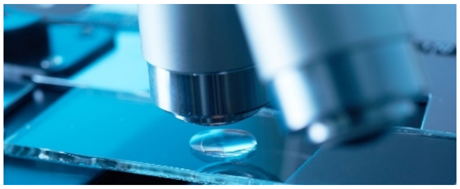
PROTOCOL

Health Outcomes around Pregnancy and Exposure to HIV/ARVs (HOPE)



June 14, 2024

Version 1.10

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HOPE
Version 1.10
Document Date: June 14, 2024
Effective Implementation Date: August 7, 2024

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Document Date: June 14, 2024
HLC IRB Approval Date: 06/21/2024
Effective Implementation Date: August 7, 2024
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Sponsored by:
The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

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List of Abbreviations and Definition of Terms

Abbreviation	Explanation
ACASI	Audio Computer-Assisted Self-Interview
AIDS	Acquired Immunodeficiency Syndrome
AMP	Adolescent Master Protocol
AMP Up	Adolescent Master Protocol for Participants 18 Years of Age and Older
AMP Up Lite	Adolescent Master Protocol for Participants 18 Years of Age and Older – Lite
ART	Antiretroviral Therapy
ARV	Antiretroviral
BIPOC	Black, Indigenous, People of Color
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CHEU	Children Who Are HIV-Exposed but Uninfected
CIN	Consent Identification Number
CRF	Case Report Form
CI	Confidence Interval
dbGaP	Database of Genotypes and Phenotypes
DDE	Direct Data Entry
DMC	Data Management Center
DNA	Deoxyribonucleic Acid
DOHD	Developmental Origins of Health and Disease
DolPHIN2	Dolutegravir in Pregnant HIV Mothers and Their Neonates
DTG	Dolutegravir
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture System
EDS	Everyday Discrimination Scale
EFV	Efavirenz
FAQs	Frequently Asked Questions
FDA	Food and Drug Administration
FSF	Frontier Science Foundation
FTC	Emtricitabine
GAD-7	Generalized Anxiety Disorder Scale
GDS	Genomic Data Sharing
GEE	Generalized Estimation Equations
GCP	Good Clinical Practice
GDM	Gestational Diabetes
GWAS	Genome-Wide Association Studies

Abbreviation	Explanation
GWG	Gestational Weight Gain
HAART	Highly Active Antiretroviral Therapy
HCV	Hepatitis C Virus
HDP	Hypertensive Disorders of Pregnancy
HHS	U.S. Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HLC	Harvard Longwood Campus
HOPE	Health Outcomes around Pregnancy and Exposure to HIV/ARVs
HPV	Human Papillomavirus
HTTPS	Hyper Text Transfer Protocol Secure
IATA	International Air Transport Association
ICH	International Conference on Harmonisation
ICSI	Intracytoplasmic Sperm Injection
IMPACT	International Maternal Pediatric Adolescent AIDS Clinical Trials
INSTI	Integrase Strand Transfer Inhibitor
IPV	Intimate Partner Violence
IRB	Institutional Review Board
IUI	Intrauterine Insemination
IVF	In Vitro Fertilization
IVI	Intravaginal Insemination
LAR	Legally Authorized Representative
LARC	Long-Acting Reversible Contraception
LDMS	Laboratory Data Management System
LOESS	Locally Estimated Scatterplot Smoothing
MAR	Missing at Random
MNPP	Manual of Network Policies and Procedures
MOP	Manual of Procedures
NCDS	Noncommunicable Disease
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health
NPHIV	Non-Perinatally Acquired HIV
OHRP	Office for Human Research Protections
OSHA	Occupational Safety and Health Administration
OR	Odds Ratio
PBMC	Peripheral Blood Mononuclear Cells
PHACS	Pediatric HIV/AIDS Cohort Study

Abbreviation	Explanation
PHI	Protected Health Information
PHIV	Perinatally Acquired HIV
PHQ-9	Patient Health Questionnaire-9
PI	Protease Inhibitor
PID	Participant Identification Number/PATID
PIN	Personal Identification Number
PLHIV	Persons Living with HIV
PrEP	Pre-Exposure Prophylaxis
PTSD	Posttraumatic Stress Disorder
QA	Quality Assurance
QNS	Query and Notification System
RNA	Ribonucleic Acid
RR	Risk Ratio
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SES	Study Enrollment System
SGA	Small for Gestational Age
SID	Subject Identification Number
sIRB	Single Institutional Review Board
SMARTT	Surveillance Monitoring for ART Toxicities
STI	Sexually Transmitted Infection
TAF	Tenofovir Alafenamide
TDF	Tenofovir Disoproxil Fumarate
TasP	Treatment as Prevention
U = U	Undetectable = Untransmittable
VESTED	Virological Efficacy and Safety of ART Combinations with TAF/TDF, EFV, and DTG
WIHS	Women’s Interagency HIV Study
WITS	Woman and Infants Study
WLHIV	Women Living with HIV
WNPHIV	Women with Non-Perinatally Acquired HIV
WPHIV	Women with PHIV

Study Abstract

Design	This is a prospective cohort study designed to evaluate the longitudinal health outcomes of young women living with HIV (WLHIV). Four populations of WLHIV at various reproductive stages will be enrolled across Health Outcomes around Pregnancy and Exposure to HIV/ARVs (HOPE) sites into the study.
Population	WLHIV who are ≥ 18 and <= 45 years of age
Sample Size	**A total of 1,630 participants will be enrolled into the study, including:** • Nulliparous and nonpregnant WLHIV (N~370) • WLHIV who are pregnant or recently delivered (≤ 3 days) (N~430) • Postpartum (> 3 days up to 12 months after delivery) nonpregnant WLHIV (N~260) • Parous, nonpregnant (> 12 months after delivery) (N~ 570) **Note:** Approximately 15% of WLHIV will be living with Perinatally Acquired HIV (PHIV).
Study Evaluations and Data Collection Measures	• **Clinical assessments:** Anthropometrics and blood pressure • **Online survey:** Social and demographic information; health literacy and healthcare engagement; physical and mental health; exposure to violence and abuse; adverse childhood experiences; sexual and reproductive health; sexual behavior; substance use; antiretroviral therapy (ART) adherence; physical activity and sleep quality; social determinants of health (e.g., food security, experiences of racism and discrimination, stigma); and health-related quality of life • **Interview**: Family and personal medical history, including social history, mental health history, and screening for current mental health conditions, reproductive history, health literacy • **Medical chart abstraction:** Diagnoses, medications, vaccinations, labs, hospitalization events, preventative health maintenance encounters • **Collection of repository specimens:** Blood, hair, saliva, vaginal, and rectal swabs
Registration/ Stratification	**Participants will be stratified at enrollment into one of four groups:** • Nulliparous and nonpregnant (N~370) • Pregnant or recently delivered (N~430) • Postpartum (> 3 days up to 12 months after delivery) nonpregnant (N~260) • Parous, nonpregnant (> 12 months after delivery) (N~570)
Study Duration	At least through February 28, 2026
Study Objectives	**Primary objectives:** • Establish the HOPE cohort to evaluate the health and well-being of WLHIV of reproductive age utilizing innovative epidemiologic study designs and cost-effective methods for enrollment, follow-up, and data collection. • Assess human immunodeficiency virus (HIV)-related outcomes and overall health of WLHIV in the HOPE cohort over their reproductive life course. • Determine the association of HIV, including timing of acquisition, treatment, disease course, and engagement in care, with overall physical and mental health of WLHIV in the HOPE cohort over their reproductive life course.

	• Assess the relationship of adverse child health outcomes with the health of WLHIV.
Domain-Specific Aims	**Reproductive Health** • Determine factors associated with a) fertility desires and b) alignment of family planning practices with stated fertility desires of reproductive-aged women living with HIV. • Assess contraception preferences and uptake, patterns of use, adherence, discontinuation, and associated individual, interpersonal, and structural factors. • Describe the unique gynecologic health problems, concerns, and needs of reproductive-age WLHIV and determine factors associated with gynecologic healthcare utilization. • Determine factors associated with pregnancy outcomes (e.g., spontaneous abortion, fetal loss, preterm birth) and complications (e.g., hypertensive disorders of pregnancy, gestational diabetes mellitus, and chorioamnionitis) • Determine factors associated with awareness of and use of HIV prevention practices and safer conception practices (i.e., methods that reduce the likelihood of transmission during attempted conception in a mixed-status couple) **Cardiometabolic Health** • Assess associations of ART use with patterns of weight change • Assess associations of mode of HIV acquisition, immune status, viral control, and ART use with hypertension • Assess associations of ART use with gestational diabetes • Evaluate the influence of sleep and physical activity on cardiometabolic health of women living with HIV. **General Health and Co-infections** • Investigate prevalence of and factors associated with self-reported severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and hospitalization for SARS-CoV-2 infection in WLHIV of reproductive age. • Identify barriers and facilitators of SARS-CoV-2 vaccine uptake among WLHIV. • Identify barriers and facilitators of influenza vaccine uptake among WLHIV. • Evaluate differences or similarities in rates of HIV viral suppression between women co-infected with Hepatitis C and HIV and those living with HIV only. **HIV Disease, Care Continuum, Care Engagement, and Treatment Adherence** • Investigate the prevalence, changes in, and HIV history-related predictors (e.g., mode of HIV acquisition) of HIV care continuum outcome components (e.g., linkage to HIV care, retention in HIV care, adherence, viral suppression, immune status), across the reproductive life course among WLHIV. • Investigate individual, interpersonal, social, and structural determinants of HIV care continuum-related outcomes (linkage to HIV care, retention in HIV care, adherence, viral suppression, immune status) across the reproductive life course among WLHIV. • Describe the transition from obstetrical care to postpartum HIV care, and barriers and facilitators to successful transition. **Substance Use** • Assess the changes in substance use behavior among WLHIV over time, including the patterns unique to individuals who experience reproductive life events such as pregnancy, the first postpartum year, and early years of parenting.

	- Assess the relationships of substance use among pregnant and postpartum WLHIV with perinatal outcomes. - Determine predictors of substance use behavior in WLHIV across the reproductive lifespan, including mental health, and social determinants (e.g., significant political events, social movements, public health policy, and healthcare systems/processes) **Stigma, Racism, and Social Determinants of Health** - Assess the relationship of structural racism and individual experiences of racism to the health of WLHIV. - Identify prevalence, predictors, and health consequences of disclosure or nondisclosure of HIV status to intimate partners, HIV-exposed children, and women's wider social networks. - Identify predictors and health-related sequelae of internalized HIV stigma and racism among WLHIV across the reproductive life course. **Mental Health and Psychosocial Conditions** - Describe the prevalence, incidence, and persistence of mental health problems, including significant symptoms of depression, anxiety, and posttraumatic stress disorder (PTSD), among WLHIV, including women living with perinatally acquired HIV (WLPHIV) and those living with non-perinatally acquired HIV (NPHIV). - Identify individual, HIV disease, treatment, pregnancy-related, and psychosocial factors associated with the presence and chronicity of mental health problems among women living with HIV. - Determine the relationship of mental health problems to adherence and HIV outcomes (viral suppression, CD4 cell count, and engagement in HIV care) among WLHIV. - Examine the relative contribution of violence exposure, mental health problems, and HIV disease factors to a) hypertension/changes in blood pressure during and after pregnancy and b) adverse pregnancy outcomes.
Risk/Benefit Category	Greater than minimal risk but presenting the prospect of direct benefit to the individual subjects

Study Schema

(Target N = 1,630)

- Nulliparous non-pregnant WLHIV (N~370)
- WLHIV who are pregnant or recently delivered (≤ 3 days), (N~430)
- Postpartum (> 3 days up to 12 months after delivery) non-pregnant WLHIV (N~260)
- Parous, non-pregnant (> 12 months after delivery) WLHIV (N~ 570)

Note: Approximately 15% of WLHIV will be living with PHIV

Confirm eligibility, obtain informed consent, and enroll.

Evaluations and Assessments at Entry[1] *(In-person study visit)*

- **Clinical assessments:** Height, weight, waist[2] and hip circumference[2], and blood pressure measurements
- **Online Survey:** Social and demographic information, HIV history, HIV and other health care access, utilization, attitudes; ART adherence, health seeking behavior, reproductive history, health, behaviors, and intentions, sexual behavior, substance use, physical and mental health, stressors and resilience, psychological and social determinants of health (e.g., experiences of racism and discrimination, food security, stigma), intimate partner violence, HIV status disclosure, adverse childhood experiences, health-related quality of life, diet, physical activity, sleep quality, and feasibility/acceptability of data collection via a wearable actigraphy device.
- **Interview:** Family and personal medical history, reproductive history, mental health, social history, health literacy.
- **Chart abstraction:** Weight, blood pressure, HIV viral load, CD4 counts, prescribed ARV and non-ARV medications, care engagement, cervical and anal dysplasia encounters and results, diagnoses and hospitalizations, pregnancy history, vaccinations, results of laboratory tests.
- **Collection of repository specimens:** blood (serum, plasma, non-viable PBMC), hair, saliva, maternal swabs (vaginal, rectal, oral) only if not already collected in AMP Up series or SMARTT studies.

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[1] The entry visit is intended to be conducted in-person. If circumstances preclude this, it can be conducted virtually. If the entry visit occurs through a virtual visit, anthropometric measures and blood pressure measurements will be collected through chart abstraction.

[2] Among non-pregnant women

Pregnant Participants

Non Pregnant Participants

Evaluations and Assessments at Delivery *(In-person study visit)*

- **Clinical assessments:** Weight and blood pressure measurements
- **Online Survey[4]:** Social and demographic information, ART adherence, health seeking behavior, infant feeding intentions/practices
- **Chart abstraction:** Weight, blood pressure, HIV viral load, CD4 counts, prescribed ARVs and non-ARV medications, care engagement, HIV-related illnesses and hospitalizations, cervical and anal dysplasia encounters and results, co-infectious and co-morbid conditions, and birth outcomes, results of laboratory tests
- **Collection of repository specimens:** blood (serum, plasma, non-viable PBMCs), maternal hair, saliva, maternal swabs [oral, vaginal (microbiome, metabolomics, and Aptima kit) and rectal [5]] only if not already collected in AMP Up Series and SMARTT Studies

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[4] To be omitted if pregnancy ends in a spontaneous abortion, induced abortion, fetal demise, or neonatal demise.

[5] Collection of the rectal and vaginal swabs (microbiome, metabolomics, and Aptima kit) should occur ONLY if they were not collected in the visit during the corresponding pregnancy.

Evaluations and Assessments at 6 Weeks Postpartum *(In-person study visit)*

- **Clinical assessments:** Weight, waist and hip circumference, and blood pressure measurements
- **Online Survey:** Social and demographic information, ART adherence, health care-related utilization, access, attitudes, behavior; reproductive health and intentions, infant feeding intentions/practices[4], breastfeeding history[4], mental health, substance use, and sleep quality
- **Interview:** Depression symptoms, anxiety
- **Chart abstraction:** Weight, blood pressure, HIV viral load, CD4 counts, prescribed ARVs and non-ARV medications, care engagement, HIV-related illnesses and hospitalizations, co-infectious, cervical and anal dysplasia encounters and results, co-morbid conditions, vaccinations, results of laboratory tests
- **Collection of repository specimens:** None

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[4] To be omitted if pregnancy ends in a spontaneous abortion, induced abortion, fetal demise, or neonatal demise.

One Year Postpartum and Annual Follow-Up Evaluations and Assessments *(Virtual Visits)*[6]

- **Clinical Assessments:** Weight, waist and hip circumference, and blood pressure only at one year postpartum and only for SMARTT co-enrollees.
- **Online Survey:** Social and demographic information, HIV history, HIV and other medical care access and utilization, ART adherence, health seeking behavior, reproductive history, health, behaviors, and intentions; sexual behavior, substance use, mental health, stressors and resilience, social and psychological determinants of health, intimate partner violence, HIV status disclosure, health-related quality of life, diet, physical activity, and sleep quality.
- **Chart abstraction:** HIV viral load, CD4 counts, prescribed ARVs and non-ARV medications, care engagement, HIV-related illnesses and hospitalizations, co-infections, pregnancy history, cervical and anal dysplasia encounters and results, blood pressures, weights, co-morbid conditions, vaccinations, results of laboratory tests.
- **Collection of repository specimens:** None

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[6] Site of virtual visit is at the discretion of the participant and can be virtual or conducted in conjunction with a SMARTT study visit or, if not enrolled in SMARTT, in person.

Participants who become pregnant after enrollment

Women Who Are Pregnant or Recently Delivered at Follow-Up[7,8]

- **Clinical assessments:** Height, weight, and blood pressure measurements
- **Interview:** Mental health
- **Chart abstraction:** Weight, blood pressure, HIV viral load, CD4 counts, prescribed ARV and non-ARV medications, care engagement, cervical and anal dysplasia encounters and results, diagnoses and hospitalizations, pregnancy history, vaccinations, results of laboratory tests.
- **Collection of repository specimens:** blood (serum, plasma, non-viable PBMC), hair, saliva, maternal swabs (vaginal, rectal, oral) only if not already collected in AMP Up series or SMARTT studies.

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[7] Defined as pregnant or up to 3 days post-delivery at follow-up.

[8] The first visit for women who are pregnant or who recently delivered at follow up can occur at either the pregnancy visit (which may occur during pregnancy up to 1 day prior to delivery) or at the delivery visit (may occur up to 2 weeks following delivery). If a woman starts on the ‘Women Who Are Pregnant or Recently Delivered at Follow-Up’ schedule during pregnancy, she should have a separate delivery visit at follow-up unless she experiences a pregnancy loss or non-live birth

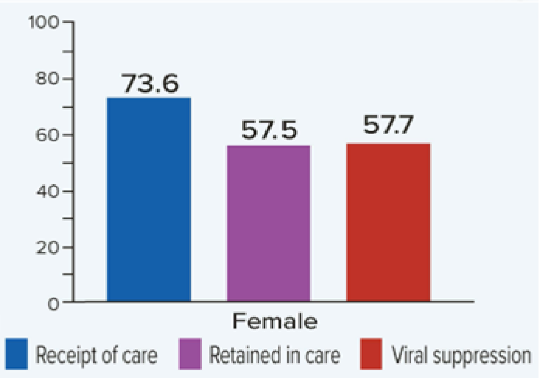
1. Introduction

1.1 Background

Globally, 18.2 million women are living with HIV (WLHIV), accounting for 56 percent of adults living with human immunodeficiency virus (HIV).[1] Each year since 2010, over 1 million WLHIV experience pregnancy, with an increasing proportion accessing antiretroviral treatment in pregnancy, up from 49 percent in 2010 to 78 percent in 2017.[2] In the United States, 33 percent of adults living with HIV are women, with 85 percent having acquired HIV through heterosexual contact.[3] Of the over 250,000 WLHIV in the United States, approximately 2 percent give birth each year.[4;5]

The HIV cascade of care has been used as a performance metric for the health of groups living with HIV and a barometer of HIV prevention, with the proportion of persons in the group of interest achieving viral suppression measuring the degree of success. In the United States, over 40 percent of WLHIV fail to achieve sustained viral suppression,[6] (Figure 1) and more than 60 percent of postpartum WLHIV are not virally suppressed 6 to 24 months after delivery.[7-10] Women with perinatally acquired HIV (PHIV) have even lower rates of viral suppression in the postpartum period.[11;12] Failure to achieve sustained viral suppression not only contributes to HIV disease progression but also impairs the long-term health and survival of WLHIV, potentially contributing to poorer health and developmental outcomes for their children. Understanding the complex milieu of biological, social, and structural events influencing the health and well-being of young WLHIV at varying stages of their reproductive life course, including women who are nulliparous, pregnant, in their first year postpartum, or beyond their first year postpartum, is critical to informing the design of interventions to optimize the long-term health of WLHIV.

Figure 1. Receipt of HIV Medical Care, Retention in Care, and Viral Suppression Among Women Living with HIV 13 Years of Age, 2016, 37 States and District of Columbia



CDC https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-national-hiv-care-outcomes.pdf

1.1.1 Reproductive Health

Improved health and significant reductions in the risk of perinatal HIV transmission have influenced the reproductive decisions of WLHIV, with more women now choosing to have children.[13-17] However, family planning is often incompletely addressed and up to 80 percent of pregnancies among WLHIV in the United States are unintended,[18-21] compared to 40-50 percent in the general population.[22] Pregnancy rates for WLHIV are similar to women without HIV, while abortion remains common.[13] Factors associated with abortion among WLHIV have been shown to be similar to the general population, including young age and greater parity, whereas HIV-specific factors have not been associated with induced abortion rates.[13] Effective contraceptive use among

WLHIV is lower than in the general population, with more WLHIV relying on non-prescription methods of birth-control[23;24] or sterilization with subsequent high rates of sterilization regret.[25;26] WLHIV also experience a greater incidence of cervical[27] and anal[28] precancerous and cancerous[29] lesions as well as STIs,[30;31] making engagement in reproductive health care, reduction of risks associated with condomless or multiple concurrent sexual partners, cancer screening and follow-up imperative. Women with perinatally acquired HIV (WPHIV) are less likely to discuss contraception with their healthcare providers,[32] which may contribute to high rates of unintended pregnancy. Further, some existing data suggest that compared to women with non-perinatally acquired HIV (WNPHIV), WPHIV may have greater pregnancy and postpartum risks, including lower rates of viral suppression, greater ART resistance, higher rates of preterm birth and cesarean delivery, and lower rates of cervical cancer screening.[33-38] Disproportionate overlapping socioeconomic, racial, and ethnic health disparities of WLHIV contribute to the reproductive health issues outlined above. Examining the multifaceted intersections of reproductive health decisions, engagement, and access to healthcare is critical to reducing inequity and improving health outcomes among WLHIV.

1.1.2 Cardiometabolic Health

Improved ART options for WLHIV have shifted morbidity and mortality from HIV-specific causes to those brought on by non-communicable disease (NCDs) such as obesity, diabetes, cardiovascular disease, hypertension, and renal dysfunction, albeit with excess risk compared with the general population.[39-44] Among WLHIV, significant strides in HIV management and treatment have also led to longer life expectancy, reduced risks of perinatal transmission, and improved overall health.[45-51] However, WLHIV face different risks for these NCDs compared with men given genetic, hormonal, and pregnancy-related factors.[52]

Pregnancy offers a critical window into the short- and long-term cardiometabolic health of a woman.[53] Maternal obesity, gestational weight gain (GWG), glucose metabolism, and hypertension in pregnancy all impact the cardiometabolic health of women beyond pregnancy.[54-57] Excess GWG is associated with preeclampsia, gestational diabetes, and long-term adiposity and obesity.[58-65] Furthermore, women with excessive versus adequate and inadequate GWG have greater adipose mass increase beyond pregnancy,[66] and the risk of postpartum weight retention has been reported to be 2-fold higher in women with excessive GWG.[67] In addition to postpartum weight retention[67] and increased abdominal adiposity later in life,[65] women with excessive GWG have a 47 percent increased risk of developing diabetes over 20 years postpartum compared to women with appropriate GWG.[56]

Both the Tsepamo study in Botswana and the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network's Virological Efficacy and Safety of ART Combinations with TAF/TDF, EFV and DTG (VESTED) study reported higher GWG in WLHIV receiving dolutegravir (DTG) versus efavirenz (EFV)-based ART.[68;69] The Tshilo Dikotla Study in Botswana demonstrated that WLHIV on DTG-based ART had higher weight through 18 months postpartum than those on EFV-based ART,[70] and data from the Dolutegravir in Pregnant HIV Mothers and Their Neonates (DolPHIN2) study showed DTG was associated with continued excess weight gain through 48 weeks postpartum compared to EFV-based ART.[71-78] Outside of the setting of pregnancy, studies of weight gain on DTG among adults found higher weight gain among women and Black and Hispanic participants.

Results of studies are conflicting as to whether WLHIV have higher rates of hypertensive disorders of pregnancy (HDP) than women without HIV or whether specific ART are associated with HDP.[79-81] The large heterogeneity of studies and rapidly changing ART used in pregnancy contribute to the challenge of disentangling these effects. Over the life course multiple studies have shown that WLHIV remain at greater risk for cardiovascular disease than their male counterparts.[82] Some data have shown that combination ART compared to no ART use or increasing duration of ART to be associated with increased risk for hypertension,[83-85] but little definitive data exists regarding specific ART associations with hypertension in WLHIV.

Sleep deprivation, or less than 7 hours of sleep on average per night, is associated with hypertension,[86-88] insulin resistance,[89-91] cardiovascular disease,[92] stroke,[93] cognitive challenges,[94] including slowed reaction time, and poorer problem solving, and has emotional consequences,[95] including depression and poor emotional regulation. On average, adults require 7-9 hours of sleep per night to feel refreshed. Sleep may be affected by variation in reproductive hormones, stress, depression, and life/role transitions.[96] Sleep disturbances are commonly reported in women experiencing premenstrual syndrome[97;98] and during pregnancy,[96] with sleep disturbances increasing in frequency and duration as pregnancy progresses. Furthermore, unpredictable sleep patterns of a newborn contribute to or exacerbate poor sleep, and are frequently responsible for daytime sleepiness in the postpartum period.[96]

Similarly, excessive sleep patterns, in excess of 9 hours are also associated with cardiovascular disease,[92] hypertension,[86] and insulin resistance.[90;91] Notably, sex is an important variable which modifies the association of sleep deprivation with incident hypertension. In a large study, the association between sleep deprivation of < 5 hours of sleep per night and incident hypertension was observed among women but not men.[99] In addition, data from the Women's Interagency HIV Study (WIHS) identified that WLHIV ages 31-40 years were 26 percent more likely to report insomnia symptoms than women without HIV (OR 1.26; 95% CI 1.01-1.59; $p < 0.05$).[100] Sleep deprivation and its health impacts have not been well studied in women of reproductive age as they transition from a nulliparous state through pregnancy and on to parenting.

Poor sleep and physical activity may be inter-related. Currently merely half of adults living with HIV have been reported to achieve the recommendations of moderate intensity physical activity per week (recommended 150-300 minutes a week of moderate-intensity activity).[101] Compared to adults without HIV, adults living with HIV also report higher sedentary behavior, with some studies demonstrating lower physical activity measured with an accelerometer.[102]

The HOPE cohort study provides an optimal opportunity to study associations between pregnancy-related metabolic alterations, and traditional risk factors including patterns of sleep and physical activity on the long-term cardiometabolic health of WLHIV of reproductive age. The cohort is uniquely positioned to address scientific gaps in understanding how various risk factors influence women's short and longer-term cardiometabolic health.

1.1.3 General Health and Co-Infections

The emergence of a novel coronavirus, SARS-CoV-2 named COVID-19, in December 2019 caused a global pandemic of severe respiratory and systemic disease, which carried significant morbidity and mortality. While ~80 percent of cases are reported to be mild to moderate, ~20 percent are life-threatening. Comorbid conditions predisposing to severe disease include arterial hypertension, obesity, diabetes, cardiopulmonary disease, older age, and immune suppression. Despite immunosuppression as a potential risk factor for severe COVID-19, anecdotal reports have not shown increased incidence or more serious disease among persons living with HIV (PLHIV).[103-105] In a retrospective series of 33 PLHIV in Germany with symptomatic SARS-CoV-2 infection, 91 percent recovered and 76 percent were classified as having mild disease.[106] However, 8 (24%) PLHIV in this series were classified as having severe disease; 14 (42%) required hospitalization, six of whom were admitted to intensive care. Three (9%) PLHIV died: one was 82 years old with detectable viremia; the second had little available data besides a "very low" pre-COVID CD4 count; and the third had hypertension, diabetes, and chronic obstructive pulmonary disease. Although the clinical characteristics of PLHIV with COVID-19 were not unlike those reported in the general population,[107] both the case fatality rate and the hospitalization rate exceeded that of the COVID-19 rates in the general population of Germany, which at the time of the report was 3.4 percent and 17 percent, respectively.[108]

Based on in vitro data and early uncontrolled studies, protease inhibitors were considered as a possible treatment option for COVID-19,[109;110] but a randomized trial of lopinavir/ritonavir in adults with severe COVID-19 did not show benefit over standard of care.[111] More data are forthcoming, as several trials of lopinavir are ongoing, including a cluster-randomized clinical trial on 3,040 participants in Spain (HCQ4COV19). Del Amo et al. investigated the risk of COVID-19 related morbidity among 77,590 individuals with HIV receiving ART across Spain, and found that receipt of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) was associated with significantly lower risk of COVID-19 diagnoses and hospital admissions, and no patients receiving these drugs died or were admitted to the intensive care unit.[112] In addition, a double blind randomized controlled trial is underway in Spain to explore the efficacy of TDF/FTC in prevention and reduction of severity of COVID-19 in 4000 health care workers.[113]

Interim guidelines from the United States HHS Panel on Antiretroviral Guidelines for Adults and Adolescents state, "the limited data currently available do not indicate that the disease course of COVID-19 in persons with HIV differs from that in persons without HIV," and "before the advent of effective combination antiretroviral therapy (ART), advanced HIV infection (i.e., CD4 cell count $<200/mm^3$) was a risk factor for complications of other respiratory infections. Whether this is also true for COVID-19 is yet unknown."[114] With regard to COVID-19 in pregnancy, the guidelines state: "Although limited, currently available data do not indicate that pregnant individuals are more susceptible to COVID-19 infection or that pregnant individuals with COVID-19 have more severe illness." Data is limited on COVID-19 and pregnancy[115] and even more limited in the context of HIV and pregnancy. However, a recent analysis by the Centers for Disease Control and Prevention (CDC) of approximately 400,000 women in the United States aged 15–44 years with symptomatic COVID-19 found that intensive care unit admission, invasive ventilation, extracorporeal membrane oxygenation, and death were more likely in pregnant women than in nonpregnant women.[115] Therefore, further investigation into the prevalence and severity of COVID-19 disease in pregnant and nonpregnant WLHIV of reproductive age is warranted.

Similar to COVID-19, co-infection with HIV and other infectious entities including Hepatitis C virus (HCV) and influenza have been associated with adverse pregnancy outcomes or more severe infectious morbidity in pregnancy. One study of 4,236 pregnant WLHIV in France found a prevalence HCV to be relatively low at 1.7 percent.[116] However, co-infection with HIV and HCV was significantly associated with preterm delivery [aOR 3.0 (95% CI 1.6-5.7), $p<0.0001$], cholestasis [aOR 4.1 (95% CI 1.5-10.8), p=0.005], lower CD4+ cell count [aOR 2.6 (95% CI 1.0-6.4), p<0.001] and detectable HIV viral load at delivery [aOR 2.3 (95% CI 1.0-5.5), p=0.06].[116] In the case of influenza, co-infection in PLHIV is associated with higher rates of mortality compared to persons without HIV, even among adults receiving a virally suppressive regimen.[117] Importantly, influenza is a vaccine preventable illness that is associated with significantly higher morbidity among pregnant women. In a meta-analysis, pregnancy was associated with a seven times greater risk of hospital admission [6.8 (95% CI 6.0 -7.7)].[118] Lessons learned in understanding influenza vaccine acceptance among pregnant WLHIV, which has been found to be offer both maternal and infant protection,[119] may inform SARS-CoV-2 vaccine uptake strategies among pregnant WLHIV.

1.1.4 HIV Disease, Care Continuum, Care Engagement, and Treatment Adherence (Includes CD4, Viral Load)

Engagement in HIV care, medication adherence, and sustained viral suppression are crucial to promoting health and long-term survival of WLHIV and reducing the risk of HIV transmission. The HIV care continuum is a framework for understanding how people living with HIV receive an HIV diagnosis, are linked and retained in HIV care, receive and adhere to ART, and ultimately become and remain virally suppressed. It has been used to monitor the health of groups living with HIV and as a barometer of HIV prevention. Among WLHIV in the United States in 2016, an estimated 74 percent received HIV care, with only 58 percent retained in care and 59 percent of those retained in care virally suppressed at their most recent clinic visit.[6] Fewer than 40 percent of postpartum WLHIV exhibit sustained viral suppression 6 to 24 months after delivery.[7;9;120] WPHIV have even lower rates of viral suppression in the postpartum period.[11;36;121] When viral suppression cannot be sustained, it contributes to HIV disease progression, immunologic changes, and risks to overall long-term health and survival of WLHIV. This in turn, may be associated with adverse health and developmental outcomes for their children. Understanding the complex milieu of individual, social, and structural conditions influencing the health and well-being of young WLHIV is critical to the design of interventions to optimize the long-term health of both WLHIV and their children.

Pregnancy is a period of enhanced engagement with clinical care[122] and represents a critical opportunity to link newly diagnosed young WLHIV to HIV care, promote retention in care, achieve viral suppression, and address HIV disease in the context of reproductive, mental health, and other psychosocial needs. In the United States, postpartum care is fragmented and sub-optimal. In fact, retention along the preconception to postpartum HIV care cascade is poor among WLHIV, with high loss to follow-up, 11-68 percent antenatally and 25-50 percent postpartum worldwide.[123] For WLHIV who conceive and continue pregnancies, the postpartum period represents a time of potential risk for interruptions in HIV care, as well as a crucial opportunity for health-promoting interventions.[124] Rates of viral suppression and ART adherence have been shown to be lower postpartum compared to the antepartum period.[7;10;123;125-128] A multi-country meta-analysis of 51 studies, comprising over 20,000 pregnant WLHIV, estimated 76 percent and 53 percent had >80 percent adherence in the antepartum and postpartum periods, respectively.[129] In addition to viremia and problems with adherence, estimates of loss to care in the first year postpartum among United States WLHIV range from 24 percent to 61 percent.[10;126;130;131]

HIV-related factors before and during pregnancy, including lower engagement in HIV care prior to pregnancy, HIV diagnosis during pregnancy, initiation of ART in pregnancy, as well as younger age have been associated with unsuppressed viral load.[10;126;132] WLHIV with a history of adverse childhood experiences and trauma who have experienced intimate partner violence (IPV) may have lower rates of adherence and viral suppression at delivery and postpartum.[124] Social factors associated with positive HIV care outcomes include trust in one's health care provider and the health care system,[133] having a provider who "knows you as a person,"[134] and social support (e.g., emotional and instrumental support). However less is known about how these factors contribute to HIV care outcomes in young women and in the context of pregnancy and the postpartum period. All of these factors have the potential to contribute to risk of secondary HIV transmission, emergence of resistance, HIV-related complications, and mortality.

Given that women may cycle in and out of care, and face multiple transitions that interrupt adherence and care, characterizing longitudinal patterns in HIV treatment and care related outcomes, by describing trajectory groupings, for example, as has been done with viral load among older women in WIHS[135] and among pregnant WPHIV in PHACS' Adolescent Master Protocol (AMP) Up study,[121] or across repeat pregnancies, is important. Examining repeat pregnancies of 610 WLHIV in the Pediatric HIV AIDS Cohort Study (PHACS) of Surveillance Monitoring for ART Toxicities (SMARTT) study,[136] O'Brien et al. found that 67 percent of women had unsuppressed viral load (>400 copies/ml) at the earliest measurement in pregnancy, which decreased to 9 percent by the end of pregnancy. However, rates of unsuppressed viral load were 50 percent by the beginning of the next pregnancy. A similar pattern of viral rebound was repeated in 166 women who had a 3rd pregnancy. The longitudinal patterns of engagement in care and viral suppression for young WLHIV in the United States, including nulliparous, pregnant, and postpartum women, remain poorly understood.

WPHIV are a unique population with lifetime exposure to HIV and ARVs who are now reaching reproductive age in the United States. In a study pooling data from SMARTT study and the IMPAACT Network P1025 study, Jao et al found that pregnant WPHIV were younger, more likely to have a CD4 count <200 cells/mm^3 during pregnancy, a delivery HIV RNA level $\geq$400 copies/mL, and receipt of $\geq$3-class ART regimens during pregnancy compared to WNPHIV, later in life.[137] Among AMP and AMP Up women, Patel et al. found that only 30 percent of pregnant WPHIV achieved sustained viral suppression in the first year postpartum, and 53 percent of women with suppressed viral load at delivery experienced rebound viremia in the first postpartum year.[121] Although pregnancy outcomes, adherence, and virologic and immunologic functioning have been compared between WPHIV and WNPHIV, few studies have determined whether barriers to or facilitators of sustained viral suppression and engagement in care are common or unique between WPHIV and WNPHIV, and whether timing of diagnoses preconception or in pregnancy for WNPHIV moderates sustained viral suppression. Identifying these factors is important for designing tailored interventions for these women. The HOPE cohort is well-poised to examine the occurrence, determinants, and consequences of interruptions in HIV care, adherence, and HIV care-related health outcomes among WLHIV/PHIV, as well as the role of repeat pregnancies and postpartum transitions in HIV care.

1.1.5 Substance Use

There is a growing opioid crisis in the United States, with ample evidence demonstrating that opioid use, driven largely by use of prescription opioids, is rising.[138;139] Non-medical opioid use (prescription misuse) is a complex public health challenge that has been reported to affect as many as 1-3 percent of pregnant and reproductive aged women;[140] concurrently, deaths from opioid overdose have risen more than 300 percent in recent years.[138;141] As in the general population, maternal opioid use has increased steeply since 2000, with data suggesting nearly one quarter of pregnant women fill an opioid prescription.[141] Opioid use and opioid use disorder have substantial implications for both perinatal outcomes and long-term health of women and children.[141] Women who use opioids during pregnancy are also much more likely to experience comorbid mental health disorders, other substance use disorders, and addiction-related risk behaviors.[141] Moreover, the postpartum period may be a particularly critical risk period for opioid initiation or increased use, as recent data demonstrate hospitalization for birth is a common reason for opioid prescribing among reproductive aged women, even when unindicated based on pain report.[142-147] However, it remains unclear whether opioid use patterns during pregnancy or postpartum among WLHIV mirror that of the general population.

Concurrent with the growing opioid epidemic in the U.S., rates of marijuana use have risen in pregnant and nonpregnant women of reproductive age.[148] Legalization of marijuana for both medical and recreational use as well as increased acceptance of marijuana use in many parts of the United States may contribute to greater use in pregnant and reproductive aged postpartum or nonpregnant women.[149-152] Despite guidelines from the American College of Obstetricians and Gynecologists discouraging the prescribing or use of marijuana during preconception, pregnancy, and lactation, it remains the most commonly used illicit drug, with rates reported to be as high as 15-28 percent among young and socioeconomically disadvantaged women and with 34-60 percent of women continuing to use marijuana during pregnancy.[149;153] Although existing data suggest marijuana use is not associated with structural fetal defects or most adverse perinatal outcomes,[153-155] heavy and early use have each been associated with low birthweight and abnormal neurodevelopment.[153] Additionally, marijuana use has been associated with other social-behavioral risk factors that could have implications for maternal and child health, such as concomitant IPV, tobacco use, and suboptimal nutrition.[153;155] Nevertheless, in the general population, marijuana use during pregnancy is common, often perceived to be safe, and has even been recommended by dispensaries for pregnancy symptoms.[149;150] Given this context, marijuana use in pregnant and postpartum WLHIV may be increasing as in the general population. The associations of such use with perinatal and long-term outcomes among WLHIV also remains unknown.

Although trends in substance use have been described among pregnant women without HIV and non-pregnant WLHIV, and to a lesser extent among pregnant WLHIV, in the United States,[156] several unanswered questions remain. Rough et al. demonstrated that overall substance use rates declined sharply from 1990 to 2012 in a U.S. sample of pregnant WLHIV enrolled in SMARTT or Women and Infants Study (WITS), although these data largely addressed tobacco, alcohol, cocaine, and heroin use.[157] Findings suggest the prevalence of substance use during pregnancy among SMARTT-enrolled WLHIV is very low for most substances, achieving levels similar to the general U.S. population.[157] However, these findings also predated the peak of the current opioid epidemic as well as the most recent sociopolitical changes in marijuana use. Additionally, little is known about the trajectories of substance use after birth. Although prior data, such as from the WIHS cohort, has identified some correlates of substance use among WLHIV, such as food insecurity, this work has been in an older population of WLHIV.[158] Few reports have examined the trajectory of use in younger reproductive aged women. Little is known regarding the extent of or changes in postpartum marijuana or opioid use among WLHIV. Currently, PHACS does not collect data on postpartum opioid use (except for heroin), which represents an important area for expansion of research on substance use.

Thus, the development of an HIV/opioid surveillance program is critically needed, and will be essential for the success of the new HHS “Ending the Epidemic” initiative (EtE).[159] The engagement of PHACS sites in HOPE will allow for surveillance monitoring, with 33 percent of HOPE Study sites (see Appendix II) situated in the top tertile of opioid overdose states, according to CDC mapping.[160]

1.1.6 Stigma, Racism, and Social Determinants of Health

Among WLHIV in the United States, disparities in health care access, comorbidities, HIV disease progression, adverse pregnancy outcomes, and mortality are not uncommon.[161-166] HIV-related stigma,[167] socioeconomic disadvantage, and racism-driven inequities are major contributors to pervasive disparities in access to care, medication adherence,[163-166] mental health,[168] pain,[169] hypertension and other comorbidities, and the overall well-being of WLHIV. These disparities are shaped by social determinants of health, individual, interpersonal, institutional, and structural level discrimination and systemic inequities that impact the distribution of risk, resources, and opportunities.

Social determinants of health, the conditions in which individuals are born live, learn, work and play, are increasingly recognized as drivers of health disparities. Social determinants of health encompass conditions of individuals’ physical and social environment which shape health-related behaviors and conditions.[170;171] These include structural factors such as HIV-related stigma,[166;172;173] violence,[174;175] racism,[176] inequity,[177] and poverty, [178] which may negatively influence both maternal HIV disease state and outcomes of children who are HIV-exposed but uninfected (CHEU) through direct or indirect pathways, potentiating health outcome disparities among WLHIV and their children.[179]

Accumulating evidence highlights the impact of internalized, interpersonal, cultural, institutional, systemic and structural racism on the health of Black, Indigenous, People of Color (BIPOC).[180-185] Racism is “a system of structuring opportunity assigning value based on the social interpretation of how one looks (which is what we call “race”), that unfairly disadvantages some individuals and communities, unfairly advantages other individuals and communities, and saps the strength of the whole society through the waste of human resources.”[186;187] Racism is also the use of power to maintain systems of oppression that perpetuate the advantages of the dominant race and social identity.[188] Stress incurred from the experience of racism and discrimination[189;190] has been associated with specific health-affecting challenges, including sleep disturbance,[191;192] substance use[193] mental health concerns,[194-196] cardiovascular disease,[197] and sexual and reproductive health issues.[176] In addition, among Black women of childbearing age, racism has been linked to disproportionate maternal and infant death,[198] high rates of pre-term birth,[199;200] and low rates and duration of breastfeeding.[201] However, few studies to date have examined the impact of racism and discrimination on the health of BIPOC WLHIV of childbearing age, despite the fact that HIV disproportionately impacts women who identify as Black and Latinx[4] in the United States.

Among pregnant BIPOC women with and without HIV, chronic and acute experiences of racism may be linked to adverse birth outcomes.[202] Such experiences include racism-related stress[203] within casual, professional and intimate relationships and resultant anxiety,[204] living in racially segregated neighborhoods with fewer resources, more environmental hazards, less access to or lower quality care,[205] and/or experiencing discrimination during medical encounters.[206;207] “Weathering,” or chronic exposure to social and economic disadvantage, increases allostatic load and has potential to accelerate aging and declines in health, and has been identified as a possible mechanism linking racism to adverse health outcomes.[208;209] Microaggressions, behaviors that are “brief and subtle verbal and or non-verbal denigrating messages”[210] directed toward women can weaken women’s sense of self-worth and increase vulnerability to negative health outcomes. Microaggressions are cumulative in nature and therefore constitute cumulative harm, which is associated with negative long-term emotional, cognitive, behavioral, physiological, and social responses. Additionally, microaggressions reinforce structural inequities and impact an individual’s ability to function adequately.[211] When microaggressions occur in the health care setting, they can undermine patient-provider interactions, and lead to disengagement from HIV and obstetric care.[162;212]

Stigma is a social phenomenon that adversely affects WLHIV. Women experiencing higher levels of perceived, anticipated, internalized, and enacted stigma may also experience higher levels of social isolation and depression, which could, in turn, contribute to poor adherence[163] and other HIV care continuum outcomes. The intersection of HIV-related stigma and other forms of stigma, including racism, classism, sexism, disability, and heterosexism,[213-215] have been associated with suboptimal HIV care and poses additional threats to positive health outcomes[216] among WLHIV.

At the structural level, racial segregation, disproportionate rates of police brutality and incarceration, and other traumatic forms of systemic racism, including legacies of slavery, redlining, and Jim Crow laws, have also contributed to adverse health outcomes for Black women. For example, Black women living in racially segregated neighborhoods have higher risk of HDP.[217] In addition, racial segregation has been linked to low birthweight and higher incidence of cardiovascular disease in the general population, yet little is known about the specific effects of racial residential segregation and other harmful social policies (e.g., living in states with more laws criminalizing HIV) on the health of WLHIV. Immigration status, and the anxiety and fear of deportation resulting from harmful social policies directed toward women who are undocumented, may also lead to disengagement from care and health disparities for BIPOC WLHIV.[218;219]

Some women experience multiple and intersecting traumas of racism, stigma, and discrimination yet maintain positive health outcomes. Understanding the role of individual and community resilience resources—that is the “ability to cope adaptively when faced with adversity or to “bounce back” following adverse experiences by navigating to and negotiating for social psychological, physical and cultural resources”[220;221]—is critical to identifying avenues for intervention to promote the health of WLHIV.[222] Family, interpersonal and institutional resources including social support[221;223] and social capital,[224] connection to religious or spiritual community,[225] political and community activism and advocacy, availability of and access to community resources, and enactment of laws aiming to protect human rights, which vary across individuals, and by state and locality, may mitigate the negative effects on women’s health and well-being and are, thus, critical avenues for investigation within HOPE.

1.1.7 Mental Health and Psychosocial Conditions

WLHIV have improved opportunities for long-term survival in the presence of effective antiretroviral therapy and adequate adherence to treatment and care. However, complications and risks associated with HIV, including adverse mental health and behavioral health conditions, are not uncommon among women with HIV, including those with PHIV, and women who acquire HIV later in life.[156;226-234] If present, mental and behavioral health problems may increase risk for inconsistent utilization of ART and detectable viral load during pregnancy and may influence pregnancy outcomes, subsequent HIV care engagement, risk behaviors, and mortality.[235;236] Mood disorders, for example, including major depression, dysthymia, and bipolar disorder, as well as substance use disorders among WLHIV, are associated with sexual risk behaviors, with potential to further complicate women's general health and well-being.[237]

Risks for mental health problems among WLHIV are likely related to biological and psychosocial factors. For example, HIV-related disease complications, including chronic inflammation and neurochemical changes during pregnancy and postpartum, confer risk for depression.[238-242] In addition, WLHIV, whether acquired perinatally or later in life, may have personal histories of adverse life events, trauma, chronic or acute stress, and inadequate individual, family, social, or community resources that further increase mental health risk.[243-247]

In their 2014 study of women enrolled in the PHACS SMARTT study, Malee et al. found that 35 percent of women screened positive for a psychiatric or substance use disorder at their initial evaluation and 61 percent of women with disorders at the initial evaluation presented with a disorder at a subsequent evaluation.[156] More than half of women with persistent disorders had comorbid mental health disorders at their initial evaluation, especially PTSD, anxiety, and depression, in varying combinations, which may adversely affect adherence and retention in HIV care. Of additional concern, among women with no disorders at their initial evaluation, 21 percent experienced an incident disorder, which underscores the dynamic nature of psychiatric conditions and the need for ongoing screening and provision of easily accessible services.

In the current era of care for WLHIV, it is unclear whether mental health problems develop, persist, worsen, or remit during pregnancy, in the one year after delivery, defined as the postpartum period, or during the near-term life course of a parenting WLHIV. Of particular concern are persistent mental health problems that are undiagnosed or untreated, placing women at heightened risk for role functional impairment, morbidity, and mortality. Similarly, their children may be at risk for negative developmental effects and mental health problems related to parental mental and behavioral health risks.[248-250]

Given that mental health risks are not uncommon among WLHIV, may be exacerbated by pregnancy, and may influence maternal health, engagement in care, and attachment and child caregiving behaviors, examination of the prevalence, incidence, and persistence of adverse mental health outcomes among women during their child-bearing years is essential. HOPE will enable collection of the mental health and biopsychosocial data needed to address these questions and identify interventions to improve the health of WLHIV across their lifespan.

1.1.8 Effect of Child's Health on Maternal Health and Well-Being

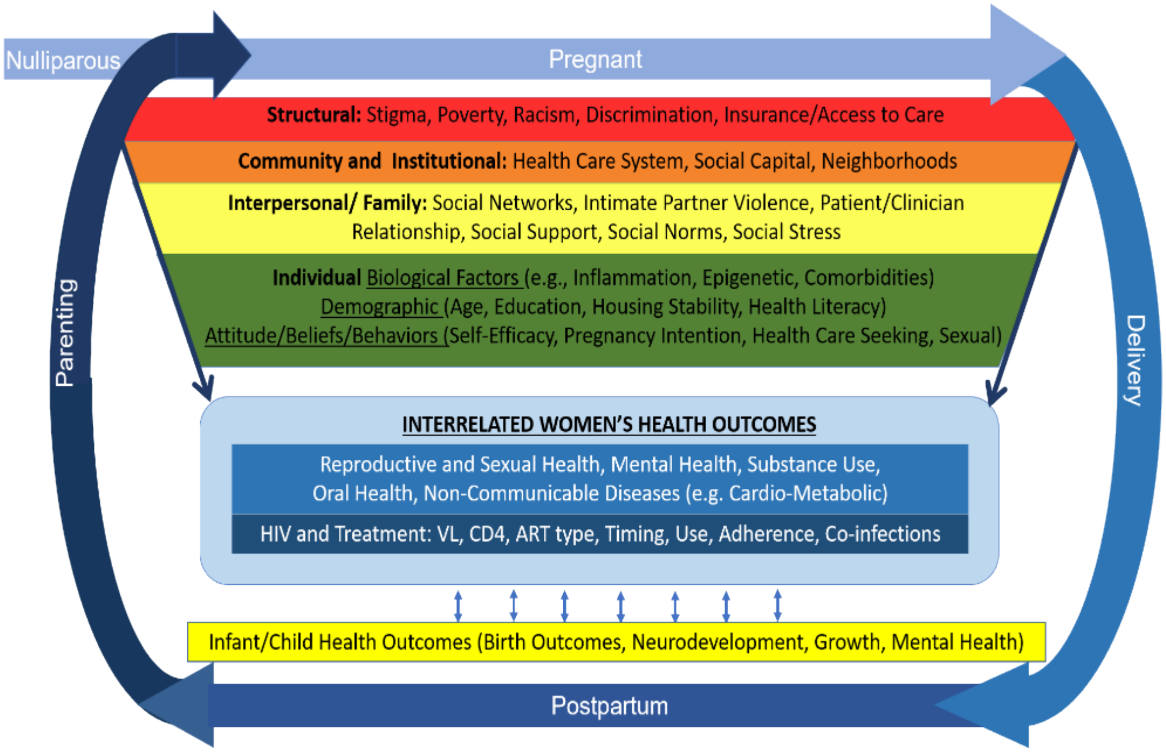
Explaining how children and their health influence maternal physical and mental health is understudied and essential to improving the health of young WLHIV. Providing appropriate parenting and care is often prioritized ahead of optimizing WLHIV's own health, including achievement of sustained viral suppression. This could have dramatic consequences for a woman's health, as well as subsequent pregnancy outcomes.

Parenting children with significant developmental delays or chronic health conditions has the potential to have short- and long-term effects on the health of caregivers.[251-255] For example, the care of children with chronic diseases has been associated with maternal anxiety, depression, diminished sleep quality and quantity, and perceived stress as well as deterioration in parents' physical health. Parenting and caring for such a child may present particular challenges for a mother with HIV, jeopardizing sustained overall healthcare engagement and increasing her risk for HIV-related complications. For example, preterm birth, a common perinatal morbidity in the SMARTT cohort,[256] has been associated with maternal stress, anxiety, and depression as well as alterations in family function and parenting interactions, both soon after the birth and many years later.[255;257-260]

Other childhood diseases, such as asthma, occurring in 13 percent of children enrolled in the SMARTT cohort, have been similarly documented to be associated with deterioration in parental health and quality of life due to the intensity of caregiving required for chronic conditions with a high burden of self-care.[261] These added risks to maternal health may have major lifelong and intergenerational consequences on the family's physical and social well-being, but their impact specifically among WLHIV is an understudied area.

1.2 Conceptual Framework

Figure 2. Conceptual Model for HOPE *(Note that WLHIV may enter HOPE during pre-pregnancy, pregnancy, postpartum, or parenting periods and cycle through these stages in varying patterns).*



The HOPE Study is informed by the Developmental Origins of Health and Disease (DOHD) framework as well as a social/ecological framework in which factors operating at multiple levels including individual, biological, interpersonal, family, community and institutional, and structural, may affect women's and children's healthy development as well as their risk of adverse outcomes.[262] (See Figure 2.) Changes in exposure to these factors, in maternal HIV disease across their lifespan, as well as changes during pregnancy and postpartum, may affect women's health and the health of their children. Maternal infections other than HIV, the mode of HIV acquisition[263;264] and timing of HIV diagnosis, and type and timing of ART use and adherence can influence engagement in care, maternal HIV outcomes, and women's overall health and that of their children.[265;266] The needs and health of children in turn may affect women's health. This cyclical and dynamic relationship, occurring in the context of structural factors including HIV-related stigma, violence, racism, inequity, and poverty may negatively influence maternal HIV disease state and outcomes of CHEU through direct or indirect pathways, potentiating health outcome disparities among WLHIV and their children.[267;268] Conversely, potential adverse effects may be mitigated by family and interpersonal resources including social support and availability and access to community resources.[124;269]

The HOPE cohort will be well-poised to address questions surrounding the long-term health of WLHIV of reproductive age through young adulthood, pregnancy, and parenting as well as the health of their children. It will leverage the well-established infrastructure of PHACS, drawing from the SMARTT cohort, which was established in 2007 as an observational study using a novel trigger-based study design to identify the short- and long-term safety of in utero fetal exposure to maternal ART,[270;271] and the AMP Up Series (AMP Up and AMP Up Lite cohorts), which follow individuals with PHIV. It will also leverage the strong research infrastructure at each HOPE participating PHACS site to recruit nulliparous WLHIV. This unique research platform provides efficiencies in study design and opportunities for multi-disciplinary and cross-cutting research, to inform public health policy for optimizing the health of WLHIV and their children in the United States.

2. Objectives and Hypotheses

2.1 Primary Study Objectives

Establish the HOPE cohort to evaluate the health and wellbeing of WLHIV of reproductive age utilizing innovative epidemiologic study designs and cost-effective methods for enrollment, follow-up, and data collection.

Assess the HIV-related outcomes and overall health of WLHIV over their reproductive life course, including:

- Reproductive health, co-infections, and long-term non-communicable diseases, as well as potential inflammatory and epigenetic processes associated with these outcomes.
- Psychosocial determinants of health including engagement in care, depression and other mental health diagnoses, stigma, racism, inequity, disclosure of HIV, and opioid and other substance use/misuse.

Determine the association of HIV, including timing of acquisition, treatment, disease course, and engagement in care, with the overall physical and mental health of WLHIV over their reproductive life course.

Assess the relationship of adverse infant or child health outcomes to the health of WLHIV including:

- Adverse birth outcomes (preterm birth) and child conditions (hospitalizations in the first 2 years) will increase the risk of adverse maternal outcomes, such as unsuppressed viral load.
- Chronic child health conditions, e.g., asthma, neurologic diagnoses, in the offspring of women will increase the risk of unsuppressed viral load and lower CD4 cell count among WLHIV after 1 year postpartum.
- The relationship of child chronic health conditions to maternal unsuppressed viral load will be mediated by maternal chronic stress, inadequate sleep, depression, and anxiety.
- The relationship of child acute and chronic health conditions to maternal physical and mental health outcomes will be moderated by presence of resilience resources (e.g., social support, less social isolation).

2.2 Domain Specific Aims and Hypotheses

2.2.1 Reproductive Health

Specific Aims:

- Determine factors associated with a) fertility desires and b) alignment of family planning practices with stated fertility desires of reproductive-aged women living with HIV.
- Assess contraception preferences and uptake, patterns of use, adherence, discontinuation, and associated individual, interpersonal, and structural factors.

- Describe the unique gynecologic health problems, concerns, and diagnoses of reproductive age WLHIV (including STIs and abnormal cytology) and determine factors associated with gynecologic healthcare utilization, including adherence to cervical cancer screening guidelines.
- Determine factors associated with pregnancy outcomes (e.g., spontaneous abortion, fetal loss, preterm birth, term live birth) and complications (e.g., HDP, gestational diabetes, chorioamnionitis).
- Determine factors associated with awareness of and use of HIV prevention practices and safer conception practices (i.e., methods that reduce the likelihood of transmission during attempted conception in a mixed status couple).

Hypotheses:

- The fertility desires of WLHIV will vary across time and by demographic, clinical, and psychosocial factors, such as pregnancy history, social support, HIV stigma, and HIV- and non-HIV-related health status.
- Greater engagement in care, better HIV control, and psychosocial markers of well-being (such as absence of mental health disorders, greater social support, and greater engagement in HIV care) will be associated with concordance between stated fertility desires and behaviors (i.e., use of effective contraception when future pregnancy is not desired).
- Contraception use and the choice of specific high-quality methods (long-acting reversible contraception [LARC] and other World Health Organization Tier 1 or 2 methods) will be associated with demographic factors (e.g., age, parity, whether partnered), clinical factors (e.g., time since last pregnancy, comorbidities, HIV control), and psychosocial factors (e.g., engagement in care, healthcare access, and mental health diagnoses).
- Reported dissatisfaction, perceived barriers, and safety misconceptions will be associated with inconsistent contraception use.
- WLHIV will have a high prevalence of gynecologic complaints and diagnoses (including uterine fibroids, dysmenorrhea, abnormal uterine bleeding, endometriosis, sexual dysfunction, urogynecologic conditions including incontinence and prolapse), and such findings will be associated with factors such as age, quality of life, HIV disease status, pregnancy history, and health care engagement.
- WLHIV with better health care engagement and better HIV control will be more likely to have received indicated gynecologic healthcare utilization (including receipt of indicated gynecologic care, such as cervical cytology screening and human papillomavirus [HPV] vaccination).
- Secondary infertility among young WLHIV will be associated with age, HIV disease status, and history of STIs.
- STI incidence will be associated with demographic (e.g., younger age, South/Southeast region, low household income), behavioral (e.g., inconsistent condom use, greater number of sex partners), clinical (e.g., greater STI history, suboptimal health care engagement, suboptimal HIV control), and psychosocial factors (e.g., HIV stigma and mental health disorders).
- Early pregnancy loss (including spontaneous abortions and ectopic pregnancy; occurring prior to or during HOPE Study participation) will be associated with demographic, clinical, and

psychosocial factors, such as older maternal age, history of chronic comorbidities (e.g., antiphospholipid antibody syndrome), poorer healthcare engagement (e.g., not using ARVs at conception), and suboptimal HIV control.

- WLHIV will experience frequent pregnancy complications (e.g., chorioamnionitis), and certain pregnancy complications such as HDP and gestational diabetes mellitus will be associated with clinical factors (such as age, chronic hypertension, and body mass index) as well as HIV-related factors (e.g., viral suppression, CD4 count, and ART at conception).
- Preterm birth among WLHIV will be associated with demographic, clinical, and psychosocial factors, including age, maternal mode of HIV acquisition, history of prior preterm birth, social stress, race/ethnicity, HIV stigma, HIV control, and chronic comorbidities.
- Better HIV care engagement, better HIV control, less HIV stigma, partner HIV status, and disclosure of HIV status to partner will be associated with awareness and uptake of biomedical HIV prevention (e.g., Preexposure prophylaxis (PrEP), undetectable = untransmissible (U=U)).
- Use of safer conception methods (e.g., PrEP use, sperm washing, home intravaginal insemination (IVI), intrauterine insemination (IUI), in vitro fertilizations (IVF) with intracytoplasmic sperm injection (ICSI), donor sperm, or donor egg) will be associated with intended pregnancies, disclosure of HIV status to partner, greater HIV or gynecologic healthcare engagement, and better HIV control. Use of safer conception methods will also be associated with better viremic control during pregnancy.

2.2.2 Cardiometabolic Health

Specific Aims:

- Assess associations of ART use with patterns of weight change.
- Assess associations of mode of HIV acquisition, immune status, viral control, and ART use with hypertension.
- Assess associations of ART use with gestational diabetes.
- Evaluate the influence of sleep and activity on cardiometabolic health of women living with HIV.

Hypotheses:

- Women on an ART regimen of DTG, TAF, and FTC will experience higher GWG and higher postpartum weight retention compared with women on other regimens.
- Women living with HIV initiating or switching to TAF/FTC/DTG outside of pregnancy and the postpartum period will exhibit more rapid weight gain over time compared with women who initiate on ART regimens without TAF or DTG.
- Differences in ART will modify the overall relationship between HDP and postpartum hypertension.
- Differences in ART will be associated with incidence of hypertension in nulliparous women.
- For nulliparous women, perinatal HIV acquisition, compared to non-perinatal HIV acquisition, will be associated with increased incidence of hypertension, defined as a systolic blood pressure > 140 mm Hg or a diastolic blood pressure > 90 mm Hg, regardless of ART regimen.

- WLHIV who experience preeclampsia or eclampsia in pregnancy will have a higher risk of a hypertension diagnosis within 3 years following the index pregnancy compared with women who do not have HIV but are diagnosed with preeclampsia or eclampsia in pregnancy.
- Protease inhibitor use vs. integrase strand transfer inhibitor (INSTI) use in pregnancy will be associated with higher risk for gestational diabetes.
- Self-reported sleep duration will be associated with incident hypertension and changes in weight over time.
- Women reporting more frequent daily moderate and/or vigorous activity will have lower incidence of hypertension.

2.2.3 General Health and Co-Infections

Specific Aims:

- Investigate prevalence and factors associated with self-reported SARS-CoV-2 infection and hospitalization for SARS-CoV-2 infection in WLHIV of reproductive age.
- Identify barriers and facilitators of SARS-CoV-2 vaccine uptake among WLHIV.
- Identify barriers and facilitators of influenza vaccine uptake among WLHIV.
- Evaluate differences or similarities in rates of HIV viral suppression between women co-infected with Hepatitis C and HIV and those living with HIV only.

Hypotheses:

- Poorer immune status will be associated with higher risk of self-reported SARS-CoV-2 infection and hospitalization for SARS-CoV-2 infection among non-pregnant WLHIV.
- Treatment with tenofovir will be associated with a lower incidence of self-reported SARS-CoV-2 infection and hospitalization for SARS-CoV-2 infection among non-pregnant WLHIV.
- Black racial identity, Hispanic ethnicity, or lower socioeconomic status will be associated with higher incidence of self-reported SARS-CoV-2 infection and hospitalization for SARS-CoV-2 infection among non-pregnant WLHIV due to experiences of discrimination and structural racism.
- Self-reported SARS-CoV-2 infection will be similar between pregnant and non-pregnant WLHIV; however, severity of COVID-19 will be higher in pregnant WLHIV.
- Influenza vaccine uptake will be facilitated by engagement in antenatal care, with a common barrier for non-pregnant WLHIV being poor integration of vaccine health services at the site where they receive their primary HIV care.
- Persons co-infected with Hepatitis C and HIV will be more likely to have detectable HIV viral loads 1 year after treatment initiation compared to women with HIV infection alone.

2.2.4 HIV Disease, Care Continuum, Care Engagement, and Treatment Adherence

Specific Aims:

- Investigate the prevalence, changes in, and HIV history-related predictors of HIV care continuum outcome components (e.g., linkage to HIV care, retention in HIV care, adherence, viral suppression, immune status) across the reproductive life course among WLHIV.
- Investigate individual, interpersonal, social, and structural determinants of HIV care continuum-related outcomes (e.g., linkage to HIV care, retention in HIV care, adherence, viral suppression, immune status) across the reproductive life course among WLHIV.
- Describe the transition from obstetrical care to postpartum HIV care, and barriers and facilitators to successful transition.

Hypotheses:

- Optimal HIV care continuum outcomes will be more prevalent during pregnant periods vs. postpartum or non-pregnant periods.
- Prevalence of and changes in HIV care continuum outcomes (e.g., time to viral suppression, rate of increase in CD4 count) will differ by mode of HIV acquisition (WPHIV vs. WNPHIV), duration since HIV acquisition, and HIV disclosure status to partners.
- Among pregnant and postpartum WLHIV, pre-pregnancy HIV care continuum-related outcomes will predict postpartum HIV care continuum-related outcomes. Presence of supportive resources will moderate this association.
- Women experiencing adversities in childhood (i.e., adverse childhood experiences) and adulthood (e.g., IPV, racism) will have suboptimal HIV care continuum outcomes. The effect of these adversities will be moderated by presence of resilience resources (e.g., social support, less social isolation).
- HIV-related stigma (e.g., internalized stigma, enacted stigma), lower trust in the healthcare system and HIV care provider, and lower levels of social support, social capital, and resilience will be associated with suboptimal HIV care continuum outcomes; these relationships will be punctuated during the pregnancy to postpartum period.
- Disparities in HIV care continuum outcomes will be observed by region and socioeconomic deprivation (e.g., access to care, food and housing security status, neighborhood poverty level) and interpersonal and family factors (e.g., having a child with an adverse health condition).
- Women with depression, anxiety, or post-traumatic stress disorder, and women with elevated substance use will have greater risk of suboptimal HIV care continuum outcomes.
- Individual demographic characteristics (e.g., age, race, ethnicity, education), capabilities (health literacy, self-efficacy), and resources (e.g., income, health insurance) will be associated with HIV care continuum outcomes.
- Health care delivery and system-related factors (e.g., use of telehealth) will be associated with HIV care continuum outcomes.

2.2.5 Substance Use

Specific Aims:

- Assess the changes in substance use behavior among WLHIV over time, including the patterns unique to individuals who experience reproductive life events such as pregnancy, the first postpartum year, and early years of parenting.
- Assess the relationships of substance use among pregnant and postpartum WLHIV with perinatal outcomes.
- Determine predictors of substance use behavior in WLHIV across the reproductive lifespan, including mental health, and social determinants (e.g., significant political events, social movements, public health policy, and health care systems/processes).

Hypotheses:

- Substance use—particularly marijuana and concomitant alcohol plus marijuana use—will continue to increase over time among pregnant postpartum WLHIV.
- Marijuana use will be more prevalent among all WLHIV in states where marijuana is medically or recreationally legal compared to WLHIV in states without legalized marijuana use.
- Tobacco use among pregnant and postpartum WLHIV will be stable over time but will be associated with concomitant use of other substances and will be associated with demographic and psychosocial factors, including age, geographic region, and HIV status.
- Opioid use or the use of other substances for the treatment of pain will continue to rise over time among all WLHIV, consistent with the U.S. opioid epidemic. Opioid use will be associated with demographic, clinical, and psychosocial factors, including geographic region, delivery route, mental health status, and healthcare engagement.
- Substance use during pregnancy will be associated with adverse maternal and perinatal outcomes, including growth restriction, intrauterine fetal demise, small for gestational age (SGA) status, neonatal intensive care unit admission, neonatal abstinence syndrome, and other adverse childhood outcomes.
- The association of substance use during pregnancy/postpartum and longer-term maternal and child health outcomes will be modified by HIV disease control (e.g., detectable viral load) and health care engagement.
- Substance use will be associated with greater viral load, lower CD4 count, poorer maintenance of viral suppression (i.e., “blips” or other evidence of viremia after initial suppression), and, among pregnant individuals, greater likelihood of viremia at the time of delivery.
- Substance use will be associated with poorer engagement in HIV-related health care, including medication adherence and appointment attendance, as well as HIV stigma.
- Substance use will be associated with greater HIV-related comorbidities and complications, including opportunistic infections.
- PHIV status may be a modifier of the relationships above.

2.2.6 Stigma, Racism, and Social Determinants of Health

Specific Aims:

- Assess the relationship of structural racism and individual experiences of racism to the health of WLHIV.
- Identify prevalence, predictors, and health consequences of disclosure or non-disclosure of HIV status to intimate partners, HIV-exposed children, and women's wider social networks.
- Identify predictors and health related secondary results of internalized HIV stigma and racism among WLHIV across the reproductive life course.

Hypotheses:

- Higher levels of racism and stigma will be associated with suboptimal HIV care continuum outcomes, including disengagement from care, suboptimal adherence, unsuppressed viral load, and declines in CD4, and will be moderated by resilience resources (e.g., presence of social support).
- The relationship of racism to suboptimal HIV care continuum outcomes, including disengagement from care, suboptimal adherence, unsuppressed viral load, and/or declines in CD4 will be mediated by higher levels of stress.
- Women who report higher levels of racism and HIV-related stigma and discrimination during or prior to pregnancy will have lower CD4 count, higher risk of perinatal depression, HDP, and adverse birth outcomes, including preterm birth, SGA, and/or low birthweight infants.
- Younger women will have lower levels of HIV-related internalized stigma relative to older women; levels of internalized stigma will not differ by mode of HIV acquisition (PHIV vs. NPHIV).
- Women with higher levels of internalized stigma will have higher levels of chronic stress, unsuppressed viral load, and lower CD4 count.
- Lower levels of trust and higher levels of racism and stigma enacted by health care providers will be associated with suboptimal HIV care continuum outcomes (e.g., disengagement from care, suboptimal adherence, unsuppressed viral load, declines in CD4) and adverse birth outcomes.

2.2.7 Mental and Psychosocial Conditions

Specific Aims:

- Describe the prevalence, incidence, and persistence of mental health problems, including significant symptoms of depression, anxiety, and PTSD, among WLHIV, including women with PHIV and those with NPHIV.
- Identify individual, HIV disease, treatment, pregnancy-related, and psychosocial factors associated with the presence and chronicity of mental health problems among WLHIV.
- Determine the relationship of mental health problems to adherence and HIV disease outcomes (e.g., viral suppression, CD4 cell count and engagement in HIV care) among WLHIV.

- Examine the relative contribution of violence exposure, mental health problems, and HIV disease factors to a) hypertension/changes in blood pressure during and after pregnancy, and b) adverse pregnancy outcomes.

Hypotheses:

- Mental health problems will be more prevalent among WPHIV vs. WNPHIV and will have earlier onset and greater chronicity; remission and recurrence among both WPHIV and WNPHIV will vary depending upon engagement in medical and mental health care.
- The prevalence of depression among women living with HIV will increase during the postpartum period; remission will be more likely among women with postpartum depression who access mental health care.
- The prevalence, incidence, and persistence of mental health problems among WLHIV will be associated with adverse life events during childhood or adolescence, higher levels of HIV-related stigma, stressful life events during adulthood (e.g., violence, HIV related health complications), and limited personal resources (e.g., income, education, access to care), regardless of timing of HIV infection.
- Exposure to specific ARVs or ARV classes will be associated with elevated risks of depression and will vary by ARV class and treatment duration.
- The factors associated with mental health problems during antepartum and postpartum will differ for women with PHIV vs. women with NPHIV diagnosed in pregnancy vs. women with NPHIV diagnosed before pregnancy.
- The risk of nonadherence and unsuppressed viral load in any period (i.e., never pregnant, pregnant, postpartum, parenting) will be greater among women with current depression, anxiety, and/or PTSD and poor engagement in mental health care.
- The relationship of current mental health problems to suboptimal HIV care outcomes and engagement in health care will be attenuated among women with more vs. fewer resiliency resources (e.g., social support, personal competence, higher family income, higher education, engagement in psychiatric care).
- Cumulative violence exposure will be associated with elevated blood pressure during and after pregnancy.
- Women with violence exposure, depression, and unsuppressed viral load at time of conception will have greater risk of hypertension and adverse pregnancy outcomes.

3. Study Design

This study will enroll up to 1,630 women living with HIV ≥ 18 and ≤ 45 years of age.

Participants will be evaluated prospectively according to an established schedule of evaluations, conducted both in person and remotely (see Appendix I).

3.1 Study Population and Sample Size

A total of 1,630 participants will be enrolled into the study as follows:

- Nulliparous non-pregnant WLHIV (N~370)
- WLHIV who are pregnant or recently delivered (≤ 3 days) (N~430)
- Postpartum (> 3 days up to 12 months after delivery), non-pregnant WLHIV (N~260)
- Parous, non-pregnant (> 12 months after delivery) WLHIV (N~ 570)

3.2 Registration and Stratification

Participants will be stratified into one of four groups at enrollment as described above in Section 3.1.

3.3 Study Duration

The study is funded for a 5-year period and subject to competitive renewal of funding. Women consenting to study participation will be followed through February 28, 2026, or longer if the study receives extended funding.

3.4 Biological Specimens

Biological specimens will be collected from HOPE participants at enrollment, and for pregnant participants, at delivery, based on the participant's choice. For women co-enrolling in HOPE and the PHACS SMARTT study during pregnancy or at the time of delivery, or in the AMP Up Series, specimens jointly collected for both studies will be labeled with the PHACS study details. For all other women enrolling in the HOPE Study or for women from whom vaginal, rectal, and oral swabs will be obtained, these specimens will be labeled as HOPE and stored in the PHACS Repository. Specimens will include serum, plasma, non-viable peripheral blood mononuclear cells (PBMCs), anal, oral, and vaginal swabs, hair specimens, and saliva. For women co-enrolled in the PHACS SMARTT study, the HOPE and SMARTT study consents include language whereby women can elect to approve stored specimens obtained from their infant at birth can be used by both the SMARTT and HOPE studies in the future.

Note: *Women may be co-enrolled in HOPE and one or more PHACS study. All HOPE biological specimens are designated for the repository. For repository specimens collected in the HOPE Study, as well as for other PHACS studies in which a woman is co-enrolled, the designated repository specimen may be acquired once and shared by both studies if the PHACS study visits occur within 90 days before the HOPE Study visit and the specimens are blood, hair, and/or the Aptima vaginal swab STI kit. Otherwise, specimens should be collected separately for each study. HOPE will abide by the PHACS specimen request policy governing this process if the stored specimen is shared between HOPE and a PHACS study. Refer to the HOPE Manual of Procedures (MOP) for additional information.*

4. Selection and Enrollment of Study Participants

4.1 Inclusion Criteria

To be considered eligible for enrollment into HOPE, an individual must meet all the criteria listed below:

- Female based on biological sex assignment at birth
- HIV infection as documented in the medical record
- 18 to ≤ 45 years of age
- Willingness to provide access to existing medical records
- Willingness to participate and provide legal consent/assent
- Able to complete study assessments in English, Spanish, or Haitian Creole

4.2 Exclusion Criteria

Individuals who meet any of the criteria listed below are not eligible for enrollment:

- Currently incarcerated
- Age > 45 years
- Male based on biological sex assignment at birth (even if self-identified as female)
- Any concurrent participation in other studies not approved by the HOPE Protocol Team

4.3 Study Registration Procedures

Prior to implementation of this study, the Harvard Longwood Campus Institutional Review Board (HLC IRB), the single IRB (sIRB) of record for HOPE, will approve the study protocol, including template informed consent forms. Subsequently, the local IRBs at HOPE sites must cede review of HOPE to the HLC IRB via the execution of a reliance agreement. All site-specific materials including fact sheets and recruitment materials must then be reviewed and approved by the HLC IRB. Finally, sites must receive protocol registration approval from the Regulatory Affairs Office at Westat. Confirmation of site registration must occur before any participant is enrolled in the protocol. Original approved regulatory documents must be maintained at the site. HOPE will follow the PHACS procedures for registration, which are outlined in the PHACS Manual of Network Policies and Procedures (MNPP). The MNPP chapter pertaining to protocol registration can also be found on the PHACS website (https://my.phacsstudy.org).

4.4 Recruitment Procedures

Potential participants will be recruited from participating HOPE sites or from their local affiliates. Clinical staff members such as case managers and healthcare providers at clinical sites will be made aware of the eligibility criteria for the study. Potential participants will be identified and referred to the clinical research team for potential enrollment. A research staff member will provide an overview of the study and gauge the potential participant’s interest in participating.

4.5 Informed Consent

The site's designated study staff member will discuss details about participation in this study with eligible participants who indicate an interest in participating as stated in Section 4.4. Once it is determined that a participant qualifies for the protocol, informed consent will be obtained prior to any study-related medical abstraction or evaluation being performed.

Study details including the information to be collected and the evaluations and assessments involved will be discussed with potential participants who show interest in the study, and all questions will be answered during the informed consent process. Designated study staff will initiate the informed consent process using informed consent forms that have been reviewed and approved by the HLC IRB (see Appendices V and VI).

The initial informed consent procedure will be conducted either: (1) at the clinical site prior to study enrollment; or (2) remote (online) consent will be available at HOPE Study sites for participants who cannot attend the clinical site in person. The online consent form may include verification of comprehension and require participants to acknowledge that they have read and agree to the consent form by checking a box following each section of the consent. Verification of identification during the consent process will be confirmed using a consent identification number (CIN) provided to the participant by the clinical site at the time of consent. Security questions may be employed for further verification. When necessary, re-consenting may occur via an online informed consent form when there are protocol amendments requiring re-consent or when the participant is no longer affiliated with the local clinical site (see next paragraph). The HOPE Protocol Team will work with the clinical sites and the HLC IRB to ensure that the online informed consent completed by each site's participants is developed in accordance with sites' local IRB requirements. If the online informed consent should occur, clinical site staff will be available for phone consultation to address questions or concerns. Participants will also be offered the option of coming to the clinic to re-consent in person. Clinical site staff will monitor whether the mental capacity of a participant changes throughout the course of the study. Each site employs psychology staff that can advise when a participant's competence to give initial or continuing consent is in question, and sites will contact the HLC IRB and/or their local IRB for guidance.

If the online consent option is chosen by the participant, the required information will be collected via an online consent form as described above and will be stored on a secure server. The electronic version of the consent mirrors the hardcopy, albeit in an electronic format, and allows for the participant to designate whether they accept or reject certain opportunities, such as being contacted after the study has ended to hear about new studies or having blood drawn in the study used for future research. The clinical site who enrolled the participant will have access to the online consent data. The online consent form is developed by Frontier Science Foundation (FSF), the Data Management Center (DMC) for HOPE, and although FSF is responsible for administration of the online survey tool, protected health information (such as the participant's name) will not be transferred to the PHACS/HOPE Study database. FSF owns the online survey tool and maintains secure servers in compliance with all requisite Federal, state, and international law as it pertains to clinical data.

4.6 Enrollment Procedures

When a participant is eligible for the study and informed consent has been obtained, the site will use the Study Enrollment System (SES) at FSF to enter participant and eligibility information. Participants who were previously enrolled in PHACS will continue to use their PHACS participant ID number (PID). A new PID will be assigned to participants who were not enrolled in any of these studies. For all participants, once confirmed eligible and enrolled, the SES will generate a study identification number (SID). In HOPE, the SID will serve as the participant's protocol-specific PIN that will be used as the participant identifier in the online survey.

4.7 Co-Enrollment Guidelines

Enrollment of HOPE participants in other studies with or without similar goals/data collection as HOPE is at the discretion of the clinical site Principal Investigators (PI) and HOPE Protocol Team. However, the PI must take into account any issues that enrollment in the additional study may impose upon the participant, or which may compromise the site's ability to fulfill HOPE protocol requirements.

Participants may be co-enrolled in the following PHACS studies without additional approval from the HOPE Protocol Team: AMP Up, AMP Up Lite, or SMARTT. Participants may also be co-enrolled into WIHS and the WIHS STAR study without additional approval from the HOPE Protocol Team, but if visits are planned to occur concurrently, consideration should be given to the blood volume required by each study.

Enrolling participants into HOPE who are already enrolled in other studies of WLHIV with similar goals and data collection as HOPE that are not listed above is at the discretion of the Protocol Co-Chairs. Sites should query for permission to enroll these individuals into HOPE.

Pregnant or delivering HOPE participants are encouraged to enroll in the PHACS SMARTT Dynamic Cohort with their unborn or newborn infant, but this is not a requirement for HOPE enrollment.

Participants who indicate they would like to be contacted for studies opening in the future will provide their contact information to the clinical site. Each site will maintain this information and, in the event a participant changes their mind and no longer wishes to be contacted, the site will track these requests and update their documentation accordingly.

5. Clinical and Laboratory Evaluations

The following clinical and laboratory evaluations will be performed on each participant, after signed informed consent is obtained, as part of participation in this study. See Appendix I for a tabulated summary of the evaluations described below and their schedule for completion.

5.1 Entry Evaluations (Pregnancy, Delivery or Non-Pregnant)

Entry time point evaluations for all participants will include clinical assessments, an interviewer-administered medical and psychosocial history questionnaire, an online survey, chart abstraction, and collection of specimens for the shared PHACS/HOPE Repository. The entry visit, including consent, study registration, and entry evaluations, is estimated to take 3 hours in total. Sites may obtain consent and conduct study registration on a different date prior to the entry evaluations if they choose.

- Clinical assessments will include height, weight, waist and hip circumference, and blood pressure measurements. Waist and hip circumference will not be measured for participants who are enrolling during pregnancy or at delivery. If an in-person visit cannot be completed at the entry visit, then height, weight, and blood pressure measurements will be collected through chart abstraction, if available.
- An interviewer-administered medical history questionnaire will be completed to collect targeted medical and medications history (including approximate year of ART initiation), and family medical history. An interviewer-administered pregnancy and reproductive history questionnaire and a brief assessment of health literacy and social history will also be completed. In addition, the interview will screen for symptoms of depression via the Patient Health Questionnaire-9 (PHQ-9), as well as anxiety symptoms via the Generalized Anxiety Disorder Scale (GAD-7), and Posttraumatic Stress Disorder via the PC-PTSD-5. Information on addressing any potential safety issues and adverse event planning for participants will be included in the HOPE MOP. All interviewer-administered questionnaires may be completed via telephone or other video-conferencing technology for participants who cannot complete an in-person visit at entry.
- The online survey will collect information on sociodemographic characteristics, including ZIP code, physical and mental health, health care-related use, access, attitudes, behavior; HIV care engagement, HIV-related history, adherence to ARVs (Wilson Three-Item Self-Report Measure for Adherence), stigma and HIV status disclosure, exposure to violence, history of physical and sexual assault, emotional abuse, and IPV, resilience, pregnancy circumstances, intentions, and desire; sexual behaviors and health, contraceptive use and satisfaction, reproductive health, sexual orientation and gender identity, breastfeeding intention and practices (for pregnant and postpartum women only), substance use, health related quality of life, social determinants of health (e.g., experiences of racism and discrimination, food and housing security, social support), adverse childhood experiences, perceived stress, health literacy, self-efficacy, diet, physical activity, sleep quality, and feasibility/acceptability of data collection via a wearable actigraphy device.

- At the entry visit, participants can consent to provide their residential address information for the purposes of geocoding. The address information will be stored at the site and will not be part of the database.
- Chart abstraction will include:
    - For women enrolling in pregnancy, at delivery, or in the postpartum period (up to 1 year after delivery), the following data will be abstracted from medical records for the period starting 6 months prior to conception of the most recent pregnancy (please refer to the MOP Section 3.9.1 to calculate the date of conception):
        1. HIV status;
        2. General medical, obstetric, and gynecological history;
        3. Medical diagnoses including but not limited to diabetes (gestational or pregestational), hypertension (including HDP, or chronic hypertension regardless of timing of diagnosis), obesity, dyslipidemia, and anemia;
        4. Mental health diagnoses including depression, anxiety, PTSD, and psychosis;
        5. HIV, primary care, OB, gynecologic, mental health care engagement; ART medications, non-ART medications, CD4 including nadir CD4, viral load, immunizations, gravidity, parity, pregnancy outcomes, results of STI testing, as well as normal and abnormal cervicovaginal cytology and histology, weight, blood pressure, and results of selected laboratory tests.
    - For nulliparous, non-pregnant women and non-pregnant women enrolling more than one year after giving birth, the following data will be abstracted for the period starting 12 months prior to the visit:
        1. HIV status;
        2. General medical, gynecological, and obstetric history (if applicable);
        3. Medical diagnoses including but not limited to diabetes (gestational or pregestational), hypertension (including HDP, or chronic hypertension regardless of timing of diagnosis), obesity, dyslipidemia, and anemia;
        4. Mental health diagnoses including depression, anxiety, PTSD, and psychosis;
        5. HIV, primary care, OB, gynecologic, mental health care engagement; ART medications, non-ART medications, CD4 including nadir CD4, viral load, results of STI testing and abnormal cervicovaginal cytology and histology, immunizations, gravidity, parity, and pregnancy outcomes, weight, blood pressure, and results of selected laboratory tests.
- Blood (serum, plasma, and PBMCs), hair, and saliva samples, and oral, vaginal, and rectal swabs will be collected for storage in the PHACS/HOPE Repository.
- For any woman co-enrolled in HOPE and another PHACS study, a link will be established between their HOPE and PHACS PID for subsequent use of the woman's data.
- For women co-enrolled in HOPE and SMARTT, who provide informed consent to share data about the health, development, and behavioral outcomes of their SMARTT enrolled child(ren) or for use of the birth specimens, for the purposes of assessing the association between conditions in children and the health and wellbeing of mothers or pregnancy

outcomes, the child's SMARTT PID will be collected at enrollment and linked to the woman's PID.

5.2 Delivery Follow-up Visit

At the delivery visit following a pregnancy visit, the following will be collected:

- Clinical assessments: These will include height (if not collected at entry), weight and blood pressure measurements.
- The online survey: This will collect information on sociodemographic characteristics, ART adherence, health care-related utilization, access, attitudes, behavior; HIV care engagement, physical and mental health, social determinants of health, breastfeeding intentions/practices, substance use, and immunizations.
- Chart abstractions: These will include anthropometrics and blood pressure, CD4, viral load, ART medications, non-ART medications, engagement in HIV and primary care, OB, gynecologic, mental health care engagement, immunizations, medical conditions, results of STI testing and abnormal cervicovaginal cytology and histology, cervical and anal dysplasia, mental health diagnoses including depression, anxiety and PTSD, results of selected laboratory tests, and pregnancy outcomes.
- Blood (serum, plasma, and PBMCs), hair and saliva samples, oral and vaginal swabs: All will be collected for storage in the PHACS/HOPE Repository.

5.3 Six-Week Postpartum Visit

Women who enroll while pregnant or up to 3 days after delivery, or who experience a pregnancy after completing their entry visit and wish to have the pregnancy followed in HOPE, will have a follow up visit after the delivery visit, when they are 6 weeks postpartum. Six-week postpartum visit evaluations for all participants will include clinical assessments, interviewer-administered mental health assessments, an online survey, chart abstraction. The six-week postpartum visit is estimated to take 1.5-2 hours.

- Clinical assessments will include height (if not obtained at entry), weight, waist and hip circumference and blood pressure measurements. If an in-person visit cannot be completed, then height, weight, and blood pressure measurements will be collected through chart abstraction, if available.
- An interview will assess depression via the Patient Health Questionnaire-9 (PHQ-9), as well as anxiety symptoms via the Generalized Anxiety Disorder Scale (GAD-7). Information on addressing any potential safety issues and adverse event planning for participants will be included in the HOPE MOP. All interviewer-administered questionnaires may be completed via telephone or other video-conferencing technology for participants who cannot complete an in-person visit.
- The online survey will collect information on sociodemographic characteristics, health care utilization, access, attitudes, behavior; HIV care engagement, ART adherence (Wilson Three-Item Self-Report Measure for Adherence), pregnancy circumstances, intentions, and desire, sexual behaviors and health, contraceptive use and satisfaction, reproductive health, breastfeeding intention and practices, substance use, health related quality of life, pain, social

determinants of health, adverse childhood experiences (only if not obtained at enrollment), perceived stress, exposure to violence, history of physical and sexual assault, emotional abuse, and IPV, health literacy, self-efficacy, diet, physical activity, sleep quality, and physical and mental health.

- Chart abstraction will include HIV viral load, CD4 counts, ART medications, non-ART medications, HIV, primary care, OB, gynecologic, mental health care engagement, HIV-related illnesses and hospitalizations, co-infections, cervical and anal dysplasia encounters and results, co-morbid conditions, mental health diagnoses including depression, anxiety and PTSD, immunizations, results of selected laboratory tests, weight, and blood pressure.

5.4 One Year Postpartum and Annual Evaluations

After the entry visit for women who were nulliparous or not pregnant at enrollment, chart abstraction and the online survey will be completed annually. For all women who enrolled during pregnancy or at delivery, chart abstraction and the online survey will be completed at 1 year postpartum and then annually. For women who enrolled during pregnancy or who experience a pregnancy after completing their entry visit and wish to have the pregnancy followed in HOPE, and are co-enrolled in SMARTT, the 1-year postpartum visit should be conducted in person, at which clinical assessments (i.e., weight, waist and hip circumference and blood pressure measurements) will be collected for HOPE.

The 1 year postpartum follow up or annual visit is estimated to take approximately 1 hour.

- The online survey may be completed remotely outside of the clinic or may be completed in the clinic at the option of the participant. Questions will include sociodemographic characteristics, health care utilization, access, attitudes and behavior; HIV care engagement, HIV medical history, ART adherence, stigma and disclosure, pregnancy circumstances, intentions, and desire, sexual behaviors and health, contraception use and satisfaction, reproductive health, sexual orientation and gender identity, breastfeeding, substance use, health related quality of life, social determinants of health, perceived stress, exposure to violence, history of physical and sexual assault, emotional abuse; and IPV, physical and mental health (depression using the PHQ-9 and anxiety symptoms using the GAD-7), health literacy, self-efficacy, diet, physical activity, and sleep quality.
- Chart abstraction will include anthropometrics, blood pressure, interval medical diagnoses, ART medications, non-ART medications, immunizations, CD4, viral load, pregnancy and pregnancy outcomes, results of STI testing, cervical and anal dysplasia, and mental health diagnoses including depression, anxiety, PTSD, and psychosis. Medical chart abstraction will be done per the schedule of evaluation (Appendix I), allowing for repeated follow up measurements of HIV disease markers (viral load, CD4 cell count); HIV, primary care, OB, gynecologic, mental health care engagement; co-infections, co-morbidities, and diagnoses of NCDs, and results of selected laboratory tests obtained in the period since the baseline or most recent assessment.

5.5 Pregnancy at Follow-Up

Participants who become pregnant during follow-up in HOPE will be encouraged to switch to the visit schedule and schedule of evaluations for women who are pregnant or recently delivered at follow-up. The assessments required at each visit are the same as those expected for a participant that enrolled during pregnancy or delivery, with the exception of the following:

- No assessment of Reproductive History, Personal and Family Medical History, and Health Literacy, PTSD, height,
- No social history interview, and
- No online survey at the pregnancy visit.

> ***Note:*** *If the participant agrees to switch schedules, they have the discretion to schedule their first visit on the new schedule during pregnancy or at delivery.*
>
> *If a pregnancy at follow-up ends in a non-live birth (i.e., spontaneous abortion, induced abortion, or fetal demise), the guidelines described in Section 8.1.1 will apply.*
>
> *In addition, for participants who switch to this schedule, all chart abstraction should start from the participant's last visit.*

5.6 Additional Surveys

From time to time, technological developments, events impacting public health, or world events may be associated with the changes in the health and wellbeing of WLHIV. As such events occur, surveys may be developed and submitted at that time to the HLC IRB as a project modification. Once approved by the HLC IRB, they would be administered to HOPE participants. These surveys may be administered as online surveys or interviews.

5.7 Feasibility and Acceptability Survey of Wearable Devices

To support and prepare for future data collection using wearable devices, a brief online survey will be administered at baseline assessing women's perceptions of feasibility and acceptability of data collection via a wearable actigraphy device. The survey will assess access to smart phones, accompanying data plans, and women's comfort level in sharing data collected on wearable devices, including data on sleep, heart rate, and physical activity. It is anticipated that the collection of such information and data will better assist HOPE in refining the conduct of such data collection in the future, providing insight into its practicality, and determining women's level of enthusiasm (or lack thereof) in the approach to data collection. Although our premise is that studies predicated on the use of mobile devices to collect data centered on general health and well-being will be of interest to participants, the questionnaire will be a first step of a broader effort to determine acceptability and feasibility of this data collection strategy.

6. Data Collection and Site Monitoring

6.1 Data Collection

Participants must not be identified by name on any case report forms (CRFs), online surveys, laboratory specimens, clinical evaluation results, or laboratory results that are part of their research record. Participants are to be identified only by the PID and SID/PIN numbers assigned by HOPE. Study research records with PID and SID/PIN numbers must be stored separately from source documents that include personal identifiers. Source documents must be securely stored at HOPE Study sites with access restricted to designated study staff. The HOPE Study sites will not share source documents containing personal identifiers with individuals or entities outside the HOPE Study or with Frontier Sciences or HOPE Study staff who are not employed by the study site, except for persons or entities noted in Section 6.3.

6.1.1 Case Report Forms

For medical record abstraction and other non-web-based data collection, CRFs will be made available on the HOPE DMC web portal. Whenever possible, sites are encouraged to complete CRFs electronically, including those that are used as source documents, through direct data entry (DDE) into the PHACS/HOPE central database. CRFs approved for use as source documents must be signed and dated by the clinical site staff member recording the data on the day of completion. CRFs not used as source documents must have corresponding source documentation on file at the clinical site to substantiate all submitted data. Please refer to the MOP for a full listing of CRFs and details.

6.1.2 Online Surveys

Online surveys will be administered using a secure cloud-based commercial software tool managed by FSF. The online surveys can be completed on any device on which the internet can be accessed, including a smartphone. Skip patterns will be programmed into the survey, and questions can be skipped by participants if they choose. Questions may be accompanied by sound. Most of the questions are incorporated into one overall survey, while other questions may be administered separately as short, stand-alone surveys. Participants will receive a link to the longer, overall survey and—if applicable—separate links for the stand-alone surveys. The participant can choose to complete both the overall and stand-alone surveys at the same time, or they can complete the stand-alone surveys later. If they will be completed later, participants will receive the links for the stand-alone surveys either from the clinical site or from Frontier Science (if they gave their permission for Frontier Science to receive their contact information from the site).

The online survey data collected using the online survey commercial software tool will be transferred using Hyper Text Transfer Protocol Secure (HTTPS) connections that adhere to the Food and Drug Administration (FDA) guidelines for secure electronic data capture. The collected data will be stored on a secure cloud server and transferred to the HOPE central database at FSF. Access to the server will be highly restrictive and limited to a small number of technical and project staff.

6.2 Data Quality Assurance

Investigators receiving Federal funding must adhere to the Code of Federal Regulations (CFR) to protect research participants and produce reliable study information. Sites participating in the HOPE Study, sponsored by the NICHD, will be required to have an internal quality assurance (QA) plan that will be employed to identify problems and correct errors in research study records. Sites are responsible for following HOPE data QA procedures.

6.3 Clinical Site Monitoring and Record Availability

Clinical site monitoring for protocol and regulatory compliance will be conducted by Westat at each participating HOPE site either in person or via remote monitoring.

The site investigator will make study documents (e.g., consent forms, CRFs, and other study data) and pertinent hospital or clinic records readily available for inspection by the local IRB, the National Institutes of Health (NIH), the Office for Human Research Protection (OHRP), and the site monitors acting on behalf of the NICHD. Site monitors will verify that the informed consent process was provided, the data collected matches source documents, and regulatory compliance is maintained.

> ***Note:*** *Participating sites are responsible for specifying these individuals and the HOPE investigators as recipients of private health information in the individual's authorization required under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule.*

7. Study Management

7.1 Data Management

This study will follow PHACS standards and recommended guidelines for data management and where necessary, specific HOPE guidelines will also be developed. The HOPE DMC (also the PHACS DMC) will provide clinical site staff with instructions concerning the collection and recording of study data, including the use of the Laboratory Data Management System (LDMS) and how to access and use the online surveys. The clinical data will be entered into an electronic case report form (eCRF) using an electronic data capture system (EDC). Each site is responsible for entering data in a timely fashion according to the standards set in the HOPE MOP. The EDC system has built-in basic error checking capability so that minor errors can be resolved at the site. The data entered will then be exported to the PHACS/HOPE central database where additional checking and processing will take place. Data will be checked for completeness, accuracy, and consistency. Data errors found during the automatic processing and loading of the data will be communicated to sites via daily update reports. Additional data checks will be performed by the study data manager and communicated via an interactive query mechanism integrated within the EDC system.

The LDMS, also used to manage specimens in the PHACS network, will be used to label, manage, and track specimens collected in the HOPE Study. The LDMS has built-in basic error checking capability so that minor errors can be resolved at the lab before data is transmitted to the PHACS/HOPE central database.

It is the responsibility of the DMC to ensure the completeness, quality, and integrity of clinical and laboratory data collected for the HOPE Study. This role extends from protocol development to generation of the final study database.

7.1.1 Rolling Implementation and New Protocol Versions

The introduction of a new protocol version may result in a period of delay between HLC IRB approval and functional roll-out of the new protocol version to sites in order to allow time for operational changes to be made. In addition, data collection instruments may need to be modified because of the approved new protocol and may not be available immediately upon receipt of HLC IRB approval. The Protocol Team will ensure that all infrastructure-based operational components required for initiating implementation of the new protocol version (including the enrollment system's eligibility checklist and the new data collection instruments) have been aligned with the updated protocol version and are completed. Sites should not enroll or follow participants under the new protocol version prior to the effective implementation date. As this study will be implemented across multiple clinical sites, implementation of the study will occur on a rolling basis as each site becomes ready.

7.2 Protocol Query Management

For the integrity of the study and the welfare of the participants, it is important for the clinical site staff to have immediate access to the research team. Queries for this study protocol should be sent to the HOPE Protocol Team using the Protocol Query and Notification System (QNS) accessible via the HOPE website (https://phacsstudy.org). The Protocol Co-Chairs or designee will respond to queries within 2 business days after receipt. Queries are automatically archived by the PHACS webmaster. Queries deemed relevant to all sites will be posted as frequently asked questions (FAQs) on the PHACS website, where they will be available to all sites for future reference. The categories of queries and the appropriate team member for responding are as follows:

- Protocol violations or adverse events, related to the protocol (see Section 9.0) should be reported to the HOPE Protocol Team via the QNS and to the sIRB as stipulated in their guidance.
- Study management issues requiring clarification should be reported via the QNS and managed by the Protocol Specialist with the help of the Protocol Co-Chairs and/or the DMC, if necessary.
- Participant management issues that fall outside the protocol parameters should be reported via the QNS and managed by the Protocol Co-Chairs or designee.

7.3 Temporary Specimen Storage/Repository Storage

Specimens will be collected for future testing as outlined in Section 5.0 (Clinical and Lab Evaluations) and Appendix I (Schedule of Evaluations). All specimens collected will be processed, stored, and batch shipped to the PHACS/HOPE repository.

Specimens collected for non-specified future testing will be placed in long-term storage at the PHACS/HOPE repository. Permission to collect/store specimens long-term for unspecified future use in the PHACS/HOPE repository will be obtained as part of the HOPE Study informed consent process. Participants may take part in this study without agreeing to the long-term storage of their specimens in the PHACS/HOPE repository.

8. Participant Management

8.1 Data Collection and Study Visits

Data collection will be conducted according to the Schedule of Evaluations in Appendix I. Study visit windows for women who are pregnant or have recently delivered (up to 3 days post-delivery) will vary from the visit schedule of non-pregnant women. Completion of online surveys and medical record abstractions should be conducted as close to the target data collection time point as possible.

According to Human Subjects Protection guidelines, a participant may voluntarily decline any specific protocol assessment or specimen collection during a study visit, and any such missed assessments will not be considered a protocol deviation. We will operate under this practice and, thus, voluntary participant refusal of any research activities does not require HLC IRB notification. The site should document the participant's decline of a specific protocol assessment or specimen collection in the participant's study record, as needed, and on the appropriate CRF.

Each scheduled study visit has a variety of assessments to be conducted and completed within a 3-month window before or after the participant's target visit date. If the participant is unable to have a visit conducted within the visit window, or unable to complete all visit assessments within their specific required timeframe according to the type of assessment, the clinical site should consult the guidelines within the HOPE MOP. Every effort should be made by the site staff to follow the IRB-approved protocol and HOPE MOP.

The HOPE study is a longitudinal study with a schedule of evaluations associated with appropriate windows for study visits and completion of online surveys by participants. From time to time a HOPE study participant may not be able to complete a visit, or a specific assessment (e.g., a specimen collection or a required online survey) within the window specified by the schedule of evaluations. If this is the case, a site must seek approval from the HOPE Protocol Co-Chairs to conduct the visit or conduct the assessment later than the designated window, as long as the extension of the window does not impact data/specimen fidelity.

8.1.1 Enrollment in Pregnancy or at Delivery

Women who enroll during pregnancy or up to 3 days post-delivery will have the following data collection windows per study visit. The entry visit for these women may be conducted any time during pregnancy and up to 2 weeks post-delivery:

- Pregnancy visit: During pregnancy and 1 day prior to delivery.
- Delivery visit: The optimal timing of this visit will be as close to the delivery date as feasible. The visit window for completion of the delivery visit is within 2 weeks starting from the date of delivery.
- 6-Weeks Postpartum Visit: The optimal timing of this visit will be 6 weeks after the date of delivery. The visit window for completion of the 6-week postpartum visit is 4-12 weeks after pregnancy end.

- 1-Year Postpartum Visit: The target date for the annual follow-up data collection time point will be the anniversary of the delivery data collection date. The visit window will be the anniversary of the delivery date +/- 3 months. The visit should occur at least 6 months after the previous data collection time point.
- Annual Visits: The window for completion of the annual follow-up online survey and chart abstraction after the 1-year postpartum visit begins 3 months prior to and closes 3 months after the anniversary date (in-person entry visit date) of the target data collection time point.

> ***Note:*** *If women enrolling during pregnancy experience a pregnancy loss (induced or spontaneous), follow-up will be based on whether the pregnancy loss occurred at < 24 weeks of gestation or ≥ 24 weeks of gestation.*

- For pregnancy loss occurring at < 24 weeks gestation there will be no “delivery” visit, no 6-week postpartum visit, and the follow-up annual visit will occur on the 1-year anniversary of enrollment into the study using the Schedule of Evaluations (SOE) for non-pregnant women.
- For non-live births ≥ 24 weeks gestation, there will be no “delivery” visit. However, 6 weeks after the end of the pregnancy, a follow-up visit will be conducted with collection of the 6-week postpartum data specified in the SOE. Follow-up annual visits will occur on the 1-year anniversary of enrollment into the study using the SOE for non-pregnant women. Special circumstances (such as co-twin demise) may be considered for different visit schedules on an individual basis.

8.1.2 Enrollment of Non-Pregnant Nulliparous Women and Parous Women Not Currently Pregnant or Within 12 Months After Delivery

WLHIV who are not pregnant, defined as those who are either in the nulliparous group (and not currently pregnant) or who are more than 3 days post-delivery, will have the following data collection windows per study visit:

- **Entry Visit:** The first data collection visit. The window for completion of the entry visit and chart abstraction is 3 months from when the participant was enrolled (entered into the SES). See MOP for details.
- **Annual Visits:** The window for the completion of the annual follow-up online survey and chart abstraction begins 3 months prior to and closes 3 months after the anniversary date (in-person entry visit date) of the target data collection time point.

8.1.3 New Pregnancy at Follow Up

Participants who become pregnant during follow-up in HOPE will be encouraged to switch to the visit schedule and schedule of evaluations for women who are pregnant or recently delivered at follow-up. Depending on the SOE the participant agrees to switch to, follow the applicable guidelines noted in Section 8.1.1 above.

8.2 Enrollment and Participation of Individuals who are Cognitively Impaired

Potential participants who are cognitively impaired and meet study eligibility criteria will not be excluded from enrollment. Enrollment of participants who are cognitively impaired is justified given that the cause of the cognitive impairment may be related to the exposures being studied and not enrolling these individuals may introduce bias into the study. HOPE is an observational study; therefore, any potential risks or negative impacts on the well-being of these individuals are minimal. Given these conditions, enrollment of participants with cognitive impairment is in line with HHS regulations.

Clinical sites will screen potential participants to evaluate for cognitive impairment prior to enrollment in HOPE. In many cases, the clinical sites will have extensive experience with and knowledge of the skills and capabilities of the participant through their previous participation in other studies. All clinical sites have psychologists on staff who can conduct further cognitive assessments when appropriate. If a potential participant's ability to consent is in question, trained site staff will assess, and in agreement with the site PI, decide whether the potential participant can consent or needs a legally authorized representative (LAR) to sign the consent. For individuals requiring a LAR, consent from the LAR is required, and participant assent or consent, as applicable will be obtained. Clinical sites will consult with the HLC IRB for guidance when needed.

The online surveys do not need to be completed by the participant if the clinical site PI determines that the participant is incapable of completing the surveys. Clinic staff has the option of administering the online surveys to participants with cognitive impairment by either telephone interview or in person at the clinic if determined to be appropriate, although in these instances, participants will not be asked to complete the reproductive health, sexual activity, or substance use modules in the presence of their LAR.

Participants with cognitive impairment will be taken off-study if it is determined that they are unduly distressed because of protocol activities. In the case of distress resulting from completion of online assessments, clinical site staff will be available to consult by telephone. Site staff may also bring participants with cognitive impairment to the clinic to complete the online surveys and monitor for signs of distress if determined to be appropriate.

8.3 Enrollment of Participants Under the Age of Majority

The age of legal adulthood is termed the age of majority and is defined by each state. Most HOPE clinical sites define the age of majority for research purposes as 18 years of age. Puerto Rico defines the age of majority as 21 years of age. For those participants who are between 18-21 years of age and are eligible to enroll in HOPE at the clinical site in Puerto Rico, LAR consent and participant assent will be obtained. When those participants have their first study visit following their 21st birthday, they will be asked to sign a new consent form to continue participation.

8.4 Participant Retention

Multiple methods will be employed to retain participants in HOPE. Remote participation during enrollment and follow-up visits will be made available to promote participant engagement and retention during the COVID-19 pandemic and any other events that might preclude in-person involvement. Remote consenting will be available, as the HOPE Study will offer electronic consenting as an option for any woman considering enrollment in HOPE.

All non-pregnancy follow-up visits for HOPE will occur as remote visits, unless the participant requests an in-person visit and staff are available to accommodate the request. Annual follow-up visits will consist of medical chart data abstraction along with an online survey that may be completed at home or in the clinic dependent on participant preferences. The online survey, available in English and Spanish, will have an audio component to support the engagement of women with limited literacy. PHACS has been very successful employing this approach for its SMARTT and AMP cohorts and anticipates similar success in HOPE.

For women enrolled during pregnancy, in-person visits will be conducted at delivery and at 6 weeks postpartum. Pregnant women enrolled in the study will have routine contact from the study site around delivery and to remind them about their 6-week postpartum visit.

Capitalizing on existing patient-provider relationships, sites will work with clinics and clinical providers throughout the course of this study to support participants with continued HOPE Study retention. Study staff will maintain contact with HOPE participants via telephone, text messaging, postal service, and/or email about every 6 months to ensure retention.

A HOPE Community Advisory Board will be established to ensure representation of participants' priorities in HOPE and to drive the creation of health education materials related to women's health and HIV. Tangible opportunities to promote participant retention will be sought from the HOPE Community Advisory Board. Two HOPE participants will also be selected to serve on the PHACS Community Task Force, which is part of the PHACS Health Education and Community Core. These Task Force Members will work to ensure representation of participants' priorities, and in collaboration with the HOPE Protocol Team and other members of the PHACS Community Task Force, will conduct reviews of and prioritize selected research proposals, advise and assist with development of resources for recruitment and retention, and support the dissemination of study findings.

8.5 Discontinuing Study Participation

The reason for prematurely discontinuing from the study will be monitored by the Protocol Team. Participants will be discontinued from study participation for any of the following reasons, which include but are not limited to:

- The participant withdraws permission;
- The participant fails to comply with the study requirements;
- The site investigator determines that further participation would be detrimental to the participant's health or well-being;
- The study is stopped by a governmental agency, including the HHS or NICHD;
- The HLC IRB decides to withdraw approval for the study due to participant safety concerns; or
- The clinical site is terminated for significant participant safety concerns, study integrity, or poor performance issues.

8.6 Participant Compensation

Participants will receive compensation for their participation in the study. Study participants will receive reimbursements for each study visit, with the standard amount of remuneration approved by the HLC IRB and any site IRB-required additional compensation included in an informed consent addendum.

9. Adverse Event Reporting

This study is not a therapeutic study, and no medications are being prescribed as part of this study. Participants enrolled in this study may develop common conditions requiring treatment during the study period. Study personnel will assist the participants in receiving care as appropriate to their roles at their sites. The participants may also experience adverse events associated with HIV infection, ART exposure, pregnancy, or therapies. Site investigators are encouraged to use the FDA's MedWatch system to report any events possibly associated with medications clinically prescribed for the participant.

10. Study Impact and Safety Monitoring

Reporting of participant or staff-associated negative study impact events to the HOPE Protocol Team will result in the examination of study procedures, as necessary, to address concerns about participant management, enrollment, recruitment, adequacy of staff training, and/or to modify study procedures.

10.1 Reporting Requirements

Any event that is deemed to have negatively impacted a participant to a moderate or major extent and is related to the study activity must be reported to the PHACS/HOPE Regulatory and Compliance Manager by the study site through QNS. Reportable events could involve study participants and/or staff members. Examples of moderate and major impact events for study participants that could be related to the study activity include:

- Significant visible distress or injury resulting from the research encounter.
- Breach of confidentiality.

The PHACS/HOPE Regulatory and Compliance Manager will be responsible for reporting such events to the HLC IRB. The PHACS/HOPE Regulatory and Compliance Manager will also work with the sites to ensure that the site's local IRB is notified of the event.

> ***Note:*** *The distinguishing feature of moderate and major impact events is the need for enlisting additional support outside the research staff and the research encounter. The online survey will include information on how and where they can obtain assistance should they have feelings of anxiety, depression, etc. after completing the survey.*

11. Statistical/Analytic Considerations

11.1 Study Design

This longitudinal cohort study will enroll WLHIV as described in Section 3.1. Women will be followed with data collected at least annually until the end of the study or up to participant self-initiated withdrawal. The entry point of a participant could be at one of four different stages of reproductive life: nulliparous, pregnant, postpartum (defined as 12 months after the birth of a child), and after the birth of a child but beyond the postpartum period. Women enrolling in the study who are not pregnant but who subsequently experience pregnancy while participating in the study will modify their timing of evaluation from annually to a visit during pregnancy, at delivery, 6 weeks after delivery, and 1 year after delivery, with annual visits thereafter, as detailed in Section 8.1.

11.2 Statistical Analysis Plan

11.2.1 Prevalence and Cross-sectional Comparison of Prevalence Between Different Exposure Groups (Binary Outcome)

The HOPE Study has been designed to evaluate the health of WLHIV over the reproductive lifecycle, with many outcomes of interest that are binary, such as preterm birth, diagnoses of hypertension or depressive disorder, linkage to HIV care, un-suppressed viral load at delivery, poor retention in HIV care, or substance use. To estimate the prevalence of a binary condition, the proportion of women with such conditions among women in the analysis population for each respective aim will be calculated with a 95 percent confidence interval (CI). The prevalence or the risk of such binary outcomes between different exposure groups will be compared. For example, we will compare the prevalence of depression during the postpartum period versus other periods of the reproductive lifecycle, or the prevalence of HIV viremia at delivery between women with and without marijuana use using chi-square tests. The exposure of interest may have a continuous measurement, for example, we may assess the association between individual experience of racism during pregnancy, measured using the Everyday Discrimination Scale (EDS), and adverse birth outcomes. We will identify potential confounders of an exposure with the risk of each binary condition and evaluate the association using risk ratios estimated by log-binomial regression models, with and without adjustment for confounders. We will not adjust for variables that could be on the causal pathway.

To evaluate the collective predictive ability of multiple risk factors, for example, how engagement in care combined with HIV disease control, psychosocial markers of well-being and age of the youngest child can predict the discordance between fertility desire and contraception use, the overall c statistic (area under the Receiver Operating Characteristic curve) of the full multivariable logistic regression model will be derived.

When prevalence of an outcome of interest is low, we can approximate the binomial distribution by Poisson distribution and estimate the Risk Ratio by Poisson regression with robust standard error estimates.

11.2.2 Cross-Sectional Comparison of Continuous Outcome

For continuous outcomes, such as body mass index (BMI) or blood pressure, we will first summarize by descriptive statistics such as mean and standard deviation, or median and quartiles if the distribution of the outcome is skewed. To study the association between an exposure and the outcome of interest, we will use general linear regression with and without adjustment for potential confounders. For outcomes with skewed distributions, log or other appropriate transformation will be performed to obtain normality before the regression analysis.

11.2.3 Incidence Rate from the Follow-Up Person-Years and Association with Exposures

Given the longitudinal nature of the HOPE Study, there is the opportunity to evaluate the incidence rate of conditions of interest. For example, the incidence rate of depressive disorder or incidence rate of hypertension, will be estimated for participants who are free of depressive disorder or hypertension at study entry, using the Poisson distribution with a person-time offset, with reporting of 95 percent CIs. We will estimate the association between an exposure and the incidence using a Poisson regression model. For example, the association between HIV-related stigma and the incidence of depressive disorder, or average sleep duration and hypertension incidence. The absolute rate of any exposure value can also be derived by introducing an intercept term in the log-linear model of the incidence rate.

Participant withdrawal from follow-up may be related to their exposure of interest and result in selection bias from administrative censoring. For potential time-dependent confounding or administrative censoring, inverse probability weighting will be utilized to account for this bias and included in each Poisson model.[272]

11.2.4 Longitudinal Analyses for Binary Outcomes Over Time

There will be many binary outcomes collected repeatedly during follow up, such as fertility desires, HIV viral suppression, psychiatric diagnosis, and substance use. To estimate the prevalence over time and analyze the association with exposures of interest, we will apply log-binomial models using generalized estimation equations (GEE) with a log link function and a binomial distribution, considering the association among the repeated measures within each participant, with and without adjustment for confounders or covariates. Both time-varying covariates within a participant (such as different periods of reproductive life) and characteristics between participants (such as mode of HIV acquisition) can be incorporated in these models. We will explore the numerical feasibility of adjusting for the clustering of clinical sites. We will use the robust empirical variance estimator to avoid misspecification of the distribution. The same GEE modeling technique can also be applied to cross-sectional studies where some participants have repeated measures, such as repeated pregnancy, to account for the association among these measures.

For some specific aims, we will be evaluating the change of a binary outcome over time, for example, GWG. In this case, the change over time will first be categorized, such as adequate vs. excessive weight gain, with use of the methods for cross-sectional analyses, such as log-binomial or log-multinomial regression analyses as appropriate.

11.2.5 Longitudinal Analyses on Trajectory of Continuous Outcome Over Time

When the interest is to study the trend of a continuous outcome over time, such as weight or $\log_{10}$ RNA, we will first describe the trajectory using locally estimated scatterplot smoothing (LOESS) plots by exposure or risk factor groups. We will then use GEE models with a linear link function to fit linear or piecewise linear regression models to the continuous outcomes over time, and compare trajectories between exposure groups, such as different categories of average sleep duration. The models can also adjust for other risk factors or potential confounders, including both time-varying covariates within a participant and characteristics between participants. Appropriate transformation will be performed to approximate normality before the regression analysis. The robust empirical variance estimator will be used to avoid misspecification of the distribution. The GEE modeling technique, with an identity link function, can also be applied to cross-sectional studies of continuous outcomes where some participants have repeated measures to account for the association among these measures.

If the pattern of trajectories and its relation to risk factors are of interest, for example, the trajectory of weight for different average length of sleep duration, finite mixture modeling techniques such as group-based trajectory modelling[273] or growth mixture modeling[274] will be applied to identify distinct patterns among all participants. The optimal number and shapes of the distinct patterns will be chosen based on model fit statistics such as Bayesian information criterion. The risk factors across identified trajectory groups can then be compared.

11.2.6 Longitudinal Analyses for Time-to-Event Outcomes

In the HOPE Study, we will be assessing associations between exposure and the time to the occurrence of an outcome of interest. The exposure may change over time. For example, we will evaluate substance use and time to viral rebound after achievement of viral suppression, or between psychiatric care and time to remission of postpartum depression. Due to interval censoring, the exact time of event will be unknown, and we will have grouped survival data for each covariate pattern. Under this circumstance, Poisson regression provides a good approximation to Cox regression,[275] especially when the event is relatively rare. Poisson regression models can also accommodate time-dependent exposures.[276]

11.3 Sample Size and Power Estimates

The HOPE Study will enroll up to 1,630 WLHIV at various stages of their reproductive life course. Some HOPE Study aims and hypotheses will apply to all women participating in the HOPE Study, while others will be specific to a participant's reproductive lifecycle stage.

Possible study populations within HOPE include the following:

1. **Nulliparous and non-pregnant Women:** 370.
2. **Pregnant Women:** 430 enrolled in pregnancy or at delivery.
3. **Postpartum Women (within 12 months after delivery):** 260 at enrollment plus 430 women enrolled in pregnancy and reaching one year postpartum for a total of more than 600 women.

4. **Not-pregnant Parous Women beyond the 12 months postpartum period:** 570 at enrollment plus women enrolled during pregnancy or postpartum and followed beyond 12 months after delivery, for a total of at least 800 up to 1,200.
5. **All women:** 1,630.

Therefore, the following power calculations were generated for a conservative range of sample sizes, that is, 300, 400, 800, 1200 and 1600, which will apply to different study aims. All power analyses were done in PASS 15.0.4.[280]

11.3.1 Cross-Sectional Comparisons Between Exposure Groups

For **binary outcomes**, Table 11.1 shows the minimum Risk Ratio (RR) we will be able to detect between two exposure groups at 80 percent power with a 0.05 significance level. For this type of comparison, the detectable RRs depend on the underlying prevalence in the reference exposure group and the sample size distribution between the two exposure groups. For simplicity, we assume that the prevalence is lower in the reference group. For example, to test whether viral suppression or depression is associated with discordance between fertility desire and contraception use among non-pregnant women, we use a sample size of 1,200 and the prevalence of discordance of 20-40 percent.[26] About 50 percent of women in the SMARTT Dynamic cohort had viral suppression at the first measure during pregnancy, which we use as the approximation of non-pregnant women and gives 50/50 percent sample size between the exposed (not viral suppressed) and unexposed groups (viral suppressed), the minimum detectable RR falls between 1.20 and 1.34. About 20 percent of SMARTT women had a diagnosis of depressive disorder,156 which gives 20/80 percent sample size between exposed and unexposed groups, and thus the minimum detectable RR falls between 1.25 and 1.45.

Many exposure variables of interest are continuous rather than binary. For example, the score of the EDS, Internalized HIV Stigma Scale, or the Medical Outcomes Study Social Support Scale. The minimal detectable RR corresponding to a one standard deviation increase above the mean score will be smaller than what is presented in Table 11-1. That is, we will have better power to detect smaller differences with continuous exposure measures. For example, to test whether more experience of discrimination are associated with higher risk of hypertensive disorder during pregnancy, using a conservative estimate of sample size of 400, and 10 percent have new onset hypertension[277] at the mean EDS score, the minimum detectable RR will be smaller than 1.99 between those with an EDS score that is 1 standard deviation (SD) higher than the mean and those with a EDS at mean value.

Table 11-1. **Minimum detectable RRs between two exposure groups at 80% power and a 0.05 maximal false positive rate for various prevalence in the reference exposure group (Group 2) with a range of sample sizes.**

Prevalence in Group 2	Percent sample size		Minimum detectable RR for given total sample size				
	Group 1	Group 2	N = 1,600	N = 1,200	N = 800	N = 400	N = 300
5%	10%	90%	2.50	2.82	3.40	4.85	5.67
	20%	80%	2.00	2.20	2.56	3.47	4.00
	30%	70%	1.82	1.98	2.26	2.96	3.37
	40%	60%	1.74	1.87	2.11	2.71	3.05
	50%	50%	1.70	1.83	2.05	2.59	2.89
10%	10%	90%	1.90	2.07	2.37	3.10	3.49
	20%	80%	1.62	1.74	1.94	2.42	2.69
	30%	70%	1.52	1.62	1.78	2.17	2.39
	40%	60%	1.48	1.56	1.70	2.05	2.24
	50%	50%	1.46	1.54	1.67	1.99	2.17
20%	10%	90%	1.53	1.62	1.78	2.14	2.32
	20%	80%	1.38	1.45	1.56	1.82	1.95
	30%	70%	1.33	1.38	1.48	1.69	1.81
	40%	60%	1.30	1.35	1.44	1.63	1.74
	50%	50%	1.29	1.34	1.42	1.61	1.71
40%	10%	90%	1.29	1.34	1.41	1.57	1.64
	20%	80%	1.22	1.25	1.31	1.43	1.50
	30%	70%	1.19	1.22	1.27	1.38	1.44
	40%	60%	1.18	1.21	1.25	1.35	1.41
	50%	50%	1.17	1.20	1.25	1.35	1.40

For **continuous outcomes**, the effect size is expressed as a difference in means between the exposure groups relative to a common SD. Table 11-2 summarizes the minimum detectable differences between two exposure groups based on a 2-sample t-test at 80 percent power and 5 percent maximum false positive rate.

Table 11-2. Detectable differences in means (relative to SD) between exposure groups at 80% power and a 0.05 maximal false positive rate for a range of total sample sizes with various sample size distribution between two exposure groups.

Percent sample size		Minimum detectable difference in means (relative to SD)				
Group 1	Group 2	N = 1,600	N = 1,200	N = 800	N = 400	N = 300
10%	90%	0.23	0.27	0.33	0.47	0.54
20%	80%	0.18	0.20	0.25	0.35	0.41
30%	70%	0.15	0.18	0.22	0.31	0.35
40%	60%	0.14	0.17	0.20	0.29	0.33
50%	50%	0.14	0.16	0.20	0.28	0.33

Once we adjust for potential confounders, we will typically lose some power, resulting in a small increase in the minimum detectable differences.

11.3.2 Longitudinal Comparison Between Exposure Groups Using GEE

In evaluating both continuous outcomes and binary outcomes, greater power will be attained in longitudinal analyses of repeated measures over time. The detectable effect size will also depend on the number of repeated measures and the correlation among the repeated measures. For example, we plan to test the association between viral suppression after delivery and trust in the health care system over the follow up period using GEE. Most women will have 2 to 5 measures of viral load for assessment of viral suppression. Assuming the correlation among viral suppression of the same women is 0.4, and 30 percent of these women reporting low or no trust of the health care system, while among the 70 percent who report high trust in the health care system, 10 percent do not have suppressed viral load at delivery, Table 11-3 shows the minimum detectable RR for detectable viral load is about 1.79 to 1.93, between women reporting low/no trust versus women reporting higher trust in the health care system.

Table 11-3. Minimum detectable RRs between two exposure groups at 80% power and a 0.05 maximal false positive rate for a range of total sample sizes with various sample size distribution between two exposure groups, prevalence in the reference exposure group (Group 2), number of repeated measures and correlation among repeated measures.

Prevalence in Group 2	Percent sample size		Number of repeated measure	Correlation among repeated measure	Minimum detectable RR for given total sample size				
	Group 1	Group 2			N = 1,600	N = 1,200	N = 800	N = 400	N = 300
5%	10%	90%	2	0.2	2.08	2.30	2.72	3.78	4.40
				0.4	2.20	2.44	2.90	4.10	4.48
			5	0.2	1.78	1.94	2.22	2.94	3.36
				0.4	1.98	2.18	2.56	3.50	4.08
	30%	70%	2	0.2	1.60	1.70	1.90	2.36	2.60
				0.4	1.66	1.78	1.98	2.48	2.72
			5	0.2	1.46	1.52	1.66	2.00	2.18
				0.4	1.56	1.66	1.82	2.24	2.48
10%	10%	90%	2	0.2	1.66	1.79	2.01	2.57	2.89
				0.4	1.73	1.87	2.11	2.73	3.09
			5	0.2	1.49	1.58	1.74	2.13	2.36
				0.4	1.61	1.72	1.93	2.43	2.72
	30%	70%	2	0.2	1.39	1.46	1.58	1.85	2.01
				0.4	1.43	1.50	1.63	1.93	2.10
			5	0.2	1.30	1.35	1.43	1.64	1.75
				0.4	1.36	1.43	1.53	1.79	1.93
20%	10%	90%	2	0.2	1.41	1.48	1.60	1.88	2.04
				0.4	1.44	1.52	1.65	1.96	2.13
			5	0.2	1.31	1.36	1.45	1.66	1.78
				0.4	1.38	1.44	1.55	1.81	1.96
	30%	70%	2	0.2	1.25	1.29	1.36	1.53	1.62
				0.4	1.27	1.32	1.40	1.57	1.67
			5	0.2	1.19	1.23	1.28	1.40	1.47
				0.4	1.23	1.27	1.34	1.49	1.57

Table 11-4. Minimum detectable differences in means (relative to SD) for repeated continuous outcomes between exposure groups at 80% power and a 0.05 maximal false positive rate, for a range of total sample sizes with various sample size distribution between two exposure groups, number of repeated measures and correlation among repeated measures.

Percent sample size		Number of repeated measure	Correlation among repeated measure	Minimum detectable difference in means (relative to SD)				
Group 1	Group 2			N=1,600	N=1,200	N = 800	N = 400	N = 300
10%	90%	2	0.2	0.18	0.21	0.26	0.36	0.42
			0.4	0.20	0.23	0.28	0.39	0.45
		5	0.2	0.14	0.16	0.20	0.28	0.32
			0.4	0.17	0.19	0.24	0.34	0.39
30%	70%	2	0.2	0.12	0.14	0.17	0.24	0.27
			0.4	0.13	0.15	0.18	0.26	0.30
		5	0.2	0.09	0.11	0.13	0.18	0.21
			0.4	0.11	0.13	0.16	0.22	0.25

11.3.3 Incidence Rate Using Poisson Models

Incidence rate is estimated among the subset without the condition of interest at the baseline, therefore the available sample size is smaller than the size of the cohort of interest. However, the longitudinal nature increases the power. For example, we will evaluate the association between self-reported stressful events and the incidence of PTSD. A 2014 study of SMARTT mothers showed 68 percent without PTSD,[156] providing a subset of about 1,000 women. Assuming an annual incidence rate for PTSD of 5 percent, and 10-40 percent of women reporting adulthood stressful events, Table 11.5 shows the minimum detectable RR is in the range of 1.7 – 2.2, assuming participants, on average, have 2 years of follow-up data. The power will be higher for longer follow-up time.

Table 11-5. Minimum detectable RRs between two exposure groups at 80% power and a 0.05 maximal false positive rate for various incidence rate in the reference exposure group (Group 2) with a range of sample sizes and 2 years of follow up for all participants.

Prevalence in Group 2	Percent sample size		Minimum detectable RR for given total sample size				
	Group 1	Group 2	N = 1600	N = 1200	N = 800	N = 400	N = 300
5%	10%	90%	1.89	2.05	2.34	3.09	3.52
	20%	80%	1.64	1.76	1.96	2.48	2.78
	30%	70%	1.56	1.65	1.83	2.27	2.52
	40%	60%	1.52	1.61	1.78	2.18	2.42
	50%	50%	1.51	1.60	1.76	2.17	2.41
10%	10%	90%	1.60	1.70	1.89	2.34	2.61
	20%	80%	1.44	1.51	1.64	1.96	2.15
	30%	70%	1.38	1.44	1.56	1.83	1.99
	40%	60%	1.35	1.41	1.52	1.78	1.92
	50%	50%	1.35	1.41	1.51	1.76	1.91
20%	10%	90%	1.41	1.48	1.60	1.89	2.05
	20%	80%	1.30	1.35	1.44	1.64	1.76
	30%	70%	1.26	1.30	1.38	1.56	1.65
	40%	60%	1.24	1.28	1.35	1.52	1.61
	50%	50%	1.24	1.28	1.35	1.51	1.60

11.4 Missing, Unused and Spurious Data

Every effort will be made to ensure that the amount of missing data is kept to a minimum as missing data complicates the statistical analyses or results in biased parameter estimates.

When data for covariates are missing, the extent and pattern of missing data will first be assessed. If data are missing for only a few cases, then data analyses will be conducted only on study participants with complete data. However, when such a strategy would result in loss of data from a substantial proportion of participants (such as greater than 10%), or if data are not deemed missing at random (MAR) (i.e., the outcomes for those with and without missing covariates are very different), then some form of imputation will be performed. Missing indicator categories can be used for categorical variables. Alternatively, we will explore probability-based imputation methods using participant characteristics and non-missing data.

Data analysis will be conducted using only data from study participants with the endpoint, excluding participants with missing primary endpoint data. We will describe the reasons for missing primary endpoints and compare patient characteristics between the group of participants with missing primary endpoint data and those with non-missing data. Assumptions needed to obtain valid statistical inferences in the presence of missing data will be thoroughly investigated. When appropriate, factors associated with the propensity of missingness will be identified and included in analyses using missing data methods, such as multiple imputation and inverse probability weighting, to correct for selection bias.[278;279]

11.5 Monitoring

Routine data monitoring, which will be performed by the protocol HOPE team, will include the following: accrual, study status/progress, data and specimen timeliness and completeness.

12. Human Subjects

This study will be conducted in compliance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH, E6, R2) Good Clinical Practice (GCP) guidelines, and 45 CFR § 46. It is the judgment of the HLC IRB that this protocol belongs under 45 CFR § 46 Subpart D: Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

12.1 Participant Confidentiality

All participants co-enrolled in a PHACS study will use the same PHACS PID number assigned for their first PHACS study. A unique SID number will be assigned by the SES when the participant is successfully enrolled into the study and would similarly be assigned to a newborn of any women co-enrolled in HOPE and SMARTT, should she consent to allow for infant specimen collection or use of her child's health data to assess how child health outcomes are associated with the health of women. The PID and SID numbers will be used for identification purposes on all laboratory specimens, evaluation forms, online assessments, and reports retained in the research records and generated by the PHACS database. A list linking the participant names with the PID and SID numbers will be securely stored at the clinical site under double locks, separate from all other research records. All research records will be stored in a secured area in locked files. Neither Frontier Science nor HOPE staff at Harvard T.H. Chan School of Public Health will be permitted access to the list linking participant names with the PID and SID numbers.

All study staff members at the clinical sites are required to sign non-disclosure forms agreeing to hold research information in confidence. All HOPE investigators and collaborators are required to sign confidentiality agreements agreeing not to seek the identity of study participants. Furthermore, if any participant identify is accidentally sent to an unauthorized person, such as an investigator or collaborator during the course of the study, breach notification policies required by the HLC IRB and local IRBs will be followed.

Study staff will work with participants to record contact information, which may also include the names and contact information of people (friends, family, or others) who may know the whereabouts of participants. Establishing this list is a voluntary exercise and, if used in the event contact is lost with a participant, only a previously agreed to level of information will be disclosed. When contact is re-established with participants who were lost, willingness to continue study participation will be ascertained and documented.

Participant may consent to share their residential address for the purpose of future geocoding. Any address provided by a study participant will be securely stored at the study site to ensure confidentiality.

Information on sexual activity and substance use reported by participants in the confidential online survey will not be disclosed to the HOPE clinical site staff or to the clinicians responsible for their health care. If a participant is unable to complete the web-based survey independently due to technical challenges or cognitive impairment, the online survey may be completed at the clinical site, where a research staff member may assist with this process as needed. In these cases, clinical site staff will make every effort to maintain participant confidentiality.

HOPE data will be stored in accordance with the PHACS Long-Term Maintenance of Hard Copy and Electronic Storage of CRFs, Study Instruments, Regulatory Documents and Medical Records Policy and the PHACS Site Closure Policy and Study Close-Out Procedures.

12.2 Certificate of Confidentiality

As an NIH-funded project using identifiable, sensitive information, HOPE is automatically covered by a Certificate of Confidentiality issued from the HHS. With this Certificate in place, HOPE researchers cannot be forced to turn over identifying information about a study participant in any Federal, state, or local criminal, administrative, legislative, or other proceedings. This Certificate does not prevent a study participant from volunteering to turn over their research information nor does it prevent researchers from providing research-related information to others when requested by the study participant or when required by law such as in cases of suspected or actual harm to or by the study participant.

12.3 Risks and Benefits

12.3.1 Risks Associated with Participation in This Study May Include:

Participation in this study involves greater than minimal risk to research participants than they may experience in normal daily life or during routine medical or psychological examinations or tests according to the HLC IRB (45 CFR § 46.405: Research Involving Greater Than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Subjects).

The evaluations that are involved in this study require venipuncture, clinical assessment, and answering questions about mental health, sexual behavior, substance use, and ART adherence. Possible risks resulting from the study include:

- Venipuncture to collect blood specimens may cause local discomfort, bleeding, or bruising; rarely a small clot or infection can occur at the blood draw site.
- Participants will be asked questions about depression, stigmatizing health conditions, illegal substance use, addiction, PTSD, childhood trauma, sexual history and IPV during in-person interviews and follow-up online surveys. A list of local support services will be provided to participants following in-person interviews or after completion of the online surveys. At the conclusion of in-person interviews, participants will be asked if they wish to receive further support. If the clinical staff performing in-person interviews deems a participant in need of counseling, they will inform the site PI and the participant will be offered further support, evaluation, and referrals, as needed.
- The information that participants provide through surveys will not be shared with medical providers without their permission unless there is serious risk of self-harm or harm to others as specified in the consent and local ethics committee requirement. This includes information about ART adherence and mental health. However, if a participant endorses plans/thoughts of self-harm on the PHQ-9 at the entry visit or during the 6-week postpartum visit, the clinical site staff will inform the site PI and the participant will be offered further support, evaluation, and referrals, as needed.
- Despite the multiple measures taken to protect participant confidentiality, online communications may be at risk for hacking, intrusions, and other violations.

Another potential risk for participants is inadvertent disclosure of their HIV status to someone who does not yet know about the infection. Research staff members will provide guidance to participants to help them to maintain their confidentiality, including while completing the online survey. Participants will be encouraged to complete their online survey in a private location on a device that is not publicly shared. Clinical sites will make space available for participants to complete surveys when a participant does not have access to a private space or device. See Appendix III for additional information that sites can provide to participants to help prevent inadvertent disclosure of HIV status due to someone accessing the web-based surveys or study website.

Repository specimens may be used in genome-wide association studies (GWAS) that includes sequencing of participant's entire DNA. Per the NIH Genomic Data Sharing (GDS) Policy to facilitate the sharing of large-scale genomic data generated from NIH-funded research, participants' DNA testing information may be deposited in NIH designated data repositories such as the NIH Database of Genotypes and Phenotypes (dbGaP). Data will be stored without a participant's name or other direct identifiers. However, each participant's genetic information is unique, and it may be possible to identify a participant based only upon his or her genomic data. Even if access to data is controlled and data security standards are met, confidentiality cannot be guaranteed.

12.3.2 Benefits

While there is no guarantee of direct benefit to the individuals who participate in this study, benefiting from participating is possible. If the participant or his or her legal guardian chooses, the information obtained in this study can be made available to their health care providers and it may inform their primary health care. Participants and legal guardians will be encouraged to make this information available to providers in order to maximize the potential for benefits.

12.4 HLC IRB Review and Informed Consent

All currently identified HOPE sites as well as those that may be identified in the future will rely on the HLC IRB as the sIRB of record.

Prior to the initiation of HOPE all participating sites will sign Reliance Agreements that will detail the roles and responsibilities of the HLC IRB in relation to sites conducting the study. The HLC IRB and the PHACS/HOPE Regulatory and Compliance Manager will retain copies of all Reliance Agreements and communications in their records and will help to facilitate the process of obtaining HLC IRB approval of all study protocols, informed consents, and recruitment documents. The HLC IRB Reliance Agreement Specialist and the PHACS/HOPE Regulatory and Compliance Manager will regularly update communications plans to ensure that all participating sites are following requirements of the HLC IRB and will maintain consistent communication with one another throughout this process.

This protocol, the informed consent documents, and any subsequent modifications will be reviewed and approved by the HLC IRB. The informed consent will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. In accordance with 45 CFR §46.116, a written informed consent will be obtained from each participant and a copy of the consent/assent form will be given to each participant.

12.5 Prisoner Participation

HOPE and NICHD have concluded that this protocol does NOT meet Federal requirements governing prisoner participation in human subjects research and should NOT be considered by local IRBs for the recruitment of prisoners. Participants who become prisoners after enrollment may not be seen for research visits if they are considered prisoners.

12.6 45 CFR § 160 and 164 Standards for Privacy of Individually Identifiable Health Information ("Privacy Rule" Pursuant to the Health Insurance Portability and Accountability Act - HIPAA)

Each site is responsible for adherence to their individual institution's HIPAA policies and procedures, as are all collaborators.

12.7 PHACS/HOPE Repository Policies

It is not expected that protected health information (PHI) will be needed to create and operate the PHACS/HOPE repository. In addition, since biologic specimens, in and of themselves, do not constitute PHI under 45 CFR § 164.501, the Privacy Rule will not apply to the creation of the PHACS/HOPE 45 CFR § 46.116, to have their specimens included in the PHACS/HOPE repository. Consent for collection of repository specimens is included within the sample study consent/assent forms (see Appendixes V and VI). Participants may participate in this study without agreeing to the long-term storage of their specimens in the PHACS/HOPE repository for future testing not necessarily related to the primary aims of this study.

12.8 Study Discontinuation

This study may be discontinued at any time by the HHS or NIH.

13. Publication of Research Findings

Publication of the results of this study will be governed by PHACS policies as outlined in the PHACS Publication Policy (available on the PHACS website).

Participant summaries of findings will be developed, approved by the HLC IRB, and provided directly to the clinical sites to distribute to participants.

14. Biohazard Containment

As the transmission of HIV and other blood borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate blood and secretion precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by the CDC. These procedures can be found at www.cdc.gov.

HOPE specimens will be transported in accordance with Federal and local laws, and in compliance with Occupational Safety and Health Administration (OSHA) blood-borne pathogens standards. This policy includes the samples being transported by ground to the local laboratory. Compliance will be achieved by education of personnel involved with packaging and transporting specimens.

All infectious specimens must be shipped as Diagnostic Specimens according to current International Air Transport Association (IATA) Shipping Guidelines for Infectious Substances Class/Div. 6.2. Refer to individual carrier guidelines (e.g., FedEx, Airborne Express) for specific instructions.

Appendix I
Schedule of Evaluations

Table I-1. Women Who Are Pregnant or Recently Delivered[1]

	Pregnancy[2]	Delivery[2,3]	6 weeks postpartum[4]	1 year postpartum and annually[5,6]	Notes
Sign consent	X	[X]			At entry visit only. In clinic or remotely (online).
Residential address information/location for geocoding purposes	X	[X]			At entry visit only via interview.
Contact and check-in between visits		X		X	Attempt every 6 months, starting 6 months after the delivery visit. Contact should be attempted at the 1 year postpartum and annual visits, as well as 6 months after these visits. If the participant does not have a delivery visit, contact should be attempted starting 6 months after the pregnancy visit.
Change in pregnancy status	X		X	X	
Clinical Assessments (Collected in-person)					
Height	X	[X]	X		If the visit is not conducted in person, collect through chart abstraction. Assess height at 6 weeks postpartum if height was not obtained at the entry visit.
Weight	X	X	X	X[7]	
Waist and hip circumference			X	X[7]	Do not collect if visit is conducted remotely.
Blood pressure	X	X	X	X[7]	If the visit is not conducted in person, collect through chart abstraction.
Interview					
Family and personal medical history	X	[X]			Interview includes date of ART initiation.
Reproductive history	X	[X]			
Depression	X	[X]	X		
Anxiety	X	[X]	X		

	Pregnancy[2]	Delivery[2,3]	6 weeks postpartum[4]	1 year postpartum and annually[5,6]	Notes
PTSD	X	[X]			
Health Literacy	X	[X]			
Social History	X	[X]			
Online Survey	X	X	X	X	See Section 5 for more information on the items included in the online survey at each time point.
Medical Chart Abstraction					
Weight	X	X	X	X	
Blood pressure	X	X	X	X	
HIV RNA level, lymphocytes and subsets	X	X	X	X	
ART Medications	X	X	X	X	
Non-ART medications	X	X	X	X	
HIV, Primary Care, OB, Gynecologic, Mental Health Care Engagement	X	X	X	X	
Immunizations	X	X	X	X	
Medical and mental health diagnoses and hospitalization	X	X	X	X	
Laboratory Test Results	X	X	X	X	
Pregnancy and pregnancy Outcomes	X	X		X	
Cervical and anal dysplasia screening	X	X	X	X	
STI Testing and Results	X	X		X	
Sample Collection/Repository[8]					
Serum, plasma (EDTA and heparin), and non-viable PBMCs[8]	X	X			Collect in clinic if in-person visit is conducted.
Rectal swab for Microbiome	X	[X]			
Vaginal swab for Microbiome	X	[X]			
Vaginal swab for Metabolomics	X	[X]			

	Pregnancy[2]	Delivery[2,3]	6 weeks postpartum[4]	1 year postpartum and annually[5,6]	Notes
Vaginal swab for STI testing[8]	X	X			
Oral swab	X	X			
Saliva	X	X			
Hair[8]	X	X			

[1] Defined as pregnant or up to 3 days post-delivery at time of enrollment

[2] The entry visit for women who are pregnant or who recently delivered can occur during pregnancy up to 1 day prior to delivery, or at the delivery visit (may occur up to 2 weeks following delivery). If a woman's entry visit is conducted during pregnancy, she should have a separate delivery visit at follow-up unless she experiences a pregnancy loss or non-live birth.

[3] The window for collection of data for women completing a delivery visit is up to 2 weeks following delivery.

[4] Target date for visit is 6 weeks post-delivery. Visit window of 4-12 weeks after pregnancy end.

[5] 1-Year Postpartum Visit: The target date for the 1-year postpartum follow-up data collection time point will be the anniversary of the delivery data collection date. The visit window will be the anniversary of the delivery date +/- 3 months. The visit should occur at least 6 months after the previous data collection time point.

[6] The window for completion of the annual follow-up online survey and chart abstraction (annual visit) after the 1-year postpartum visit begins 3 months prior to and closes 3 months after the anniversary date (in-person entry visit date) of the target data collection time point.

[7] Collect only for women who are co-enrolled in SMARTT, only at the 1-year postpartum visit, in person.

[8] Up to 30 mL of blood will be collected from participants. A small sample of approximately 100 strands of hair will be collected. Refer to the Laboratory Processing Chart (LPC) for collection, processing, and storage instructions of all repository specimens. For repository specimens collected in the HOPE Study, as well as for other PHACS studies in which a woman is co-enrolled, the designated repository specimen may be acquired once and shared by both studies if the PHACS study visits occur within 90 days before the HOPE Study visit and the specimens are blood, hair, and/or the Aptima vaginal swab STI kit. Otherwise, specimens should be collected separately for each study. HOPE will abide by the PHACS specimen request policy governing this process if the specimen is shared between HOPE and a PHACS study.

Notes:

- If women enrolling during pregnancy experience a pregnancy loss (induced or spontaneous), follow-up will be based on whether the pregnancy loss occurred at < 24 weeks of gestation or ≥ 24 weeks of gestation.
  - For pregnancy loss occurring at < 24 weeks gestation there will be no "delivery" visit, no 6-week postpartum visit, and the follow-up annual visit will occur on approximately the 1-year anniversary of enrollment into the study using the SOE for non-pregnant women.
  - For non-live births ≥ 24 weeks gestation, there will be no "delivery" visit. However, 6 weeks after the end of the pregnancy, a follow-up visit will be conducted with collection of the 6-week postpartum data specified in the SOE. Follow-up annual visits will occur on approximately the 1-year anniversary of entry into the study using the SOE for non-pregnant women. Special circumstances (such as co-twin demise) may be considered for different visit schedules on an individual basis.
- Brackets [ ] indicate that the assessment will take place at delivery only if the delivery visit is an entry visit.
- Note: If women become pregnant again at follow-up, they will be encouraged to shift to the schedule of evaluations for Women Who Are Pregnant or Recently Delivered at Follow Up.

Table I-2. Women Who Are Not Pregnant[1]

	Entry[2]	Annually[3]	Notes
Sign consent	X		At entry visit only. In clinic or remotely (online).
Residential address information/location for geocoding purposes	X		At entry visit only, via interview. Document in participant chart.
Contact and check in between visits	X	X	Attempt every 6 months, starting 6 months after the entry visit. Contact should be attempted at the annual visits, as well as 6 months after these visits.
Change in pregnancy status		X	
Clinical Assessments (Collected in person)			
Height	X		If the visit is not conducted in person, collect through chart abstraction.
Weight	X	X	
Waist and hip circumference	X		Do not collect if visit is conducted remotely.
Blood pressure	X	X	If the visit is not conducted in person, collect through chart abstraction.
Interview			
Family and personal medical history	X		Interview includes date of ART initiation.
Reproductive history	X		
Depression	X		
PAnxiety	X		
PTSD	X		
Health Literacy	X		
Social History	X		
Online Survey	X	X	See Section 5 for more information on the items included in the online survey at each time point.
Medical Chart Abstraction			
Weight	X	X	
Blood pressure	X	X	

	Entry[2]	Annually[3]	Notes
HIV RNA level, lymphocytes, and subsets	X	X	
ART Medications	X	X	
Non-ART Medications	X	X	
HIV, Primary Care, OB, Gynecologic, Mental Health Care Engagement	X	X	
Immunizations	X	X	
Medical and Mental Health Diagnoses	X	X	
Laboratory Test Results	X	X	
Pregnancy and pregnancy outcomes	X	X	
Cervical and anal dysplasia screening	X	X	
STI testing and results	X	X	
Sample Collection Repository[4]			
Serum, plasma (EDTA and heparin), and non-viable PBMCs[4]	X		Collect in clinic if in-person visit is conducted.
Rectal Swab for Microbiome	X		
Vaginal Swab for Microbiome	X		
Vaginal Swab for Metabolomics	X		
Vaginal Swab for STI Testing[4]	X		
Saliva	X		
Oral Swab	X		
Hair[4]	X		

[1] Defined as either nulliparous or more than 3 days after giving birth.

[2] The window for completion of the entry visit participant-facing components and chart abstraction is 3 months from when the participant was enrolled (entered into the SES). Ideally, the participant would be registered into the SES within 2 business days of consenting. See MOP for details.

[3] The window for completion of the annual follow-up online survey and chart abstraction (annual visit) after the 1-year postpartum visit begins approximately 3 months prior to and closes approximately 3 months after the anniversary date (in-person entry visit date) of the target data collection time point.

[4] Up to 30 mL of blood will be collected from participants. A small sample of approximately 100 strands of hair will be collected. Refer to the LPC for collection, processing, and storage instructions of all repository specimens. For repository specimens collected in the HOPE Study, as well as for other PHACS studies in which a woman is co-enrolled, the designated repository specimen may be acquired once and shared by both studies if the PHACS study visits occur within 90 days before the HOPE Study visit and the specimens

are blood, hair, and/or the Aptima vaginal swab STI kit. Otherwise, specimens should be collected separately for each study. HOPE will abide by the PHACS specimen request policy governing this process if the specimen is shared between HOPE and a PHACS study.

Note: If women become pregnant, they will be encouraged to shift to the schedule of evaluations for Women Who Are Pregnant or Recently Delivered at Follow Up.

Table I-3. Women Who Are Pregnant or Recently Delivered at Follow-Up[1]

	New-Pregnancy[2]	New-Delivery[2,3]	New-6 weeks postpartum[4]	New-1 year postpartum and annually[5,6]	Notes
Residential address information/location for geocoding purposes		X			
Contact and check-in between visits		X		X	Attempt every 6 months, starting 6 months after the delivery visit. Contact should be attempted at the 1 year postpartum and annual visits, as well as 6 months after these visits. If the participant does not have a delivery visit, contact should be attempted starting 6 months after the pregnancy visit.
Change in pregnancy status	X		X	X	
Clinical Assessments (Collected in-person)					
Weight	X	X	X	X[7]	If the visit is not conducted in person, collect through chart abstraction.
Waist and hip circumference			X	X[7]	Do not collect if visit is conducted remotely.
Blood pressure	X	X	X	X[7]	If the visit is not conducted in person, collect through chart abstraction.
Interview					
Depression	X	[X]	X		
Anxiety	X	[X]	X		
Online Survey		X	X	X	See Section 5 for more information on the items included in the online survey at each time point.
Medical Chart Abstraction					
Weight	X	X	X	X	
Blood pressure	X	X	X	X	
HIV RNA level, lymphocytes and subsets	X	X	X	X	
ART Medications	X	X	X	X	
Non-ART medications	X	X	X	X	

	New-Pregnancy[2]	New-Delivery[2,3]	New-6 weeks postpartum[4]	New-1 year postpartum and annually[5,6]	Notes
HIV, Primary Care, OB, Gynecologic, Mental Health Care Engagement	X	X	X	X	
Immunizations	X	X	X	X	
Medical and mental health diagnoses and hospitalization	X	X	X	X	
Laboratory Test Results	X	X	X	X	
Pregnancy and pregnancy Outcomes	X	X		X	
Cervical and anal dysplasia screening	X	X	X	X	
STI Testing and Results	X	X		X	
Sample Collection/Repository[8]					
Serum, plasma (EDTA and heparin), and non-viable PBMCs[8]	X	X			Collect in clinic if in-person visit is conducted.
Rectal swab for Microbiome	X	[X]			
Vaginal swab for Microbiome	X	[X]			
Vaginal swab for Metabolomics	X	[X]			
Vaginal swab for STI testing[8]	X	X			
Oral swab	X	X			
Saliva	X	X			
Hair[8]	X	X			

[1] Defined as pregnant or up to 3 days post-delivery at follow-up.

[2] The first visit on this schedule for women who are pregnant or who recently delivered at follow up can occur at either the pregnancy visit (which may occur during pregnancy up to 1 day prior to delivery) or at the delivery visit (may occur up to 2 weeks following delivery). If a woman starts this visit schedule during pregnancy, she should have a separate delivery visit at follow-up unless she experiences a pregnancy loss or non-live birth.

[3] The window for collection of data for women completing a delivery visit is up to 2 weeks following delivery.

[4] Target date for visit is 6 weeks post-delivery. Visit window of 4-12 weeks after pregnancy end.

[5] 1-Year Postpartum Visit: The target date for the 1-year postpartum follow-up data collection time point will be the anniversary of the delivery data collection date. The visit window will be the anniversary of the delivery date +/- approximately 3 months. The visit should occur at least 6 months after the previous data collection time point.

[6] The window for completion of the annual follow-up online survey and chart abstraction (annual visit) after the 1-year postpartum visit begins approximately 3 months prior to and closes approximately 3 months after the anniversary date (in-person entry visit date) of the target data collection time point.

[7] Collect only for women who are co-enrolled in SMARTT, only at the 1-year postpartum visit, in person.

[8] Up to 30 mL of blood will be collected from participants. A small sample of approximately 100 strands of hair will be collected. Refer to the Laboratory Processing Chart (LPC) for collection, processing, and storage instructions of all repository specimens. For repository specimens collected in the HOPE Study, as well as for other PHACS studies in which a woman is co-enrolled, the designated repository specimen may be acquired once and shared by both studies if the PHACS study visits occur within 90 days before the HOPE Study visit and the specimens are blood, hair, and/or the Aptima vaginal swab STI kit. Otherwise, specimens should be collected separately for each study. HOPE will abide by the PHACS specimen request policy governing this process if the specimen is shared between HOPE and a PHACS study.

Notes:

- If women who start this schedule during pregnancy experience a pregnancy loss (induced or spontaneous), follow-up will be based on whether the pregnancy loss occurred at < 24 weeks of gestation or ≥ 24 weeks of gestation.
  - For pregnancy loss occurring at < 24 weeks gestation there will be no “delivery” visit, no 6-week postpartum visit, and the follow-up annual visit will occur on approximately the 1-year anniversary of the pregnancy visit using the SOE for non-pregnant women.
  - For non-live births ≥ 24 weeks gestation, there will be no “delivery” visit. However, 6 weeks after the end of the pregnancy, a follow-up visit will be conducted with collection of the 6-week postpartum data specified in the SOE. Follow-up annual visits will occur on approximately the 1-year anniversary of the pregnancy visit using the SOE for non-pregnant women. Special circumstances (such as co-twin demise) may be considered for different visit schedules on an individual basis.
- Brackets [ ] indicate that the assessment will take place at delivery only if the delivery visit is the first visit the participant attends on this SOE for a pregnancy at follow-up.

Appendix II
Participating HOPE Sites

The following are PHACS sites eligible to participate in the Health Outcomes around Pregnancy and Exposure to HIV/ARV (HOPE):

1. Site 4 – University of Alabama, Birmingham – Birmingham, AL
2. Site 5 – University of Southern California – Los Angeles, CA
3. Site 7 – St. Jude Children's Research Hospital – Memphis, TN
4. Site 8 - SUNY Downstate – Brooklyn, NY
5. Site 9 – University of Colorado, Denver – Denver, CO
6. Site 12 – Children's Diagnostic and Treatment Center – Ft. Lauderdale, FL
7. Site 13 – Bronx Lebanon Hospital – Bronx, NY
8. Site 14 – University of Florida, Jacksonville – Jacksonville, FL
9. Site 16 – University of Puerto Rico Medical Center – San Juan, Puerto Rico
10. Site 18 – University of Miami – Miami, FL
11. Site 19 – Baylor College of Medicine – Houston, TX
12. Site 20 – Tulane University Health Sciences Center– New Orleans, LA
13. Site 23 - Jacobi Medical Center – Bronx, NY
14. Site 24 – Ann & Robert H. Lurie Children's Hospital of Chicago – Chicago, IL

Appendix III
Online Survey Completion Tips

Tips to Protect your Privacy When Filling Out the Online Survey

We understand that your privacy is very important to you, and it is very important to us as well. We want to make sure it is protected while you are filling out our surveys. Here are some tips for how to do that.

Where to complete your survey:

- If possible, fill out your survey on a personal computer or device.
- Take extra precautions if you use a shared computer in a public place like school, work, or the library. Shared computers may not give you much privacy because so many other people also use them.
- Before you start the surveys, make sure you are answering the questions in a space where you feel comfortable. Some people might feel uncomfortable if they take a web-based survey while surrounded by people in a public place.
- Remember that you are always welcome to go to the study clinic to complete your web-based survey.

Privacy tips for shared computers:

- Do not leave the computer while the survey is open on the screen.
- If you are logged in to the study website, make sure to log out and close the browser before you leave the computer.
- If possible, clear the cache on the browser you used. This will help prevent the browser from storing your information.
- Turn on the “privacy” feature on the web browser. This will stop the browser from saving a record of your visit to the study website. All of the main browsers like Microsoft Edge, Safari, Google Chrome, and Firefox have a privacy feature.

Privacy tips for personal computers:

- Create a password to protect your personal computer, even if you are the only person using it. This will prevent anybody else from being able to log in and see your information.
- Use firewalls for your hardware and software. Firewalls can prevent others from getting access to your computer through the internet. One effective free software firewall is available from Zone Alarm. Firewalls are also included in many virus protection programs. One example is AVG, which also offers a free version. Both programs are easy to find and download from the internet.
- Make sure you are using the most recent versions of operating systems. For example, “Windows” and “Mac OS” are examples of operating systems.
- Make sure you are using the most recent versions of web browsers and software. For example, “Microsoft Edge” is a web browser, and “Microsoft Word” is software.
- Make sure to update your operating system, browsers, and software regularly.

References

1. UNAIDS. (2018). *UNAIDS data 2018*. Retrieved April 15, 2019 from http://www.unaids.org/en/resources/documents/2018/unaids-data-2018
2. UNAIDS. (2017). *UNAIDS 2017 estimates*. Retrieved December 2, 2018 from http://www.unaids.org/en/resources/documents/2017/2017_data_book
3. Centers for Disease Control and Prevention. (2020). Estimated HIV incidence and prevalence in the United States, 2014–2018. *HIV Surveillance Supplemental Report 2020; 25*(1). Retrieved September 4, 2020 from http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html
4. Centers for Disease Control and Prevention. (2020). *HIV and women*. Retrieved June 3, 2020 from https://www.cdc.gov/hiv/group/gender/women/index.html
5. Nesheim, S. R., FitzHarris, L. F., Lampe, M. A., & Gray, K. M. (2018). Reconsidering the number of women with HIV infection who give birth annually in the United States. *Public Health Reports*, *133*(6), 637-643.
6. Centers for Disease Control and Prevention. (2019). *Selected national HIV prevention and care outcomes in the United States*. Retrieved April 15, 2019 from https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-national-hiv-care-outcomes.pdf
7. Mellins, C., Chu, C., Malee, K., Allison, S., Smith, R., Harris, L., Higgins, A., Zorrilla, C., Landesman, S., & Serchuck, L. (2008). Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. *AIDS Care*, *20*(8), 958-968.
8. Chen, J. S., Pence, B. W., Rahangdale, L., Patterson, K. B., Farel, C. E., Durr, A. L., Antono, A. C., Zakharova, O., Eron, J. J., & Napravnik, S. (2019). Postpartum HIV care continuum outcomes in the Southeastern US. *AIDS*, *33*(4), 637.
9. Patel, M., Tedaldi, E., Armon, C., Nesheim, S., Lampe, M., Palella, F., Jr., Novak, R., Sutton, M., Buchacz, K., & HOPS Investigators. (2018). HIV RNA Suppression during and after Pregnancy among Women in the HIV Outpatient Study, 1996 to 2015. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*, *17*, 2325957417752259. https://doi.org/10.1177/2325957417752259
10. Swain, C.-A., Smith, L. C., Nash, D., Pulver, W. P., Lazariu, V., Anderson, B. J., Warren, B. L., Birkhead, G. S., & McNutt, L.-A. (2016). Postpartum loss to HIV care and HIV viral suppression among previously diagnosed HIV-infected women with a live birth in New York State. *PLoS One*, *11*(8), e0160775.
11. Meade, C. M., Hussen, S. A., Momplaisir, F., Badell, M., Hackett, S., & Sheth, A. N. (2018). Long term engagement in HIV care among postpartum women with perinatal HIV infection in the United States. *AIDS Care*, *30*(4), 488-492.
12. Patel, K., Karalius, B., & Powis, K., et al. (2018, March). *Pregnancy rates and postpartum virologic control among perinatally HIV-infected young women in the US.* 22nd International Workshop on HIV and Hepatitis Observational Databases (IWHOD), Fuengirola, Spain.
13. Haddad, L. B., Wall, K. M., Mehta, C. C., Golub, E. T., Rahangdale, L., Kempf, M.-C., Karim, R., Wright, R., Minkoff, H., & Cohen, M. (2017). Trends of and factors associated with live-birth and abortion rates among HIV-positive and HIV-negative women. *American Journal of Obstetrics and Gynecology*, *216*(1), 71.e71-71.e16. https://doi.org/10.1016/j.ajog.2016.09.079

14. Blair, J. M., Hanson, D. L., Jones, J. L., & Dworkin, M. S. (2004). Trends in pregnancy rates among women with human immunodeficiency virus. *Obstetrics & Gynecology*, *103*(4), 663-668. https://doi.org/10.1097/01.AOG.0000117083.33239.b5

15. Huntington, S. E., Thorne, C., Bansi, L. K., Anderson, J., Newell, M.-L., Taylor, G. P., Pillay, D., Hill, T., Tookey, P. A., & Sabin, C. A. (2013). Predictors of pregnancy and changes in pregnancy incidence among HIV-positive women accessing HIV clinical care at 13 large UK clinics. *AIDS*, *27*(1), 95.

16. Sharma, A., Feldman, J. G., Golub, E. T., Schmidt, J., Silver, S., Robison, E., & Minkoff, H. (2007). Live birth patterns among human immunodeficiency virus-infected women before and after the availability of highly active antiretroviral therapy. *American Journal of Obstetrics and Gynecology*, *196*(6), 541. e541-541. e546.

17. Massad, L. S., Springer, G., Jacobson, L., Watts, H., Anastos, K., Korn, A., Cejtin, H., Stek, A., Young, M., & Schmidt, J. (2004). Pregnancy rates and predictors of conception, miscarriage and abortion in US women with HIV. *AIDS*, *18*(2), 281-286.

18. Koenig, L. J., Espinoza, L., Hodge, K., & Ruffo, N. (2007). Young, seropositive, and pregnant: Epidemiologic and psychosocial perspectives on pregnant adolescents with human immunodeficiency virus infection. *American Journal of Obstetrics and Gynecology*, *197*(3), S123-S131.

19. Sutton, M. Y., Patel, R., & Frazier, E. L. (2014). Unplanned pregnancies among HIV-infected women in care—United States. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *65*(3), 350-358.

20. Rahangdale, L., Stewart, A., Stewart, R. D., Badell, M., Levison, J., Ellis, P., Cohn, S. E., Kempf, M.-C., Lazenby, G. B., & Tandon, R. (2014). Pregnancy intentions among women living with HIV in the United States. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *65*(3), 306.

21. Lindsay, M. K., Grant, J., Peterson, H. B., Willis, S., Nelson, P., & Klein, L. (1995). The impact of knowledge of human immunodeficiency virus serostatus on contraceptive choice and repeat pregnancy. *Obstetrics & Gynecology*, *85*(5), 675-679.

22. Finer, L. B., & Zolna, M. R. (2016). Declines in unintended pregnancy in the United States, 2008–2011. *New England Journal of Medicine*, *374*(9), 843-852.

23. Champaloux, S. W., Tepper, N. K., Curtis, K. M., Zapata, L. B., Whiteman, M. K., Marchbanks, P. A., & Jamieson, D. J. (2015). Contraceptive use among women with medical conditions in a nationwide privately insured population. *Obstetrics & Gynecology*, *126*(6), 1151-1159.

24. Haddad, L. B., Monsour, M., Tepper, N. K., Whiteman, M. K., Kourtis, A. P., & Jamieson, D. J. (2017). Trends in contraceptive use according to HIV status among privately insured women in the United States. *American Journal of Obstetrics and Gynecology*, *217*(6), 676. e671-676. e611. https://doi.org/10.1016/j.ajog.2016.09.079

25. Raziano, V., Smoots, A., Haddad, L., & Wall, K. (2017). Factors associated with sterilization among HIV-positive US women in an urban outpatient clinic. *AIDS Care*, *29*(5), 612-617.

26. Badell, M. L., Lathrop, E., Haddad, L. B., Goedken, P., Nguyen, M. L., & Cwiak, C. A. (2012). Reproductive healthcare needs and desires in a cohort of HIV-positive women. *Infectious Diseases in Obstetrics and Gynecology*, *2012*, 107878. https://doi.org/10.1155/2012/107878

27. Denslow, S. A., Rositch, A. F., Firnhaber, C., Ting, J., & Smith, J. S. (2014). Incidence and progression of cervical lesions in women with HIV: A systematic global review. *International Journal of STD & AIDS*, *25*(3), 163-177.

28. Stier, E. A., Sebring, M. C., Mendez, A. E., Ba, F. S., Trimble, D. D., & Chiao, E. Y. (2015). Prevalence of anal human papillomavirus infection and anal HPV-related disorders in women: A systematic review. *American Journal of Obstetrics and Gynecology*, *213*(3), 278-309.

29. Ghebre, R. G., Grover, S., Xu, M. J., Chuang, L. T., & Simonds, H. (2017). Cervical cancer control in HIV-infected women: Past, present and future. *Gynecologic Oncology Reports*, *21*, 101-108.

30. Satterwhite, C. L., Torrone, E., Meites, E., Dunne, E. F., Mahajan, R., Ocfemia, M. C. B., Su, J., Xu, F., & Weinstock, H. (2013). Sexually transmitted infections among US women and men: Prevalence and incidence estimates, 2008. *Sexually Transmitted Diseases*, *40*(3), 187-193.

31. Reda, S., Gonçalves, F. A., Mazepa, M. M., & De Carvalho, N. S. (2018). Women infected with HIV and the impact of associated sexually transmitted infections. *International Journal of Gynecology & Obstetrics*, *142*(2), 143-147.

32. Echenique, M., Rodriguez, V. J., LaCabe, R. P., Privette, C. K., Jones, D. L., Potter, J. E., & Fischl, M. A. (2017). Behaviorally and perinatally HIV-infected young women: Targets for preconception counseling. *AIDS Care*, *29*(3), 372-377.

33. Badell, M. L., Kachikis, A., Haddad, L. B., Nguyen, M. L., & Lindsay, M. (2013). Comparison of pregnancies between perinatally and sexually HIV-infected women: An observational study at an urban hospital. *Infectious Diseases in Obstetrics and Gynecology*, *2013*, 301763. https://doi.org/10.1155/2013/301763

34. Byrne, L., Sconza, R., Foster, C., Tookey, P. A., Cortina-Borja, M., & Thorne, C. (2017). Pregnancy incidence and outcomes in women with perinatal HIV infection. *AIDS*, *31*(12), 1745.

35. Phillips, U. K., Rosenberg, M. G., Dobroszycki, J., Katz, M., Sansary, J., Golatt, M. A., Wiznia, A. A., & Abadi, J. (2011). Pregnancy in women with perinatally acquired HIV-infection: Outcomes and challenges. *AIDS Care*, *23*(9), 1076-1082.

36. Munjal, I., Dobroszycki, J., Fakioglu, E., Rosenberg, M. G., Wiznia, A. A., Katz, M., Steiner, A., Sansary, J., Heo, M., & Abadi, J. (2013). Impact of HIV-1 infection and pregnancy on maternal health: Comparison between perinatally and behaviorally infected young women. *Adolescent Health, Medicine and Therapeutics*, *4*, 51-58.

37. Lazenby, G. B., Mmeje, O., Fisher, B. M., Weinberg, A., Aaron, E. K., Keating, M., Luque, A. E., Willers, D., Cohan, D., & Money, D. (2016). Antiretroviral resistance and pregnancy characteristics of women with perinatal and nonperinatal HIV infection. *Infectious Diseases in Obstetrics and Gynecology*, *2016*.

38. Setse, R., Siberry, G. K., Moss, W. J., Gravitt, P., Wheeling, T., Bohannon, B., Dominguez, K., & Consortium, L. (2012). Cervical pap screening cytological abnormalities among HIV-infected adolescents in the LEGACY cohort. *Journal of Pediatric and Adolescent Gynecology*, *25*(1), 27-34.

39. Freiberg, M. S., & So-Armah, K. (2016). HIV and cardiovascular disease: We need a mechanism, and we need a plan. *Journal of the American Heart Association*, *4*(3), e003411. https://doi.org/10.1161/JAHA.116.003411

40. Triant, V. A., Lee, H., Hadigan, C., & Grinspoon, S. K. (2007). Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *Journal of Clinical Endocrinology and Metabolism*, *92*(7), 2506-2512. https://doi.org/10.1210/jc.2006-2190

41. Womack, J. A., Chang, C. C., So-Armah, K. A., Alcorn, C., Baker, J. V., Brown, S. T., Budoff, M., Butt, A. A., Gibert, C., Goetz, M. B., Gottdiener, J., Gottlieb, S., Justice, A. C., Leaf, D., McGinnis, K., Rimland, D., Rodriguez-Barradas, M. C., Sico, J., Skanderson, M., Tindle, H., Tracy, R. P., Warner, A., & Freiberg, M. S. (2014). HIV infection and cardiovascular disease in women. *Journal of the American Heart Association*, *3*(5), e001035. https://doi.org/10.1161/JAHA.114.001035

42. Fahme, S. A., Bloomfield, G. S., & Peck, R. (2018). Hypertension in HIV-infected adults: Novel pathophysiologic mechanisms. *Hypertension*, *72*(1), 44-55. https://doi.org/10.1161/HYPERTENSIONAHA.118.10893

43. Wyatt, C. M. (2017). Kidney disease and HIV infection. *Topics in Antiviral Medicine*, *25*(1), 13-16.

44. Feinstein, M. J., Bahiru, E., Achenbach, C., Longenecker, C. T., Hsue, P., So-Armah, K., Freiberg, M. S., & Lloyd-Jones, D. M. (2016). Patterns of cardiovascular mortality for HIV-infected adults in the United States: 1999 to 2013. *American Journal of Cardiology*, *117*(2), 214-220. https://doi.org/10.1016/j.amjcard.2015.10.030

45. Palella Jr, F. J., Delaney, K. M., Moorman, A. C., Loveless, M. O., Fuhrer, J., Satten, G. A., Aschman, D. J., Holmberg, S. D., & Investigators, H. O. S. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *New England Journal of Medicine*, *338*(13), 853-860.

46. May, M., Gompels, M., Delpech, V., Porter, K., Post, F., Johnson, M., Dunn, D., Palfreeman, A., Gilson, R., & Gazzard, B. (2011). Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study. *BMJ*, *343*, d6016.

47. European Collaborative Study. (2005). Mother-to-child transmission of HIV infection in the era of highly active antiretroviral therapy. *Clinical Infectious Diseases*, *40*(3), 458-465.

48. Mandelbrot, L., Tubiana, R., Le Chenadec, J., Dollfus, C., Faye, A., Pannier, E., Matheron, S., Khuong, M.-A., Garrait, V., & Reliquet, V. (2015). No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. *Clinical Infectious Diseases*, *61*(11), 1715-1725.

49. Smith, C. J., Ryom, L., Weber, R., Morlat, P., Pradier, C., Reiss, P., Kowalska, J. D., de Wit, S., Law, M., & el Sadr, W. (2014). Trends in underlying causes of death in people with HIV from 1999 to 2011 (D: A: D): A multicohort collaboration. *The Lancet*, *384*(9939), 241-248.

50. Stone, L., Looby, S. E., & Zanni, M. V. (2017). Cardiovascular disease risk among women living with HIV in North America & Europe. *Current Opinion in HIV and AIDS*, *12*(6), 585.

51. Casper, C., Crane, H., Menon, M., & Money, D. (2017). HIV/AIDS comorbidities: Impact on cancer, noncommunicable diseases, and reproductive health. In K. Holmes, S. Bertozzi, B. Bloom, & et al. (Eds.), *Major infectious diseases* (3rd ed.). Washington, DC: The International Bank for Reconstruction and Development/The World Bank.

52. Hanna, D. B., Ramaswamy, C., Kaplan, R. C., Kizer, J. R., Daskalakis, D., Anastos, K., & Braunstein, S. L. (2020). Sex- and poverty-specific patterns in cardiovascular disease mortality associated with Human Immunodeficiency Virus, New York City, 2007-2017. *Clinical Infectious Diseases*, *71*(3), 491-498. https://doi.org/10.1093/cid/ciz852

53. Saade, G. R. (2009). Pregnancy as a window to future health. *Obstetrics & Gynecology*, *114*(5), 958-960. https://doi.org/10.1097/AOG.0b013e3181bf5588

54. Lowe, W. L., Jr., Scholtens, D. M., Lowe, L. P., Kuang, A., Nodzenski, M., Talbot, O., Catalano, P. M., Linder, B., Brickman, W. J., Clayton, P., Deerochanawong, C., Hamilton, J., Josefson, J. L.,

Lashley, M., Lawrence, J. M., Lebenthal, Y., Ma, R., Maresh, M., McCance, D., Tam, W. H., Sacks, D. A., Dyer, A. R., Metzger, B. E., & Group, H. F.-u. S. C. R. (2018). Association of gestational diabetes with maternal disorders of glucose metabolism and childhood adiposity. *JAMA*, *320*(10), 1005-1016. https://doi.org/10.1001/jama.2018.11628

55. Leddy, M. A., Power, M. L., & Schulkin, J. (2008). The impact of maternal obesity on maternal and fetal health. *Reviews in Obstetrics & Gynecology*, *1*(4), 170-178.
56. Al Mamun, A., Mannan, M., O'Callaghan, M. J., Williams, G. M., Najman, J. M., & Callaway, L. K. (2013). Association between gestational weight gain and postpartum diabetes: Evidence from a community based large cohort study. *PLoS One*, *8*(12), e75679. https://doi.org/10.1371/journal.pone.0075679
57. Wu, P., Haththotuwa, R., Kwok, C. S., Babu, A., Kotronias, R. A., Rushton, C., Zaman, A., Fryer, A. A., Kadam, U., Chew-Graham, C. A., & Mamas, M. A. (2017). Preeclampsia and future cardiovascular health: A systematic review and meta-analysis. *Circulation. Cardiovascular Quality and Outcomes*, *10*(2). https://doi.org/10.1161/circoutcomes.116.003497
58. Goldstein, R. F., Abell, S. K., Ranasinha, S., Misso, M., Boyle, J. A., Black, M. H., Li, N., Hu, G., Corrado, F., Rode, L., Kim, Y. J., Haugen, M., Song, W. O., Kim, M. H., Bogaerts, A., Devlieger, R., Chung, J. H., & Teede, H. J. (2017). Association of gestational weight gain with maternal and infant outcomes: A systematic review and meta-analysis. *JAMA*, *317*(21), 2207-2225. https://doi.org/10.1001/jama.2017.3635
59. Macdonald-Wallis, C., Tilling, K., Fraser, A., Nelson, S. M., & Lawlor, D. A. (2013). Gestational weight gain as a risk factor for hypertensive disorders of pregnancy. *American Journal of Obstetrics and Gynecology*, *209*(4), 327 e321-317. https://doi.org/10.1016/j.ajog.2013.05.042
60. Widen, E. M., Whyatt, R. M., Hoepner, L. A., Ramirez-Carvey, J., Oberfield, S. E., Hassoun, A., Perera, F. P., Gallagher, D., & Rundle, A. G. (2015). Excessive gestational weight gain is associated with long-term body fat and weight retention at 7 y postpartum in African American and Dominican mothers with underweight, normal, and overweight prepregnancy BMI. *American Journal of Clinical Nutrition*, *102*(6), 1460-1467. https://doi.org/10.3945/ajcn.115.116939
61. Catalano, P. M., & Shankar, K. (2017). Obesity and pregnancy: Mechanisms of short term and long term adverse consequences for mother and child. *BMJ*, *356*, j1. https://doi.org/10.1136/bmj.j1
62. Truong, Y. N., Yee, L. M., Caughey, A. B., & Cheng, Y. W. (2015). Weight gain in pregnancy: Does the Institute of Medicine have it right? *American Journal of Obstetrics and Gynecology*, *212*(3), 362 e361-368. https://doi.org/10.1016/j.ajog.2015.01.027
63. Johnson, J., Clifton, R. G., Roberts, J. M., Myatt, L., Hauth, J. C., Spong, C. Y., Varner, M. W., Wapner, R. J., Thorp, J. M., Jr., Mercer, B. M., Peaceman, A. M., Ramin, S. M., Samuels, P., Sciscione, A., Harper, M., Tolosa, J. E., Saade, G., Sorokin, Y., Eunice Kennedy Shriver National Institute of Child, H., & Human Development Maternal-Fetal Medicine Units, N. (2013). Pregnancy outcomes with weight gain above or below the 2009 Institute of Medicine guidelines. *Obstetrics & Gynecology*, *121*(5), 969-975. https://doi.org/10.1097/AOG.0b013e31828aea03
64. Egan, A. M., Dennedy, M. C., Al-Ramli, W., Heerey, A., Avalos, G., & Dunne, F. (2014). ATLANTIC-DIP: Excessive gestational weight gain and pregnancy outcomes in women with

gestational or pregestational diabetes mellitus. *Journal of Clinical Endocrinology and Metabolism*, *99*(1), 212-219. https://doi.org/10.1210/jc.2013-2684

65. McClure, C. K., Catov, J. M., Ness, R., & Bodnar, L. M. (2013). Associations between gestational weight gain and BMI, abdominal adiposity, and traditional measures of cardiometabolic risk in mothers 8 y postpartum. *American Journal of Clinical Nutrition*, *98*(5), 1218-1225. https://doi.org/10.3945/ajcn.112.055772
66. Berggren, E. K., Groh-Wargo, S., Presley, L., Hauguel-de Mouzon, S., & Catalano, P. M. (2016). Maternal fat, but not lean, mass is increased among overweight/obese women with excess gestational weight gain. *American Journal of Obstetrics and Gynecology*, *214*(6), 745 e741-745. https://doi.org/10.1016/j.ajog.2015.12.026
67. Vesco, K. K., Dietz, P. M., Rizzo, J., Stevens, V. J., Perrin, N. A., Bachman, D. J., Callaghan, W. M., Bruce, F. C., & Hornbrook, M. C. (2009). Excessive gestational weight gain and postpartum weight retention among obese women. *Obstetrics & Gynecology*, *114*(5), 1069-1075. https://doi.org/10.1097/AOG.0b013e3181baeacf
68. Caniglia, E., Shapiro, R., Diseko, M., Wylie, B., Zera, C., Davey, S., Isaacson, A., Mayondi, G., Mabuta, J., Luckett, R., Makhema, J., Mmalane, M., Lockman, S., Zash, R., & The Tsepamo Study. (2019, July). *Weight gain during pregnancy among women initiating dolutegravir in Botswana.* International AIDS Society (IAS), Mexico City.
69. Chinula, L., Brummel, S., Ziemba, L., Stranix-Chibanda, L., Coletti, A., Krotje, C., Jean-Philippe, P., Fairlie, L., Vhembo, T., & IMPAACT. (2020, March). *Safety and efficacy of DTG vs EFV and TDF vs TAF in pregnancy: IMPAACT 2010 Trial.* Conference on Retroviruses and Opportunistic Infections (CROI), Boston.
70. Jao, J., Sun, S., Legbedze, J., Jacobson, D., Mmasa, K., Kgole, S., Masasa, G., Makhema, J., Moyo, S., Mmalane, M., Banda, F., Nkomo, B., Gerschenson, M., Abrams, E., & Powis, K. (2020, March). *Dolutegravir use is associated with higher postpartum weight compared to Efavirenz.* Conference on Retroviruses and Opportunistic Infections (CROI), Boston.
71. Malaba, T., Chen, T., Kintu, K., Papamichael, C., Reynolds, H., Nakibuka, N., Waitt, C., Hodel, E., Colbers, A., Orrell, C., Wang, D., Lamorde, M., Khoo, S., & Myer, L. (2020, March). *Postpartum weight changes in women initiating DTG vs EFV in pregnancy: DolPHIN-2.* Conference on Retroviruses and Opportunistic Infections (CROI), Boston.
72. Menard, A., Meddeb, L., Tissot-Dupont, H., Ravaux, I., Dhiver, C., Mokhtari, S., Tomei, C., Brouqui, P., Colson, P., & Stein, A. (2017). Dolutegravir and weight gain: An unexpected bothering side effect? *AIDS*, *31*(10), 1499-1500. https://doi.org/10.1097/qad.0000000000001495
73. Lake, J. E., Wu, K., Erlandson, K. M., Bares, S. H., Debroy, P., Godfrey, C., Koethe, J. R., McComsey, G. A., Palella, F. J., & Tassiopoulos, K. (2019, March). *Risk factors for excess weight gain following switch to integrase inhibitor-based ART.* Conference on Retroviruses and Opportunistic Infections (CROI), Seattle.
74. Palella, F. J., Rayeed, N., Li, J., Ward, D., Fuhrer, J., Purinton, S., Tedaldi, E., Novak, R., & Buchacz, K. (2019, March). *Weight gain among virally suppressed persons who switch to INSTI-based ART.* Conference on Retroviruses and Opportunistic Infections (CROI), Seattle.
75. McComsey, G. A., Moser, C., Currier, J., Ribaudo, H. J., Paczuski, P., Dubé, M. P., Kelesidis, T., Rothenberg, J., Stein, J. H., & Brown, T. T. (2016). Body composition changes after initiation of raltegravir or protease inhibitors: ACTG A5260s. *Clinical Infectious Diseases*, *62*(7), 853-862. https://doi.org/10.1093/cid/ciw017

76. Lennox, J. L., Dejesus, E., Berger, D. S., Lazzarin, A., Pollard, R. B., Ramalho Madruga, J. V., Zhao, J., Wan, H., Gilbert, C. L., Teppler, H., Rodgers, A. J., Barnard, R. J., Miller, M. D., Dinubile, M. J., Nguyen, B. Y., Leavitt, R., & Sklar, P. (2010). Raltegravir versus Efavirenz regimens in treatment-naive HIV-1-infected patients: 96-week efficacy, durability, subgroup, safety, and metabolic analyses. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *55*(1), 39-48. https://doi.org/10.1097/QAI.0b013e3181da1287

77. Rockstroh, J. K., Lennox, J. L., Dejesus, E., Saag, M. S., Lazzarin, A., Wan, H., Walker, M. L., Xu, X., Zhao, J., Teppler, H., Dinubile, M. J., Rodgers, A. J., Nguyen, B. Y., Leavitt, R., & Sklar, P. (2011). Long-term treatment with raltegravir or efavirenz combined with tenofovir/emtricitabine for treatment-naive human immunodeficiency virus-1-infected patients: 156-week results from STARTMRK. *Clinical Infectious Diseases*, *53*(8), 807-816. https://doi.org/10.1093/cid/cir510

78. Sax, P. E., Erlandson, K. M., Lake, J. E., McComsey, G. A., Orkin, C., Esser, S., Brown, T. T., Rockstroh, J. K., Wei, X., Carter, C. C., Zhong, L., Brainard, D. M., Melbourne, K., Das, M., Stellbrink, H. J., Post, F. A., Waters, L., & Koethe, J. R. (2020). Weight gain following initiation of antiretroviral therapy: Risk factors in randomized comparative clinical trials. *Clinical Infectious Diseases*, *71*(6), 1379-1389. https://doi.org/10.1093/cid/ciz999

79. Premkumar, A., Dude, A. M., Haddad, L. B., & Yee, L. M. (2019). Combined antiretroviral therapy for HIV and the risk of hypertensive disorders of pregnancy: A systematic review. *Pregnancy Hypertens*, *17*, 178-190. https://doi.org/10.1016/j.preghy.2019.05.015

80. Saums, M. K., King, C. C., Adams, J. C., Sheth, A. N., Badell, M. L., Young, M., Yee, L. M., Chadwick, E. G., Jamieson, D. J., & Haddad, L. B. (2019). Combination antiretroviral therapy and hypertensive disorders of pregnancy. *Obstetrics & Gynecology*, *134*(6), 1205-1214. https://doi.org/10.1097/AOG.0000000000003584

81. Sebitloane, H. M., Moodley, J., & Sartorius, B. (2017). Associations between HIV, highly active anti-retroviral therapy, and hypertensive disorders of pregnancy among maternal deaths in South Africa 2011-2013. *International Journal of Gynecology & Obstetrics*, *136*(2), 195-199. https://doi.org/10.1002/ijgo.12038

82. Solomon, D., Sabin, C. A., Mallon, P. W. G., Winston, A., & Tariq, S. (2018). Cardiovascular disease in women living with HIV: A narrative review. *Maturitas*, *108*, 58-70. https://doi.org/10.1016/j.maturitas.2017.11.012

83. Sarfo, F. S., Nichols, M., Singh, A., Hardy, Y., Norman, B., Mensah, G., Tagge, R., Jenkins, C., & Ovbiagele, B. (2019). Characteristics of hypertension among people living with HIV in Ghana: Impact of new hypertension guideline. *Journal of Clinical Hypertension*, *21*(6), 838-850. https://doi.org/10.1111/jch.13561

84. Bergersen, B. M., Sandvik, L., Dunlop, O., Birkeland, K., & Bruun, J. N. (2003). Prevalence of hypertension in HIV-positive patients on highly active retroviral therapy (HAART) compared with HAART-naive and HIV-negative controls: Results from a Norwegian study of 721 patients. *European Journal of Clinical Microbiology & Infectious Diseases*, *22*(12), 731-736. https://doi.org/10.1007/s10096-003-1034-z

85. Baekken, M., Os, I., Sandvik, L., & Oektedalen, O. (2008). Hypertension in an urban HIV-positive population compared with the general population: Influence of combination antiretroviral therapy. *Journal of Hypertension*, *26*(11), 2126-2133. https://doi.org/10.1097/HJH.0b013e32830ef5fb

86. Gottlieb, D. J., Redline, S., Nieto, F. J., Baldwin, C. M., Newman, A. B., Resnick, H. E., & Punjabi, N. M. (2006). Association of usual sleep duration with hypertension: The Sleep Heart Health Study. *Sleep*, *29*(8), 1009-1014. https://doi.org/10.1093/sleep/29.8.1009

87. Wang, Q., Xi, B., Liu, M., Zhang, Y., & Fu, M. (2012). Short sleep duration is associated with hypertension risk among adults: A systematic review and meta-analysis. *Hypertension Research*, *35*(10), 1012-1018. https://doi.org/10.1038/hr.2012.91

88. Calhoun, D. A., & Harding, S. M. (2010). Sleep and hypertension. *Chest*, *138*(2), 434-443. https://doi.org/10.1378/chest.09-2954

89. Henst, R. H. P., Pienaar, P. R., Roden, L. C., & Rae, D. E. (2019). The effects of sleep extension on cardiometabolic risk factors: A systematic review. *Journal of Sleep Research*, *28*(6), e12865. https://doi.org/10.1111/jsr.12865

90. Gottlieb, D. J., Punjabi, N. M., Newman, A. B., Resnick, H. E., Redline, S., Baldwin, C. M., & Nieto, F. J. (2005). Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Archives of Internal Medicine*, *165*(8), 863-867. https://doi.org/10.1001/archinte.165.8.863

91. Shan, Z., Ma, H., Xie, M., Yan, P., Guo, Y., Bao, W., Rong, Y., Jackson, C. L., Hu, F. B., & Liu, L. (2015). Sleep duration and risk of type 2 diabetes: A meta-analysis of prospective studies. *Diabetes Care*, *38*(3), 529-537. https://doi.org/10.2337/dc14-2073

92. Cappuccio, F. P., Cooper, D., D'Elia, L., Strazzullo, P., & Miller, M. A. (2011). Sleep duration predicts cardiovascular outcomes: A systematic review and meta-analysis of prospective studies. *European Heart Journal*, *32*(12), 1484-1492. https://doi.org/10.1093/eurheartj/ehr007

93. Leng, Y., Cappuccio, F. P., Wainwright, N. W., Surtees, P. G., Luben, R., Brayne, C., & Khaw, K. T. (2015). Sleep duration and risk of fatal and nonfatal stroke: A prospective study and meta-analysis. *Neurology*, *84*(11), 1072-1079. https://doi.org/10.1212/WNL.0000000000001371

94. Honn, K. A., Halverson, T., Jackson, M. L., Krusmark, M., Chavali, V. P., Gunzelmann, G., & Van Dongen, H. P. A. (2020). New insights into the cognitive effects of sleep deprivation by decomposition of a cognitive throughput task. *Sleep*, *43*(7). https://doi.org/10.1093/sleep/zsz319

95. Ben Simon, E., Vallat, R., Barnes, C. M., & Walker, M. P. (2020). Sleep loss and the socio-emotional brain. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2020.02.003

96. Nowakowski, S., Meers, J., & Heimbach, E. (2013). Sleep and women's health. *Sleep Medicine Research*, *4*(1), 1-22. https://doi.org/10.17241/smr.2013.4.1.1

97. Baker, F. C., & Driver, H. S. (2007). Circadian rhythms, sleep, and the menstrual cycle. *Sleep Medicine*, *8*(6), 613-622. https://doi.org/10.1016/j.sleep.2006.09.011

98. Jehan, S., Auguste, E., Hussain, M., Pandi-Perumal, S. R., Brzezinski, A., Gupta, R., Attarian, H., Jean-Louis, G., & McFarlane, S. I. (2016). Sleep and premenstrual syndrome. *Journal of Sleep Medicine and Disorders*, *3*(5).

99. Cappuccio, F. P., Stranges, S., Kandala, N. B., Miller, M. A., Taggart, F. M., Kumari, M., Ferrie, J. E., Shipley, M. J., Brunner, E. J., & Marmot, M. G. (2007). Gender-specific associations of short sleep duration with prevalent and incident hypertension: The Whitehall II Study. *Hypertension*, *50*(4), 693-700. https://doi.org/10.1161/HYPERTENSIONAHA.107.095471

100. Jean-Louis, G., Weber, K. M., Aouizerat, B. E., Levine, A. M., Maki, P. M., Liu, C., Anastos, K. M., Milam, J., Althoff, K. N., & Wilson, T. E. (2012). Insomnia symptoms and HIV infection among

participants in the Women's Interagency HIV Study. *Sleep*, *35*(1), 131-137. https://doi.org/10.5665/sleep.1602

101. Vancampfort, D., Mugisha, J., De Hert, M., Probst, M., Firth, J., Gorczynski, P., & Stubbs, B. (2016). Global physical activity levels among people living with HIV: A systematic review and meta-analysis. *Disability and Rehabilitation*, 1-10.

102. Vancampfort, D., Mugisha, J., De Hert, M., Probst, M., & Stubbs, B. (2017). Sedentary behavior in people living with HIV: A systematic review and meta-analysis. *Journal of Physical Activity & Health*, *14*(7), 571-577. https://doi.org/10.1123/jpah.2016-0507

103. Wong, A. T., Tsang, O. T., Wong, M. Y., Lim, W. L., Zheng, B. J., Lee, S. S., Lai, S. T., Yuen, K. Y., Choi, K. W., Tso, E. Y., Chau, T. N., Tong, W. L., Chiu, M. C., & Yu, W. C. (2004). Coronavirus infection in an AIDS patient. *AIDS*, *18*(5), 829-830. https://doi.org/10.1097/00002030-200403260-00021

104. Blanco, J. L., Ambrosioni, J., Garcia, F., Martínez, E., Soriano, A., Mallolas, J., & Miro, J. M. (2020). COVID-19 in patients with HIV: Clinical case series. *Lancet HIV*, *7*(5), e314-e316. https://doi.org/10.1016/s2352-3018(20)30111-9

105. Zhu, F., Cao, Y., Xu, S., & Zhou, M. (2020). Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China. *Journal of Medical Virology*, *92*(6), 529-530. https://doi.org/10.1002/jmv.25732

106. Härter, G., Spinner, C. D., Roider, J., Bickel, M., Krznaric, I., Grunwald, S., Schabaz, F., Gillor, D., Postel, N., Mueller, M. C., Müller, M., Römer, K., Schewe, K., & Hoffmann, C. (2020). COVID-19 in people living with human immunodeficiency virus: A case series of 33 patients. *Infection*, *48*(5), 681-686. https://doi.org/10.1007/s15010-020-01438-z

107. Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H., & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *The Lancet*, *395*(10229), 1054-1062. https://doi.org/10.1016/s0140-6736(20)30566-3

108. Robert Koch Institut. (2020). *Coronavirus Disease 2019 (COVID-19) - Daily situation report of the Robert Koch Institute*. Retrieved April 25, 2020 from https://www.rki.de/EN/Content/infections/epidemiology/outbreaks/COVID-19/Situationsberichte_Tab.html

109. Wang, Z., Chen, X., Lu, Y., Chen, F., & Zhang, W. (2020). Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment. *Bioscience Trends*, *14*(1), 64-68. https://doi.org/10.5582/bst.2020.01030

110. Wu, J., Li, W., Shi, X., Chen, Z., Jiang, B., Liu, J., Wang, D., Liu, C., Meng, Y., Cui, L., Yu, J., Cao, H., & Li, L. (2020). Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). *Journal of Internal Medicine*, *288*(1), 128-138. https://doi.org/10.1111/joim.13063

111. Cao, B., Wang, Y., Wen, D., Liu, W., Wang, J., Fan, G., Ruan, L., Song, B., Cai, Y., Wei, M., Li, X., Xia, J., Chen, N., Xiang, J., Yu, T., Bai, T., Xie, X., Zhang, L., Li, C., Yuan, Y., Chen, H., Li, H., Huang, H., Tu, S., Gong, F., Liu, Y., Wei, Y., Dong, C., Zhou, F., Gu, X., Xu, J., Liu, Z., Zhang, Y., Li, H., Shang, L., Wang, K., Li, K., Zhou, X., Dong, X., Qu, Z., Lu, S., Hu, X., Ruan, S., Luo, S., Wu, J., Peng, L., Cheng, F., Pan, L., Zou, J., Jia, C., Wang, J., Liu, X., Wang, S., Wu, X., Ge, Q., He, J., Zhan, H., Qiu, F., Guo, L., Huang, C., Jaki, T., Hayden, F. G., Horby, P. W., Zhang, D., & Wang, C. (2020). A trial of lopinavir-

ritonavir in adults hospitalized with severe Covid-19. *New England Journal of Medicine*, *382*(19), 1787-1799. https://doi.org/10.1056/NEJMoa2001282

112. Del Amo, J., Polo, R., Moreno, S., Díaz, A., Martínez, E., Arribas, J. R., Jarrín, I., & Hernán, M. A. (2020). Incidence and severity of COVID-19 in HIV-positive persons receiving antiretroviral therapy: A cohort study. *Annals of Internal Medicine*, *173*(7), 536-541. https://doi.org/10.7326/m20-3689
113. Plan Nacional sobre el Sida (PNS), & Effice Servicios Para la Investigacion S.L. (2020). *Randomized clinical trial for the prevention of SARS-CoV-2 Infection (COVID-19) in healthcare personnel.* (ClinicalTrials.gov registration number: NCT04334928). https://clinicaltrials.gov/show/NCT04334928
114. Office of AIDS Research Advisory Council, National Institutes of Health. (2020). *Interim guidance for COVID-19 and persons with HIV*. Retrieved May 19, 2020 from https://clinicalinfo.hiv.gov/en/guidelines/covid-19-and-persons-hiv-interim-guidance/interim-guidance-covid-19-and-persons-hiv
115. Zambrano, L. D., Ellington, S., Strid, P., Galang, R. R., Oduyebo, T., Tong, V. T., Woodworth, K. R., Nahabedian, J. F., 3rd, Azziz-Baumgartner, E., Gilboa, S. M., & Meaney-Delman, D. (2020). Update: Characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020. *MMWR. Morbidity and Mortality Weekly Report*, *69*(44), 1641-1647. https://doi.org/10.15585/mmwr.mm6944e3
116. Benhammou, V., Tubiana, R., Matheron, S., Sellier, P., Mandelbrot, L., Chenadec, J. L., Marel, E., Khoshnood, B., & Warszawski, J. (2018). HBV or HCV coinfection in HIV-1-infected pregnant women in France: Prevalence and pregnancy outcomes. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *77*(5), 439-450. https://doi.org/10.1097/qai.0000000000001618
117. Cohen, C., Simonsen, L., Sample, J., Kang, J. W., Miller, M., Madhi, S. A., Campsmith, M., & Viboud, C. (2012). Influenza-related mortality among adults aged 25-54 years with AIDS in South Africa and the United States of America. *Clinical Infectious Diseases*, *55*(7), 996-1003. https://doi.org/10.1093/cid/cis549
118. Mertz, D., Lo, C. K., Lytvyn, L., Ortiz, J. R., & Loeb, M. (2019). Pregnancy as a risk factor for severe influenza infection: An individual participant data meta-analysis. *BMC Infectious Diseases*, *19*(1), 683. https://doi.org/10.1186/s12879-019-4318-3
119. Madhi, S. A., Cutland, C. L., Kuwanda, L., Weinberg, A., Hugo, A., Jones, S., Adrian, P. V., van Niekerk, N., Treurnicht, F., Ortiz, J. R., Venter, M., Violari, A., Neuzil, K. M., Simões, E. A., Klugman, K. P., & Nunes, M. C. (2014). Influenza vaccination of pregnant women and protection of their infants. *New England Journal of Medicine*, *371*(10), 918-931. https://doi.org/10.1056/NEJMoa1401480
120. Chen, J. S., Pence, B. W., Rahangdale, L., Patterson, K. B., Farel, C. E., Durr, A. L., Antono, A. C., Zakharova, O., Eron, J. J., & Napravnik, S. (2019). Postpartum HIV care continuum outcomes in the southeastern USA. *AIDS*, *33*(4), 637-644. https://doi.org/10.1097/qad.0000000000002094
121. Patel, K., Karalius, B., Powis, K., Kacanek, D., Berman, C., Moscicki, A. B., Paul, M., Tassiopoulos, K., & Seage, G. R., 3rd. (2020). Trends in post-partum viral load among women living with perinatal HIV infection in the USA: A prospective cohort study. *Lancet HIV*, *7*(3), e184-e192. https://doi.org/10.1016/s2352-3018(19)30339-x

122. Yee, L. M., Simon, M. A., Grobman, W. A., & Rajan, P. V. (2021). Pregnancy as a "golden opportunity" for patient activation and engagement. *American Journal of Obstetrics and Gynecology*, *224*(1), 116-118. https://doi.org/10.1016/j.ajog.2020.09.024

123. Geldsetzer, P., Yapa, H. M. N., Vaikath, M., Ogbuoji, O., Fox, M. P., Essajee, S. M., Negussie, E. K., & Bärnighausen, T. (2016). A systematic review of interventions to improve postpartum retention of women in PMTCT and ART care. *Journal of the International AIDS Society*, *19*(1), 20679.

124. Momplaisir, F. M., Storm, D. S., Nkwihoreze, H., Jayeola, O., & Jemmott, J. B. (2018). Improving postpartum retention in care for women living with HIV in the United States. *AIDS*, *32*(2), 133-142.

125. Bardeguez, A. D., Lindsey, J. C., Shannon, M., Tuomala, R. E., Cohn, S. E., Smith, E., Stek, A., Buschur, S., Cotter, A., Bettica, L., & Read, J. S. (2008). Adherence to antiretrovirals among US women during and after pregnancy. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *48*(4), 408-417. https://doi.org/10.1097/QAI.0b013e31817bbe80

126. Adams, J. W., Brady, K. A., Michael, Y. L., Yehia, B. R., & Momplaisir, F. M. (2015). Postpartum engagement in HIV care: An important predictor of long-term retention in care and viral suppression. *Clinical Infectious Diseases*, *61*(12), 1880-1887. https://doi.org/10.1093/cid/civ678

127. Swain, C. A., Smith, L. C., Nash, D., Pulver, W. P., Gordon, D., Bian, F., Miranda, W., Anderson, B. J., Chicoine, J., Birkhead, G. S., & McNutt, L. A. (2016). Postpartum Human Immunodeficiency Virus care among women diagnosed during pregnancy. *Obstetrics & Gynecology*, *128*(1), 44-51. https://doi.org/10.1097/aog.0000000000001454

128. O'Brien, B. E., Williams, P. L., Huo, Y., Kacanek, D., Chadwick, E. G., Powis, K. M., Correia, K., Haddad, L. B., Yee, L. M., & Chakhtoura, N. (2020). Repeat pregnancies among US women living with HIV in the SMARTT Study: Temporal changes in HIV disease status and predictors of preterm birth. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *85*(3), 346-354.

129. Nachega, J. B., Uthman, O. A., Anderson, J., Peltzer, K., Wampold, S., Cotton, M. F., Mills, E. J., Ho, Y. S., Stringer, J. S., McIntyre, J. A., & Mofenson, L. M. (2012). Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: A systematic review and meta-analysis. *AIDS*, *26*(16), 2039-2052. https://doi.org/10.1097/QAD.0b013e328359590f

130. Rana, A. I., Gillani, F. S., Flanigan, T. P., Nash, B. T., & Beckwith, C. G. (2010). Follow-up care among HIV-infected pregnant women in Mississippi. *Journal of Women's Health*, *19*(10), 1863-1867. https://doi.org/10.1089/jwh.2009.1880

131. Siddiqui, R., Bell, T., Sangi-Haghpeykar, H., Minard, C., & Levison, J. (2014). Predictive factors for loss to postpartum follow-up among low income HIV-infected women in Texas. *AIDS Patient Care and STDs*, *28*(5), 248-253. https://doi.org/10.1089/apc.2013.0321

132. Hodgson, I., Plummer, M. L., Konopka, S. N., Colvin, C. J., Jonas, E., Albertini, J., Amzel, A., & Fogg, K. P. (2014). A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. *PLoS One*, *9*(11), e111421.

133. Michel, K., Wang, C., Wilson, T., Anastos, K., Cohen, M., Greenblatt, R., Fischl, M., Ofotokun, I., Kempf, M., Adimora, A., Milam, J., Ocampo, J., Gange, S., Plankey, M., & Kassaye, S. (2018, March). *Healthcare provider trust linked to long-term HIV viral suppression.* Conference on Retroviruses and Opportunistic Infections (CROI), Boston.

134. Beach, M. C., Keruly, J., & Moore, R. D. (2006). Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? *Journal of General Internal Medicine*, *21*(6), 661-665. https://doi.org/10.1111/j.1525-1497.2006.00399.x

135. Kassaye, S. G., Wang, C., Ocampo, J. M. F., Wilson, T. E., Anastos, K., Cohen, M., Greenblatt, R. M., Fischl, M. A., Otofukun, I., Adimora, A., Kempf, M. C., Sharp, G. B., Young, M., & Plankey, M. (2019). Viremia trajectories of HIV in HIV-positive women in the United States, 1994-2017. *JAMA Network Open*, *2*(5), e193822. https://doi.org/10.1001/jamanetworkopen.2019.3822

136. O'Brien, B. E., Williams, P. L., Kacanek, D., Chadwick, E. G., Powis, K. M., Correia, K., Haddad, L. B., Yee, L. M., Chakhtoura, N., Dola, C., & Van Dyke, R. B. (2018, October). *Repeat pregnancies among US women living with HIV in the SMARTT Study: Temporal changes in HIV disease status and predictors of preterm birth.* IDWeek, San Francisco.

137. Jao, J., Kacanek, D., Williams, P. L., Geffner, M. E., Livingston, E. G., Sperling, R. S., Patel, K., Bardeguez, A. D., Burchett, S. K., & Chakhtoura, N. (2017). Birth weight and preterm delivery outcomes of perinatally vs nonperinatally human immunodeficiency virus-infected pregnant women in the United States: Results from the PHACS SMARTT study and IMPAACT P1025 protocol. *Clinical Infectious Diseases*, *65*(6), 982-989.

138. Schuchat, A., Houry, D., & Guy, G. (2017). New data on opioid use and prescribing in the United States. *JAMA*, *318*(5), 425-426.

139. Centers for Disease Control and Prevention. (2017). *Opioid prescribing: Where you live matters*. Retrieved September 12, 2018 from https://www.cdc.gov/vitalsigns/opioids/index.html

140. Kozhimannil, K., Graves, A., Jarlenski, M., Kennedy-Hendricks, A., Gollust, S., & Barry, C. (2017). Non-medical opioid use and sources of opioids among pregnant and non-pregnant reproductive-aged women. *Drug and Alcohol Dependence*, *174*, 201-208.

141. American College of Obstetricians and Gynecologists. (2017). Committee Opinion No. 711: Opioid use and opioid use disorder in pregnancy. *Obstetrics & Gynecology*, *130*(e81-94).

142. Badreldin, N., Grobman, W., Chang, K., & Yee, L. (2018). Opioid prescribing patterns among postpartum women. *American Journal of Obstetrics and Gynecology*, *219*(1), 103.e101-108.

143. Badreldin, N., Grobman, W., & Yee, L. (2018). Inpatient opioid use after vaginal delivery. *American Journal of Obstetrics and Gynecology*, *219*(6), 608.e601-608.e607. https://doi.org/10.1016/j.ajog.2018.08.039

144. Badreldin, N., Grobman, W., Chang, K., & Yee, L. (2018). Patient and health care provider factors associated with prescription of opioids after delivery. *Obstetrics & Gynecology*, *132*(4), 929-936. https://doi.org/10.1097/AOG.0000000000002862

145. Prabhu, M., Garry, E., Hernandez-Diaz, S., MacDonald, S., Huybrechts, K., & Bateman, B. (2018). Frequency of opioid dispensing after vaginal delivery. *Obstetrics & Gynecology*, *132*(2), 459-465.

146. Osmundson, S., Schornack, L., Grasch, J., Zuckerwise, L., Young, J., & Richardson, M. (2017). Postdischarge opioid use after cesarean delivery. *Obstetrics & Gynecology*, *130*(1), 36-41.

147. Jarlenski, M., Bodnar, L., Kim, J., Donohue, J., Krans, E., & Bogen, D. (2017). Filled prescriptions for opioids after vaginal delivery. *Obstetrics & Gynecology*, *129*(3), 431-437.

148. Brown, Q., Sarvet, A., Shmulewitz, D., Martins, S., Wall, M., & Hasin, D. (2017). Trends in marijuana use among pregnant and nonpregnant reproductive-aged women, 2002-2014. *JAMA*, *317*(2), 207-209.

149. Dickson, B., Mansfield, C., Guiahi, M., Allshouse, A., Borgelt, L., Sheeder, J., Silver, R., & Metz, T. (2018). Recommendations from cannabis dispensaries about first-trimester cannabis use. *Obstetrics & Gynecology*, *131*(6), 1031-1038.

150. Mark, K., Gryczynski, J., Axenfeld, E., Schwartz, R., & Terplan, M. (2017). Pregnant women's current and intended cannabis use in relation to their views toward legalization and knowledge of potential harm. *Journal of Addiction Medicine*, *11*(3), 211-216.

151. Ko, J., Farr, S., Tong, V., Creanga, A., & Callaghan, W. (2015). Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. *American Journal of Obstetrics and Gynecology*, *213*(2), 201.e201-210.

152. Cerda, M., Wall, M., Feng, T., Keyes, K., Sarvet, A., Schulenberg, J., O'Malley, P., Liccardo Pacula, R., Galea, S., & Hasin, D. (2017). Association of state recreational marijuana laws with adolescent marijuana use. *JAMA Pediatrics*, *171*(2), 142-149.

153. American College of Obstetricians and Gynecologists. (2017). Committee Opinion No. 637: Marijuana use in pregnancy and lactation. *Obstetrics & Gynecology*, *130*(4), e205-209.

154. Dotters-Katz, K., Smid, M., Manuck, T., & Metz, T. (2017). Risk of neonatal and childhood morbidity among preterm infants exposed to marijuana. *Journal of Maternal-Fetal & Neonatal Medicine 30*(24), 2933-2939.

155. Chabarria, K., Racusin, D., Antony, K., Kahr, M., Suter, M., Mastrobattista, J., & Aagaard, K. (2016). Marijuana use and its effects in pregnancy. *American Journal of Obstetrics and Gynecology*, *215*(4), 506.e501-507.

156. Malee, K., Mellins, C. A., Huo, Y., Tassiopoulos, K., Smith, R., Sirois, P. A., Allison, S., Kacanek, D., Kapetanovic, S., Williams, P., Grant, M., Marullo, D., Aidala, A., & Pediatric HIV/AIDS Cohort Study. (2014). Prevalence, incidence and persistence of psychiatric and substance use disorders among mothers living with HIV. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *65*(5), 526-534. https://doi.org/10.1097/QAI.0000000000000070

157. Rough, K., Tassiopoulos, K., Kacanek, D., Griner, R., Yogev, R., Rich, K., Seage, G. r., & for the Pediatric HIV/AIDS Cohort Study. (2015). Dramatic decline in substance use by HIV-infected pregnant women in the United States from 1990 to 2012. *AIDS*, *29*(1), 117-123.

158. Whittle, H., Sheira, L., Frongillo, E., Palar, K., Cohen, J., Merenstein, D., Wilson, T., Adedimeji, A., Cohen, M., Adimora, A., Ofotokun, I., Metsch, L., Turan, J., Wentz, E., Tien, P., & Weiser, S. (2019). Longitudinal associations between food insecurity and substance use in a cohort of women with or at risk for HIV in the United States. *Addiction*, *114*(1), 127-136. https://doi.org/10.1111/add.14418

159. Department of Health and Human Services. (2019). *Ending the HIV epidemic: A plan for America*. Retrieved February 11, 2019 from https://www.hhs.gov/sites/default/files/ending-the-hiv-epidemic-fact-sheet.pdf

160. National Institute on Drug Abuse, National Institutes of Health. (2019). *Opioid summaries by state*. Retrieved April 23, 2019 from https://www.drugabuse.gov/drugs-abuse/opioids/opioid-summaries-by-state

161. Geter, A., Herron, A. R., & Sutton, M. Y. (2018). HIV-related stigma by healthcare providers in the United States: A systematic review. *AIDS Patient Care and STDs*, *32*(10), 418-424. https://doi.org/10.1089/apc.2018.0114

162. Dale, S. K., Dean, T., Sharma, R., Reid, R., Saunders, S., & Safren, S. A. (2019). Microaggressions and discrimination relate to barriers to care among black women living with HIV. *AIDS Patient Care and STDs*, *33*(4), 175-183. https://doi.org/10.1089/apc.2018.0258

163. Turan, B., Smith, W., Cohen, M. H., Wilson, T. E., Adimora, A. A., Merenstein, D., Adedimeji, A., Wentz, E. L., Foster, A. G., Metsch, L., Tien, P. C., Weiser, S. D., & Turan, J. M. (2016). Mechanisms for the negative Effects of internalized HIV-related stigma on antiretroviral therapy adherence in women: The mediating roles of social isolation and depression. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *72*(2), 198-205. https://doi.org/10.1097/qai.0000000000000948

164. Bradley, E. L. P., Frazier, E. L., Carree, T., Hubbard McCree, D., & Sutton, M. Y. (2019). Psychological and social determinants of health, antiretroviral therapy (ART) adherence, and viral suppression among HIV-positive black women in care. *AIDS Care*, *31*(8), 932-941. https://doi.org/10.1080/09540121.2019.1612022

165. Sayles, J. N., Wong, M. D., Kinsler, J. J., Martins, D., & Cunningham, W. E. (2009). The association of stigma with self-reported access to medical care and antiretroviral therapy adherence in persons living with HIV/AIDS. *Journal of General Internal Medicine*, *24*(10), 1101-1108. https://doi.org/10.1007/s11606-009-1068-8

166. Katz, I. T., Ryu, A. E., Onuegbu, A. G., Psaros, C., Weiser, S. D., Bangsberg, D. R., & Tsai, A. C. (2013). Impact of HIV-related stigma on treatment adherence: Systematic review and meta-synthesis. *Journal of the International AIDS Society*, *16*(3 Suppl 2), 18640. https://doi.org/10.7448/ias.16.3.18640

167. Sweeney, S. M., & Vanable, P. A. (2016). The association of HIV-related stigma to HIV medication adherence: A systematic review and synthesis of the literature. *AIDS and Behavior*, *20*(1), 29-50. https://doi.org/10.1007/s10461-015-1164-1

168. Chapman Lambert, C., Westfall, A., Modi, R., Amico, R. K., Golin, C., Keruly, J., Quinlivan, E. B., Crane, H. M., Zinski, A., Turan, B., Turan, J. M., & Mugavero, M. J. (2020). HIV-related stigma, depression, and social support are associated with health-related quality of life among patients newly entering HIV care. *AIDS Care*, *32*(6), 681-688. https://doi.org/10.1080/09540121.2019.1622635

169. Crockett, K. B., Esensoy, T. A., Johnson, M. O., Neilands, T. B., Kempf, M. C., Konkle-Parker, D., Wingood, G., Tien, P. C., Cohen, M., Wilson, T. E., Logie, C. H., Sosanya, O., Plankey, M., Golub, E., Adimora, A. A., Parish, C., S, D. W., Turan, J. M., & Turan, B. (2020). Internalized HIV stigma and pain among women with HIV in the United States: The mediating role of depressive symptoms. *AIDS and Behavior*, *24*(12), 3482-3490. https://doi.org/10.1007/s10461-020-02919-w

170. Kawachi, I., & Berkman, L. (2014). Social capital, social cohesion and health. In L. Berkman, I. Kawachi, & M. Glymour (Eds.), *Social epidemiology* (2nd ed., pp. 290-319). New York: Oxford University Press.

171. Office of Disease Prevention and Health Promotion, Department of Health and Human Services. (n.d.). *Healthy People 2030*. Retrieved November 20, 2020 from https://health.gov/healthypeople/objectives-and-data/social-determinants-health

172. Earnshaw, V. A., Bogart, L. M., Dovidio, J. F., & Williams, D. R. (2013). Stigma and racial/ethnic HIV disparities: Moving toward resilience. *American Psychologist*, *68*(4), 225-236. https://doi.org/10.1037/a0032705

173. Turan, J. M., & Nyblade, L. (2013). HIV-related stigma as a barrier to achievement of global PMTCT and maternal health goals: A review of the evidence. *AIDS and Behavior*, *17*(7), 2528-2539.

174. Onono, M., Odwar, T., Abuogi, L., Owuor, K., Helova, A., Bukusi, E., Turan, J., & Hampanda, K. (2020). Effects of depression, stigma and intimate partner violence on postpartum women's adherence and engagement in HIV care in Kenya. *AIDS and Behavior*, *24*(6), 1807-1815. https://doi.org/10.1007/s10461-019-02750-y

175. Vives-Cases, C., Torrubiano-Domínguez, J., Escribà-Agüir, V., Ruiz-Pérez, I., Montero-Piñar, M. I., & Gil-González, D. (2011). Social determinants and health effects of low and high severity intimate partner violence. *Annals of Epidemiology*, *21*(12), 907-913. https://doi.org/10.1016/j.annepidem.2011.02.003

176. Prather, C., Fuller, T. R., Marshall, K. J., & Jeffries, W. L. (2016). The impact of racism on the sexual and reproductive health of African American women. *Journal of Women's Health*, *25*(7), 664-671. https://doi.org/10.1089/jwh.2015.5637

177. Sharpe, T. T., Voûte, C., Rose, M. A., Cleveland, J., Dean, H. D., & Fenton, K. (2012). Social determinants of HIV/AIDS and sexually transmitted diseases among black women: Implications for health equity. *Journal of Women's Health*, *21*(3), 249-254. https://doi.org/10.1089/jwh.2011.3350

178. Katz, I. T., Leister, E., Kacanek, D., Hughes, M. D., Bardeguez, A., Livingston, E., Stek, A., Shapiro, D. E., & Tuomala, R. (2015). Factors associated with lack of viral suppression at delivery among highly active antiretroviral therapy-naive women with HIV: A cohort study. *Annals of Internal Medicine*, *162*(2), 90-99. https://doi.org/10.7326/m13-2005

179. Gadson, A., Akpovi, E., & Mehta, P. K. (2017). Exploring the social determinants of racial/ethnic disparities in prenatal care utilization and maternal outcome. *Seminars in Perinatology*, *41*(5), 308-317. https://doi.org/10.1053/j.semperi.2017.04.008

180. Jones, C. P. (2000). Levels of racism: A theoretic framework and a gardener's tale. *American Journal of Public Health*, *90*(8), 1212-1215. https://doi.org/10.2105/ajph.90.8.1212

181. Williams, D. R., Lawrence, J. A., & Davis, B. A. (2019). Racism and health: Evidence and needed research. *Annual Review of Public Health*, *40*, 105-125. https://doi.org/10.1146/annurev-publhealth-040218-043750

182. Bailey, Z. D., Krieger, N., Agénor, M., Graves, J., Linos, N., & Bassett, M. T. (2017). Structural racism and health inequities in the USA: Evidence and interventions. *The Lancet*, *389*(10077), 1453-1463. https://doi.org/10.1016/s0140-6736(17)30569-x

183. Cobbinah, S. S., & Lewis, J. (2018). Racism & health: A public health perspective on racial discrimination. *Journal of Evaluation in Clinical Practice*, *24*(5), 995-998. https://doi.org/10.1111/jep.12894

184. Trent, M., Dooley, D. G., & Dougé, J. (2019). The impact of racism on child and adolescent health. *Pediatrics*, *144*(2). https://doi.org/10.1542/peds.2019-1765

185. Liu, W. M., Liu, R. Z., Garrison, Y. L., Kim, J. Y. C., Chan, L., Ho, Y. C. S., & Yeung, C. W. (2019). Racial trauma, microaggressions, and becoming racially innocuous: The role of acculturation

and White supremacist ideology. *American Psychologist*, *74*(1), 143-155. https://doi.org/10.1037/amp0000368

186. Jones, C. P. (2002). Confronting institutionalized racism. *Phylon (1960-)*, 7-22.

187. Jones, C. P., Truman, B. I., Elam-Evans, L. D., Jones, C. A., Jones, C. Y., Jiles, R., Rumisha, S. F., & Perry, G. S. (2008). Using "socially assigned race" to probe white advantages in health status. *Ethn Dis*, *18*(4), 496-504.

188. Hoyt, C., Jr. (2012). The pedagogy of the meaning of racism: Reconciling a discordant discourse. *Social Work*, *57*(3), 225-234. https://doi.org/10.1093/sw/sws009

189. Clark, R., Anderson, N. B., Clark, V. R., & Williams, D. R. (1999). Racism as a stressor for African Americans. A biopsychosocial model. *American Psychologist*, *54*(10), 805-816. https://doi.org/10.1037//0003-066x.54.10.805

190. Heard-Garris, N. J., Cale, M., Camaj, L., Hamati, M. C., & Dominguez, T. P. (2018). Transmitting trauma: A systematic review of vicarious racism and child health. *Social Science & Medicine*, *199*, 230-240. https://doi.org/10.1016/j.socscimed.2017.04.018

191. Hicken, M. T., Lee, H., Ailshire, J., Burgard, S. A., & Williams, D. R. (2013). "Every shut eye, ain't sleep": The role of racism-related vigilance in racial/ethnic disparities in sleep difficulty. *Race and Social Problems*, *5*(2), 100-112. https://doi.org/10.1007/s12552-013-9095-9

192. Yip, T., Cheon, Y. M., Wang, Y., Cham, H., Tryon, W., & El-Sheikh, M. (2020). Racial disparities in sleep: Associations with discrimination among ethnic/racial minority adolescents. *Child Development*, *91*(3), 914-931. https://doi.org/10.1111/cdev.13234

193. Vu, M., Li, J., Haardörfer, R., Windle, M., & Berg, C. J. (2019). Mental health and substance use among women and men at the intersections of identities and experiences of discrimination: Insights from the intersectionality framework. *BMC Public Health*, *19*(1), 108. https://doi.org/10.1186/s12889-019-6430-0

194. Williams, D. R. (2018). Stress and the mental health of populations of color: Advancing our understanding of race-related stressors. *Journal of Health and Social Behavior*, *59*(4), 466-485. https://doi.org/10.1177/0022146518814251

195. Mouzon, D. M., & McLean, J. S. (2017). Internalized racism and mental health among African-Americans, US-born Caribbean Blacks, and foreign-born Caribbean Blacks. *Ethnicity & Health*, *22*(1), 36-48. https://doi.org/10.1080/13557858.2016.1196652

196. Williams, D. R., & Williams-Morris, R. (2000). Racism and mental health: The African American experience. *Ethnicity & Health*, *5*(3-4), 243-268. https://doi.org/10.1080/713667453

197. Wyatt, S. B., Williams, D. R., Calvin, R., Henderson, F. C., Walker, E. R., & Winters, K. (2003). Racism and cardiovascular disease in African Americans. *American Journal of the Medical Sciences*, *325*(6), 315-331. https://doi.org/10.1097/00000441-200306000-00003

198. Owens, D. C., & Fett, S. M. (2019). Black maternal and infant health: Historical legacies of slavery. *American Journal of Public Health*, *109*(10), 1342-1345. https://doi.org/10.2105/ajph.2019.305243

199. Beck, A. F., Edwards, E. M., Horbar, J. D., Howell, E. A., McCormick, M. C., & Pursley, D. M. (2020). The color of health: How racism, segregation, and inequality affect the health and well-being of preterm infants and their families. *Pediatric Research*, *87*(2), 227-234. https://doi.org/10.1038/s41390-019-0513-6

200. Bower, K. M., Geller, R. J., Perrin, N. A., & Alhusen, J. (2018). Experiences of racism and preterm birth: Findings from a pregnancy risk assessment monitoring system, 2004 through 2012. *Womens Health Issues*, *28*(6), 495-501. https://doi.org/10.1016/j.whi.2018.06.002

201. Griswold, M. K., Crawford, S. L., Perry, D. J., Person, S. D., Rosenberg, L., Cozier, Y. C., & Palmer, J. R. (2018). Experiences of racism and breastfeeding initiation and duration among first-time mothers of the Black Women's Health Study. *Journal of Racial and Ethnic Health Disparities*, *5*(6), 1180-1191. https://doi.org/10.1007/s40615-018-0465-2

202. Davis, D. A. (2019). Obstetric racism: The racial politics of pregnancy, labor, and birthing. *Medical Anthropology*, *38*(7), 560-573. https://doi.org/10.1080/01459740.2018.1549389

203. Thomas, M. D., Michaels, E. K., Reeves, A. N., Okoye, U., Price, M. M., Hasson, R. E., Chae, D. H., & Allen, A. M. (2019). Differential associations between everyday versus institution-specific racial discrimination, self-reported health, and allostatic load among black women: Implications for clinical assessment and epidemiologic studies. *Annals of Epidemiology*, *35*, 20-28.e23. https://doi.org/10.1016/j.annepidem.2019.05.002

204. Latendresse, G. (2009). The interaction between chronic stress and pregnancy: Preterm birth from a biobehavioral perspective. *Journal of Midwifery & Womens' Health*, *54*(1), 8-17. https://doi.org/10.1016/j.jmwh.2008.08.001

205. Mendez, D. D., Hogan, V. K., & Culhane, J. F. (2014). Institutional racism, neighborhood factors, stress, and preterm birth. *Ethnicity & Health*, *19*(5), 479-499. https://doi.org/10.1080/13557858.2013.846300

206. Relf, M. V., Pan, W., Edmonds, A., Ramirez, C., Amarasekara, S., & Adimora, A. A. (2019). Discrimination, medical distrust, stigma, depressive symptoms, antiretroviral medication adherence, engagement in care, and quality of life among women living with HIV in North Carolina: A mediated wtructural equation model. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *81*(3), 328-335. https://doi.org/10.1097/qai.0000000000002033

207. Fair, C. D., & Berk, M. (2018). Provider perceptions of stigma and discrimination experienced by adolescents and young adults with pHiV while accessing sexual and reproductive health care. *AIDS Care*, *30*(2), 178-181. https://doi.org/10.1080/09540121.2017.1344349

208. Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *American Journal of Public Health*, *96*(5), 826-833. https://doi.org/10.2105/ajph.2004.060749

209. Allen, A. M., Wang, Y., Chae, D. H., Price, M. M., Powell, W., Steed, T. C., Rose Black, A., Dhabhar, F. S., Marquez-Magaña, L., & Woods-Giscombe, C. L. (2019). Racial discrimination, the superwoman schema, and allostatic load: Exploring an integrative stress-coping model among African American women. *Annals of the New York Academy of Sciences*, *1457*(1), 104-127. https://doi.org/10.1111/nyas.14188

210. Cruz, D., Rodriguez, Y., & Mastropaolo, C. (2019). Perceived microaggressions in health care: A measurement study. *PLoS One*, *14*(2), e0211620. https://doi.org/10.1371/journal.pone.0211620

211. Friedlaender, C. (2018). On microaggressions: Cumulative harm and individual responsibility. *Hypatia*, *33*(1), 5-21. https://doi.org/10.1111/hypa.12390

212. Slaughter-Acey, J. C., Sneed, D., Parker, L., Keith, V. M., Lee, N. L., & Misra, D. P. (2019). Skin tone matters: Racial microaggressions and delayed prenatal care. *American Journal of Preventive Medicine*, *57*(3), 321-329. https://doi.org/10.1016/j.amepre.2019.04.014

213. Rice, W. S., Logie, C. H., Napoles, T. M., Walcott, M., Batchelder, A. W., Kempf, M. C., Wingood, G. M., Konkle-Parker, D. J., Turan, B., Wilson, T. E., Johnson, M. O., Weiser, S. D., & Turan, J. M. (2018). Perceptions of intersectional stigma among diverse women living with HIV in the United States. *Social Science & Medicine*, *208*, 9-17. https://doi.org/10.1016/j.socscimed.2018.05.001

214. Wagner, A. C., Girard, T., McShane, K. E., Margolese, S., & Hart, T. A. (2017). HIV-related stigma and overlapping stigmas towards people living with HIV among health care trainees in Canada. *AIDS Education and Prevention*, *29*(4), 364-376. https://doi.org/10.1521/aeap.2017.29.4.364

215. Parsons, J. A., Bond, V. A., & Nixon, S. A. (2015). 'Are we not human?' Stories of stigma, disability and HIV from Lusaka, Zambia and their implications for access to health services. *PLoS One*, *10*(6), e0127392. https://doi.org/10.1371/journal.pone.0127392

216. Logie, C., James, L., Tharao, W., & Loutfy, M. (2013). Associations between HIV-related stigma, racial discrimination, gender discrimination, and depression among HIV-positive African, Caribbean, and Black women in Ontario, Canada. *AIDS Patient Care and STDs*, *27*(2), 114-122. https://doi.org/10.1089/apc.2012.0296

217. Mayne, S. L., Yellayi, D., Pool, L. R., Grobman, W. A., & Kershaw, K. N. (2018). Racial residential segregation and hypertensive disorder of pregnancy among women in Chicago: Analysis of electronic health record data. *American Journal of Hypertension*, *31*(11), 1221-1227. https://doi.org/10.1093/ajh/hpy112

218. Castañeda, H., Holmes, S. M., Madrigal, D. S., Young, M. E., Beyeler, N., & Quesada, J. (2015). Immigration as a social determinant of health. *Annual Review of Public Health*, *36*, 375-392. https://doi.org/10.1146/annurev-publhealth-032013-182419

219. Ojikutu, B. O., Nnaji, C., Sithole-Berk, J., Masongo, D., Nichols, K., Weeks, N., Ngminebayihi, M., Bishop, E., & Bogart, L. M. (2018). African born women living with HIV in the United States: Unmet needs and opportunities for intervention. *AIDS Care*, *30*(12), 1542-1550. https://doi.org/10.1080/09540121.2018.1497767

220. Ungar, M. (2013). Resilience, trauma, context, and culture. *Trauma, Violence, & Abuse*, *14*(3), 255-266. https://doi.org/10.1177/1524838013487805

221. Dale, S. K., & Safren, S. A. (2018). Resilience takes a village: Black women utilize support from their community to foster resilience against multiple adversities. *AIDS Care*, *30*(sup5), S18-s26. https://doi.org/10.1080/09540121.2018.1503225

222. Dale, S. K., Reid, R., & Safren, S. A. (2019). Factors associated with resilience among Black women living with HIV and histories of trauma. *Journal of Health Psychology*, *26*(5). https://doi.org/10.1177/1359105319840690

223. Davtyan, M., Farmer, S., Brown, B., Sami, M., & Frederick, T. (2016). Women of color reflect on HIV-related stigma through PhotoVoice. *Journal of the Association of Nurses in AIDS Care*, *27*(4), 404-418. https://doi.org/10.1016/j.jana.2016.03.003

224. Ransome, Y., Thurber, K. A., Swen, M., Crawford, N. D., German, D., & Dean, L. T. (2018). Social capital and HIV/AIDS in the United States: Knowledge, gaps, and future directions. *SSM - Population Health*, *5*, 73-85. https://doi.org/10.1016/j.ssmph.2018.05.007

225. Odom, E. C., & Vernon-Feagans, L. (2010). Buffers of racial discrimination: Links with depression among rural African American mothers. *Journal of Marriage and the Family*, *72*(2), 346-359. https://doi.org/10.1111/j.1741-3737.2010.00704.x

226. Mellins, C. A., Ehrhardt, A. A., & Grant, W. F. (1997). Psychiatric symptomatology and psychological functioning in HIV-infected mothers. *AIDS and Behavior*, *1*(4), 233-245. https://doi.org/10.1023/A:1026227418721

227. Mellins, C. A., Ehrhardt, A. A., Rapkin, B., & Havens, J. F. (2000). Psychosocial factors associated with adaptation in HIV-infected mothers. *AIDS and Behavior*, *4*(4), 317-328. https://doi.org/10.1023/A:1026494221011

228. Mellins, C. A., Kang, E., Leu, C. S., Havens, J. F., & Chesney, M. A. (2003). Longitudinal study of mental health and psychosocial predictors of medical treatment adherence in mothers living with HIV disease. *AIDS Patient Care and STDs*, *17*(8), 407-416. https://doi.org/10.1089/108729103322277420

229. Kapetanovic, S., Christensen, S., Karim, R., Lin, F., Mack, W. J., Operskalski, E., Frederick, T., Spencer, L., Stek, A., & Kramer, F. (2009). Correlates of perinatal depression in HIV-infected women. *AIDS Patient Care and STDs*, *23*(2), 101-108.

230. Morrison, M. F., Petitto, J. M., Ten Have, T., Gettes, D. R., Chiappini, M. S., Weber, A. L., Brinker-Spence, P., Bauer, R. M., Douglas, S. D., & Evans, D. L. (2002). Depressive and anxiety disorders in women with HIV infection. *American Journal of Psychiatry*, *159*(5), 789-796. https://doi.org/10.1176/appi.ajp.159.5.789

231. Taylor, E. R., Amodei, N., & Mangos, R. (1996). The presence of psychiatric disorders in HIV-infected women. *Journal of Counseling and Development: JCD*, *74*(4), 345.

232. Kapetanovic, S., Dass-Brailsford, P., Nora, D., & Talisman, N. (2014). Mental health of HIV-seropositive women during pregnancy and postpartum period: A comprehensive literature review. *AIDS and Behavior*, *18*(6), 1152-1173.

233. Angrand, R. C., Sperling, R., Roccobono, K., Osborne, L. M., & Jao, J. (2018). Depression in perinatally HIV-infected pregnant women compared to non-perinatally HIV-infected and HIV-uninfected pregnant women. *AIDS Care*, *30*(9), 1168-1172.

234. Nguyen, N., Choi, C. J., Robbins, R., Korich, R., Raymond, J., Dolezal, C., Leu, C. S., Wiznia, A., Abrams, E. J., & Mellins, C. A. (2020). Psychiatric trajectories across adolescence in perinatally HIV-exposed youth: The role of HIV infection and associations with viral load. *AIDS*, *34*(8), 1205-1215. https://doi.org/10.1097/qad.0000000000002529

235. Brittain, K., Remien, R. H., Mellins, C. A., Phillips, T. K., Zerbe, A., Abrams, E. J., & Myer, L. (2018). Determinants of suboptimal adherence and elevated HIV viral load in pregnant women already on antiretroviral therapy when entering antenatal care in Cape Town, South Africa. *AIDS Care*, *30*(12), 1517-1523. https://doi.org/10.1080/09540121.2018.1503637

236. Haberer, J. E., Bwana, B. M., Orrell, C., Asiimwe, S., Amanyire, G., Musinguzi, N., Siedner, M. J., Matthews, L. T., Tsai, A. C., Katz, I. T., Bell, K., Kembabazi, A., Mugisha, S., Kibirige, V., Cross, A., Kelly, N., Hedt-Gauthier, B., & Bangsberg, D. R. (2019). ART adherence and viral suppression are high among most non-pregnant individuals with early-stage, asymptomatic HIV infection: An observational study from Uganda and South Africa. *Journal of the International AIDS Society*, *22*(2), e25232. https://doi.org/10.1002/jia2.25232

237. Cook, J. A., Burke-Miller, J. K., Steigman, P. J., Schwartz, R. M., Hessol, N. A., Milam, J., Merenstein, D. J., Anastos, K., Golub, E. T., & Cohen, M. H. (2018). Prevalence, comorbidity, and

correlates of psychiatric and substance use disorders and associations with HIV risk behaviors in a multisite cohort of women living with HIV. *AIDS and Behavior*, *22*(10), 3141-3154. https://doi.org/10.1007/s10461-018-2051-3

238. Remien, R. H., Stirratt, M. J., Nguyen, N., Robbins, R. N., Pala, A. N., & Mellins, C. A. (2019). Mental health and HIV/AIDS: The need for an integrated response. *AIDS*, *33*(9), 1411-1420. https://doi.org/10.1097/qad.0000000000002227
239. Dantzer, R., & Kelley, K. W. (2007). Twenty years of research on cytokine-induced sickness behavior. *Brain, Behavior, and Immunity*, *21*(2), 153-160. https://doi.org/10.1016/j.bbi.2006.09.006
240. Kiecolt-Glaser, J. K., & Glaser, R. (2002). Depression and immune function: Central pathways to morbidity and mortality. *Journal of Psychosomatic Research*, *53*(4), 873-876. https://doi.org/10.1016/s0022-3999(02)00309-4
241. Longone, P., Rupprecht, R., Manieri, G. A., Bernardi, G., Romeo, E., & Pasini, A. (2008). The complex roles of neurosteroids in depression and anxiety disorders. *Neurochemistry International*, *52*(4-5), 596-601. https://doi.org/10.1016/j.neuint.2007.10.001
242. Raison, C. L., Capuron, L., & Miller, A. H. (2006). Cytokines sing the blues: Inflammation and the pathogenesis of depression. *Trends in Immunology*, *27*(1), 24-31. https://doi.org/10.1016/j.it.2005.11.006
243. Dyer, T. P., Stein, J. A., Rice, E., & Rotheram-Borus, M. J. (2012). Predicting depression in mothers with and without HIV: The role of social support and family dynamics. *AIDS and Behavior*, *16*(8), 2198-2208. https://doi.org/10.1007/s10461-012-0149-6
244. Leenerts, M. H. (1999). The disconnected self: Consequences of abuse in a cohort of low-income white women living with HIV/AIDS. *Health Care for Women International*, *20*(4), 381-400. https://doi.org/10.1080/073993399245674
245. Machtinger, E. L., Wilson, T., Haberer, J. E., & Weiss, D. S. (2012). Psychological trauma and PTSD in HIV-positive women: A meta-analysis. *AIDS and Behavior*, *16*(8), 2091-2100.
246. McIntosh, R. C., & Rosselli, M. (2012). Stress and coping in women living with HIV: A meta-analytic review. *AIDS and Behavior*, *16*(8), 2144-2159. https://doi.org/10.1007/s10461-012-0166-5
247. Wyatt, G. E., Myers, H. F., & Loeb, T. B. (2004). Women, trauma, and HIV: An overview. *AIDS and Behavior*, *8*(4), 401-403. https://doi.org/10.1007/s10461-004-7324-3
248. Lippard, E. T. C., & Nemeroff, C. B. (2020). The devastating clinical consequences of child abuse and neglect: Increased disease vulnerability and poor treatment response in mood disorders. *American Journal of Psychiatry*, *177*(1), 20-36. https://doi.org/10.1176/appi.ajp.2019.19010020
249. Mebrahtu, H., Simms, V., Chingono, R., Mupambireyi, Z., Weiss, H. A., Ndlovu, P., Malaba, R., Cowan, F. M., & Sherr, L. (2018). Postpartum maternal mental health is associated with cognitive development of HIV-exposed infants in Zimbabwe: A cross-sectional study. *AIDS Care*, *30*(sup2), 74-82. https://doi.org/10.1080/09540121.2018.1468015
250. Gentile, S. (2017). Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. *Neuroscience*, *342*, 154-166. https://doi.org/10.1016/j.neuroscience.2015.09.001

251. Ireys, H. T., Chernoff, R., DeVet, K. A., & Kim, Y. (2001). Maternal outcomes of a randomized controlled trial of a community-based support program for families of children with chronic illnesses. *Archives of Pediatrics & Adolescent Medicine*, *155*(7), 771-777.

252. Raina, P., O'Donnell, M., Rosenbaum, P., Brehaut, J., Walter, S. D., Russell, D., Swinton, M., Zhu, B., & Wood, E. (2005). The health and well-being of caregivers of children with cerebral palsy. *Pediatrics*, *115*(6), e626-e636.

253. Meltzer, L. J., & Mindell, J. A. (2006). Impact of a child's chronic illness on maternal sleep and daytime functioning. *Archives of Internal Medicine*, *166*(16), 1749-1755.

254. Moskowitz, J. T., Butensky, E., Harmatz, P., Vichinsky, E., Heyman, M. B., Acree, M., Wrubel, J., Wilson, L., & Folkman, S. (2007). Caregiving time in sickle cell disease: Psychological effects in maternal caregivers. *Pediatric Blood & Cancer*, *48*(1), 64-71.

255. Treyvaud, K., Lee, K. J., Doyle, L. W., & Anderson, P. J. (2014). Very preterm birth influences parental mental health and family outcomes seven years after birth. *The Journal of Pediatrics*, *164*(3), 515-521.

256. Watts, D. H., Williams, P. L., Kacanek, D., Griner, R., Rich, K., Hazra, R., Mofenson, L. M., Mendez, H. A., & Pediatric HIV/AIDS Cohort Study. (2013). Combination antiretroviral use and preterm birth. *The Journal of Infectious Diseases*, *207*(4), 612-621.

257. Henderson, J., Carson, C., & Redshaw, M. (2016). Impact of preterm birth on maternal well-being and women's perceptions of their baby: A population-based survey. *BMJ Open*, *6*(10), e012676.

258. Treyvaud, K. (2014). Parent and family outcomes following very preterm or very low birth weight birth: A review. *Seminars in Fetal and Neonatal Medicine*, *19*(2), 131-135.

259. Gerstein, E. D., Njoroge, W. F., Paul, R. A., Smyser, C. D., & Rogers, C. E. (2019). Maternal depression and stress in the neonatal intensive care unit: Associations with mother−child interactions at age 5 years. *Journal of the American Academy of Child & Adolescent Psychiatry*, *58*(3), 350-358. e352.

260. Treyvaud, K., Anderson, V. A., Lee, K. J., Woodward, L. J., Newnham, C., Inder, T. E., Doyle, L. W., & Anderson, P. J. (2010). Parental mental health and early social-emotional development of children born very preterm. *Journal of Pediatric Psychology*, *35*(7), 768-777.

261. Eccleston, C., Fisher, E., Law, E., Bartlett, J., & Palermo, T. M. (2015). Psychological interventions for parents of children and adolescents with chronic illness. *Cochrane Database of Systematic Reviews*, *4*(4), CD009660. https://doi.org/10.1002/14651858.CD009660.pub3

262. Barker, D. J. (1990). The fetal and infant origins of adult disease. *BMJ*, *301*(6761), 1111.

263. Jao, J., Agwu, A., Mhango, G., Kim, A., Park, K., Posada, R., Abrams, E. J., Hutton, N., & Sperling, R. S. (2015). Growth patterns in the first year of life differ in infants born to perinatally vs. non-perinatally HIV-infected women. *AIDS*, *29*(1), 111.

264. Jao, J., Sigel, K. M., Chen, K. T., Rodriguez-Caprio, G., Posada, R., Shust, G., Wisnivesky, J., Abrams, E. J., & Sperling, R. S. (2012). Small for gestational age birth outcomes in pregnant women with perinatally acquired HIV. *AIDS*, *26*(7), 855-859. https://doi.org/10.1097/QAD.0b013e328351f6ef

265. Katz, I. T., Leister, E., Kacanek, D., Hughes, M. D., Bardeguez, A., Livingston, E., Stek, A., Shapiro, D. E., & Tuomala, R. (2015). Factors associated with lack of viral suppression at delivery

among highly active antiretroviral therapy–naive women with HIV: A cohort study. *Annals of Internal Medicine*, *162*(2), 90-99.

266. Momplaisir, F. M., Brady, K. A., Fekete, T., Thompson, D. R., Diez Roux, A., & Yehia, B. R. (2015). Time of HIV diagnosis and engagement in prenatal care impact virologic outcomes of pregnant women with HIV. *PLoS One*, *10*(7), e0132262.

267. Shonkoff, J. P., Garner, A. S., Siegel, B. S., Dobbins, M. I., Earls, M. F., McGuinn, L., Pascoe, J., Wood, D. L., Committee on Psychosocial Aspects of Child Family Health, Committee on Early Childhood, Adoption, and Dependent Care, & Section on Developmental and Behavioral Pediatrics. (2012). The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*, *129*(1), e232-e246.

268. Bronfenbrenner, U. (2005). *Making human beings human: Bioecological perspectives on human development*. Thousand Oaks, CA: Sage Publications.

269. Phiri, S., Tweya, H., van Lettow, M., Rosenberg, N. E., Trapence, C., Kapito-Tembo, A., Kaunda-Khangamwa, B., Kasende, F., Kayoyo, V., Cataldo, F., Stanley, C., Gugsa, S., Sampathkumar, V., Schouten, E., Chiwaula, L., Eliya, M., Chimbwandira, F., & Hosseinipour, M. C. (2017). Impact of facility- and community-based peer support models on maternal uptake and retention in Malawi's Option B+ HIV prevention of mother-to-child transmission program: A 3-arm cluster randomized controlled trial (PURE Malawi). *Journal of Acquired Immune Deficiency Syndromes: JAIDS*, *75*(Suppl 2), S140-S148. https://doi.org/10.1097/qai.0000000000001357

270. Williams, P. L., Seage III, G. R., Van Dyke, R. B., Siberry, G. K., Griner, R., Tassiopoulos, K., Yildirim, C., Read, J. S., Huo, Y., & Hazra, R. (2012). A trigger-based design for evaluating the safety of in utero antiretroviral exposure in uninfected children of human immunodeficiency virus-infected mothers. *American Journal of Epidemiology*, *175*(9), 950-961.

271. Van Dyke, R. B., Chadwick, E. G., Hazra, R., Williams, P. L., & Seage III, G. R. (2016). The PHACS SMARTT study: Assessment of the safety of in utero exposure to antiretroviral drugs. *Frontiers in Immunology*, *7*, 199.

272. Hernán, M. A., & Robins, J. M. (2019). *Causal inference: What if*. Boca Raton: Chapman & Hall/CRC.

273. Nagin, D. S., & Odgers, C. L. (2010). Group-based trajectory modeling in clinical research. *Annual Review of Clinical Psychology*, *6*, 109-138. https://doi.org/10.1146/annurev.clinpsy.121208.131413

274. Muthen, B. (2004). Latent variable analysis: Growth mixture modeling and related techniques for longitudinal data. In D. Kaplan (Ed.), *The Sage handbook of quantitative methodology for the social sciences* (pp. 345–368). Thousand Oaks, CA: Sage.

275. Laird, N., & Olivier, D. (1981). Covariance analysis of censored survival data using log-linear analysis techniques. *Journal of the American Statistical Association*, *76*(374), 231-240. https://doi.org/10.1080/01621459.1981.10477634

276. Villeneuve, P. J., Goldberg, M. S., Krewski, D., Burnett, R. T., & Chen, Y. (2002). Fine particulate air pollution and all-cause mortality within the Harvard Six-Cities Study: Variations in risk by period of exposure. *Annals of Epidemiology*, *12*(8), 568-576. https://doi.org/10.1016/s1047-2797(01)00292-7

277. Chadwick, E. G. (2020). *SMARTT study [unpublished raw data].* (Personal communication).

278. Adhikari, S., Lecci, F., Becker, J. T., Junker, B. W., Kuller, L. H., Lopez, O. L., & Tibshirani, R. J. (2019). High-dimensional longitudinal classification with the multinomial fused lasso. *Statistics in Medicine*, *38*(12), 2184-2205. https://doi.org/10.1002/sim.8100

279. Perkins, N. J., Cole, S. R., Harel, O., Tchetgen Tchetgen, E. J., Sun, B., Mitchell, E. M., & Schisterman, E. F. (2018). Principled approaches to missing data in epidemiologic studies. *American Journal of Epidemiology*, *187*(3), 568-575. https://doi.org/10.1093/aje/kwx348

280. PASS 15 Power Analysis and Sample Size Software. Kaysville, UT: NCSS, LLC; 2017. Available from: http://ncss.com/software/pass. Accessed: 2023/09/06.