Research Update

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A semi-annual look at select DLH research activities.

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We are excited to share the latest volume of the DLH Research Update, a semi-annual look at select research activities from across our organization.

Research is essential to understanding the world around us, uncovering key insights, and driving improved outcomes. DLH advances knowledge, tackles challenges, and accelerates innovation through our core capabilities:

- Science, Research, & Development
- Digital Transformation & Cybersecurity, and
- Systems Engineering & Integration.

The work of our researchers spans sectors and markets. We dig into challenges associated with cancer, diabetes, and HIV. We leverage data to advance combat casualty care and enhance warfighter readiness. We develop methodologies for informed decision-making to improve response, recovery, and future preparedness for disaster-related events such as wildfires, droughts, and hurricanes.

Thank you to each member of Team DLH for your unwavering commitment to positive change. Your contributions are shaping a better world for all.

Thank you for reading.

Jeanine Christian
President, Public Health & Scientific Research

Brief Report. **Preexposure Prophylaxis Use Among U.S. Veterans Using Veterans Health Administration Services, 2014-2022**

DLH researchers **Lei Yu** and **Wei Wei** were among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Online: January 2025). It is important to monitor national HIV preexposure prophylaxis (PrEP) use in the United States. However, PrEP use data in the Veterans Health Administration (VHA) system are not included in the current monitoring surveillance. To address this gap, the authors examined the trends in PrEP use among U.S. veterans receiving health services in the VHA system. 2014-2022 VHA data was analyzed to identify the annual number and prevalence of persons aged ≥18 years prescribed PrEP, stratified by sex, age, race/ethnicity, and region. The number of veterans prescribed PrEP increased from 361 in 2014 to 6,050 in 2022 with an estimated annual percent change of 29.6%. Of 6,050 veterans with PrEP prescriptions in 2022, 95.2% were men, 4.8% were women, 50.4% were White, 24.5% Black or African American (Black), and 14.0% Hispanic or Latino. The prevalence of Black and Hispanic or Latino individuals prescribed PrEP increased significantly from 2014 to 2022. VHA data fill a gap in monitoring PrEP use in the United States. An increasing trend was observed in the number of veterans prescribed PrEP similar to trends among persons with commercial or public health insurance. *The other authors are researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention, VA Puget Sound Health Care System, VA Portland Health Care System, Oregon Health & Science University, and the University of Washington School of Medicine.*

Stressful Life Events Are Associated With the Diagnosis of Systemic Autoimmune Rheumatic Diseases Among Adults

DLH researcher **Nastaran Bayat** was among the authors of an article published in *Clinical and Experimental Rheumatology* (Online: January 2025). The study objective was to assess the association between life events and subsequent diagnosis of systemic autoimmune rheumatic diseases (SARDs) by comparing siblings discordant for SARDs and unrelated controls. Life events 12 months prior to SARD diagnosis/reference date were queried using the Interview for Recent Life Events in 227 adults (96 probands with SARDs, 78 siblings, 53 controls). Probands were matched by age, sex, and race with their unaffected siblings or with unrelated controls. Logistic regression was used to calculate the relative odds of SARDs in relation to life events scores, adjusting for age, sex, race/ethnicity, education, and ever smoking. The study identified consistent trends of probands reporting greater numbers of total and highly stressful events, and higher stress ratings than their unaffected siblings. Probands reported greater numbers and higher stress ratings of total, uncontrollable, and undesirable events compared to unrelated controls. The number of highly stressful events and the scores of weighted major events were also greater in probands and siblings compared to unrelated controls. The number of total, major, uncontrollable, undesirable, and highly stressful life events, along with their corresponding stress ratings, were associated with higher odds of SARD diagnosis, based on probands compared to controls. This case-control study of life events preceding SARDs diagnosis using a validated life events questionnaire provides support for an aetiologic role of negative life events and psychological stress in SARDs among adults. *The other authors are researchers from the National Institute of Environmental Health Sciences, the National Institute of Dental and Craniofacial Research, the University of Chicago, and the Italian National Institute of Health (Rome).*

Level of Tuberculosis-Related Stigma and Associated Factors in Ugandan Communities
DLH researchers **Derrick Kimuli**, **Norah Namuwenge**, **Barbara Amuron**, and **Daraus Bukenya** were among the authors of an article published in *PLoS One* (Online: January 2025). Tuberculosis (TB) stigma remains a significant barrier to TB control efforts globally, especially in countries with a high TB burden. Studies about TB stigma done in Uganda so far have been limited in scope and focused on data collected health facilities. In this study, the authors reported TB-related stigma at the community level for the period 2021/2022. They used the 2021/22 Lot Quality Assurance Sampling (LQAS) data from a sample of 33,349 participants across 77 districts to measure TB stigma determine factors associated. Demographic characteristics, knowledge, and participant perspectives were included as study variables. The data set had equal proportions of males and females. The largest age group was 20-29 years old (38.47%). Most participants were married (62.94%) and had primary level education (65.80%). Overall, 45.48% of participants had TB stigma scores above the median. Variations in TB stigma levels were observed across different districts. Factors associated with higher TB stigma included older age, higher education levels, urban residence, and TB knowledge. To reduce TB stigma and misinformation that can make an impact on TB response, community interventions should balance increasing awareness with minimizing fear. These interventions should be well-rounded and context-specific to address disparities within communities and bolster TB control efforts in the country. *The other authors include researchers from the Ministry of Health Uganda, U.S. Agency for International Development, and the U.S. Centers for Disease Control and Prevention.*

Fine Particulate Matter From Burning Oil and Gas and Associated Neurological Symptoms Among Deepwater Horizon Oil Spill Cleanup Workers
DLH researchers **Braxton Jackson** and **Kate Christenbury** were among the authors of an article published in *Environmental Science Processes & Impacts* (Online: January 2025; Print: February 2025). Burning and flaring of oil and gas following the 2010 Deepwater Horizon (DWH) oil spill generated high airborne concentrations of fine particulate matter (PM2.5). Neurological effects of PM2.5 have been previously reported, but this relationship has received limited attention in the context of oil spills. The authors evaluated associations between burning-related PM2.5 and prevalence of self-reported neurological symptoms during, and 1-3 years after, the DWH disaster cleanup. For 9914 DWH disaster responders in the Gulf Long-term Follow-up Study who worked on the water, the authors examined aggregate outcomes (central nervous system [CNS; dizziness, sweating, palpitations, nausea, or migraine/severe headache] and peripheral nervous system [PNS; tingling/numbness in extremities, blurred vision, or stumbling] symptoms) and individual symptoms (CNS and PNS symptoms, plus insomnia, vomiting, seizures, and fatigue). Log-binomial regression was used to estimate adjusted prevalence ratios (PR) and 95% confidence intervals, accounting for age, race, ethnicity, and sex, and DWH disaster-related co-exposures to benzene, toluene, ethylbenzene, xylene, and n-hexane (BTEX-H). Effect measure modification was examined by age, race, smoking, and BTEX-H exposure. During the disaster, 34% of participants experienced at least one symptom (23% CNS, 12% PNS); 1-3 years later, 30% did (19% CNS, 17% PNS). Evidence of associations with PM2.5 was most consistent for CNS symptoms, although exposure-response trends were not observed. Associations with PM were more apparent among those with lower BTEX-H exposure and among older workers. Some evidence was found of an association between burning-related PM2.5 and prevalence of neurologic symptoms during the DWH disaster response and 1-3 years later. Understanding these relationships can inform responses to future disasters to better protect human health. *The other authors include researchers from the*

Gillings School of Global Public Health at the University of North Carolina at Chapel Hill, the National Institute of Environmental Health Sciences, and the School of Public Health at the University of Minnesota.

***Commentary.* Advancing Reproducible Research Through Version Control Technology**
DLH researchers **Ghassan Hamra**, **Ian Buller**, **Audrey Brown**, and **Nathaniel MacNell** were among the authors of a commentary published in *Epidemiology* (Epub: January 2025; Print: May 2025). *[No abstract available]. The other authors are researchers from the University of California at Berkeley and the University of Washington at Seattle.*

Concentrations of Blood Styrene and Neurobehavioral Function Among Gulf State Residents in the U.S.
DLH researcher **Braxton Jackson** was among the authors of an article published in the *International Journal of Environmental Health Research* (Online Ahead of Print: February 2025). The objective was to investigate relationships between blood styrene concentrations and neurobehavioral function among US Gulf State residents. The study included 328 Gulf state residents enrolled in the Gulf Long-term Follow-up Study with data on blood styrene concentrations (2012-2013) and neurobehavioral test results (2014-2016, Behavioral Assessment and Research System and trail making test). The authors estimated the differences in test scores by blood styrene quartiles and explored effect measure modification by smoking. Styrene was detected in 77% of participants. The authors observed only weak associations and no apparent dose-response relationships between styrene levels and performance on any neurobehavioral tests, although some associations were more prominent in males. For some neurobehavioral tests, modestly stronger associations were observed among participants with higher cotinine levels. The authors found limited support for an association between low-level blood styrene concentration and neurobehavioral test performance, although some associations were stronger among smokers. *The other authors include researchers from the University of North Carolina at Chapel Hill, the National Institute on Aging, the National Institute of Environmental Health Sciences, and the National Cancer Institute.*

Indoor Allergen Exposure in Relation to Sleep Health Among US Adults
DLH researcher **Jesse Wilkerson** was among the authors of an article published in the *Journal of Allergy and Clinical Immunology* (Online: February 2025). Common indoor allergens can accumulate within the sleep microenvironment (e.g., bedding) and may contribute to poor sleep health. The authors sought to examine bedroom allergen exposure in relation to multiple sleep dimensions among US adults. Data for this study (N = 3399) were collected during the 2005 to 2006 National Health and Nutrition Examination Survey. Concentrations of 8 bedroom allergens were assessed and classified as elevated when levels exceeded 75th/90th percentile thresholds. Self-reported sleep measures included having trouble sleeping, any sleep disorder, snoring, and sleep medication use. Adjusting for confounders, the authors used Poisson regression to estimate associations between bedroom allergen exposures and sleep dimensions overall and by race/ethnicity, sex/gender, and socioeconomic status. Among adults, elevated pet allergen exposure was the most prevalent (41.2%). Elevated pest allergen exposure was associated with a lower likelihood of a reported sleep disorder diagnosis. For Hispanic/Latino participants, elevated pet allergen exposure was associated with having trouble sleeping and frequent snoring. Elevated fungal allergen exposure was associated with any sleep disorder diagnosis among participants with moderate socioeconomic status and a higher prevalence of sleep medication use for Hispanic/Latino participants. Elevated exposures to pet and fungal allergens were also associated with being diagnosed with any sleep disorder among women. In a nationally representative sample of US adults, exposure

to elevated levels of bedroom allergens was associated with poor sleep health, and the magnitude of the associations was generally the strongest among minoritized racial/ethnic groups and women. *The other authors include researchers from the National Institute of Environmental Health Sciences, Department of Occupational and Environmental Health at the University of Iowa, and the National Institute on Minority Health and Health Disparities.*

Virologic Effects of Broadly Neutralizing Antibodies VRC01LS and VRC07-523LS on Chronic HIV-1 Infection

DLH researcher **Jhoanna Roa** was among the authors of an article published in *JCI Insight* (Online: February 2025). HIV-1-specific broadly neutralizing monoclonal antibodies (bNAbs) have emerged as promising interventions with the potential to effectively treat and prevent HIV-1 infections. The authors conducted a phase I clinical trial evaluating the potent CD4-binding site-specific (CD4bs-specific) bNAbs VRC01LS and VRC07-523LS in people with HIV-1 (PWH) not receiving antiretroviral therapy (ART). Participants received a single intravenous 40 mg/kg dose of either VRC01LS (n = 7) or VRC07-523LS (n = 9) and did not initiate ART for a minimum of 14 days. The primary study objective was to evaluate safety and tolerability; the secondary study objectives were to evaluate pharmacokinetics (PK) and the impact of administered bNAbs on viral loads (VL) and CD4+ T cell counts in the absence of ART. This trial enrolled 16 PWH aged 20 to 57 years. Both bNAbs were safe and well tolerated. Mild local reactogenicity was only reported in participants who received VRC07-523LS, while both bNAbs were associated with mild systemic symptoms. VRC07-523LS administration significantly decreased VL in 8 out of 9 participants. In contrast, VRC01LS administration resulted in a smaller average decline, and 3 out of 7 participants showed no change in VL. Postinfusion maximum decline in VL correlated with post hoc baseline in vitro viral susceptibility results for both bNAbs. The results of this trial support inclusion of potent CD4bs-specific bNAbs, such as VRC07-523LS, into next-generation treatment regimens for HIV-1. [The protocol number and *clinicaltrials.gov* identifier are VRC607/ACTG A5378 and NCT02840474, respectively.] *The other authors include researchers from the National Institute of Allergy and Infectious Diseases, Department of Microbiology, Immunology, and Tropical Medicine at George Washington University, and the Frederick National Laboratory for Cancer Research.*

Lessons Learned From Evaluating Defined Chemical Mixtures in a High-Throughput Estrogen Receptor Assay System

DLH researcher **Gregg Dinse** was among the authors of an article published in *Toxicological Sciences* (Online Ahead of Print: February 2025: Print: May 2025). In this paper, the authors provided a proof of concept evaluating the utility of the U.S. Tox21 high-throughput screening approach to assess the hazard of chemical mixtures using two estrogen receptor assays. A subset of chemicals identified in Phase I of the Tox21 program as active in the estrogen receptor (ER) agonist assay were used to design mixtures for testing in Phase II. Individual chemicals and mixtures were evaluated in two cell-based estrogen receptor alpha (ERα) activation assays: One incorporating a transfected ligand-binding domain in an ERα β-lactamase reporter cell line (ER-bla) and the full-length endogenous receptor in the MCF7 cell line with a luciferase reporter gene (ER-luc). Concentration-response data from individual chemicals were used to predict the joint effect based on mixtures modeling methods and were compared to observed mixtures data to assess model fit. The models tended to overpredict mixture responses in the ER-bla assay, while predictions were closer to observed responses in the ER-luc assay, indicating that a full-length endogenous estrogen receptor is a preferred model for high-throughput mixture analysis. Lessons learned from this research include the

importance of analyzing the individual chemicals used for predictions and the mixtures in the same experimental paradigm to minimize variation, developing methods for imputing missing values from incomplete concentration-response curves, and establishing criteria to determine when inactive chemicals should be omitted from mixture predictions. *The other authors include researchers from the National Institute of Environmental Health Sciences and the U.S. Environmental Protection Agency.*

Developmental Immunotoxicity Study of Tris(Chloropropyl) Phosphate in Hsd:Sprague Dawley SD Rats Exposed Through Dosed Feed

DLH researcher **Guanhua Xie** was among the authors of an article published in *Toxicological Sciences* (Online Ahead of Print: February 2025; Print: May 2025). Tris(chloropropyl) phosphate (TCPP) is a member of organophosphate flame retardants (OPFRs) used commonly as a replacement for polybrominated diphenyl ethers in consumer and commercial products. Flame retardants have been shown to modulate immune function in vivo and in vitro and there is evidence that at least some related compounds such as organophosphate pesticides can cause developmental immunotoxicity. Developmental immunotoxicology studies were conducted by administering 0, 2500, 5000, or 10,000 ppm TCPP in feed to pregnant Hsd:Sprague Dawley® SD® rats from gestation day (GD) 6 through weaning on postnatal day (PND) 28. Feed exposure to TCPP was continued in the F1 offspring until terminal euthanasia at approximately 16-21 weeks of age when assessments for developmental immunotoxicity were conducted. Innate, humoral, and cell-mediated immune function were assessed in the F1 adults. The antibody forming cells (AFC) response to sheep red blood cells (SRBC) was reduced in male and female F1 rats in the 10,000 ppm treatment group but coincided with reduced bodyweights. The AFC response was also significantly reduced in male rats exposed to 5,000 ppm where only moderate effects on bodyweights occurred. TCPP exposure affected baseline T-cell proliferation without stimulation; however, the relevance of this change for immunotoxicity risk is unknown. TCPP exposure did not affect cytotoxic T-lymphocyte activity. Only minor and inconsistent treatment related effects on hematology, innate NK cell function, and immune cell population distributions in the spleen were observed. Taken together, these data indicate that TCPP has the potential to impact humoral immune responses following developmental exposure. *The other authors include researchers from the National Institute of Environmental Health Sciences.*

Impact of a Minimal Monitoring HCV Treatment Approach on Health-Related Quality of Life

DLH researcher **Chanelle Wimbish** was among the authors of an article published in *Quality of Life Research* (Online Ahead of Print: February 2025; Print: June 2025). Direct-acting antivirals (DAA) are highly effective for the management of HCV disease. This study aimed to evaluate changes in health-related quality of life (HQoL) among people with HCV who were treated with DAAs using a minimal monitoring (MINMON) approach. The MINMON strategy proposed for evaluation in this study included the following components: a) No pre-treatment genotyping; b) entire treatment course (84 tablets) given to participant at baseline; c) no scheduled on-treatment clinic visits; d) no scheduled on-treatment monitoring; and e) remote contact with participants at week 4 (adherence counseling and locator update) and week 22 (scheduling of SVR visit and locator update). ACTG A5360 was a multicenter, international (Brazil, South Africa, Thailand, Uganda, and USA) trial to assess the feasibility and efficacy of the MINMON approach in people with HCV. Overall, 394 individuals were included; most did not have cirrhosis (360; 91%) or problematic alcohol use (278; 71%). The authors found HQoL improvements for

participants from Brazil and Thailand, but not for the USA. Participants reported high rates of pain/discomfort and anxiety/depression, with decreases over time only for Brazil. Factors associated with larger improvements in VAS scores included: cirrhosis at baseline, and non-use or problematic use of other substances (apart from tobacco/marijuana) compared to non-problematic use. HQoL improvements were found among people with HCV following DAA treatment with variability across countries. The authors findings reinforce the importance of DAA treatment, especially among those with advanced HCV disease. Continuous mental health care including depression and substance use support should be offered to individuals after HCV treatment. *The other authors include researchers from the Instituto Nacional de Infectologia Evandro Chagas (Brazil), Center for Biostatistics in AIDS Research at the Harvard T. H. Chan School of Public Health, and the Johns Hopkins University School of Medicine, as well as researchers from institutes in Brazil, Thailand, Uganda, and South Africa.*

Racial-Ethnic Residential Segregation and Sleep Health Among US Adults: Associations by Race and Ethnicity, Sex/Gender, and Neighborhood-Level Poverty
DLH researchers **Jesse Wilkerson**, **Nathaniel MacNell**, and **Braxton Jackson** were among the authors of an article published in the *Journal of Racial and Ethnic Health Disparities* (Online Ahead of Print: March 2025). Although racial-ethnic residential segregation (RRS) is hypothesized to contribute to sleep disparities by concentrating poverty and impairing sleep among minoritized racial-ethnic groups, feelings of belonging within relatively homogenous neighborhoods may be protective against poor sleep. Yet, empirical studies are sparse. To investigate RRS-sleep health associations and determine potential modifiers among US adults, the authors linked National Health Interview Survey data (2011-2017) to 2012 and 2017 American Community Survey census tract-level data. Among 126,539 participants (mean age ±SE = 46±0.1 years), high RRS was most common among non-Hispanic (NH)-Black (38%), followed by NH-Asian and non-Mexican Latine (34%), Mexican Latine (30%), and NH-White adults (17%). Across races-ethnicities and sexes/genders, high vs. low RRS was associated with a 6% lower prevalence of short sleep duration, an 11% lower prevalence of long sleep duration, and a 2% higher prevalence of restorative sleep. Associations with a lower prevalence of trouble falling asleep were stronger among men vs. women. Race-ethnicity-by-sex/gender group membership and neighborhood-level poverty modified associations with sleep duration and quality without consistent patterns. RRS was associated with more favorable sleep health among US adults with variation by key modifiers (e.g., sex). Strategies that leverage potentially protective social factors while promoting equitable resources across diverse neighborhoods may help address sleep health disparities. *The other authors include researchers from the National Institute of Environmental Health Sciences and the National Institute on Minority Health and Health Disparities.*

Burden of Non-Malignant Liver and Pancreatic Diseases in the United States Population: Rates and Trends
DLH researcher **Constance Ruhl** was a coauthor of an article published in *Clinical Gastroenterology and Hepatology* (Online Ahead of Print: March 2025). Non-malignant liver and pancreatic diseases are common in the United States and lead to significant morbidity, mortality, and health care utilization. The authors used national survey and claims databases to investigate rates and trends in the liver and pancreatic disease burden over the past decade in the United States. The Nationwide Emergency Department Sample, National Inpatient Sample, Vital Statistics of the U.S.: Multiple Cause-of-Death Data, Optum Clinformatics® Data Mart, and Centers for Medicare and Medicaid Services

Medicare 5% Sample and Medicaid files were used to estimate claims-based prevalence, medical care use, and mortality with an all-listed liver or pancreatic disease diagnosis. In the U.S. population, liver disease contributed to 2.7 million emergency department visits, 2.0 million hospital stays, and 134,000 deaths in 2021. Pancreatitis was a less common but still significant cause of health care use contributing to 733,000 emergency department visits, 552,000 hospital stays, and 9,000 deaths in 2021. For both conditions, male and American Indian/Alaska Native persons had a greater mortality and medical care use burden. During the study period, both medical care use and mortality rates with a liver disease diagnosis rose, concerningly reversing previously declining trends. For pancreatitis, medical care use rates stabilized or declined during recent years and the mortality rate declined through 2019 and then rose through 2021. The burden of non-malignant liver and pancreatic diseases in the United States is substantial. The rise in liver disease mortality rates following the reversal of a previous downward trend is particularly concerning. Hence ongoing surveillance of liver disease and pancreatitis prevalence may better inform research programs. *The other author is a researcher at the National Institute of Diabetes and Digestive and Kidney Diseases.*

Oil Spill Cleanup Related Exposures to Benzene, Toluene, Ethylbenzene, Xylenes, and N-Hexane and Incident Diabetes Mellitus

DLH researcher **Kate Christenbury** was among the authors of an article published in *Environmental Research* (Online Ahead of Print: March 2025). Exposure to benzene, toluene, ethylbenzene, xylenes, and n-hexane (BTEX-H) may contribute to the development of diabetes. Oil spill response and cleanup (OSRC) workers are exposed to BTEX-H but there are few relevant studies. Incident diabetes was studied over 10 years of follow-up among OSRC workers. This analysis included 21,726 participants (82.2 % male, mean age 39.9 years; 66.5 % White race) in the Gulf Long-term Follow-up Study—a prospective cohort of Deepwater Horizon (DWH) oil spill OSRC workers followed from 2011 to 2013 through 2021. Individual estimates of cumulative work-related exposures to specific BTEX-H chemicals and an aggregate sum (total BTEX-H) were derived from a job-exposure matrix that linked exposure group estimates derived from exposure measurements to self-reported DWH work histories. Differences in associations were examined by neighborhood disadvantage using the Area Deprivation Index (ADI) and by self-classified race in stratified analyses. Exposure to the BTEX-H chemicals was associated with diabetes, with elevated hazard ratios for third and fourth quartiles of exposure compared to the first quartile. Stratified analyses showed little variation by race and suggestions of variation by ADI. Exposures to BTEX-H chemicals were associated with incident diabetes among OSRC workers for the individual BTEX-H chemicals, total BTEX-H, and the BTEX-H mixture. The range of exposures in this study make these findings relevant to other low to moderate exposure settings. *The other authors include researchers from the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill, the National Institute of Environmental Health Sciences, and the National Cancer Institute.*

Quality of Care in Adults With Diabetes

DLH senior epidemiologist and researcher **Sarah Casagrande** served as an editor for an article published in *Diabetes in America*, a National Institute of Diabetes and Digestive and Kidney Diseases compilation and assessment of epidemiologic, public health, clinical research, and clinical trial data focused on diabetes, its complications and treatment, health care utilization, and diabetes prevention in the United States. (Online: March 2025). *Excerpt:* This article reviews the evidence behind current quality metrics and evaluates how well diabetes care in the United States meets high-quality standards at the individual

and organizational levels. Clinical recommendations for diabetes focus on managing risk factors to prevent and treat microvascular and macrovascular complications. These clinical recommendations have been the primary source materials for current quality indicators for diabetes care. These indicators include achieving targeted glycemic control (glycated hemoglobin [A1C] levels <7% or <8%), maintaining blood pressure <130/80 or <140/90 mmHg, reaching low-density lipoprotein (LDL) cholesterol levels <100 mg/dL for those without atherosclerotic cardiovascular disease (ASCVD) or <70 mg/dL for those with ASCVD, smoking cessation, annual screenings for eye, kidney, and foot health, and receiving specific immunizations (pneumococcal vaccine and annual influenza vaccine). A composite measure of controlling glycemia, blood pressure, and cholesterol and avoiding tobacco is also used, identifying individuals with control of all four factors. Since the late 1990s, the population with diagnosed diabetes in the United States has become older, more diverse, and more insured. Risk factor control in people with diabetes in the United States has seen improvements but has plateaued over the last decade. Racial and ethnic disparities persist, with non-Hispanic Black and Hispanic individuals less likely to achieve A1C control <8.0% and blood pressure <140/90 mmHg compared to non-Hispanic White individuals. Uninsured individuals are also less likely to achieve risk factor control compared to individuals with insurance, including A1C <8.0%, LDL cholesterol control, and the composite measure of risk factor control. Similarly, younger adults age 20–44 years demonstrate poorer outcomes in glycemic and lipid control, smoking cessation, and composite risk factors compared to older adults. National data highlight a high prevalence of diabetes-related complications, including ASCVD, chronic kidney disease (CKD), and retinopathy. Annual hospitalization rates for diabetes-related discharges have increased over time with notable increases in diabetic ketoacidosis (from 2.15 cases per 100 people in 2000 to 4.15 cases per 100 people in 2020) and hypoglycemia (from 0.08 cases per 100 people in 2000 to 0.57 cases per 100 people in 2020). This article concludes by identifying key areas for improvement in diabetes quality-of-care measurement. With growing recognition that diabetes varies in phenotypes and severity, there is an emphasis on tailoring quality indicators and thresholds to population subgroups based on risk level. As such, clinical guidelines are beginning to incorporate personalized treatment recommendations based on genetic, clinical, and social factors. Expanding quality-of-care standards to include novel indicators could improve outcomes for individuals and identify system-wide improvements in diabetes care.

Psychosocial and Behavioral Health Among Youth and Adults With Diabetes
DLH senior epidemiologist and researcher **Sarah Casagrande** served as an editor for an article published in *Diabetes in America*, a National Institute of Diabetes and Digestive and Kidney Diseases compilation and assessment of epidemiologic, public health, clinical research, and clinical trial data focused on diabetes, its complications and treatment, health care utilization, and diabetes prevention in the United States. (Online: March 2025). *Excerpt:* Psychosocial and behavioral health concerns for people with diabetes have received increased attention over the past several years, and since the publication of the American Diabetes Association's position statement calling for psychosocial care for people with diabetes, screening and treatment options have become more widespread. In this review, the authors use national data sets to describe the prevalence of psychosocial and behavioral health conditions in people with diabetes, which occur at higher rates than in the general population. Lifetime prevalence of depression in adults with diabetes is 25% (compared to 20% in the general adult population); anxiety diagnoses are reported by 20% of adults with diabetes (compared to 17.5% of adults without diabetes); eating disorders occur in 10% of females with diabetes, and disordered eating occurs in up to 38% of people with diabetes. Diabetes distress is also commonly experienced by people

with diabetes; >30% of people with both type 1 and type 2 diabetes report clinically significant levels of diabetes distress. In addition, the authors highlighted the correlates and consequences of the psychosocial concerns most commonly experienced by people with diabetes, including depression, diabetes distress, anxiety, and disordered eating, as well as serious mental illnesses. Specifically, the authors noted that females and young adults with diabetes are more likely to experience clinical diagnoses of depression, anxiety, and eating disorders than males or older adults with diabetes. Depression has been consistently associated with elevated glycemic outcomes in adults and youth, including higher glycated hemoglobin (A1C) levels and greater risk for diabetic ketoacidosis. In recent years, more studies have explored these topics in youth with diabetes and in representative populations. Finally, the authors identified measurement issues and review options for treatment and implications for clinical practice and future research.

Suppression of the T-Dependent Antibody Response Following Oral Exposure to Selected Polycyclic Aromatic Compounds in B6C3F1/N Mice

DLH researcher **Shawn Harris** was among the authors of an article published in *Frontiers in Toxicology* (Online: March 2025). The ability of polycyclic aromatic compounds (PACs), most notably benzo(a) pyrene [B(a)P], to suppress antibody responses in experimental animals is well documented. Very little information, however, is available on the immunotoxicity of related PACs despite their widespread presence in the environment. Additionally, there are several weaknesses in existing immunotoxicity databases for PACs in experimental animals, limiting their applicability in quantitative risk assessment. Careful characterization of strong positive and clear negative PACs is needed in order to lay the foundation for generating robust immunotoxicity data for structurally diverse PACs that have not yet been evaluated. In the current study, adult B6C3F1/N female mice were treated daily for 28 consecutive days by oral administration of B(a)P to provide dose levels ranging between 2 and 150 mg/kg bodyweight/day. In addition, phenanthrene and pyrene, non-carcinogenic PACs, were tested at dose ranges between 12.5 and 800 mg/kg bodyweight/day and 3.1 and 200 mg/kg bodyweight/day, respectively. Immune assessments following PAC exposure included organ weights and immunopathology, hematology, quantification of immune cell types in the spleen, and T-dependent antibody response (TDAR) to sheep red blood cells (SRBC). Benzo(a)pyrene exposure resulted in significant decreases in lymphoid organ weights, immune cell populations in the spleen and TDAR. The most sensitive indicator for immunotoxicity from B(a)P treatment was suppression of antibody responses, where an ~75% decrease occurred at a dose level of 9 mg/kg bodyweight/day and ~32% decrease at the lowest tested dose of 2 mg/kg bodyweight/day. Antibody suppression was associated with significant immune cell loss in the spleen; however, it was clear that the suppression of the TDAR was more sensitive than cell loss indicating that cell function impairments were involved. Phenanthrene treatment also resulted in suppression of the antibody response but only at dose levels ≥50 mg/kg bodyweight/day without significant effects on other parameters, while pyrene showed no significant immune effects. Suppression of the TDAR to SRBC immunization was the most sensitive immune endpoint being 33 times more sensitive than changes in liver weight, a commonly used outcome for risk assessment for PACs. Benzo(a)pyrene was the most potent PAC regarding suppression of humoral immunity whereas pyrene did not affect the immune responses tested. These studies lay the foundation for evaluating diverse PACs with a range of immunotoxicological potencies. *The other authors include researchers from the National Institute of Environmental Health Sciences.*

***Preprint.* ACTG A5409 (RAD-TB): Study Protocol for a Phase 2 Randomized, Adaptive, Dose-Ranging, Open-Label Trial of Novel Regimens for the Treatment of Pulmonary Tuberculosis**

This is a preprint, and has not yet been peer reviewed by a journal. The National Library of Medicine is running a pilot to include preprints that result from research funded by NIH in PMC and PubMed.

DLH researchers **Austin Van Grack** and **Jhoanna Roa** were among the authors of a preprint published on the open-source platform *Research Square* (Online: March 2025). The standard of care (SOC) treatment for drug-susceptible pulmonary tuberculosis (DS-TB) consists of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE). New treatment regimen options for DS-TB are needed as HRZE is long in duration (6 months), associated with frequent adverse events, unforgiving of adherence lapses, and complicated by rifamycin-based drug-drug interactions. The recent resurgence of TB drug development, particularly in the context of drug-resistant TB, offers promise for additional regimens for persons with DS-TB, provided they are sufficiently effective and well-tolerated. The authors spotlight wave 1 of the RAD-TB platform trial (ACTG A5409, NCT06192160) that will investigate new chemical entities for the treatment of DS-TB. In wave 1 of the RAD-TB platform, adult participants initiating treatment for DS-TB will be randomized to SOC (HRZE, Arm 1) or one of five experimental arms for the 8-week intensive phase. The experimental treatment arms will consist of a bedaquiline and pretomanid backbone (BPa) in combination with one of three oxazolidinones. Arm 2 will study linezolid (BPaL) at a dose of 600 mg daily, Arms 3A and 3B will study TBI-223 at 1200 mg and 2400 mg daily, respectively, and Arms 4A and 4B will study sutezolid at 800 mg and 1600 mg daily, respectively. The primary efficacy objective is to compare sputum culture time to positivity (TTP) slope over the first 6 weeks of treatment for each experimental treatment arm to SOC. The primary safety objective is to compare new Grade 3 or higher adverse events over the first 8 weeks of treatment for each experimental treatment arm to SOC. After the intensive phase, all participants will receive the standard isoniazid and rifampicin (HR) continuation phase for 18 weeks and will be followed for 52 weeks after TB treatment initiation to assess long-term outcomes. Discussion: Wave 1 of the RAD-TB platform aims to identify the optimal oxazolidinone(s), with regard to both efficacy and safety, to combine with the BPa backbone for the treatment of DS-TB. Subsequent waves of this platform trial may add a fourth drug to the regimen, study new diarylquinolines to substitute for bedaquiline, or study novel agents from other TB drug classes. *The other authors include researchers from Harvard University T.H. Chan School of Public Health, the University of California San Francisco, Emory University, Johns Hopkins University, the National Institute of Allergy and Infectious Diseases, the University of Cape Town, and the Global Alliance for TB Drug Development: TB Alliance.*

Association Between Socioeconomic Position and Lung Cancer Incidence in 16 Countries: A Prospective Cohort Consortium Study

DLH researcher **Victoria Stevens** was among the authors of an article published in *EClinicalMedicine* (Online: March 2025). Studies have reported higher lung cancer incidence among groups with lower socioeconomic position (SEP). However, it is not known how this difference in lung cancer incidence between SEP groups varies across different geographical settings. Furthermore, most prior studies that assessed the association between SEP and lung cancer incidence were conducted without detailed adjustment for smoking. Therefore, the authors aimed to assess this relationship across world regions. In this international prospective cohort consortium study, data was used from the Lung Cancer Cohort Consortium (LC3), which includes 20 prospective population

cohorts from 16 countries in North America, Europe, Asia, and Australia. Participants were enrolled between 1985 and 2010 and followed for cancer outcomes using registry linkages and/or active follow-up. Among 2,487,511 participants, 53,830 developed lung cancer during a 13.5-year median follow-up. Among participants with a smoking history, higher education was associated with decreased lung cancer incidence in nearly every cohort after detailed smoking adjustment. By world region, this association was observed in North America, Europe, and Asia, but not in the Australian study. By histological subtype, education associated most strongly with squamous cell carcinoma and more weakly with adenocarcinoma. Among participants who never smoked, there was no association between education and lung cancer incidence in any cohort, except the USA Southern Community Cohort Study. Based on longitudinal data from 2.5 million participants from 16 countries, findings suggest that higher educational attainment was associated with lower lung cancer risk among participants with a smoking history, but not among participants who never smoked. Limitations of the study include that cohort participants cannot fully represent the general populations of the geographical regions included, and education was the only measure of SEP consistently available across our consortium. *The other authors include researchers from the Lombardi Comprehensive Cancer Center at Georgetown University Medical Center, the National Cancer Institute, and the Johns Hopkins Bloomberg School of Public Health, as well as researchers from institutes in Australia, France, United Kingdom, Germany, Singapore, Norway, Iran, and Spain.*

Demonstrating Tactical Combat Casualty Care in Simulated Environments to Enable Passive, Autonomous Documentation: Protocol for a Prospective Simulation-Based Study

DLH researchers **James Gaudaen** and **Todd Hall** were among the authors of an article published in *JMIR Research Protocols* (Online: March 2025). The Telemedicine & Advanced Technology Research Center (TATRC) commenced a new research portfolio specifically addressing Autonomous Casualty Care (AC2) in 2023. The first project within this portfolio addresses the current and historical challenges of capturing tactical combat casualty care (TCCC) data at the point of injury in an operational setting. The initial autonomous casualty care effort, the Passive Data Collection using Autonomous Documentation research project, conducted systematic, simulated patient and casualty care scenarios, leveraging suites of passive sensor inputs to populate a data repository that will provide the foundation for future automated patient and medical regulation. To obtain the required datasets, TATRC engaged care provider participants who provided consent in one of six randomized simulated TCCC scenarios leveraging an institutional review board-approved office protocol. These simulations leveraged mannikins (low and high fidelity) and live simulated patients (e.g., human actors who provided consent). All consenting participants (e.g., both the care providers and live simulated patients) were equipped with suites of sensors that passively collected data on care delivery actions and patient physiology. Simulated data are being collected at Fort Detrick, Maryland; Fort Sam Houston, Texas; Fort Indiantown Gap, Pennsylvania; Fort Liberty, North Carolina; and a commercial site in Greenville, North Carolina. Across all research locations, TATRC is collecting and annotating approximately 2,500 simulation procedures tasks. These study data will generate the first machine learning and artificial intelligence algorithms to populate Department of Defense (DD) Form 1380 fields accurately and reliably. Additional data collected past March 2025 will be used to continue to refine and mature the algorithm. The military health care system (MHS) lacks real-world datasets for TCCC care at the point of injury. Developing a data repository of simulated TCCC data is required as an essential step toward automating TCCC care. If TATRC's research efforts result in the ability to automate care delivery documentation, this will alleviate the cognitive burden of TCCC

care providers in austere, chaotic environments. By generating a TCCC data repository through this Autonomous Documentation research project, TATRC will have opportunities to leverage this research data to create machine learning and artificial intelligence models to advance passive, automated medical documentation across the health care continuum. *The authors are also researchers from the Telemedicine and Advanced Technology Research Center (TATRC) at Fort Detrick, MD.*

Periods of Susceptibility for Associations Between Phthalate Exposure and Preterm Birth: Results From a Pooled Analysis of 16 US Cohorts

DLH researcher **Kate Christenbury** was among the authors of an article published in *Environment International* (Epub: March 2025; Online: April 2025). Phthalate exposure during pregnancy has been associated with preterm birth, but mechanisms of action may depend on the timing of exposure. The authors' objective was to investigate critical periods of susceptibility during pregnancy for associations between urinary phthalate metabolite concentrations and preterm birth. Individual-level data were pooled from 16 US cohorts (N = 6,045, n = 539 preterm births). Trimester-averaged urinary phthalate metabolite concentrations were examined. Most phthalate metabolites had 2248, 3703, and 3172 observations in the first, second, and third trimesters, respectively. The primary analysis used logistic regression models with generalized estimating equations under a multiple informant approach to estimate trimester-specific odds ratios of preterm birth and significant heterogeneity in effect estimates by trimester. Differences in trimester-specific associations between phthalate metabolites and preterm birth were most evident for di-2-ethylhexyl phthalate (DEHP) metabolites. The association of preterm birth with gestational biomarkers of DEHP exposure, but not other phthalate metabolites, differed by the timing of exposure. First and second trimester exposures demonstrated the greatest associations. The study also highlighted methodological considerations for critical periods of susceptibility analyses in pooled studies. *The other authors include researchers from the National Institute of Environmental Health Sciences, the National Cancer Institute, and the National Center for Environmental Health at the Centers for Disease Control and Prevention.*

Skin Conditions Associated With Dermal Exposure to Oil Spill Chemicals Among Deepwater Horizon Disaster Response and Cleanup Workers

DLH researchers **Kate Christenbury** and **Braxton Jackson** were among the authors of an article published in *Ecotoxicology and Environmental Safety* (Epub: March 2025; Online: April 2025). Previous studies have associated oil spill response and cleanup (OSRC) work with skin symptoms, but evidence is lacking on the specific exposure agents that contributed to these skin effects. OSRC-related exposures were investigated, including dermal exposure to specific chemical agents, in relation to acute and longer-term skin conditions among the 2010 Deepwater Horizon (DWH) OSRC workers. At GuLF Study enrollment, workers reported duration of work, jobs performed, and skin contact with crude oil/tar, dispersants, and decontamination chemicals. Cumulative dermal exposure to polycyclic aromatic hydrocarbons (PAHs) from oil/tar was estimated based on the "GuLF DREAM model." The authors used Poisson regression with robust standard errors to evaluate associations of exposures with prevalent skin conditions during spill cleanup and at enrollment (1-3 years later) and incident eczema diagnoses after the start of OSRC work. The authors examined modification of associations between exposures and prevalent conditions by use of rubber/synthetic gloves. Duration of OSRC work was positively associated with skin conditions and eczema diagnoses. Workers in operations, response, and decontamination jobs had higher skin condition prevalence (during cleanup,

at enrollment) and eczema risk compared to support workers. After adjusting for co-exposures, the authors saw associations of skin conditions during cleanup with dermal exposure to oil/tar, decontamination chemicals, dispersants, and PAHs. These associations remained apparent at enrollment. Eczema diagnosis was associated with exposure to oil/tar and PAHs. Effect estimates were on average 21% lower among workers who used rubber/synthetic gloves. Duration of work, working in non-support jobs, and dermal exposure to oil/tar, dispersants, decontamination chemicals, and PAHs were associated with acute and longer-term skin effects among the DWH OSRC workers. *The other authors include researchers from the National Institute of Environmental Health Sciences, the Centre for Human Exposure Science at the Institute of Occupational Medicine (UK), and the Gillings School of Global Public Health at the University of North Carolina.*

Risk of Major Gynecologic Surgery Before Age 40 Among Daughters of Young Mothers
DLH researcher **Aimee D'Aloisio** was among the authors of an article published in *Human Reproduction* (Online Ahead of Print: March 2025; Print: May 2025). *Study question:* Is being born of a young mother associated with worse gynecologic health, as indicated by a bilateral oophorectomy or hysterectomy before age 40? *Summary answer:* Daughters of mothers younger than 25 did not have reduced parity but did have a higher risk of having bilateral oophorectomy or hysterectomy before age 40, particularly if their mother was younger than 20 years at their birth. Three recent studies have reported lower fecundability among daughters of mothers younger than 20 years; adverse socioeconomic conditions may explain part of that association. This study reports cumulative, primarily retrospective, accrual of outcomes up to age 40 among 41,450 women recruited into the US-based Sister Study between 2003 and 2009. The analysis sample included women ≥41 years at the time of the latest follow-up and <66 years at recruitment. Using log-binomial regression, the authors estimated adjusted relative risks (RRs) of having major gynecologic surgery (bilateral oophorectomy or hysterectomy) before age 40 by age of the participant's mother (G1) when she gave birth to the participant (G2). All models were adjusted for father's age at G2's birth, daughter's self-identified race/ethnicity, and year of birth. Possible effect modification was assessed by stratifying the analyses by self-reported G2's family income level during childhood (poor-low, medium-high) and G2's educational level (categorized as below bachelor's degree and bachelor's degree or higher) and, in the following step, by G2's age at first birth. Compared with daughters born to mothers aged 30-34, daughters of mothers <20 and 20-24 years had an RR of 1.74 and 1.35, respectively, of major gynecologic surgery before age 40. Although lower childhood income, G2 education, and giving birth before age 25 were strongly associated with outcome risk, the RRs changed little after accounting for those factors. This is a descriptive study of a proxy indicator of poor gynecologic health. Furthermore, all information was self-reported and, for nearly all women, recalled after the event. The measures used for socioeconomic status may have been insufficient. Daughters of younger mothers did not have reduced parity but appeared to have a higher risk of major gynecologic surgery before age 40. This study adds to prior evidence that daughters of young mothers have worse gynecologic health. *The other authors include researchers from the National Institute of Environmental Health Sciences and McGill University and Research Institute in Montreal.*

A Novel Method for Assessing Poor Quality of Life Among People With HIV
DLH researcher **Jen-Feng Lu** was among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Online Ahead of Print: March 2025; Print: June 2025). The U.S. National HIV/AIDS Strategy (NHAS) prioritizes improving QoL

among people with HIV (PWH) but co-occurrence of different aspects of QoL is not well described. The authors developed and applied a novel, multi-item assessment of poor quality of life (QoL) among PWH, and examined associations with selected outcomes. *Setting:* 2018-2021 CDC Medical Monitoring Project data on 15,855 U.S. PWH. The poor QoL index, measured by the number of indicators of poor QoL experienced included: poor/fair self-rated health, unmet needs for mental health services, and subsistence needs (hunger/food insecurity, unstable housing/homelessness, unemployment). Associations with selected adverse outcomes were assessed, including not being retained in care, missing ≥1 HIV medical appointments, missing ≥1 ART dose, not having sustained viral suppression, and having ≥1 emergency room visit or ≥1 hospitalization. Overall, 55.1% of PWH had ≥1 indicator of poor QoL; 8.4% had ≥3 indicators. Over a quarter (26.5%) of people who inject drugs experienced ≥3 indicators of poor QoL. A large percentage of people aged 18-24 years and transgender women had subsistence needs; 36.4% of cisgender Black women had poor/fair self-rated health. After adjusting for age, race/ethnicity, and gender, higher poor QoL index scores-and each indicator of poor QoL-were associated with worse outcomes. The authors demonstrated the utility in using the poor QoL index to identify those at higher risk of experiencing health challenges. Expanding national recommendations to include this QoL assessment could help in meeting NHAS goals for improving PWH's well-being. *The other authors are researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention.*

Geosocial-Networking App Use Among Men Who Have Sex With Men in High HIV Community Viral Load Areas of Baltimore City

DLH researcher **Zaneta Gaul** was among the authors of an article published in *AIDS and Behavior* (Epub: March 2025; Print: July 2025). Geosocial networking applications (GSN apps) are important tools for HIV/sexually transmitted infection prevention among men who have sex with men (MSM). Strategies for identifying high transmission and acquisition among GSN app users are needed to prioritize public health response. Community viral load (CVL) is associated with HIV transmission and can be used to identify populations with behaviors/environment associated with HIV/STI risk. The authors sought to determine user profile characteristics and utilization patterns associated with GSN app use in high CVL census tracts (CTs). They used routine HIV surveillance data from in-care individuals and their viral loads at the point of diagnosis to estimate CVL in 200 CTs across Baltimore City. Among GSN user profiles, multiple imputation methods were used to complete missing profile characteristics. Imputed datasets were then used to explore the association between profile characteristics, app utilization times, and app use in high CVL CTs. Data on 606 profiles were collected originally and imputed 50 times to create a complete data set for analysis. GSN app users were aged 18-65 years, with 52.2% Black, 6.8% living with HIV, 39.1% in high CVL CTs, 50.6% use at nighttime, and 51.6% use during the weekend. Black MSM users were associated with GSN app use in high CVL CTs. MSM with profiles listing versatile sex position preference and profiles listing top sex position preference were associated with GSN app use in high and medium CVL CTs. GSN app user profiles of people in high and medium CVL CTs, especially Black MSM and those who report top and versatile sexual positions, may benefit from online prevention messages and real-time notification of health resources presently available in their communities to reduce HIV transmission. *The other authors are researchers from the John Hopkins School of Medicine, the Johns Hopkins School of Public Health, and the Division of HIV Prevention at the Centers for Disease Control and Prevention.*

Geographic Patterns in Wildland Fire Exposures and County-Level Lung Cancer Mortality in the United States

DLH researcher **Ian Buller** was among the authors of an article published in the *International Journal of Health Geographics* (Online: April 2025). Emissions from wildfire plumes are composed of modified biomass combustion by-products, including carcinogens. However, studies of the association between wildland fire (WF; includes wildfires, prescribed burns, and resource management fires) exposure and lung cancer are limited. The authors evaluated geographic patterns in these exposures and their association with lung cancer mortality (LCM) rates across the conterminous United States (US). Data were extracted from the Monitoring Trends in Burn Severity program (1997-2003) and derived county-level exposure metrics: WF density by area, WF density by population, the ratio between total burned land area and county area, and the ratio between total burned land area by population. Sex-specific, county-level LCM rates were obtained for 2016-2020 from the National Center for Health Statistics. There were positive (high WF exposures and high LCM rate) clusters for males and females in counties within the mid-Appalachian region and Florida, and modest differences across WF metrics in the cluster patterns were observed across the Western US and Central regions. The most positive clusters were seen between WF density by area and LCM rates among women (N = 82 counties) and a similar geographic pattern among men (N = 75 counties). Similar patterns were observed for males and females in the western US, with clusters of high WF exposures and low LCM rates. After adjusting for multiple comparisons, a positive cluster pattern among both sexes persisted in Kentucky and Florida with area-based exposure metrics. The analysis identified counties outside the western US with wildfires associated with lung cancer mortality. Studies with individual-level exposure-response assessments are needed to evaluate this relationship further. *The other authors include researchers from the National Cancer Institute, the U.S. Department of Agriculture, and the Daugherty Water for Food Global Institute and School of Natural Resources at the University of Nebraska.*

Approaches to Harmonize Mortality Data Sets in Three Diverse Radiation Worker Cohorts

DLH researcher **Sarah Cohen** was among the authors of an article published in the *Journal of Radiological Protection* (Online: April 2025). While there is a well-established link between ionizing radiation and cancer, there are uncertainties with effects following low doses delivered at low dose rates. To address these gaps, the ongoing Million Person Study of Radiation Workers and Veterans (MPS) is investigating health effects following chronic exposure to low dose-rate ionizing radiation. One challenge is combining and harmonizing diverse cohorts with widely different measures of socioeconomic status, birth cohorts, dose distributions, and sex ratios. This analysis combined three cohorts for which dose reconstructions have been completed: Rocketdyne (Atomics International, California, 1948-2008), Mound (Dayton, Ohio, 1944-2009), and nuclear weapons test participants (Atomic Veterans, 1945-2012). Heart disease mortality was chosen for illustrating different statistical approaches. In all three cohorts, radiation dose estimates were distributed very differently by different measures of socioeconomic status. Further, the effect of birth cohort was significantly different for heart disease mortality in all three cohorts. The authors identified five different methods to combine the results of these three datasets: the simple pooled analysis, pooled analysis including study interactions, traditional stratified analysis, and both fixed and random effects meta-analysis. The similarities and differences between the combined results using these approaches are described. These three cohorts represent a small fraction of the overall Million Person Study (MPS) but provide valuable insight into methods of combining and harmonizing data from multiple diverse cohorts that can later be considered for all MPS cohorts. The goal of

this paper is not to quantify radiation effects based on these combined cohorts and it would be inappropriate to do so. Rather these cohorts are used to illustrate approaches for combining multiple data sets that incorporate the full set of individual confounder and cofactor information available from each cohort, though widely different. *The other authors include researchers from the Department of Preventive Medicine at the University of Southern California, the U.S. Environmental Protection Agency, Brigham and Women's Hospital and Harvard Medical School, and the Oak Ridge National Laboratory.*

Comparison of HIV Prevention Indicators Among Adolescent Girls and Young Women in DREAMS and Non-DREAMS Intervention Districts in Uganda

DLH researchers **Norah Namuwenge**, **Derrick Kimuli**, **Rebecca Nsubuga**, **Timothy Sserunga**, **Barbara Amuron**, and **Daraus Bukenya** were among the authors of an article published in *PLoS One* (Online: April 2025). In sub-Saharan Africa, a significant number of new human immunodeficiency virus (HIV) infections occur among adolescent girls and young women (AGYW). The 2023 Uganda Annual Spectrum estimates indicated that about one-third of all new HIV infections are among AGYW. In 2016, the Ministry of Health in partnership with the United States President's Emergency Plan for AIDS Relief (PEPFAR) initiated the Determined, Resilient, Empowered, AIDS-Free, Mentored and Safe (DREAMS) program to reduce the vulnerability of AGYW to HIV by offering various direct and indirect HIV-related prevention services. These services influence the level of various HIV prevention indicators in the age group. Fifteen HIV prevention indicators were independently compared between 8 DREAMS and 8 non-DREAMS districts. Of the 9,290 records of AGYW reviewed, 52.40% were of AGYW residing in DREAMS districts. Between DREAMS and non-DREAMS districts, significant differences in level of knowledge of HIV prevention methods, condom use, knowledge of HIV testing points, having multiple sex partners, and HIV testing, among other indictors. AGYW in DREAMS districts had better outcomes for all indicators except multiple sex partners. Although this factor likely contributed to the initial selection of DREAMS-intervention districts, its persistence may continue to influence overall efforts towards the reduction of HIV prevalence. Moreover, this potentially mitigates the benefits from other better performing indicators. *The other authors include researchers from the U.S. Agency for International Development Strategic Information Technical Support Activity in Uganda and the U.S. Agency for International Development Uganda.*

Abatacept for the Treatment of Myositis-Associated Interstitial Lung Disease (ATtackMy-ILD)

DLH researcher **Jesse Wilkerson** was among the authors of an article published in *Rheumatology (Oxford)* (Online Ahead of Print: April 2025). This randomized, placebo-controlled pilot trial evaluated the efficacy and safety of abatacept in patients with anti-synthetase syndrome-associated interstitial lung disease (ASyS-ILD). Participants with active ASyS-ILD were randomized to receive abatacept (n = 9) or placebo (n = 11) for 24 weeks, followed by a 24-week open-label extension with abatacept for all participants. The primary end point was a change in % predicted forced vital capacity (%FVC) from baseline to week 24. Secondary endpoints included changes in the FVC (ml), % predicted diffusing capacity for carbon monoxide (%DLCO), shortness of breath questionnaire (SOBQ), and pulmonary disease activity on a visual analogue scale (VAS) at weeks 24 and 48. Pre-post baseline analysis of FVC and quantitative image analysis (QIA) of high-resolution computed tomographic scans were performed. Data was analyzed using a generalized linear mixed model. The study was not powered for primary or secondary endpoints. At week 24, there was no significant difference in the primary end point of %FVC change

between abatacept and placebo and in all secondary endpoints. However, by week 48, trends favoring abatacept in %FVC, FVC (ml), %DLCO, and SOBQ were observed without statistical significance. There was a significant improvement in pulmonary disease activity VAS and pre-post baseline slopes of %FVC and QIA scores in the abatacept arm. Abatacept was generally well tolerated. Abatacept did not significantly improve %FVC at 24 weeks. However, trends at 48 weeks suggest potential benefits, supporting the need for a larger, long-term randomized controlled trial. *The other authors include researchers from the University of Pittsburgh, Mahidol University in Bangkok, and the University of California Los Angeles David Geffen School of Medicine.*

Colossus: Software for Radiation Epidemiological Studies With Big Data
DLH researcher **Sarah Cohen** was among the authors of an article published in the *Journal of Radiological Protection* (Online: April 2025). The software package Colossus was designed to meet a growing need for survival analysis software capable of analyzing tens of millions of rows of radiation epidemiological data. Colossus is an R package devised to offer scalable survival analysis for the Million Person Study, which includes numerous large cohort studies with long follow-up of individuals with low-dose radiation exposure. The total and relative rate equations available in Colossus are outlined in this article, which are used in conjunction with Cox proportional hazards, Poisson, and Fine-Grey regression models. Following a comparison with existing software, validation with epidemiological cohort data is described. For demonstration purposes, exposure data and specific causes of death among workers at Los Alamos National Laboratory and U.S. nuclear power plants were analyzed by Colossus as well as 32-bit Epicure and compared with previously published results. Colossus results agreed with the results of existing software and previous publications. *The other authors include researchers from the Kansas State University, Memorial Sloan-Kettering Cancer Center, and NASA Langley Research Center.*

Prevalence of Cardiovascular Disease Risk Factors Associated With Residential Natural Hazard Risk
DLH researchers **Kaitlyn Lawrence**, **Marina Sweeney**, **Ian Buller**, **Braxton Jackson**, and **Kate Christenbury** were among the authors of an article published in *The Science of the Total Environment* (Epub: April 2025; Online: May 2025). Specific natural hazards are associated with increased chronic disease risk. Less is known about the impact of living in regions with elevated natural hazards risk. The authors evaluated cross-sectional associations between predicted residential natural hazard risk and CVD-related risk factors using data from the Gulf Long-term Follow-up Study, a prospective cohort enrolled following the Deepwater Horizon disaster (N = 32,608). Diabetes prevalence among 29,714 participants who provided enrollment data on self-reported physician diagnosis of diabetes was evaluated. In separate analyses, obesity and hypertension were evaluated using data from 10,727 home visit participants with measured height, weight, and blood pressure. Geocoded residential enrollment and home visit addresses were linked to the National Risk Index (NRI, 1960-2020), a monetized risk score that quantifies overall and hazard-specific risk at the census-tract level. The highest quartile of overall NRI was associated with hypertension but not diabetes or obesity. All quartiles of hurricane risk were associated with higher diabetes prevalence. Increasing quartiles of heatwave risk were associated with increasing prevalence of diabetes, hypertension, and obesity. Residing in areas prone to natural disasters is associated with higher prevalence of key cardiovascular disease risk factors. *The other authors include researchers from the National Institute of Environmental Health Sciences, the Federal Emergency Management Agency, and the National Center for Integrated Coastal Research at the University of Central Florida.*

Greenspace Proximity in Relation to Sleep Health Among a Racially and Ethnically Diverse Cohort of US Women

DLH researchers **Marina Sweeney**, **Erline Martinez-Miller**, and **Braxton Jackson** were among the authors of an article published in *Environmental Research* (Epub: April 2025; Online: August 2025). Sleep is essential for overall health. Greenspace may contribute to sleep health through, for instance, improving mood, reducing sleep disruptors (e.g., poor air quality), and promoting physical activity. Although greenspace likely differs across populations, few studies have included diverse populations. To investigate greenspace-sleep health associations, overall and by age, race and ethnicity, and socioeconomic status, the authors used data collected at enrollment (2003-2009) from women in the Sister Study (n = 1612 Hispanic/Latina, n = 4421 non-Hispanic (NH)-Black, and n = 41,657 NH-White). Participants' geocoded home addresses were linked to NASA's Moderate Resolution Imaging Spectroradiometer Normalized Difference Vegetation Index data to capture greenspace tertiles. Participants reported seven sleep dimensions, which were assessed individually, along with a multidimensional sleep health measure (categories: favorable, moderate, poor). Among participants (mean ± SD age = 55.7 ± 9.0 years), those with low/moderate vs. high greenspace had a lower prevalence of favorable sleep. Magnitudes of associations were higher among NH-White women vs. minoritized racial-ethnic groups and women with higher vs. lower educational attainment. Higher greenspace was associated with favorable sleep, with stronger associations among groups with more social advantages. *The other authors include researchers from the National Institute of Environmental Health Sciences, the University of North Carolina at Chapel Hill, the School of Environmental and Forest Sciences at the University of Washington, and the National Cancer Institute.*

Social Determinants of Health and Unmet Needs for Services Among Young Adults With HIV: Medical Monitoring Project, 2018-2021

DLH researcher **Priya Nair** was among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Online: May 2025). Persons aged 13-24 years are a priority population in the National HIV/AIDS Strategy. Young adults with HIV have poorer health outcomes-including not being retained in care, antiretroviral nonadherence, and not being virally suppressed-than other persons with HIV. Using Centers for Disease Control and Prevention's Medical Monitoring Project data collected June 2018 through May 2022, the authors compared demographic characteristics, social determinants of health, and mental health between persons aged 18-24 years with HIV versus persons aged ≥25 years with HIV. Among those aged 18-24 years, the authors analyzed total and unmet needs for ancillary services, defined as those that support care engagement, viral suppression, and overall health and well-being among people with HIV. Persons aged 18-24 years were more likely to have a household income <100% of the federal poverty level (48% vs. 39%), and experience unstable housing or homelessness (37% vs. 18%) or hunger/food insecurity (29% vs. 18%) than those aged ≥25 years. Persons aged 18-24 years had higher median HIV stigma scores (40 vs. 29) and were more likely to experience symptoms of generalized anxiety disorder (21% vs. 15%) than those aged ≥25 years. Of persons aged 18-24 years, 96% had a need for ≥1 ancillary service, of whom 56% had ≥1 unmet need; unmet needs were highest for subsistence services (53%) and non-HIV medical services (41%). Addressing unmet needs for subsistence and non-HIV medical services could help reduce disparities in social determinants of health and mental health that drive inequities in health outcomes among persons with HIV aged 18-24 years. *The other authors are researchers from the National Center for HIV, Viral Hepatitis, STD, and TB Prevention at the Centers for Disease Control and Prevention.*

Development and Pilot Testing of an Addiction Clinic-Based Pre-Exposure Prophylaxis Uptake and Adherence Intervention for Women with Substance Use Disorders: Protocol for a Pilot Randomized Trial

DLH researcher **Zaneta Gaul** was among the authors of an article published in *JMIR Research Protocols* (Online: May 2025). Black and Hispanic women in the United States continue to bear disproportionate incidence of HIV related to sexual transmission and injection drug use. Specifically, women with substance use disorders (SUDs) are more likely to engage in vaginal or anal condomless sex associated with HIV transmission. Pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention tool but is not widely used by racial or ethnic minority women. Effective interventions for engaging women with SUDs in HIV prevention interventions that are culturally appropriate and, therefore, more appealing to racial or ethnic minority women with SUDs are critically needed. This three-phased study, including a pilot randomized controlled trial (RCT), will assess the initial efficacy, feasibility, and acceptability of an addiction clinic-based behavioral and PrEP services intervention to increase the uptake and adherence to PrEP among racial or ethnic minority women. The pilot RCT will enroll and randomize 60 women to either the standard SUD treatment program or SUD treatment integrated with PrEP services. The addiction clinic-based behavioral intervention will include four motivational counseling sessions guided by the Information-Motivation-Behavioral Skills Model to increase the uptake of PrEP. A mobile health app will be used to engage participants with the intention of motivating PrEP initiation and supporting adherence to PrEP. Following phase 3, generalized linear modeling will be used to model effects of the proportion of participants who fill their prescription and take at least 1 dose as a function of the intervention group. Findings from individual qualitative interviews informed the development of the addiction clinic-based behavioral intervention. Study recruitment for the randomized pilot (phase 3) launched in May 2024. Additional statistical analyses will be performed upon completion of the study. This addiction clinic-based behavioral intervention aims to increase PrEP uptake and adherence among racial or ethnic minority women who engage in sexual and substance use behaviors associated with increased susceptibility to HIV transmission. The addiction clinic-based behavioral intervention has the potential to reduce HIV-related disparities among Black and Hispanic women with SUDs. Findings from this study will provide a foundation for future HIV prevention interventions for racial or ethnic minority women with SUDs. *The other authors are researchers from the University of Texas Health Science Center at Houston and the National Center for HIV, Viral Hepatitis, STD, and TB Prevention at the Centers for Disease Control and Prevention.*

Depression, Antidepressant Use, and Breast Cancer Incidence in the Sister Study Cohort

DLH researcher **Aimee D'Aloisio** was among the authors of an article published in *Breast Cancer Research (BCR)* (Online: May 2025). Depression could affect breast cancer risk; however, epidemiologic findings are mixed. The authors assessed the association of breast cancer risk with self-reported history of diagnosed depression and time-dependent antidepressant use. Data were analyzed from 45,746 women in the Sister Study cohort (2003-2009). During follow-up (mean = 11.7 years), 3,899 breast cancers were diagnosed. There was no association between history of diagnosed depression and risk of breast cancer. However, antidepressant use was associated with reduced risk of breast cancer. Comparison of antidepressant drug classes revealed a suggestion of an inverse association with selective serotonin reuptake inhibitors. Reduction was stronger in those with BMI <25. Depression was not associated with breast cancer risk. A suggestion of a reduction in risk associated with antidepressant use was observed. The analysis evaluating the association by specific drug types, showed a suggestion of a reduction in breast cancer risk

associated with use of SSRIs. The negative association with overall antidepressant use and SSRIs was stronger in those with BMI <25, which could reflect a dose effect. This was the first study to examine the association between depression, antidepressant use, and breast cancer risk in a large genetic-risk-enriched cohort. *The other authors include researchers from the National Institute of Environmental Health Sciences and the University of North Carolina Gillings School of Global Public Health.*

Barriers to Rapid Enrollment and ART Initiation Among U.S. HIV Care Facilities
DLH researchers **Xin Yuan** and **Jen-Feng Lu** were among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Online Ahead of Print: May 2025). Rapid linkage to HIV care and antiretroviral therapy (ART) initiation is now the standard of care for treating people with HIV (PWH). Understanding and intervening on barriers to rapid enrollment and ART initiation are needed to meet the goals of the Ending the HIV Epidemic in the U.S. initiative. The authors analyzed 2021 data from the Medical Monitoring Project on characteristics of 455 facilities providing care to a national probability sample of U.S. PWH. Overall, only 19.9% of HIV facilities could routinely offer a first appointment in <1 business day (rapid enrollment). The most commonly reported barriers to rapid enrollment were insufficient provider capacity (56%), patient preference (50%), and patients lacking required documents (19%). The most commonly reported documents required for enrollment were positive HIV antibody or detectable viral load (52%), government-issued identification (36%), proof of residence (24%), and proof of income (22%). Ryan White HIV/AIDS Program (RWHAP)-funded facilities more frequently required these documents than non-RWHAP-funded facilities. Most facilities (73%) were routinely able to obtain a 30-day supply of ART during the first HIV care provider visit (rapid ART initiation). The most commonly reported barriers to rapid ART included unavailable test results (56%), delays in getting medication paid for (49%), unavailable starter packs (36%), inability to afford copayment (31%), and patient preference (29%). The authors concluded that structural, provider-related, or patient-level barriers may delay rapid clinic enrollment or ART initiation. HIV care programs can benefit from removing barriers to care, easing requirements for clinical enrollment and ART prescriptions, and improving patient readiness. *The other authors are researchers from the Centers for Disease Control and Prevention.*

Conceptual GeoHealth Framework for Disaster Response Research: Case Study for Wildland Urban Interface (WUI) Fires and Data Integration
DLH researchers **Jacqui Barkoski**, **Erin Van Fleet**, and **Steven Ramsey** recently published an article in *GeoHealth* (Online: May 2025), presenting a novel conceptual framework for wildfire and disaster-related research. The article was featured as an *Eos* Research Spotlight, titled: "*Charting a Path from Fire Features to Health Outcomes*," recognizing its potential to advance research and preparedness in the face of rapidly evolving extreme weather events. With the increased frequency and severity of extreme weather events like wildfires, droughts, and hurricanes, there is a growing need for coordinated research efforts to understand the impact of these events on human health. Specialized research frameworks can help interdisciplinary teams organize and visualize complex exposure-health pathways, identify knowledge gaps, and enhance coordination and communication across diverse groups of stakeholders. This article describes the development and application of a novel conceptual framework for wildfire-related exposures, human health outcomes, and disaster-related research. This framework serves as a tool for integrating data resources and mapping known and hypothesized connections, between complex wildfire exposures and human health outcomes, across the lifecycle of a wildland urban

interface (WUI) fire. The GeoHealth Framework for WUI Fires illustrates complex linkages between wildfire-related exposures and health outcomes and highlights areas for future study. Given the destruction and complexity of WUI fires, this framework provides an important resource that can assist with evaluating these complex exposure-health relationships, guiding and coordinating data collection, and informing communities and decision-makers to improve response, recovery, and future preparedness for such events in the United States and globally. *The other authors are researchers from the National Institute of Environmental Health Sciences.*

Sleep Health by Sexual Orientation Among Women in the United States and Interrelations With Race/Ethnicity, Age, and Generational Cohort

DLH researchers **Erline Martinez-Miller** and **Braxton Jackson** were among the authors of an article published in the *International Journal of Women's Health* (Print and Online: May 2025). The authors examined associations between sexual orientation and sleep; interrelations with race/ethnicity, age, and generation; and mediation by perceived sexual orientation discrimination among United States (US) women. Eligible Sister Study participants (N=50,790) identified as heterosexual or non-heterosexual at enrollment (2003-2009), and self-reported sleep duration, sleep quality, and sleep mask and sleep medication use. The authors used latent class analyses to determine patterns of sleep health (good, moderate, poor), and investigated race/ethnicity, age, and generation as modifiers. Perceived sexual orientation discrimination was assessed as a modifier and/or mediator. Median age was 55 (interquartile range: 49-62) years; 2% identified as non-heterosexual; 86% identified as non-Hispanic White, 9% non-Hispanic Black (NHB), and 5% Hispanic/Latina. Overall, sleep masks were more common among non-heterosexuals than heterosexuals; other sexual orientation-sleep associations were not identified. Among NHB women, sleep medications were more prevalent among non-heterosexual orientation. Among women who ever perceived discrimination, shorter than recommended duration was less common among non-heterosexuals than heterosexuals as was moderate sleep health compared to good sleep health. Among women who never perceived discrimination, poor sleep health was more common among non-heterosexuals. Prevalent sleep aid use among sexual minoritized women may help reduce sleep disparities by sexual orientation. Differential sleep experiences among intersecting identities can shape health inequities, and identification of mediating pathways can inform interventions. *The other authors include researchers from the National Institute of Environmental Health Sciences and the National Institute on Minority Health and Health Disparities.*

Ambient Air Pollution in Critical Windows of Exposure and Spontaneous Miscarriage in a Preconception Cohort

DLH researchers **Kathryn Konrad** and **Ian Buller** were among the authors of an article published in *Environmental Research* (Epub: May 2025; Online: September 2025). Air pollution may increase the risk of spontaneous pregnancy loss, potentially through inflammation. Prior studies are heterogeneous, and none have used an exposure mixtures approach. The authors used data from participants who conceived in a prospective time-to-pregnancy study (N = 446) in North Carolina to examine spontaneous pregnancy loss, defined as a positive home pregnancy test and a self-reported pregnancy loss before gestational week 20 (N = 101). Sensitivity analyses were stratified by vitamin D level (an anti-inflammatory). In exposure mixtures models, while the confidence intervals were wide, the magnitude and direction of several estimates were consistent with increased risk of spontaneous pregnancy loss with increasing air pollutant exposure: spermatogenesis, early follicle development, and luteal phase. Associations were stronger among those with

low vitamin D; for example, increasing ozone was associated with increased spontaneous pregnancy loss only among those with low vitamin D. Air pollutants may be associated with small increases in risk of spontaneous pregnancy loss, but larger exposure mixtures studies are needed. Further study of low vitamin D and air pollution risk is important for understanding the public health implications of vitamin D supplementation. *The other authors include researchers from the National Institute of Environmental Health Sciences, the National Cancer Institute, and the University of North Carolina at Chapel Hill.*

Access to Language Interpretation Services at Health Care Facilities Providing Care to Adults Diagnosed With HIV in the United States, 2019

DLH researcher **Jen-Feng Lu** was among the authors of an article published in *Current HIV Research* (Online Ahead of Print: June 2025). People with limited English proficiency (LEP) experience barriers to healthcare access and optimal outcomes. Language interpretation services can facilitate clear communication-which is key to effective HIV care and treatment. The authors analyzed weighted data from the 2019 cycle of the Medical Monitoring Project (MMP), a cross-sectional, complex sample survey of U.S. adults with diagnosed HIV, and data from the 2021 MMP Facility Survey, a survey of facilities providing care to 2019 MMP respondents. The authors estimated the percentage of people with HIV (PWH) with LEP who received care at facilities offering language interpretation services and facilities providing language interpretation services, overall and by selected characteristics. Overall, 89.9% of PWH with LEP received care at a facility with language interpretation services, and 83.6% of facilities provided language interpretation services. PWH with LEP who were unemployed were less likely than those who were employed to receive care at a facility with language interpretation services. Facilities that were Federally Qualified Health Centers, were not private practices, received Ryan White HIV/AIDS Program funding, and accepted public health care coverage were more likely to provide language interpretation services than facilities without these characteristics. Findings demonstrated that most HIV care facilities are providing access to language services to PWH with LEP in the United States. *The other authors are researchers from the Division of HIV Prevention at the Centers for Disease Control and Prevention.*

Transferability, Reproducibility and Sensitivity of Mutation Quantification by Duplex Sequencing

DLH researcher **Shawn Harris** was among the authors of an article published in *Environmental and Molecular Mutagenesis* (Online Ahead of Print: June 2025). Duplex Sequencing (DS) is an ultra-accurate, error-corrected next generation sequencing (ecNGS) technology for mutation analysis. A working group (WG) within Health and Environmental Sciences Institute's Genetic Toxicology Technical Committee is investigating the suitability of ecNGS for regulatory mutagenicity testing, using DS as a model. Initial steps to promote acceptance require demonstrating technical reproducibility across DS-experienced and inexperienced laboratories and establishing the method's sensitivity relative to conventional tests. Thus, the WG conducted a "reconstruction experiment" to evaluate the transferability, reproducibility, and sensitivity of DS. TwinStrand Biosciences first applied DS to establish mutation frequency (MF) in DNA samples extracted from the livers of an untreated Sprague Dawley rat, or rats treated with either 100 mg/kg/day benzo[a]pyrene (B[a]P) for 10 days or 40 mg/kg/day N-ethyl-N-nitrosourea (ENU) for 3 days. Using the measured MF in these original samples, mixtures were then constructed using the B[a]P- and ENU-treated samples to create "MF standards" with target MFs 1.2-, 1.5-, and 2-fold greater than the untreated control. Aliquots of these standards were distributed to seven laboratories in North America and Europe. DS libraries were prepared by each

laboratory and TwinStrand. All eight laboratories met library preparation and assay performance metrics to yield high quality sequencing data with MF in the expected "MF standard" range. The measured MF and mutation spectra were nearly identical across the laboratories and a two-fold increase in MF could readily be identified in all labs relative to the untreated controls. The results confirm the high reproducibility and sensitivity of DS for mutagenicity assessment. *The other authors include researchers from the U.S. Food and Drug Administration, the Environmental Health Science and Research Bureau at Health Canada, and the Division of Translational Toxicology at the National Institute of Environmental Health Sciences.*

Novel and Legacy Per- and Polyfluoroalkyl Substances in Humans: Long-Term Temporal Variability and Metabolic Perturbations

DLH researcher **Che-Jung Chang** was among the authors of an article published in *Environment International* (Epub: June 2025; Online: July 2025). As legacy per- and polyfluoroalkyl substances (PFAS) are phased out, numerous substitutes have emerged, raising concerns about their potential health impacts. Using targeted and untargeted approaches, the authors evaluated plasma PFAS on an -omic scale, examining temporal variability and associated metabolomic disruptions. A total of 400 blood samples from 200 Sister Study participants (collected in 2007-2008 and 2013-2014) were analyzed using liquid chromatography with high-resolution mass spectrometry. Network analysis, metabolome-wide association studies, and pathway analysis were used to evaluate the impacts of PFAS mixtures on the human metabolome. The authors detected 24 legacy PFAS via the targeted approach and 1,802 features annotated as potential PFAS via the untargeted approach (21 confirmed by reference standards). While legacy PFAS demonstrated low temporal variability, novel PFAS, especially those that have increased in abundance over time, demonstrated greater temporal variability. The legacy PFAS mixture was associated with lipid and amino acid metabolism, while other PFAS mixtures consisting of novel PFAS affected a wider range of metabolic pathways in addition to amino and lipid metabolism, such as carbohydrate, cofactor and vitamin, and endocrine metabolism. These findings underscore the need for further research on these novel PFAS and their health effects. *The other authors include researchers from the National Institute of Environmental Health Sciences, Emory University, and the National Cancer Institute.*

Infections Preceding Diagnosis Associated With Myositis Phenotypes in a National Patient Registry

DLH researchers **Jesse Wilkerson** and **Nastaran Bayat** were among the authors of an article published in *Clinical and Experimental Rheumatology* (Epub: June 2025; Print: July 2025). The authors investigated the association of antecedent infections with clinical subgroups and phenotypes in the idiopathic inflammatory myopathies (IIMs). Adult IIM patients (362 with dermatomyositis (DM), 250 with polymyositis (PM), and 256 with inclusion body myositis (IBM)) enrolled in a national myositis patient registry. One hundred thirty-four patients had symptoms of lung disease plus fever and/or arthritis (LD+), and 103 with systemic autoimmune rheumatic disease-associated overlap myositis (OM). Self-reported infections and antibiotic usage within 12 months prior to IIM diagnosis were examined. Infections before IIM diagnosis were more frequent in DM and PM than IBM. Febrile illness and gastroenteritis were more frequent in DM than IBM, and in PM than IBM. Patients with LD+ and OM had higher odds of reported infections than those without these phenotypes, with pneumonia the most strongly associated infection. Antibiotic usage within 1 year before diagnosis did not differ among DM, PM, and IBM patients, nor in OM. Antibiotics were used more frequently used in patients with LD+ compared to no LD,

but this was attenuated after adjusting for infections. Antecedent infections, particularly respiratory and gastrointestinal infections may contribute to adult IIM phenotypes. Pneumonia showed the strongest association with myositis phenotypes accompanied by frequent lung disease. *The other authors include researchers from the National Institute of Environmental Health Sciences and the Division of Rheumatology at the Cincinnati Children's Hospital Medical Center.*

Research Snapshot (1479). **Evaluation of State-of-the-Art Object Detection System During Simulated Combat Casualty Care**

DLH researcher **Jaeyeon Lee** was among the authors of a research snapshot published in *Critical Care Medicine* (Online: January 2025). Combat casualty care (C3) is done in challenging environments where clinical documentation (CD) is low, inhibiting effective triage and logistic response. The researchers sought to automate CD through passive use of video and other sensors to infer casualty status, caregiver activities, and resource use. Computer vision (CV) models such as the state-of-the-art "you only look once" (YOLO) neural networks, are excellent at object detection but were developed on civilian and non-clinical datasets with no evidence of accuracy during C3. The researchers tested the latest YOLO models on realistic human and manikin C3 simulations (sims). Pilot study exploring accuracy of YOLO CV models at body detection during C3 sims using trained Army combat medics wearing helmet-mounted cameras while providing care to realistic manikins in pre-defined clinical scenarios aligned with combat medic guidelines. Sims recorded using 720p resolution at 30fps, covering 5-6 clinical activities and lasting 10-20 mins. The researchers applied YOLO models and assessed their detection of patient, medic and body posture. They manually adjudicated quality of detection on every 100th frame of the videos (~1 every 3 secs). High quality (HQ) detection occurred when all major body parts and separation of medic and patient were identified without reasonable (e.g., non-detection of a few pixels of a limb) error. False alarms (FA) detected more people than present. Qualitative assessment of inaccurate detections was performed. 10 sims were performed yielding 59.5 minutes of video. YOLOv8, YOLOv8-pose, YOLOv9, and YOLOv9-seg model detections were each adjudicated on 1,080 frames. All models correctly detected all people in 17% of frames, correctly detected at least one person in 82% of frames, with a FA rate of 45-47%. HQ rates of 34%, 19%, 34% and 35% were found for v8, v8-pose, v9, and v9-seg respectively. Qualitative analysis revealed errors that: combined medic and patient limbs; omitted partial or complete bodies due to camouflage; resulted from image blur and close views. The authors found that state-of-the-art CV models lack accuracy for clinical utility in identifying body composition and differentiation between the medic during simulated C3 using helmet-mounted cameras. Customization and tuning for C3 use cases are necessary to support autonomous CD. *The other authors include researchers from the U.S. Army Telemedicine and Advanced Technology Research Center at Fort Detrick, MD.*