



# Research Update

Fall-Winter 2023

A semi-annual look at select DLH research activities.

I am excited to share the Fall-Winter 2023 edition of the DLH Research Update, a semiannual look at select research activities from across our company's Public Health & Scientific Research (PHSR) operating unit.

Alongside our partners in government and academia, our team has accomplished so much in recent years. From groundbreaking discoveries to critical interventions, each successful undertaking is a testament to our staff's collective expertise and commitment to improving health outcomes for all. Our team's work is instrumental in addressing the most crucial of health challenges and safeguarding the well-being of communities both near and far. We are taking the needed and innovative steps toward a healthier and more resilient world.

DLH researchers shape the future of public health by creating lasting positive change. Whether in the field, the office, or the lab, their collaboration and innovation are the driving forces behind our success and every milestone we have achieved. We pursue advancements in the treatment of mental health and aim to address health inequities in those with HIV. We look to identify risk factors for Parkinson's disease and conduct clinical research on diabetes. Our staff's contributions are invaluable. I am always inspired to work alongside such talented individuals and am grateful for the power we have to change lives for the better.

As we continue to navigate through the complexities of public health and scientific research, I am filled with immense pride and gratitude for each and every one of the individuals on our team. Your unwavering passion and dedication to our mission are truly inspiring. I am honored to lead such an exceptional team, and thank you for all that you do.

Sincerely,

**Jeanine Christian**

President

Public Health & Scientific Research



## **Comparison of Demographic Characteristics and Social Determinants of Health Between Adults With Diagnosed HIV and All Adults in the U.S.**

DLH researcher **Xin Yuan** was among the authors of an [article](#) published in *AJPM Focus* (Online: June 2023; eCollection 2023 September). Quantifying disparities in social determinants of health between people with HIV and the total population could help address health inequities, and ensure health and well-being among people with HIV in the U.S., but estimates are lacking. Several representative data sources were used to assess differences in social determinants of health between adults with diagnosed HIV (Centers for Disease Control and Prevention Medical Monitoring Project) and the total adult population (U.S. Census Bureau's decennial census, American Community Survey, Household Pulse Survey, the Current Population Survey Annual Social and Economic Supplements; the Department of Housing and Urban Development's point-in-time estimates of homelessness; and the Bureau of Justice Statistics). Overall, 35.6% of people with HIV were living in a household with an income at or below the federal poverty level, and 8.1% recently experienced homelessness. Additionally, 42.9% had Medicaid and 27.6% had Medicare; 39.7% were living with a disability. Over half (52.3%) lived in large central metropolitan counties and 20.6% spoke English less than very well based on survey responses. After adjustment, poverty, homelessness, coverage through Medicaid or Medicare, and disability were higher among people with HIV than the total U.S. population. The percentage of people with HIV living in large central metropolitan counties or who were recently incarcerated was higher than the total U.S. population. These findings provide a baseline for assessing national-level disparities in social determinants of health between people with HIV and the total U.S. population, and it can be used as a model to assess local disparities. Addressing social determinants of health is essential for achieving health equity, requiring a multipronged approach with interventions at the provider, facility, and policy levels. *Other authors include researchers from the Centers for Disease Control and Prevention.*

## **Parkinson's Disease Case Ascertainment in the Sister Study: A Cohort for Environmental Health Research**

DLH researchers **Aimee D'Aloisio** and **Lourdes Suarez** were among the authors of an [article](#) published in the *Journal of Parkinson's Disease* (Print: July 2023). Large prospective studies are essential for investigating the environmental causes of Parkinson's disease (PD), but PD diagnosis via clinical exams is often infeasible in such studies. The researchers' objective was to present case ascertainment strategy and data collection in a US cohort of women. In the Sister Study (n = 50,884, baseline ages 55.6±9.0), physician-made PD diagnoses were first reported by participants or their proxies. Cohort-wide follow-up surveys collected data on subsequent diagnoses, medication usage, and PD-relevant motor and nonmotor symptoms. The researchers contacted self-reported PD cases and their treating physicians to obtain relevant diagnostic and treatment history. Diagnostic adjudication was made via expert review of all available data, except nonmotor symptoms. Associations of nonmotor symptoms with incident PD was examined using multivariable logistic regression models and reported odds ratio and 95% confidence intervals. Of the 371 potential PD cases identified, 242 diagnoses were confirmed. Compared with unconfirmed cases, confirmed cases were more likely to report PD diagnosis from multiple sources, medication usage, and motor and nonmotor features consistently during the follow-up. Hyposmia, dream-enacting behaviors, constipation, depression, unexplained weight loss, dry eyes, dry mouth, and fatigue were significantly related to PD risk. Only one of the eight negative control symptoms was associated with incident PD. The authors' findings support their PD case ascertainment approach in this

large cohort of women. PD prodromal presentation is likely beyond its well-documented profile. *Other authors include researchers from the National Institute of Environmental Health Sciences, National Institute on Aging, and the Center for Alzheimer's and Related Dementias (NIH).*

### **Association Between Spill-Related Exposure to Fine Particulate Matter and Peripheral Motor and Sensory Nerve Function Among Oil Spill Response and Cleanup Workers Following the Deepwater Horizon Oil Spill**

DLH researcher **W. Braxton Jackson II** was among the authors of an [article](#) published in the *Journal of Exposure Science & Environmental Epidemiology* (Online Ahead of Print: July 2023). Burning/flaring of oil/gas during the Deepwater Horizon oil spill response and cleanup (OSRC) generated high concentrations of fine particulate matter (PM<sub>2.5</sub>). Personnel working on the water during these activities may have inhaled combustion products. Neurologic effects of PM<sub>2.5</sub> have been reported previously but few studies have examined lasting effects following disaster exposures. The association of brief, high exposures and adverse effects on sensory and motor nerve function in the years following exposure have not been examined for OSRC workers. The authors assessed the relationship between exposure to burning/flaring-related PM<sub>2.5</sub> and measures of sensory and motor nerve function among OSRC workers. Quantitative measures of sensory and motor nerve function were obtained 4-6 years after the disaster during a clinical exam restricted to those living close to two clinics in Mobile, AL or New Orleans, LA. The authors did not find strong evidence of associations between exposure to PM<sub>2.5</sub> and sensory or motor nerve function, although there was a suggestion of impairment based on single-leg stance among individuals with high exposure to PM<sub>2.5</sub>. Remediating environmental disasters is essential for long-term human and environmental health. During the Deepwater Horizon oil spill disaster, burning and flaring of oil and gas were used to remove these pollutants from the environment, but led to potentially high fine particulate matter exposures for spill response workers working on the water. The authors investigated the potential adverse effects of these exposures on peripheral nerve function; understanding the potential health harm of remediation tactics is necessary to inform future clean up approaches and protect human health. *Other authors include researchers from the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill and the National Institute of Environmental Health Sciences.*

### **Use of Nonsteroidal Anti-Inflammatory Drugs and Poor Olfaction in Women**

DLH researcher **Aimee D'Aloisio** was among the authors of an [article](#) published in the *International Forum of Allergy & Rhinology* (Online Ahead of Print: August 2023 [Print: March 2024]). It is unclear whether regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with poor olfaction in older adults. The researchers selected 4020 participants, aged 50 to 79 years in 2018, from 36,492 eligible participants in the National Institute of Environmental Health Sciences Sister Study, according to their self-reported olfaction status. Of these, 3406 women completed the 12-item Brief Smell Identification Test. Poor olfaction was defined as a test score  $\leq 9$  in the primary analysis. Overall, NSAID use was not associated with poor olfaction. However, evidence was found for potential multiplicative interactions. Specifically, the OR comparing regular versus never use of aspirin was 1.8 among women who had not regularly used nonaspirin NSAIDs, while the corresponding OR was 0.8 among nonaspirin NSAID users. Similar results were seen for ibuprofen alone versus ibuprofen with other NSAID use. Among women using either drug alone, associations with poor olfaction increased with increasing duration and cumulative dose. Post hoc analyses showed that the interactions could not be readily explained by

potential biases. Other NSAIDs were not associated with olfaction. The authors concluded that long-term regular use of aspirin or ibuprofen was associated with poor olfaction among women who never regularly used other types of NSAIDs. These preliminary findings warrant independent confirmation. *Other authors include researchers from Michigan State University College of Human Medicine, The University of Chicago, and the National Institute of Environmental Health Sciences.*

### **Pitavastatin to Prevent Cardiovascular Disease in HIV Infection**

DLH researcher **Jhoanna Roa** was among the authors of an [article](#) published in *The New England Journal of Medicine* (Epub: July 2023; Print: August 2023). DLH researcher **Laura Moran** was the co-Clinical Trials Specialist on this study. The risk of cardiovascular disease is increased among persons with human immunodeficiency virus (HIV) infection, so data regarding primary prevention strategies in this population are needed. In this phase 3 trial, the authors randomly assigned 7769 participants with HIV infection with a low-to-moderate risk of cardiovascular disease who were receiving antiretroviral therapy to receive daily pitavastatin calcium or placebo. The primary outcome was the occurrence of a major adverse cardiovascular event, which was defined as a composite of cardiovascular death, myocardial infarction, hospitalization for unstable angina, stroke, transient ischemic attack, peripheral arterial ischemia, revascularization, or death from an undetermined cause. The median age of the participants was 50 years; the median CD4 count was 621 cells per cubic millimeter, and the HIV RNA value was below quantification in 5250 of 5997 participants (87.5%) with available data. The trial was stopped early for efficacy after a median follow-up of 5.1 years. The incidence of a major adverse cardiovascular event was 4.81 per 1000 person-years in the pitavastatin group and 7.32 per 1000 person-years in the placebo group. Muscle-related symptoms occurred in 91 participants (2.3%) in the pitavastatin group and in 53 (1.4%) in the placebo group; diabetes mellitus occurred in 206 participants (5.3%) and in 155 (4.0%), respectively. Participants with HIV infection who received pitavastatin had a lower risk of a major adverse cardiovascular event than those who received placebo over a median follow-up of 5.1 years. *Other authors include researchers from the Massachusetts General Hospital and Harvard Medical School, Harvard T.H. Chan School of Public Health, Brigham and Women's Hospital, Hospital Clinic and University of Barcelona, Instituto de Salud Carlos III (Madrid), the National Heart, Lung, and Blood Institute, and the Division of AIDS at the National Institute of Allergy and Infectious Diseases.*

### **Problems Paying Medical Bills Among Adults With Diagnosed HIV in the United States**

DLH researcher **Xin Yuan** was among the authors of an [article](#) published in *The Journal of the Association of Nurses in AIDS Care: JANAC* (Online Ahead of Print: July 2023; Print: September/October 2023). Problems paying medical bills may affect HIV outcomes among people with HIV (PWH), thus limiting progress toward achieving national HIV prevention goals. The authors analyzed nationally representative data from CDC's Medical Monitoring Project collected during 6/2018-5/2020. Among 8,108 PWH, weighted percentages of characteristics were reported and associations examined between problems paying medical bills and clinical outcomes using prevalence ratios with predicted marginal means, adjusting for potential confounding. Nineteen percent of PWH reported problems paying medical bills. Problems paying medical bills were more prevalent among persons who experienced homelessness. People with problems paying medical bills were more likely to have adverse HIV outcomes and were more likely to have  $\geq 1$  emergency room visit or hospitalization in the past year. Identifying PWH experiencing financial barriers and expanding access to safety net programs could improve access to care and outcomes. *Other authors include researchers from the Centers for Disease Control and Prevention.*

## **Benefits of Frequent HIV Testing in the THRIVE Demonstration Project: United States, 2015-2020**

DLH researcher **Lei Yu** was among the authors of an [article](#) published in the *American Journal of Public Health* (Epub: July 2023; Print: September 2023). The authors' objectives were to describe HIV testing among clients in the Targeted Highly Effective Interventions to Reverse the HIV Epidemic (THRIVE) demonstration project and evaluate testing frequency. The authors identified factors associated with an average testing frequency of 180 days or less compared with more than 180 days using adjusted Poisson regression models. Among 5710 clients with 2 or more tests and no preexposure prophylaxis (PrEP) prescription, 42.4% were tested frequently. Black/African American clients were 21% less likely and Hispanic/Latino clients were 18% less likely to be tested frequently than were White clients. Among 71 Black/African American and Hispanic/Latino cisgender men who have sex with men and transgender women with HIV diagnoses, those with frequent testing had a median time to diagnosis of 137 days, with a diagnostic testing yield of 1.5% compared with those tested less frequently, with 559 days and 0.8% yield. The authors concluded that HIV testing at least every 6 months resulted in earlier HIV diagnosis and was efficient. Persons in communities with high rates of HIV who are not on PrEP can benefit from frequent testing, and collaborative community approaches may help reduce disparities. *Other authors include researchers from the Centers for Disease Control and Prevention, New York City Department of Health and Mental Hygiene, the District of Columbia Department of Health, and the Johns Hopkins School of Medicine.*

## **Cannabis Use and Sleep Disturbances Among White, Black, and Latino Adults in the United States: A Cross-sectional Study of National Comorbidity Survey-Replication (2001-2003) Data**

DLH researcher **W. Braxton Jackson II** was among the authors of an [article](#) published in *Sleep Health* (Epub: August 2023; Print: October 2023). Research investigating cannabis use and sleep health is limited, and results are mixed. Few studies were nationally representative with racially-ethnically diverse samples or assessed potential modifiers. The objective was to investigate cross-sectional associations between reported cannabis use and sleep disturbances by potential modifiers among non-Hispanic White, non-Hispanic Black, and Hispanic/Latino men and women in the United States. The authors used nationally representative National Comorbidity Survey-Replication data collected from 2001 to 2003 among 3929 adults. Models adjusted for sociodemographic, health behavior, and clinical characteristics were stratified by race-ethnicity and by race-ethnicity along with sex/gender, and age, separately. Over half of adults reported cannabis use (52%-ever/lifetime vs 48%-never). Two latent classes were identified: multiple sleep disturbances with daytime sleepiness and no sleep disturbances with some daytime sleepiness. Prevalence of multiple sleep disturbances with daytime sleepiness was higher among participants reporting lifetime cannabis use (23% vs 20%). Associations did not vary by race-ethnicity or sex/gender. Lifetime vs never cannabis use was marginally associated with a higher prevalence of multiple sleep disturbances with daytime sleepiness only among adults aged 25-29 years. The authors concluded that associations between cannabis use and sleep may vary by age. Replication with more recent data and prospective studies that investigate intersectional identities among diverse populations with objective assessments are warranted. *Other authors include researchers from the National Institute of Environmental Health Sciences, National Institute on Alcohol Abuse and Alcoholism, and the Department of Biobehavioral Health at the Pennsylvania State University.*

## **Moon, Mars and Minds: Evaluating Parkinson's Disease Mortality Among U.S. Radiation Workers and Veterans in the Million Person Study of Low-Dose Effects**

DLH researcher **Sarah Cohen** was among the authors of an [article](#) published in *Zeitschrift für Medizinische Physik* (Epub: August 2023 [Print: February 2024]). Radiation is one of the most important stressors related to missions in space beyond Earth's orbit. Epidemiologic studies of radiation-exposed workers have reported elevated rates of Parkinson's disease but the relationship between cognitive dysfunction and low-dose radiation in humans remains poorly defined. A meta-analysis was conducted of six cohorts in the Million Person Study (MPS) of low-dose health effects to assess whether there is consistent evidence that Parkinson's disease is associated with radiation dose to the brain. The six cohorts include medical radiation workers, industrial radiographers, nuclear power plant workers, atomic veterans, and Manhattan Project workers at the Los Alamos National Laboratory and at Rocky Flats. Consistent methods were used for all cohorts to estimate organ-specific brain doses and to obtain vital status and cause of death. The meta-analysis includes 517,608 workers and 17,219,001 person-years of observation. Five of the six cohorts revealed positive associations with Parkinson's disease. The overall summary estimate from the meta-analysis was statistically significant based on 1573 deaths due to Parkinson's disease. The authors concluded that Parkinson's disease was positively associated with radiation in the MPS cohorts, indicating the need for careful evaluation as to causality in other studies, delineation of possible mechanisms, and assessing possible implications for space travel as well as radiation protection guidance for terrestrial workers. *Other authors include researchers from the Memorial Sloan Kettering Cancer Center, University of Zürich, and National Council on Radiation Protection and Measurements.*

## **Polygenic Risk Score for Parkinson's Disease and Olfaction Among Middle-Aged to Older Women**

DLH researcher **Aimee D'Aloisio** was among the authors of an [article](#) published in *Parkinsonism & Related Disorders* (Epub: August 2023; Online: October 2023). Olfactory impairment and Parkinson's disease (PD) may share common genetic and environmental risk factors. This study investigates the association of a PD polygenic risk score (PRS) with olfaction, and whether the associations are modified by environmental exposures of PM2.5, NO2, or smoking. This analysis included 3358 women (aged 50-80) from the Sister Study with genetic data and results from the Brief Smell Identification Test (B-SIT) administered in 2018-2019. As expected, PD PRS was strongly associated with the odds of having PD. For individual B-SIT items, the highest PRS quartile was generally associated with lower odds of correctly identifying the odorant, albeit only statistically significant for pineapple, soap, and rose. The association of PD PRS with olfactory impairment was not modified by airborne environmental exposures or smoking. These preliminary data suggest that high PD genetic susceptibility is associated with olfactory impairment in middle-aged and older women. *Other authors include researchers from Michigan State University College of Human Medicine, National Institute on Aging, Georgetown University, National Institute of Environmental Health Sciences, and the National Institute of Neurological Disorders and Stroke.*

## **Ambient Air Pollutants and Olfaction Among Women 50-79 Years of Age from the Sister Study**

DLH researchers **Aimee D'Aloisio**, **Lourdes Suarez**, and **Sandra Deming-Halverson** were among the authors of an [article](#) published in *Environmental Health Perspectives* (Epub/Online: August 2023). Poor olfaction is common in older adults and may have

profound adverse implications on their health. However, little is known about the potential environmental contributors to poor olfaction. The authors investigated ambient fine particulate matter [PM  $\leq 2.5\mu\text{m}$  in aerodynamic diameter (PM<sub>2.5</sub>)] and nitrogen dioxide (NO<sub>2</sub>) in relation to poor olfaction in middle-aged to older women. The Sister Study is a nationwide cohort of 50,884 women in the United States with annual average air pollutant exposures estimated based on participants' residences from enrollment (2003-2009) through 2017. This analysis was limited to 3,345 women, 50-79 years of age as of January 2018, who completed the Brief Smell Identification Test (B-SIT) in 2018-2019. Poor olfaction was defined as a B-SIT score of  $\leq 9$  in the primary analysis. Overall, the authors found little evidence for associations of air pollutants with poor olfaction. Results were similar in the analyses using the most recent (2017) or the cumulative average (2006-2017) air pollutant exposure data. Secondary analyses suggested potential association in certain subgroups. The OR per IQR was 1.35 for PM<sub>2.5</sub> among younger participants (<54.2 years of age) and 1.87 for NO<sub>2</sub> among current smokers. This study did not find convincing evidence that air pollutants have lasting detrimental effects on the sense of smell of women 50-79 years of age. The subgroup analyses are exploratory, and the findings need independent confirmation. *Other authors include researchers from Michigan State University College of Human Medicine, National Institute of Environmental Health Sciences, and the University of Washington School of Medicine.*

### **Postpartum Family Planning Uptake in Uganda: Findings From the Lot Quality Assurance Sampling Survey**

DLH researchers **Florence Nakaggwa, Derrick Kimuli, Kenneth Kasule, Justine Fay Katwesige, Norah Namuwenge, Rebecca Nsubuga, Barbara Amuron, Daraus Bukenya, and Bonnie Wandera** were among the authors of an [article](#) published in *Contraception and Reproductive Medicine* (Online: August 2023). The initiation and use of family planning (FP) services within the first 12 months following childbirth, postpartum family planning (PPFP), promotes safe motherhood by reducing unintended pregnancies and ensuring appropriate pregnancy spacing. However, there is a paucity of information on PPFP uptake from community surveys. This study aimed to quantify the reported use of PPFP and identify predictors and barriers to PPFP uptake from a large community survey. The authors analyzed data collected from the 2021 Lot Quality Assurance Sampling (LQAS) survey, a cross-sectional community and household survey that covered 68 districts in Uganda. Data collected from mothers of children aged 12 months or younger on reproductive health and FP were abstracted and analyzed. PPFP use was defined as the reported use of modern FP by the mother or their partner. Overall, 8103 mothers of children aged less than 12 years were included in the analysis; the majority of mothers, 55.8% were above 24 years while 11.7% were 19 years and under. 98% of the mothers attended at least one antenatal care visit and 86.3% delivered at a health facility. Only 10% of mothers who participated in the survey reported PPFP use at the time of the survey. Reporting of PPFP use was 5 times higher among mothers of children aged 7-12 months, 50% higher among mothers with secondary education, 80% higher among breastfeeding mothers, and 30% lower among those that did not receive a health worker visit within 3 months preceding the survey. Among 4.6% who stated a reason for non-use of PPFP, the most cited reasons for not using were breastfeeding 43%, fear of side effects 26.9%, respondent/partner opposition 17.6%, and infrequent sex 12.1%. The researchers concluded the analysis showed a low proportion of PPFP uptake among mothers of children under 12 years. Possible barriers included child age, education, a health worker visit, and side effects, and perceived benefits of possibly improperly implementing lactation amenorrhea method. Integration of social, community, and health services could provide a more



holistic approach to improving PFP uptake. *Other authors include researchers from the Office of Health and HIV at USAID/Uganda and the Office of Family Planning and Reproductive Health at USAID (Washington, DC).*

### **Association of Genital Talc and Douche Use in Early Adolescence or Adulthood With Uterine Fibroids Diagnoses**

DLH researcher **Aimee D'Aloisio** was among the authors of an [article](#) published in the *American Journal of Obstetrics and Gynecology* (Epub: August 2023; Online: December 2023). Genital talc and douching are practices that can involve exposure to chemical compounds linked to certain gynecologic cancers. However, it is unclear if they are associated with fibroid risk or age at fibroid diagnosis among women. This study aimed to evaluate the impact of early-adolescence genital talc use and douching on prevalence of fibroids diagnosed before the age of 35 and 50 years among Black/African American and non-Hispanic White women. Data were derived from the Sister Study (2003-2020), a prospective cohort of 50,884 US women aged 35 to 74 years at enrollment. Participants were asked if they ever had a fibroid diagnosis and at what age, and if they used genital talc and/or douched between the ages of 10 and 13 years or in the past 12 months. After applying predefined exclusion criteria, the analytical sample size was n=46,316 (Black, n=4310; non-Hispanic White, n=42,006). The authors adjusted for early life factors (in utero diethylstilbestrol exposure, singleton or multiple birth, fed soy formula during infancy), childhood socioeconomic status, and relative weight and height compared with peers at age 10. Results were stratified by race/ethnicity given that Black women are more likely to develop fibroids at a younger age than non-Hispanic White women. Among Black/African American women, 29% had fibroids diagnosed before age 35. Both genital talc use at age 10 to 13 and douching were associated with higher odds of having a fibroid diagnosed before age 35. Douching without talc use was not associated with increased odds, but combined use of genital talc and douche was associated with 52% increased odds of fibroids. Among non-Hispanic White women, 9% reported fibroids diagnosed before age 35. Genital talc use but not douching at age of 10 to 13 years was associated with having a fibroid diagnosed before age 35. Similar patterns were observed for non-Hispanic White women when fibroids were diagnosed before age 50, but neither practice was associated with fibroids diagnosed before age 50 in Black women. Genital talc use in early adolescence, alone and in combination with douching (but not douching alone), is associated with prevalence of fibroids diagnosed before age 35 among Black/African American women and before ages 35 and 50 among non-Hispanic White women. Early adolescence may be a window of susceptibility for fibroid development, suggesting that adolescent girls should be educated on abstention from or alternatives to talc use and douching. *Other authors include researchers from the National Institute of Environmental Health Sciences and the National Cancer Institute.*

### **Immunotoxicity of N-Butylbenzenesulfonamide: Impacts on Immune Function in Adult Mice and Developmentally Exposed Rats**

DLH researcher **Caroll Co** was among the authors of an [article](#) published in *Toxicological Sciences* (Online Ahead of Print: August 2023; Print: October 2023). N-Butylbenzenesulfonamide (NBBS) is a high production volume plasticizer that is an emerging contaminant of concern for environmental and human health. To understand the risks and health effects of exposure to NBBS, studies were conducted in adult exposed mice and developmentally exposed rats to evaluate the potential for NBBS to modulate the immune system. Beginning between 8-9 weeks of age, dosed feed containing NBBS at concentrations of 0, 313, 625, 1250, 2500, and 5000 ppm was continuously provided

to B6C3F1/N female mice for 28 days. Dosed feed was also continuously provided to time-mated Harlan Sprague Dawley (HSD: Sprague Dawley® SD®) rats at concentrations of 0, 250, 500 and 1000 ppm NBBS from gestation day 6 to postnatal day 28 and in F1 rats until 11-14 weeks of age. Functional assessments of innate, humoral and cell-mediated immunity were conducted in adult female mice and F1 rats following exposure to NBBS. In female mice, NBBS treatment suppressed the antibody forming cell response to SRBC with small increases in T cell responses and NK cell activity. In developmentally exposed rats, NBBS treatment-related immune effects were sex-dependent. A positive trend in natural killer (NK) cell activity occurred in male F1 rats while a negative trend occurred in female F1 rats. The AFC response to SRBC was decreased in female F1 rats but not in male F1 rats. These data provide evidence that oral exposure to NBBS has the potential to produce immunomodulatory effects on both innate and adaptive immune responses, and these effects appear to have some dependence on species, sex, and period of exposure (developmental vs. adult). *Other authors include researchers from the National Institute of Environmental Health Sciences.*

### **The Capacity of HIV Care Facilities to Implement Strategies Recommended by the Ending the HIV Epidemic Initiative: The Medical Monitoring Project Facility Survey**

DLH researcher **Anne Xin Yuan** was among the authors of an [article](#) published in the *Journal of Acquired Immune Deficiency Syndromes* (Online Ahead of Print: August 2023; Print: December 2023). Data are needed to assess the capacity of HIV care facilities to implement recommended Ending the HIV Epidemic (EHE) activities. The researchers analyzed 2021 survey data from a census of 514 U.S HIV care facilities providing care to a national probability sample of U.S. adults with HIV. Weighted estimates were presented of facility characteristics, services, and policies, and estimates of the proportion of all U.S. HIV patients attending these facilities. Among HIV care facilities, 37% were private practices, 72% were in areas with population >1 million, and 21% had over 1000 HIV patients. Most provided preexposure prophylaxis (PrEP, 83%) and postexposure prophylaxis (PEP, 84%). Over 67% of facilities provided HIV-specific stigma or discrimination training for all staff (covering 70% of patients) and 66% provided training on cultural competency (covering 74% of patients). A majority of patients attended facilities that provided on-site access to HIV/STI transmission risk reduction counseling (89%); fewer had on-site access to substance use disorders treatment (35%). Low provision of on-site assistance was found with food banks or meal delivery (14%) and housing (33%). Approximately 71% of facilities reported using data to systematically monitor patient retention in care. On-site access to adherence tools was available at 58% of facilities; 29% reported notifying patients of missed prescription pickups. The results indicate some strengths that support EHE-recommended strategies among HIV care facilities, such as high availability of PrEP/PEP, as well as areas for improvement, such as provision of staff anti-stigma trainings and adherence supports. *Other authors include researchers from the Centers for Disease Control and Prevention.*

### **Evaluating the Impact of Point-of-Care HIV Viral Load Assessment on Linkage to Care in Baltimore, MD: A Randomized Controlled Trial**

DLH researcher **Debra Daugherty** was among the authors of an [article](#) published in *BMC Infectious Diseases* (Online: September 2023). Integration of a sensitive point-of-care (POC) HIV viral load (VL) test into screening algorithms may help detect acute HIV infection earlier, identify people with HIV (PWH) who are not virally suppressed, and facilitate earlier referral to antiretroviral therapy (ART), or evaluation for pre-exposure prophylaxis (PrEP). This report describes a randomized clinical trial sponsored by the

Centers for Disease Control and Prevention (CDC): “Ending the HIV Epidemic Through Point-of-Care Technologies” (EHPOC). The study’s primary aim is to evaluate the use of a POC HIV VL test as part of a testing approach and assess the impact on time to linkage to ART or PrEP. The study will recruit people in Baltimore, Maryland, including patients attending a hospital emergency department, patients attending an infectious disease clinic, and people recruited via community outreach. The secondary aim is to evaluate the performance characteristics of two rapid HIV antibody tests approved by the United States Food and Drug Administration (FDA). The study will recruit people 18 years or older who have risk factors for HIV acquisition and are not on PrEP, or PWH who are not taking ART. Participants will be randomly assigned to either the control arm or the intervention arm. Participants randomized to the control arm will only receive the standard-of-care (SOC) HIV screening tests. Intervention arm participants will receive a POC HIV VL test in addition to the SOC HIV diagnostic screening tests. Follow-up will consist of an interim phone survey conducted at week 4 and an in-person week 12 visit. Demographic and behavioral information, and oral fluid and blood specimens will be collected at enrollment and at week 12. Survey data will be captured in a Research Electronic Data Capture (REDCap) database. Participants in both arms will be referred for either ART or PrEP based on their HIV test results. The EHPOC trial will explore a novel HIV diagnostic technology that can be performed at the POC and provide viral assessment. The study may help inform HIV testing algorithms and contribute to the evidence to support same day ART and PrEP recommendations. *Other authors include researchers from the Centers for Disease Control and Prevention and Johns Hopkins University.*

### **Using Serial Cross-Sectional Surveys to Create a Retrospective Nested Cohort to Determine HIV Incidence from 20 U.S. Cities**

DLH researcher **Julie Berg** was among the authors of an [article](#) published in *AIDS (London, England)* (Epub: September 2023; Print: December 2023). The aim is to estimate HIV incidence using successive cross-sectional surveys by creating retrospective nested cohorts among men who have sex with men (MSM), people who inject drugs (PWID), and heterosexually active persons (HET). Cohorts were created among participants who had at least one repeat observation across four surveillance cycles from National HIV Behavioral Surveillance in 20 U.S. cities. Repeat participants were identified using a combination of date of birth, race/ethnicity, metropolitan statistical area, and gender. The analysis was limited to participants who tested negative for HIV at baseline and were assumed to be at-risk between cycles. HIV incidence was higher among younger MSM, Black MSM (compared to white MSM), and PWID residing in the South and Territories (compared to the Midwest). These estimates are consistent with previously published incidence estimates from prospective cohort studies among these populations. Using repeat cross-sectional surveys to simulate a cohort may serve as another strategy in estimating HIV incidence. *Other authors include researchers from the Centers for Disease Control and Prevention and Ghent University Hospital (Belgium).*

### **Ambient Fine Particulate Matter and Breast Cancer Incidence in a Large Prospective US Cohort**

DLH researcher **Marina Sweeney** was among the authors of an [article](#) published in the *Journal of the National Cancer Institute* (Online Ahead of Print: September 2023 [Print: January 2024]). Fine particulate matter (PM<sub>2.5</sub>) has been inconsistently associated with breast cancer incidence, however few studies have considered historic exposure when levels were higher. Outdoor residential PM<sub>2.5</sub> concentrations were estimated using a nationwide spatiotemporal model for women in the NIH-AARP Diet and Health Study, a

prospective cohort located in 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan) and enrolled in 1995-1996 (N = 196,905). Annual average PM<sub>2.5</sub> concentrations were estimated for a 5-year historical period 10 years prior to enrollment (1980-1984). With follow-up through 2017, 15,870 breast cancer cases were identified. A 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> was significantly associated with overall breast cancer incidence. The association was evident for ER+, but not ER- tumors. Overall, breast cancer HRs were >1 across the catchment areas; ranging from a HR = 1.26 for North Carolina to a HR = 1.04 for Louisiana. In this large U.S. cohort with historical air pollutant exposure estimates, PM<sub>2.5</sub> was associated with risk of ER+ breast cancer. State-specific estimates were imprecise but suggest that future work should consider region-specific associations and the potential contribution of PM<sub>2.5</sub> chemical constituency in modifying the observed association. *Other authors include researchers from the National Institute of Environmental Health Sciences, National Cancer Institute, and the University of Washington School of Public Health.*

### **Adverse Pregnancy Outcomes Among HIV-infected Women Taking Isoniazid Preventive Therapy During the First Trimester**

DLH researcher **Laura Moran** was among the authors of an [article](#) published in *Clinical Infectious Diseases* (Online Ahead of Print: September 2023). Tuberculosis prevention using isoniazid (IPT) is recommended for people with HIV, yet data on the safety of first-trimester pregnancy exposure are limited. The method was a planned secondary analysis in a TB prevention trial of adverse pregnancy outcomes among participants assigned to 9-month IPT who became pregnant during (IPT-exposed) or after (unexposed) IPT. Regression models compared binary outcomes of a composite adverse outcome (any non-live birth, excluding induced abortion); preterm delivery <37 weeks; and low birth weight <2500 g) among exposure groups. Models were adjusted for latent TB infection, maternal age, CD4 count, and antiretroviral therapy (ART). The results showed that 128 participants had a known pregnancy outcome; 39 IPT-exposed and 89 unexposed. At pregnancy outcome, ART use was lower in IPT-exposed (79%) than unexposed women (98%). Overall, 29 pregnancies ended in a composite adverse outcome (25 spontaneous abortions, 2 stillbirths, and 2 ectopic pregnancies), 15 preterm deliveries, and 10 infants with low birth weight. IPT was associated with the composite adverse outcome adjusting for covariates at enrollment, but the effect was attenuated when adjusted for covariates at pregnancy outcome; IPT was not associated with preterm delivery or low birth weight. The authors concluded first-trimester IPT exposure was associated with nearly two-fold increased risk of fetal demise, mostly spontaneous abortion, though the association was attenuated when adjusted for covariates proximal to pregnancy outcome including ART use. Further study is needed to inform TB prevention guidelines. *Other authors include researchers from Johns Hopkins University School of Medicine, Harvard TH Chan School of Public Health, Thai Red Cross AIDS Research Centre and Center of Excellence in Tuberculosis, University of Witwatersrand (South Africa), Les Centres GHESKIO (Haiti), and Botswana Harvard AIDS Institute Partnership.*

### **Genetic Deletion of α7 nAChRs Reduces Hippocampal Granule and Pyramidal Cell Number in Both Sexes But Impairs Pattern Separation in Males Only**

DLH researcher **Gary Larson** was among the authors of an [article](#) published in *Frontiers in Neuroscience* (eCollection 2023, Online: September 2023). Neurogenesis within the dentate gyrus is thought to play an important role in cognitive processes such as reversal learning and pattern separation. The α7 nicotinic acetylcholine receptor (α7 nAChR) is expressed early in newly formed granule cells of the dentate gyrus, though its role in

neurogenesis and related cognitive function is not fully understood. To better characterize relevant function of  $\alpha 7$  nAChRs, the authors performed unbiased stereology to quantify hippocampal granule cells, pyramidal cells, and total volume and used a touchscreen operant spatial discrimination/reversal task to test pattern separation in a global  $\alpha 7$  nAChR knockout mouse line. The knockout resulted in an  $\approx 22\%$  reduction in granule cells and a  $\approx 20\%$  reduction in pyramidal cells in both sexes, with no change in total hippocampal volume. However, the knockout impaired performance in the touchscreen task for males only. The sex-dependent difference in behavioral, but not stereological, results suggest a divergence in the structure-function relationship in males versus females. Detailed analyses revealed males were more biased by the initial reversal contingency relative to females indicating a potential source of the sex-specific interaction with the loss of  $\alpha 7$  nAChRs. These findings argue that the  $\alpha 7$  nAChR plays a critical role in hippocampal development, not just granule cell neurogenesis, and plays a sex-dependent role in cognitive function. *The other authors are researchers from the National Institute of Environmental Health Sciences.*

### **Epidemiology of Infantile Ureteropelvic Junction Obstruction in the US**

DLH researchers **Chyng-Wen Fwu** and **Kara Bennett** were among the authors of an [article](#) published in *Urology* (Epub: October 2023 [Print: January 2024]). The objective was to describe sex- and diagnosis-specific comorbidities, outcomes, and secular trends associated with ureteropelvic junction obstruction (UPJO) in a large, real-world population diagnosed with hydronephrosis in infancy. The authors identified all infants  $\leq 1$  year old with  $\geq 1$  claim in the Optum<sup>©</sup> Clinformatics<sup>®</sup> 2007-2020 nationwide population database and used univariable and multivariable Cox regression analyses to estimate associations of demographic and clinical characteristics of infants with a UPJO diagnosis with surgical status. Of 22,349 infants with hydronephrosis, 1722 had UPJO. Follow-up was  $\geq 1$  year in 1,198 and  $\geq 3$  years in 555 cases, and UPJO repair was performed in 542 children; 77.7% within 1 year and 97.3% within 3 years. UPJO repair was associated with prior UTI and South or Midwest geographic region but did not change over time. This population-based study provides a real-world view of postnatally diagnosed hydronephrosis, focusing on UPJO, for which 522 cases had  $\geq 3$  years continuous coverage. UPJO-associated comorbidities were more common in females, and the frequencies of UPJO-associated surgery and comorbidities were higher than in other studies. Other than UTI, no other associated kidney or urinary tract diagnoses were associated with UPJO repair. The authors identified unique sex- and diagnosis-specific differences in associated comorbidities and interventions in children diagnosed with UPJO in the first year of life. *The other authors are researchers from the National Institute of Diabetes and Digestive and Kidney Diseases.*

### **Probable Parasomnias and Mortality: A Prospective Study in US Men**

DLH researcher **Samantha Molsberry\*** was among the authors of an [article](#) published in *Mayo Clinic Proceedings* (Print: October 2023). The objective was to examine the association between parasomnias, including rapid eye movement sleep behavior disorder (RBD) and sleepwalking (SW), and mortality risk in a large-scale population-based cohort. This prospective cohort study was based on 25,695 participants from the Health Professionals Follow-up Study, a population-based cohort of male health professionals in the United States. Of the studied population, 223 reported probable SW (pSW) and 2720 reported probable rapid eye movement sleep behavior disorder (pRBD). During 6 years of follow-up (2012 to 2018), 4743 mortality cases were documented. The co-occurrence of both probable parasomnias was associated with higher all-cause mortality risk, and

the adjusted hazard ratio (HR) of mortality was 1.65 compared with participants without either probable parasomnia after adjustment for major lifestyle, sleep, and metabolic risk factors, and chronic diseases. Significant associations were found for mortality attributed to neurodegenerative diseases and accidents. Having pSW alone was associated with all-cause mortality, and pSW and pRBD were individually associated with mortality attributed to neurodegenerative diseases and accidents too. Probable parasomnia was associated with a higher risk of all-cause mortality and mortality attributed to neurodegenerative diseases and accidents. \*Dr. Molsberry completed this research as a follow-up to her post-doctoral research performed while at the Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, Massachusetts. *Other authors include researchers from the Pennsylvania State University, Brigham and Women's Hospital and Harvard Medical School, Harvard T.H. Chan School of Public Health, Massachusetts General Hospital, and Fudan University (China).*

### **Association of Redlining and Natural Environment with Depressive Symptoms in Women in the Sister Study**

DLH researcher **Aimee D'Aloisio** was among the authors of an [article](#) published in *Environmental Health Perspectives* (Epub: October 2023). Improving mental health is recognized as an important factor for achieving global development goals. Despite strong evidence that neighborhood greenery promotes better mental health, there are environmental justice concerns over the distribution of neighborhood greenery. Underlying these concerns are present-day consequences of historical discriminatory financial investment practices, such as redlining, which was established by the U.S. Federal Home Owners' Loan Corporation (HOLC) in the 1930s. The impacts of redlining on environmental and health disparities have been researched extensively. However, the influences of redlining on the associations between neighborhood environment and health outcomes have not been fully assessed. The aim of this study was to examine whether associations between residential tree cover and depressive symptoms vary across areas subject to HOLC practices. Depressive symptoms were defined by the 10-item Center for Epidemiologic Studies Depression Scale collected during the period 2008-2012 for 3,555 women in the Sister Study cohort residing in cities subject to HOLC practices across the United States. HOLC rating maps were obtained from the Mapping Inequality Project, University of Richmond, with neighborhoods graded as A (best for financial investment, green), B (still desirable, blue), C (declining, yellow), and D (hazardous, red-known as redlined). Tree cover within 500m and 2,000m from residences was estimated using 2011 U.S. Forest Service Percent Tree Canopy Cover. Tree cover was significantly higher in neighborhoods with better HOLC grades. A 10% increase in tree cover was associated with reduced odds of depressive symptoms for the full study population. Across HOLC grades, the strongest associations were observed in redlined neighborhoods. Findings support a remediation strategy focused on neighborhood greenery that would address multiple public health priorities, including mental health and environmental justice. *The other authors are researchers from the U.S. Environmental Protection Agency and the National Institute of Environmental Health Sciences.*

### **Level of Minimum Acceptable Diet and Its Associated Factors Among Children Aged 12-23 Months in Ugandan Districts**

DLH researchers **Derrick Kimuli, Florence Nakaggwa, Kenneth Kasule, Immaculate Kiconco, Justine Fay Katwesige, Rebecca Nsubuga, Barbara Amuron, Daraus Bukenya, Bonnie Wandera, and Norah Namuwenge** were among the authors of an [article](#) published in *PLoS One* (eCollection 2023, Online: October 2023). Uganda has made notable progress

in improving child nutrition indicators, albeit not fast enough to meet global targets. Navigating the landscape of child nutrition in Uganda demands attention, particularly in light of the necessity for a minimum acceptable diet (MAD) for children aged 12-23 months. While the focus on local nutritional planning is crucial, the absence of routine-specific nutritional status data creates a significant information gap. To bridge this void, this study used datasets from the 2021 Lot Quality Assurance Sampling (LQAS) survey. Data were analyzed using multilevel mixed-effects logistic regression (clustering districts based on regional boundaries). Of the 7,111 children surveyed, 3,256 (49.20%) received the minimum meal frequency, 695 (9.80%) received the minimum dietary diversity, and only 380 (5.34%) received the MAD. There was a notable variation in the proportion of children that received the MAD across regions and districts. Children living in urban areas, children whose mothers had a higher education, and children whose mothers had a diverse diet were more likely to receive the MAD. Children were less likely to receive the MAD if they lived in a household that did not receive a health worker visit within the year. These findings suggest a need to prioritize initiatives aimed at increasing dietary diversity among children in Uganda. This could be done through a variety of approaches, such as leveraging the use of home gardens to boost nutrition through diverse crop cultivation, demonstration gardens, and offering nutrition counselling through village health teams. *The DLH authors are also researchers from the United States Agency for International Development (USAID) Strategic Information Technical Support Activity, Kampala, Uganda; the other authors are researchers from USAID Uganda, US Mission Compound-South Wing, Kampala, Uganda.*

### **High Pesticide Exposures Events, Pesticide Poisoning, and Shingles: A Medicare-Linked Study of Pesticide Applicators in the Agricultural Health Study**

DLH researchers **Darya Leyzarovich** and **Shelly-Ann Love** were among the authors of an [article](#) published in *Environment International* (Epub: October 2023; Online: November 2023). Self-reported shingles was associated with history of high pesticide exposure events (HPEE) in licensed pesticide applicators aged >60 years in the Agricultural Health Study (AHS). In the current study, using AHS-linked Medicare claims data, the authors examined incident shingles in relation to pesticide-related illness and pesticide poisoning, as well as HPEE. The authors studied 22,753 licensed private pesticide applicators (97% white males, enrolled in the AHS 1993-97), aged  $\geq 66$  years with >12 consecutive months of Medicare fee-for-service hospital and outpatient coverage between 1999 and 2016. Incident shingles was identified based on having  $\geq 1$  shingles claim(s) after 12 months without claims. At AHS enrollment, participants were asked if they ever sought medical care or were hospitalized for pesticide-related illness, and a supplemental questionnaire (completed by 51%) asked about HPEE and poisoning. Over 192,053 person-years (PY), 2396 applicators were diagnosed with shingles, with higher rates among those reporting hospitalization for pesticide-related illness, pesticide poisoning, and HPEE. In adjusted models, shingles was associated with hospitalization for pesticide-related illness, poisoning, and HPEE, especially HPEE plus medical care/poisoning. These novel findings suggest that acute, high-level, and clinically impactful pesticide exposures may increase risk of shingles in subsequent years to decades following exposure. *Other authors include researchers from the National Institute of Environmental Health Sciences and the National Cancer Institute.*

## **Association of Obesity, Metabolic Syndrome, and Diabetes With Urinary Incontinence and Chronic Kidney Disease: Analysis of the National Health and Nutrition Examination Survey, 2003-2020**

DLH researcher **Chyng-Wen Fwu** was among the authors of an [article](#) published in the *Journal of Urology* (Epub: October 2023 [Print: January 2024]). Diabetes and obesity, components of the metabolic syndrome (MetS), are risk factors for urinary incontinence (UI) and chronic kidney disease (CKD). The authors interrogated US population-based data to explore independent, sex-specific associations between nondiabetic MetS, with and without obesity, and UI and/or CKD. The authors analyzed data from 8586 males and 8420 females  $\geq 20$  years from the National Health and Nutrition Examination Survey. Multivariable logistic regression models were used to examine associations of UI or CKD with diabetes and 4 nondiabetic obesity/metabolic phenotypes: non-MetS/nonobese, MetS/nonobese, non-MetS/obese, and MetS/obese. Male MetS/obese participants had increased odds of any UI and urgency UI, compared with non-MetS/nonobese participants. Female MetS/obese participants had increased odds of any UI, stress UI, and mixed UI compared with non-MetS/nonobese participants. The odds of co-occurring UI/CKD were increased relative to either condition alone in persons with diabetes, and in males with MetS/obese phenotypes and females with MetS phenotypes as compared to same sex participants with neither obesity nor MetS. The authors found novel associations between MetS/obese and urgency UI in males without diabetes, and between SUI and both MetS and obesity in females without diabetes. Odds estimates for UI/CKD were increased by existing obesity or MetS as compared to those for UI or CKD alone. Improved understanding of modifiable factors associated with UI will inform prevention and treatment opportunities. *The other authors are researchers from the National Institute of Diabetes and Digestive and Kidney Diseases.*

## **Partial or Complete Loss of Norepinephrine Differentially Alters Contextual Fear and Catecholamine Release Dynamics in Hippocampal CA1**

DLH researcher **Kathryn Konrad** was among the authors of an [article](#) published in *Biological Psychiatry Global Open Science* (Print: October 2023). Contextual fear learning is heavily dependent on the hippocampus. Despite evidence that catecholamines contribute to contextual encoding and memory retrieval, the precise temporal dynamics of their release in the hippocampus during behavior is unknown. In addition, new animal models are required to probe the effects of altered catecholamine synthesis on release dynamics and contextual learning. The authors generated two new mouse models of altered locus coeruleus-norepinephrine (NE) synthesis and utilized them together with GRABNE and GRABDA sensors and in vivo fiber photometry to investigate NE and dopamine (DA) release dynamics in the dorsal hippocampal CA1 during contextual fear conditioning. Aversive foot shock increased both NE and DA release in the dorsal CA1, while freezing behavior associated with recall of fear memory was accompanied by decreased release. The authors found that freezing at the recent time point was sensitive to both partial and complete loss of locus coeruleus-NE synthesis throughout prenatal and postnatal development, similar to previous observations of mice with global loss of NE synthesis beginning postnatally. In contrast, freezing at the remote time point was compromised only by complete loss of locus coeruleus-NE synthesis beginning prenatally. Overall, these findings provide novel insights into the role of NE in contextual fear and the precise temporal dynamics of both NE and DA during freezing behavior and highlight complex relationships between genotype, sex, and NE signaling. *The other authors are researchers from the National Institute of Environmental Health Sciences and the Connecticut Institute for the Brain & Cognitive Sciences.*



## **Unmet Needs for Ancillary Services and Associations with Clinical Outcomes Among Transgender Women with Diagnosed HIV: Medical Monitoring Project, United States, 2015-2020**

DLH researcher **Tamara Carree** was among the authors of an [article](#) published in *LGBT Health* (Epub: October 2023 [Print: February-March 2024]). Access to ancillary services—including HIV support services, non-HIV clinical services, and subsistence services—can support care engagement and viral suppression and reduce disparities among people with HIV (PWH). The authors used representative U.S. data to assess differences in unmet needs for ancillary services between transgender women with HIV and other PWH. In addition, associations between unmet needs and clinical outcomes were examined among transgender women. 2015-2020 Medical Monitoring Project data among transgender women (N = 362), cisgender men (N = 17,319), and cisgender women (N = 6016) with HIV were analyzed. Among transgender women, unmet needs were highest for dental care (24.9%), shelter or housing (13.9%), and transportation assistance (12.6%). Transgender women were more likely than cisgender men to have unmet subsistence needs. Among transgender women, unmet needs for ancillary services were negatively associated with many clinical outcomes after adjusting for age and race/ethnicity. Unmet needs for subsistence services were associated with higher levels of antiretroviral therapy nonadherence and detectable viral loads, emergency room visits, and depression or anxiety symptoms. Transgender women with HIV were more likely than cisgender men with HIV to experience unmet needs for subsistence services—likely a reflection of substantial socioeconomic disadvantage. Addressing unmet needs is an essential step for improving care outcomes among transgender women with HIV. *The other authors are researchers from the Centers for Disease Control and Prevention.*

## **Longitudinal Study of Comorbidities and Clinical Outcomes in Persons with Gallstone Disease Using Electronic Health Records**

DLH senior epidemiologist **Constance Ruhl** and DLH epidemiologist **Jane Der** co-authored an [article](#) published in the *Journal of Gastrointestinal Surgery* (Epub: November 2023; Print: December 2023). Gallstone disease (GSD) is common and leads to significant morbidity, mortality, and health care utilization in the USA. The authors examined comorbidities and clinical outcomes among persons with GSD using electronic health records (EHR). In this retrospective study of 1,381,004 adults, GSD was defined by ICD-9 code 574 or ICD-10 code K80 using Optum® longitudinal EHR from January 2007 to March 2021. The authors obtained diagnosis, procedure, prescription, and vital sign records, and evaluated associations between demographics, comorbidities, and medications with cholecystectomy, digestive cancers, and mortality. Among persons with GSD, 30% had a cholecystectomy and were more likely to be women, White, and younger, and less likely to have comorbidities, except for obesity, gastroesophageal reflux disease (GERD), abdominal pain, hyperlipidemia, and pancreatitis. Among persons with GSD, 2.2% had a non-colorectal digestive cancer diagnosis during follow-up and risk was 40% lower among persons with a cholecystectomy. Non-colorectal digestive cancer predictors included older age, male sex, non-White race-ethnicity, lower BMI, other cancers, diabetes, chronic liver disease, pancreatitis, GERD, and abdominal pain. Among persons with GSD, mortality was 15.1% compared with 9.7% for the whole EHR sample. Persons with a cholecystectomy had 40% lower mortality risk and mortality predictors included older age, male sex, Black race, lower BMI, and most comorbidities. In this EHR analysis of persons with GSD, 30% had a cholecystectomy. Mortality was higher compared with the whole EHR sample. Persons with cholecystectomy were less likely to have non-colorectal digestive cancer or to die. *A third co-author is a researcher from the National Institute of Diabetes and Digestive and Kidney Diseases.*

## **Environmental Management of Asthma in Clinical Practice: Results from the 2012 National Ambulatory Medical Care Survey**

DLH researcher **Jesse Wilkerson** was among the authors of an [article](#) published in the *Journal of Allergy and Clinical Immunology Global* (Online: November 2023). The National Asthma Education and Prevention Program guidelines emphasize environmental control as an integral part of asthma management; however, limited national-level data exist on how clinicians implement environmental control recommendations. The authors analyzed data on clinicians' self-reported use of recommended environmental control practices in a nationally representative sample (n = 1645) of primary care physicians, asthma specialists, and advanced practice providers from the National Asthma Survey of Physicians, a supplemental questionnaire to the 2012 National Ambulatory Medical Care Survey. Clinician and practice characteristics were examined as well as clinicians' decisions and strategies regarding environmental trigger assessment and environmental control across provider groups. A higher percentage of specialists assessed asthma triggers at home, school, and/or work than primary care or advanced practice providers. Almost all clinicians recommended avoidance of secondhand tobacco smoke, whereas recommendations regarding cooking appliances (e.g., proper ventilation) were infrequent. Although assessment and recommendation practices differed between clinician groups, modeling results showed that clinicians who reported almost always assessing asthma control were 5- to 6-fold more likely to assess environmental asthma triggers. Use of asthma action plans was also strongly associated with implementation of environmental control recommendations. Environmental assessment and recommendations to patients varied among asthma care providers. High adherence to other key guideline components, such as assessing asthma control, was associated with environmental assessment and recommendation practices on environmental control. *Other authors include researchers from National Institute of Environmental Health Sciences, Centers for Disease Control and Prevention, United States Public Health Service, and US Environmental Protection Agency.*

## **HIV Preexposure Prophylaxis Provision Among Adolescents: 2018 to 2021**

DLH researchers **Wei Wei** and **Ishwarya Ravichandran** were among the authors of an [article](#) published in *Pediatrics* (Online: November 2023). HIV preexposure prophylaxis (PrEP) is safe, effective, and was approved for adolescents in 2018. Adolescents and young adults make up 20% of HIV diagnoses in the United States. The authors' objective was to describe trends in adolescents prescribed PrEP during 2018 through 2021 and characteristics of these adolescents and their PrEP providers. The authors identified adolescents aged 13 to 19 years with oral PrEP prescriptions during 2018 through 2021 in a national pharmacy database using a validated algorithm. Trends were assessed by calculating the overall percentage change and estimated annual percentage change with 95% confidence intervals. Characteristics of adolescents and their PrEP providers in 2021 were described. The number of adolescents prescribed PrEP increased 76.2% from 2018 to 2021, despite decreases in 2020. Increases were observed among all sex and age groups, with larger increases among older adolescents aged 18 to 19 years. The majority of the 6444 adolescents prescribed PrEP in 2021 were male (82.6%) and aged 18 to 19 years (87.8%). Among 2455 physician PrEP providers, 29.6% were pediatricians, with varying specialty distributions by adolescent age group. Among the 217 pediatricians who prescribed PrEP to adolescents aged 13 to 17 years, 67.7% were general pediatricians. PrEP provision for adolescents has increased, largely among older and male adolescents. The availability of PrEP provides an important opportunity for pediatric providers to take an active role in HIV prevention. *The other authors are researchers from the Centers for Disease Control and Prevention and Emory University School of Medicine.*

## **Pubertal Girls With Overweight/Obesity Have Higher Androgen Levels—Can Metabolomics Tell Us Why?**

DLH researcher **Samantha Molsberry** was among the authors of an [article](#) published in the *Journal of Clinical Endocrinology and Metabolism* (Online Ahead of Print: November 2023). Pubertal girls with higher total body fat (TBF) demonstrate higher androgen levels. The cause of this association is unknown but is hypothesized to relate to insulin resistance. The objective was to investigate the association between higher TBF and higher androgens in pubertal girls using untargeted metabolomics. Sixty-six pubertal, premenarchal girls (aged  $10.9 \pm 1.39$  SD years; 60% White, 24% Black, 16% Other; 63% normal weight, 37% overweight/obese) contributed an average of 2.29 blood samples. Body mass Index (BMI) and TBF were negatively associated with most features including raffinose (a plant trisaccharide) and several bile acids. For BMI, RaMP-DB (Relational database of Metabolomic Pathways) identified many enriched pathways related to bile acids. Androstenedione also showed strong negative associations with raffinose and bile acids. Metabolomic analyses of samples from pubertal girls did not identify an insulin resistance signature to explain the association between higher TBF and androgens. Instead, we identified potential novel signaling pathways that may involve raffinose or bile acid action at the adrenal gland. *The other authors are researchers from the National Institute of Environmental Health Sciences.*

## **Inequities Along the Human Immunodeficiency Virus (HIV) Pre-exposure Prophylaxis Services Continuum for Black Women in the United States, 2015-2020**

DLH researcher **Lei Yu** was among the authors of an [article](#) published in *Obstetrics and Gynecology* (Epub: November 2023 [Print: February 2024]). The study objectives were to estimate the number of women who received human immunodeficiency virus (HIV) and sexually transmitted infection (STI) testing and HIV pre-exposure prophylaxis (PrEP) services by race and ethnicity in seven THRIVE (Targeted Highly Effective Interventions to Reverse the HIV Epidemic)-funded jurisdictions and to estimate associations of age and syphilis and gonorrhea diagnoses with receipt of HIV PrEP services. The authors analyzed data collected from 2015 to 2020 in Birmingham, Alabama; Baltimore City, Maryland; Washington, DC; New Orleans, Louisiana; Brooklyn, New York; Philadelphia, Pennsylvania; and Hampton Roads, Virginia. Black women and women of additional racial and ethnic groups were compared by age, HIV status at enrollment, receipt of STI testing and test positivity, and steps in the PrEP continuum (screened, eligible, referred, linked, and prescribed). Also examined was the association of age, syphilis, or gonorrhea with the following steps in the PrEP continuum: screened, referred, linked, and prescribed. Black women made up 69.2% of women served in THRIVE. Compared with non-Black women, Black women were more likely to have a positive test result for syphilis, gonorrhea, chlamydia, or more than one STI. Among women with negative HIV test results or unknown HIV status, Black women were more likely to be screened for PrEP eligibility. Among Black women, the proportion screened for PrEP was higher among those diagnosed with syphilis or gonorrhea than among those without an STI. Among 219 Black women who presented with syphilis, only 10 were prescribed PrEP; among 407 with gonorrhea, only 11 were prescribed PrEP. Although most Black women seeking services received STI testing, the proportion of Black women who were eligible for PrEP and prescribed PrEP was low. To achieve national HIV-prevention goals, it is imperative that Black women have access to PrEP information and services. *Other authors include researchers from the Centers for Disease Control and Prevention, the District of Columbia Department of Health, Johns Hopkins School of Medicine, the Louisiana Office of Public Health, the University of Alabama at Birmingham, and the New York City Department of Health and Mental Hygiene.*

## **Developing a Comparative Effective Methodology for Technology Usability During a Simulated Casualty Event**

DLH researchers **Holly Ortman, James Gaudaen, and Benjamin Knisely** were among the authors of an [article](#) published in *Military Medicine* (Print: November 2023). Future combat environments will be complex, making effective care for multi-domain battlefield injuries more challenging. Technology and resources are essential to reduce provider burden enabling more accurate assessments, decision-making support, expanded treatment, and outcome improvements. Experimentation exercises to evaluate concepts and technologies to incorporate into the Army's future force ensure rapid and continuous integration across air, land, sea, space, and cyberspace domains to overmatch adversaries. The authors describe a project to develop a method for empirically comparing devices intended to support combat casualty care through high-fidelity simulation in preparation for an Army experimentation exercise. Six medics participated in a series of high-fidelity simulation medical casualty injury scenarios with and without technology devices. The participants provided usability information about their care delivery experiences using the System Usability Scale and Adapted Telehealth Usability Questionnaire-Telemedicine and Advanced Technology Research Command and qualitative feedback. A comparative effectiveness design compared the devices regarding their usability, size, weight, and power with the addition of cost, connectivity, and cyber security, and the qualitative feedback this methodology holistically assessed the technologies as they were applied in the combat casualty care scenario. Results were used by decision makers to determine technology inclusion in experimentation exercise, develop proof of concept methodology to scale for the exercise, and provide technology developers feedback for iterative updates of their devices before participation in experimentation exercise. This project supports the body of simulation studies conducted to understand combat casualty care. It is one of few empirical medical technology assessments with medical personnel end user input that has been reported. The methodology incorporates a user-centered design for rapid technology improvements before fielding. *The other authors are researchers from the US Army Telemedicine and Advanced Technology Research Center (Fort Detrick, Maryland) and the Geneva Foundation (Bethesda, Maryland).*

## **Sociodemographic and Health-Related Factors Associated With Exclusive Breastfeeding in 77 Districts of Uganda**

DLH researchers **Derrick Kimuli, Florence Nakaggwa, Norah Namuwenge, Rebecca Nsubuga, Paul Isabirye, Kenneth Kasule, Justine Fay Katwesige, Barbara Amuron, and Daraus Bukenya** were among the authors of an [article](#) published in the *International Breastfeeding Journal* (Online: December 2023). Uganda surpasses many African nations and the global average in exclusive breastfeeding (EBF) rates. Yet, malnutrition is a critical issue, with stunting impacting roughly 29% of children under 5 years. Enhancing EBF could mitigate such nutritional challenges. This study focused on determining the current EBF prevalence and identifying associated factors across 77 surveyed districts. Pooled data from the Lot Quality Assurance Sampling (LQAS) surveys conducted in 77 districts in Uganda during 2021 and 2022 were analyzed. The analysis involved 7,210 mothers of children under 6 months, EBF was considered as the proportion of infants who received breast milk only in the 24 hours before the survey. A mother practicing EBF was (1) currently breastfeeding (2) had not started giving foods other than breastmilk (3) had not given any other probed liquids or (4) semi-solid foods the previous day or night. The prevalence of EBF was 62.3%. In the adjusted analysis, EBF was more common among older mothers 20-24 years, 25-29 years and 30+ years compared to teenage mothers. Also, EBF was more likely among mothers who lived in rural areas compared

to urban areas and those who attended antenatal care (ANC). On the contrary, EBF was less common for children aged 3-5 months compared to younger, and children who had received Vitamin A supplementation. The study suggests that most districts in Uganda might not have made significant strides in improving EBF rates over the last 20 years, pointing to possible ongoing hurdles that need urgent attention. Particularly, there is a pressing need to focus on teenage mothers. Maintaining and strengthening programs that advocate EBF, such as ANC, is crucial to bridge the gaps and bring about more equitable rates among different groups. *The other authors are researchers from the United States Agency for International Development Uganda.*

### **Health Insurance and Diabetes**

DLH researcher **Sarah Casagrande** was among the authors of an [article](#) published in *Diabetes in America* (Internet; National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); December 2023). National survey data from 2019 indicate that among adults age  $\geq 18$  years with diabetes, 93.4% had health insurance coverage, including 88.9% of those age 18–64 years and 98.8% of those age  $\geq 65$  years. An estimated 1.56 million adults with diabetes had no health insurance coverage, including 1.43 million adults age 18–64 years and 130,000 adults age  $\geq 65$  years. Following the enactment of the Patient Protection and Affordable Care Act (ACA) in 2010, the proportion of individuals with health insurance in the United States increased. For adults age 18–64 years with diabetes, health insurance coverage increased from 84.7% in 2009 to 90.1% in 2016, 88.9% in 2019, and 89.8% in 2021. In 2019, for adults with diabetes age 18–64 years, Hispanic people had a lower prevalence of health insurance coverage (75.8%) compared to people who were non-Hispanic White (93.2%), non-Hispanic Black (90.5%), and non-Hispanic Asian (98.3%). The majority of adults age 18–64 years with diabetes had private insurance coverage (57.4%); other forms of insurance were Medicaid (23.9%), Medicare (16.0%), and military benefits (4.1%). Finally, the proportion of income spent on private insurance premiums was greater for those whose income was closest to the poverty level compared to those with higher income. During 2017 through March 2020, insured adults with diabetes had greater health care utilization compared to uninsured adults with diabetes, including more often seeing a doctor in the past year and having an eye exam. In addition, insured adults age 20–64 years with diabetes more often checked their blood glucose  $\geq 1$  time per day (45%) and had their glycosylated hemoglobin (A1c) checked regularly (88%) compared to their uninsured adult counterparts (18% and 54%, respectively). Finally, insured adults with diabetes had better A1c and cholesterol control compared to those without insurance. *The other authors are researchers from the Centers for Disease Control and Prevention and the University of Michigan School of Medicine.*

### **Association of Hormonal and Reproductive Factors With Differentiated Thyroid Cancer Risk in Women: A Pooled Prospective Cohort Analysis**

DLH researcher **Aimee D'Aloisio** was among the authors of an [article](#) published in the *International Journal of Epidemiology* (Online Ahead of Print: December 2023 [Online: February 2024]). The incidence of differentiated thyroid cancer (DTC) is higher in women than in men but whether sex steroid hormones contribute to this difference remains unclear. Studies of reproductive and hormonal factors and thyroid cancer risk have provided inconsistent results. Original data from 1,252,907 women in 16 cohorts in North America, Europe, Australia, and Asia were combined to evaluate associations of DTC risk with reproductive and hormonal factors. During follow-up, 2142 women were diagnosed with DTC. Factors associated with higher risk of DTC included younger age at menarche, younger and older ages at menopause, ever use of menopausal hormone therapy

and previous hysterectomy or bilateral oophorectomy. Factors associated with lower risk included longer-term use of oral contraceptives among those who ever used oral contraception and baseline post-menopausal status. No associations were observed for parity, duration of menopausal hormone therapy use, or lifetime number of reproductive years or ovulatory cycles. The study provides some evidence linking reproductive and hormonal factors with risk of DTC. Results should be interpreted cautiously considering the modest strength of the associations and potential for exposure misclassification and detection bias. Prospective studies of pre-diagnostic circulating sex steroid hormone measurements and DTC risk may provide additional insight. *Other authors include researchers from the National Cancer Institute, National Institute of Environmental Health Sciences, University at Albany School of Public Health, Albert Einstein College of Medicine, and research institutions in France, Norway, Sweden, Australia, and England.*

### **Racial and Ethnic Disparities in Phthalate Exposure and Preterm Birth: A Pooled Study of Sixteen U.S. Cohorts**

DLH researcher **Kate Christenbury** was among the authors of an [article](#) published in *Environmental Health Perspectives* (Epub and Online: December 2023). Phthalate exposures are ubiquitous during pregnancy and may contribute to racial and ethnic disparities in preterm birth. The authors investigated race and ethnicity in the relationship between biomarkers of phthalate exposure and preterm birth by examining: a) how hypothetical reductions in racial and ethnic disparities in phthalate metabolites might reduce the probability of preterm birth; and b) exposure-response models stratified by race and ethnicity. Individual-level data were pooled on 6,045 pregnancies from 16 U.S. cohorts. Covariate-adjusted differences were investigated in nine urinary phthalate metabolite concentrations by race and ethnicity [non-Hispanic White (White, 43%), non-Hispanic Black (Black, 13%), Hispanic/Latina (38%), and Asian/Pacific Islander (3%)]. In comparison with concentrations among White participants, adjusted mean phthalate metabolite concentrations were consistently higher among Black and Hispanic/Latina participants by 23%-148% and 4%-94%, respectively. Asian/Pacific Islander participants had metabolite levels that were similar to those of White participants. Hypothetical interventions to reduce disparities in metabolite mixtures were associated with lower probabilities of preterm birth for Black and Hispanic/Latina participants. Odds ratios for preterm birth in association with phthalate metabolites demonstrated heterogeneity by race and ethnicity for two individual metabolites (mono-n-butyl and monoisobutyl phthalate), with positive associations that were larger in magnitude observed among Black or Hispanic/Latina participants. Phthalate metabolite concentrations differed substantially by race and ethnicity. The results show hypothetical interventions to reduce population-level racial and ethnic disparities in biomarkers of phthalate exposure could potentially reduce the probability of preterm birth. *Other authors include researchers from the National Cancer Institute, National Institute of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, and the Harvard T.H. Chan School of Public Health at Harvard University.*

### **Stressful Life Events, Social Support, and Epigenetic Aging in the Women's Health Initiative**

DLH researcher **Shelly-Ann Love** was among the authors of an [article](#) published in the *Journal of the American Geriatrics Society* (Epub: December 2023 [Print: February 2024]). Elevated psychosocial stress has been linked with accelerated biological aging, including composite DNA methylation (DNAm) markers that predict aging-related outcomes ("epigenetic age"). However, no study has examined whether stressful life events (SLEs) are associated with epigenetic age acceleration in postmenopausal women, an aging

population characterized by increased stress burden and disease risk. The authors leveraged the Women's Health Initiative, a large multi-ancestry cohort of postmenopausal women with available psychosocial stress measures over the past year and epigenomic data. SLEs and social support were ascertained via self-report questionnaires. Whole blood DNAm array data were used to calculate five DNAm-based predictors of chronological age, health span and life span, and telomere length (HorvathAge, HannumAge, PhenoAge, GrimAge, DNAmTL). After controlling for potential confounders, higher SLE burden was significantly associated with accelerated epigenetic aging, as measured by GrimAge and DNAmTL. Exploratory analyses showed that SLEs-GrimAge associations were stronger in Black women as compared to other races/ethnicities and in those with lower social support levels. In women with lower social support, SLEs-DNAmTL associations showed opposite association in Hispanic women as compared to other race/ethnicity groups. The authors' findings suggest that elevated stress burden is associated with accelerated epigenetic aging in postmenopausal women. Lower social support and/or self-reported race/ethnicity may modify the association of stress with epigenetic age acceleration. These findings advance understanding of how stress may contribute to aging-related outcomes and have important implications for disease prevention and treatment in aging women. *Other authors include researchers from the University of North Carolina at Chapel Hill, British Columbia Cancer Research Institute, and the Fred Hutchinson Cancer Research Center.*

### **Unmet Needs for HIV Ancillary Services Among Persons With Diagnosed HIV Aged 55 Years and Older**

DLH researcher **Jen-Feng Lu** was among the authors of an [article](#) published in the *Journal of Acquired Immune Deficiency Syndromes* (Online Ahead of Print: December 2023). Approximately two in five persons with HIV (PWH) in the United States are aged  $\geq 55$  years. HIV ancillary services, such as case management and transportation services, can help older PWH remain engaged in care. The authors used data from the Medical Monitoring Project (MMP) to describe the prevalence of unmet needs for ancillary services among persons with diagnosed HIV aged  $\geq 55$  years. The Medical Monitoring Project is an annual cross-sectional study that reports representative estimates on adults with diagnosed HIV in the United States. The authors used MMP data collected during 6/2019-5/2021 to calculate weighted percentages of cisgender men and cisgender women with HIV aged  $\geq 55$  years with unmet needs for ancillary services, overall and by selected characteristics (N=3,200). Unmet need was defined as needing but not receiving a given ancillary service. Differences between groups were assessed using prevalence ratios (PRs) and 95% confidence intervals (CIs) with predicted marginal means. Overall, 37.7% of cisgender men and women with HIV aged  $\geq 55$  years had  $\geq 1$  unmet need for ancillary services. Overall, 16.6% had  $\geq 1$  unmet need for HIV support services, 26.9% for non-HIV medical services, and 26.7% for subsistence services. There were no statistically significant differences in unmet needs for services by gender. The prevalence of  $\geq 1$  unmet need was higher among non-White persons, persons who experienced housing instability, and those without any private insurance. A large percentage of older PWH have unmet needs for ancillary services. Given the challenges that older PWH face related to the interaction of HIV and aging-associated factors, deficits in the provision of ancillary services should be addressed. *The other authors are researchers from the Centers for Disease Control and Prevention.*

## Launch of Diabetes in America

[\*Diabetes in America\*](#) is the National Institute of Diabetes and Digestive and Kidney Diseases' compilation and assessment of epidemiologic, public health, clinical research, and clinical trial data focused on diabetes, its complications and treatment, health care utilization, and diabetes prevention in the United States. DLH researcher and senior epidemiologist **Sarah Casagrande** is an editor on the publication. There have been three previous *Diabetes in America* editions published in 1984, 1995, and 2018. *Diabetes in America* has been migrated to an exclusively digital format. Starting in December 2023, each updated or new article will be available on the National Library of Medicine's NCBI Bookshelf. *Diabetes in America* is organized into four broad topic areas—Section I: Spectrum of Diabetes; Section II: Complications of Diabetes and Related Conditions; Section III: Medical Care for Diabetes; and Section IV: Prevention of Diabetes.



# DLH Research Posters and Presentations 2023

- **Dr. Chyng-Wen Fwu presented a poster at the Kidney Week Meeting in November.**  
**Fwu CW, Barthold JS, Kimmel PL, Eggers PW, Norton JM, Chan C, Mendley SR, Star RA, Schulman IH. Association of Obesity, Metabolic Syndrome, and Diabetes with Chronic Kidney Disease in Men and Women: National Health and Nutrition Examination Survey (NHANES), 2003-2020. Kidney Week 2023, Philadelphia, PA.**
- **The following is a North American Registry for Care and Research in Multiple Sclerosis (NARCRMS) poster presented at Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS), February 23-25, 2023, San Diego, California.**

Relative Impact of Cognitive and Motor Impairments in Multiple Sclerosis and their Impact on Employment. *Preliminary Findings from the North American Registry for Care and Research in Multiple Sclerosis.*

*Kottil Rammohan, University of Miami, David Li, The University of British Columbia, June Halper, Consortium of Multiple Sclerosis Centers (CMSC), Sara McCurdy Murphy, Social & Scientific Systems, Inc (SSS), Audrey Brown, SSS, Lisa Patton, SSS, and Ramon Flores Gonzalez, University of Miami, and on behalf of the NARCRMS Site Investigators.*



**Relative Impact of Cognitive and Motor Impairments in Multiple Sclerosis and their Impact on Employment.**  
**Preliminary Findings from the North American Registry for Care and Research in Multiple Sclerosis.**  
Kottil Rammohan, University of Miami, David Li, The University of British Columbia, June Halper, Consortium of Multiple Sclerosis Centers (CMSC)  
 Sara McCurdy Murphy, Social & Scientific Systems, Inc (SSS), Audrey Brown, SSS, Lisa Patton, SSS, Ramon Flores Gonzalez, University of Miami  
 and on behalf of the NARCRMS Site Investigators



**Abstract**

**Background:**  
 The North American Registry for Care and Research in Multiple Sclerosis (NARCRMS) is a longitudinal registry that examines the course of MS in the disease-modifying era. Under or unemployment in multiple sclerosis (MS) may be due to a number of factors, among them cognition and motor impairment.

**Objective:**  
 In this study we examine the relative roles of cognition and motor function in under or unemployment in patients with MS.

**Methods:**  
 Cognitive and motor impairment were examined in a subgroup of patients enrolled into NARCRMS at the enrollment visit. Their employment status was recorded and if employed part-time, patients were queried if their status was based on their self-perceived impairments due to MS.

**Results:**  
 Complete data was available on 366 subjects where cognition was examined by the 3-second Paced Auditory Sequential Addition Test (PASAT 3). Patients' ages ranged from 20 to 65 years (median 40 years) and Male:Female ratio of 1:2.5. The median extended disability status scale (EDSS) was 1.50, mean dominant 9 hole-peg test (9HPT) 23.05 seconds, 25-foot timed walk (25FTW) 5.82 seconds, and fatigue was reported by 63.16% (Table 1). Approximately a third of the subjects were unemployed; 15% reported part-time employment with 44% indicating that the impairments from MS precluded full-time employment. Approximately 21% of patients employed full time or part time indicated that MS affected how often they would like to work and 14.8% of employed patients indicated MS affected their ability to work. Patients were grouped into quartiles based on the PASAT scores from the highest functioning subjects in the 1st quartile to the lowest performers in the 4th (Table 2). Significant interquartile differences were not observed for EDSS with motor function approaching but not meeting significance (Table 3). Employment status however was statistically significant favoring the higher functioning subjects (Q1 v. Q4, p=0.0206) (Table 4).

**Conclusions:**  
 Preliminary studies from this limited data set reaffirms that under or unemployment in those diagnosed with MS correlated best with cognitive rather than motor impairment in this cohort of subjects with relatively early MS.

**Data and Analysis (Data as of November 10, 2022)**

**Table 1. Demographics and Physical Function by PASAT Quartile**

	Q1	Q2	Q3	Q4
<b>Sex</b>	Female = 55 (15.45%) Male = 26 (7.3%)	Female = 63 (17.7%) Male = 27 (7.58%) Transgender Male = 1 (0.28%)	Female = 71 (19.94%) Male = 21 (5.9%)	Female = 65 (18.26%) Male = 26 (7.3%) Transgender Male = 1 (0.28%)
<b>Age</b>	N = 81 Median: 41 Mean: 42.53	N = 91 Median: 40 Mean: 40.83	N = 91 Median: 39 Mean: 40.24	N = 92 Median: 39 Mean: 39.47
<b>EDSS</b>	N = 82 Median: 1.5 Mean: 1.70	N = 94 Median: 1.5 Mean: 1.76	N = 99 Median: 2 Mean: 1.91	N = 92 Median: 2 Mean: 2.01
<b>Average 9 Hole Peg (Dom)</b>	N = 82 Median: 20.5 Mean: 21.46	N = 91 Median: 20.5 Mean: 22.26	N = 97 Median: 21 Mean: 22.28	N = 89 Median: 23 Mean: 26.11
<b>25 Foot Walk</b>	N = 81 Median: 5 Mean: 5.51	N = 93 Median: 5 Mean: 5.68	N = 99 Median: 5.5 Mean: 5.8	N = 90 Median: 6 Mean: 6.26

**Table 2. Employment by PASAT Quartile**

	Q1	Q2	Q3	Q4
Original Grouping				
<b>Employed</b>	N = 66 23.01%	N = 75 21.31%	N = 71 20.17%	N = 59 16.76%
<b>Not Employed</b>	N = 15 4.26%	N = 15 4.26%	N = 20 5.68%	N = 31 8.81%
New Grouping				
<b>Employed Full Time</b>	N = 53 15.14%	N = 53 15.14%	N = 51 14.57%	N = 40 11.43%
<b>Unemployed / Under-employed</b>	N = 27 7.71%	N = 37 10.57%	N = 40 11.43%	N = 49 14%

**Table 3. Analysis of Maximum Likelihood & Odds Ratios Estimates for Physical Function by PASAT Quartile**

	Q2	Q3	Q4	
<b>EDSS</b>	Pr > ChiSq	0.7754	0.3376	0.1593
	Point Estimate	1.032	1.109	1.164
	95% Wald Confidence Limits	0.830/1.284	0.898/1.370	0.942/1.439
<b>25 Foot Walk</b>	Pr > ChiSq	0.6126	0.4091	0.1077
	Point Estimate	1.038	1.059	1.114
	95% Wald Confidence Limits	0.899/1.197	0.924/1.215	0.977/1.271
<b>Average 9 Hole Peg (Dom)</b>	Pr > ChiSq	0.3338	0.3213	0.0123
	Point Estimate	1.029	1.029	1.071
	95% Wald Confidence Limits	0.971/1.089	0.972/1.089	1.015/1.131

**Table 4. Analysis of Maximum Likelihood & Odds Ratios Estimates for Employment by PASAT Quartile (Original vs. New Groupings)**

	Q2	Q3	Q4	
Original Grouping				
<b>Employed</b>	Pr > ChiSq	0.7506	0.5741	0.0206
	95% Wald Confidence Limits	0.400/1.96	0.586/2.620	1.137/4.700
New Grouping				
<b>Employed Full Time</b>	Pr > ChiSq	0.3235	0.1735	0.0058
	95% Wald Confidence Limits	0.390/1.364	0.394/1.209	0.223/0.776

Note: Descriptive and logistic regression analyses were conducted in SAS 9.4 (SAS Institute, Inc., Cary, North Carolina). The original grouping for employment was assessed solely as unemployed (no employment at the time of analysis) or employed (part-time or full-time, regardless of underemployment due to self-perceived impairments due to MS). The new grouping for employment utilized the classification of full-time employment (without indication of underemployment due to MS) and a second classification for those that were full-time employed (with an indication of underemployment due to MS, part-time employed, and unemployed).

## • **STAT2 Contracts Accomplishments**

### **January 2023**

- **Sandra McBride, Lauar Bets, Shawn Harris:** Contributors on publication in the DNT Technical Report on the Toxicity of Sodium Metavanadate and Vanadyl Sulfate in HSD Rats.
- **Caroll Co:** Presented at ASA Conference on Statistical Practice, “Efficient simulation studies using designed experiments.”

### **February 2023**

- **Kate Konrad:** Presented at North Carolina State University Center for Human Health and Environment 7th Annual Symposium, “Male and Female Differences across Age in Control Rat Neurobehavioral Test Assays.”
- **Kate Konrad:** Presentation on Reproducibility of DNT studies at CHHE Symposium: “Sex Difference in Response to Environment Exposures.”
- **Guan Xie:** Black Cohosh [paper](#) won the Editor’s Choice paper for the December 2022 issue of Environmental and Molecular Mutagenesis.
- **Caroll Co:** Conference presentation at Conference on Statistical Practice (CSP), “Efficient simulation studies with design of experiments.”

### **March 2023**

- **Kate Konrad:** NIEHS mechanistic toxicology branch talk on Reproducibility of DNT studies.
- **Caroll Co:** Appointed to serving on the steering committee for the Conference on Statistical Practice (CSP) 2024, 2025.

### **April 2023**

- **Kate Konrad:** Conference poster presentation at Triangle Society for Neuroscience Conference “Male and Female Differences across Age in Control Rat Neurobehavioral Assays.”
- **Sandra McBride, Lauar Bets, Shawn Harris:** Contributors to DNT, Acetoin/Pentanedione Technical Report.

### **May 2023**

- **Gary Larson, Guan Xie:** Conference presentations at the Symposium for Data Science and Statistics (SDSS).
- **Gary Larson:** “A comparison of dynamic versus static regression coefficients in a generalized linear model for longitudinal rodent neurobehavioral data.”
- **Guan Xie:** “Quantitative High Throughput Screening Data Quality Control Analysis R Shiny Application.”

### **June 2023**

- **Caroll Co:** Conference presentation at Society of Epidemiologic Research Annual Meeting, “Exposure to chemicals in personal care products among women with high daily use.” Coauthors: **Angela Jeffers**, Peter Egeghy, Steven Prince, Daniel Stout II, Raquel Silva, Lillian Alston, Richard Walker, Helen Cunny, Timothy Buckley, Andrew Rooney, Kyla Taylor.
- **Shawn Harris:** Conference presentation at Society of Birth Defects Research “Statistical Analysis of Fetal Defect Data: A Cautionary Tale.” Coauthors: Helen Cunny, Karr Stinson, Keith Shockley.
- **Sandra McBride, Lauar Bets, Shawn Harris:** Contributors to DNT, TCPP Technical Report.

### **July 2023**

- **Matt Bridge:** Paper submitted for publication to Neurophotonics, “FiPhA: An Open-Source Fiber Photometry Analysis Platform in R/Shiny.”

### **August 2023**

- **Caroll Co:** Contributor on DTT Technical Report (NBBS).
- **Caroll Co:** Recorded JMP Discovery Summit, “Time-efficient strategy for selecting a test set in the validation of an image detection algorithm.”
- **Kate Konrad:** Conference presentation at Joint Statistical Meetings (JSM), “A Framework for Assessing Reproducibility and Variability in Control Rat Neurobehavioral Test Assays.”
- **Angela Jeffers:** Conference presentation at Joint Statistical Meetings (JSM), “Statistical Issues in Developmental and Reproductive Toxicology Studies.”

### **September 2023**

- **Shawn Harris, Angela Jeffers, Gary Larson:** Abstracts accepted for the Lab Animal Special Issue.
- **Shawn Harris:** “Accounting for Animal Survival in Pathology Analyses.”
- **Angela Jeffers:** “Simulation Studies to Determine Statistical Power in Animal Research Methodologies.”
- **Gary Larson:** “An Introduction to Bayesian Statistical Concepts with Examples from Rodent Toxicology Studies.”

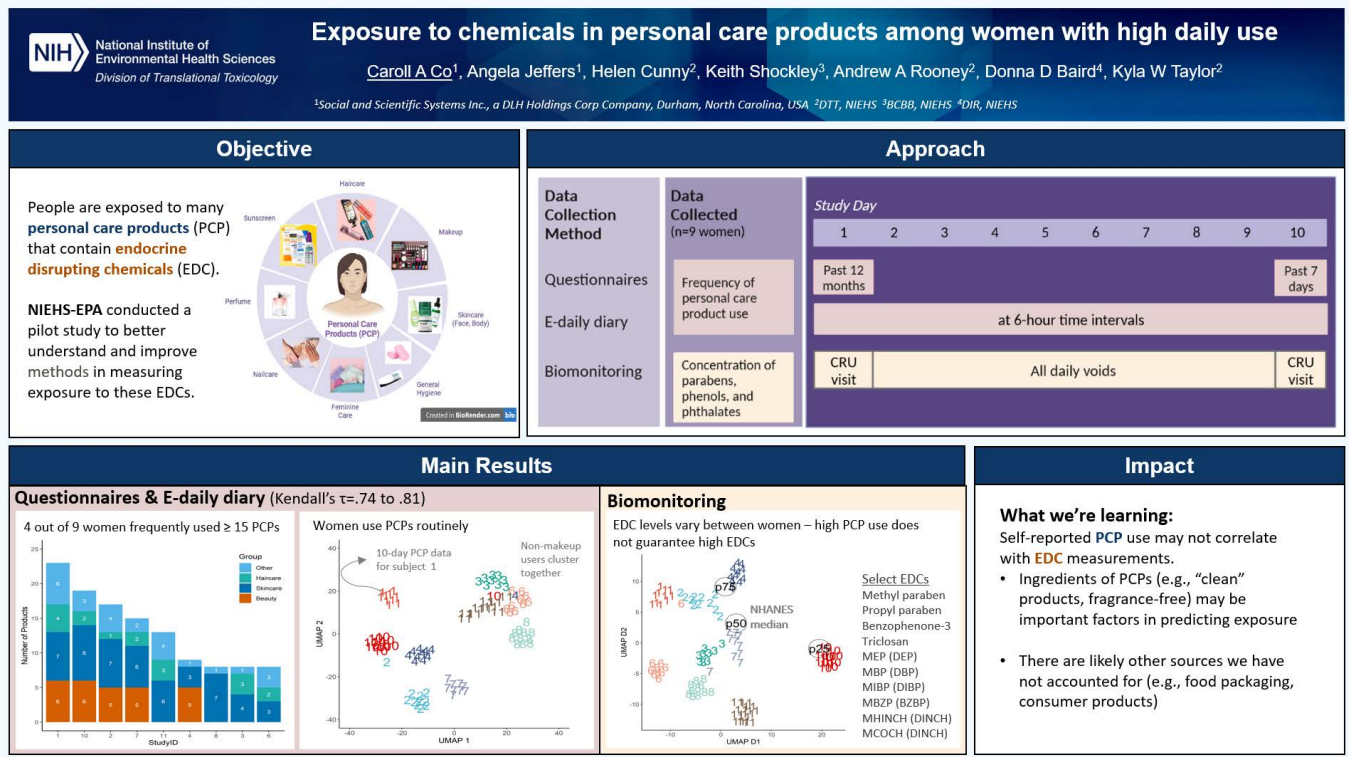
### **October 2023**

- **Caroll Co:** Presented “Time-efficient strategy for selecting a test set in the validation of an image detection algorithm” at JMP Discovery Summit (in person; also recorded as a resource in August).

### **November 2023**

- **Matt Bridge:** Conference presentation at Society for Neuroscience (SFN), “FiPhA: An Open-Source Fiber Photometry Analysis Platform in R/Shiny.”
- **Marjo Smith, Sandra McBride, Shawn Harris:** Published Research Report 19 on the trend test for binary data; [Website](#). [Bookshelf](#).

- **Poster Presentation: Carol Co's** poster, which was presented at [SER](#) and the NIEHS' DTT poster day, highlights the potentially harmful chemicals in personal care products, such as makeup and skincare, that women are exposed to daily, and features an interesting machine learning approach to analysis.



- **Phenotypic Susceptibility to VRC07-523LS and the Correlates in the ACTG A5357 Study**

Babafemi O. Taiwo, Jackie Reeves, Yu (Evelyn) Zheng, Katherine Rodriguez, Yolanda Lie, Leah Burke, Lucio Gama, Christos Petropoulos, Pablo F. Belaunzaran-Zamudio, Richard Koup, Jennifer Tiu, Jenifer Baer, Jennifer Kiser, Paul Wannamaker, Katharine Bar, Pablo Tebas; for the ACTG A5357 Team

