



# Research Update

## Spring - Summer 2022

A semi-annual look at select DLH research activities.

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# **Jeanine Christian**

## **President, Public Health & Scientific Research**

I am excited to share with you the Spring - Summer 2022 edition of the DLH Research Update. This update is a semi-annual look at select research activities from across our company's Public Health & Scientific Research operating unit. DLH researchers continuously analyze reams of data that helps support our customer's critical missions and learning goals.

The research findings summarized in the following articles will contribute to knowledge-building aimed at improving health and readiness outcomes for millions across the globe. This collection showcases the wide array of populations, locations, and scientific fields into which we contribute - spanning clinical trials, behavioral studies, and real-world response to health crises - and issues ranging from Covid-19 vaccinations, to racial disparities in healthcare, and assessing exposure from oil spills, and a clinical trial for HPV treatment. I hope you will enjoy learning more about our team's work and our efforts to support public health research.

As always, I am proud of our team's innovative findings and the remarkable expertise our researchers exemplify in their fields. My sincere gratitude goes to all authors listed in this update and the many members of our workforce and partner organizations who contributed to this work. I am proud of all your accomplishments and I look forward to seeing you continue to excel.

Sincerely,

**Jeanine Christian**

**President**

**Public Health & Scientific Research**





*American Society of Nephrology* (Online Ahead of Print: January 2022; Print: July 2022). The role of kidney transplantation in differential survival in Black and White patients with childhood-onset kidney failure is unexplored. The researchers analyzed 30-year cohort data of children beginning rapid resolution therapy (RRT) before 18 years of age between January 1980 and December 2017 (n=28,337) in the US Renal Data System. Black children comprised 24% of the cohort and their crude 30-year survival was 39% compared with 57% for White children. Black children had 45% higher risk of death, 31% lower incidence of first transplant, and 39% lower incidence of second transplant. Children and young adults are likely to require multiple transplants, yet even after their first transplant, Black patients had 11% fewer total transplants. In Black patients, grafts failed earlier after first and second transplants. Overall, Black patients spent 24% less of their RRT time with a transplant than did White patients. Transplantation compared with dialysis strongly protected against death by time-varying analysis. Mediation analyses estimated that equalizing transplant duration could prevent 35% of excess deaths in Black patients. The authors concluded that equalizing time with a functioning transplant for Black patients may equalize survival of childhood-onset end-stage kidney disease with White patients. *Other authors include researchers from the National Institute of Diabetes and Digestive and Kidney Diseases and Rush University Medical Center.*

### **Hygiene Hypothesis Indicators and Prevalence of Antinuclear Antibodies in US Adolescents**

DLH researchers **Jesse Wilkerson** and **Gregg Dinse** were among the authors of an [article](#) published in *Frontiers in Immunology* (Online: January 2022). Autoimmunity prevalence, as measured by antinuclear antibodies (ANA), is increasing in U.S. adolescents. Improved hygiene and cleaner environments in childhood may reduce exposure to infections and other immune challenges, resulting in improper immune responses to later-life exposures. The researchers examined associations of hygiene hypothesis indicators, including asthma, allergies, and antibodies to infectious agents, with ANA prevalence, measured by HEp-2 immunofluorescence, in adolescents (aged 12-19 years) over a 25-year time span in the National Health and Nutrition Examination Survey (NHANES) (N=2,709). Prevalence of ANA in adolescents increased from 5.0% in 1988-1991 to 12.8% in 2011-2012. ANA were positively associated with diagnosis of asthma in early childhood, and the effect estimate for current hay fever was elevated but not statistically significant. Fewer than 2% of those with ANA in 1988-1991 had been diagnosed with asthma, compared with 18% in 1999-2000, and 27% in 2003-2004 and 2011-2012. ANA trended negatively with *Helicobacter pylori* antibodies. ANA may be useful as an additional indicator of inadequate immune education in adolescence, a critical period of growth and development. *Other authors include researchers from the University of Michigan and the National Institute of Environmental Health Sciences.*

### **Behavioral Efficacy of a Sexual Health Mobile App for Men Who Have Sex With Men: Randomized Controlled Trial of Mobile Messaging for Men**

DLH researcher **Evelyn Olansky** was among the authors of an [article](#) published in the *Journal of Medical Internet Research* (Epub: February 2022). Gay, bisexual, and other men who have sex with men (GBMSM) face the highest burden of HIV in the United States, and there is a paucity of efficacious mobile health (mHealth) HIV prevention and care interventions tailored specifically for GBMSM. A mobile app was tested that combined prevention messages and access to core prevention services for GBMSM. The study aimed to measure the efficacy of the Mobile Messaging for Men (M-cubed) app and related services to increase HIV prevention and care behaviors in diverse GBMSM in the US. A randomized open-label study was conducted with a waitlist control group among GBMSM in three groups (low-risk HIV-negative group, high-risk HIV-negative group, and living-with-HIV [LWH] group) recruited online and in venues in Atlanta, Detroit, and New York City. Participants were randomly assigned to receive access to the app immediately or at 9 months after randomization. The app provided prevention messages in six domains of sexual health and offered ordering of at-home HIV and sexually transmitted infection test kits, receiving preexposure prophylaxis (PrEP) evaluations and navigation, and service locators. Serostatus- and risk-specific prevention outcomes were evaluated at baseline, at the end of the

intervention period, and at 3, 6, and 9 months after the intervention period. Access to the M-cubed app was associated with increased HIV testing and PrEP use among high-risk HIV-negative GBMSM in three US cities. The app could be made available through funded HIV prevention providers. Additional efforts are needed to understand optimal strategies to implement the app outside of the research setting. *Other authors include researchers from Rollins School of Public Health at Emory University, University of Michigan, The State University of New York Downstate Health Sciences University, Emory University School of Medicine, and the Division of HIV Prevention at Centers for Disease Control and Prevention.*

### **Roadbumps at the Crossroads of Integrating Behavioral and In Vitro Approaches for Neurotoxicity Assessment**

DLH researchers **Sandra McBride** and **Matthew Bridge** were among the authors of an [article](#) published in *Frontiers in Toxicology* (eCollection: February 2022). Given that behavior results from a complicated series of nervous system interactions, neurobehavioral phenotyping and assessment have seen a resurgence as the investigation of both biological and neurological mechanisms becomes more commonplace in vivo with the assistance of modern technologies. However, the appreciation of behavioral testing as a sensitive tool does not often translate well to pre-clinical or chemical neurotoxicity studies. This article presents a review of behavioral testing in the context of developmental neurotoxicity and discusses the roles that experimental design, data analysis, and interpretation play in reporting valuable developmental data with insights from the mechanistic aspects of nervous system function derived from historical in vitro experimentation. *Other authors include researchers from the National Toxicology Program at the National Institute of Environmental Health Sciences, Institut de Biologie Paris Seine at Sorbonne Université, and the French Agency for Food, Environmental and Occupational Health & Safety at the Université de Lyon.*

### **Geographical Differences in the Self-Reported Functional Impairment of People with HIV and Associations with Cardiometabolic Risk**

DLH researcher **Laura Moran** was among the authors of an [article](#) published in *Clinical Infectious Diseases* (Online Ahead of Print: February 2022). Researchers sought to explore multinational differences in functional status by Global Burden of Disease (GBD) regions in the REPRIEVE cohort. REPRIEVE is a prospective, double-blind, randomized, placebo-controlled, multicenter, phase III primary cardiovascular prevention study of pitavastatin calcium versus placebo among people with HIV (PWH) ages 40-75 on antiretroviral therapy (ART). Of 7736 participants, the majority were from high-income countries, were male, and had received ART for  $\geq 10$  years. In adjusted analyses, functional impairment was significantly more frequent among participants from Southeast/East Asia. Other factors associated with greater impairment included female sex, Black race, older age, current/former smoking, higher body mass index, use of ART for  $\geq 10$  years, and select ART regimens; differences were seen in risks across GBD regions. Functional impairment was associated with increased cardiometabolic risk. The authors concluded that over one-third of middle-aged and older PWH in a global cohort across diverse GBD regions demonstrate functional impairments. The associations between Duke Activity Status Instrument and cardiometabolic risk suggest that a measure of functional status may improve risk prediction. These longitudinal associations will be further investigated over REPRIEVE trial follow-up. *Other authors include researchers from the University of Colorado, Massachusetts General Hospital and Harvard Medical School, Center for Biostatistics in AIDS Research at the Harvard T.H. Chan School of Public Health, Duke Global Health Institute, Johns Hopkins University School of Medicine, and researchers from institutions in India, Thailand, Botswana, and Brazil.*

### **Fine Particulate Matter and Lung Function Among Burning-Exposed Deepwater Horizon Oil Spill Workers**

DLH researcher **W. Braxton Jackson II** was among the authors of an [article](#) published in *Environmental Health Perspectives* (Epub: February 2022). During the 2010 Deepwater Horizon (DWH) disaster, controlled burning was

conducted to remove oil from the water. Workers near combustion sites were potentially exposed to increased fine particulate matter [with aerodynamic diameter  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>)] levels. Exposure to PM<sub>2.5</sub> has been linked to decreased lung function, but to the authors' knowledge, no study has examined exposure encountered in an oil spill cleanup. The association between estimated PM<sub>2.5</sub> only from burning/flaring of oil/gas and lung function measured 1-3 years after the DWH disaster was investigated. Workers who participated in response and cleanup activities on the water during the DWH disaster and had lung function measured at a subsequent home visit were included. The researchers concluded that, among oil spill workers, exposure to PM<sub>2.5</sub> specifically from controlled burning of oil/gas was associated with significantly lower forced expiratory volume (FEV<sub>1</sub>) and FEV<sub>1</sub>/FVC (forced vital capacity) when compared with workers not involved in burning. *Other authors include researchers from the Epidemiology Branch and Office of the Director at the National Institute of Environmental Health Sciences, Gillings School of Global Public Health at the University of North Carolina at Chapel Hill, and the Division of Cancer Epidemiology and Genetics at the National Cancer Institute.*

### **Association of Deepwater Horizon Oil Spill Response and Cleanup Work With Risk of Developing Hypertension: The Association Between Blood Metals and Hypertension in the GuLF Study**

DLH researchers **W. Braxton Jackson II** and **John McGrath** were among the authors of an [article](#) published in *JAMA Network Open* (Epub: February 2022). Exposure to hydrocarbons, fine particulate matter (PM<sub>2.5</sub>), and other chemicals from the April 20, 2010, Deepwater Horizon disaster may be associated with increased blood pressure and newly detected hypertension among oil spill response and cleanup workers. The objective was to determine whether participation in cleanup activities following the disaster was associated with increased risk of developing hypertension. Participants were 6,846 adults who had worked on the oil spill cleanup (workers) and 1,505 others who had completed required safety training but did not do cleanup work (nonworkers). Eligible participants did not have diagnosed hypertension at the time of the oil spill. Engagement in cleanup activities following the Deepwater Horizon oil spill disaster, job classes, quintiles of cumulative total hydrocarbons exposure level, potential exposure to burning or flaring oil, and estimated PM<sub>2.5</sub> were examined. Systolic and diastolic blood pressure measurements were collected during home exams from 2011 to 2013 using automated oscillometric monitors. Newly detected hypertension was defined as antihypertensive medication use or elevated blood pressure since the spill. The researchers concluded that oil spill exposures were associated with newly detected hypertension after the Deepwater Horizon disaster. These findings suggest that blood pressure screening should be considered for workers with occupational hydrocarbon exposures. *Other authors of the article included researchers from the National Institute of Environmental Health Sciences, Department of Environmental and Occupational Health at Drexel University, and the Bloomberg School of Public Health at Johns Hopkins University.*

### **No Differences Between Lopinavir/Ritonavir and Nonnucleoside Reverse Transcriptase Inhibitor-Based Antiretroviral Therapy on Clearance of Plasmodium falciparum Subclinical Parasitemia in Adults Living With HIV Starting Treatment (A5297)**

DLH researcher **Evelyn Hogg** was among the authors of an [article](#) published in the *Journal of Acquired Immune Deficiency Syndromes* (Print: February 2022). HIV protease inhibitors anti-Plasmodium falciparum activity in adults remains uncertain. In AIDS Clinical Trials Group study A5297, adults with HIV CD4+ counts  $>200$  cells/mm<sup>3</sup> starting antiretroviral therapy (ART) with P. falciparum subclinical parasitemia (Pf SCP) were randomized 1:1 to (Step 1) protease inhibitor lopinavir/ritonavir (LPV/r)-based (Arm A) or nonnucleoside reverse transcriptase inhibitor (nNRTI)-based ART (Arm B) for 15 days. In Step 2, participants received nNRTI-based ART and trimethoprim/sulfamethoxazole prophylaxis for 15 days. The authors concluded that in a small, randomized study of adults starting ART with Pf SCP, no statistically significant differences were seen between LPV/r- and nNRTI-based ART in Pf SCP clearance after 15 days of treatment. *Other authors include researchers from the U.S. Centers for Disease Control and Prevention (Kigali, Rwanda, at the time of research), College of Medicine Johns*

### **The Geospatial Distribution of Myositis and Its Phenotypes in the United States and Associations With Roadways: Findings From a National Myositis Patient Registry**

DLH researchers **Jesse Wilkerson** and **John McGrath** were among the authors of an [article](#) published in *Frontiers in Medicine* (Lausanne) (eCollection: March 2022). Little is known about the spatial distribution of idiopathic inflammatory myopathies (IIM) in the U.S., or their geospatial associations. The researchers studied a national myositis patient registry, with cases diagnosed in the contiguous U.S. from 1985-2011 and comprised of dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM) patients. There was a trend of a higher prevalence of IIM and its major phenotypes among people living within 50 m of a roadway relative to living beyond 200 m. Demographic characteristics, rural-urban commuting area, and female percentage were significantly associated with the prevalence of IIM and with major phenotypes. The researchers concluded that, using a large U.S. database to evaluate the spatial distribution of IIM and its phenotypes, this study suggests clustering in some regions of the U.S. and a possible association of proximity to roadways. *Other authors include researchers from Cincinnati Children's Hospital and Medical Center, National Institute of Environmental Health Sciences, and the Myositis Association.*

### **Assessment of Self-reported Sense of Smell, Objective Testing, and Associated Factors in Middle-Aged and Older Women**

DLH research scientist and epidemiologist **Aimee D'Aloisio** and **Sandra Deming-Halverson** were among the authors of an [article](#) published in *JAMA Otolaryngology--Head & Neck Surgery* (Online Ahead of Print: March 2022; Print: May 2022). Poor olfaction is common in older adults and signifies multiple adverse health outcomes, but it often goes unrecognized. The researchers' objective was to characterize the self-awareness of poor olfaction in women, including its prevalence, associated factors, reporting reliability, validity against an objective test, and factors associated with validity. Of the 41,118 women (mean age, 64.3 years) included in the analysis, 3,322 self-reported poor olfaction. Higher prevalence was associated with older age, not being married, current smoking status, frequent coffee drinking, overweight or obesity, less than optimal health, Parkinson disease, cognitive impairment, depression, anxiety, and seasonal allergy, whereas a lower prevalence was associated with non-Hispanic Black race and physical activity. The researchers concluded that, in this case-control study, the self-awareness and reporting accuracy of poor olfaction in middle-aged and older women were low, particularly in non-Hispanic Black women. Given its potential health implications, awareness of this common sensory deficit should be raised. *Other authors of the article include researchers from the Department of Epidemiology and Biostatistics at Michigan State University College of Human Medicine, The University of Chicago, and the Epidemiology Branch at the National Institute of Environmental Health Sciences.*

### **Plasma Concentrations of Tris(1-chloro-2-propyl) Phosphate and a Metabolite bis(2-chloroisopropyl) 1-carboxyethyl phosphate in Sprague-Dawley Rats and B6C3F1/N Mice from a Chronic Study of Tris(chloropropyl) Phosphate Via Feed**

DLH researcher **Laura Betz** was among the authors of an [article](#) published in *Toxicology Reports* (eCollection: March 2022). Tris(chloropropyl) phosphate (TCPP) is an organophosphorus flame retardant and plasticizer used in manufacturing and multiple consumer products. Commercial TCPP is a ubiquitous environmental contaminant, and TCPP or its metabolites have been detected in human plasma and urine. In response to the demonstrated widespread human exposure and lack of toxicity data, the Division of the National Toxicology Program is investigating the chronic toxicity of TCPP following perinatal exposure in HSD:Sprague Dawley®SD® (HSD) rats and adult exposure in B6C3F1/N mice to TCPP via feed. Systemic exposure and bioaccumulation were assessed by measuring plasma concentrations of tris(1-chloro-2-propyl)phosphate (TCIPP), the most abundant TCPP

isomer. TCIPP concentrations in TCPP-exposed rats and mice ranged from 3.43 to 1180 ng/mL and increased with exposure concentration at all time points. No sex differences were observed in rats, but male mice had higher TCIPP concentrations than females. TCIPP did not bioaccumulate in rats or mice over the course of the study. Low TCIPP concentrations were seen in some control rats and mice that were attributed to background TCPP present during sample collection, preparation, and/or analysis. Bis(2-chloroisopropyl) 1-carboxyethyl phosphate (BCPCP), a TCPP metabolite, was quantified in plasma from control and selected exposed animals. Results showed increases in BCPCP concentration that were proportional to exposure concentration in rats and mice at concentrations much higher than TCIPP, indicating that BCPCP might be a more suitable biomarker of TCPP exposure. *Other authors include researchers from the Division of the National Toxicology Program at the National Institute of Environmental Health Sciences.*

### **Prevalence and Correlates of Electrocardiographic Abnormalities in Adults With HIV: Insights From the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE)**

DLH researcher **Laura Moran** was among the authors of an [article](#) published in the *Journal of Acquired Immune Deficiency Syndromes* (Print: March 2022). People with HIV (PWH) are at increased risk of cardiovascular disease (CVD) and sudden cardiac death. Previous work has suggested an association between HIV infection and electrocardiographic (ECG) abnormalities. There are limited data on the burden of ECG abnormalities among PWH in a multiracial, multiethnic globally representative population. The researchers analyzed data for 7720 PWH (99% of participants) (median age 50 years, 69% male participants). There were 3346 (43%) Black or African American, 2680 (35%) White, and 1139 (15%) Asian participants. Nearly half of the participants had at least one ECG abnormality. QTc prolongation was more common among male than female participants, and nearly twice as common among Asian participants when compared with other racial groups. The authors concluded that prolonged QTc is common among male, Asian, and REPRIEVE participants with higher viral loads. These relationships warrant future investigation of linkages to ensuing CVD events among PWH. *Other authors include researchers from Duke Clinical Research Institute, Harvard T.H. Chan School of Public Health, and the Epidemiology Branch at the National Institute of Environmental Health Sciences.*

### **A Randomized Clinical Trial of HPV Test-and-Treat as Compared to Cytology-Based Screening for Prevention of Cervical Cancer Among Women Living with HIV: AIDS Clinical Trials Group Protocol A5282**

DLH researcher **Reena Naranjo** was among the authors of an [article](#) published in *Clinical Infectious Diseases* (Online Ahead of Print: March 2022). Women living with HIV/AIDS are at greater risk of human papillomavirus (HPV) infection. Untreated or undertreated high-risk HPV (hrHPV) infection may lead to pre-invasive cervical disease and cervical cancer. More than 85% of the global burden of cervical cancer occurs in resource-limited settings. Cytology-based (“Pap smear”) cervical cancer screening followed by confirmation and treatment of biopsy-proven high-grade squamous intraepithelial (bHSIL) is effective in reducing cancer, provided that coverage is high and screening is performed relatively frequently. These programs are difficult to implement in resource-constrained settings. The researchers hypothesized an alternative approach—hrHPV testing followed by immediate cryotherapy of women with hrHPV (HPV test-and-treat)—may improve outcomes. The clinical trial was a randomized, open-label, phase 2, multinational trial that enrolled 288 women living with HIV (WLHIV) age 18 or older with cervical hrHPV who had no cervical lesions or lesions appropriate for cryotherapy. HPV test-and-treat using cryotherapy treatment was not associated with improved outcomes as compared to cytology-based screening. However, the HPV test-and-treat strategy was acceptable to WLHIV as evidenced by a high completion rate and study retention. These results suggest that optimization of cervical treatments to be used within the paradigm of test-and-treat programs are needed to achieve desired cervical cancer prevention outcomes. *Other authors include researchers from Weill Cornell Medicine, Harvard School of Public Health, the National Cancer Institute, Office of the Global AIDS Coordinator at Department of State, as well as researchers from South Africa, Malawi, Zimbabwe, Botswana, Haiti, and India.*



### **Systemic Exposure and Urinary Excretion of Vanadium Following Perinatal Subchronic Exposure to Vanadyl Sulfate and Sodium Metavanadate Via Drinking Water**

DLH researcher **Guanhua Xie** was among the authors of an [article](#) published in *Toxicology Letters* (Epub: March 2022; Print: May 2022). Vanadium is a ubiquitous environmental contaminant although there are limited data to assess potential adverse human health impact following oral exposure. In support of studies investigating the subchronic toxicity of vanadyl sulfate (V4+) and sodium metavanadate (V5+) following perinatal exposure via drinking water in male and female rats, the researchers determined the internal exposure and urinary excretion of total vanadium at the end of study. Water consumption decreased with increasing exposure concentration following exposure to both compounds. Plasma and urine vanadium concentration normalized to total vanadium consumed per day increased with the exposure concentration of vanadyl sulfate and sodium metavanadate, suggesting absorption increased as the exposure concentration increased. Animals exposed to sodium metavanadate had up to three-fold higher vanadium concentration in plasma and urine compared to vanadyl sulfate-exposed animals, when normalized to total vanadium consumed per day, demonstrating differential absorption, distribution, metabolism, and excretion properties between V5+ and V4+ compounds. These data will aid in the interpretation of animal toxicity data of V4+ and V5+ compounds and determine the relevance of animal toxicity findings to human exposures. *Other authors include researchers from the National Institute of Environmental Health Sciences and Battelle Memorial Institute.*

### **Association of Dietary and Plasma Carotenoids with Urinary F2-Isoprostanes**

DLH researcher **Jenna Lilyquist** was among the authors of an [article](#) published in the *European Journal of Nutrition* (Online Ahead of Print: March 2022; Print: August 2022). Carotenoids may protect against chronic diseases including cancer and cardiometabolic disease by mitigating oxidative stress and/or inflammation. The researchers cross-sectionally evaluated associations between carotenoids and biomarkers of oxidative stress or inflammation. The authors concluded that plasma carotenoids and supplemental  $\beta$ -carotene were associated with lower concentrations of 8-iso-PGF2 $\alpha$  metabolite. Plasma carotenoids associations may reflect antioxidant effects. *Other authors include researchers from the National Institute of Environmental Health Sciences, Department of Epidemiology at the University of North Carolina at Chapel Hill, and the Division of Clinical Pharmacology at Vanderbilt University Medical Center.*

### **Baseline Factors Associated with Self-reported Disease Flares Following COVID-19 Vaccination Among Adults with Systemic Rheumatic Disease: Results from the COVID-19 Global Rheumatology Alliance Vaccine Survey**

DLH researchers **Jesse Wilkerson** and **Rebecca Ritter** were among the authors of an [article](#) published in *Rheumatology (Oxford)* (Online Ahead of Print: April 2022; Print: June 2022). The researchers examined the frequency of, and risk factors for, disease flare following COVID-19 vaccination in patients with systemic rheumatic disease (SRD). An international study was conducted from April 2 to August 16, 2021, using an online survey of 5619 adults with SRD for adverse events following COVID-19 vaccination, including flares of disease requiring a change in treatment. Flares requiring a change in treatment following COVID-19 vaccination were reported by 4.9% of patients. Compared with rheumatoid arthritis, certain SRD, including systemic lupus erythematosus, psoriatic arthritis, and polymyalgia rheumatica were associated with higher odds of flare, while idiopathic inflammatory myopathies were associated with lower odds for flare. The Oxford-AstraZeneca vaccine was associated with higher odds of flare relative to the Pfizer-BioNTech vaccine, as were a prior reaction to a non-COVID-19 vaccine and female sex. The authors concluded that SRD flares requiring changes in treatment following COVID-19 vaccination were uncommon in this large international study. Several potential risk factors, as well as differences by disease type, warrant further examination in prospective cohorts. *Other authors include researchers from the National Institute of Environmental Health Sciences, McMaster University, Division of*

Rheumatology and Clinical Immunology at the University of Pittsburgh, and Department of Epidemiology and Population Health, and Immunology and Rheumatology (Department of Medicine) at Stanford University School of Medicine.

### **Demographic and Geospatial Analysis of Buprenorphine and Methadone Prescription Rates**

DLH statistician **Tejal Vashi** was among the authors of an [article](#) published in *Cureus* (eCollection May 2022). The medical community continues to seek to understand both the causes and consequences of opioid use disorder (OUD). The recent 2019 public release of the Automation of Reports and Consolidated Orders System (ARCOS) database from the years 2006 to 2012 provides a unique opportunity to analyze a critical period of the opioid epidemic with unprecedented data granularity. This study aims to use the ARCOS dataset to (1) determine significant contributory variables to opioid overdose death rates, (2) determine significant contributory variables to the relative prescription of buprenorphine and methadone, and (3) evaluate the existence of statistically significant geospatial clusters in buprenorphine and methadone prescription rates. This study utilizes multiple databases, including the Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER), the Drug Enforcement Administration (DEA) prescription drug data, and the United States (US) Census demographics, to examine the relationship between the different treatments of OUD. Methadone prescriptions, racial demographics, and poverty were found to significantly correspond to opioid overdose death rates. Buprenorphine prescriptions were not found to be significant. Opioid overdoses, metro character, racial categorization, and education were found to significantly correspond to the ratio of buprenorphine to methadone prescribed. The researchers concluded that, historically, methadone prescriptions have been higher in areas with high overdose rates. Buprenorphine and methadone prescribing patterns have historically demonstrated different geographic trends. *Other authors include researchers from the Carle Foundation Hospital and Carle Illinois College of Medicine.*

### **Nutrient Intake Differs Among Persons With Celiac Disease and Gluten-Related Disorders in the United States**

DLH senior epidemiologist **Constance Ruhl** was among the authors of an [article](#) published in *Scientific Reports* (Online: April 2022). Persons with celiac disease (CD) may develop nutritional deficiencies, while individuals following a gluten-free diet (GFD) may lack essential nutrients. The authors examined nutrient intake from diet and supplements among persons with CD and GFD in the cross-sectional National Health and Nutrition Examination Survey, 2009-2014. Among 15,610 participants 20 years and older, CD was identified based on positive serology for immunoglobulin A against tissue transglutaminase, health care provider diagnosis, and adherence to a GFD. People without CD avoiding gluten (PWAG) adhered to a GFD without a diagnosis of CD. Two 24-hour recalls assessed nutrient intake from diet and supplements. Compared to participants without CD or PWAG, persons with diagnosed CD had lower intake of total energy, carbohydrates, fat, and saturated and monounsaturated fatty acids. In contrast, persons with undiagnosed CD and positive serology had higher intake of those nutrients, sugar, and protein. Total carbohydrate and sugar intake was lower among PWAG. Persons with diagnosed CD had higher vitamin A and E intake, while those with undiagnosed CD had increased intake of calcium, phosphorus, magnesium, iron, zinc, copper, sodium, potassium, vitamin A, alpha-carotene, folic acid, and choline. PWAG had higher beta-carotene and lutein/zeaxanthin and lower folic acid intake. In the U.S. population over a 6-year period, total energy and macronutrient intake was decreased among persons with diagnosed CD, while intake of total energy, macronutrients, and multiple micronutrients was increased among persons with undiagnosed CD. Nutriomics studies of multiple analytes measured simultaneously across affected persons and populations are needed to inform screening for malabsorption and treatment strategies. *Other authors include researchers from the National Institute of Diabetes and Digestive and Kidney Diseases.*

### **Assessing Exposures from the Deepwater Horizon Oil Spill Response and Clean-up**

DLH researcher **Kate Christenbury** was among the authors of an [article](#) published in *Annals of Work Exposure*



*and Health* (Epub: April 2022). The GuLF Study is investigating adverse health effects from work on the response and clean-up after the Deepwater Horizon explosion and oil release. An essential and necessary component of that study was the exposure assessment. Bayesian statistical methods, and over 135,000 measurements of total hydrocarbons (THC), benzene, ethylbenzene, toluene, xylene, and n-hexane (BTEX-H) were used to estimate inhalation exposures to these chemicals for >3400 exposure groups (EGs) formed from three exposure determinants: job/activity/task, location, and time period. Exposures to oil mist were assessed using professional judgment. Potential 1-hour particulate matter sized 2.5 µm or less (PM2.5) air concentrations experienced by some workers may have been as high as 550 µg m<sup>3</sup>. Dispersant aerosol air concentrations were very low, but vapor concentrations may have exceeded occupational exposure excursion guidelines for 2-butoxyethanol under certain circumstances. The daily arithmetic means of dermal exposure estimates showed large contrasts among the study participants. The estimates are being used to evaluate exposure-response relationships in the GuLF Study. *Other authors include researchers from the School of Public Health at West Virginia University, Dornsife School of Public Health at Drexel University, School of Population and Public Health at the University of British Columbia, and the Bloomberg School of Public Health at Johns Hopkins University.*

### **Participant Perspectives and Experiences Following an Intensively Monitored Antiretroviral Pause in the United States: Results from the AIDS Clinical Trials Group A5345 Biomarker Study**

DLH researcher **Evelyn Hogg** was among the authors of an [article](#) published in *AIDS Research and Human Retroviruses* (Epub: April 2022; Print: June 2022). The A5345 study (NCT03001128) included an intensively monitored antiretroviral pause (IMAP), during which participants (people living with HIV [PLWH] on suppressive antiretroviral treatment [ART]) temporarily stopped ART in an effort to identify biomarkers that could predict HIV rebound. The researchers evaluated the potential impact of the IMAP on study participants in the United States by administering longitudinal sociobehavioral questionnaires following the IMAP (when ART resumed) and again at the end of the study. Descriptive data from the questionnaires were summarized. Open-ended responses were analyzed using conventional content analysis. Reactions to pausing ART involved a mixture of curiosity and satisfaction from contributing to science. All participants indicated adherence with the ART pause. About half (9/17) of post-IMAP questionnaire respondents reported having sexual partner(s) during the IMAP, and of those, nearly all (8/9) did not find it difficult to use measures to prevent HIV transmission to partners. The majority of participants believed that they benefited from the study, although some had elevated anxiety. Most (24/29) respondents who completed the end-of-study questionnaire would recommend the study to other PLWH. The findings underscored the relevance of the psychosocial aspects of participating in studies that involve IMAP. Understanding how participants experience this research is invaluable for informing the design of future research aimed at sustained ART-free virologic suppression. *Other authors of the article include researchers from the UNC's Gillings School of Global Public Health, the Community Scientific Sub-Committee of the AIDS Clinical Trials Group, and the Division of AIDS (National Institute of Allergy and Infectious Diseases/NIH).*

### **High Prevalence of Tuberculosis Infection and Disease in Child Household Contacts of Adults With Rifampin-resistant Tuberculosis**

DLH researcher **Linda Naini** was among the authors of an [article](#) published in the *Pediatric Infectious Disease Journal* (Epub: May 2022). Household contact (HHC) investigation is an important strategy to identify individuals with tuberculosis (TB) exposure, infection, and disease, including those who may benefit from tuberculosis preventive therapy (TPT). Data in children exposed to rifampin-resistant TB are limited. Of 303 child HHCs, median age (range) 7 years (0-14), 57% had a positive interferon-gamma release assay result (TB infected). TB infection was associated with the index case smoking, being the parent or sleeping in the same room, and the child HHC being age ≥5 years and having attended school. Four had study-defined confirmed TB and 9 had probable TB, a prevalence of 4.3%. Using the international consensus definitions, 4 had confirmed TB and 49 had unconfirmed TB, a prevalence of 17.2%. Twenty (7%) children had received TPT. The researchers concluded that,

the prevalence of TB infection and disease was high in child HHC exposed to rifampin-resistant TB. Few children had routinely received TPT. High-quality evidence is needed to inform strong recommendations for and access to TPT in children exposed to TB resistant to rifampin. *Other authors include researchers from the Harvard T.H. Chan School of Public Health, Division of AIDS/National Institutes of Health, Emory University Rollins School of Public Health, Johns Hopkins University, and researchers from South Africa, Peru, India, Botswana, and Haiti.*

### **Duration of Replication-Competent SARS-CoV-2 Shedding Among Patients with Severe or Critical Coronavirus Disease 2019 (COVID-19)**

DLH researcher **Daniel Zaccaro** was among the authors of an [article](#) published in *Clinical Infectious Diseases* (Online Ahead of Print: May 2022). Patterns of shedding replication-competent SARS-CoV-2 in severe or critical COVID-19 are not well-characterized. The researchers investigated the duration of replication-competent SARS-CoV-2 shedding in upper and lower airway specimens from patients with severe or critical COVID-19. Patients with active or recent severe or critical COVID-19 who were admitted to a tertiary care hospital intensive care unit (ICU) or long-term acute care hospital (LTACH) because of COVID-19 were enrolled. The researchers collected 529 respiratory specimens from 78 patients. Replication-competent virus was detected in 4 of 11 immunocompromised patients up to 45 days after symptom onset, and in 1 of 67 immunocompetent patients 10 days after symptom onset. All culture-positive patients were in the ICU cohort and had persistent or recurrent symptoms of COVID-19. Immunocompromise and persistent or recurrent symptoms were associated with shedding of replication-competent SARS-CoV-2, supporting the need for improving respiratory symptoms in addition to time as criteria for discontinuation of transmission-based precautions. Results suggested that the period of potential infectiousness among immunocompetent patients with severe or critical COVID-19 may be similar to that reported for patients with milder disease. *Other authors include researchers from the Division of Infectious Diseases at Rush University Medical Center and the Chicago Department of Public Health.*

### **Serum Antioxidant Vitamins and Respiratory Morbidity and Mortality: A Pooled Analysis**

DLH researchers **Jesse Wilkerson**, **Samantha Molsberry**, and **Lydia Feinstein** were among the authors of an [article](#) published in *Respiratory Research* (Print: June 2022). Oxidative stress plays a key role in the pathogenesis of respiratory diseases; however, studies on antioxidant vitamins and respiratory outcomes have been conflicting. The researchers evaluated whether lower serum levels of vitamins A, C, D, and E were associated with respiratory morbidity and mortality in the U.S. adult population. A pooled analysis of data from the 1988-1994 and 1999-2006 National Health and Nutrition Examination Survey (participants aged  $\geq 20$  years) was conducted. Analysis of nationally representative data on over 34,000 participants showed that lower serum levels of vitamins A, C, D, and  $\alpha$ -tocopherol vitamin E are associated with increased respiratory morbidity and/or mortality in U.S. adults. The results underscore the importance of antioxidant vitamins in respiratory health. *Other authors include researchers from the National Institute of Environmental Health Sciences, Department of Environmental and Public Health Sciences at the University of Cincinnati College of Medicine, and the Department of Occupational and Environmental Health at the University of Iowa.*

### **The Association Between Oil Spill Cleanup-Related Total Hydrocarbon Exposure and Diabetes**

DLH researcher **Matthew Curry** was among the authors of an [article](#) published in *Environmental Research* (Epub: June 2022; Print: September 2022). Although evidence suggests relationships between some crude oil components and glycemic dysregulation, no studies have examined oil spill-related chemical exposures in relation to type 2 diabetes mellitus (DM) risk. This study examined the relationship between total hydrocarbon (THC) exposure among workers involved in the 2010 Deepwater Horizon (DWH) oil spill and risk of DM up to 6 years afterward. Participants comprised 2660 oil-spill cleanup or response workers in the prospective GuLF Study who completed a clinical exam and had no self-reported DM diagnosis prior to the spill. An exposure-response relationship between maximum daily ordinal THC exposure level and incident DM was

observed, especially among overweight participants. The researchers observed suggestively increasing DM risk with increasing THC exposure level among overweight participants, but not among normal weight or obese participants. *Other authors include researchers from the UNC Gillings School of Global Public Health and the Epidemiology Branch of the National Institute of Environmental Health Sciences.*

### **Pharmacokinetics of Standard Versus High-Dose Isoniazid for Treatment of Multidrug-Resistant Tuberculosis**

DLH researcher **Laura Moran** was among the authors of an [article](#) published in the *Journal of Antimicrobial Chemotherapy* (Online Ahead of Print: June 2022; Print: August 2022). The WHO-endorsed shorter-course regimen for MDR-TB includes high-dose isoniazid. The pharmacokinetics of high-dose isoniazid within MDR-TB regimens has not been well described. The objectives were to characterize isoniazid pharmacokinetics at 5-15 mg/kg as monotherapy or as part of the MDR-TB treatment regimen. A total of 58 and 103 participants from the INHindsight and PODRtb studies, respectively, were included in the analysis. Participants treated with the MDR-TB regimen had a 65.6% lower AUC compared with participants on monotherapy. Ethionamide co-administration was associated with a 29% increase in isoniazid AUC. Markedly lower isoniazid exposures were observed in participants on combination MDR-TB treatment compared with monotherapy. Isoniazid displays saturable kinetics at doses >10 mg/kg. The safety implications of these phenomena remain unclear. *Other authors include researchers from the University of Cape Town (South Africa), Johns Hopkins University School of Medicine, Harvard T.H. Chan School of Public Health, and the Division of AIDS at the National Institute of Allergy and Infectious Diseases.*

### **Neighborhood Social Cohesion and Serious Psychological Distress Among Asian, Black, Hispanic/Latinx, and White Adults in the United States: A Cross-Sectional Study**

DLH researcher **W. Braxton Jackson II** was among the authors of an [article](#) published in *BMC Public Health* (June 2022). Serious psychological distress (SPD) is common and more prevalent in women, older adults, and individuals with a low income. Prior studies have highlighted the role of low neighborhood social cohesion in potentially contributing to SPD; however, few have investigated this association in a large, nationally representative sample of the United States. Therefore, the objective was to investigate the overall and racial/ethnic-, sex/gender-, self-rated health status-, age-, and household income-specific relationships between neighborhood social cohesion and SPD. Data were used from survey years 2013 to 2018 of the National Health Interview Survey to investigate neighborhood social cohesion and SPD among Asian, Non-Hispanic (NH)-Black, Hispanic/Latinx, and NH-White men as well as women in the United States and to determine modification by race/ethnicity, sex/gender, self-rated health status, age, and annual household income. Neighborhood social cohesion was measured by asking participants four questions related to the trustworthiness and dependability of their neighbors. Among 168,573 participants, most were Non-Hispanic-White (69%), and mean age was 47 years. Low neighborhood social cohesion was associated with higher SPD in the overall population and the magnitude of the association was higher in Asian men, participants who reported good health, older participants, and Hispanic/Latinx adults with higher household incomes. Future research should continue to examine how neighborhood contexts can affect health across various sociodemographic groups, especially among groups with multiple marginalized social identities. *Other authors include researchers from the National Institute of Environmental Health Sciences, the Harvard T.H. Chan School of Public Health, and the National Institute on Minority Health and Health Disparities.*

### **Expanded Assessment of Xenobiotic Associations with Antinuclear Antibodies in the United States, 1988-2012**

DLH researchers **Gregg Dinse, Carol Co,** and **Guanhua Xie** were among the authors of an [article](#) published in *Environment International* (Online Ahead of Print: June 2022). The prevalence of autoimmunity in the U.S. has increased recently for undetermined reasons. Little is known about associations between autoimmunity and

environmental causes. In a large representative sample of the U.S. population, the researchers expanded their prior exploratory study of how exposures to selected xenobiotics and dioxin-like (DL) mixtures related to antinuclear antibodies (ANA), the most common biomarker of autoimmunity. Cross-sectional data on 12,058 participants aged  $\geq 12$  years (14% were ANA-positive) from three time periods of the National Health and Nutrition Examination Survey between 1988 and 2012 were analyzed. Observed ANA associations were positive for most DL compounds and non-DL polychlorinated biphenyls (PCBs), negative for most phthalates, and mixed for other xenobiotic classes. This study identified potential associations between ANA and various xenobiotics. Further investigation to confirm these observations and elucidate effects of certain xenobiotics on immune regulation could have important mechanistic, preventive, and treatment implications for a variety of immune-mediated disorders. *Other authors include researchers from the University of Florida and the National Institute of Environmental Health Sciences.*

### **Evaluation of Access Disparities to Biologic Disease-Modifying Antirheumatic Drugs in Rural and Urban Communities**

DLH statistician **Tejal Vashi** was among the authors of an [article](#) published in *Cureus* (eCollection: June 2022). The American College of Rheumatology guidelines provide a strong recommendation for the use of biologic disease-modifying antirheumatic drugs (bDMARDs) when conventional rheumatoid arthritis treatments fail to meet treatment targets. Although bDMARDs are an effective and important treatment component, access inequalities remain a challenge in many communities worldwide. The purpose of this analysis is to assess nationwide trends in bDMARD access in the United States, with a specific focus on rural and urban access gaps. This study combined multiple county-level databases to assess bDMARD prescriptions from 2015 to 2019. Counties were classified according to prescription levels to assess for hotspots and coldspots. The analysis identified statistically significant hotspot and coldspot prescription clusters within the United States. Coldspot clusters with low access to bDMARDs were located predominantly in the rural west North Central region, extending down to Oklahoma and Arkansas. Hotspot clusters were seen in urban and metro areas of Wisconsin, Minnesota, Pennsylvania, North Carolina, Georgia, Oregon, and the southern tip of Texas. Comparing coldspot to hotspot areas of bDMARD access revealed that the Medicare populations were older, more rural, less educated, less impoverished, and less likely to get their bDMARDs from a rheumatologist. *Other authors include researchers from Carle Foundation Hospital and Carle Illinois College of Medicine, University of Cincinnati College of Medicine, and Emory University Hospital Midtown.*

### **Third-Line Antiretroviral Therapy, Including Raltegravir (RAL), Darunavir (DRV/r) and/or Etravirine (ETR), Is Well Tolerated and Achieves Durable Virologic Suppression Over 144 Weeks in Resource-Limited Settings: ACTG A5288 Strategy Trial**

DLH researcher **Evelyn Hogg** was among the authors of an [article](#) published in the *Journal of the International AIDS Society* (June 2022). AIDS Clinical Trials Group A5288 was a strategy trial conducted in diverse populations from multiple continents of people living with HIV (PLWH) failing second-line protease inhibitor (PI)-based antiretroviral therapy (ART) from 10 low- and middle-income countries (LMICs). Participants resistant to lopinavir (LPV) and/or multiple nucleotide reverse transcriptase inhibitors were started on third-line regimens that included raltegravir (RAL), darunavir/ritonavir (DRV/r) and/or etravirine (ETR) according to their resistance profiles. At 48 weeks, 87% of these participants achieved HIV-1 RNA  $\leq 200$  copies/mL. Long-term outcomes over 144 weeks are reported. Study participants were enrolled from 2013 to 2015, prior to the availability of dolutegravir in LMICs. The authors concluded that third-line regimens that included RAL, DRV/r, and/or ETR were very well tolerated and had high rates of durable virologic suppression among PLWH in LMICs who were failing on second-line PI-based ART prior to the availability of dolutegravir. *Other authors include researchers from the Harvard T.H. Chan School of Public Health, the Division of AIDS at the National Institute of Allergy and Infectious Disease, and HIV researchers in Thailand, Uganda, Brazil, Kenya, South Africa, India, Haiti, Zimbabwe, and Malawi.*