



Research Update

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A semi-annual look at select DLH research activities

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Jeanine Christian

President

Public Health & Scientific Research

I am proud to present the latest edition of the DLH Research Update, a semi-annual look at select research activities from across our company's Public Health & Scientific Research operating unit. I remain inspired by the dedication our researchers show in their fields, and hope that you will draw as much excitement and interest out of their work as I did.

There is a wide array of subject matter covered in the pages that follow. But there is one thing you will quickly pick up on—our team's passion for improving lives. From identifying gaps in COVID-19 control measures amongst minority groups, managing food insecurity and diet quality for those with diabetes, determining better treatment options for fertility, to building comprehensive HIV prevention services—our scientists, analysts, engineers, and others work each day to make this vital research a reality.

My wholehearted thanks and appreciation go to those who contributed to the research included in this collection. I look forward to seeing the work that follows from each of you.

Proud as always to be a part of DLH,

Jeanine Christian

Unless another funding source is named, the research activities described below were funded wholly or in part by the federal government.

Recent Publications

Evaluation of Skin Sensitization Induced by Four Ionic Liquids

DLH programmer/analyst **Shawn Harris** is among the authors of an [article](#) published in the *Journal of Applied Toxicology* (Epub: August 2021; Print: March 2022). Ionic liquids (ILs) are synthetic solvents used as replacements for volatile organic solvents. Human exposure occurs through dermal or oral routes. In rodents, several ILs were reported to induce dermal toxicity, irritation, and sensitization. Due to the potential for occupational exposure, and industrial use as nonvolatile solvents, 1-ethyl-3-methylimidazolium chloride (EMIM), 1-butyl-3-methylimidazolium chloride (BMIM), 1-butyl-1-methylpyrrolidinium chloride (BMPY), and N-butylpyridinium chloride (NBuPY) were nominated to the National Toxicology Program and evaluated for skin sensitization. In vitro, BMIM was positive in the Human Cell Line Activation Test (h-CLAT); BMPY and NBuPY were positive in the h-CLAT and KeratinoSens™ assay. NBuPY induced skin irritation; BMIM and BMPY increased lymph node cell proliferation in the local lymph node assay, collectively indicating that BMIM and BMPY may induce weak to mild sensitization. *Other authors include researchers from the National Institute of Environmental Health Sciences and Virginia Commonwealth University.*

Receipt of Baseline Laboratory Testing Recommended by the HIV Medicine Association for People Initiating HIV Care, United States, 2015-2019

DLH researcher **Jen-Feng Lu** is among the authors of an [article](#) published in *Open Forum Infectious Diseases* (Online: June 2022; eCollection: July 2022). The HIV Medicine Association of the Infectious Disease Society of America publishes Primary Care Guidance for Persons with Human Immunodeficiency Virus. The authors assessed receipt of recommended baseline tests among newly diagnosed patients initiating HIV care. The Medical Monitoring Project is a Centers for Disease Control and Prevention survey designed to produce nationally representative estimates of behavioral and clinical characteristics of adults with diagnosed HIV in the United States. The authors analyzed data for 725 participants in the 2015-2019 data collection cycles who received an HIV diagnosis within the past 2 years and had ≥ 1 HIV provider visit. The authors estimated the prevalence of having recommended tests after the first HIV provider visit and between 3 months before and 3/6 months after the first HIV provider visit, and estimated prevalence differences of having four combinations of tests by sociodemographic and clinical characteristics. Within 6 months of care initiation, HIV monitoring tests were performed for 91.3% of patients; coinfection blood tests, 27.5%; site-based STI tests, 59.7%; and blood chemistry and hematology tests, 50.8%. Patients who were younger, gay, or bisexual were more likely to receive site-based STI tests, and patients receiving care at Ryan White HIV/AIDS Program (RWHAP)-funded facilities were more likely than patients at non-RWHAP-funded facilities to receive all test combinations. The authors concluded that, receipt of recommended baseline tests among patients initiating HIV care was suboptimal but was more likely among patients at RWHAP-funded facilities. Embedding clinical decision support in HIV provider workflow could increase recommended baseline testing. *Other authors include researchers from the Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention, and the Division of Infectious Diseases at Emory University School of Medicine.*

Diet in a Global Cohort of Adults With HIV at Low-to-Moderate Traditional Cardiovascular Disease Risk

DLH researcher **Laura Moran** is among the authors of an [article](#) published in *AIDS (London, England)* (Epub: July 2022; Print: November 2022). To characterize diet quality across a global cohort of people with HIV (PWH) using a cross-sectional analysis, the authors leveraged REPRIEVE data from baseline across five Global Burden of Disease (GBD) regions and analyzed participant responses to the Rapid Eating Assessment for Participants

questionnaire. An overall diet quality score and scores for specific diet components were generated, with higher scores indicating better diet quality. Among 7,736 participants (median age 50 years, 30% women, median BMI 25.8 kg/m²), overall diet quality score was optimal in 13% of participants and good, suboptimal, or poor in 45, 38, and 4% of participants, respectively. Diet quality scores differed across GBD region with the highest scores reported in the South Asia region and lowest in the sub-Saharan Africa region; 61% of participants in the South Asia region reported optimal diet quality compared with only 6% in the sub-Saharan Africa region. Higher atherosclerotic cardiovascular risk scores were seen with worsening diet quality. The researchers concluded that, among PWH eligible for primary CVD prevention, diet quality was suboptimal or poor for almost half of participants, and there were substantial variations in diet quality reported by GBD region. *Other authors include researchers from Massachusetts General Hospital, Icahn School of Medicine at Mount Sinai, University of Puerto Rico, and researchers from India, Thailand, and South Africa.*

Isoniazid Adherence Reduces Mortality and Incident Tuberculosis at 96 Weeks Among Adults Initiating Antiretroviral Therapy With Advanced Human Immunodeficiency Virus in Multiple High-Burden Settings

DLH researcher **Evelyn Hogg** is among the authors of an [article](#) published in *Open Forum Infectious Diseases* (eCollection/Online: July 2022). People with human immunodeficiency virus (HIV) and advanced immunosuppression initiating antiretroviral therapy (ART) remain vulnerable to tuberculosis (TB) and early mortality. To improve early survival, isoniazid preventive therapy (IPT) or empiric TB treatment have been evaluated; however, their benefit on longer-term outcomes warrants investigation. The authors performed a 96-week preplanned secondary analysis among 850 ART-naïve outpatients enrolled in a multicountry, randomized trial of efavirenz-containing ART plus either 6-month IPT or empiric 4-drug TB treatment. By 96 weeks, 85 deaths and 63 TB events occurred. Tuberculosis medication adherence lowered the hazards of death by ≥23% in empiric and ≥20% in IPT and incident TB by ≥17% only in IPT. The authors concluded that empiric TB treatment offered no longer-term advantage over IPT in their population with advanced immunosuppression-initiating ART. High IPT adherence significantly lowered death and TB incidence through 96 weeks, emphasizing the benefit of ART plus IPT initiation and completion, in persons with advanced HIV living in high TB-burden, resource-limited settings. *Other authors include researchers from Johns Hopkins University, the Harvard T.H. Chan School of Public Health, and researchers from Malawi, Haiti, Kenya, South Africa, Uganda, Zimbabwe, Peru, and Brazil.*

Sexual Health Discussion Practices and HIV Clinical Care Provided by Primary Care Providers in the Southeast United States, K-BAP Study (2017-2018)

DLH researcher **Zaneta Gaul** is among the authors of an [article](#) published in *Family Practice* (Online Ahead of Print: July 2022). Research underscores the importance of providers having routine discussions with patients about their sexual health. The authors examined the occurrences and association of routine sexual health discussion practices and human immunodeficiency virus clinical care among primary care providers (PCPs) in areas with high HIV prevalence. Data collected between April and August 2017 from an online survey that assessed PCPs knowledge, behaviors, attitudes, and practices of HIV-related care in six Southeast US jurisdictions (Atlanta, Baltimore, Baton Rouge, District of Columbia, Miami, and New Orleans) were analyzed. Among PCPs, the researchers found that 39.2% routinely obtained sexual health histories, 78.5% offered HIV testing, and 16.0% ever prescribed preexposure prophylaxis (PrEP). Based on adjusted prevalence ratios and 95% confidence intervals, the proportion of PCPs who routinely obtained sexual histories was higher among female PCPs, PCPs who had a patient population that was >50% men who have sex with men, offered HIV testing, and ever prescribed PrEP. The authors concluded that improving patient-provider discussions are needed to reduce HIV-related service barriers for disproportionately affected populations. Routine discussions can reduce barriers to important HIV prevention and care services and help reduce disparities among patients living in highly prevalent HIV locations. *Other authors include researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention.*

Employment Industry and Occupational Class in Relation to Serious Psychological Distress in the United States

DLH researcher **W. Braxton Jackson II** is among the authors of an [article](#) published in the *International Journal of Environmental Research and Public Health* (Print: July 2022). Occupational characteristics may influence serious psychological distress (SPD) and contribute to health inequities; yet, few studies have examined multiple employment industries and occupational classes in a large, racially diverse sample of the United States. Using data from the National Health Interview Survey, the authors investigated employment industry and occupational class in relation to SPD in the overall population and by race/ethnicity, gender, age, household income, and health status. Among the 245,038 participants, the mean age was 41.7 ±0.1 years, 73% were Non-Hispanic (NH)-White, and 1.5% were categorized as having SPD. Compared to the professional/administrative/management industry, working in other industries (e.g., manufacturing/construction and educational services) was associated with lower SPD. Working in support services and laborer versus professional/management positions were both associated with 19% higher prevalence of SPD. Furthermore, working in a support services or laborer versus professional/management position was associated with higher SPD in most employment industries. Industry-specific workplace interventions to equitably improve mental health are warranted. *Other authors include researchers from the National Institute of Environmental Health Sciences and the National Institute on Minority Health and Health Disparities.*

Associations Between Airborne Crude Oil Chemicals and Symptom-Based Asthma

DLH researchers **W. Braxton Jackson II** and **Kate Christenbury** are among the authors of an [article](#) published in *Environment International* (Epub: July 2022; Print: September 2022). The 2010 Deepwater Horizon (DWH) oil spill response and cleanup (OSRC) workers were exposed to airborne total hydrocarbons (THC), benzene, toluene, ethylbenzene, o-, m-, and p-xylenes and n-hexane (BTEX-H) from crude oil and PM2.5 from burning/flaring oil and natural gas. Little is known about asthma risk among oil spill cleanup workers. The authors assessed the relationship between asthma and several oil spill-related exposures including job classes, THC, individual BTEX-H chemicals, the BTEX-H mixture, and PM2.5, using data from the Gulf Long-Term Follow-up (GuLF) Study, a prospective cohort of 24,937 cleanup workers and 7,671 nonworkers following the DWH disaster. The analysis largely focused on the 19,018 workers without asthma before the spill who had complete exposure, outcome, and covariate information. Incident asthma 1-3 years following exposure was defined using both self-reported wheeze and self-reported physician diagnosis of asthma. Results showed that OSRC workers had greater asthma risk than nonworkers. Higher estimated THC exposure levels were associated with increased risk in an exposure-dependent manner. Asthma risk also increased with increasing exposure to individual BTEX-H chemicals and the chemical mixture: A simultaneous quartile increase in the BTEX-H mixture was associated with an increased asthma risk of 1.45. With fewer cases, associations were less apparent for physician-diagnosed asthma alone. The researchers concluded that THC and BTEX-H were associated with increased asthma risk defined using wheeze symptoms as well as a physician diagnosis. *Other authors include researchers from the National Institute of Environmental Health Sciences, and the UNC Gillings School of Global Public Health.*

Evolution of Healthcare Costs for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia

DLH researcher **Erline Martinez-Miller** is among the authors of an [article](#) published in *International Urology and Nephrology* (Epub: July 2022; Print: November 2022). With the ubiquity of lower urinary tract symptoms due to benign prostatic hyperplasia (LUTS/BPH) in older men, costs related to this highly prevalent disease are likely significant but not well defined. With this study, the authors hoped to define costs related to LUTS/BPH care. The Optum© de-identified Clinformatics® Data Mart Database (CDM) for privately insured male enrollees aged

40-64 years with LUTS/BPH and the Centers for Medicare and Medicaid Services Medicare 5% Sample for male beneficiaries aged 65 + years with LUTS/BPH were utilized. Annual LUTS/BPH-related expenditures from 2004 to 2013 were age standardized and calculated overall and by age and service location. The Medicare cohort demonstrated a 23% increase in total costs over the study period with a 28% decrease in CDM costs. Decreases in inpatient hospital charges were offset by increasing hospital-based outpatient fees. Overall, a total cost of at least \$1.9 billion for treatment of men with LUTS/BPH was estimated for 2013. Per-person expenditures increased with age within cohorts with an average per-person cost of \$269 (CDM) and \$248 (Medicare) in 2013. The authors concluded that the distribution of healthcare expenditures for LUTS/BPH shifted across practice settings from 2004 to 2013, with increasing outpatient relative to inpatient expenditures. Total direct costs for LUTS/BPH in 2013 were at least \$1.9 billion, not accounting for indirect costs or certain unmeasured populations. *Other authors include researchers from the National Institute of Diabetes and Digestive and Kidney Diseases and the Gillings School of Global Public Health at the University of North Carolina.*

Association of Diet and Physical Activity With All-Cause Mortality Among Adults With Parkinson Disease

DLH researcher **Samantha Molsberry*** is among the authors of an [article](#) published in *JAMA Network Open* (Online: August 2022). Greater diet quality and physical activity level are associated with a lower risk of developing Parkinson disease (PD). However, information regarding the association between lifestyle behaviors and survival after PD diagnosis remains limited. The objective was to examine the association of prediagnosis and postdiagnosis overall diet quality and physical activity with all-cause mortality among individuals with PD. This population-based cohort study analyzed male participants in the Health Professionals Follow-up Study from 1986 to 2012 and female participants in the Nurses' Health Study from 1984 to 2012. Participants who were diagnosed with PD and had complete baseline dietary assessment data were included. Data were analyzed from January 2021 to February 2022. Prediagnosis diet quality, assessed by the Alternative Healthy Eating Index, and physical activity, assessed by metabolic equivalent task hours per week reported on questionnaires, were the primary exposures of interest to minimize reverse causation. Mortality, which was followed up until 2018, was the primary outcome. The sample comprised 1251 individuals with PD, which included 652 men with a median age at diagnosis of 73.4 years. During the 32 to 34 years of follow-up, 942 participants died. In the joint analyses of diet quality and physical activity before the PD diagnosis, the adjusted hazard ratio (HR) was 0.51 for individuals in the highest versus lowest tertiles for both variables. The HR for diet quality and physical activity after the diagnosis was 0.35. Results of this study showed that a healthy dietary pattern and an active lifestyle were associated with a lower rate of all-cause mortality among individuals with PD. Consuming a healthy diet and engaging in physical activity or exercise could be targeted to improve PD outcomes. *Other authors include researchers from Brigham and Women's Hospital and Harvard Medical School, Harvard T.H. Chan School of Public Health, and Fudan University (China).* *Author Samantha Molsberry contributed to this article while at the Department of Nutrition at the Harvard T.H. Chan School of Public Health.

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* (Online Ahead of Print: September 2022; Print: January 2023). Black and Hispanic/Latino men who have sex with men (MSM) are disproportionately affected by HIV. In the THRIVE demonstration project, seven 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 2014-2019 among Black, Hispanic/Latino, and White MSM in seven THRIVE-eligible Metropolitan Statistical Areas (MSAs) that were awarded funding and 12 THRIVE-eligible MSAs that were not awarded funding. Larger estimated decreases in HIV diagnosis rates were found 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 U.S. Ending the HIV Epidemic initiative, effective interventions aimed to increase Pre-Exposure Prophylaxis use need to be focused on Black and Hispanic/Latino MSM. *Other authors of the article are researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention.*

Feasibility of Leveraging Menstrual Cycle Tracking Apps for Preconception Research Recruitment

DLH researcher **Nathaniel MacNell** is among the authors of an [article](#) published in *Frontiers in Reproductive Health* (eCollection: September 2022; Print: September 2022). Mobile applications (apps) present a new opportunity to study menstrual cycles and time to pregnancy. Understanding the characteristics of cycle tracking app users is important to evaluate the feasibility of recruiting participants for preconception research. Users of a cycle tracking smartphone app, Ovia Fertility, aged 18 or older in the U.S., were randomly invited via email to complete a “fertility research” questionnaire that included demographic and reproductive characteristics. Among those attempting pregnancy without medical assistance, attempt duration, factors influencing pregnancy planning, health history, and behaviors while attempting to conceive were queried. Respondents could choose to enter a raffle for a \$50 gift card. Initially, 639 people responded to the demographics portion of the survey representing 49 states and Washington DC. Of these, 344 (54%) were trying to conceive and of those, 297 (86%) were not using medical treatments. Of those not trying to conceive, 12% reported that they planned to start in the next 3 months. Most participants were ages 26-35, of White race, reported non-Hispanic ethnicity, had at least a bachelor’s degree, and an income between \$50,000 and \$200,000. One-third were of recommended BMI, 24% overweight, and 41% obese. Most participants reported no fertility-related health conditions. Forty-eight participants (17%) had been trying to conceive for 1 month or less, 88 (31%) had been trying for 2 months or less, and 122 (43%) for 3 months or less. Interruptions in pregnancy attempts were common, 31% reported periods without intercourse. Of those attempting pregnancy, 47% of partners completed their own questionnaire. The authors concluded that this first-of its-kind analysis describes users of a cycle-tracking smartphone app who could be eligible for recruitment to a prospective time-to-pregnancy study. Survey respondents were diverse with respect to geographic location, BMI, and income. However, special recruitment efforts will be needed to recruit participants and partners who identify as other than non-Hispanic White. Participants with fertility-related conditions are not overly represented among app users who are trying to conceive. Targeting and pre-enrolling app users who are planning to begin a pregnancy attempt in the next 3 months may be an advantage of app-based recruitment. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

PrEP Use and Adherence Among Transgender Persons in Chicago, IL (SHIPP Study, 2014-2018, USA)

DLH researcher **Tiffany Williams** is among the authors of an [article](#) published in *AIDS and Behavior* (Online Ahead of Print: September 2022). Few studies investigating daily oral preexposure prophylaxis (PrEP) focus on transgender persons. The Sustainable Health Center Implementation PrEP Pilot (SHIPP) Study included a large observational cohort of transgender persons with implications for PrEP in the United States. Data from SHIPP’s observational cohort and its Medication Adherence Substudy (MAS) was examined to understand adherence among transgender participants in Chicago, IL. Adherence was assessed by the proportion of days covered (PDC) for PrEP medication prescriptions, self-reported interview data, and concentrations of intracellular tenofovir diphosphate (TFV-DP) in dried blood spot (DBS) samples. Between 2014 and 2018, there were 510 transgender participants, 349 (68.4%) transgender women and 152 (29.8%) transgender men. Forty-five of these participants were enrolled in the MAS, 31 (68.9%) transgender women and 9 (20.0%) transgender men. By the 3-month follow up, 100% of MAS participants who completed an interview reported taking 4 or more doses of PrEP in the previous week. At 6, 9, and 12 months, taking 4 or more doses in the past week was reported by 81.0%, 94.1%, and 83.3% of participants, respectively. Results from TFV-DP DBS indicated that fewer participants reached the same level of adherence (4 or more doses/week) at clinical visits compared to self-report and even

fewer participants reached this level of adherence based on the calculated PDC. Among participants who remained on PrEP throughout the study, DBS adherence levels declined after the first 3 months. There remains a critical need to develop strategies to address barriers and interventions that support PrEP adherence among transgender people. *Other authors include researchers from the Division of HIV Prevention and the National Center for HIV, Viral Hepatitis, STD, and TB Prevention at the Centers for Disease Control and Prevention; and Howard Brown Health.*

Associations Between Prenatal Urinary Biomarkers of Phthalate Exposure and Preterm Birth: A Pooled Study of 16 US Cohorts

DLH researcher **Kate Christenbury** is among the authors of an [article](#) published in *JAMA Pediatrics* (Print: September 2022). Phthalate exposure is widespread among pregnant women and may be a risk factor for preterm birth. The authors' objective was to investigate the prospective association between urinary biomarkers of phthalates in pregnancy and preterm birth among individuals living in the US. Individual-level data were pooled from 16 preconception and pregnancy studies conducted in the US. Pregnant individuals who delivered between 1983 and 2018 and provided one or more urine samples during pregnancy were included. Exposures: Urinary phthalate metabolites were quantified as biomarkers of phthalate exposure. Concentrations of 11 phthalate metabolites were standardized for urine dilution and mean repeated measurements across pregnancy were calculated. The final analytic sample included 6045 participants (mean [SD] age, 29.1 years). Overall, 802 individuals (13.3%) were Black, 2323 (38.4%) were Hispanic/Latina, 2576 (42.6%) were White, and 328 (5.4%) had other race and ethnicity (including American Indian/Alaskan Native, Native Hawaiian, >1 racial identity, or reported as other). Most phthalate metabolites were detected in more than 96% of participants. Among approximately 90 preterm births per 1000 live births in this study population, hypothetical interventions to reduce the mixture of phthalate metabolite levels by 10%, 30%, and 50% were estimated to prevent 1.8, 5.9, and 11.1 preterm births, respectively. Results from this large US study population suggest that phthalate exposure during pregnancy may be a preventable risk factor for preterm delivery. *Other authors include researchers from the National Institute of Environmental Health Sciences and the Centers for Disease Control and Prevention.*

Vitamin D and Uterine Fibroid Growth, Incidence, and Loss: A Prospective Ultrasound Study

DLH researchers **Sheri Denslow** and **Frankie LaPorte** are among the authors of an [article](#) published in *Fertility and Sterility* (Epub: September 2022; Print: December 2022). Fibroid treatments that have few side effects and can preserve fertility are a clinical priority. The authors studied the association between serum vitamin D and uterine fibroid growth, incidence, and loss. A prospective community cohort study (enrollment 2010-2012) was designed with 4 study visits over 5 years to conduct standardized ultrasounds, measure 25-hydroxyvitamin D (25(OH)D), and update covariates. Patients were self-identified African-American or Black women aged 23-34 at enrollment without previous clinical diagnosis of fibroids. At enrollment among 1,610 participants with ≥ 1 follow-up ultrasound, the mean age was 29.2 years, 73% had deficient vitamin D, and only 7% had sufficient vitamin D. Serum 25(OH)D ≥ 20 ng/mL compared with < 20 ng/mL was associated with an estimated 9.7% reduction in fibroid growth. Serum 25(OH)D ≥ 30 ng/mL compared with < 30 ng/mL was associated with an imprecise 22% reduction in incidence. The ≥ 30 ng/mL group also had a 32% increase in fibroid loss. The authors' data supported the hypothesis that high concentrations of vitamin D decrease fibroid development but are limited by the few participants with serum 25(OH)D ≥ 30 ng/mL. Interventional trials that raise and maintain 25(OH)D concentrations ≥ 30 ng/mL and then prospectively monitor fibroid development are needed to further assess supplemental vitamin D efficacy and determine optimal treatment protocols. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Prepandemic Prevalence Estimates of Fatty Liver Disease and Fibrosis Defined by Liver Elastography in the United States

DLH senior epidemiologist **Constance Ruhl** co-authored an [article](#) published in *Digestive Diseases and Sciences* (Online Ahead of Print: September 2022). Fatty liver disease is a growing public health burden. The researchers estimated prepandemic fatty liver disease prevalence determined by transient elastography-assessed hepatic steatosis and fibrosis, and examined associations with lifestyle and other factors in a United States population sample. Liver stiffness and controlled attenuation parameter (CAP) were assessed on 7923 non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and Hispanic men and women aged 20 years and over in the National Health and Nutrition Examination Survey (NHANES) 2017-March 2020 prepandemic data. The prevalence of fatty liver disease was 28.8% and fibrosis was 10.4%. Only 7.2% of participants with fatty liver disease and 10.9% with fibrosis reported being told by a health care provider that they had liver disease. In addition to known risk factors such as metabolic factors and ALT, persons with fatty liver disease were less likely to meet physical activity guidelines, more likely to be sedentary for ≥ 12 hours a day, and reported a less healthy diet. Persons with fibrosis were less likely to have a college degree and reported a less healthy diet. The authors concluded that, in the U.S. population, most persons with fatty liver disease are unaware of their condition. Physical activity and dietary modifications might reduce the fatty liver disease burden. There is an urgent need for fatty liver disease management in high-risk individuals using transient elastography or other noninvasive methods to intervene in disease progression. *The other author is a researcher from the National Institute of Diabetes and Digestive and Kidney Diseases.*

Benzophenone-3 and Antinuclear Antibodies in U.S. Adolescents and Adults Ages 12-39 Years

DLH researcher **Jesse Wilkerson** is among the authors of an [article](#) published in *Frontiers in Immunology* (Online: September 2022). Between 1988 and 2012, prevalence of antinuclear antibodies (ANA) increased in the U.S., especially in adolescents and non-Hispanic Whites. Female predominance of ANA suggests a role for hormonal factors, including xenobiotic exposures that may disrupt endocrine signaling. Benzophenone-3 (BP-3) is one such chemical with increasing exposure through sunscreen use. The authors investigated whether urinary BP-3 levels were related to ANA in adolescents and young adults. In a sample of 1,785 individuals ages 12-39 years in the National Health and Nutrition Examination Survey (NHANES; 2003-4, 2011-12), cross-sectional associations of ANA were examined with urinary BP-3, and other phenols bisphenol-A, triclosan, and parabens. BP-3 concentrations (detected in >98.5% of individuals) did not differ by ANA positivity in the summer, but in winter were higher among ANA-positives. ANA was associated with $\log_{10}(\text{BP-3})$ in winter but not summer. Triclosan, parabens, and bisphenol-A levels were unrelated to ANA overall or by season. The authors concluded that the association of urinary BP-3 with ANA in the winter may reflect different exposure patterns or unmeasured confounders. Findings warrant replication in prospective studies and including past and year-round exposures. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Increasing Prevalence of Antinuclear Antibodies in the United States

DLH researchers **Gregg Dinse**, **Caroll Co**, and **Jesse Wilkerson** are among the authors of an [article](#) published in *Arthritis & Rheumatology* (Epub: October 2022; Print: December 2022). Growing evidence suggests increasing frequencies of autoimmunity and autoimmune diseases, but findings are limited by the lack of systematic data and evolving approaches and definitions. This study was undertaken to investigate whether the prevalence of antinuclear antibodies (ANA), the most common biomarker of autoimmunity, changed over a recent 25-year span in the US. Serum ANA were measured by standard indirect immunofluorescence assays on HEp-2 cells in 13,519 participants age ≥ 12 years from the National Health and Nutrition Examination Survey, with approximately one-third from each of three time periods: 1988-1991, 1999-2004, and 2011-2012. The prevalence of ANA was 11.0% in 1988-1991, 11.4% in 1999-2004, and 16.1% in 2011-2012, corresponding to ~22.3, ~26.6, and ~41.5 million affected individuals, respectively. Among adolescents age 12-19 years, ANA prevalence increased substantially, with odds ratios of 2.07 and 2.77 in the second and third time periods relative to the first. ANA prevalence increased in both sexes (especially in men), older adults (age ≥ 50 years), and non-Hispanic whites. These increases were not

explained by concurrent trends in weight (obesity/overweight), smoking exposure, or alcohol consumption. The authors concluded that the prevalence of ANA in the US has increased considerably in recent years. Additional studies to determine factors underlying these increases could elucidate causes of autoimmunity and enable the development of preventative measures. *Other authors include researchers from the National Institute of Environmental Health Sciences and the University of Florida Health Science Center.*

Caregiver Willingness to Give TPT to Children Living With Drug-Resistant TB Patients

DLH researcher **Linda Naini** is among the authors of an [article](#) published in the *International Journal of Tuberculosis and Lung Disease* (Print: October 2022). Pediatric household contacts (HHCs) of patients with multidrug-resistant TB (MDR-TB) are at high risk of infection and active disease. Evidence of caregiver willingness to give MDR-TB preventive therapy (TPT) to children is limited. This was a cross-sectional study of HHCs of patients with MDR-TB to assess caregiver willingness to give TPT to children aged <13 years. Of 743 adult and adolescent HHCs, 299 reported caring for children aged <13 years of age. The median caregiver age was 35 years; 75% were women. Among caregivers, 89% were willing to give children MDR TPT. In unadjusted analyses, increased willingness was associated with TB-related knowledge, belief that one can die of MDR-TB, concern for MDR-TB transmission to child, confidence in properly taking TPT, comfort telling family about TPT, and willingness to take TPT oneself. The authors concluded that a high percentage of caregivers living with MDR- or rifampicin-resistant TB patients were willing to give children a hypothetical MDR TPT. These results provide important evidence for the potential uptake of effective MDR TPT when implemented. *Other authors include researchers from GHESKIO Centers (Haiti), Weill Cornell Medicine, Johns Hopkins Medical Institutions, and researchers from South Africa, Botswana, Peru, and India.*

Food Insecurity, Diet Quality, and Suboptimal Diabetes Management Among US Adults With Diabetes

DLH research scientist/epidemiologist **Sarah Casagrande** is among the authors of an [article](#) published in *BMJ Open Diabetes Research & Care* (Online: October 2022). A healthy diet is recommended to support diabetes management, including HbA1c, blood pressure, and cholesterol (ABC) control, but food insecurity is one barrier to consuming a healthy diet. As such, the authors determined the prevalence of food insecurity and diet quality among US adults with diabetes and the associations with ABC management. Cross-sectional analyses were conducted among 2075 adults ≥20 years with diagnosed diabetes who participated in the 2013-2018 National Health and Nutrition Examination Surveys. Food insecurity was assessed using a standard questionnaire, and diet quality was assessed using quartiles of the 2015 Healthy Eating Index. Overall, 17.6% of adults had food insecurity/low diet quality; 14.2% had food insecurity/high diet quality; 33.1% had food security/low diet quality; and 35.2% had food security/high diet quality. Compared with adults with food security/high diet quality, those with food insecurity/low diet quality were significantly more likely to have HbA1c ≥7.0% and HbA1c ≥8.0%; food insecurity/high diet quality was significantly associated with elevated HbA1c; and food security/low diet quality with elevated A1c. The authors concluded that food insecurity, regardless of diet quality, was significantly associated with elevated A1c. For people with food insecurity, providing resources to reduce food insecurity could strengthen the overall approach to optimal diabetes management. *Other authors include researchers from the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases (NIH).*

Resident Racial and Ethnic Composition, Neighborhood-Level Socioeconomic Status, and COVID-19 Infections in California SNFs

DLH researcher **Joseph Engeda** is among the authors of an [article](#) published in the *Journal of the American Geriatrics Society* (Online Ahead of Print: October 2022). In California, >29,000 residents in skilled nursing facility (SNFs) were diagnosed with novel coronavirus disease 2019 (COVID-19) between March 2020 and November 2020. Prior research suggests that SNFs serving racially and ethnically minoritized residents often have fewer

resources and lower quality of care. The researchers performed a cross-sectional analysis of COVID-19 incidence among residents in California SNFs, assessing the association of SNF-level racial and ethnic compositions and facility- and neighborhood-level (census tract- and county-level) indicators of socioeconomic status. SNFs were grouped based on racial and ethnic composition using data from the Centers for Medicare and Medicaid Services; categories included SNFs with $\geq 88\%$ White residents, SNFs with $\geq 32\%$ Black or Latinx residents, SNFs with $\geq 32\%$ Asian residents, or SNFs not serving a high proportion of any racial and ethnic composition (mixed). SNF resident-level COVID-19 infection data were obtained from the National Healthcare Safety Network from May 25, 2020 to August 16, 2020. Multilevel mixed-effects negative binomial regressions were used to estimate incidence rate ratios for confirmed COVID-19 infections among residents. Among 971 SNFs included in the sample, 119 had $\geq 88\%$ White residents; 215 had $\geq 32\%$ Black or Latinx residents; 78 had $\geq 32\%$ Asian residents; and 559 were racially and ethnically mixed. SNFs with $\geq 32\%$ Black or Latinx residents and SNFs with mixed racial and ethnic composition both had higher COVID-19 incidence rates than SNFs with $\geq 88\%$ White residents. COVID-19 incidence rates were also found to be higher in SNFs with low SES neighborhoods compared to those in high SES neighborhoods. The authors concluded that public health personnel should consider SNF- and neighborhood-level factors when identifying facilities to prioritize for COVID-19 outbreak prevention and control. *Other authors include researchers from the California Department of Public Health (Healthcare-Associated Infections Program, Richmond; Office of Health Equity, Sacramento).*

Transient Elastography Measures of Hepatic Steatosis and Fibrosis Are Associated With Body Composition Among US Adolescents

DLH senior epidemiologist **Constance Ruhl** co-authored an [article](#) published in the *Journal of Pediatric Gastroenterology and Nutrition* (Print: October 2022). Obesity-related fatty liver disease impacts long-term adolescent liver health. The authors examined transient elastography assessed hepatic steatosis and fibrosis distributions and relationships with body composition and lifestyle factors in a United States national adolescent population sample. Liver stiffness and controlled attenuation parameter (CAP) were assessed on 1080 non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and Hispanic boys and girls aged 12-19 years in the National Health and Nutrition Examination Survey (NHANES) 2017-2018. Participants underwent anthropometry and dual-energy x-ray absorptiometry (DXA). Compared with girls, boys had higher mean CAP and liver stiffness. CAP and liver stiffness increased markedly with body mass index (BMI). In multivariable-adjusted analysis, CAP in the upper quartile was associated with Hispanic and non-Hispanic Asian ethnicity and increased BMI, waist-to-hip ratio, systolic blood pressure, and sedentary time, and decreased physical activity and Healthy Eating Index-2015 score. In multivariable-adjusted analysis, liver stiffness in the upper quartile was associated with male sex, non-Hispanic black ethnicity, and increased BMI, alanine aminotransferase, CAP, and serum cotinine. DXA total percent fat and trunk fat percent were positively related to CAP, but not to liver stiffness with multivariable adjustment. Results were similar with CAP and liver stiffness as continuous characteristics. The authors concluded that, in US adolescents, increased anthropometric and DXA body composition measures and lifestyle factors were associated with higher CAP and liver stiffness. Transient elastography and similar noninvasive markers may be utilized for early detection of liver disease in high-risk pediatric populations. *The other author is a researcher from the National Institute of Diabetes and Digestive and Kidney Diseases.*

Fine Particulate Matter and Incident Coronary Heart Disease Events Up to 10 Years of Follow-Up Among Deepwater Horizon Oil Spill Workers

DLH researchers **W. Braxton Jackson II** and **Joseph Engeda** are among the authors of an [article](#) published in *Environmental Research* (Epub: November 2022; Print: January 2023). During the 2010 Deepwater Horizon (DWH) disaster, in-situ burning and flaring were conducted to remove oil from the water. Workers near combustion sites were potentially exposed to burning-related fine particulate matter (PM_{2.5}). Exposure to PM_{2.5}

has been linked to increased risk of coronary heart disease (CHD), but no study has examined the relationship among oil spill workers. The authors investigated the association between estimated PM_{2.5} from burning/flaring of oil/gas and CHD risk among the DWH oil spill workers. Workers who participated in response and cleanup activities on the water during the DWH disaster were included. Increased CHD hazard was observed among workers with higher levels of average daily maximum exposure. Also observed was suggestively elevated HRs among workers with higher cumulative daily maximum exposure. The authors concluded that, among oil spill workers, exposure to PM_{2.5} from flaring/burning of oil/gas was associated with increased risk of CHD. *Other authors include researchers from the Gillings School of Global Public Health at the University of North Carolina and the National Institute of Environmental Health Sciences.*

Association Between Gestational Diabetes and 6-Year Incident Diabetes: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

DLH research scientist/epidemiologist **Sarah Casagrande** is among the authors of an [article](#) published in *BMJ Open Diabetes Research & Care* (Online: November 2022). Type 2 diabetes and gestational diabetes (GDM) disproportionately affect those of Hispanic/Latino heritage. This study examined the association between GDM and prevalent and incident diabetes in a community-based study of Hispanic/Latina women living in the USA. Participants were women aged 18-74 years in the Hispanic Community Health Study/Study of Latinos who had at least one pregnancy and had information on self-reported history of GDM at baseline (n=6389). Logistic regression was used to determine the association between GDM and prevalent (2008-2011) and incident (2014-2017) diabetes and interactions between GDM and risk factors for incident diabetes. At baseline, 8.7% of participants reported a history of GDM and 18.6% had prevalent diabetes. Women with Mexican heritage had the highest prevalence of GDM history (11.3%) vs women of Cuban (5.0%), Central American (4.9%), and South American (3.8%) heritage). Women with self-reported GDM were four times more likely to have prevalent diabetes compared with women without GDM, after adjusting for sociodemographic characteristics and cardiometabolic risk factors. Overall incidence of diabetes was 14.3/100 women. Women with GDM at baseline had a threefold increased odds of incident diabetes compared with women without GDM. Women with Cuban or Puerto Rican heritage and GDM had significantly higher odds of incident diabetes compared with women with Mexican heritage. The authors concluded that self-reported GDM was significantly associated with a threefold higher risk of incident diabetes among Hispanic/Latino women in the USA even after adjusting for several significant predictors of diabetes. *Other authors include researchers from the National Institute of Minority Health and Health Disparities and the National Institute of Diabetes and Digestive and Kidney Diseases (NIH).*

Analysis of Incidence Data in Developmental Toxicity Studies: Statistical Tests to Account for Litter Effects in Fetal Defect Data

DLH researchers **Shawn Harris**, **Sandra McBride**, and **Marjolein Smith** are among the authors of an [article](#) published in *Birth Defects Research* (Online Ahead of Print: November 2022). When analyzing fetal defect incidence in laboratory animal studies, correlation in responses within litters (i.e., litter effects) can lead to increased false-positive rates if litter effects are not incorporated into the analysis. Studies of fetal defects require analysis methods that are robust across a broad range of defect types, including those with zero or near-zero incidence rates in control groups. A simulation study compared power and false-positive rates for six approaches across a range of background defect rates and litter size distributions. Statistical methods evaluated included ignoring the litter effect as well as parametric and nonparametric approaches based on litter proportions, generalized linear mixed models (GLMMs), the Rao-Scott Cochran-Armitage (RSCA) trend test, and a modification to the RSCA (mRSCA) introduced here to improve estimation at low background rates. These methods were also applied to a common and a rare defect from two prenatal developmental toxicology studies conducted by the National Toxicology Program (NTP). At background defect rates of 1%, the mRSCA and parametric litter proportion methods provided gains in power over the nonparametric litter proportion method,

the GLMM method, and the RSCA method. Simulations involving litter loss in high-dose groups showed loss of power for both litter proportion methods. The authors concluded that the mRSCA test developed here compares favorably with other litter-based approaches and is robust across a range of background defect rates and litter size distributions, making it a practical choice for prenatal developmental toxicology studies involving both common and rare fetal defects. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

A Cross-Sectional Clinical Study in Women to Investigate Possible Genotoxicity and Hematological Abnormalities Related to the Use of Black Cohosh Botanical Dietary Supplements

DLH researchers **Sandra McBride** and **Guanhua Xie** are among the authors of an [article](#) published in *Environmental and Molecular Mutagenesis* (Epub: November 2022; Print: December 2022). Black cohosh (BC; *Actaea racemosa* L.), a top-selling botanical dietary supplement, is marketed to women primarily to ameliorate a variety of gynecological symptoms. Due to widespread usage, limited safety information, and sporadic reports of hepatotoxicity, the Division of the National Toxicology Program (DNTP) initially evaluated BC extract in female rats and mice. Following administration of up to 1000 mg/kg/day BC extract by gavage for 90 days, dose-related increases in micronucleated peripheral blood erythrocytes were observed, along with a nonregenerative macrocytic anemia resembling megaloblastic anemia in humans. Because both micronuclei and megaloblastic anemia may signal disruption of folate metabolism, and inadequate folate levels in early pregnancy can adversely affect neurodevelopment, the DNTP conducted a pilot cross-sectional study comparing erythrocyte micronucleus frequencies, folate and B12 levels, and a variety of hematological and clinical chemistry parameters between women who used BC and BC-naïve women. Twenty-three women were enrolled in the BC-exposed group and 28 in the BC-naïve group. Use of any brand of BC-only supplement for at least 3 months was required for inclusion in the BC-exposed group. Supplements were analyzed for chemical composition to allow cross-product comparisons. All participants were healthy, with no known exposures (e.g., x-rays, certain medications) that could influence study endpoints. Findings revealed no increased micronucleus frequencies and no hematological abnormalities in women who used BC supplements. Although reassuring, a larger, prospective study with fewer confounders (e.g., BC product diversity and duration of use) providing greater power to detect subtle effects would increase confidence in these findings. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Generalized Mean Residual Life Models for Survival Data With Missing Censoring Indicators

DLH researcher **Gregg Dinse** is among the authors of an [article](#) published in *Statistics in Medicine* (Epub: November 2022; Print: February 2023). The mean residual life (MRL) function is an important and attractive alternative to the hazard function for characterizing the distribution of a time-to-event variable. In this article, the authors studied the modeling and inference of a family of generalized MRL models for right-censored survival data with censoring indicators missing at random. To estimate the model parameters, augmented inverse probability weighted estimating equation approaches were developed, in which the non-missingness probability and the conditional probability of an uncensored observation were estimated by parametric methods or nonparametric kernel smoothing techniques. Asymptotic properties of the proposed estimators were established and finite sample performance was evaluated by extensive simulation studies. An application to brain cancer data was presented to illustrate the proposed methods. *Other authors include researchers from the East China Normal University in Shanghai and the University of Haifa (Israel).*

Cisgender Women With HIV in the United States: How Have HIV Care Continuum Outcomes Changed Over Time? 2015-2020

DLH researcher **Xin Yuan** is among the authors of an [article](#) published in *AIDS (London, England)* (Epub: November 2022; Print: February 2023). The objective was to evaluate HIV care continuum trends over time

among women with HIV (WWH). The Medical Monitoring Project (MMP) is a complex sample survey of adults with diagnosed HIV in the United States. The researchers used 2015-2019 MMP data collected from 5139 adults with diagnosed HIV infection who identified as cisgender women. Weighted percentages were calculated with 95% confidence intervals (CIs) for all characteristics and estimated annual percentage change (EAPC) and the associated 95% CI to assess trends. EAPCs were considered meaningful from a public health perspective if at least 1% with P values less than 0.05. Results showed that, among cisgender women with diagnosed HIV infection during 2015-2019, 58.8% were Black or African American, 19% were Hispanic/Latina, and 16% were Non-Hispanic White persons. There was a meaningful increase in the percentage who ever had stage 3 HIV disease from 55.8% in 2015 to 61.5% in 2019. There were no meaningful changes over time among women, overall, in retention in care, antiretroviral therapy (ART) prescription, ART adherence, missed appointments, or recent or sustained viral suppression. The authors concluded that the HIV care continuum outcomes among WWH did not meaningfully improve from 2015 to 2019, raising a concern that Ending the HIV Epidemic in the US initiative goals will not be met. To improve health and reduce transmission of HIV among WWH, multifaceted interventions to retain women in care, increase ART adherence, and address social determinants of health are urgently needed. *Other authors include researchers from the Centers for Disease Control and Prevention.*

HIV Pre-exposure Prophylaxis Services for Black and Hispanic or Latino Gay, Bisexual, and Other Men Who Have Sex with Men and Transgender Women in THRIVE, 2015-2020

DLH researchers **Lei Yu** and **Tameka Hayes** are among the authors of an [article](#) published in the *Journal of Acquired Immune Deficiency Syndromes* (Online Ahead of Print: December 2022). From 2015-2020, the THRIVE (Targeted Highly Effective Interventions to Reverse the HIV Epidemic) project supported seven U.S. health departments to improve HIV prevention services for Black or African American (Black) and Hispanic or Latino gay, bisexual, and other men who have sex with men (GBM) and transgender women (TGW). The authors described services provided in the THRIVE pre-exposure prophylaxis (PrEP) continuum. Using Poisson regression models, associations were estimated between race or ethnicity and age and PrEP screening, linkage, and prescription. Associations were examined between co-location of services and PrEP linkage and prescription for two sites. THRIVE served 12,972 GBM without HIV; 37% of PrEP-eligible GBM were prescribed PrEP. THRIVE served 1,185 TGW without HIV; 45% of PrEP-eligible TGW were prescribed PrEP. Black and Hispanic or Latino GBM were 29% and 19% less likely, respectively, to be prescribed PrEP than White GBM. GBM 18-24 years and ≥55 years were 19% and 22% less likely, respectively, to be prescribed PrEP compared to those 35-44 years. Co-located services were associated with a 54% and a 31% greater likelihood of PrEP linkage and prescription respectively compared to services at different locations. The authors concluded that THRIVE provided PrEP to higher proportions of PrEP-eligible persons than current national estimates; however, PrEP use disparities persist. Co-location of services may be a useful component of jurisdictional strategies to increase PrEP coverage. Other authors included researchers from the Centers for Disease Control and Prevention, University of Alabama at Birmingham, Louisiana Office of Public Health, Virginia Department of Health, District of Columbia Department of Health, Baltimore City Health Department, and the New York City Department of Health and Mental Hygiene.

Association of Distance to Swine Concentrated Animal Feeding Operations With Immune-Mediated Diseases: An Exploratory Gene-Environment Study

DLH researchers **Nathaniel MacNeill** and **John McGrath** are among the authors of an [article](#) published in *Environment International* (Epub: December 2022; Print: January 2023). Concentrated animal feeding operations (CAFOs) are a source of environmental pollution and have been associated with a variety of health outcomes. Immune-mediated diseases (IMD) are characterized by dysregulation of the normal immune response and, while they may be affected by gene and environmental factors, their association with living in proximity to a CAFO is unknown. The authors explored gene, environment, and gene-environment (GxE) relationships between IMD,

CAFOs, and single nucleotide polymorphisms (SNPs) of prototypical xenobiotic response genes AHR, ARNT, and AHRR and prototypical immune response gene PTPN22. The exposure analysis cohort consisted of 6,464 participants who completed the Personalized Environment and Genes Study Health and Exposure Survey and a subset of 1,541 participants who were genotyped. The association between participants' residential proximity to a CAFO in gene, environment, and GxE models was assessed. In White participants, ARNT SNP rs11204735 was associated with autoimmune diseases and rheumatoid arthritis (RA), and ARNT SNP rs1889740 was associated with RA. In a transethnic genetic analysis, ARNT SNPs rs11204735 and rs1889740 and PTPN22 SNP rs2476601 were associated with autoimmune diseases and RA. In participants living closer than 1 mile to a CAFO, the log-distance to a CAFO was associated with autoimmune diseases and RA. In a GxE interaction model, White participants with ARNT SNPs rs11204735 and rs1889740 living closer than eight miles to a CAFO had increased odds of RA and autoimmune diseases, respectively. The transethnic model revealed similar GxE interactions. The authors' results suggest increased risk of autoimmune diseases and RA in those living in proximity to a CAFO and a potential role of the AHR-ARNT pathway in conferring risk. Also reported is the first association of ARNT SNPs rs11204735 and rs1889740 with RA. The researchers' findings, if confirmed, could allow for novel genetically-targeted or other preventive approaches for certain IMD. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Reproductive and Developmental Toxicity Following Exposure to Organophosphate Ester Flame Retardants and Plasticizers, Triphenyl Phosphate and Isopropylated Phenyl Phosphate, in Sprague Dawley Rats

DLH researcher **Jeff Krause** is among the authors of an [article](#) published in *Toxicological Sciences* (Online Ahead of Print: December 2022). Two organophosphate esters (OPEs) used as flame retardants and plasticizers, triphenyl phosphate (TPHP) and isopropylated phenyl phosphate (IPP), have been detected in environmental samples around the world. Human exposure primarily occurs via oral ingestion with reported higher concentrations in children. Currently, there are no data to evaluate potential risk from exposure to either TPHP or IPP during fetal development. These short-term perinatal studies in rats provide preliminary toxicity data for TPHP and IPP, including information on transfer to fetus/offspring and across the pup blood brain barrier. In separate experiments, TPHP or IPP were administered via dosed feed at concentrations 0, 1000, 3000, 10,000, 15,000, or 30,000 ppm to time-mated Hsd: Sprague Dawley® SD® rats from gestation day (GD) 6 through postnatal day (PND) 28; offspring were provided dosed feed at the same concentration as their dam (PND28-PND 56). TPHP and IPP-related toxicity resulted in removal of both 30,000 ppm groups on GD12 and 15,000 ppm IPP group after parturition. Body weight and organ weights were impacted with exposure in remaining dams. Reproductive performance was perturbed at ≥10,000 ppm TPHP and all IPP exposure groups. In offspring, both TPHP and IPP-related toxicity was noted in pups at ≥10,000 ppm as well as reduction in bodyweights, delays in pubertal endpoints, and/or reduced cholinesterase enzyme activity starting at 1000 ppm TPHP or IPP. Preliminary internal dose assessment indicated gestational and lactational transfer following exposure to TPHP or IPP. These findings demonstrate that offspring development is sensitive to 1000 ppm TPHP or IPP exposure. *Other authors include researchers from the National Institute of Environmental Health Sciences.*

Neighborhood Disadvantage and Immune-Related Illnesses Among Residents Living in the US Gulf States

DLH researchers **Mark Bodkin** and **W. Braxton Jackson II** are among the authors of an article published in *Annals of Epidemiology* (Epub: December 2022; Print: February 2023). Neighborhood disadvantage has been associated with increased risk for pneumonia and influenza-associated hospitalizations. Few studies have investigated how neighborhood disadvantage may influence immune-related illnesses. The aim of this study was to examine the association between neighborhood disadvantage and immune-related illnesses. The authors used data from the Gulf Long-term Follow-up (GuLF) Study. Analytic sample included home visit participants who

had complete information on exposure and covariates. Neighborhood disadvantage was assessed using the 2013 Area Deprivation Index (ADI), which assigns a ranking of 1 to 100 for lowest to highest disadvantage. ADI was linked to participants' geocoded enrollment addresses at the census block group level. ADI was categorized into quartiles based on the national distribution with the first quartile as the referent. Immune-related illnesses self-reported at the home visit (May 2011-May 2013) included occurrence of shingles, pneumonia, cold sores, flu, and colds since the Deepwater Horizon oil spill (April 2010). An aggregated outcome, based on occurrence of any pneumonia, cold sores, flu, and frequent colds since the spill, was also examined. The authors found elevated prevalence ratios for pneumonia associated with ADI in the third and fourth quartiles. Prevalence ratios for frequent colds were also elevated for increasing ADI quartiles, but with confidence intervals including the null value. The observed associations of frequent colds and pneumonia with increasing neighborhood disadvantage may warrant further research on this topic. *Other authors include researchers from the National Institute of Environmental Health Sciences and the UNC Gillings School of Public Health.*



Motor Impairment in Multiple Sclerosis:
Analysis from the North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)

Kottil Rammohan¹, David K.B. Li², June Halper³, Sara McCurdy Murphy⁴, Lisa Patton⁴, Chao Zheng¹, Seema Khurana¹
¹University of Miami, ²The University of British Columbia, ³Consortium of MS Centers, ⁴Social & Scientific Systems



Background:

NARCRMS is a longitudinal registry studying the course of MS in the disease-modifying era.

Objective:

To examine motor performance metrics of upper and lower extremity function in NARCRMS participants at enrollment, using the Expanded Disability Status Scale (EDSS) and 25-foot walk times.

Methods:

Recruitment began in 2016 and by July 30, 2021, 900 patients were enrolled at 27 MS sites across the US and Canada. People with any sub type of MS within 15 years of disease onset and an EDSS of up to 6.5 are eligible for enrollment. Various clinical metrics are collected including motor performance for upper and lower extremities. Our initial observations about EDSS, 25-foot timed walk and the 9-hole peg test are reported below.

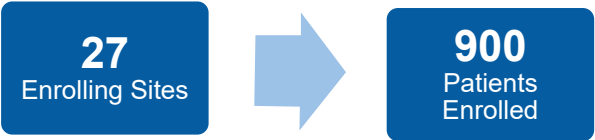
Results:

A mean 25-foot walking speed of 5.0 seconds was recorded in patients with EDSS 0 with progressive decline (5.6 and 8.3 seconds at EDSS 3.0 and 4.0 respectively) to 18.3 seconds at EDSS 6.5. For upper limb function, patients with EDSS 0 had a mean 9-HP test speed of 19.7 seconds in dominant (D) and 20.8 seconds in non-dominant (ND) hands, with decline starting at EDSS 2.5 (24.4 and 23.5 seconds for D and ND hands respectively) progressing to 37.3 and 47.4 seconds for the D and ND hands at EDSS 6.5.

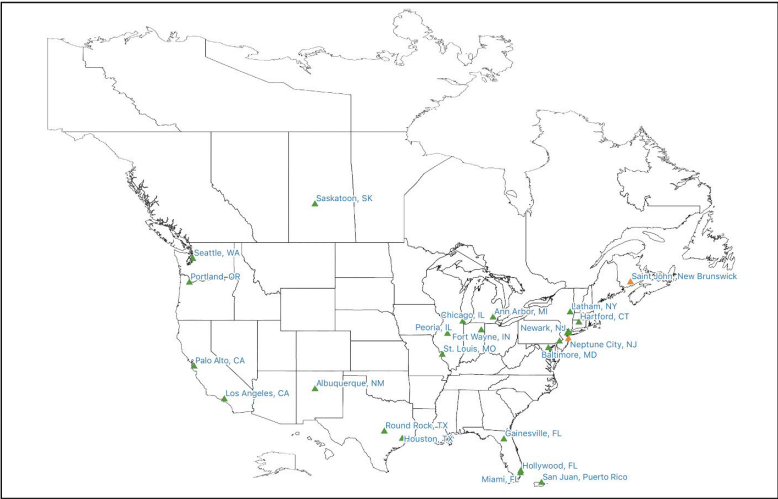
Conclusions:

Correlation of 25-foot walking speed to EDSS scale reiterated EDSS is a "walking scale". Decline in hand function beginning at EDSS 2.5 was unexpected as it is generally thought to be less affected in early MS. Progressive decline of hand function with EDSS confirms 9-HP test as a good measure of declining hand function and should be included in clinical monitoring.

* Data as of July 30, 2021



Geographic Distribution of NARCRMS Sites:



Demographics at Enrollment:

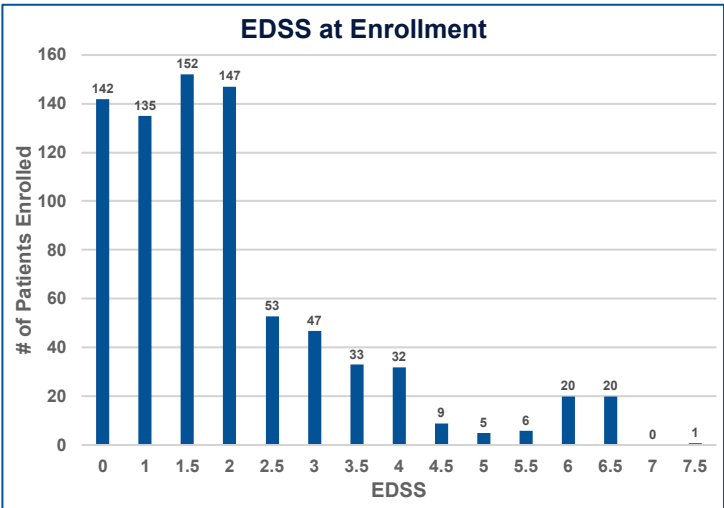
Gender	
Male	215
Female	647
Transgender Male	3
No Information (NI)	8

Race	
Caucasian/White	741
African American/Black	92
Aboriginal/Native America/Alaskan Native	2
Asian South Asian	6
Asian East Asian	2
Asian Southeast Asian	1
Pacific Islander/Hawaiian	1
Unknown	14
Caucasian/White & African American/Black	3
Caucasian/White & Aboriginal/Native American/Alaskan Native	1
African American/Black & Asian East Asian	1
No Information (NI)	9

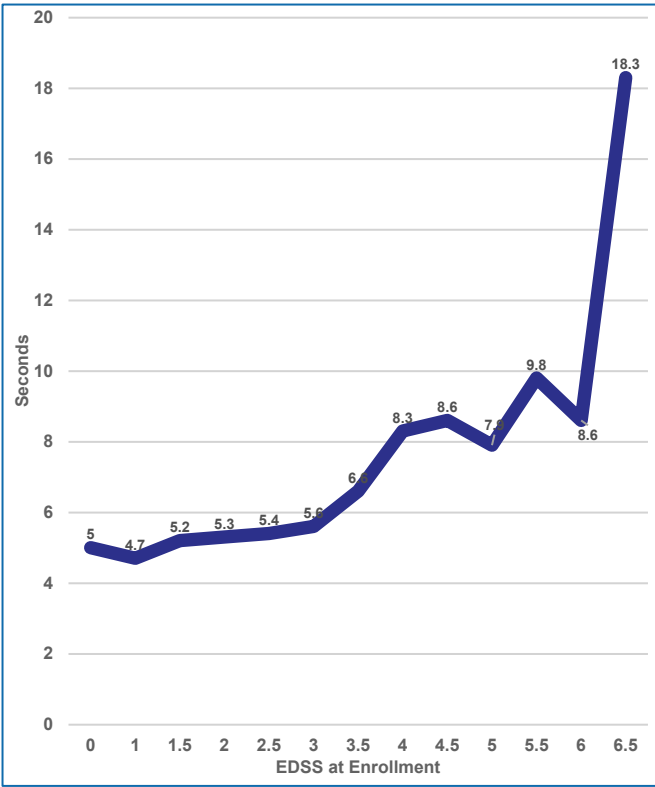
Ethnicity	
Hispanic/Latino	182
Non-Hispanic	669
Unknown	10
No Information (NI)	12

Inclusion Criteria:

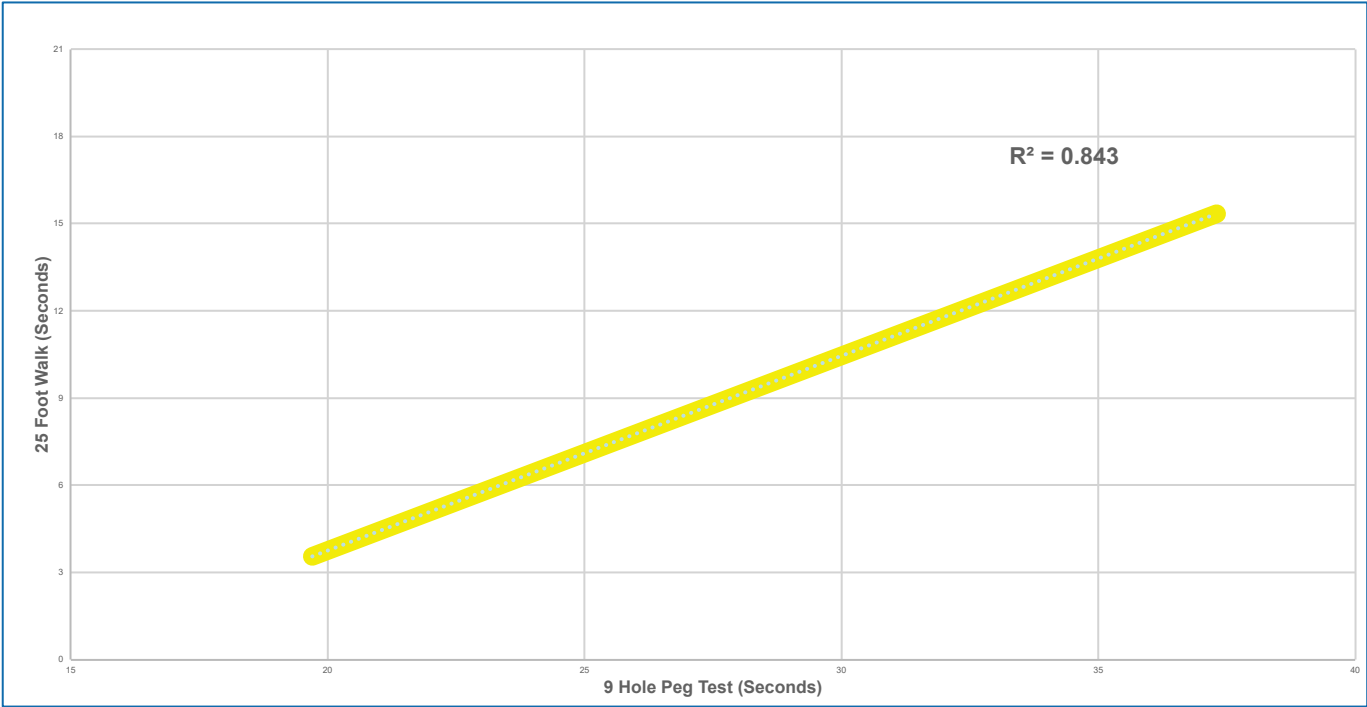
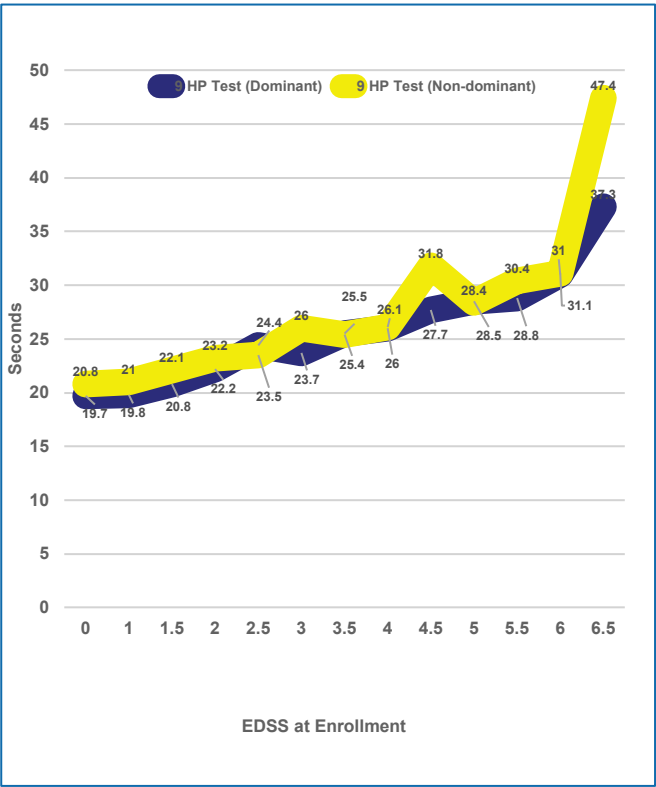
- Age 18 to 65 years
- Relapsing or Progressive MS with clear date of MS onset within 15 years.
- Evidence of Clinical Isolated Syndrome (CIS) typical of demyelination
- In patients with Progressive MS, the date of onset is the date at which the first neurological symptom was identified.
- EDSS of 6.5 or less
- Willingness to participate and contribute data on an on-going basis



EDSS vs. 25 Foot Walk:




EDSS vs. 9-Hole Peg Test:




Funding & Acknowledgments

NARCRMS is supported by the Consortium of Multiple Sclerosis Centers (CMSC) and receives funding from several pharmaceutical industry sponsors including Biogen Idec, Inc., BMS (formerly) Celgene Corporation, EMD Serono, Genentech Inc., Genzyme, Novartis Pharmaceutical Corporation and Teva Pharmaceuticals. NARCRMS gratefully acknowledges the contribution of sites, Site PIs, site staff and patients who contribute to NARCRMS.



Cognitive and Motor impairment in Multiple Sclerosis and their relative impact on Employment Status.
Preliminary findings from the North American Registry for Care and Research in Multiple Sclerosis.
Kottil Rammoohan¹, David Li², June Halper³, Sara McCurdy Murphy⁴, Lisa Patton⁴, Audrey Brown⁴, R. Flores Gonzalez¹, and on behalf of NARCRMS Site PIs
¹The University of Miami, ²The University of British Columbia, ³The Consortium of MS Centers, ⁴Social & Scientific Systems, A DLH Holdings Company



NARCRMS
North American Registry for Care and Research in Multiple Sclerosis

Abstract

Background:
NARCRMS is a longitudinal registry studying the course of MS in the era of disease modifying therapy.

Objective:
Underemployment or unemployment in multiple sclerosis (MS) is caused by multiple factors, among them cognition and motor impairment. In this study we examine the relative impact of cognition and motor function in employment status in patients with MS.

Methods:
Cognitive and motor impairment were examined in a subgroup of patients enrolled into the North American Registry for Care and Research in Multiple Sclerosis (NARCRMS) at the enrollment visit. Their employment status was recorded and if employed part-time, patients were queried if their status was based on their self-perceived impairments due to MS.

Results:
Complete data was available on 351 subjects as of May 18, 2022 where cognition was examined by the 3-second Paced Auditory Sequential Addition Test (PASAT 3). Patients ranged from 20 to 64 years (median 39 years) and M:F ratio of 1:2.5. The median extended disability status scale (EDSS) was 1.50, mean dominant 9 hole-peg test (9HPT) 23.07 seconds, 25-foot timed walk (25FTW) 5.82 seconds, and fatigue was reported by 63.41%. Approximately a third of the subjects were unemployed and 15% reported part-time employment and 44% indicated that the impairments from MS precluded full-time employment. Patients were grouped into quartiles based on the PASAT scores from the highest functioning subjects in the 1st quartile to the lowest performers in the 4th. Significant interquartile differences were not observed for EDSS or motor function. Although motor function approached but did not meet significance, employment status was statistically significant favoring the higher functioning subjects (Q1 v. Q4, p=0.0375).

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

Data and Analysis

	Q1	Q2	Q3	Q4
Sex	Female = 53 (15.6%) Male = 24 (7.06%)	Female = 66 (19.4%) Male = 27 (7.9%) Transgender Male = 1 (0.29%)	Female = 60 (17.6%) Male = 19 (5.6%)	Female = 64 (18.8%) Male = 25 (7.4%) Transgender Male = 1 (0.29%)
Age	N = 77 Median: 41 Mean: 42.9	N = 94 Median: 39 Mean: 39.9	N = 78 Median: 40 Mean: 40.6	N = 90 Median: 38.5 Mean: 39.4
EDSS	N = 78 Median: 1.5 Mean: 1.72	N = 97 Median: 1.5 Mean: 1.8	N = 86 Median: 2 Mean: 1.91	N = 90 Median: 2 Mean: 1.98
Average 9 Hole Peg (Dom)	N = 78 Median: 20.75 Mean: 21.4	N = 94 Median: 20.5 Mean: 22.4	N = 84 Median: 21.25 Mean: 22.1	N = 87 Median: 23 Mean: 26.1
25 Foot Walk	N = 77 Median: 5 Mean: 5.6	N = 96 Median: 5 Mean: 5.7	N = 86 Median: 5.5 Mean: 5.8	N = 88 Median: 6 Mean: 6.2

	Q1	Q2	Q3	Q4
Original Grouping				
Employed	N = 62 18.45%	N = 77 22.92%	N = 59 17.56%	N = 58 17.26%
Not Employed	N = 15 4.46%	N = 16 4.76%	N = 19 5.65%	N = 30 8.93%
New Grouping				
Employed Full Time	N = 52 15.52%	N = 58 17.31%	N = 45 13.43%	N = 40 11.94%
Unemployed/Under-employed	N = 25 7.46%	N = 35 10.45%	N = 33 9.85%	N = 47 14.03%

		Q2	Q3	Q4
EDSS	Pr > ChiSq	0.7928	0.3827	0.2291
	Point Estimate	1.029	1.102	1.14
	95% Wald Confidence Limits	0.829/1.278	0.886/1.369	0.921/1.411
25 Foot Walk	Pr > ChiSq	0.7805	0.502	0.1553
	Point Estimate	1.02	1.048	1.097
	95% Wald Confidence Limits	0.887/1.173	0.914/1.201	0.965/1.248
Average 9 Hole Peg (Dom)	Pr > ChiSq	0.2153	0.3596	0.0114
	Point Estimate	1.038	1.029	1.076
	95% Wald Confidence Limits	0.979/1.101	0.968/1.094	1.017/1.139

		Q2	Q3	Q4
Original Grouping				
Employed	Pr > ChiSq	0.7022	0.4638	0.0375
	95% Wald Confidence Limits	0.394/1.873	0.619/2.861	1.045/4.374
	New Grouping			
Employed Full Time	Pr > ChiSq	0.4831	0.2065	0.0059
	95% Wald Confidence Limits	0.422/1.5	0.34/1.26	0.216/0.77

Statistical evaluation of an image analysis algorithm trained to detect and score rodent cardiomyopathy

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Problem

In cardiotoxicology, microscopic evaluation of rodent hearts is performed to detect and grade the severity of histopathologic changes due to test article exposure. Although there is standard diagnostic criteria for semi-quantitative human-grading of progressive cardiomyopathy (PCM) in the literature, challenges remain in the consistency of grading across pathologists and across studies.

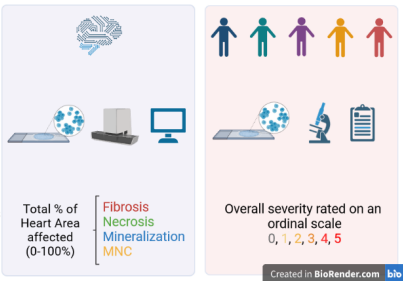
Approach


Evaluate image algorithm trained to detect PCM by comparing AI scores with severity grades rated by pathologists from different centers.

Computer vs Humans

Digital vs Glass slides

Continuous vs ordinal data





National Institute of Environmental Health Sciences




Social & Scientific Systems



A well-trained and validated **AI** can be a useful **tool** in helping humans **quantify microscopic features** of **cardiomyopathy** in rodents.

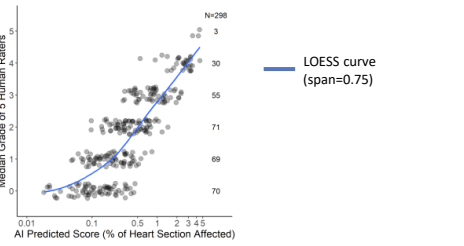
Whole slide image showing AI detection of lesions

Fibrosis
Necrosis
Mineralization
Mononuclear cell infiltration (MNC)

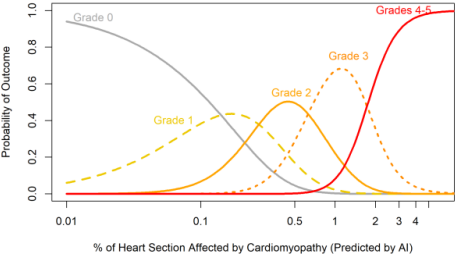


Scan for more info

Data & Results



Using a multinomial logistic regression model, we found a strong positive correlation between the AI predicted score and the median severity grading reached by a panel of pathologists.



Acknowledgments
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