Health of AMP Up Young Women
Finally, there is a study that looked at women in AMP Up after they had a baby. Researchers looked at the birth outcomes and found that there was a lower rate of pregnancy in women born with HIV but almost 42% had at least one pregnancy. Researchers found that VLs were not always suppressed when the women got pregnant. During pregnancy most of the women reached undetectable VLs, but after the baby was born the VLs often became detectable again. Researchers determined that health care providers need to support medication adherence in women born with HIV when they get pregnant.

HIV Cohorts and Networks: The Importance of Collaboration
Dr. Russ Van Dyke talked about the second day of the meeting. A guest speaker talked about HIV cohorts and networks. She talked about the importance of collaboration. The Office of AIDS Research (OAR) within the NIH recently sent a request to the public asking for input about HIV research. NIH wanted to get feedback about what research questions they should be looking to answer. The OAR encouraged collaboration between HIV cohort studies. PHACS continues to collaborate with other HIV cohort studies.

Genomics Studies
Dr. Van Dyke talked about genomics studies. Genomics is the study of a person's genes (DNA) and seeing how genes relate to different outcomes, including both developing illness and remaining healthy. A genome refers to part or all of a person's DNA. Researchers in PHACS have completed whole genome sequencing on most participants in AMP. Whole genome sequencing is the process by which researchers can map out the entire set of a person's DNA. Genome sequencing was done on DNA only for participants and caregivers who consented for the research. Researchers in PHACS are doing a genomics study to study why some ARV medications work better in some people than others. Researchers are also interested in learning how HIV disease progresses and why side effects develop. Genetics can be a very

important predictor of outcomes. A person may be prone to developing a particular health outcome if they have a genetic predisposition to it. An example of this is how fast a person's body will eliminate medications. Some people eliminate medications faster than others. If someone processes medications slowly, they may develop toxicity from that medication because they're exposed to it at higher levels. If they eliminate it quickly, the medication level may be low and therefore less effective.

The PHACS genome sequencing data has been transferred to a database. PHACS researchers are currently learning how to use the data. There are a lot of challenges to analyzing the data. Studies will need to involve very powerful computers and people who have experience looking at large datasets. Researchers in PHACS are close to starting to answer questions about how the genetics of participants in PHACS influence their health outcomes.

Using Networks to Map Biological Drivers
Gene mutations are changes in gene structures. In the past, people thought that a single gene mutation led to a single problem or disease. This is true for diseases like sickle cell disease. Researchers have learned that most health outcomes are actually due to many different minor mutations in the genome. This is because many genes work together. This means that research in genomics can be very complicated. Researchers in PHACS may consider looking at genomic data from other studies to understand the results from the genomes of PHACS participants.

Language Acquisition and Neurocognition
Previous studies outside of PHACS have suggested that genes can be related to how a child develops language skills. These studies have suggested that genetic mutations may be associated with children developing language skills later than other children. Additionally, other studies done outside of PHACS have suggested that there may be gene mutations that explain why some children have lower IQ or develop cognitive skills later than other children.

Status of PHACS Genomics Project and Bone Mineralization
Many participants in PHACS were given Dual-energy X-ray absorptiometry (DXA) scans. These scans help researchers look at bone density. Some research done outside of PHACS suggested that gene mutations can be related to bone density. PHACS researchers are interested in learning whether HIV or some of the ARVs are associated with bone density. Some of the research in PHACS has already suggested that certain ARVs may be associated with lower bone density. With the genomics data, PHACS researchers want to look into how the genomes of participants in PHACS impact the association between ARV exposure, HIV, and their outcomes related to bone density. Researchers in PHACS submitted a grant proposal to NIH to do a follow up study looking at the changes in bone density over time.

Chronic Lung Disease and Immune Imbalance in U.S. and Kenya Youth with Perinatally-Acquired HIV
Dr. Van Dyke talked about a study on chronic lung disease and immune imbalance in U.S. and Kenya youth with perinatally-acquired HIV. Researchers are looking at lung function data collected in AMP. The goal is to compare the data with data from a study done in children in Kenya. Results from the study done in Kenya suggested that the youth born with HIV had a substantial amount of lung disease, but these children are also exposed to a lot of smoke because many homes always have a fire lit inside the home for cooking and/or heating purposes.

Cardiac Substudy
Dr. Van Dyke talked about the cardiac substudy. Many years ago before ARV medications were widely available, many people living with HIV developed poor heart function or other heart complications. Now, better ARV medications are available and there is less heart disease in people living with HIV. Many years ago in PHACS, a cardiac echocardiogram study was done in AMP that showed there were small differences in the hearts of youth born with HIV and HEU youth. This raised the concern that that youth born with HIV may develop heart problems later in life. This study is a follow up study to see if there have been any changes over time since the echocardiograms were performed several years ago. Researchers will do echocardiograms on the same youth to see if there are any changes. In addition, researchers will look at pulse wave velocity. Pulse wave velocity is a measure of blood vessel disease. It is a measure of the stiffness of the blood vessel. The way it works is by placing two probes on a person's neck and groin. Researchers measure how fast the pulse moved in that same blood vessel from the neck to the groin. How fast the pulse moves helps researchers determine the stiffness of the

blood vessel. The reason this research is being done is because previous studies have suggested that there may be a higher rate of premature heart and blood vessel disease in youth born with HIV.

NOTE: The next CAB call will be on Thursday, June 28, 2018 at 12:00 pm EST.