Public Health and Scientific Research

Research Update

Spring-Summer 2023

A semi-annual look at select DLH research activities.

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I am honored to present the Spring-Summer 2023 edition of the PHSR Research Update, a semi-annual look at select research activities from across our company's Public Health & Scientific Research operating unit.

Science can be abstract at times. For those of us entrenched in the realms of microscopic organisms, invisible waves, and mind-numbingly large data sets, the vital real-world impact of our work can slip from top of mind. But as I read through this volume, I was struck by the breadth of the everyday issues our researchers and analysts dedicate their careers to solving. From housing policy, to opioid usage, food insecurity, breast cancer risk, and beyond, DLH researchers work each day to glean insight into some of the health problems communities across the globe find most troubling.

Some research topics are long-standing and enduring—racial health disparities, HIV treatment, hazardous waste, and more—while others have emerged more recently. Read on to learn how investigators are examining the ways the scientific community can integrate Machine Learning into complex survey analysis—and the ramifications of such advanced technology for our industry.

I am proud to work alongside colleagues who contribute so much to the advancement of knowledge. Their expertise, sophistication, and ingenuity are made apparent through the research that follows. I remain inspired by our team's commitment to improving lives in the communities in which we live and work. Thank you.

Sincerely,

Jeanine Christian
President
Public Health & Scientific Research

Needs for Shelter or Housing Assistance Among People With Diagnosed HIV by Jurisdiction: United States, 2015-2020

DLH researchers **Jen-Feng Lu**, **Xin Yuan**, and **Priya Nair** are among the authors of an article published in *AIDS* (Epub: December 2022; Print: March 2023). The authors' objective was to describe the landscape of needs for housing assistance among people with HIV (PWH) and availability of Housing Opportunities for People with AIDS (HOPWA) funding with respect to housing service needs, nationally and for 17 US jurisdictions. The CDC Medical Monitoring Project (MMP) is an annual, cross-sectional survey designed to report nationally and locally representative estimates of characteristics and outcomes among adults with diagnosed HIV in the United States. The authors analyzed 2015-2020 data from MMP and 2019 funding data from HOPWA. Nationally, 1 in 4 PWH had shelter or housing service needs. Among those who needed housing services, 2 in 5 did not receive them. Reasons for unmet needs were multifactorial and varied by jurisdiction. Available 2019 HOPWA funding per person in need would cover up to 1.24 months of rent per person nationally, and may not have matched housing assistance needs among PWH in certain jurisdictions. Addressing housing service needs necessitates a multipronged approach at the provider, jurisdiction, and national level. Locally, jurisdictions should work with their partners to understand and address housing service needs among PWH. Nationally, distribution of HOPWA funding for housing services should be aligned according to local needs; the funding formula could be modified to improve access to housing services among PWH. *The other authors are researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention and the National HIV/AIDS Housing Coalition*.

Implementing Machine Learning Methods with Complex Survey Data: Lessons Learned on the Impacts of Accounting Sampling Weights in Gradient Boosting

DLH researchers **Nathaniel MacNell**, **Lydia Feinstein**, **Jesse Wilkerson**, and **Samantha Molsberry** are among the authors of an article published in *PLoS One* (eCollection 2023: January 2023). Despite the prominent use of complex survey data and the growing popularity of machine learning methods in epidemiologic research, few machine learning software implementations offer options for handling complex samples. A major challenge impeding the broader incorporation of machine learning into epidemiologic research is incomplete guidance for analyzing complex survey data, including the importance of sampling weights for valid prediction in target populations. Using data from 15,820 participants in the 1988-1994 National Health and Nutrition Examination Survey cohort, the authors determined whether ignoring weights in gradient boosting models of all-cause mortality affected prediction. In simulations, the authors additionally assessed the impact of sample size, weight variability, predictor strength, and model dimensionality. For sample sizes <5,000, sampling weights had little impact in simulations that more closely resembled a simple random sample (low weight variability) or in models with strong predictors, but findings were inconsistent under other analytic scenarios. Failing to account for sampling weights in gradient boosting models may limit generalizability for data from complex surveys, dependent on sample size and other analytic properties. In the absence of software for configuring weighted algorithms, post-hoc re-calculations of unweighted model performance using weighted observed outcomes may more accurately reflect model prediction in target populations than ignoring weights entirely. *Other authors include researchers from the University of Iowa's College of Public Health and the National Institute of Environmental Health Sciences.*

Predictors of Virologic Outcome Among People Living With HIV Who Continue a Protease Inhibitor-Based Antiretroviral Regimen Following Virologic Failure With No or Limited Resistance

DLH researcher **Evelyn Hogg** is among the authors of an article published in *AIDS Research and Therapy* (Print: January 2023). Treatment management after repeated failure of antiretroviral therapy (ART) is difficult due to resistance and adherence challenges. For people who have failed non-nucleoside reverse transcriptase inhibitor-(NNRTI-) and protease inhibitor-(PI-) based regimens with no or limited resistance, remaining on PI-based ART is an option. Using data from an ART strategy trial (A5288) in low/middle-income countries that included this option, the authors explored whether predictors can be identified distinguishing those who experienced further virologic failure from those who achieved and maintained virologic suppression. Study A5288 enrolled people with confirmed HIV-1 RNA ≥1000 copies/mL after ≥24 weeks of PI-based ART and prior failure on NNRTI-based ART. Fifty-six percent of participants were female. At study entry, median age was 40 years, time on ART 7.8 years, CD4 count 169 cells/mm^3, HIV-1 RNA 20,444 copies/mL; and 37% had NRTI resistance. Only 13% of participants developed new NRTI or PI resistance mutations. The authors concluded that a simple count of five predictors might have value for identifying risk of continued virologic failure. Novel antiretroviral and adherence support interventions are needed to improve virologic outcomes for higher risk individuals. *Other authors include researchers from Case Western Reserve University, Instituto Nacional de Infectologia Evandro Chagas (Brazil), Harvard T.H. Chan School of Public Health, and the University of Washington at Seattle.*

Decreased Human Immunodeficiency Virus Diagnosis Rates Among Black and Hispanic or Latino Men Who Have Sex With Men in US Jurisdictions Supported by the THRIVE Demonstration Project, 2014-2019

DLH researcher **Xueyuan Dong** is among the authors of an article published in *Clinical Infectious Diseases* (Print: January 2023). Black and Hispanic/Latino men who have sex with men (MSM) are disproportionately affected by human immunodeficiency virus (HIV). In the Targeted Highly Effective Interventions to Reverse the HIV Epidemic (THRIVE) demonstration project, 7 community collaboratives were developed to provide comprehensive HIV prevention services for these populations. The authors analyzed National HIV Surveillance System data to determine the number of HIV diagnoses for each year from 2014 to 2019 among Black, Hispanic/Latino, and White MSM in 7 THRIVE-eligible Metropolitan Statistical Areas (MSAs) that were awarded funding and 12 THRIVE-eligible MSAs that were not awarded funding. They found larger estimated decreases in HIV diagnosis rates in THRIVE jurisdictions compared with non-THRIVE jurisdictions. The authors concluded that the THRIVE community collaborative model was associated with a decrease in HIV diagnoses among Black and Hispanic/Latino MSM. To achieve the goals of the US Ending the HIV Epidemic initiative, effective interventions aimed to increase PrEP use need to be focused on Black and Hispanic/Latino MSM. *The other authors are researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention.*

A Prospective Case-Cohort Analysis of Plasma Metabolites and Breast Cancer Risk

DLH researcher **Victoria Stevens** is the lead author of an article published in *Breast Cancer Research* (Print: January 2023; Correction: February 2023). Breast cancer incidence rates have not declined despite an improvement in risk prediction and the identification of modifiable risk factors, suggesting the need to identify novel risk factors and etiological pathways involved in this cancer. Metabolomics has emerged as a promising tool to find circulating metabolites associated with breast cancer risk. Untargeted metabolomic analysis was done on prediagnostic plasma samples from a

case-cohort study of 1695 incident breast cancer cases and a 1983 women subcohort drawn from Cancer Prevention Study 3. A total of 11 metabolites were associated with breast cancer at false discovery rate (FDR) <0.05 with the majority having inverse association and one having a positive association. An additional 50 metabolites were associated at FDR <0.20 with inverse associations ranging from RR = 0.88 to RR = 0.91 and positive associations ranging from RR = 1.13 to RR = 1.11. Several of these associations validated the findings of previous metabolomic studies. These included findings that several progestogen and androgen steroids were associated with increased risk of breast cancer in postmenopausal women and four phospholipids, and the amino acids glutamine and asparagine were associated with decreased risk of this cancer in pre- and postmenopausal women. Several novel associations were also identified, including a positive association for syringol sulfate, a biomarker for smoked meat, and 3-methylcatechol sulfate and 3-hydroxypyridine glucuronide, which are metabolites of xenobiotics used for the production of pesticides and other products. The study validated previous metabolite findings and identified novel metabolites associated with breast cancer risk, demonstrating the utility of large metabolomic studies to provide new leads for understanding breast cancer etiology. The authors' novel findings suggest that consumption of smoked meats and exposure to catechol and pyridine should be investigated as potential risk factors for breast cancer. *The other authors are researchers from the American Cancer Society.*

Opioid Prescription and Diabetes Among Medicare Beneficiaries

DLH researcher **Sarah Stark Casagrande** is among the authors of an article published in *Diabetes Research and Clinical Practice* (Epub: January 2023; Print: February 2023). The aims were to determine the prevalence of opioid prescriptions among U.S. Medicare beneficiaries by diabetes status, and predictors of opioid prescription among those with diabetes. This retrospective study used claims data from the Centers for Medicare and Medicaid Services among beneficiaries age ≥65 years who were continuously enrolled in Part A, Part B, and Part D Medicare between 2017 and 2019. Overall, the prevalence of any opioid prescription was 30.8% among persons with diabetes and 24.2% in those without diabetes; chronic use was 8.0% and 7.4%, respectively. Those with diabetes had a 45% higher odds of having an opioid prescription compared to those without diabetes after adjusting for sociodemographic characteristics. After adjustment for comorbidities/complications, the association reversed. Persons with diabetes who had hypertension, obesity, CVD, neuropathy, amputation, liver disease, COPD, cancer, osteoporosis, depression, or alcohol/drug abuse had a 20%-140% higher odds of opioid prescription compared to those without these conditions. The authors concluded that comorbidities and complications accounted for the higher odds of opioid prescriptions among those with diabetes. *Other authors include researchers from the National Institute of Diabetes and Digestive and Kidney Diseases/NIH and Rush University.*

Pharmacokinetics of Dose-Adjusted Levonorgestrel Emergency Contraception Combined With Efavirenz-Based Antiretroviral Therapy or Rifampicin-Containing Tuberculosis Regimens

DLH researcher **Elizabeth Woolley** is among the authors of an article published in *Contraception* (Epub: January 2023; Print: May 2023). The objectives were to determine if double-dose levonorgestrel emergency contraception (EC) in combination with efavirenz or rifampicin, two drugs known to decrease levonorgestrel exposure, resulted in similar pharmacokinetics compared to standard-dose levonorgestrel EC without drug-drug interactions. The authors conducted a phase 2, open-label, multicenter, partially

randomized, 4 parallel group trial in pre-menopausal females ≥16 years old without an indication for EC and not on hormonal contraception. Participants on dolutegravir-based antiretroviral therapy (ART) received levonorgestrel 1.5 mg (control group); those on rifampicin-containing tuberculosis therapy received levonorgestrel 3 mg; those on efavirenz-based ART were randomized 1:2 to levonorgestrel 1.5 mg or 3 mg. Plasma was collected through 48 hours post-dose to assess levonorgestrel pharmacokinetics. The median age for all participants was 34 years and BMI was 23.2 kg/m^2. Participants receiving levonorgestrel 1.5 mg plus efavirenz had 50% lower $AUC_{0\text{-}8h}$ compared to the control group. Participants receiving levonorgestrel 3 mg had a similar $AUC_{0\text{-}8h}$ when receiving either efavirenz or rifampicin compared to control. Levonorgestrel 3 mg resulted in similar or higher maximum concentration with either efavirenz or rifampicin compared to the control group. The authors concluded that doubling the dose of levonorgestrel EC successfully increased levonorgestrel exposure over the first 8 hours in participants receiving either efavirenz-based ART or rifampicin-containing tuberculosis therapy. Adjusting levonorgestrel emergency contraception from 1.5 mg to 3 mg improves levonorgestrel pharmacokinetic exposure in participants receiving either efavirenz-based antiretroviral regimens or rifampicin-containing tuberculosis therapy. These data support guideline recommendations to double the dose of levonorgestrel emergency contraception in persons on medications that decrease levonorgestrel exposure by inducing levonorgestrel metabolism. *Other authors include researchers from the National Institute of Allergy and Infectious Diseases, University of Nebraska Medical Center, Harvard T.H. Chan School of Public Health, and the Office of Research on Women's Health (NIH), as well as researchers from South Africa, Thailand, Brazil, and Malawi.*

Increasing Gallstone Disease Prevalence and Associations with Gallbladder and Biliary Tract Mortality in the United States

DLH senior epidemiologist **Constance Ruhl** co-authored an article published in *Hepatology* (Epub: January 2023; Print: June 2023). The authors examined gallbladder and biliary tract mortality predictors in the US National Health and Nutrition Examination Survey (NHANES), 1988-1994, with 31 years of linked mortality data, and gallstone disease prevalence trends and associations in NHANES 2017-March 2020 prepandemic data. In NHANES 1988-1994, 18,794 participants were passively followed for mortality, identified by death certificate underlying or contributing causes, by linkage to the National Death Index through 2019. In NHANES 2017-March 2020, gallstone disease history was ascertained from 9232 adults. During NHANES 1988-2019 follow-up, 8580 deaths occurred from all causes and 72 deaths with gallbladder or biliary tract disease. In multivariable-adjusted analysis, older age, male sex, prediabetes or diabetes, and physical inactivity were associated with gallbladder and biliary tract mortality, and non-Hispanic Black and Mexican American race-ethnicity were inversely associated. Between 1988-1994 and 2017-March 2020, gallstone disease prevalence increased from 7.4% to 13.9% and gallbladder surgery from 6.0% to 11.6%. In 2017-March 2020 in multivariable-adjusted analysis, female sex, diabetes, liver disease, proton pump inhibitors, abdominal pain, increased age, BMI, and liver stiffness were associated with gallstone disease, and non-Hispanic Black and non-Hispanic Asian race and alcohol were inversely associated. The authors concluded that, in the US population, gallstone disease prevalence doubled over three decades, possibly because of the worsening of metabolic risk factors and growth of laparoscopic cholecystectomy. Gallbladder and biliary tract mortality and gallstone disease associations included factors such as prediabetes or diabetes, liver stiffness, and

proton pump inhibitors. *The other author is a researcher from the National Institute of Diabetes and Digestive and Kidney Diseases.*

Racial Differences in Social Determinants of Health and Outcomes Among Hispanic/Latino Persons with HIV—United States, 2015-2020

DLH researchers **Tamara Carree** and **Xin Yuan** are among the authors of an article published in the *Journal of Racial and Ethnic Health Disparities* (Online Ahead of Print: February 2023). Hispanic/Latino people with HIV (PWH) experience disparities in health outcomes compared with other racial and ethnic groups. Disaggregated data based on race for Hispanic/Latino PWH in the United States are rarely reported, potentially masking inequities. The Medical Monitoring Project (MMP) is a complex sample survey of adults with diagnosed HIV. The authors used weighted interview and medical record data collected from June 2015-May 2021 to examine differences in social determinants of health (SDH) and health outcomes by self-reported race among Hispanic/Latino adults with diagnosed HIV. Compared with White Hispanic/Latino PWH, Black Hispanic/Latino PWH were more likely to be unemployed, have a disability, have experienced homelessness, and have been incarcerated. American Indian/Alaska Native (AI/AN) and multiracial Hispanic/Latino PWH were more likely to have experienced homelessness than White Hispanic/Latino PWH. Black and multiracial Hispanic/Latino PWH were more likely to be virally unsuppressed than White Hispanic/Latino PWH. Black, multiracial, and AI/AN Hispanic/Latino PWH experience disparities in SDH and HIV outcomes. Lumping Hispanic/Latino people into one racial and ethnic category obscures health disparities, which might limit progress towards reaching national HIV goals. Future studies should consider disaggregating by other factors such as Hispanic origin, place of birth, immigration status, and primary language. Doing so recognizes the diversity of the Hispanic/Latino population. *Other authors are researchers from the Centers for Disease Control and Prevention.*

Higher Dose Oral Fluconazole for the Treatment of AIDS-Related Cryptococcal Meningitis (HIFLAC) - Report of A5225, a Multicentre, Phase I/II, Two-Stage, Dose-Finding, Safety, Tolerability and Efficacy Randomised, Amphotericin B-Controlled Trial of the AIDS Clinical Trials Group

DLH researcher **Evelyn Hogg** is among the authors of an article published in *PLoS One* (eCollection 2023, February 2023). The WHO recommended 1200 mg/day of fluconazole (FCZ) in the induction phase of cryptococcal meningitis (CM) in HIV prior to 2018 in regions where amphotericin-B (AMB) was unavailable. A 2-stage AMB-controlled, dose-escalation study to determine the maximum tolerated dose and the safety/efficacy of an induction-consolidation strategy of higher doses FCZ (1200 mg-2000 mg/day), adjusted for weight and renal function (eGFR)in adults with CM was undertaken. In Stage-1, three induction doses of FCZ (1200 mg/day, 1600 mg/day, and 2000 mg/day) were tested in sequential cohorts and compared with AMB in a 3:1 ratio. In Stage-2, the 1200 mg dose was excluded per protocol because of increased mortality, and participants were randomised to 1600 mg, 2000 mg FCZ, or AMB in a 1:1:1 ratio. One hundred and sixty eight participants were enrolled with 48, 50, and 48 in the AMB, 1600 mg, and 2000 mg cohorts. There were no life-threatening changes in electrocardiogram QTc, which were similar across all doses of FCZ and AMB. Induction phase weight and renal-adjusted doses of 1600 mg and 2000 mg/day FCZ for CM were safe and well tolerated except for increased GI side effects in the 2000 mg/day dose, and had similar times to achieve CSF sterilization, but took significantly longer than AMB. The WHO recommended 1200 mg FCZ was associated with a high mortality. While not statistically significant, mortality was

numerically lower in the AMB compared to 1600 mg and 2000 mg FCZ. These data make a case for a phase 3 study of higher doses of FZC. *Other authors include researchers from the Durban University of Technology (South Africa), Harvard T.H. Chan School of Public Health, and George Washington University, as well as researchers from Uganda, Kenya, India, Thailand, Zimbabwe, Peru, and South Africa.*

HIV Knowledge Among African Americans Living with HIV in the Rural South: Implications for Improving HIV Prevention and Care Outcomes

DLH researcher **Zaneta Gaul** is among the authors of an article published in the *Journal of Racial and Ethnic Health Disparities* (Online Ahead of Print: February 2023). This study examines the HIV knowledge of people living with HIV (PLWH) and its implications for improved healthcare outcomes. The study design was a descriptive cross-sectional study, and a total of 41 PLWH were recruited from a larger faith-based anti-stigma study. Data were collected using a semi-structured self-administered questionnaire and analyzed using SAS. In addition, a literature review was conducted using search engines to gauge existing literature from 2013 to 2022 in areas of HIV knowledge and healthcare outcomes among PLWH. The 41 PLWH enrolled consisted of 51% males and 49% females. Sixteen (39%) were aged ≥51 years, 17 (41%) had been living with HIV for >10 years, 15 (37%) had < high school diploma, and 100% were currently in HIV care. HIV knowledge scores were below average for 20 (49%) of the PLWH. Substantial knowledge deficits were noted in areas of HIV transmission and risk reduction strategies. Lower scores were not significantly associated with the participant's gender, education level, or length of time being HIV-infected. The results of the literature review showed limited research in this area. The authors concluded that the study and literature review results showed that HIV knowledge and health literacy may contribute to racial disparities in retention in care leading to poor health outcomes. Healthcare providers and health facilities in rural areas should be equipped with culturally tailored HIV educational tools to strengthen ongoing care for PLWH, foster patient-provider relationships, and eliminate internalized stigma detrimental to improved healthcare outcomes among PLWH. *Other authors include researchers from Vitalera Integrated Consults (Nigeria) and the University of Alabama at Tuscaloosa.*

Nicotine Exposure Decreases Likelihood of SARS-CoV-2 RNA Expression and Neuropathology in the hACE2 Mouse Brain But Not Moribundity

DLH researcher **Matthew Bridge** is among the authors of an article published in *Scientific Reports* (Print: February 2023). Individuals infected by SARS-CoV-2 are at risk of developing neurological-related post-acute disorders. Disputed epidemiological data indicated nicotine may reduce the severity of infection. Here we find exposure to nicotine in drinking water does not alter the moribundity of hACE2 mice. However, pre-exposure to nicotine decreased the likelihood of SARS-CoV-2 RNA expression and pathology in the brain. These results suggest mechanisms involving targets of nicotine could be leveraged to prevent the neurovirulence of SARS-CoV-2. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

The Cooperative Re-Engagement Controlled Trial (CoRECT): Durable Viral Suppression Assessment

DLH researcher **Tiffany Williams** is among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Epub: February 2023; Print: June 2023). A collaborative, data-to-care strategy to identify persons with HIV (PWH) newly out-of-care, combined with an active public health intervention, significantly increases the proportion of PWH re-engaged in HIV care. The authors assessed this strategy's impact

on durable viral suppression (DVS). A multi-site, prospective randomized controlled trial for out-of-care individuals using a data-to-care strategy and comparing public health field services to locate, contact, and facilitate access to care versus the standard of care (SOC). DVS was defined as the last viral load (VL), the VL at least three months prior, and any VL between the two were all <200 copies/mL during the 18 months post-randomization. Alternative definitions of DVS were also analyzed. Between August 1, 2016 and July 31, 2018, 1,893 participants were randomized from Connecticut, Massachusetts, and Philadelphia. There was no association between DVS and the intervention adjusting for site, age categories, race/ethnicity, birth sex, CD4 categories, and exposure categories. A collaborative, data-to-care strategy, and active public health intervention did not increase the proportion of PWH achieving DVS, suggesting additional support to promote retention in care and antiretroviral adherence may be needed. Initial linkage and engagement services, through data-to-care or other means, are likely necessary but insufficient for achieving DVS for all PWH. *The other authors are researchers from the Centers for Disease Control and Prevention, Philadelphia Department of Public Health, Massachusetts Department of Public Health, Yale University School of Medicine, and the Connecticut Department of Public Health.*

Changes in Body Mass Index with Longer-Term Integrase Inhibitor Use: A Longitudinal Analysis of Data from the Randomized Trial to Prevent Vascular Events in Human Immunodeficiency Virus (REPRIEVE)

DLH researcher **Jhoanna Roa** is among the authors of an article published in *Clinical Infectious Diseases* (Epub: February 2023; Print: June 2023). Weight gain with longer-term integrase strand transfer inhibitor (INSTI)-based regimens remains unknown. Over 2-years of follow-up in REPRIEVE, INSTI use was associated with weight gain among those on an INSTI entry regimen <2 years, but not those on an INSTI regimen >2 years at entry. *Other authors include researchers from Massachusetts General Hospital and Harvard Medical School, Division of Infectious Diseases at Ohio State University Medical Center, Division of Infectious Diseases at University of Cincinnati College of Medicine, and Division of Infectious Diseases at Icahn School of Medicine at Mount Sinai.*

Residential Proximity to Metal-Containing Superfund Sites and Their Potential as a Source of Disparities in Metal Exposure Among U.S. Women

DLH researcher **Nathaniel MacNell** is among the authors of an article published in *Environmental Health Perspectives* (Epub: March 2023; Print: March 2023). More than 73 million people in the United States live within 3 mi (5 km) of a Superfund site, which can be sources of uncontrolled hazardous waste. These sites tend to be in areas of lower socioeconomic status or with higher proportions of people of color. Many Superfund sites release metals into different environmental media, making the sites plausible sources of exposure for nearby communities. The authors aimed to evaluate associations between residential proximity to metal-containing Superfund sites and toenail metal biomarker concentrations, with consideration of how these associations varied by race to assess the potential for unequal burden of exposure. Overall, results suggested that living near a metal-containing Superfund site is positively associated with toenail metal concentrations and that associations for lead and cadmium are strongest for non-Hispanic Black women in comparison with non-Hispanic White women. Negative control results suggested that Superfund sites that do not contain lead are located proximal to other sources of lead. These findings are important from a public health standpoint because people continue to be exposed to toxic chemicals—released from such sites—that have well-established adverse health effects. It is imperative that these sites, as well as other sources of exposure that may be colocated with Superfund sites, continue to be

remediated to reduce exposure to hazardous chemicals such as metals. *Other authors include researchers from the National Institute of Environmental Health Sciences, Gillings School of Global Public Health at the University of North Carolina at Chapel Hill, and the National Cancer Institute.*

Performance of the 2016 ACR-EULAR Myositis Response Criteria in Adult Dermatomyositis/Polymyositis Therapeutic Trials and Consensus Profiles

DLH researchers **Christian Douglas**, **Brian Erman**, **Jesse Wilkerson**, and **John McGrath** are among the authors of an article published in *Rheumatology (Oxford)* (Online Ahead of Print: March 2023). The ACR-EULAR myositis response criteria (MRC) were developed as a composite measure using absolute percentage change in six core set measures (CSMs). The authors aimed to further validate the MRC by assessing the contribution of each CSM, frequency of strength versus extramuscular activity improvement, representation of patient-reported outcome measures (PROM), and frequency of CSM worsening. Data from adult dermatomyositis/polymyositis patients in the rituximab, etanercept, and abatacept trials, and consensus patient profiles were evaluated. Of 412 adults with dermatomyositis/polymyositis, there were 37%, 24%, 25%, and 14% with no, minimal, moderate, and major MRC improvement, respectively. The authors concluded that the ACR-EULAR MRC performs consistently across multiple studies, further supporting its use as an efficacy end point in future myositis therapeutic trials. *Other authors include researchers from the University of Pittsburgh, National Institute of Arthritis Musculoskeletal and Skin Diseases, and the National Institute of Environmental Health Sciences.*

Performance of the 2016 ACR-EULAR Myositis Response Criteria in Juvenile Dermatomyositis Therapeutic Trials and Consensus Profiles

DLH researchers **Christian Douglas**, **Jesse Wilkerson**, **Brian Erman**, and **John McGrath** are among the authors of an article published in *Rheumatology (Oxford)* (Online Ahead of Print: March 2023). The 2016 ACR-EULAR Response Criteria for juvenile dermatomyositis (JDM) was developed as a composite measure with differential weights of six core set measures (CSMs) to calculate a Total Improvement Score (TIS). The authors assessed the contribution of each CSM, representation of muscle-related and patient-reported CSMs towards improvement, and frequency of CSM worsening across myositis response criteria (MRC) categories in validation of MRC. Data from JDM patients in the Rituximab in Myositis trial, PRINTO JDM trial, and consensus patient profiles were included. Of 457 JDM patients with IMACS CSMs and 380 with PRINTO CSMs, 9-13% had minimal, 19-23% had moderate, and 41-50% had major improvement. The authors concluded that the ACR-EULAR MRC perform consistently across multiple studies, supporting its further use as an efficacy end point in JDM trials. *Other authors include researchers from the National Institute of Arthritis Musculoskeletal and Skin Diseases, University of Chicago, University of Pittsburgh, and the National Institute of Environmental Health Sciences.*

Factors Associated with Prevalent Mycobacterium Tuberculosis Infection and Disease Among Adolescents and Adults Exposed to Rifampin-Resistant Tuberculosis in the Household

DLH researcher **Linda Naini** is among the authors of an article published in *PLoS One* (eCollection 2023, March 2023). Understanding factors associated with prevalent Mycobacterium tuberculosis infection and prevalent TB disease in household contacts of patients with drug-resistant tuberculosis (TB) may be useful for TB program staff conducting contact investigations. Using data from a cross-sectional study that enrolled index participants with rifampin-resistant pulmonary TB and their household contacts

(HHCs), the authors evaluated HHCs age ≥15 years for factors associated with two outcomes: Mycobacterium tuberculosis infection and TB disease. Seven hundred twelve HHCs age ≥15 years enrolled from 279 households in eight high-TB burden countries were a median age of 34 years, 63% female, 22% current smokers and 8% previous smokers, 8% HIV-positive, and 11% previously treated for TB. Multivariable modeling showed interferon-gamma release assay (IGRA) positivity was more common in HHCs aged 25-49 years; reporting prior TB treatment; reporting incarceration, substance use, and/or a period of daily alcohol use in the past 12 months; sharing a sleeping room or more evenings spent with the index participant; living with smokers; or living in a home of materials typical of low socioeconomic status. Forty-six HHCs age ≥15 years had prevalent TB disease. Multivariable modeling showed higher prevalence of TB disease among HHCs aged ≥50 years; reporting current or previous smoking; reporting a period of daily alcohol use in the past 12 months; and reporting prior TB treatment. The authors identified overlapping and distinct characteristics associated with Mycobacterium tuberculosis infection and TB disease that may be useful for those conducting household TB investigations. *Other authors include researchers from Frontier Science Foundation, Harvard T.H. Chan School of Public Health, Emory University Rollins School of Public Health, and researchers from South Africa, India, Peru, Haiti, Thailand, Brazil, and Kenya.*

Evaluation of the Herbicide Glyphosate, (Aminomethyl)Phosphonic Acid, and Glyphosate-Based Formulations for Genotoxic Activity Using In Vitro Assays

DLH researchers **Shawn Harris**, **Sandra McBride**, and **Gary Larson** are among the authors of an article published in *Environmental and Molecular Mutagenesis* (Epub: March 2023; Print: April 2023). Glyphosate, the most heavily used herbicide world-wide, is applied to plants in complex formulations that promote absorption. The National Toxicology Program reported in 1992 that glyphosate, administered in feed to rats and mice for 13 weeks at doses up to 50,000 ppm, showed little evidence of toxicity, with no induction of micronuclei to the mice. Subsequently, mechanistic studies of glyphosate and glyphosate-based formulations (GBFs) that have focused on DNA damage and oxidative stress suggest that glyphosate may have genotoxic potential. However, few of these studies directly compared glyphosate to GBFs, or effects among GBFs. To address these data gaps, the authors tested glyphosate, glyphosate isopropylamine (IPA), and (aminomethyl)phosphonic acid (AMPA, a microbial metabolite of glyphosate), 9 high-use agricultural GBFs, 4 residential-use GBFs, and additional herbicides (metolachlor, mesotrione, and diquat dibromide) present in some of the GBFs in bacterial mutagenicity tests, and in human TK6 cells using a micronucleus assay and a multiplexed DNA damage assay. Results showed no genotoxicity or notable cytotoxicity for glyphosate or AMPA at concentrations up to 10 mM, while all GBFs and herbicides other than glyphosate were cytotoxic, and some showed genotoxic activity. An in vitro to in vivo extrapolation of results for glyphosate suggests that it is of low toxicological concern for humans. In conclusion, these results demonstrate a lack of genotoxicity for glyphosate, consistent with observations in the NTP in vivo study, and suggest that toxicity associated with GBFs may be related to other components of these formulations. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Process Development for a 1H-Indazole Synthesis Using an Intramolecular Ullmann-Type Reaction

DLH researcher **Katherine Allen** is among the authors of an article published in the *Journal of Organic Chemistry* (Epub: March 2023; Print: April 2023). Fluorinated indazole was needed to develop a new route to an active pharmaceutical ingredient intermediate.

Although an established route was in place, it was undesirable due to safety and selectivity concerns. A concise and improved route was developed to form the desired indazole, which takes advantage of an electronically directed metalation/formylation sequence followed by condensation with methyl hydrazine to form a hydrazone and culminates in a copper-catalyzed intramolecular Ullmann cyclization. The Ullmann reaction was plagued with difficulties ranging from poor reactivity to thermal hazard concerns, but through use of high-throughput screening, statistical modeling, and an unusual isolation method for fine chemicals, safe and optimal conditions were found that produce high-purity isolated material in excellent yields at a laboratory scale. *The other authors are researchers from Lilly Research Laboratories.*

A Gene-Acculturation Study of Obesity Among US Hispanic/Latinos: The Hispanic Community Health Study/Study of Latinos

DLH researcher **Julia Ward** is among the authors of an article published in *Psychosomatic Medicine* (Epub: March 2023; Print: May 2023). In the United States, Hispanic/Latino adults face a high burden of obesity; yet, not all individuals are equally affected, partly due in part to this ethnic group's marked sociocultural diversity. The authors sought to analyze the modification of body mass index (BMI) genetic effects in Hispanic/Latino adults by their level of acculturation, a complex biosocial phenomenon that remains understudied. Among 11,747 Hispanic/Latino adults in the Hispanic Community Health Study/Study of Latinos aged 18 to 76 years from four urban communities (2008-2011), the authors (a) tested their hypothesis that the effect of a genetic risk score (GRS) for increased BMI may be exacerbated by higher levels of acculturation, and (b) examined if GRS acculturation interactions varied by gender or Hispanic/Latino background group. Results suggested the presence of effect modification by acculturation, with stronger effects on BMI among highly acculturated individuals and female immigrants. Future studies of obesity in the Hispanic/Latino community should account for sociocultural environments and consider their intersection with gender to better target obesity interventions. *Other authors include researchers from Pennsylvania State University, University of North Carolina at Chapel Hill, and the University of Texas Southwestern Medical Center.*

Perceived Neighborhood Social Cohesion and Type 2 Diabetes Mellitus by Age, Sex/Gender, and Race/Ethnicity in the United States

DLH researcher **W. Braxton Jackson II** is among the authors of an article published in *Preventive Medicine* (Epub: March 2023; Print: May 2023). In prior research, perceived low neighborhood social cohesion (nSC) has been associated with prevalence of type 2 diabetes mellitus (T2DM); however, few studies have investigated the nSC-T2DM relationship among a large, racially/ethnically diverse, and nationally representative sample of the U.S. population. The authors used National Health Interview Survey (2013-2018) data to determine overall, age-, sex/gender-, and racial/ethnic-specific associations between nSC and T2DM among 170,432 adults. Self-reported nSC was categorized as low, medium, and high. T2DM was determined by participants being told they had diabetes by a health professional. Mean age was 47.4 ± 0.1 years, 52% were women, and 69% self-identified as Non-Hispanic (NH)-White. Low vs. high nSC was associated with a higher prevalence of T2DM, after adjustment. A higher prevalence of T2DM was observed among participants 31-49 years old who perceived low vs. high nSC and among participants ≥50 years old. Hispanic/Latinx women 18-30 years old in neighborhoods with low vs. high social cohesion had a higher prevalence of T2DM, whereas NH-Black women 18-30 years old in neighborhoods with medium vs. high social cohesion had a lower prevalence of T2DM. The authors' findings support the literature by demonstrating an association between

neighborhood environment and T2DM as well as extend it by identifying determinants for intervention for T2DM. *Other authors include researchers from the National Institute of Environmental Health Sciences, National Institute on Minority Health and Health Disparities, and the Massachusetts Institute of Technology.*

Utilizing Community Based Participatory Research Methods in Black/African American and Hispanic/Latinx Communities in the US: The CDC Minority HIV Research Initiative (MARI-Round 4)

DLH researcher **Zaneta Gaul** is among the authors of an article published in the *Journal of Community Health* (Epub: March 2023; Print: August 2023). The Centers for Disease Control and Prevention Minority HIV Research Initiative (MARI) funded 8 investigators in 2016 to develop HIV prevention and treatment interventions in highly affected communities. We describe MARI studies who used community-based participatory research methods to inform the development of interventions in Black/African American and Hispanic/Latinx communities focused on sexual minority men (SMM) or heterosexual populations. Each study implemented best practice strategies for engaging with communities, informing recruitment strategies, navigating through the impacts of COVID-19, and disseminating findings. Best practice strategies common to all MARI studies included establishing community advisory boards, engaging community members in all stages of HIV research, and integrating technology to sustain interventions during the COVID-19 pandemic. Implementing community-informed approaches is crucial to intervention uptake and long-term sustainability in communities of color. MARI investigators' research studies provide a framework for developing effective programs tailored to reducing HIV-related racial/ethnic disparities. *Other authors include researchers from the Centers for Disease Control and Prevention, University of Central Florida, Brown University, and Johns Hopkins School of Medicine.*

HIV Prevention Services for Hispanic/Latino Persons in THRIVE, 2015-2020

DLH researcher **Tameka Hayes** is among the authors of an article published in the *American Journal of Preventive Medicine* (Epub: March 2023; Print: August 2023). Hispanic/Latino men who have sex with men (MSM) and transgender women (TGW) are disproportionately affected by HIV in the U.S. The study evaluated HIV prevention services and outcomes among Hispanic/Latino MSM and TGW in the targeted highly effective interventions to reduce the HIV epidemic (THRIVE) demonstration project and consider lessons learned. The authors described the THRIVE demonstration project services provided to Hispanic/Latino MSM and TGW in 7 U.S. jurisdictions from 2015 to 2020. HIV prevention service outcomes were compared between 1 site with (2,147 total participants) and 6 sites without (1,129 total participants) Hispanic/Latino-oriented pre-exposure prophylaxis clinical services. The THRIVE demonstration project served 2,898 and 378 Hispanic/Latino MSM and TGW, respectively, with 2,519 MSM and 320 TGW receiving ≥1 HIV screening test. Among 2,002 MSM and 178 TGW eligible for pre-exposure prophylaxis, 1,011 MSM and 98 TGW received pre-exposure prophylaxis prescriptions, respectively. The THRIVE demonstration project delivered comprehensive HIV prevention services to Hispanic/Latino MSM and TGW. Hispanic/Latino-oriented clinical settings may improve HIV prevention service delivery to persons in Hispanic/Latino communities. *Other authors include researchers from the Centers for Disease Control and Prevention, District of Columbia Department of Health, Johns Hopkins School of Medicine, New York City Department of Health and Mental Hygiene, and the Office of Public Health at the Louisiana Department of Health in New Orleans.*

Whole-Genome Sequencing to Predict Antimicrobial Susceptibility Profiles in Neisseria Gonorrhoeae

DLH researcher **Sara McCurdy Murphy** is among the authors of an article published in the *Journal of Infectious Diseases* (Print: April 2023). Neisseria gonorrhoeae is a major public health problem due to increasing incidence and antimicrobial resistance. Genetic markers of reduced susceptibility have been identified; the extent to which those are representative of global antimicrobial resistance is unknown. The authors evaluated the performance of whole-genome sequencing (WGS) used to predict susceptibility to ciprofloxacin and other antimicrobials using a global collection of N. gonorrhoeae isolates. Susceptibility testing of common antimicrobials and the recently developed zolifodacin was performed using agar dilution to determine minimum inhibitory concentrations (MICs). Resistance alleles were identified at loci known to contribute to antimicrobial resistance in N. gonorrhoeae from WGS data. The ability of each locus was tested to predict antimicrobial susceptibility. A total of 481 N. gonorrhoeae isolates, collected between 2004 and 2019 and making up 457 unique genomes, were sourced from 5 countries. All isolates with demonstrated susceptibility to ciprofloxacin had a wild-type gyrA codon 91. Multilocus approaches were needed to predict susceptibility to other antimicrobials. All isolates were susceptible to zoliflodacin, defined by an MIC ≤0.25 µg/mL. The authors concluded that single marker prediction can be used to inform ciprofloxacin treatment of N. gonorrhoeae infection. A combination of molecular markers may be needed to determine susceptibility for other antimicrobials. *Other authors include researchers from the University of California San Diego, Harvard T.H. Chan School of Public Health, University of Washington, University of California Los Angeles, and the University of Saskatchewan.*

Neighborhood Social Cohesion and Obesity in the United States

DLH researcher **W. Braxton Jackson II** is among the authors of an article published in *Endocrine and Metabolic Science* (Epub: April 2023; Print: June 2023). Low neighborhood social cohesion (nSC) has been associated with obesity. Still, few studies have assessed the nSC-obesity relationship among a large, nationally representative, and racially/ethnically diverse sample of the United States population. To address this literature gap, the authors examined cross-sectional associations among 154,480 adult participants of the National Health Interview Survey (NHIS) from 2013 to 2018. They also determined if associations varied by race/ethnicity, sex/gender, age, annual household income, and food security status. Based on a 4-item scale from the Project on Human Development in Chicago Neighborhoods Community Survey, nSC was categorized as low, medium, and high. Based on body mass index (BMI) recommendations, obesity was categorized as ≥30 kg/m2. Study participants' mean age ± standard error was 47.1 ± 0.1 years; most (69.2%) self-identified as Non-Hispanic (NH)-White; and 51.0 % were women. NH-Black and Hispanic/Latinx adults comprised more of the population in neighborhoods with low nSC (14.0% NH-Black, 19.1% Hispanic/Latinx, and 61.8% NH-White) versus high nSC (7.7% NH-Black, 10.4% Hispanic/Latinx, and 77.0% NH-White). Low vs. high nSC was associated with a 15% higher prevalence of obesity, and the magnitude of the association was more substantial among NH-White adults compared to associations among Hispanic/Latinx and NH-Black adults. Low vs. high nSC was associated with a 20% higher prevalence of obesity in women compared to a 10% higher prevalence in men. Low vs. high nSC was associated with a 19% higher prevalence of obesity among adults ≥50 years old compared to a 7% higher prevalence of obesity among adults <50 years old. Efforts to address nSC may improve health and address health disparities. *Other authors include researchers from the National Institute of Environmental Health Sciences and National Institute on Minority Health and Health Disparities.*

Readmission and Mortality After Hospitalization With Acute Kidney Injury
DLH researchers **Jane Der**, **Helen Corns**, **Bryan Sayer**, and **Duc Anh Ngo** are among the authors of an article published in the *American Journal of Kidney Diseases* (Epub: April 2023; Print: July 2023). Acute kidney injury (AKI) carries high rates of morbidity and mortality. This study quantified various short- and long-term outcomes after hospitalization with AKI. The study design was a retrospective propensity score (PS)-matched cohort study. Optum Clinformatics, a national claims database, was used to identify patients hospitalized with and without an AKI discharge diagnosis between January 2007 and September 2020. Among patients with prior continuous enrollment for at least 2 years without AKI hospitalization, 471,176 patients hospitalized with AKI were identified and PS-matched to 471,176 patients hospitalized without AKI. After PS matching, rehospitalization, and death incidences were estimated using the cumulative incidence function method and compared using Gray's test. Overall and stratified analyses were performed to evaluate for interaction between an AKI hospitalization and preexisting chronic kidney disease (CKD). After PS matching, AKI was associated with higher rates of rehospitalization for any cause, end-stage renal disease, heart failure, sepsis, pneumonia, myocardial infarction, and volume depletion at 90 days after discharge compared with the group without AKI, with similar findings at 365 days. Mortality rate was higher in the group with AKI than in the group without AKI at 90 and 365 days. The higher risk of outcomes persisted when participants were stratified by CKD status. The authors concluded that AKI during hospitalization in patients with and without CKD is associated with increased risk of 90- and 365-day all-cause/selected-cause rehospitalization and death. *The other authors are researchers from the National Institute of Diabetes and Digestive and Kidney Diseases.*

Immunogenicity and Safety of Hepatitis B Virus (HBV) Vaccine With a Toll-Like Receptor 9 Agonist Adjuvant in HBV Vaccine-Naive People with Human Immunodeficiency Virus
DLH researcher **Christina Vernon** is among the authors of an article published in *Clinical Infectious Diseases* (Epub: April 2023; Print: August 2023). In this international, multicenter open-label study (ACTG A5379) of HepB-CpG vaccine in people with HIV without prior Hepatitis B Virus (HBV) vaccination, all 68 participants achieved HBV seroprotective titers after the 3-dose series in the primary analysis. No unexpected safety issues were observed. *The other authors are researchers from Weill Cornell Medicine, Harvard T.H. Chan School of Public Health, Johns Hopkins University, and the National Institute of Allergy and Infectious Diseases.*

Food Insecurity and Sleep Health by Race/Ethnicity in the United States
DLH researcher **W. Braxton Jackson II** is among the authors of an article published in the *Journal of Nutritional Sciences* (eCollection 2023; May 2023). Food insecurity, poised to increase with burgeoning concerns related to climate change, may influence sleep, yet few studies examined the food security-sleep association among racially/ethnically diverse populations with multiple sleep dimensions. The authors determined overall and racial/ethnic-specific associations between food security and sleep health. Using National Health Interview Survey data, food security was categorized as very low, low, marginal, and high. Sleep duration was categorized as very short, short, recommended, and long. Sleep disturbances included trouble falling/staying asleep, insomnia symptoms, waking up feeling unrested, and using sleep medication (all ≥3 d/times in the previous week). Among 177,435 participants, with a mean age of 47.2 ±0.1 years, 52.0% were women, and 68.4% were non-Hispanic (NH)-White. A higher percent of NH-Black (7.9%) and Hispanic/Latinx (5.1%) lived in very low food security households than NH-White (3.1%) participants. Very

low vs. high food security was associated with a higher prevalence of very short sleep duration as well as trouble falling asleep. Very low vs. high food security was associated with a higher prevalence of very short sleep duration among Asian and NH-White participants compared with NH-Black and Hispanic/Latinx participants. Food insecurity was associated with poorer sleep in a racially/ethnically diverse US sample. *The other authors are researchers from the National Institute of Environmental Health Sciences and the National Institute on Minority Health and Health Disparities.*

Antiretroviral Therapy Intensification for Neurocognitive Impairment in Human Immunodeficiency Virus

DLH researcher **Jhoanna Roa** is among the authors of an article published in *Clinical Infectious Diseases* (Online Ahead of Print: May 2023). Neurocognitive impairment (NCI) in people with HIV (PWH) on antiretroviral therapy (ART) is common and may result from persistent HIV replication in the central nervous system. A5324 was a randomized, double-blind, placebo-controlled trial of ART intensification with dolutegravir (DTG) +MVC, DTG+Placebo, or Dual-Placebo in PWH with plasma HIV RNA <50 copies/mL on ART and NCI. Assessments were repeated at 24, 48, 72, and 96 weeks. The primary outcome was the change from baseline to week 48 on the normalized total z-score (i.e., the mean of the individual NC test z-scores). Of 357 screened, 191 enrolled: 71% male, 51% Black race, 22% Hispanic ethnicity; mean age 52 years; mean CD4+ T-cells 681 cells/µL. Most (65%) had symptomatic HIV-associated NC disorder. Adjusting for age, sex, race, study site, efavirenz use, or baseline z-score did not alter the results. Body mass index modestly increased over 96 weeks and did not differ between arms. This is the largest, randomized, placebo-controlled trial of ART intensification for NCI in PWH. The findings do not support empiric ART intensification as a treatment for NCI in PWH on suppressive ART. They also do not support that DTG adversely affects cognition, mood, or weight. *Other authors include researchers from the University of California San Diego, Harvard T.H. Chan School of Public Health, and Division of AIDS/National Institute of Allergy and Infectious Diseases.*

Risk Factors and Trends for HPV-Associated Subsequent Malignant Neoplasms Among Adolescent and Young Adult Cancer Survivors

DLH researcher **Judy Ou** is among the authors of an article published in *Cancer Epidemiology, Biomarkers & Prevention* (Print: May 2023). Subsequent malignant neoplasms (SMN; new cancers that arise after an original diagnosis) contribute to premature mortality among adolescent and young adult (AYA) cancer survivors. Because of the high population prevalence of human papillomavirus (HPV) infection, the authors identified demographic and clinical risk factors for HPV-associated SMNs (HPV-SMN) among AYA cancer survivors in the SEER-9 registries diagnosed from 1976 to 2015. Outcomes included any HPV-SMN, oropharyngeal-SMN, and cervical-SMN. Follow-up started 2 months after their original diagnosis. Of 374,408 survivors, 1,369 had an HPV-SMN, occurring on average 5 years after first cancer. Compared with the general population, AYA survivors had 70% increased risk for any HPV-SMN and 117% for oropharyngeal-SMN; cervical-SMN risk was generally lower in survivors, but Hispanic AYA survivors had an 8.4 significant increase in cervical-SMN. AYAs first diagnosed with Kaposi sarcoma, leukemia, Hodgkin, and non-Hodgkin lymphoma had increased HPV-SMN risks compared with the general population. Oropharyngeal-SMN incidence declined over time in APC models. Chemotherapy and radiation were associated with any HPV-SMN among survivors with first HPV-related cancers, but not associated among survivors whose first cancers were not HPV-related. The authors concluded that HPV-SMN in AYA survivors are driven by oropharyngeal cancers despite temporal declines in oropharyngeal-SMN. Hispanic survivors are at risk for cervical-SMN relative to the general

population. *Other authors include researchers from the University of Utah, Brigham Young University, and Oak Ridge National Laboratory (U.S. Department of Energy). Note: Dr. Ou conducted this work while at the University of Utah.*

Volatile Hydrocarbon Exposures and Incident Coronary Heart Disease Events: Up to Ten Years of Follow-up Among *Deepwater Horizon* Oil Spill Workers

DLH researcher **W. Braxton Jackson II** is among the authors of an article published in *Environmental Health Perspectives* (Epub: May 2023; Print: May 2023). During the 2010 *Deepwater Horizon* (DWH) disaster, response and cleanup workers were potentially exposed to toxic volatile components of crude oil. However, to the authors' knowledge, no study has examined exposure to individual oil spill-related chemicals in relation to cardiovascular outcomes among oil spill workers. The authors aimed to investigate the association of several spill-related chemicals [benzene, toluene, ethylbenzene, xylene, n-hexane (BTEX-H)] and total hydrocarbons (THC) with incident coronary heart disease (CHD) events among workers enrolled in a prospective cohort. Cumulative exposures to THC and BTEX-H across the cleanup period were estimated via a job-exposure matrix that linked air measurement data with self-reported DWH spill work histories. The authors ascertained CHD events following each worker's last day of cleanup work as the first self-reported physician-diagnosed myocardial infarction (MI) or a fatal CHD event. Among 22,655 workers with no previous MI diagnoses, 509 experienced an incident CHD event through December 2019. Workers in higher quintiles of each exposure agent had increased CHD risks in comparison with the referent group (Q1) of that agent, with the strongest associations observed in Q5. However, most associations were nonsignificant, and there was no evidence of exposure-response trends. Stronger associations were observed among ever smokers, workers with ≤high school education, and workers with body mass index <30kg/m2. No apparent positive association was observed for the BTEX-H mixture. The authors concluded that higher exposures to volatile components of crude oil were associated with modest increases in risk of CHD among oil spill workers, although exposure-response trends were not observed. *Other authors include researchers from the University of North Carolina at Chapel Hill, Johns Hopkins University, the National Institute of Environmental Health Sciences, the National Cancer Institute, and the National Institute on Aging.*

One-Year Incidence of Tuberculosis Infection and Disease Among Household Contacts of Rifampin- and Multi-Drug Resistant Tuberculosis

DLH researcher **Linda Naini** is among the authors of an article published in *Clinical Infectious Diseases* (Online Ahead of Print: May 2023). Tuberculosis infection (TBI) and tuberculosis disease (TBD) incidence remains poorly described following household contact (HHC) rifampin-/multidrug-resistant tuberculosis exposure. The authors sought to characterize TBI and TBD incidence at 1 year in HHCs and to evaluate tuberculosis preventive therapy (TPT) use in high-risk groups. The authors previously conducted a cross-sectional study of HHCs of rifampin-/multidrug-resistant tuberculosis in 8 high-burden countries and re-assessed TBI (interferon-gamma release assay, HHCs ≥5 years) and TBD (HHCs all ages) at 1 year. Incidence was estimated across age and risk groups (age <5 years; age ≥5 years, HIV-positive; age ≥5 years, HIV-negative/unknown, baseline TBI positive) by logistic or log-binomial regression fitted using generalized estimating equations. Of 1016 HHCs, 850 from 247 households were assessed. Among 242 HHCs, 52 tested interferon-gamma release assay-positive, yielding a 1-year 21.6% TBI cumulative incidence. Sixteen of 742 HHCs developed confirmed, probable, or possible TBD, yielding a 2.3% one-year cumulative incidence for confirmed/probable TBD. TBI and TBD incidence

continued through 1 year in rifampin-/multidrug-resistant tuberculosis HHCs. Low TPT coverage emphasizes the need for evidence-based prevention and scale-up, particularly among high-risk groups. *Other authors include researchers from Johns Hopkins University School of Medicine, Harvard T.H. Chan School of Public Health, and Frontier Science Foundation, and researchers from South Africa, India, Peru, Haiti, Botswana, Brazil, and Kenya.*

Short-Term Toxicity Studies of Thallium (I) Sulfate Administered in Drinking Water to Sprague Dawley Rats and B6C3F1/N Mice

DLH researcher **Laura Betz** is among the authors of an article published in *Toxicology Reports* (eCollection 2023, May 2023). Thallium is a heavy metal that is known to induce a broad spectrum of adverse health effects in humans including alopecia, neurotoxicity, and mortality following high-dose acute poisoning events. Widespread human exposure to thallium may occur via consumption of contaminated drinking water; limited toxicity data are available to evaluate the corresponding public health risk. To address this data gap, the Division of Translational Toxicology conducted short-term toxicity studies of a monovalent thallium salt, thallium (I) sulfate. Thallium (I) sulfate was administered via dosed drinking water to time-mated Sprague Dawley rats and their offspring from gestation day (GD) 6 until up to postnatal day (PND) 28 at concentrations of 0, 3.13, 6.25, 12.5, 25, or 50 mg/L, and adult male and female B6C3F1/N mice for up to 2 weeks at concentrations of 0, 6.25, 12.5, 25, 50, or 100 mg/L. Exposure to thallium (I) sulfate at concentrations ≤12.5 mg/L did not impact dam body weights, maintenance of pregnancy, littering parameters, or pup survival. However, in pups, exposure to 12.5 mg/L thallium (I) sulfate resulted in decreased body weight gains relative to control rats and onset of whole-body alopecia. Measurement of thallium concentrations in dam plasma, amniotic fluid, fetuses, and pup plasma indicated marked maternal transfer of thallium to offspring during gestation and lactation. Mice exposed to 100 mg/L thallium (I) sulfate were removed early due to overt toxicity, and mice exposed to ≥25 mg/L exhibited exposure concentration-related decreases in body weight. Lowest-observed-effect levels of 12.5 mg/L (rats) and 25 mg/L (mice) were determined based on the increased incidence of clinical signs of alopecia in rat pups and significantly decreased body weights for both rats and mice. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Understanding Disparities in Antiretroviral Therapy Adherence and Sustained Viral Suppression Among Black, Hispanic/Latina, and White Women in the United States - Medical Monitoring Project, United States, 2015-2019

DLH researcher **Xin Yuan** is among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Epub: May 2023; Print: August 2023). Racial and ethnic disparities in antiretroviral therapy (ART) adherence and sustained viral suppression (SVS) have been documented among women with HIV. The authors examined factors that may account for these racial/ethnic differences among women to inform interventions that increase health equity. Data from the 2015-2019 cycles of the Medical Monitoring Project were used, a probability sample of U.S. adults with diagnosed HIV. After adjusting for poverty, transportation needs, health literacy, and gap in health insurance/coverage, the Black-White PD in adherence decreased by 11%. After adjusting for adherence, poverty, type of health insurance, and gap in health insurance/coverage, the Black-White PD in SVS reduced 37% and was no longer statistically different. The Hispanic/Latina-White PD in adherence reduced 24% after adjusting for poverty, health literacy and transportation needs. The unadjusted Hispanic/Latina-White PD in SVS was not significantly different. The authors concluded that racial/ethnic disparities in HIV outcomes among women

taking ART were substantially reduced after accounting for social determinants of health (SDOH) and other factors, although differences remained. Structural interventions to improve SDOH are needed to improve health equity for women with HIV.
The other authors are researchers from the Centers for Disease Control and Prevention.

Exposure to Volatile Hydrocarbons and Neurologic Function Among Oil Spill Workers Up to 6 Years After the Deepwater Horizon Disaster
DLH researchers **W. Braxton Jackson II** and **Kate Christenbury** are among the authors of an article published in *Environmental Research* (Epub: May 2023; Print: August 2023). During the 2010 Deepwater Horizon (DWH) disaster, oil spill response and cleanup (OSRC) workers were exposed to toxic volatile components of crude oil. Few studies have examined exposure to individual volatile hydrocarbon chemicals below occupational exposure limits in relation to neurologic function among OSRC workers. The authors investigated the association of several spill-related chemicals (benzene, toluene, ethylbenzene, xylene, n-hexane, i.e., BTEX-H) and total petroleum hydrocarbons (THC) with neurologic function among DWH spill workers enrolled in the Gulf Long-term Follow-up Study. Cumulative exposure to THC and BTEX-H across the oil spill cleanup period were estimated using a job-exposure matrix that linked air measurement data to detailed self-reported DWH OSRC work histories. The authors ascertained quantitative neurologic function data via a comprehensive test battery at a clinical examination that occurred 4-6 years after the DWH disaster. The authors did not find evidence of adverse neurologic effects from crude oil exposures among the overall study population. However, among workers ≥50 years of age, several individual chemical exposures were associated with poorer vibrotactile acuity of the great toe, with statistically significant effects observed in Q3 or Q4 of exposures. Also observed were suggestive adverse associations among those ≥ age 50 years for tests of postural stability and single-leg stance, although most effect estimates did not reach thresholds of statistical significance. Higher exposures to volatile components of crude oil were associated with modest deficits in neurologic function among OSRC workers who were age 50 years or older at study enrollment. *Other authors include researchers from the University of North Carolina at Chapel Hill, the National Institute of Environmental Health Sciences, Johns Hopkins University, and the National Institute on Aging.*

Reliability of Low Mass Toenail Samples as Biomarkers of Chronic Metal Exposure
DLH researcher **W. Braxton Jackson II** is among the authors of an article published in the *Journal of Exposure Science & Environmental Epidemiology* (Online Ahead of Print: June 2023). Toenails are a promising matrix for chronic metal exposure assessment, but there are currently no standard methods for collection and analysis. Questions remain about sample mass requirements and the extent to which metals measured in this matrix are representative of chronic body burden. This study proposed a method to maximize sample conservation for toenail metals analysis using inductively coupled plasma mass spectrometry (ICP-MS). The authors demonstrated the reliability of an ~25 mg toenail sample (typically 1-2 clippings) for metals analysis and evaluated the intra-individual variability of multiple metals in this matrix over time in men from the Gulf Long-term Follow-up (GuLF) Study. Toenail samples from 123 GuLF Study participants were collected at two visits 3 years apart and analyzed for 18 elements using ICP-MS. Results were not reported for Cd, Co, Mo, Sb, and V (detected in <60% of the samples). This toenail reliability study found that a low-mass (~25 mg) toenail sample (1-2 clippings) is suitable for the determination of most elements using ICP-MS and helps to increase the analytical capacity of limited toenail biospecimens collected in cohort studies. The results highlight

differences in the suitability of toenails for chronic metal exposure assessment by element and underscore the need to consider intra-person variability, especially when comparing results across studies. The authors also provided recommendations for analytical standardization and the partitioning of the total collected toenail sample into multiple analytic subsamples for future studies using toenail biospecimen for multiple assays. *The other authors are researchers from Johns Hopkins Bloomberg School of Public Health, National Institute of Environmental Health Sciences, and the University of North Carolina Gillings School of Global Public Health.*

Anti-Dense Fine Speckled 70 (DFS70) Autoantibodies: Correlates and Increasing Prevalence in the United States

DLH researchers **Gregg Dinse** and **Caroll Co** are among the authors of an article published in *Frontiers in Immunology* (eCollection 2023, Online: June 2023). Recent studies report high-titer anti-dense fine speckled 70 (DFS70) autoantibodies in persons with inflammatory conditions, but the clinical significance remains unclear. The researchers sought to estimate anti-DFS70 autoantibody prevalence, identify correlates, and assess time trends. Serum antinuclear antibodies (ANA) were measured by indirect immunofluorescence assay on HEp-2 cells in 13,519 participants ≥12 years old from three time periods (1988-1991, 1999-2004, 2011-2012) of the National Health and Nutrition Examination Survey. ANA-positive participants with dense fine speckled staining were evaluated for anti-DFS70 antibodies by enzyme-linked immunosorbent assay. Women were more likely than men, black persons were less likely than white persons, and active smokers were less likely than nonsmokers to have anti-DFS70 antibodies. The prevalence of anti-DFS70 antibodies increased from 1.6% in 1988-1991 to 2.5% in 1999-2004 to 4.0% in 2011-2012, which corresponds to 3.2 million, 5.8 million, and 10.4 million seropositive individuals, respectively. This increasing time trend in the US population was modified in some subgroups and was not explained by concurrent changes in tobacco smoke exposure. Some, but not all, anti-DFS70 antibody correlates and time trends resembled those reported for total ANA. The authors concluded that more research is needed to elucidate anti-DFS70 antibody triggers, their pathologic or potentially protective influences on disease, and their possible clinical implications. *Other authors include researchers from the National Institute of Environmental Health Sciences, Department of Oral Biology at the University of Florida, and Shanghai Jiao Tong University.*

Blood Glucose, Blood Pressure, and Cholesterol Testing Among Adults With Diabetes Before and During the COVID-19 Pandemic, USA, 2019 vs 2021

DLH researcher **Sarah Stark Casagrande** is one of two authors of an article published in *BMJ Open Diabetes Research & Care* (Online: June 2023). Regular blood glucose/A1c, blood pressure (BP), and cholesterol (ABC) testing is important for diabetes management. It is unknown whether pandemic-related disruptions in medical care were negatively associated with ABC testing among US adults with diagnosed diabetes. A cross-sectional analysis was conducted among adults ≥18 years with diagnosed diabetes who participated in the 2019 or 2021 National Health Interview Survey. Adults with diabetes self-reported sociodemographic and diabetes-related characteristics, ABC testing in the past year, and delays or not getting medical care due to the pandemic (2021 only). Descriptive statistics were used to determine differences in ABC testing in 2019 vs 2021. Logistic regression models were used to assess the association between delays or not getting medical care due to the pandemic and ABC testing, adjusting for sociodemographic characteristics, diabetes duration, and diabetes medication use. Overall, the prevalence of having a blood glucose/A1c or a BP test in the past year was high but it was significantly lower in 2021 compared with 2019. Cholesterol testing

remained stable. In logistic regression analysis, after full adjustment, adults who reported delaying or not getting medical care when needed due to the pandemic were 50% less likely to get an ABC test in the past year compared with those who promptly received medical care. The authors concluded that disruptions in medical care during the pandemic were associated with a decrease in ABC testing. Future research is needed to assess whether blood glucose/A1c and BP testing returns to prepandemic levels and if reductions in these tests result in excess diabetes-related complications. *The other author is a researcher from the National Institute of Diabetes and Digestive and Kidney Diseases.*

Pharmacogenetic Interactions of Efavirenz or Rifampin and Isoniazid With Levonorgestrel Emergency Contraception During Treatment of HIV or Tuberculosis
DLH researcher **Elizabeth Woolley** is among the authors of an article published in *Pharmacogenetics and Genomics* (Epub: June 2023; Print: August 2023). In AIDS Clinical Trials Group study A5375, a pharmacokinetic trial of levonorgestrel emergency contraception, double-dose levonorgestrel (3 mg versus standard dose 1.5 mg) offset the induction effects of efavirenz or rifampin on plasma levonorgestrel exposure over 8 hours post-dose. The authors characterized the pharmacogenetics of these interactions. Cisgender women receiving efavirenz- or dolutegravir-based HIV therapy, or on isoniazid-rifampin for tuberculosis, were followed after a single oral dose of levonorgestrel. Of 118 evaluable participants, 17 received efavirenz/levonorgestrel 1.5 mg, 35 efavirenz/levonorgestrel 3 mg, 34 isoniazid-rifampin/levonorgestrel 3 mg, and 32 (control group) dolutegravir/levonorgestrel 1.5 mg. There were 73 Black and 33 Asian participants. Regardless of genotype, women on efavirenz and isoniazid-rifampin had higher levonorgestrel clearance. The authors concluded that CYP2B6 poor metabolizer genotypes exacerbate the efavirenz-levonorgestrel interaction, likely by increased CYP3A induction with higher efavirenz exposure, making the interaction more difficult to overcome. NAT2 slow acetylator genotypes attenuate the rifampin-levonorgestrel interaction, likely by increased CYP3A inhibition with higher isoniazid exposure. *Other authors include researchers from Tufts University School of Medicine, University of Nebraska Medical Center, Harvard TH Chan School of Public Health, the Office of Research on Women's Health/NIH, National Institute of Allergy and Infectious Diseases, Office of the Global AIDS Coordinator/Department of State, and researchers from South Africa, Brazil, Thailand, and Malawi.*