PHACS CAB Members,

Welcome to the PHACS Fall 2018 Network Meeting! As you may have noticed, the sessions look a little different this year. Sessions are shorter, more interactive, and focused on ongoing studies in progress and updates on important findings.

This packet includes areas to write down your questions and comments from the sessions. Several pages also include brief summaries of certain sessions for your reference. We highly encourage you to write down your questions as we will review them with the PHACS Leadership on our October CAB Conference Call.

Please turn in your questions to Megan during the following times:

- **Monday, September 17 at 6:10-6:30 PM**: CAB Working Session (Old Georgetown Room)
- **Tuesday, September 18 at 11:30 AM-12:30 PM**: Lunch (Terrace/ Diplomat/Ambassador)
- **Wednesday, September 19 at 8:20-9:20 AM**: CAB Retreat (Susquehanna Room)

We will be reviewing questions together during the CAB Working Session on Monday and during the CAB Retreat on Wednesday.

Thank you!

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

Notes:

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

Notes:

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

Notes:

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

Notes:

Panel Discussion

Notes:

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

Late Breaker Title: Temporal Trends in ARV Use in Pregnancy

Presentation Description: Since 1994, the Department of Health and Human Services (DHHS) has issued recommendations on which antiretrovirals (ARVs) provide the best outcomes in managing HIV in pregnancy. These recommendations also take into account what is safe for moms to take in pregnancy and babies to take immediately after birth. The DHHS developed these recommendations with a panel of people with expertise caring for pregnant women living with HIV and their babies.

These guidelines are known as the Perinatal ARV Treatment Guidelines. The guidelines categorize ARVs or the combination of three ARVS as follows:

Category	Explanation
Preferred	The guidelines committee found enough evidence to say that this is a good drug or combination of drugs to manage HIV in pregnancy. It is safe for moms and babies.
Alternative	While this drug or combination of drugs is not the first pick of the committee, it is a reasonable option for pregnant women living with HIV.
Special Circumstances	This category is assigned because the drug or combination of drugs is deemed a good option among certain women. For example, this could refer to women with both Hepatitis B and HIV in pregnancy.
Not Mentioned	While this is not a guideline category, we added it because there were some drugs that were not mentioned in the guidelines but were prescribed.
Insufficient Evidence	This category was given when a drug or drug combination had not been used much in pregnancy. Also there was very little information on its ability to manage HIV disease in pregnancy. There also was little information on these drugs safety when used by pregnant women or for their babies.
Not Recommended	This category was given to a drug or drug combination when there was safety data to suggest that it should not be used in pregnancy.

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

We looked at data from women enrolled in the SMARTT Dynamic cohort from January 1, 2008 through July 1, 2017. We looked at how well doctors who prescribed ARVS in pregnancy followed the guidelines.

Overall, the SMARTT Dynamic women included in this study were divided into three groups:

- **Group 1:** Women who were taking ARVs prior to pregnancy
- **Group 2:** Women who started taking ARVs for the first time in pregnancy
- **Group 3:** Women who had taken ARVs previously, were not taking ARVs at the time they became pregnant but started taking ARVs again in pregnancy

For this late breaker, we will focus on women who either started taking ARVs for the first time in pregnancy (Group 2) or those who starting taking ARVs again in pregnancy (Group 3). We will review the factors associated with why a clinician (doctor, nurse practitioner) was prescribing either a "preferred" or a "preferred/ alternative" regimen as the very first regimen for women in pregnancy. We wanted to locate which factors might predict the ARVs a clinician might initially prescribe. Here are those factors:

SMARTT Site Location by Region

Child's Insurance Coverage (Medicaid versus Private Insurer)

Guideline Period (Year the ARV prescription was written)

Maternal HIV Disease Characteristics
- Mode HIV Acquisition (Birth versus other modes)
- Trimester of starting ARVs in pregnancy (initiation)
- Timing of HIV Diagnosis
- Earliest CD4 count/Viral Load in pregnancy

Maternal Characteristics
- Age when a woman became pregnant
- Race
- Ethnicity
- Highest Education Level
- Household Income

Obstetric Care
- How many weeks pregnant was a woman when she went to her first obstetric appointment?

Other Illness of a Woman
- Hepatitis B or Hepatitis C
- Tuberculosis with need to take specific medications
- Mental Health Diagnosis with need to take specific medications

Maternal Habits
- Alcohol use in pregnancy
- Tobacco use in pregnancy
- Illicit drug use in pregnancy

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

There were 450 women in the SMARTT Dynamic cohort who had initiated ARVs for the first time in pregnancy (Group 2). There were 625 who starting taking ARVs again in pregnancy (Group 3).

When we considered all the possible predictors in the table above for women resuming ARVs in pregnancy (Group 3), clinicians were more likely to prescribe a "Preferred" ARV in pregnancy if women had viral loads of more than 1,000 copies/ml and were attending a PHACS/SMARTT site in the Midwest region of the United States. This is as compared to those attending a site in Western United States. Women resuming ARVS in pregnancy were less likely to be prescribed a "Preferred" regimen if they were taking a psychiatric medication. This makes sense, because some of the psychiatric medications taken with ARVs can cause side effects.

When we considered all the possible predictors for women initiating ARVs for the first time in pregnancy (Group 2), clinicians were more likely to prescribe a "Preferred" regimen to women with viral loads > 1,000 copies/ml or with low CD4 counts (< 200) early in pregnancy, and for women who attended a PHACS/SMARTT site in the Midwest region of the country. Women who had Hepatitis B in addition to HIV were less likely to be prescribed a "Preferred" regimen. This also makes sense, since these women should be treated under the guidelines that outline "Special Circumstances".

We looked at it a second way – We looked at being prescribed either a "Preferred" or an "Alternative" regimen in pregnancy as an appropriate practice. When we considered women resuming ARVs in pregnancy who were prescribed a "Preferred" or "Alternative" regimen, having a high viral load (above 1,000 copies/ml) was again predictor. Having lower CD4 counts was less of a predictor of receiving a "Preferred" or "Alternative" regimen. This finding is a bit confusing, as we would want to make sure a woman is receiving a regimen in pregnancy that suppresses her viral load and improves her CD4 count. Both "Preferred" and "Alternative" are recommended by the experts for this reason.

Among women who newly initiated ARVs in pregnancy, being Hispanic and attending a PHACS/SMARTT site in the Midwest region of the United States were the only two predictors of clinicians prescribing a "Preferred" or "Alternative" regimen.

Overall, 43% of women initiating ARVs in pregnancy received a "Preferred" regimen and 69% received either a "Preferred" or "Alternative" regimen. Among women who restarted ARVs in pregnancy, 29% received a "Preferred" regimen and 53% received a "Preferred" or "Alternative" regimen. This analysis suggests that there are regional differences in prescribing practices of ARVs. This requires more research to understand why regional differences exist. Our data also highlight that many women living with HIV in the United States are not being prescribed "Preferred" or "Alternative" regimens.

Finally, we looked at women who had initiated ARVs for the first time in pregnancy and were prescribed a regimen with "Insufficient Evidence." This means not enough is known about the safety or effectiveness of the regimen to recommend that a pregnant woman use the regimen. We recognize that many PHACS/SMARTT sites are home to clinicians who have the latest data on ARVs and may prescribe certain ARV regimens ahead of guideline recommendations. During the session, we will report how many women newly starting ARVs in pregnancy who were prescribed a regimen before 2015 classified as "Insufficient Evidence" would have been considered as receiving a "Preferred" or "Alternative" regimen if the prescription had been written after 2015, when more safety information was available.

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

Notes:

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

We wanted to know if infants born to women with perinatally-acquired HIV (PHIV) are at risk for poor neurodevelopment when they are 1 year old. We compared infants born to women with PHIV with infants born to women who have non-perinatally-acquired HIV (NPHIV) infection. Our three questions were:

1. **Are infants born to women with PHIV more likely to have problems with language development?**
2. **Are infant born to women with PHIV more likely to have problems moving around (crawling, walking, etc.)**
3. **Are infants born to women with PHIV more likely to have problems with learning or other neurodevelopment?**

Successful treatment for children born with HIV has helped them live longer. Girls born with HIV are now having babies. However, we do not know much about whether their infants have more problems. We do not know if their infants have problems with development.

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

Who we studied: We studied 678 infants who were born to 550 women with HIV from the PHACS SMARTT study. All of these babies were uninfected. There were 125 babies born to PHIV mothers and 553 babies born to mother with NPHIV. We only studied women who had their baby after 1982 and did not have twins.

What we did: We used a test called the Bayley Scales of Infant and Toddler Development to see how the infant was developing at 1 year old. This tests the infant's development in language, moving around (crawling, walking, etc.), and learning.

What we found: Women with PHIV had babies at a younger age than other HIV-infected mothers (average age 23 vs. 25 years). The mothers with PHIV had lower CD4 counts and higher levels of HIV virus when they were pregnant. Pregnant women with PHIV took more complex HIV medication regimens. Overall, infants born to women with PHIV were not developmentally delayed at 1 year of age compared to infants born to women with NPHIV.

What we learned: Infants born to women with PHIV do not seem to be at risk for being developmentally delayed in the first year of life. This is good news. Since the study was only in infants up to 1 year of age, it will be important to keep following infants of women with PHIV and make sure that development continues to be good after 1 year of age.

Notes:

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

Previous studies have looked at how children do after they start their first HIV treatment. But there are only a few studies that have looked at how children do when they fail their first HIV treatment and switch to their second HIV treatment, also called "second-line." This analysis looked at: CD4 counts, weight, loss-to-follow-up, and death on second-line HIV treatment among children living with HIV from around the world.

We found that CD4 counts got better in the first two years after starting second-line HIV treatment, but weight didn't really improve. Children still tended to be small for their age in the first two years after starting second-line HIV treatment. Few children tended to be lost to follow-up in the first two years on second-line treatment but more children were lost in African countries compared to the United States. Few children also tended to die in the first two years on second-line treatment but again, more children died in Africa than in the United States.

This study shows that children from around the world do pretty well on second-line treatment but we have to make sure that they take their medications so they don't fail it and need third-line treatment which is usually hard to get in countries in Africa.

Notes:

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

Notes:

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

Notes:

Kathy Tassiopoulos - AMP Up early transition to adult care outcome

Notes:

Interactive Session – How Can We Retain HEU Young Adults in SMARTT When Maternal HIV Status is Not Disclosed?

Notes:

Stephanie Shiau - Epigenetic profiles in South African children with PHIV

Notes:

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

The ability of an person to recognize and repeat back speech stimuli is dependent, in part, on hearing sensitivity, cognitive and language abilities.

From PHACS AMP hearing data, youth born with HIV (PHIV) have higher risk of hearing loss than youth born HIV -exposed but uninfected (PHEU) children. However, in this new study in AMP Up, PHIV young adults were significantly less likely to have poorer words-in-noise (WIN) scores as compared to PHEU young adults. This is after we adjusted for age. For young adults with normal (i.e., ³70) non-verbal cognitive scores, PHIV young adults had a lower percentage of poorer WIN scores compared to PHEU young adults. However, the difference was only very slightly significant. For young adults with impaired non-verbal cognitive function, the opposite was the case. PHIV young adults had a higher percentage of poorer WIN scores compared with PHEU young adults, but the number of participants was too small to have enough statistical evidence. Similarly, for young adults with normal (i.e., ³70) verbal cognitive scores, PHIV young adults had a lower percentage of WIN scores compared to PHEU young adults, but without enough statistical evidence. Only 20 young adults (17 PHIV and 3 PHEU) had impaired verbal cognitive function, so any formal statistical evaluation was limited.

It is not currently known why PHEU young adults have poorer WIN scores compared to PHIV young adults for those with normal cognitive function when previous data has shown that PHIV adolescents have significantly poorer hearing. Additional hearing data are being collected in AMP Up participants in an effort to further evaluate the effects of HIV status on hearing and speech communication.

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

Notes:

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

At the in-person visits of the AMP Up study, participants complete an interview to screen for depression. They also do computer-based tests of memory and learning, and answer questions (also on the computer) about their friendships, social support, and self-efficacy (this is their believe that they can achieve their goals). In this talk we present some data from these interviews and computer tests that were done at the entry visit and the Year 3 visit.

Notes:

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

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Interactive Session - Hearing/Language and ND/ Neurodevelopmental Working Groups

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

Notes:

Update Sessions

Notes: