WORKING GROUP (WG) PRESENTATION SUMMARIES

Instructions: Please read the following summaries about each WG's presentation. Please take notes and remember to write down any questions you have for the WG's based on the lay summary or topics from their presentation. Please note that **bolded** words are glossary words. Please refer to the "glossary" document for a full list of glossary words used in these presentations. Use the WG Presentation Summaries and Glossary documents to follow along with each WG's presentation. The **glossary** may be found at the end of this document.

ND/NEUROLOGY WG (BRAIN DEVELOPMENT AND MENTAL HEALTH) THURSDAY, OCTOBER 29TH 10:30 - 11:45 AM

<u>Summary</u>

Co-Chairs: Kay Malee, PhD, Psychologist, Ann & Robert H. Lurie Children's Hospital of Chicago, Renee Smith, PhD, Pediatric Research Psychologist, University of Illinois at Chicago, and Katherine Tassiopoulos, DSc, Senior Research Scientist, Harvard T. H. Chan School of Public Health

Effects of HIV and ARV Exposure on Child Health and Neurodevelopment, Botswana

In Botswana, Dr. Kammerer and her colleagues followed babies who were not born with HIV but whose mothers are living with HIV. They also followed babies whose mothers who are not living with HIV. The mothers living with HIV had different kinds of **antiretroviral** (ARV) treatment. The study team looked at differences in **mortality** and in the babies' development at two years of age.

Betsy Kammerer, PhD

Associate in Psychology, Department of Psychiatry, Boston Children's Hospital Assistant Professor of Psychology, Harvard Medical School

Multimodal imaging in large scale studies of the developing brain

This presentation will talk about changes over time in the relationship between the brain and behaviors during childhood and teen years.

Terry L. Jernigan, PhD

Professor of Cognitive Science, Psychiatry, and Radiology Director, UCSD Center for Human Development University of California, San Diego

Long-term effects of perinatally-acquired HIV on the subcortical shape of the adolescent brain

ND/NEUROLOGY WG (BRAIN DEVELOPMENT AND MENTAL HEALTH) THURSDAY, OCTOBER 29TH 10:30 - 11:45 AM BALLROOM A-B-C

This presentation will describe a study of 40 youth born with HIV. Brain images were done to see if there was an association between **subcortical** brain volume loss and worse HIV disease severity. The association also considered youths' age, sex, and substance use.

Lei Wang, PhD

Assistant Professor in Psychiatry and Behavioral Sciences and Radiology Northwestern University Feinberg School of Medicine

<u>Are there any specific capsules, concept sheets, or</u> manuscripts you will reference ?

Dr. Wang's presentation is based on the "Long-term effects of perinatally-acquired HIV on the subcortical shape of the adolescent brain" concept sheet (see attachment at end of this WG Presentation Summaries document). Drs. Kammerer's and Jernigan's presentations are about non-PHACS related research.

What are the main takeaways from your WG's presentation?

We encourage CAB members to ask questions at the end of the presentation. CAB members can also write questions to the presenter or WG co-chairs at the end of the meeting so they can follow-up and give answers.

Do you have any specific ideas about how the CAB can collaborate with your research and writing teams?

- Provide regular input to WG co-chairs regarding CAB's priorities for analyses and publications.
- Given the strict journal requirements for authorship, it is challenging to include as co-authors anyone who had not participated in most if not all aspects of the process. This includes study design, data collection, statistical analyses, interpretation of data, manuscript writing and editing. However, investigators value input from CAB members and encourage them to provide comments and suggestions during the project development and writing process.

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MATERNAL EXPOSURES WG THURSDAY, OCTOBER 29TH 11:45 AM - 1:00 PM BALLROOM A-B-C

Summary

<u>Notes</u>

<u>Co-Chairs</u>: Ellen Chadwick, MD, PHACS Principal Investigator, Ann & Robert H. Lurie Children's Hospital of Chicago and Deborah Kacanek, ScD, Social Epidemiologist, — Harvard T. H. Chan School of Public Health

Dr. Steve Nesheim, US Centers for Disease Control and Prevention:

HIV-exposed uninfected infants in the United -States

The number of babies born to mothers living with HIV every year in the United States (known as "HIV exposed infants") needs to be kept in mind as we keep track of efforts to prevent HIV in babies. State HIV programs are encouraged to get information on pregnant women living with HIV and their babies (infected or uninfected). This helps us to measure our progress with prevention. Examples of this kind of information are:

- When were pregnant women living with HIV diagnosed with HIV?
- Was it before or during pregnancy, at delivery, later?
- How many women, and how many of their babies got medicine to prevent HIV in the baby?
- Are babies delivered by Cesarean Section (C-Section) method when such a delivery may occur? It is tough to know the number of babies exposed to HIV exactly, but it is estimated to be 8700 per year.

Dr. Fatima Kakkar, Dept. of Pediatrics, University of Montreal:

Infectious disease outcomes and hospitalizations among HIV-exposed uninfected infants in Canada

 Worldwide, about 1.3 million pregnant women living with

 HIV will give birth to babies who do not have HIV every

 year. While it is a great success that these babies are not

 born with HIV, we are starting to realize that they may

 still be affected by either exposure to HIV during pregnancy, or exposure to the medications used to prevent

 HIV.

Studies from different parts of the world have shown higher rates of infections (such as pneumonia, **gastroenteritis**), hospital admissions, and even death, among **HIV-exposed uninfected youth (HEU)** when compared to other non-HIV exposed youth. My research looks at trying to understand why HEU youth may be sicker from infectious diseases.

MATERNAL EXPOSURES WG THURSDAY, OCTOBER 29TH 11:45 AM - 1:00 PM BALLROOM A-B-C

My research also looks at what these diseases may be Notes and if we can identify those HEU children who may be at highest risk of severe infections. My research on HEU children in Canada has found that babies born to mothers whose HIV is not well-controlled during pregnancy may be at highest risk of hospitalization and infections. This may be due to differences in their immune system. However, we need to study this among many more HEU children to be certain of these findings.

Dr. Ellen Caniglia, Dept. of Epidemiology, Harvard School of Public Health

Trimester of atazanavir exposure in utero and neurodevelopment in infants: A comparative safety study

In this presentation, I will describe the findings of our study that looked at the safety of in utero exposure to atazanavir with regards to neurodevelopment in peri**natal**ly HIV-exposed but uninfected babies. Using data from the SMARTT protocol of PHACS, we compared women living with HIV who started taking antiretroviral medications during pregnancy that contained atazanavir with women who started taking antiretroviral medications during pregnancy that did not contain atazanavir. Brain growth and development at 9-15 months was evaluated using the Bayley Scales of Infant and Toddler Development-Third Edition assessment.

COMPLICATIONS WG (HIV COMPLICATIONS) THURSDAY, OCTOBER 29TH 2:00 - 3:15 PM BALLROOM A-B-C

<u>Summary</u>

<u>Notes</u>

Co-chairs: Kunjal Patel, DSc, Research Scientist, Harvard T. H. Chan School of Public Health and Russell Van Dyke, MD, PHACS Principal Investigator, PHACS Coordinating Center, Tulane University

The Complications working group seeks to identify **infec-tious** and non-infectious issues among youths born with HIV. We then check whether they are related to HIV and its treatment. Our working group mostly focuses on the AMP protocol of PHACS. This protocol includes both youth born with HIV and those exposed to HIV during pregnancy but uninfected. Our session will have presentations by four researchers:

1) <u>Anne Neilan - Pediatric infectious disease doctor</u> <u>at Massachusetts General Hospital, Boston, MA.</u>

Anne will present results on how often teens and young adults living with HIV get various infectious and non-infectious medical events. "Incidence" or "incidence rate" is a measure of how often an event occurs. A higher incidence rate means that more events were seen while participants were followed in the study.

We found that young adults living with HIV 18-24 years of age had higher **incidences** of sexual health events, AIDS-defining diagnoses, and were more likely to die than younger participants. They were also more likely to have poor control of their HIV disease (higher HIV viral loads and lower CD4 counts). These results show that we need to improve care for 18-24 year old young adults living with HIV so they can be healthy now and in the future.

2) Deborah Persaud - Pediatric infectious disease doctor at Johns Hopkins Children's Center, Baltimore, MD.

Debbie works on identifying a cure for youth born with HIV. To do this, we first need to know how many cells in the body are infected with HIV. We then see if the number of infected cells gets smaller the longer a child is on successful HIV treatment. Treatment is successful when it keeps the HIV viral load in the blood low. The terms "reservoir" and "proviral burden" are used to describe the cells in the body that are infected with HIV. A **small reservoir or low proviral burden** means that fewer cells are infected with HIV.

We found that the number of infected cells in the body gets smaller the longer youth remain on effective **an-tiretroviral** therapy. Also, the number of infected cells got smaller faster in youth who started successful treatment before 1 year of age, compared to those who started between 1-5 years of age.

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From this analysis, we learned that it may be important Notes to start treatment early in youth born with HIV. This helps to maintain low viral loads so that the number of infected cells in the body can continue to decrease over time.

3) Steve Nesheim - Pediatric infectious disease doctor at the Centers for Disease Control and Prevention (CDC) – Atlanta, GA.

Before PHACS, the CDC conducted studies in the United States that enrolled **perinatal**ly HIV-infected children and adolescents. These studies were called Legacy and the Pediatric Spectrum of Disease Study. Steve will talk about the data from these studies and how we can work together to help learn more about HIV-infection among youth born with HIV.

4) Allison Agwu - Pediatric infectious disease doctor at Johns Hopkins Children's Center, Baltimore, MD.

Allison is interested in understanding the heart health of perinatally HIV-infected young adults who are on successful **antiretroviral** therapy. She is specifically interested in whether heart health is related to markers in the blood which show that the system that fights infection in the body is working hard. These markers are called markers of inflammation and immune activation. Allison is going to present a proposal to measure these markers in young adults living with HIV and see whether they are related to a measure of heart health called pulse wave velocity. Pulse wave velocity measures how flexible blood vessels are in the body. Blood vessels that are not very flexible are not very good for heart health.

CARDIOPULMONARY WG (HEART AND LUNG HEALTH) THURSDAY, OCTOBER 29TH 4:45 - 6:00 PM BALLROOM A-B-C

<u>Summary</u>

Co-chairs: William Shearer, MD, PhD, PHACS Principal Investigator, Baylor College of Medicine, Steve Lipshultz, MD, Pediatric Cardiologist and Chairman of Pediatrics at – Wayne State University, Detroit, MI, and Paige Williams, PhD, Senior Statistician, Harvard T. H. Chan School of Public Health

The Cardiopulmonary Working Group (CPWG) looks at heart and lung problems in children living with HIV and children born to mothers living with HIV. For children __ with HIV, we have found that current treatment strategies using a combination of HIV medications have helped a lot in preventing more severe heart problems. However, children living with HIV may be at a greater risk of developing asthma. For children born to mothers living with HIV, we want to make sure that the HIV medications given to mothers during pregnancy are safe for their children's hearts and lungs.

Our session will have three presentations:

Bill Shearer, Pediatric infectious disease doctor at Baylor College of Medicine:

Bill will present some recent findings from a substudy of the PHACS AMP study, which looks specifically at children's lung function. Over the past decade, research has found that youth living with HIV may be at a greater risk of developing asthma. **Asthma** is an obstructive lung disorder that makes the airways narrower. Patients with asthma have symptoms, such as wheezing, shortness of breath, coughing, and chest tightness. To relieve asthma symptoms, a **bronchodilator** can be used to open the airways and increase airflow to the lungs. Doctors find that when HIV+ patients' CD4 counts rise after starting **antiretroviral** treatment, breathing symptoms might begin or increase. It is not clear how HIV infection impacts **pulmonary** (lung) responses.

The PHACS **pulmonary** substudy included 188 HIV+ and 132 **HIV-exposed but uninfected (HEU)** youth from the AMP study who were given pulmonary function tests (PFTs) before and after they used a bronchodilator. Pulmonary function tests (PFTs) measure the amount of air you breathe in and out, and tell the doctors how well the lungs are working. Doctors compared the PFT results before and after the bronchodilator to assess whether or not these patients' outcomes were improved after use of a bronchodilator. This improvement is called reversibility. The percentage of youth with obstructive or restrictive pulmonary disease before using the bronchodilator did not differ between HIV+ and HEU youth. However, more HEU youth had **reversibility** compared to HIV-infected youth. Youth with obstructive disease not improved after using a bronchodilator may have an undiagnosed lung disease that could be dangerous.

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Steve Lipshultz, pediatric cardiologist and Chairman of Pediatrics at Wayne State University, Detroit, MI:

During this presentation Dr. Lipshultz will discuss results from cardiac (heart) studies completed in both the HIVinfected (AMP) and HIV-exposed uninfected (SMARTT) groups of children including:

- 1. A report showing how heart failure is now very rare in youth living with HIV treated with **highly active antiretroviral therapy (HAART)** compared to a period 20 years ago when this treatment was not available.
- 2. Results from several reports which found changes _ in the **echocardiograms** (ultrasound of the heart) of some children in both AMP and SMAART although the children appear well and have no heart symptoms and what this means for these children, their families and their doctors.
- Results from a study in SMAART children which found higher than normal levels of certain blood tests called **cardiac biomarkers** in some children although the children have no heart symptoms and what this means for these children their families, and their doctors.
- 4. A study in children in the AMP group which calculated a risk score to determine if they already have **atherosclerosis** ("hardening of the arteries") and how they and their doctors can discuss healthy lifestyle and other approaches to decrease their risk of a future heart attack or other heart problem as adults.
- 5. A proposal for a new study in the AMP and AMP/ -UP groups to better understand those changes in echocardiograms and cardiac biomarkers _ described above and what they mean for these adolescents and young adults regarding their future heart health.

<u>Paige Williams, biostatistician at Harvard Universi-</u> – <u>ty</u>:

Paige will show some new data on the relationship between vitamin D levels and heart function (a cardiologist named Renee Margossian is leading this project but was not able to attend the meeting). People with low vitamin D levels may have higher risk of heart problems. Some research has also shown that both children and adults living with HIV are more likely to have low vitamin D than those without HIV. Since the medications used to treat HIV might increase the risk of heart problems, the extra risk of low vitamin D might be particularly important in heart problems.



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The specific ways in which vitamin D might affect the heart are still not completely understood, especially in children.

Our study included both children living with HIV and HEU children from the AMP study who had an **echocardio-gram** and a blood sample to measure vitamin D. We looked at the AMP children to better understand the link between low vitamin D with heart function and structure. We are using measures of the heart taken during an echocardiograph, which is an ultrasound of the heart. The echocardiograph allows us to measure how well the heart is pumping blood (eg., the ejection fraction), and the size and shape of the heart. In our study, we created standardized values of these measurements using z-scores, by comparing them to a group of similarly-aged healthy volunteers at Boston Children's Hospital.

Some of the key measures of the heart are based on the size of the left ventricle (LV) of the heart, including the overall size (mass and volume), and the thickness of certain walls of the heart (LV wall thickness, septal thickness). We wanted to see whether children with low vitamin D levels had lower function of the heart (lower ejection fraction) and increased size of the heart. When the heart has to work harder to pump blood, it often ends up getting bigger, so higher values for LV mass and volume are considered bad. We also wanted to see if the relationship between vitamin D and heart function and structure was similar for HIV+ and HEU children in AMP.

ADOLESCENTS AND YOUNG ADULTS WG FRIDAY, OCTOBER 30TH 8:00 - 9:15 AM BALLROOM A-B-C

<u>Summary</u>

<u>Notes</u>

Co-chairs: Claude Mellins, PhD, Professor of Clinical Psychology, Columbia University, Barbara Moscicki, MD, Professor of Pediatrics, University of California Los Angeles, – and Katherine Tassiopoulos, DSc, Senior Research Scientist, Harvard T. H. Chan School of Public Health

1. Overview of the NIH Sponsored Adolescent HIV Prevention Meeting and Mature Minor Consent Meeting

Susannah Allison, PhD Division of AIDS Research, National Institute of Mental ______ Health National Institutes of Health

This past summer, NIH had two meetings on HIV prevention research in adolescents. The first meeting talked – about what we know about how to prevent HIV among adolescents around the world. It asked participants to come up with suggestions about what research we still need to do. The second meeting focused on the ethical and legal challenges to enrolling youth into HIV prevention research studies in the US. We will summarize the meetings and some of the suggestions from participants.

2. AMP Up Update

Kathy Tassiopoulos, DSc, MPH Senior Research Scientist, Dept of Epidemiology Harvard T.H. Chan School of Public Health

We will go over how many people have enrolled in AMP Up. We will talk about how many people in AMP Up were in AMP before, and how many were instead in the P219C or P1074 studies. We will describe the AMP Up participants by age, race, and sex. We'll end the talk by going over some of the answers to the online survey, both at the Entry visit and the Year 1 visit.

3. Off into the Unknown: Transitioning Youth/ Young Adults Living with HIV from Pediatric/ Adolescent to Adult Medical Care

Allison Agwu, MD

Associate Professor, Divisions of Pediatric & Adult Infectious Diseases

Johns Hopkins University School of Medicine

As young people living with HIV get older, they usually must stop going to their pediatric HIV clinics and start going to adult clinics. This usually means they see a new doctor and have to tell a new clinic and staff about their health. During this time of change from pediatric to adult care young people may have problems leaving going to the new adult clinic. We will go over studies that look at what makes it hard for young people to transfer their care. We will talk about how young people do when they transfer, and what can be done to make the transfer better for young people living with HIV.

HEARING AND LANGUAGE WG FRIDAY, OCTOBER 30TH 10:00 - 11:15 AM BALLROOM A-B-C

<u>Summary</u>

Co-chairs: Mabel Rice, PhD, Distinguished Professor, Child Language Doctoral Program, University of Kansas, Peter Torre, PhD, Associate Professor, School of Speech, Language, and Hearing Science, San Diego State University, and Tzy-Jyun Yao, PhD, Senior Statistician, Harvard T. H. Chan School of Public Health

Presentation 1: Causal Pathways for Language Impairments in Children: Nonverbal Cognitive Abilities are Tricky Mabel Rice

The language studies in PHACS aim to figure out if HIV and/or HIV regimens increase the risk of language impairments in youth. This requires us to focus on possible causes of language impairments in children with or without exposure to HIV or HIV medications. In this presentation the relation between children's **language acquisition** and their nonverbal **cognitive abilities** will be summarized. We'll first talk about studies of 5-year-old children and then we will talk about evidence from the PHACS data.

The picture is complicated. Children with low nonverbal IQ abilities can have good language outcomes; children with low language abilities can have good nonverbal IQ abilities. The conclusion is that the causes for **language acquisition** are significantly different than the causes for nonverbal intellectual development. We cannot assume a child with language impairments is intellectually impaired. We also cannot assume that a child with intellectual issues will have language issues or impairments.

Presentation 2: Longitudinal Evaluation of Language Impairment in the AMP Cohort Study Sample Sean Redmond

We previously looked at higher **prevalence** of language impairment (LI) in participants from the Adolescent Master Protocol (AMP). We compared the **prevalence** to similar participants in other studies. This presentation is an update on their outcomes 18 months later.

Key findings of the analyses include:

- Persistence of language impairment (LI) in 78% of the original cases and the appearance of 21 _ (10%) new cases of LI;
- 2) Female participants were more likely to resolve their LI;
- 3) African-American participants were more likely to show improved language scores;

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- Participants with a positive family history of LI and learning disabilities were more likely to show decreased scores; and
- 5) For the youth born with HIV, not being on cART medications at the first time of measurement and low CD4 counts decreased their likelihood of improving their language scores/resolving their LI. Additional follow-up is needed to figure out the long -term impacts of these risk and protective factors.

<u>Presentation 3: Epidemiology of Hearing Impair-</u> <u>ment – Present Knowledge and Research Needs</u> Howard Hoffman

The presentation will talk about the **prevalence** and **incidence** of **hearing impairment** in countries like the United States. It will also talk about the worldwide **prevalence** of **hearing impairment**. This information is based on recent findings by the 2010 Global Burden of – Disease (GBD) Hearing Loss Expert Team.

The presentation will also look into knowledge about **hearing impairment** in the United States. The importance of major risk factors for hearing loss – age/aging, loud noise exposure, **congenital** and other heritable factors, infection (including otitis media), and **oto-toxicity** – will be talked about. A survey of recent and on -going studies of **hearing impairment**, funded by the NIDCD, will be talked about. The presentation will look at pediatric research studies like childhood hearing **epide-miology** (newborn screening, **otitis media**, hearing studies that were in women from pregnancy through early-to-middle childhood). Finally, we will look at how childhood hearing problems, both **conductive** and **neuro-sensory**, can later impact hearing in adults of all ages.

Presentation 4: WIN Test Data Collection in AMP Up Peter Torre

The Words-in-Noise (WIN) test evaluates how well people repeat words in various listening environments. The listening environment changes from easy to difficult, and this is done raising the volume of a background noise when the words are being presented. The words and the noise are presented to the person while they are wearing earphones and the number words correctly repeated is calculated. Those individuals with a great number of words correctly repeated may have better hearing than those individuals who repeat few words correctly.

The goal of the presentation is to describe what the WIN test is and what problems that test administrators may have. Further, it is hoped that Community Advisory – Board (CAB) members will recognize the importance of the WIN test and assist in conveying that importance to – all AMP Up participants.

NUTRITION, GROWTH, AND METABOLISM WG FRIDAY, OCTOBER 30TH 1:00 - 2:15 PM BALLROOM A-B-C

<u>Summary</u>

<u>Co-chairs</u>: Denise Jacobson, PhD, Senior Research Scientist, Harvard T. H. Chan School of Public Health and Tracie Miller, MD, Director, Division of Pediatric Clinical – Research, University of Miami

Since **antiretroviral** medications were made, people living with HIV have longer life expectancies living with other chronic conditions, such as metabolic and heart disease, becoming more common in this population. In some reports, **cART** is associated with a "metabolic syndrome" in adults. This is characterized by unhealthy body composition, **insulin resistance**, abnormal glucose metabolism (how the body processes glucose), and abnormal **lipids** (fats) in the blood that places people at higher risk for heart disease.

Increased rates of **insulin resistance** have also been reported in youth living with HIV as has the presence of risks factors for future heart disease. We plan to compare the frequency of **insulin resistance** in children born to mothers living with HIV both infected and uninfected, evaluate associations of **insulin resistance** and vitamin D insufficiency/deficiency, and determine how often **insulin resistance** and abnormal glucose metabolism increase or decrease over time.

We will look at these in youth living with HIV with the goal to find the factors that make these changes happen. (See attachments at the end of this Working Group Presentation Summaries Document, "Factors Associated with Insulin Resistance among Children and Adolescents Perinatally Infected with HIV-1 in the Pediatric HIV/AIDS Cohort Study" and "Insulin Sensitivity in HIV+ vs HIV-Exposed but Uninfected Children in AMP/PHACS: Changes over Time and Associated Factors in HIV+ Children.")

The key factors that predict **insulin resistance** in youth living with HIV are the same as seen in the general population (for example: female sex, larger body mass index – (BMI), and bigger waist size).

The key factors that predict the end of **insulin re-sistance** among youth living with HIV are the same as would be expected in the general population (for example: male sex, smaller body mass index (BMI), and lower waist circumference).

No obvious relationship between new **insulin resistance** or the end of existing **insulin resistance** in youth living with HIV and any HIV disease-specific characteristic or treatment regimen, or vitamin D, was noted.

Notes

NUTRITION, GROWTH, AND METABOLISM WG FRIDAY, OCTOBER 30TH 1:00 - 2:15 PM BALLROOM A-B-C

Summary of Maternal Anemia and Birth Outcomes Notes

Background:

Anemia is defined as not having enough healthy red blood cells or not having enough hemoglobin. Hemoglobin is a protein molecule in the red blood cells that carries oxygen from the lungs to the tissues and returns carbon dioxide from the tissues back to the lungs. Anemia is common in pregnant women and it is often due to poor dietary intake of iron or not enough of the correct vitamin supplements. Some studies have shown that women who are anemic in pregnancy are more likely to deliver their baby too early (prematurity) and to have babies with low birth weight. In other studies, when pregnant women were given iron tablets their anemia got better and it increased the baby's birth weight, but it had no effect on prematurity, gestational age, small-for gestational age or birth length.

In a study in which HIV-infected pregnant women in Tanzania were given multivitamins, they saw a decrease in fetal death, low birth weight, and preterm birth (born too early) and it also improved the **CD4 counts** and **hemoglobin** levels of the mothers. In Uganda, increases in **hemoglobin** during the pregnancy of mothers living with HIV decreased the risk of small for gestational age births (this is babies who are too small when they are born). We don't have much data on the relationship of anemia and vitamins involved in red blood cell health and birth outcomes in pregnant mothers living with HIV in the US.

We had several objectives in this analysis.

- 1. Describe intake and serum levels of iron, B6, B12 and folate in the women.
- 2. Figure out how many of the women had anemia when they were pregnant.
- 3. Figure out if anemia was associated with poorer birth outcomes, including lower birth weight, lower birth length and shorter gestational age.
- 4. Figure out if intake and serum levels of iron, B6, B12 and folate was associated with anemia.

Methods

We enrolled pregnant mothers living with HIV in SMARTT into the Nutrition Substudy during their third trimester of pregnancy. We recorded their diet and supplement use and took blood to measure levels of certain nutrients. We calculated z-scores for baby weight, length and weightfor-length. The z-score tells us how a baby compares to healthy babies in the population. We compared the average z-score for each infant outcome between two groups. The groups were babies born to mothers with anemia and babies born to mothers without anemia.

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Results

Maternal characteristics

There were 285 pregnant women living with HIV in the _____ Nutrition Substudy who had at least one evaluable **dietary recall** in the third trimester. The median age of the mothers was 28.4 years; 71% were black and 34% were Hispanic. English only was spoken at home by 68% of women, 53% had income < \$10,000 per year. Sixty-nine percent were born on the mainland of the US. The median pre-pregnancy body mass index was 27.4 among the 231 women with available data. Illicit drugs, alcohol, or tobacco were ever used during pregnancy by 10%, 10% and 19%, respectively. Among the 280 women with information about food security, 25% had low food security and 12% had very low food security. _____

Baby characteristics

Seventeen percent of the babies were born preterm (too early) and 16% were small for gestational age. The average birth weight z-score was lower in our babies compared to healthy babies, but the birth lengths were similar to healthy babies. Eleven percent had a low weight for their length.

Overall, 12% of the women had a low intake of iron and folate and 6% had low intake of B6 and B12. However, compared to women without anemia, anemic women had a similar intake of B6, B12, iron and folate as non-anemic women. Of the 267 women with a **hemoglobin** measure in the third trimester, 50% were anemic and 6% had severe anemia. Women with anemia also had lower blood levels of all four nutrients.

Association between hemoglobin and birth outcomes

Weight z-scores and length z-scores were similar in babies born to women with low **hemoglobin** compared to those born to mothers with normal hemoglobin levels. Gestational age was on 3.5 days shorter for babies born of women with low **hemoglobin** levels.

<u>Take away message</u>

There might be many reasons for the high rate of prematurity in babies born to mothers living with HIV in the United States. Maternal anemia may be an important factor. If women eat foods that are rich in iron and B vitamins and take the appropriate prenatal vitamins, they might be able to improve their **hemoglobin** levels and decrease anemia. This may result in better outcomes for the baby. Our study has contributed important information about this topic. It needs to be studied further.

CAB collaboration

As we continue to explore the data from the Nutrition Substudy, CAB members may help us to identify factors that might explain why some women eat better than others during pregnancy. They could also help us to understand what the challenges are to getting good nutrition during pregnancy.

GLOSSARY

AMP: Adolescent Master Protocol.

<u>Anemia</u>: Defined as not having enough healthy red blood cells or not having enough hemoglobin (See hemoglobin).

Antiretroviral (ARV): An anti-HIV medicine (See antiretroviral therapy).

Antiretroviral Therapy (ART): A treatment developed to suppress a retrovirus, such as HIV. It is a course of treatment with anti-HIV medicine or medicines.

<u>Asthma</u>: An obstructive lung disorder that makes the airways narrower. Patients with asthma have symptoms, such as wheezing, shortness of breath, coughing, and chest tightness.

Atherosclerosis: Hardening of the arteries.

<u>BP</u>: blood pressure (in the Cardiopulmonary WG presentation, BP is measured during the echocardiogram).

Bronchodilator: A drug that causes widening of the bronchi, e.g., any of those taken by inhalation for the alleviation of asthma.

<u>Cardiac Biomarkers</u>: Substances that are released into the blood when the heart is damaged or stressed. **<u>cART</u>**: Some specific combinations of HIV medications.

<u>CD4</u> count: A lab test that measures the CD4 T lymphocytes in a sample of blood. An indicator of how well your immune system is working.

<u>CELF</u>: Clinical Evaluation of Language Fundamentals, a general purpose standardized language test.

<u>Cesarean Section (C-Section)</u>: a surgical operation for delivering a child by cutting through the wall of the mother's abdomen.

<u>CI</u>: "Cognitive impairment", a testing profile consisting of language performance within the normal range and cognitive performance below the normal range.

<u>CLI</u>: "Concomitant language and cognitive impairment", a testing profile consisting of language and cognitive performance below the normal range (comorbidity).

<u>Conductive Hearing Loss</u>: Hearing loss due to poor sound conduction through the outer ear and middle ear (includes ear drum and ossicles, tiny bones in the middle ear).

Cognitive Abilities: Brain-based skills we need to carry out any task from the simplest to the most complex. They have more to do with the mechanisms of how we learn, remember, problem-solve, and pay attention rather than with any actual knowledge.

Congenital: Present from birth.

Dietary Recall: This measure is used in a study where researchers ask participants to tell them what they ate and drank in a certain time period.

Echocardiograms: ultrasound of the heart.

ED: end diastolic, the period when the ventricle is filling up with blood.

Epidemiology: The branch of medicine that deals with the incidence, distribution, and possible control of diseases and other factors relating to health.

ES: end systolic, the period when the ventricle contracts to pump blood out.

<u>Gastroenteritis</u>: An intestinal infection marked by diarrhea, cramps, nausea, vomiting, and fever. Also known as the stomach flu.

<u>Gestational Age</u>: The length of time that the baby is in the mother's uterus until it is born.

GLOSSARY

Hearing Impairment: Often defined by reference to hearing thresholds assessed at different (audible) frequencies (tones people hear).

Hemoglobin: A protein molecule in the red blood cells that carries oxygen from the lungs to the tissues and returns carbon dioxide from the tissues back to the lungs.

<u>Highly Active Antiretroviral Therapy (HAART)</u>: Treatment for HIV infection using a combination of ARVs from at least two different classes.

HIV-Exposed but Uninfected (HEU): Refers to babies without HIV who were born to mothers living with HIV.

HOMA-IR: Homeostatic model assessment (HOMA) is a method for assessing β -cell function and insulin resistance (IR) from basal (fasting) glucose and insulin or C-peptide concentrations.

In Utero: In a pregnant woman's uterus; before birth.

Incidence, Incidence Rate: A measure of how often an event occurs.

Infectious: (of a disease or disease-causing) likely to be transmitted to people through the environment.

Insulin Resistance: A resistance to the hormone insulin, resulting in increasing blood sugar. Insulin is a hormone produced in the pancreas that regulates the amount of glucose sugar in the blood. The lack of insulin causes a form of diabetes.

Language Acquisition: The process by which humans acquire the capacity to perceive and comprehend language, as well as to produce and use words and sentences to communicate.

Language Impairment: Children whose language ability is in the bottom 15th percentile of their age peers on a language test.

Lipids: Fats

 \underline{LV} : left ventricular, this is referring to one of the chambers of the heart that is most involved with pumping blood.

Mortality: Death

Neurodevelopment: Growth and development of the brain or central nervous system.

<u>Neurosensory Hearing Loss</u>: Hearing loss due to damage in the inner ear (cochlea) or in the nerve pathways from the inner ear to the brain.

Nonverbal IQ: Cognitive ability that does not require language ability, such as the ability to solve visual puzzles or build a block design.

Nonverbal IQ Impairment: Children whose nonverbal cognitive ability is in the bottom 10-15th percentile of their age peers on a nonverbal IQ test.

Obstructive Disease: When a person has difficulty breathing out all of the air from the lung.

<u>Otitis media</u>: Ear infection, may be classified as acute, recurrent, or chronic, typically with fluid (effusion) in the middle ear space. Otitis media (OM) may be the cause of conductive hearing loss, which usually doesn't last very long, but may become a semi-permanent or permanent condition.

Ototoxicity: Damage or destruction of sensory structures in the ear ("oto" = Greek prefix meaning "ear"). Some important medications such as aminoglycoside antibiotics (e.g., gentamicin) and cancer chemotherapy drugs such as cisplatin and carboplatin are ototoxic.

Perinatal: Immediately before and after birth while a baby is inside a mother's uterus.

<u>Persistence</u>: continuation or prolonged existence.

GLOSSARY

PLI: "Primary language impairment", a testing profile consisting of language performance below the normal range and cognitive performance within the normal range.

Prematurity: When the baby spends less than 37 weeks in the mother's uterus.

Prevalence: The number, or proportion, of individuals with the 'condition', e.g., hearing impairment, at the present time, or during a defined period of time (how common something is).

<u>PTH</u>: parathyroid hormone, related to vitamin D, controls calcium in the body; levels above 65 are considered elevated.

Pulmonary: Of or relating to the lungs.

Pulmonary function tests (PFTs): Pulmonary Function Tests, which are a group of tests that measure how well your lungs work and can be used to help diagnose asthma, allergies, and other lung problems. A pulmonary function test may include spirometry, which measures the amount of air you breathe in and out.

Pulse Wave Velocity: Measures how flexible blood vessels are in the body.

<u>Restrictive Disease</u>: When a person has reduced lung capacity so that they can't breathe in as much air as needed.

Reversibility: Improvement in breathing after receiving a bronchodilator.

<u>SEM</u>: Standard error of measurement, used to interpret individual test scores by taking the test's stability into account.

Small Reservoir, Low Proviral Burden: Fewer cells are infected with HIV.

Sponsor: The entity that initiates a clinical investigation, but does not actually conduct the investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization.

Statistician: A scientific specialist responsible for analyzing all of the data collected in a clinical trial to determine trial results. Statisticians are part of the protocol team, and are important in designing clinical trials.

Subcortical: A part of the brain that is below the cortex part of the brain.

TLC: "Typical language and cognition", a testing profile consisting of performance within the normal range on language and cognitive tests.

Trigger: A clinical or laboratory result, which falls outside a predetermined acceptable limit. This result is said to "trigger" additional testing.

Undetectable Viral Load: A viral load test result showing that the amount of virus in the blood sample is too low to be detected by the laboratory. An undetectable viral load usually shows that treatment is effective and/or that the person is at low risk of disease progression.

WAIS: Wechsler Adult Intelligence Scale, a standardized achievement test (16 and older).

WISC-IV: Wechsler Intelligence Scale for Children, a standardized achievement test. Nonverbal sub-tests were used.

Working Group: Within PHACS, a group of scientists, clinicians, and community members that reviews the data, monitor triggers, and develops conference and publication materials in a particular area of interest.

<u>25 OHD</u>: 25-Hydroxyvitamin D, used to measure how much vitamin D is in someone's body.