DLH

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RESEARCH UPDATE

A semi-annual look at select research activities from across our organizaton

DLH delivers best-in-class, science-forward health research. The work our researchers, scientists, and statisticians support builds knowledge which prolongs life, promotes health readiness, and prevents disease. We inject advanced technology and utilize state-of-the-art methods to transform data into actionable information, producing cutting-edge clinical and population health research.

The pages that follow highlight just some of our work from the past half-year. The breadth of expertise and passion that our team brings to bear is immediately apparent. Our research professionals relentlessly pursue excellence in advancing human health and well-being.

The real-world impact of our work is clear from a mere glance at some of the subject matter highlighted in this edition:

- Stroke and diabetes in adults
- Trends in forgoing care due to the cost of insurance for Americans with Diabetes
- Associations between hypertension and environmental exposure
- Drug resistance in people living with HIV
- The risk of miscarriage

We pass along our sincere thanks to each and every DLH researcher who contributed to the work that follows. Your knowledge and passion impress your colleagues, customers, and communities each day.

Jeanine Christian
President
Public Health & Scientific Research

Virology Outcomes of Tenofovir-Lamivudine-Dolutegravir in Treatment-Naïve and Virologically Suppressed Individuals Switching From an NNRTI-Based Regimen: An Observational Analysis at 13 Sites

DLH researcher **Elizabeth Woolley** was among the authors of an article published in *Open Forum Infectious Diseases* (Online: May 2025; eCollection: July 2025). Tenofovir/lamivudine/dolutegravir (TLD) is widely prescribed worldwide. Virologic and resistance outcomes are reported for patients initiating or switching to TLD. A prospective observational study was performed at 13 AIDS Clinical Trials Group sites in 6 President's Emergency Plan for AIDS Relief-supported countries coincident with TLD rollout. This report includes results from two groups: group 1 (Gp1) were virally suppressed on nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy (ART) and group 2 (Gp2) were ART-naïve at TLD initiation. The primary objective was to estimate the proportions of participants with HIV-1 RNA ≤1000 copies/mL and frequency of dolutegravir resistance mutations 6 months after TLD initiation. From October 2019 through July 2022, 425 participants were enrolled in Gp1 and 179 in Gp2. Two in Gp1 (0.5%) and 3 in Gp2 (1.7%) discontinued TLD by 6 months due to adverse events considered related to TLD (n = 4) and participant decision (n = 1). Ninety-three percent of participants in Gp1 and 92% in Gp2 who were still on TLD had a 6-month plasma HIV-1 RNA. Plasma HIV-1 RNA ≤1000, ≤200, and <50 copies/mL was achieved in 99%, 98%, and 96% in Gp1 and in 90%, 87%, and 85% in Gp2, respectively. A new integrase mutation (T97A/T) was observed in 1 participant in Gp1 and none in Gp2. TLD was well tolerated and achieved or maintained viral suppression (≤1000 copies/mL) in 90% of ART-naïve and 99% of participants with preswitch viral suppression. An emerging integrase strand transfer inhibitor mutation of uncertain significance was detected in only 1 participant. These data support early tolerability, virologic efficacy, and rare integrase strand transfer inhibitor resistance emergence with TLD transition or initiation in programmatic settings. *The other authors include researchers from the Joint Clinical Research Centre (Uganda), the Harvard T.H. Chan School of Public Health, Les Centres GHESKIO Clinical Research Site (Haiti), The Johns Hopkins University School of Medicine, as well as researchers from South Africa, Kenya, and Malawi.*

Immunotoxicity Studies on the Insecticide 2-((1-(4-Phenoxyphenoxy)propan-2-yl)oxy)pyridine (MPEP) in Hsd:Harlan Sprague Dawley SD® Rats

DLH researcher **Shawn Harris** was among the authors of an article published in *Toxics* (Online: July 2025). The broad-spectrum insect growth regulator (IGR) and insecticide 2-((1-(4-Phenoxyphenoxy)propan-2-yl) oxy)pyridine (MPEP; also known as pyriproxyfen) is increasingly being used to address public health programs for vector control, initiated by the spread of Zika virus in 2015-2016. While considered relatively safe for humans under normal conditions, limited toxicology data are available. Current studies were undertaken to address the data gap regarding potential immunotoxicity of MPEP, with particular emphasis on host resistance to viral infection. Hsd:Harlan Sprague Dawley SD® rats were treated for 28 days by oral gavage with doses of 0, 62.5, 125, 250, or 500 mg/kg/day of MPEP in corn oil. There was a dose-dependent increase in liver weights, which is consistent with the liver playing a dominant role in MPEP metabolism. However, no histological correlates were observed. Following treatment, rats were subjected to a battery of immune tests as well as an established rat model of influenza virus infection to provide a comprehensive assessment of immune function and host resistance. While several of the immune tests showed minor exposure-related changes, evidenced by negative dose-response trends, most did not show significant differences in any of the MPEP treatment groups relative to vehicle control. Most notable was a negative trend in pulmonary mononuclear cell phagocytosis with increases in dose of MPEP. There was also a positive trend in early humoral immune response (5 days after immunization) to keyhole limpet hemocyanin (KLH) as evidenced by increased serum anti-KLH IgM antibodies which was followed later (14 days following immunization) by decreasing trends in anti-KLH IgM and IgG antibody levels. However, MPEP treatment had no effect on the ability of rats to clear the influenza virus nor the T-dependent IgM and IgG antibody response to the virus. The lack of effects of MPEP on host resistance to influenza suggests the immune effects were minimal and unlikely to present a hazard with respect to susceptibility to respiratory viral infection. *The other authors include researchers from the National Institute of Environmental Health Sciences.*

Descriptive Analysis of Municipal Policies Addressing Shade in Eight Southwest and Northeast States in the United States

DLH researcher **Ian Buller** was among the authors of an article published in *Frontiers in Public Health* (Online: July 2025). Shade is an essential environmental feature to prevent heat illnesses and skin cancer. Written policies related to shade were described in municipalities in four southwest and four northeast U.S. states. Municipal codes, planning documents, and manuals/guidelines from municipalities (N = 48) in eight U.S. states were coded by research assistants for content related to shade. They used a standardized protocol to assign numeric codes to each document to assess the type of document, type of shade, location, resource allocation, accountability, and design standards. Results were summarized using descriptive statistics. Three-quarters of municipalities (75.0%) had a policy document addressing shade, including municipal codes (54.2%), planning documents (29.2%), and manuals/guidelines (12.5%). Protecting from heat (31.3%) was mentioned in policies more often than protecting from ultraviolet radiation (8.3%), and natural shade (56.3%) was mentioned more often than constructed shade (25.0%). Policies prescribed several design standards, most frequently shade material, proportion of area covered, and attractiveness. Half (50.0%) of municipalities mentioned accountability for shade in the policy, but only a third (35.4%) addressed resource allocation. Regional differences were observed in policy document types, shade types, locations, design standards, and resource allocation. Many municipalities had policies that mentioned shade, but only a minority indicated that the purpose was protection from heat or ultraviolet radiation. In northeast municipalities, which may have local home-rule traditions, policies on shade appeared almost entirely in municipal codes. Southwest municipalities often included policies in planning documents that may have less legal force than municipal codes. *The other authors include researchers from the Department of Health Sciences at Providence College (RI) and the Rutgers Cancer Institute at Rutgers University.*

HepB-CpG Vaccine in People With HIV and Prior Nonresponse to HBV Vaccine: The BEe-HIVe Trial End-of-Study Results

DLH researcher **Parita Rathod** was among the authors of an article published in *JAMA* (Online Ahead of Print: July 2025; Print: September 2025). Hepatitis B virus (HBV) remains a leading cause of liver disease morbidity and mortality worldwide, and inadequate vaccination and waning immunity account for new HBV infections in adults. In people with HIV with prior HBV vaccine nonresponse, the BEe-HIVe trial demonstrated that 2- and 3-dose hepatitis B vaccine with a cytosine phosphoguanine adjuvant (HepB-CpG) achieved a superior seroprotection response compared with 3-dose hepatitis B vaccine with an aluminum hydroxide adjuvant (HepB-alum). Durability of seroprotection response, 1 year or more after the vaccination series, is now reported. *The other authors include researchers from Weill Cornell Medicine, the Harvard T.H. Chan School of Public Health, The Johns Hopkins University School of Medicine, the National Institute of Allergy and Infectious Diseases, as well as researchers from institutes in Thailand, Zimbabwe, Kenya, and Brazil.*

Association of Oil Spill Cleanup-Related Hydrocarbon Exposure With Hypertension and Blood Pressure in the Gulf Long-Term Follow-Up Study

DLH researcher **Braxton Jackson** was among the authors of an article published in *The Science of the Total Environment* (Epub: July 2025; Online: September 2025). Although several studies have demonstrated a relationship between crude oil exposures and cardiovascular disease, little is known about associations with hypertension. The authors' study examined associations of oil spill cleanup-related benzene, toluene, ethylbenzene, xylene, and n-hexane (BTEX-H) exposures with hypertension prevalence and blood pressure (BP). Participants comprised 6693 Deepwater Horizon (DWH) oil spill cleanup and response workers who completed a home visit in the Gulf Long-term Follow-up Study. Cumulative exposures to individual components of BTEX-H and total BTEX-H (ppb-days) were estimated via a job-exposure matrix linking detailed self-reported DWH response and cleanup work histories to air monitoring data. Trained examiners measured BP during the home visit. Hypertension was defined as systolic ≥140 or diastolic ≥90 mmHg, or self-reported antihypertensive medication use. BTEX-H exposures were modestly associated with hypertension prevalence and systolic and diastolic BP. Strongest associations with hypertension were observed in quartile

4 versus quartile 1 of most exposures. The BTEX-H mixture was associated with small elevations in systolic and diastolic BP. BTEX-H exposures were associated with small elevations in hypertension prevalence and blood pressure. *The other authors include researchers from the UNC Gillings School of Public Health and the National Institute of Environmental Health Sciences.*

Implementing Secondary Findings Analysis in a Genetic and Environmental Research Study
DLH researcher **Jennifer Emerson** was among the authors of an article published in *Genetics in Medicine* (Epub: July 2025; Online: September 2025). Optimizing return of secondary findings (SFs) in research settings requires an understanding of the complexities and challenges. Genome sequence was generated for 4737 participants in a genetic and environmental health study, and 4630 of them consented to SF return. Variants in the American College of Medical Genetics and Genomics v3.0 genes were classified using the American College of Medical Genetics and Genomics/Association for Molecular Pathology criteria with ClinGen-approved modifications. Eighty-six variants were eligible for return to 102 participants. Average time to initial recontact attempt was 5.8 years. Recontact attempts reached 95 of 102 individuals. Results were returned to 57 participants. The remainder passively declined (25), actively declined (11), were lost to follow-up (5), were deceased (3), or had prior knowledge of the result (1). Return of results was positively associated with education status. The interest in receiving SFs was high at the time of consenting, but a clinically validated result was returned to just over half of the individuals with an SF. Approximately 1 in 3 participants with an SF who had consented to receive them subsequently actively or passively declined receipt of the result. Given the health importance of return of SF, minimizing the time from consent to results return and tailoring outreach to education level may optimize uptake of SF return. *The other authors are researchers from the National Human Genome Research Institute and the National Institute of Environmental Health Sciences.*

Hyaluronan Ameliorates Viral Pneumonia in Mice and Humans by Inhibiting Transcription Factor E2F1
DLH researchers **Daniel Zaccaro** and **Jane Der** were among the authors of an article published in the *American Journal of Respiratory Cell and Molecular Biology* (Online Ahead of Print: July 2025; Print: January 2026). Viral lung infections are a major cause of morbidity and mortality worldwide. Despite significant advances in vaccines and antivirals, there remains a tremendous need for broadly applicable treatments that can be utilized across viral infections. Prior to infecting epithelial cells, viruses interact with the epithelial glycocalyx, which contains high molecular weight hyaluronan (HMWHA), a glycosaminoglycan that has beneficial effects in lung injury. The study objective was to determine the role of HMWHA in viral pneumonia. The authors infected mice with influenza or SARS-Cov2 and treated them with prophylactic or therapeutic doses of HMWHA or saline control. The authors performed in vitro experiments of infection with viruses of respiratory and non-respiratory human and animal cells and evaluated the effect of HMWHA on infection. Existing databases were analyzed for expression of hyaluronan and the transcription factor E2F1. Finally, a clinical trial with HMWHA in patients with severe COVID-19 was performed. Exogenously applied HMWHA improved survival in SARS-CoV2 and influenza infection in mice by ameliorating inflammation via the inhibition of E2F1. In a clinical study, inhaled HMWHA improved outcomes in patients with severe COVID-19. Furthermore, airway epithelia naturally express HMWHA, which is induced during viral infection and prevents infection via macromolecular crowding of viruses. The authors concluded that their provided a mechanistic justification for the use of HMWHA as a broadly effective prophylactic and therapeutic agent in viral airway infection. *The other authors include researchers from the National Institute of Environmental Health Sciences, Fondazione Policlinico Campus Bio-Medico (Rome, Italy), and the University of California at Berkeley.*

Phase 2 Trial of Long-Acting Cabotegravir and VRC07-523LS for Viral Suppression in Adults With HIV-1: ACTG A5357
DLH researcher **Parita Rathod** was among the authors of an article published in *Clinical Infectious Diseases* (Online Ahead of Print: July 2025: Print: February 2026). Long-acting regimens are needed to expand antiretroviral therapy (ART) options for people with HIV-1 (PWH). Combining broadly neutralizing antibodies (bNAbs) with long-acting small-molecule antiretrovirals may offer an alternative to daily oral therapy. The authors conducted a Phase 2, open-label, single-arm trial at AIDS Clinical Trials Group (ACTG, now Advancing

Clinical Therapeutics Globally for HIV and Other Infections) sites across the U.S. Eligible adults had HIV-1 virologically suppressed on ART for ≥2 years, CD4 ≥350 cells/mm³, and susceptibility to VRC07-523LS (IC50 ≤0.25 µg/mL; inhibition >98%). Participants completed an oral cabotegravir (CAB) lead-in (Step 1), then received intravenous VRC07-523LS (40 mg/kg every 8 weeks) plus intramuscular CAB-LA (every 4 weeks) for 48 weeks (Step 2), followed by a return to standard ART (Step 3). Primary outcomes were treatment-related Grade ≥3 adverse events (AEs), treatment discontinuation, and confirmed HIV-1 RNA ≥200 copies/mL by week 44. Seventy-four participants were enrolled (median age 54; 26% female; 51% White non-Hispanic). Twelve (17%) experienced a primary safety event: 11 (15%) had Grade ≥3 AEs, primarily transient infusion reactions, and one discontinued due to a Grade 1 infusion event. The cumulative probability of virologic failure by week 44 was 7%. One participant developed the R263K integrase resistance mutation. The VRC07-523LS plus CAB-LA regimen maintained viral suppression in 93% of participants, with only transient infusion reactions observed; however, instances of virologic breakthrough suggest that future studies should focus on optimizing efficacy outcomes. These results support continued investigation of bNAb-based long-acting ART combinations. *The other authors include researchers from Northwestern University, Harvard T.H. Chan School of Public Health, Yale New Haven Health, the Vaccine Research Center at NIH, and the Division of AIDS at the National Institute of Allergy and Infectious Diseases.*

Short Course Therapy With Glecaprevir/Pibrentasvir for Early Hepatitis C Virus Infection: PURGE-C

DLH researcher **Chanelle Wimbish** was among the authors of an article published in *Clinical Infectious Diseases* (Online Ahead of Print: July 2025; Print: February 2026). Shorter treatment courses for early hepatitis C virus (HCV) infection could simplify treatment approaches, particularly in key populations. PURGE-C (A5380) was a single-arm, multicenter trial evaluating the treatment of early HCV (primary or reinfection) with 4 weeks of glecaprevir/pibrentasvir (G/P). Early HCV was defined as new detectable HCV RNA or alanine aminotransferase (ALT) elevation within 24 weeks of study entry. The primary endpoint was sustained virologic response (SVR) 12 weeks after prescribed treatment completion (SVR12). Re-treatment outcomes were also collected. Forty-five participants (98% male, 51% White, 31% Hispanic, median age 36 years, 51% with human immunodeficiency virus [HIV], 27% self-reported injecting drugs) were enrolled from the United States and Brazil between November 2019 and January 2023. Median time from HCV diagnosis to entry was 31 days. Overall, 38 of 45 (84%) participants achieved SVR12. All four participants who were re-treated and had outcome data achieved SVR12. In this population with elevated risk of onward HCV transmission, 84% were cured with 4 weeks of G/P. Failing this short-course treatment did not compromise retreatment. This study suggests that people with early HCV infection can achieve moderately high cure rates with abbreviated courses of direct-acting antivirals. Simplified approaches to treatment are critical for HCV elimination and are particularly relevant for populations difficult to retain in care. *The other authors include researchers from Massachusetts General Hospital, the Center for Biostatistics in AIDS Research at Harvard T.H. Chan School of Public Health, Instituto Nacional de Infectologia Evandro Chagas-Fundação Oswaldo Cruz (Rio de Janeiro, Brazil), Whitman-Walker Institute (Washington, DC), and the Division of AIDS at the National Institute of Allergy and Infectious Diseases.*

Multiple Psychosocial Stressors and Coping Strategies in Relation to Sleep Health

DLH researchers **Frankie LaPorte**, **John McGrath**, and **Braxton Jackson** were among the authors of an article published in *Sleep* (Online Ahead of Print: July 2025; Print: March 2026). The study objectives were to determine associations between multiple domains of psychosocial stressors and coping strategies in relation to sleep health among Black/African American (BAA) women. Among 1,678 BAA participants with complete data enrolled in the Study of Environment, Lifestyle and Fibroids, the authors conducted principal components analysis on 43 self-reported stressors yielding 6 components of psychosocial stressors and 3 components of coping strategies. Self-reported sleep measures included sleep duration (very short, short, vs. recommended sleep), frequent insomnia symptoms (trouble falling or staying asleep 15+ days/month vs. <15 days/month), and waking up feeling unrested (4+ days/week vs. <4 days/week). Median age (interquartile range) was 29.3 (26.3-32.0) years and 45% had an annual household income of <$20,000. The following psychosocial stressors were

highly prevalent: perceived racism (84.5%), financial strain (84.1%), and emotional distress (73.7%). Emotional distress and financial strain were associated with more frequent insomnia symptoms. Social/emotional support and resilience/personal strength were associated with lower prevalence of very short sleep duration. BAA women reporting experiences with racism versus not had a higher prevalence of short sleep. Among women who did shift work, financial strain was associated with a 22% higher prevalence of short sleep. These findings may inform interventions aimed at addressing stressors associated with poor sleep. *The other authors are researchers from the National Institute of Environmental Health Sciences, the University of North Carolina at Charlotte, the University of Alabama, and the National Institute on Minority Health and Health Disparities.*

The Impact of Multiple Sclerosis on Work Productivity: A Preliminary Look at the North American Registry for Care and Research in Multiple Sclerosis

DLH researchers **Sara McCurdy Murphy**, **Lisa Patton**, and **Jesse Wilkerson** were among the authors of an article published in *NeuroSci* (Online: August 2025). The authors aimed to quantify multiple sclerosis (MS)-related work productivity and to illustrate the longitudinal trends for relapses, disease progression, and utilization of health care resources in a nationally representative cohort of working North Americans living with MS. The North American Registry for Care and Research in Multiple Sclerosis (NARCRMS) was a multicentered physician-reported registry that prospectively collected clinical information including imaging data over a long period of time from people living with MS across the U.S. and Canada. The Health Economics Outcomes Research (HEOR) Advisory Group also incorporated Health-Related Productivity and Health Resource Utilization questionnaires, which collected information about health care economics of people living with MS and its effects on daily life. Sociodemographic, clinical, and health economic outcome data were collected through previously validated and structured questionnaires. Six hundred and eighty-two (682) people with MS were enrolled in NARCRMS and completed HEOR questionnaires at the time of the analysis. Among the participants, 61% were employed full-time and 11% were employed part-time. Fatigue was the leading symptom reported to impact both work and household chores. Among the employed participants, 13% reported having missed work with a median of 6.8 missed hours due to MS symptoms (absenteeism), while 35% reported MS having impacted their work output (presenteeism). The odds of higher disease severity were 2.29 times higher for participants who identified reduction of work output. Fatigue was the most identified symptom attributed to work output reduction. Among all participants, 33% reported having missed planned household work with a median of 3.0 hours. The odds of higher disease severity were 2.49 times higher for participants who identified reduction in household work output, and 1.70 times higher for those whose fatigue affected housework output as compared to other symptoms. A preliminary review of the first 682 patients showed that people with MS had reduced work and housework productivity even at an early disease state. Multiple sclerosis can significantly impair individuals' ability to function fully at work and at home, with fatigue overwhelmingly identified as the primary contributing factor. The economic value of finding an effective treatment for MS-related fatigue is substantial, underscoring the importance of these findings for policy development, priority setting, and the strategic allocation of healthcare resources for this chronic and disabling condition. *The other authors include researchers from the Autoimmunity Center of Excellence at the University of Michigan Medical School, Division of Multiple Sclerosis at the University of Miami Miller School of Medicine, and the Multiple Sclerosis Center of Excellence at the Oklahoma Medical Research Foundation Oklahoma City.*

Development and Testing of a Novel Whole-Body Exposure System for Investigative Studies of Radiofrequency Radiation in Rodents

DLH researchers **Katherine Allen**, **Laura Betz**, **Shawn Harris**, and **Guanhua Xie** were among the contributors to an NIEHS report published by the National Institute of Environmental Health Sciences (Online: August 2025). *Executive Summary:* The predominant source of human exposure to radiofrequency radiation (RFR) occurs through the use of cell phone handsets. Previous toxicology studies on RFR, conducted in support of the National Toxicology Program (NTP) by researchers at the National Institute of Environmental Health Sciences (NIEHS), found exposure-related effects on body temperature and DNA damage. The studies reported herein were conducted by NIEHS researchers in the Division of Translational

Toxicology to better understand the biological mechanisms that produced tumor development and DNA damage in exposed rodents. These studies were not conducted as part of the NTP. The goals of the current research were to design, construct, and use a small-scale RFR exposure system to conduct toxicological research in rats and mice. One of the primary specific objectives of this research was to test and use new, experimental methods to collect physiological data from animals in real time during RFR exposures, including assessment of body temperature and use of videos for clinical observations. Previously, such data collections were not feasible without cessation of RFR exposure. A new RFR exposure system based on the technical parameters of the system used in the previous NTP toxicology and carcinogenesis studies was developed for small-scale investigative studies with fewer animals. The system was designed with enhanced capabilities and more flexibility, including the ability to generate additional radiofrequency (RF) signals with frequencies and modulations used in more current wireless communication technologies. A series of 5-day studies was conducted in male or female Sprague Dawley (Hsd:Sprague Dawley® SD®) rats or B6C3F1/N mice to evaluate the effect of exposure to the same Code Division Multiple Access (CDMA)- or Global System for Mobile Communications (GSM)-modulated RF signals used in the previous NTP studies. Video from the cameras in the exposure chambers demonstrated no visible response in either rats or mice at the first time the exposure system was activated, at subsequent system on/off transitions, or during the periods of exposure. Exposure to RFR for 5 days did not induce DNA damage in brain cells (frontal cortex, hippocampus, and cerebellum), or in liver, heart, or blood cells of rats and mice, as measured using the comet assay. These investigative studies of RFR exposure were technically challenging to conduct and, unfortunately, measurement by two different methods did not yield data useful for assessing body temperature during exposure. Despite a number of difficulties (i.e., engineering requirements, system modifications, measurement of body temperature during exposure), this small-scale RFR exposure system presents a prototype for investigative toxicological studies by researchers interested in conducting experimental RFR studies in rodent models. High-quality studies to understand the effects of RFR exposure on biological responses are needed given the widespread human exposure to RFR associated with cell phone use. The aim of this report is to share knowledge and facilitate advancement in research methodologies for investigating the potential health effects of RFR.

Weight Cycling and Cancer Risk in the Sister Study

DLH researchers **Victoria Stevens**, **Jessica Priest**, **Jesse Wilkerson**, and **Aimee D'Aloisio** were among the authors of an article published in the *American Journal of Epidemiology* (Online Ahead of Print: August 2025). Weight cycling, when weight is repeatedly lost intentionally and then regained, may perturb biological processes that could influence cancer development. However, results from epidemiologic studies of weight cycling are mixed and provide no clear answer as to whether this behavior alters cancer risk. The authors examined the association of weight cycling and cancer incidence among 45,004 women enrolled in the Sister Study (2003-2009) and followed through October 12, 2020. Weight cycling was defined using baseline responses about the number of times ≥20 pounds (9 kilograms) was lost and then regained. Multivariable-adjusted hazards ratios and 95% confidence intervals for all cancers and five individual cancers (breast, endometrial, ovarian, colorectal, and kidney) were estimated using Cox proportional hazards regression modeling. Weight cycling was not associated with an increased risk of any cancer after bodyweight was adjusted for and was inversely associated with risk of all cancers and breast cancer. The inverse trend for breast cancer was only seen in obese and in postmenopausal women. These findings suggest that weight cycling, independent of bodyweight, does not increase cancer risk and, for breast cancer, is associated with decreased risk. *A researcher from the Epidemiology Branch of the National Institute of Environmental and Health Sciences co-wrote this article.*

Viral Suppression and Continued Participation in the Community Retail Pharmacy Drug Distribution Point Model Among People Living With HIV in Uganda

DLH researcher **Derrick Kimuli** was among the authors of an article published in *BMC Health Services Research* (Online: August 2025). Approximately 1.3 million people living with HIV (PLHIV) receive antiretroviral treatment (ART) from health facilities in Uganda. The Uganda Ministry of Health (MoH) introduced the Community Retail Pharmacy Drug Distribution Points (CRPDDP) to decongest health facilities, improve

efficiency, convenience and patient-centered care while maintaining service quality. This study examined continued model participation and viral load suppression among PLHIV enrolled in CRPDDP for at least 1 year at Iganga District Hospital, Uganda. This was a retrospective cohort study conducted from January to March 2024 using a census approach. Records of 360 PLHIV enrolled in the CRPPDP model between October 2021 and December 2022 were reviewed. The period was chosen to account for the rolling enrollment. Inclusion required at least 12 months since enrollment by the time of the study, regardless of whether clients remained in the model. Continued participation in the model, viral load at enrollment, latest viral load (at study time), and associated factors were assessed. The mean age of the participants was 43.5 (± 9.8) years; most participants were female (62.2%) and married (53.9%). The continued participation in the model was 94.7%. The mean viral suppression while in the model was 96.3 copies/mL compared to 63.2 copies/mL before enrollment in the model. Nineteen (5.2%) PLHIV had dropped out of the model at the time of the data abstraction: 1 lost from care, 2 relocated, and 16 returned to facility-based care. The increase in the mean viral load count observed after enrollment was not statistically significant. Participants on the second-line ART regimen were less likely to be retained compared to those on the first-line regimen. Under real-world programmatic conditions, at a public peri-urban hospital in Uganda, the CRPDDP model sustained high continued participation and viral load suppression among PLHIV who had spent at least 1 year in the model, demonstrating its potential as an alternative to facility-based ART distribution. However, the lower continued participation among PLHIV on second-line regimens underscores the need for specialized support strategies. Moreover, the viral load increased slightly, although the change was not statistically significant, this warrants further investigation. Longer follow-up studies that also overcome other limitations of this study could provide more insightful results and long-term sustainability. *The other authors include researchers from the Makerere University Joint AIDS Program (Kampala) and the United States Agency for International Development (Kampala).*

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

DLH researchers **Austin Van Grack** and **Jhoanna Roa** were among the authors of an article published in *Trials* (Online: August 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 on 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. Participants will be followed for 52 weeks after TB treatment initiation to assess long-term outcomes. 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 the Harvard T.H. Chan School of Public Health, the UCSF Center for Tuberculosis at the University of California, the Emory/Georgia Tuberculosis Research Advancement Center, and the Division of AIDS at the National Institute of Allergy and Infectious Diseases, as well as researchers from institutes in South Africa, Malawi, Peru, and Haiti.*

Decreased Cigarette Smoking May Partially Explain the Increased Prevalence of Antinuclear Antibodies in the United States

DLH researchers **Gregg Dinse**, **Caroll Co**, and **Jessica Priest** were among the authors of an article published in *Frontiers in Immunology* (Online: August 2025). Despite well-known harmful health effects of smoking, research supports an inverse association with some autoimmune diseases. High-titer antinuclear antibodies (ANA) are associated with autoimmune diseases, and ANA prevalence in the US increased between 1988 and 2012. Tobacco smoking decreased during those years while vaping of electronic cigarettes (e-cigarettes) increased after their introduction in 2007. Carbon monoxide (CO) may ameliorate autoimmunity, and e-cigarettes deliver much less CO than regular cigarettes. The authors explored interdependencies among ANA, smoking, and time. The authors analyzed cross-sectional data on ANA and the primary nicotine metabolite, cotinine, in 13,288 participants ≥12 years old from three time periods (1988-1991, 1999-2004, 2011-2012) of the US National Health and Nutrition Examination Survey. Smoking exposure (none, passive, active) was inferred from serum cotinine. Logistic regression to analyze ANA prevalence, adjusted for sex, age, and race/ethnicity, was used. Over the study periods, ANA prevalence was highest (13.3-19.2%) for nonsmokers but non-trending; lower (11.1-15.5%) for "passive" smokers but steadily increasing; and even lower for active smokers but increasing from 7.4% in 1999-2004 to 13.3% in 2011-2012. The increases in ANA among passive and active smokers were mainly in adolescents (ages 12-19 years). Smokers had reduced odds of ANA in 1999-2004, with an odds ratio (OR) of 0.65 and a 95% confidence interval (CI) of 0.45-0.93, but this association was weaker in 1988-1991 and 2011-2012. Although smoking causes harmful health effects, ANA data are consistent with smoking playing a role in decreasing autoimmunity. Recent vaping among adolescents may partially explain their large increase in ANA prevalence. The inverse ANA association with smoking strengthened between 1988-1991 and 1999-2004 but then weakened by 2011-2012. The initial strengthening was potentially because nonsmokers were exposed to progressively less CO (and/or other components of secondhand smoke), due to tightened smoking restrictions, while the potential nicotine-associated protection against ANA may have weakened after e-cigarettes became a source. Smoking should not be recommended given its negative health impacts. However, further studies could elucidate new mechanisms, perhaps involving components of tobacco smoke or vaping, possibly enabling development of novel preventative or treatment measures. *The other authors include researchers from the National Institute of Environmental Health Sciences.*

Associations Between Airborne Crude Oil Chemicals and Neurological Symptoms Among Workers in the Gulf Long-Term Follow-Up Study

DLH researchers **Braxton Jackson** and **Frankie LaPorte** were among the authors of an article published in *The Science of the Total Environment* (Epub: August 2025; Online: October 2025). Many volatile organic compounds may be neurotoxic at occupational levels. However, little is known about the neurotoxicity of these chemicals below occupational exposure limits, including among oil spill response and cleanup (OSRC) workers. The authors studied associations of neurological symptoms with exposure to benzene, toluene, ethylbenzene, xylenes, and n-hexane (BTEX-H) individually and as a mixture among 23,641 OSRC workers enrolled in the Gulf Long-Term Follow-up (GuLF) Study, a cohort following the 2010 Deepwater Horizon disaster. At enrollment, participants reported frequencies of neurological symptoms in the preceding 30 days. Cumulative inhalation exposure to the BTEX-H chemicals (ppb-days) and to total hydrocarbons (THC; ppm-days) were estimated using a job exposure matrix linking exposure group estimates to detailed individual OSRC work histories. Twenty-eight percent of participants reported experiencing at least one, and 5% reported two or more, neurological symptoms. Increased exposure to THC was associated with increased prevalence of two or more neurological symptoms, with similar results observed for other BTEX-H chemicals. Exposure to the BTEX-H mixture was associated with a per-quartile increased risk of two or more neurological symptoms of prevalence ratios = 1.21. *The other authors include researchers from the University of North Carolina at Chapel Hill, the National Institute of Environmental Health Sciences, and the National Institute on Aging.*

Abstracts of the 26th International Workshop on Clinical Pharmacology of HIV, Hepatitis and other Antiviral Drugs 2025, 3-4 September 2025, Amsterdam, the Netherlands

DLH researcher **Lara Hosey** was among the authors of an abstract titled, "**Population pharmacokinetics of tecovirimat in persons with mpox: Initial results from ACTG A5418**," published in a supplement of the *British Journal of Clinical Pharmacology* (Online: September 2025). The Study of Tecovirimat for Human Mpox Virus (STOMP) (ACTG A5418) assessed the safety, efficacy, and pharmacokinetics (PK) of tecovirimat in clade II mpox infection. The researchers previously showed lower tecovirimat exposures among participants in the open-label arm in comparison to healthy volunteers (HVs), though predicted concentrations at the end of the dosing interval (Ctau) were comparable or above the therapeutic target in non-human primates (NHPs). In clinical trials, tecovirimat did not reduce time to clinical resolution vs. placebo, highlighting the need to examine factors affecting tecovirimat PK in persons with mpox and the adequacy of current dosing strategies. Here, the initial population PK modelling of tecovirimat in persons with mpox and comparisons with historical data in HVs is reported. Participants in the randomized and open-label arms received oral tecovirimat 600 mg either twice daily (weight 40–<120 kg) or three times daily (weight ≥120 kg) for 14 days. PK data were available in 75 participants (41 participants with 315 intensive+30 sparse observations; 34 participants with 59 sparse observations; 404 observations total). Conclusions: Lower tecovirimat exposures and greater PK variability were observed in A5418 participants vs. HVs, but simulated Ctau estimates exceeded the NHP therapeutic target in ~91.5% of cases. Investigation into the mechanism of these differences and their relationship to clinical/virologic outcomes is warranted. *The other authors include researchers from the University of Colorado, University of California Los Angeles, University of North Carolina Chapel Hill, Harvard Medical School/Massachusetts General Hospital, Johns Hopkins University, and the Division of AIDS at the National Institute of Allergy and Infectious Diseases.*

Prospective Study of Oil Spill Cleanup-Related Exposure to Volatile Organic Compounds and Glycemic Dysregulation

DLH researcher **Kate Christenbury** was among the authors of an article published in *Environmental Health* (Online: September 2025). Exposures to volatile organic compounds could influence glycemic regulation. This study examines hemoglobin A1c (HbA1c) in a cohort of oil spill cleanup workers up to 6 years post-exposure in relation to benzene, toluene, ethylbenzene, and xylenes (BTEX) exposures, individually and as a mixture, as well as a separate estimation of the aggregate sum of BTEX (total BTEX). Data for this analysis are from the Gulf Long-term Follow-up (GuLF) Study—a prospective cohort of workers involved in the 2010 Deepwater Horizon oil spill cleanup. HbA1c and medication information were obtained at Home Visit and Clinical Exam phases 1–3 years and up to 6 years post-exposure, respectively. Cumulative inhalation exposure to the individual BTEX chemicals and to total BTEX were estimated using a job-exposure matrix linking air measurements to detailed individual worker cleanup work histories. The authors used Tobit regression models to examine associations between exposure to the chemicals and latent, untreated HbA1c, accounting for medication-reduced HbA1c; quantile g-computation to examine exposure to the mixture of BTEX chemicals and HbA1c was used. In results examining Home Visit HbA1c, the authors observed no discernable patterns but found suggestive evidence of an association with total BTEX. In results for Clinical Exam HbA1c, monotonic patterns were not observed, but rather an inverted-U pattern with elevations in Q2 or Q3 or no clear pattern. Similarly, in results for final HbA1c adjusting for initial HbA1c, total BTEX difference estimates showed an inverted-U pattern in point estimates across Q2, Q3, and Q4, compared to Q1. Exposures to the moderate levels of the BTEX chemicals observed in this study population, individually and as an aggregate, may be associated with elevated HbA1c up to 6 years after exposure, with an inverted-U pattern. *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 Joe C. Wen School of Population & Public Health at the University of California-Irvine.*

Program Implementation and Evaluation of De Casa en Casa: A Tailored Community-Based Cervical Cancer Screening Program for Underserved Hispanic Women

DLH data analyst **Adam Alomari** was among the authors of an article published in *Health Education Research* (Online: September 2025). Women on the US-Mexico border have a higher cervical cancer incidence rate, are diagnosed at later stages, and have higher mortality compared to non-Border women in the US. The authors identified key barriers to screening through various qualitative methods and have designed a program that addresses the needs of our community and creates a coordinated program of education, outreach, service delivery, navigation, and capacity building for the future. A multicomponent, culturally tailored, bilingual, evidence-based cervical cancer screening program was developed at Texas Tech University Health Sciences Center El Paso (TTUHSC El Paso). The program was implemented in El Paso and Hudspeth counties. Key program components were (i) theory-based and culturally tailored education delivered by bilingual community health workers; (ii) no-cost Pap and HPV screening; (iii) diagnostic and treatment colposcopy; and (iv) patient navigation and tracking. A total of 2318 women were recruited into the program and offered services. 2206 women were eligible for screening: mean age of the population was 44.8 years, 4.7% (N = 108) had never had a Pap smear, and 40.9% (N = 945) last received a Pap over 5 years previously. Screening uptake was 71.6% (N = 1 569); 7.8% (N = 114) of those tested were positive for high-risk HPV. 101 colposcopies were indicated and 98.0% (N = 99) were completed. Two cancers were diagnosed. A comprehensive cervical cancer screening program can achieve significant screening uptake rates in a high-risk population with historically low screening uptake and has the potential to significantly impact cervical cancer incidence and mortality in this border region. *The other authors include researchers from the University of Texas at Austin, Texas Tech University Health Sciences Center El Paso, and the University of Texas at Tyler.*

Blood Concentrations of Volatile Organic Compounds and Hypertension in the GuLF Study

DLH researchers **Kaitlyn Lawrence** and **Kate Christenbury** were among the authors of an article published in *The Science of the Total Environment* (Epub: September 2025; Online: October 2025). While certain criteria air pollutants have been associated with elevated blood pressure and risk of hypertension, there is limited research on the relationship of hazardous air pollutants, including volatile organic compounds (VOC), to these outcomes. The authors investigated associations of blood concentrations of selected VOCs with hypertension prevalence and blood pressure among participants in the Gulf Long Term Follow-up (GuLF) Study, a large prospective cohort study of individuals who participated in cleanup of the 2010 Deepwater Horizon oil spill. The authors examined 582 participants who had blood concentrations of benzene, toluene, ethylbenzene, m/p-xylene, o-xylene, styrene, 1,4-dichlorobenzene, and furan measured in samples collected 2-3 years after the spill. Because blood concentrations and blood pressure were collected/measured years after the spill and these VOCs have biological half-lives of <1-2 days, these blood VOC measurements reflect at the time of blood collection and are not related to spill-related cleanup work. The authors used modified Poisson regressions and generalized linear models to explore the associations of blood VOC concentrations with hypertension prevalence and with blood pressure levels, including analyses stratified by tobacco-smoke exposure, BMI, and age to assess potential effect measure modification. Blood concentrations of benzene, toluene, ethylbenzene, m/p-xylene, o-xylene, styrene, 1,4-dichlorobenzene, and furan were not associated with increased hypertension prevalence or blood pressure. Rather, evidence of possible inverse associations between blood concentrations of certain VOCs, particularly among tobacco smoke-exposed individuals, was observed. *The other authors include researchers from the Gillings School of Global Public Health at the University of North Carolina, the Division of Neuroscience at the National Institute on Aging, and the Epidemiology Branch of the National Institute of Environmental Health Sciences.*

Cancer Mortality After Protracted Low-Level Radiation Exposure for Early and Contemporary Workers in Two Large Occupational Cohorts in the U.S. Million Person Study

DLH researcher **Sarah Cohen** was among the authors of an article published in *Radiation Research* (Online Ahead of Print: September 2025; Print: November 2025). An evaluation is presented of differences in radiation-related solid cancer mortality risk for early versus contemporary subgroups of radiation workers in two

constituent Million Person Study (MPS) cohorts. The two previously analyzed MPS cohorts are 123,401 industrial radiographers monitored from 1939-2011 and followed through 2019 and 135,193 nuclear power plant workers monitored from 1957-1984 and followed through 2011. This analysis was conducted to compare to recently published risk estimates for early versus contemporary workers in the International Nuclear Workers Study (INWORKS) with pooled U.S., French, and UK nuclear worker data, particularly for the U.S. component. For all solid cancer mortality, the US-INWORKS study reported a low and non-significant excess relative risk (ERR) per Sv cumulative equivalent dose for the whole cohort of 0.19, whereas for contemporary workers the ERR per Sv was 2.23, approximately 10 times higher than the entire US-INWORKS cohort. The risk for the full INWORKS cohort was 0.52 per Gy colon dose, whereas, for contemporary workers, the risk was 1.44, nearly 3 times higher. These risks for contemporary workers are both larger than risks informing radiation protection and much higher (7.0 and 4.5 times) than the Japanese A-bomb survivor's risk for males exposed acutely between the ages of 20 and 60 years of 0.32. Limitations of the INWORKS analysis include missing information on organ doses from radionuclide intake as well as neutrons, and the absence of adjustment for non-radiation risk factors (notably asbestos exposure). The analysis of the MPS cohorts addresses these dosimetric- and asbestos-related limitations. For all solid cancer mortality, industrial radiographers showed similar Poisson ERRs per 100 mGy colon dose for early and contemporary workers of 0.06 and 0.07, respectively. The results for nuclear power plant workers were 0.10 and 0.02, respectively. It appears premature to conclude that there is a difference in excess risk between early and contemporary workers from radiation exposures. *The other authors are researchers from the University of Zürich, the Memorial Sloan Kettering Cancer Center Department of Medical Physics, Vanderbilt Institute for Clinical and Translational Research and the Division of Epidemiology at the Vanderbilt University Medical Center, the International Epidemiology Institute (Rockville, Maryland), and the National Council on Radiation Protection and Measurements (Bethesda, Maryland).*

The National Dementia Workforce Study: The Plan for Organization Sample Frames and Data Collection

DLH researcher **Jennifer Kelley** was among the authors of an article published in the *Journal of the American Geriatrics Society* (Epub: September 2025; Print: November 2025). The National Dementia Workforce Study was designed to improve understanding of the individuals and systems who care for people with dementia, but designing and implementing such a study is challenging due to the large number of patient care organizations, clinical and direct care roles, and locations in which care is provided. Specifically, developing a probability sample of organizations and staff caring for people with dementia is a complex and difficult process. While there are national sampling frames available for federally certified nursing homes (i.e., via data from the Centers for Medicare and Medicaid Services), there are no national sampling frames for assisted living communities or home care agencies. The latter frames must be developed through querying state-level regulatory agencies and through other, supplemental strategies such as working with professional organizations, large employers, and organizations that provide services (e.g., payroll services) to this sector. Further, since there are no national sampling frames that allow for direct sampling of staff working in any of these types of organizations, the authors opted for a two-stage design. In the first stage, organizations are identified, sampled, recruited to participate in an organizational-level survey, and asked to provide a roster of eligible staff. In the second stage, individual staff members are recruited for a staff-level survey. The authors describe the plan for sampling and recruitment procedures to be used in each stage and discuss limitations, including implications for coverage of the target population. Data collected through these surveys will be available to the research community. *The other authors include researchers from the University of Michigan, Philip R. Lee Institute for Health Policy Studies and Healthforce Center at the University of California San Francisco, and the School of Social Work and Cecil G. Sheps Center for Health Services Research at the University of North Carolina at Chapel Hill.*

Protecting Households on Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients: Study Protocol for the PHOENIx Phase 3 Clinical Trial

DLH researcher **Linda Naini** was among the authors of an article published in *Contemporary Clinical Trials* (Epub: September 2025; Online: November 2025). Data to guide tuberculosis (TB) preventive treatment (TPT) of close contacts of people with multidrug-resistant tuberculosis (MDR-TB) are limited. While levofloxacin-

based TPT has been shown safe and efficacious, alternatives are needed for those exposed to fluoroquinolone-resistant Mycobacterium tuberculosis (M. tb). The PHOENIx trial evaluates whether using a novel nitroimidazole, delamanid, in high-risk household contacts (HHCs) of patients with MDR-TB reduces their risk of developing active TB. PHOENIx is a phase 3, open-label, multicenter clinical trial with a cluster-randomized superiority design (households form the clusters). The study objectives are to compare efficacy and safety of 26 weeks of delamanid versus isoniazid for preventing confirmed or probable TB during 96 weeks of follow-up among HHCs of adults with pulmonary MDR-TB. HHCs are defined as young children <5 years, people living with HIV or non-HIV immunosuppression, or people with evidence of M. tb infection. The study was originally designed to enroll 3452 HHCs to provide 90% power to detect a 50% reduction in the cumulative proportion of HHCs developing confirmed or probable TB during 96 weeks of follow-up from 5% in the isoniazid arm to 2.5% in the delamanid arm. The design included a sample size re-evaluation to address uncertainty in study design assumptions. Preventing MDR-TB is a global priority. Alternatives to levofloxacin-based TPT are needed since fluoroquinolone resistance is growing. PHOENIx, a phase 3 trial evaluating delamanid, is poised to inform WHO guidelines. *The other authors include researchers from the Center for Biostatistics in AIDS Research at the Harvard T.H. Chan School of Public Health, the Division of AIDS at the National Institute of Allergy and Infectious Diseases, and the Byramjee Jeejeebhoy Government Medical College-Johns Hopkins Clinical Research Site (India).*

Assessing Replicability and Power Estimates of Behavioral Performance of Control Rats Across Standardized Pre-Clinical and Toxicology Studies

DLH researchers **Kathryn Konrad**, **Laura Betz**, and **Sandra McBride** were among the authors of an article published in *Neurotoxicology and Teratology* (Epub: September 2025; Online: November-December 2025). Behavioral assays are critical in evaluating impacts on nervous system function in rodents due to genetic or environmental factors and are frequently incorporated into regulatory decision-making studies. Despite numerous sources of guidance for such studies, results across behavioral assays are reputed to be highly variable with questionable replicability. Behavioral data obtained from control rats within four contract laboratory studies were used to evaluate replicability across studies, calculate the level of statistical power, and estimate the number of animals required for a specific effect size. For the three behaviors evaluated here (motor activity, acoustic startle response, and learning and memory), control rats from all studies showed the expected pattern of behavior, e.g., open field acclimation, startle habituation, % prepulse inhibition (PPI) over pre-pulse intensities, and acquisition and goal quadrant preference in the Morris Water Maze (MWM). For selected representative individual endpoints, power analyses were conducted to evaluate sample size requirements. Across all endpoints, a drop in power occurred as differences between two groups became smaller. Power analysis of multiple representative endpoints suggested that a sample size of 20 may detect a 30% effect with 80% power. Sample size requirements changed with the effect size, and achieving 80% power with a 20% effect size generally required a sample size of 30 rats. While the behavioral performance was replicated over the Study Cohorts, power analyses suggested a need for moderation of expectations regarding detectable differences if decisions relied on single endpoints or small effect sizes. Reporting results from a low powered study can have significant and wide-ranging impacts, including undermining confidence in data interpretation, misleading future research, and failing to adhere to the ethical framework of the 3 Rs. *The other authors are researchers from the National Institute of Environmental Health Sciences.*

Air Pollutants and Breast Cancer Risk: A Parallel Analysis of Five Large US Prospective Cohorts

DLH researcher **Marina Sweeney** was among the authors of an article published in the *American Journal of Public Health* (Epub: September 2025; Print: December 2025). To determine whether outdoor air pollution exposure is associated with breast cancer incidence, residential-level concentrations of nitrogen dioxide (NO_2, parts per billion [ppb]), fine particulate matter ($PM_{2.5}$; ≤2.5 μ/m³) and ozone (ppb) in the United States were estimated for participants of the Nurses' Health Studies, Women's Health Initiative Clinical Trials and Observational Study Cohort, and Sister Study using high-resolution spatiotemporal models. Cox proportional hazards regression estimated cohort-specific hazard ratios (HRs) and 95% confidence intervals, and a random effects model determined summary HRs, overall and by estrogen receptor (ER)/progesterone receptor (PR)

subtype and census region. NO_2 was positively associated with overall breast cancer incidence (n = 28,811 cases), with little variation by subgroups. $PM_{2.5}$ was associated with higher incidence of ER-/PR- tumors (n = 2367 cases) and with higher overall incidence in the Midwest. Ozone was not associated with overall incidence, but was associated with ER-/PR- tumors (n = 3406 cases). In this largest US study to date, the authors confirmed an association between NO_2 and breast cancer, and novel associations of $PM_{2.5}$ and ozone with ER-/PR- tumors are presented. *The other authors include researchers from the National Institute of Environmental Health Sciences, Harvard T. H. Chan School of Public Health, and the University of Washington School of Public Health.*

Use of Hair Straighteners and Chemical Relaxers and Incidence of Non-Reproductive Cancers

DLH researcher **Che-Jung Chang** was among the authors of an article published in the *Journal of the National Cancer Institute* (Online Ahead of Print: September 2025; Print: January 2026). Use of hair straighteners and chemical relaxers has been associated with increased incidence of breast, uterine, and ovarian cancers. However, their potential association with non-reproductive cancers remains unknown, despite evidence that some ingredients in these products may be genotoxic. The authors therefore examined use of hair straighteners/chemical relaxers in relation to the incidence of non-reproductive cancers. Data was analyzed from 46,287 cancer-free women from the Sister Study, a U.S.-wide cohort enrolled between 2003-2009 (ages 35-74). Participants reported frequency of hair straightener/chemical relaxer use in the 12 months prior to enrollment. Incident cancers (melanoma, thyroid, lung, non-Hodgkin's lymphoma, leukemia, pancreatic, colorectal, and kidney cancers) were self-reported during the follow-up period through September 30, 2021, and were confirmed by pathology reports when available. The authors used multivariable Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for hair straighteners/chemical relaxer use and incident cancers, adjusting age, race and ethnicity, educational attainment, and smoking status. During a median follow-up of 13.1 years, use of hair straighteners/chemical relaxers was associated with a higher incidence of thyroid cancer (n = 225 cases), non-Hodgkin's lymphoma (n = 313 cases), and pancreatic cancer (n = 138 cases). There was little evidence of dose-response with increasing frequency of use. The authors observed negligible or imprecise associations for the remaining cancer types. Use of hair straighteners/chemical relaxers may be associated with a higher incidence of thyroid cancer, non-Hodgkin's lymphoma, and pancreatic cancer. Further research is needed to confirm these findings. *The other authors are researchers from the Rollins School of Public Health at Emory University and the Epidemiology Branch of the National Institute of Environmental Health Sciences.*

Antiretroviral Therapy Intensification With Dolutegravir and/or Maraviroc Did Not Affect HIV-1 Cell-Associated DNA, RNA, and 2–LTR Circles Over 12 Weeks

DLH researcher **Jhoanna Roa** was among the authors of an article published in *Open Forum Infectious Diseases* (Online: October 2025). Neurocognitive impairment (NCI) among people living with human immunodeficiency virus (HIV; PWH) on antiretroviral therapy (ART) may result from residual viral replication. The A5324 trial found that ART intensification with dolutegravir (DTG) with or without maraviroc (MVC) did not affect NCI in PWH. The authors evaluated the impact of ART intensification on peripheral virological measures during the first 12 weeks of intensification. The A5324 study was a randomized, double-blind, placebo (PBO)-controlled, 96-week trial of ART intensification with either dual PBO, DTG + PBO, or DTG + MVC in PWH with NCI on ART who were naive to integrase strand transfer inhibitors and MVC. At baseline and weeks 2, 4, and 12, HIV-1 RNA was measured in plasma with a low-copy assay, while HIV-1 cell-associated DNA (caDNA), cell-associated unspliced RNA (caRNA), and cell-associated 2-long terminal repeat circles (ca2LTR) were quantified from peripheral blood mononuclear cells using droplet digital polymerase chain reaction. Of the 171 participants, 59 were randomized to dual PBO, 57 to DTG + PBO, and 55 to DTG + MVC. Changes in caDNA and caRNA and detection of plasma RNA did not differ between treatment arms over 12 weeks. Detection of ca2LTR was less frequent at weeks 2-4 in the DTG + MVC arm (40.4%) than in the dual-PBO (70.7%) and DTG + PBO (68.4%) arms. However, this difference diminished by week 12, and baseline ca2LTR detection in the DTG + MVC arm was lower than in the other groups. DTG intensification had no effect on peripheral markers of HIV-1 persistence. DTG + MVC intensification reduced ca2LTR detection at weeks 2-4, though this effect did not

persist through week 12. These findings indicate the minimal impact of intensification on the HIV-1 peripheral reservoir, consistent with prior studies. *The other authors include researchers from the University of Washington School of Medicine, the Harvard T.H. Chan School of Public Health, the University of North Carolina at Chapel Hill, and the Division of AIDS at the National Institute of Allergy and Infectious Diseases (NIH).*

Effect of HIV on Bedaquiline and Delamanid Pharmacokinetics in Patients With Multidrug-Resistant TB

DLH researcher **Laura Moran** was among the authors of an article published in *The International Journal of Tuberculosis and Lung Disease* (Print: October 2025). Bedaquiline and delamanid are key drugs in the treatment of multidrug-resistant TB. It is unclear whether HIV affects the pharmacokinetics of bedaquiline and delamanid. Participants with multidrug-resistant TB were randomized to treatment with bedaquiline, delamanid, or both, plus a standard-of-care treatment. Intensive pharmacokinetic sampling was performed after 8 weeks of therapy. The authors performed non-compartment analysis to describe bedaquiline and delamanid pharmacokinetics, comparing exposures between HIV-positive and HIV-negative participants using geometric mean ratios (GMRs), and explored covariates associated with bedaquiline and delamanid AUC, using multivariable regression modelling. Twenty-six participants were assigned to bedaquiline, 25 received delamanid, and 24 received both drugs. Fifty and 49 participants were treated with bedaquiline and delamanid, respectively. The GMR of bedaquiline $AUC_{0\text{-}22}$ and C_{max} in HIV-positive compared with HIV-negative participants was 0.76 and 0.94, respectively. The GMR of delamanid $AUC_{0\text{-}23}$ and C_{max} in HIV-positive compared with HIV-negative participants was 0.93 and 0.79, respectively. HIV infection was associated with a 24% reduction in bedaquiline $AUC_{0\text{-}22}$, the significance of which requires further exploration. Delamanid exposure was unaffected by HIV status. *The other authors are researchers from the University of Cape Town, the Harvard T.H. Chan School of Public Health, the Asociacion Civil Impacta Salud y Educacion (Peru), and Vanderbilt University Medical Center.*

Estimated Major Adverse Cardiovascular Events Averted Among Persons With HIV If Treated With a Moderate-Intensity Statin

DLH researcher **Yishiow Kuo** was among the authors of an article published in *AIDS (London, England)* (Epub: October 2025; Print: February 2026). The objective was to estimate 10-year atherosclerotic cardiovascular disease (ASCVD) risk among U.S. adults with diagnosed HIV (PWH) and number of first major adverse cardiovascular events (MACE) that are potentially preventable over a 5-year period, if U.S. Department of Health and Human Services recommendations for statin therapy for PWH were fully implemented. This is a cross-sectional study of nationally representative, individual-level data on behavioral and clinical characteristics of U.S. PWH. Using data from standardized questionnaires and medical records abstraction collected from June 2022-May 2023, the authors calculated weighted estimates of the following among PWH aged 40-75 years without documented cardiovascular disease (N = 2,155): 10-year ASCVD risk; statin prescription by risk level; number potentially avoidable first MACE over 5 years with moderate-intensity statin treatment. Among PWH eligible for therapy, 72.5% were male, 42.5% were aged 50-59 years, and 35.9% were Black, non-Hispanic persons. The overall median risk score was 7.1%. Among those with low (<5%) and moderate risk (5%-<20%), 19.8% and 36.9% were on statin therapy, respectively. An estimated 7,418 additional first MACE could be prevented over 5 years if eligible PWH received moderate-intensity statin therapy. Fully implementing statin therapy recommendations for PWH in the United States could substantially reduce MACE among this population. *The other authors are researchers from the Division of HIV Prevention and the Division of Heart Disease and Stroke Prevention at the Centers for Disease Control and Prevention.*

Prevention of Type 2 Diabetes in Adults

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: November 2025). *Excerpt:* Type 2 diabetes is a progressive condition that can lead to multiple organ damage,

disability, and premature death. Prediabetes, a high-risk state marked by elevated blood glucose levels below the diagnostic threshold for type 2 diabetes, currently affects 98 million U.S. adults. Individual-level interventions, including intensive lifestyle programs and select medications, have proven effective in delaying or preventing the progression from prediabetes to type 2 diabetes. Landmark clinical trials in the 1990s established the efficacy of these treatment approaches, with lifestyle changes demonstrating greater benefits than medications such as metformin, alpha-glucosidase inhibitors, or lipase inhibitors and more favorable safety than thiazolidinediones. These findings catalyzed translational research to enhance the feasibility, acceptability, and sustainability of delivering intensive lifestyle interventions in real-world settings. Adapted interventions remained effective and were found cost-effective, contributing to policies that established the U.S. National Diabetes Prevention Program (NDPP) and reimbursement from public and private payors. The NDPP now exists to expand access to evidence-based lifestyle intervention programs nationwide and has reached nearly 819,000 adults through a nationwide network of almost 1,400 community-based organizations and healthcare partnerships. The Centers for Medicare and Medicaid Services leveraged the NDPP infrastructure to offer Diabetes Prevention Program (DPP)-like intervention services as a covered health benefit for high-risk Medicare beneficiaries. However, despite these remarkable examples of translating research into policy and practice, only a small proportion of U.S. adults living with prediabetes today are aware they are at high risk for type 2 diabetes, and far fewer have knowledge of or have taken part in a DPP-like intervention program. Emerging research highlights the need for innovative strategies to improve engagement, including leveraging technology and tailoring interventions to diverse social and cultural contexts. Although multiple medications have efficacy in type 2 diabetes prevention, none have received U.S. Food and Drug Administration approval for this indication, and many expert groups recommend their use only when lifestyle interventions are ineffective or unavailable; subsequent utilization remains low and health payor coverage is limited. While new medications, such as glucagon-like peptide-1 (GLP-1) receptor agonists, show promise for type 2 diabetes prevention, their long-term impacts and use in real-world clinical settings remain under investigation. This article presents a narrative scoping review of the extremely active area of type 2 diabetes prevention science during the last three decades. We focus on the U.S. experience and in areas where research to date has been the strongest, namely individual-level intensive lifestyle interventions and select medications that have been studied rigorously. We include a focused evidence review of seminal efficacy trials, as well as the translational research that advanced the implementation and dissemination of intensive lifestyle interventions into the health care and population health sectors. Finally, we review the current state of U.S. diabetes prevention policy and practice, and we conclude with prevailing challenges, unanswered questions, and areas needing further research and action.

Factors Associated With Interstitial Lung Disease Among Patients With Idiopathic Inflammatory Myopathies

DLH researcher **Jesse Wilkerson** was the lead author, and DLH researchers **Matthew Bridge** and **Gary Larson** were co-authors of an article published in *Rheumatology (Oxford, England)* (Online Ahead of Print: November 2025). Idiopathic inflammatory myopathies (IIM) are heterogeneous disorders that often affect the lungs as IIM-associated interstitial lung disease (IIM-ILD). The authors used Meta-ANalysis of Transethnic Associations (MANTRA) and machine learning methods to evaluate predictors of IIM-ILD. Subjects (N = 450) were enrolled in studies at the National Institutes of Health. The authors studied adult (N = 262) and juvenile (N = 188) dermatomyositis (N = 276), polymyositis (N = 109), and overlap myositis (N = 61) patients with clinical, autoantibody, human leucocyte antigen (HLA), and single nucleotide polymorphism (SNP) data, with (N = 162) or without (N = 288) ILD. Logistic regression and MANTRA analyses were used to evaluate the associations of SNPs (Muc5b rs35705950, TOLLIP rs5743890 and rs3750920, TLR5 rs5744168, and TERT rs2736100) previously identified as risks for idiopathic pulmonary fibrosis (IPF). Classification and Regression Tree (CART) and gradient boosting machine learning were used to simultaneously evaluate the clinical, autoantibody, HLA, and SNP data for their relative predictive power of ILD. Smoking status, older age, African American heritage, and certain HLA genes were associated with IIM-ILD, but anti-synthetase, myositis-associated, and anti-MDA5 autoantibodies showed the strongest risk associations, with an increased odds of ILD by up to 20-fold. Conversely, anti-signal recognition particle, anti-TIF1 (P155/140), and anti-

NXP2 autoantibodies showed the strongest protective effects, with decreased odds of ILD by up to 40%. The effects of some HLA allele groups and IPF SNPs on ILD were inconsistent and weaker. This sample of IIM patients showed autoantibodies to be the strongest predictive or protective factors for ILD, yet the full range of associations of IIM-ILD remain undefined. *The other authors are researchers from the National Institute of Environmental Health Sciences and the National Institute on Aging.*

Association of Serum Biomarkers with Outcomes and Treatment Success of Inhaled Hyaluronan in COVID19

DLH researcher **Jane Der** was lead author of an article published in *Lung* (Online: November 2025). Viral pneumonia causes significant morbidity and mortality worldwide. However, there is limited ability to predict outcomes and treatment responses. The authors analyzed data from a recently published placebo-controlled trial of inhaled high molecular weight hyaluronan (HMWHA) in 146 patients with severe COVID-19 pneumonia, to determine whether admission cytokines and demographic information is associated with disease outcomes and response to HMWHA treatment. The authors found that serum levels of CXCL10 are strongly associated with both endpoints. Their data thus identify CXCL10 as a possible predictor of viral pneumonia outcome and response to anti-inflammatory treatment. *The other authors are researchers from the Università Campus Bio-Medico di Roma, the Fondazione Policlinico Campus Bio-Medico, and the National Institute of Environmental Health Sciences.*

Bile Acids: Potential Links to Overweight/Obesity and Androgen Levels in Pubertal Girls

DLH researchers **Sheri Denslow** and **Samantha McNeley** were among the authors of an article published in *Frontiers in Endocrinology (Lausanne)* (Online: November 2025). Pubertal girls with higher body mass index (BMI) or total body fat (TBF) have higher androgens. The authors demonstrated that several bile acids (BAs) were associated with BMI, TBF, and androstenedione in an untargeted metabolomics study. The study objective was to investigate the relationship between body composition, BAs, and androgens in pubertal girls. Blood samples were collected at up to seven study visits that included Tanner staging, breast ultrasound, and dual-energy x-ray absorptiometry. Serum total testosterone, free testosterone (FT), androstenedione, dehydroepiandrosterone sulfate, and 18 BAs were measured by liquid chromatography mass spectrometry. Generalized estimating equations estimated associations between TBF percent or BMI z-score, hormones, and BAs adjusted for time since enrollment, age, menarche status, race, and breast morphological stage. Eighty-two participants (aged 10.9 ± 1.4 SD years; 55% non-Hispanic White, 29% non-Hispanic Black, 11% Hispanic, 6% Other; 65% normal weight, 35% overweight/obese) contributed an average of 2.59 samples. BAs were stable over time and not associated with menarchal status. BMI and TBF were negatively associated with total BAs. BAs are important signaling molecules with roles in metabolic and endocrine function. BMI and TBF were inversely associated with BAs, and two BAs were nominally positively associated with FT in girls across a spectrum of body weights. These results suggest novel biological links between altered BA signaling, overweight/obesity, and androgen production among pubertal girls. *The other authors are researchers from the Clinical and Translational Research Branch and the NIEHS Mass Spectrometry Research Center at the National Institute of Environmental Health Sciences (NIH).*

In Utero and Early Life Exposures to Smoking Are Associated With Systemic Autoimmune Rheumatic Diseases

DLH researcher **Nastaran Bayat** was among the authors of an article published in *Seminars in Arthritis and Rheumatism* (Epub: November 2025; Online: December 2025). Systemic autoimmune rheumatic diseases (SARDs) are influenced by genetic and environmental factors. The authors examined pregnancy complications, early life events (birth season, birth order, feeding), and exposures to tobacco smoking in relation to SARD diagnosis. In a case-control study, probands with SARDs were compared to same-sex close-in-age unaffected siblings (US), and demographically matched unrelated controls (UC); 329 children (probands=124, US=115, UC=90) and 184 adults (probands=76, US=63, UC=45) were included. Conditional and unconditional logistic regression were used to examine proband-US and proband-UC comparisons. The authors examined

associations between SARDs and exposures to smoking while adjusting for HLA-DRB1*03:01 in White probands and UC. No specific pregnancy complication was associated with SARDs; however, the total number of pregnancy complications was greater in juvenile probands. A higher proportion of juvenile-onset probands than UC were exposed to tobacco smoking, both in utero and after birth (prenatal, 20% vs. 4%; household smoking before age 3, 14% vs. 3%). Among adult-onset probands and US, household smoking exposure before age 10 was associated with SARDs (60% vs. 42%). Among White subjects, HLA-DRB1*03:01 was associated with SARDs. After adjusting for HLA-DRB1*03:01, household smoking exposure was associated with juvenile- and adult-onset SARDs. Early life exposure to tobacco smoking is associated with SARDs; the effect remained after adjusting for the genetic risk of HLA. These findings support a role for early environmental exposures in autoimmune diseases. *The other authors are researchers from the National Institute of Environmental Health Sciences, the National Institute of Dental and Craniofacial Research, and the Department of Transfusion Medicine at the NIH Clinical Center.*

Air Pollution and Breast Cancer Incidence in a United States-Wide Prospective Cohort Study: Examining Sensitive Periods of Exposure

DLH researcher **Judy Ou** was among the authors of an article published in *Environment International* (Epub: November 2025; Online: December 2025). Mounting evidence supports that air pollution is related to a higher breast cancer risk, yet the importance of exposure timing in this relationship remains unclear. In the Sister Study, a United States-wide prospective cohort (n = 50,884, 2003-2009), the authors estimated time-varying annual concentrations of nitrogen dioxide (NO_2) and fine particulate matter ($PM_{2.5}$) from 1990 to 2017 at residential addresses using validated spatiotemporal models. Self-reported breast cancer diagnoses were validated using medical records. The authors evaluated breast cancer overall and by estrogen receptor (ER) status and tumor extent [ductal carcinoma in situ (DCIS) versus invasive]. Limited evidence was found that air pollutant exposure during the time of a woman's first birth, most recent birth, or menopause transition was associated with heightened risk for breast cancer. When examining exposure flexibly over the long-term, a 10-ppb increase in NO_2 across lag years 1-11 significantly contributed to the risk of ER-positive and DCIS breast cancer, whereas $PM_{2.5}$ experienced during lag years 11-13 was associated with ER-negative breast cancer. The authors identified unique periods of susceptibility to NO_2 and $PM_{2.5}$ for breast cancer risk by ER status. *The other authors are researchers from the National Institute of Environmental Health Sciences, Huntsman Cancer Institute at the University of Utah School of Medicine, and the Department of Environmental & Occupational Health Sciences at the University of Washington.*

Associations of Specific Pesticides and Incident Rheumatoid Arthritis Among Female Spouses in the Agricultural Health Study

DLH researchers **Darya Leyzarovich** and **Ghassan Hamra** were among the authors of an article published in *Arthritis & Rheumatology* (Epub: November 2025; Print: January 2026). Growing evidence suggests farming and agricultural pesticide use may be associated with rheumatoid arthritis (RA), but few studies have examined specific pesticides and RA among farm women, who may personally use pesticides or be indirectly exposed. The authors investigated pesticide use and RA risk among female spouses of licensed pesticide applicators in the Agricultural Health Study; participants enrolled in 1993-1997 in North Carolina and Iowa (N=32,126). Incident RA cases were identified in follow-up questionnaires (1999-2021) and confirmed by medical records, relevant medication use, or Medicare claims data (1999-2016), or from Medicare claims if lacking questionnaire data on RA. Non-cases reported no RA and had no RA Medicare claims. Among those with complete covariate data (N=410 cases and 21,850 non-cases), the authors examined associations with pesticide classes and 32 specific pesticides (personal lifetime use reported at enrollment, updated in 1999-2003). Odds ratios and 95% confidence intervals were calculated, adjusting for age, state, education, smoking pack-years smoking, body mass index, and correlated pesticides. Incident RA was associated with use of organochlorine (DDT, lindane) and organophosphate insecticides (coumaphos, malathion), the carbamate insecticide carbofuran, and permethrin or pyrethroid insecticides use on crops or livestock. RA was not associated with using herbicides, except for metribuzin. The fungicides captan and metalaxyl were also associated with RA. These findings indicate that persistent organochlorine insecticides and some pesticides also used in public health or residential settings may

increase RA risk in women. *The other authors are researchers from the National Institute of Environmental Health Sciences, Brigham and Women's Hospital and Harvard Medical School, and the Division of Cancer Epidemiology and Genetics at the National Cancer Institute.*

Rural Sleep Health and Sleep Health Disparities Among Children and Adults in the United States

DLH researchers **Christopher Payne** and **Braxton Jackson** were among the authors of an article published in *Sleep Health* (Epub: November 2025; Print: February 2026). Sleep health is essential for health promotion and disease prevention. In the United States, rural communities face unique challenges (e.g., low access to health-promoting resources like food options, healthcare, and social services due to geographic isolation) that may exacerbate sleep disturbances. Yet sleep in this group is rarely characterized. Therefore, the authors sought to perform a descriptive study of sleep health characteristics among children and adults living in rural counties in the United States. Reported sleep duration (among adults only) and disturbances such as nonrestorative sleep (among children and adults) were described by age group using cross-sectional data from the 2020 and 2022 National Health Interview Survey. Differences in sleep were additionally assessed by sociodemographic characteristics (e.g., sex, race and ethnicity, socioeconomic status) using Poisson regression with robust variance to estimate prevalence ratios and 95% confidence intervals (PR [95% CI]). Among 1429 children and 8673 adults, sleep disturbances were prevalent across all age groups. As age increased among children, sleep disturbances were more prevalent, while consistent bed and wake times were less prevalent. Consistent disparities emerged among 6-13-year-olds, including higher sleep disturbances among children with lower versus higher socioeconomic status. Sex disparities occurred among adolescents (14-17 years old). Among adults (≥18 years old), sleep duration and disturbances varied across all sociodemographic characteristics, with generally higher prevalence among groups with adverse social conditions (e.g., divorced/separated/widowed; low socioeconomic status). Sleep disturbances and disparities are prevalent among rural populations, particularly among children aged 6-13 years and adults. *The other authors are researchers from the National Institute of Environmental Health Sciences and the National Institute on Minority Health and Health Disparities.*

Characteristics of HIV Time-Space Alerts in the United States, 2018-2021

DLH researcher **Mary Plaster** was among the authors of an article published in the *Journal of Acquired Immune Deficiency Syndromes* (Online Ahead of Print: November 2025: Print: March 2026). HIV time-space cluster detection is routinely conducted by CDC and health departments to identify counties with elevated diagnoses compared with historical levels. These analyses, originally applied to all diagnoses and persons who inject drugs (PWID), generate "alerts" for review that may indicate clusters or outbreaks. The reoccurrence of alerts has not been previously described nationally. In 50 U.S. states and the District of Columbia, quarterly, during 2018-2021, the number of HIV infections diagnosed during the preceding 12 months among each group of interest (all people ["overall alerts"], PWID, men who have sex with men [MSM], or MSM who inject drugs) was compared with the annual mean for that group from the preceding 36 months. An alert was generated if the number of diagnoses was >2 standard deviations and >2 diagnoses above the baseline mean. For counties with initial alerts during 2018-2019, reoccurrences of alerts during any of the following 8 quarters were assessed. During 2018-2021, compared to counties with alerts among PWID (n=154), 5 times as many counties had overall alerts (n=824) and nearly 3 times as many counties had alerts among MSM (n=445). Reoccurrences of alerts in ≥2 subsequent quarters were lowest among MSM and MSM who inject drugs (10% and 19% of counties respectively). Applying time-space cluster detection criteria to populations beyond PWID results in numerous alerts nationally, many of which represent transient increases. Additional work to refine time-space cluster detection criteria, or to prioritize additional follow-up or investigation, is necessary. *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.*

Characteristics Associated With Sustained Viral Suppression Status Among People With HIV Who Were Incarcerated in the Past 12 Months, 2015-2022

DLH researchers **Xin Yuan** and **Priya Nair** were among the authors of an article published in *Public Health Reports* (Online Ahead of Print: November 2025; Print: March/April 2026). People with HIV (PWH) who transition back into the community after incarceration often experience treatment disruptions, increasing the risk of poor outcomes. The authors examined factors associated with sustained viral suppression (SVS) after release. Data from 2015-2022 were analyzed data from a nationally representative sample of PWH (N = 1012). Among PWH who were incarcerated at least once in the past 12 months, only 30.0% achieved SVS postrelease. PWH aged 18 to 29 years and 30 to 39 years were significantly more likely to not have SVS than PWH aged ≥50 years. PWH released within 180 days were significantly more likely to not have SVS than PWH released after ≥181 days. PWH with ≥3 incarcerations within the past 12 months were significantly more likely to not have SVS than PWH who were incarcerated once. PWH with SVS were significantly more likely to be retained in HIV care, taking antiretroviral therapy (ART), or adherent to ART than PWH without SVS. SVS outcomes among recently incarcerated PWH could improve through adherence support, discharge planning, and postrelease support, particularly for young or frequently incarcerated individuals. *The other authors include researchers from the Centers for Disease Control and Prevention.*

Mesoscopic Analysis of GABAergic Marker Expression in Acetylcholine Neurons in the Whole Mouse Brain

DLH researchers **Caroll Co** and **Sandra McBride** were among the authors of an article published in *iScience* (Online: December 2025). In the central nervous system, acetylcholine (ACh) neurons coordinate neural network activity required for higher brain functions, such as attention, learning, and memory, as well as locomotion. Disturbances in cholinergic signaling have been described in many diseases of the developing and mature brain. Interestingly, ACh neurons can co-transmit GABA to support essential roles in brain function. However, the contributions of ACh/GABA co-transmission to brain function remain unclear. This underscores the need to better understand the heterogeneity of ACh neurons, particularly the sub-population of ACh neurons co-expressing GABAergic markers. We used various combinations of transgenic mouse lines to systematically label ACh neuron populations positive for different GABAergic markers in the brain. We developed a workflow combining tissue clearing, light-sheet fluorescence microscopy, and machine learning to image entire mouse brain hemispheres followed by quantification of ACh neurons throughout the brain. With this approach, we assessed whether (1) the loss of GABA co-transmission in ACh neurons, through the genetic ablation of the vesicular GABA transporter in ACh neurons, reduces ACh neuron count and (2) quantified ACh and ACh/GABA neuron sub-populations in the brain. Our results suggest that GABA co-transmission from ACh neurons is not required to maintain the regular ACh neuron count in the brain. Furthermore, we report that a large subset of ACh neurons can potentially synthesize GABA by co-expressing the marker Gad2. However, most of these ACh neurons do not express vGAT, which would enable these neurons to release GABA. Based on the overlap of fluorescent reporter signals, we propose that GABA co-transmission likely occurs only from a small population of ACh neurons restricted to few brain nuclei. *The other authors are researchers from the National Institute of Environmental Health Sciences, the Center on Compulsive Behaviors at the National Institutes of Health, and Systems Neuroscience Imaging Resource at the National Institute of Mental Health.*

Stroke and Diabetes in Adults

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: December 2025). *Excerpt:* Diabetes is a risk factor for both incident and recurrent stroke. Stroke etiology in persons with diabetes is similar to that in the general population and is often associated with large artery atherosclerosis, cardioembolism, and cerebral small vessel disease. A unique feature of stroke in persons with diabetes is that they tend to have more subclinical strokes and different magnetic resonance imaging

characteristics of stroke, including more white matter hyperintensities, lacunar infarcts, and other evidence of small vessel disease in the brain. Standard vascular risk factors, including hypertension, smoking, dyslipidemia, and atrial fibrillation, increase the risk of stroke among individuals with both type 1 and 2 diabetes, and treatment of hypertension is a cornerstone of stroke prevention in persons with diabetes. Diabetes-specific stroke risk factors include hyperglycemia, glycemic variability, metabolic syndrome and insulin resistance, albuminuria, and diabetic retinal diseases. Other predictors of stroke risk among persons with diabetes include proteomic biomarkers, obstructive sleep apnea, and autonomic neuropathy. While epidemiologic studies have found an association between hyperglycemia and stroke risk, randomized clinical trials of intensive glycemic control have not demonstrated a reduction in stroke risk. However, specific glycemic control agents, including the glucagon-like peptide-1 analogues semaglutide and dulaglutide, have been shown to reduce stroke risk in high-risk persons with type 2 diabetes. Further, a thiazolidinedione has been shown to reduce risk of recurrent stroke among persons with type 2 diabetes (PROactive trial) and to prevent recurrent cardiovascular disease events in patients with recent stroke or transient ischemic attack with insulin resistance but not diabetes. Diabetes is associated with higher post-stroke mortality and worse neurologic and functional outcomes, although results have not been consistent across all studies. Despite higher degree of hyperglycemia being associated with worse outcomes in epidemiologic studies, intensive glucose control following an acute ischemic stroke has not been shown to improve outcomes compared with standard glucose control.

Prevalence and Incidence of Type 1 Diabetes Among Children and Adults in the United States and Comparison With Other Countries

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: December 2025). *Excerpt:* Type 1 diabetes is one of the most common chronic diseases of childhood in the United States, although it can manifest at any age. In 2017, based on data from the SEARCH for Diabetes in Youth study (SEARCH), the overall prevalence of type 1 diabetes among U.S. youth age <20 years was 215 cases per 100,000 population. Type 1 diabetes prevalence was similar by sex but increased with age. In 2017–2018, the annual incidence of type 1 diabetes in youth <20 years was 22.2 per 100,000, representing an annual increase of 2.02% since 2002–2003. Among non-U.S. youth, the prevalence of type 1 diabetes varies widely and was lowest in Burkina Faso, Africa (1.76 per 100,000 in 2022) and highest in Qatar, in the Middle East (386.2 per 100,000 in 2018–2020). In 2022, the lowest incidence was reported in Burkina Faso, Africa (0.34 per 100,000) and the highest in Sardinia, Italy (76.3 per 100,000). Compared to data in youth, data on the prevalence and incidence of type 1 diabetes in U.S. adults are very limited. According to the National Health Interview Survey (NHIS), the prevalence of type 1 diabetes in adults age ≥20 years in 2019–2023 was 390 per 100,000 population. The higher prevalence in adults compared to children is expected, as it comprises individuals diagnosed in both childhood and adulthood. Furthermore, recent data suggest that type 1 diabetes incidence in adults may be at least as high as in children, challenging the historical belief that type 1 diabetes is primarily a childhood disease. Specifically, data from a California healthcare system database estimated that the annual incidence in adults age 20–45 years was 30.1 per 100,000 population in 2017 and was higher in men (32.5 per 100,000) compared with women (27.2 per 100,000). Additional studies on incidence in adults are critically needed to better understand the growing burden of type 1 diabetes in the United States. Among non-U.S. regions reporting data on the incidence of type 1 diabetes among adults, overall rates ranged from 3.84 per 100,000 in China (2021) to 32.07 per 100,000 per year in Ireland (2011–2016). Although vital for determining the burden of type 1 diabetes in the population and guiding effective prevention and control strategies, surveillance of type 1 diabetes faces challenges, particularly given the absence of standardized case definitions and consistent ascertainment methodologies. Administrative and electronic health record databases may serve as tools for estimating diabetes incidence and prevalence; however, while these databases offer promising opportunities, their reliability and validity remain uncertain and require further investigation. Ultimately, standardizing diabetes classification and improving data ascertainment are critical steps toward

improving our understanding of the growing burden of type 1 diabetes and developing effective mitigation strategies.

Diabetes in Children and Adolescents
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: December 2025). *Excerpt:* Diabetes is one of the most common chronic diseases among children and adolescents under age 20 years in the United States. Classifying diabetes in youth as either type 1 or type 2 is challenging, especially as obesity—once associated primarily with type 2 diabetes—is now common in youth with type 1 diabetes. Between 2001 and 2017, the estimated prevalence of type 1 diabetes in U.S. youth increased by 45%, with the largest increases among non-Hispanic White and non-Hispanic Black youth. During the same period, the prevalence of type 2 diabetes increased by 95%, with the largest increases among non-Hispanic Black and Hispanic youth. Risk factors for type 1 diabetes include genetics, particularly the human leukocyte antigen (HLA) region, as well as environmental factors such as viruses and early-life diet and growth. Type 2 risk factors include genetics, intrauterine exposure to maternal obesity and diabetes, high gestational weight gain, and postnatal obesity. Youth with type 2 diabetes often experience complications that are more severe compared to those with type 1 diabetes at the same age and disease duration, as well as compared to people with adult-onset type 2 diabetes. Cardiovascular disease risk factors, such as high blood pressure and abnormal lipids, appear shortly after type 2 diabetes diagnosis, especially in youth of non-White racial and ethnic backgrounds. As more youth develop diabetes, especially in disadvantaged populations, addressing disparities in care and preventing complications are critical to reducing both health and economic burdens.

Sit to Stand and Timed Up and Go in Idiopathic Inflammatory Myopathies
DLH researcher **Jesse Wilkerson** was among the authors of an article published in *Scientific Reports* (Online Ahead of Print: December 2025). Idiopathic inflammatory myopathies can significantly impair physical function, of which Sit to Stand (STS) and Timed Up and Go (TUG) are quick, operator-independent measures. The authors aimed to evaluate psychometric properties of STS and TUG compared to established core set measures of disease activity; and assess feasibility of patients self-performing these tests remotely. Data from a 6-month prospective observational study (Myositis Patient Centered Tele-Research Study -My PACER) were analyzed. Patient-reported and functional assessments were collected monthly over 6 months. A total of 120 patients (75% female, 81% White, mean age 55.5 ± 13.4 years,52% Dermatomyositis, 39% Polymyositis, 9% Necrotizing Myopathy) participated. There was strong test-retest reliability between baseline and month one for STS and TUG. At baseline, STS and TUG showed a very strong correlation with each other and with most core set measures (CSMs). Strong correlations were seen with Muscle Disease Activity and a validated Patient Reported Outcome measure of physical function, PROMIS-PF 20. At 6 months, STS and TUG were significantly better among patients who improved according to Total Improvement Score. STS and TUG showed good reliability, even when self-performed remotely using video instructions, with excellent construct validity and responsiveness. *The other authors include researchers from the University of Pittsburgh and Massachusetts General Hospital.*

Virological and Drug-Resistance Outcomes for People Living With HIV Initiating or Switching to Tenofovir, Lamivudine, and Dolutegravir in Six PEPFAR-Supported Countries: A Prospective Cohort Study
DLH researcher **Elizabeth Woolley** was among the authors of an article published in *The Lancet HIV* (Online: December 2025). A combined regimen of tenofovir disoproxil fumarate, lamivudine, and dolutegravir is widely prescribed for people living with HIV in programs supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). This study aimed to assess long-term virological and drug-resistance outcomes in response to initiation of or switching to the tenofovir-lamivudine-dolutegravir combination among individuals receiving

care through such programs. The Advancing Clinical Therapeutics Globally (ACTG) A5381-Hakim Study was a prospective cohort study of participants aged 10 years or older initiating or switching to tenofovir-lamivudine-dolutegravir therapy at 13 PEPFAR-supported sites in Haiti, Kenya, Malawi, South Africa, Uganda, and Zimbabwe. Group 1 switched from non-nucleoside reverse transcriptase inhibitor-based antiretroviral therapy (ART), group 2 switched from protease inhibitor-based ART, and group 3 was ART-naive; before switching, group 1A and group 2A had HIV-1 RNA of more than 1000 copies per mL and group 1B and group 2B had 1000 copies per mL or less. Viral suppression (HIV-1 RNA ≤1000 copies per mL), emergence of dolutegravir-resistance mutations, and adverse events were assessed up to 36 months. Adherence, based on tenofovir diphosphate concentrations in dried blood spots, was evaluated in a nested case-control study. *Findings:* Between October 28, 2019, and September 27, 2022, 1241 participants were enrolled in the study, four of whom were excluded (two in group 2B who started tenofovir-lamivudine-dolutegravir before enrolment and two in group 3 who did not start tenofovir-lamivudine-dolutegravir). Therefore, 1237 participants were included in the full analysis population: 44 in group 1A, 425 in group 1B, 173 in group 2A, 416 in group 2B, and 179 in group 3. 65% were female, 35% were male. 12 (1%) participants discontinued tenofovir-lamivudine-dolutegravir therapy because of adverse events. Among participants for whom viral load data were available and who did not discontinue tenofovir-lamivudine-dolutegravir before viral load measurement, HIV-1 RNA of 1000 copies per mL or less was recorded in 88% (37 of 42 participants) at 6 months and 76% (16 of 21 participants) at 24 months in group 1A; 99% (380 of 384 participants) and 98% (368 of 375 participants) in group 1B; 72% (118 of 165 participants) and 70% (45 of 64 participants) in group 2A; 95% (376 of 395 participants) and 93% (190 of 204 participants) in group 2B; and 90% (136 of 151 participants) and 90% (128 of 143 participants) in group 3. Mutations associated with decreased dolutegravir susceptibility were detected in three participants in group 2A (G118R, R263K) and in no participants in the other groups. Of 87 case-control pairs analyzed at 6 months, tenofovir diphosphate concentrations were lower among participants with HIV-1 RNA of more than 1000 copies per mL than among those with 1000 copies per mL or less. High rates of viral suppression in response to tenofovir-lamivudine-dolutegravir therapy in individuals who had suppression before switching support international treatment guidelines for this population. Findings on resistance mutations and tenofovir diphosphate concentrations suggest that incomplete adherence was a key factor in the suboptimal outcomes of people with virological failure at the time of switching treatment. *The other authors include researchers from the Harvard T.H. Chan School of Public Health, the Emory Rollins School of Public Health, the Division of Infectious Diseases at the University of Pittsburgh, as well as researchers from institutes in Haiti, South Africa, Uganda, Malawi, Kenya, and Zimbabwe.*

Association of Oil Spill Cleanup-Related Hydrocarbon Exposure With Incident Hypertension Up to 11 Years After Exposure in the Gulf Long-Term Follow-Up Study

DLH researchers **Kate Christenbury** and **Braxton Jackson** were among the authors of an article published in *Environmental Health* (Online: December 2025). While several studies have found positive associations between exposure to oil spill cleanup-related chemicals and hypertension, no study has examined these associations longitudinally. This study examined associations of oil spill-related benzene, toluene, ethylbenzene, xylene, and n-hexane (BTEX-H) exposures, individually and as both the aggregate sum (total) of BTEX-H and the BTEX-H mixture with incident hypertension among Gulf Long-term Follow-up (GuLF) Study participants. Participants were 18,619 Deepwater Horizon (DWH) oil spill cleanup and response workers who enrolled in the GuLF Study (2011-2013). Cumulative exposures to each BTEX-H chemical were estimated with a job-exposure matrix linking detailed self-reported DWH participant work histories to exposure group estimates developed from air monitoring data. The authors defined incident hypertension as the first self-reported physician diagnosis of hypertension or high blood pressure after each worker's last date of cleanup work, as reported at enrollment or a follow-up interview (2013-2016 or 2017-2021). Approximately 20% (n = 3,779) of workers reported an incident hypertension diagnosis. Exposures to the individual BTEX-H chemicals were highly correlated (r = 0.87-0.95). The HRs comparing the highest to lowest quartiles of individual BTEX-H and total BTEX-H exposures ranged from 1.27 to 1.35. The authors found evidence of exposure-response trends across increasing quartiles of exposure. Each one quartile increase in the BTEX-H mixture was positively associated with incident hypertension. Oil spill cleanup work-related BTEX-H exposures were associated

with the risk of incident hypertension, extending prior findings of cross-sectional associations. Since BTEX-H exposures are common in occupational and population settings, these findings may have broader public health implications. *The other authors include researchers from the UNC Gillings School of Public Health in Chapel Hill, the Epidemiology Branch of the National Institute of Environmental Health Sciences, and the UNC School of Medicine.*

Trends in Delaying and Forgoing Medical Care Due to Cost and the Association With Insurance Status Among US Adults With Diabetes, 2009-2023

DLH researcher **Sarah Casagrande** was the lead author of an article published in *BMJ Open Diabetes Research & Care* (Online: December 2025). Adults with diabetes require regular medical care that can be costly, but little is known about factors associated with delaying or forgoing medical care due to cost among US adults with diabetes. Data were from the 2009-2010, 2014-2015, and 2022-2023 cycles of the cross-sectional National Health Interview Survey and included participants age ≥18 years who self-reported a physician diagnosis of diabetes. Among US adults aged 18-64 years with diabetes, delaying or forgoing medical care due to cost decreased from 18.1% to 10.6% and from 14.6% to 10.2%, respectively, between 2009 and 2023. In 2022-2023, the prevalence of delaying medical care due to cost for adults aged 18-64 years was highest for non-Hispanic black adults (13.3%), those with a high school education or less and poverty income ratio <4.0 (12%-13%). In 2022-2023, uninsured adults ≥18 years were significantly more likely to delay medical care compared with those who were insured (adjusted OR =7.5, 4.8-11.8, age 18-64 years [adjusted for sociodemographic and clinical characteristics]). Adults aged 18-64 years with Medicaid were significantly less likely to delay medical care compared with those who had private insurance. There was a decreasing trend for delaying or forgoing medical care across all subpopulations, but adults with lower education and income and who were uninsured more often reported delays in medical care due to cost. The expansion of Medicaid may have reduced the likelihood of delaying or forgoing medical care due to cost among adults aged 18-64 years with Medicaid coverage. *The other author is a researcher from the National Institute of Diabetes and Digestive and Kidney Diseases.*

The Investigation of Vitamin D and Menstrual Cycles Trial (the inVitD Trial): A Clinical Trial of Vitamin D Supplementation on the Hypothalamic-Pituitary-Ovarian Axis

DLH researchers **Olivia Kohrman** and **Braxton Jackson** were among the authors of an article published in *Contemporary Clinical Trials* (Epub: December 2025; Online: January 2026). While there is evidence that vitamin D deficiency is associated with long menstrual cycles, delayed ovulation, and reduced fertility, it is yet unknown if increasing vitamin D levels can regulate menstrual cycles, and thus possibly improve fertility. The primary objective of this randomized clinical trial (RCT) is to test the hypothesis that vitamin D supplementation influences the hypothalamic-pituitary-ovarian axis. This two-site RCT (NCT05050916) required participants to be aged 19-40 years old, having spontaneous menstrual cycles, and without certain chronic diseases or contraindications for vitamin D supplementation. At baseline participants provided information on their demographics and health history. Blood was drawn at the first clinic visit after which participants collected daily urine samples for one menstrual cycle (phase 1). Those with a 25-hydroxyvitamin D level less than 20 ng/ml ("low") received cholecalciferol supplementation (randomized to either 4200 IU/week or 50,000 IU/week). A random sample of those without low vitamin D received placebo. Supplement (or placebo) was taken for three menstrual cycles which included collection of daily urine samples and home ovulation testing (phase 2). Participants collected self-administered vaginal and oral swabs and a subset collected menstrual effluent samples. Finally, participants kept a daily menstrual diary and weekly behavior diaries. The primary endpoints were mid-luteal progesterone, rate of estrogen rise, and pre-ovulatory luteinizing hormone. Findings from this RCT will provide insight into the relationship between vitamin D supplementation and menstrual cycle hormones. Vitamin D shows promise as a low-cost, non-hormonal intervention to regulate menstrual cycles. *The other authors include researchers from the National Institute of Environmental Health Sciences and the University of North Carolina at Chapel Hill.*

Power Calculations for Larval Zebrafish in Light-Dark Transition Test for Developmental Neurotoxicity

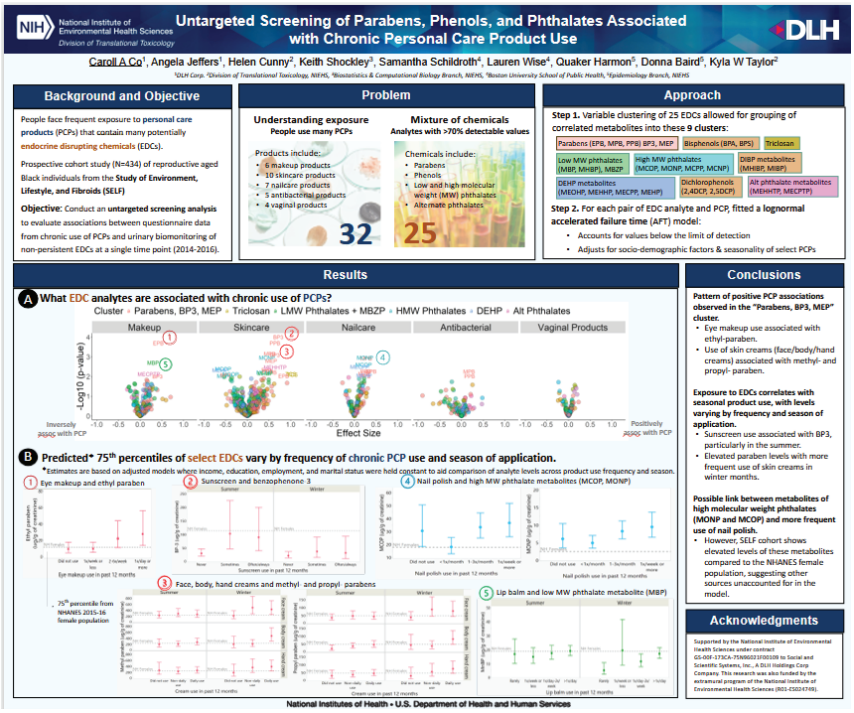
DLH researchers **Kathryn Konrad** and **Katherine Allen-Moyer** were among the authors of an article published in *Neurotoxicology* (Epub: December 2025; Online: January 2026). The link between environmental chemical exposures and neurodevelopmental disorders such as autism and attention-deficit/hyperactivity disorder underscores the need to develop efficient developmental neurotoxicity (DNT) assays for chemical evaluation. The zebrafish Light-Dark Transition Test (LDTT) assesses changes in zebrafish larval behavioral responses to chemical exposure by recording their distance moved under alternating light and dark conditions. To gain confidence in classifying a chemical as having a DNT effect for the LDTT assay, it is important to determine the minimum sample size to obtain a robust behavioral response. The authors calculated statistical power under common models based on LDTT data collected from four laboratories using standard protocol parameters, where each 96-well plate contained 5-7 test concentrations and 12-16 vehicle control wells (1 larva/well). Power calculations were conducted to identify concentration effects using t-tests, analysis of variance (ANOVA), and repeated measures ANOVA (RMANOVA), with data from four endpoints: Total Distance, Movement Similarity, Distance Change, and Distance Shift. The tests showed the highest power for the Movement Similarity and Distance Change endpoints, which had the lowest intra- and inter-laboratory variability, resulting in a smaller necessary sample size to estimate dose effects. The use of these endpoints more than doubled the power of the statistical tests for the Total Distance endpoints using the same sample size and typically required between 8 and 32 samples to achieve 80% power at a 20% effect size. This work demonstrates that the LDTT can be improved for detecting DNT effects by careful consideration of endpoint selection, data transformation, and type of statistical test. *The other authors are researchers from the National Research Council of Canada (Halifax, NS), the National Institute for Public Health and the Environment (Utrecht, the Netherlands), BBD BioPhenix SLU (Spain), ZeClinics SL (Spain), Oregon State University, and the National Institute of Environmental Health Sciences.*

Risk of Spontaneous Miscarriage by Gestational Week Among 12,390 Pregnancies From Six Pooled Cohort Studies of Pregnancy Planners Not Using Assisted Reproductive Technologies (ART)

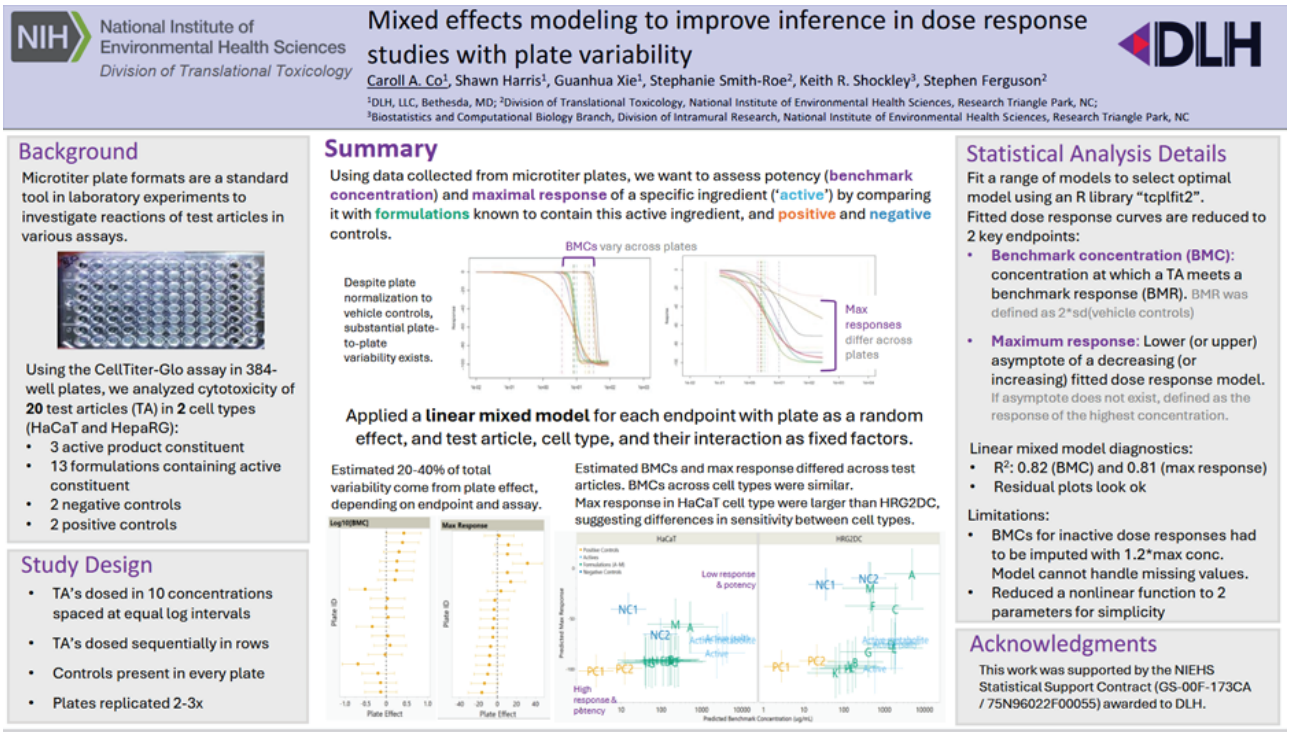
DLH researchers **Sheri Denslow** and **Gary Larson** were among the authors of an abstract published in *Fertility and Sterility* (Online: December 2025). *Objective:* Estimate risk of miscarriage (spontaneous intrauterine pregnancy loss <20 weeks of gestational age [GA]). GA was defined as: 1) weeks since last menstrual period (LMP) and 2) weeks since ovulation. *Materials and Methods:* Individual-level data were pooled from: the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial, the Early Pregnancy Study (EPS), the Longitudinal Investigation of Fertility and the Environment (LIFE), Pregnancy Study Online (PRESTO), Right from the Start (RFTS), and Time to Conceive (TTC). Each study enrolled participants early in their pregnancy attempt and not using ART, followed them for conception, and if they conceived, collected pregnancy outcome and timing via self-reported questionnaires, ultrasounds, or medical record abstraction. Pregnancies with known outcome type and GA, and timing of positive pregnancy test (PPT, at home or lab) were included. Ovulation was estimated using an ovulation predictor kit (TTC), a fertility monitor (LIFE, EAGeR), or with lab assays (EPS). Week-specific probability (risk) of miscarriage was calculated as the number of pregnancies ending each week divided by the number of pregnancies at risk at the start of that week, defined as a PPT prior to or in that week. *Results:* In 12,390 pregnancies, there were 2,635 spontaneous miscarriages. The median time from LMP to PPT was 4 weeks (25th, 75th percentiles: 3, 4) in all studies except EPS which was 3 weeks (25th, 75th: 3, 4). The risk of miscarriage was highest at ≤6 weeks from LMP (4%), then declined until weeks 13-19, where it was less than 0.5%. By ovulation, risk of miscarriage was highest at ≤2 weeks GA (8%) with a steep decline at week 3 and became less than 0.5% at weeks 11-17. In EPS, with early, sensitive, daily hCG assays, risk was 20% at ≤2 weeks from ovulation. *Conclusions:* Miscarriage risk was highest at very early GA when pregnancy recognition is typically low, indicating that clinic-based samples would underestimate risk. Lab-based PPTs will identify more miscarriages at earlier GA than couples would observe at home. *Impact Statement:* This is the largest analysis of spontaneous miscarriage risk at early GA in pregnancy planners. These data are important for clinician and patient education and counseling.

DLH Research Posters and Presentations

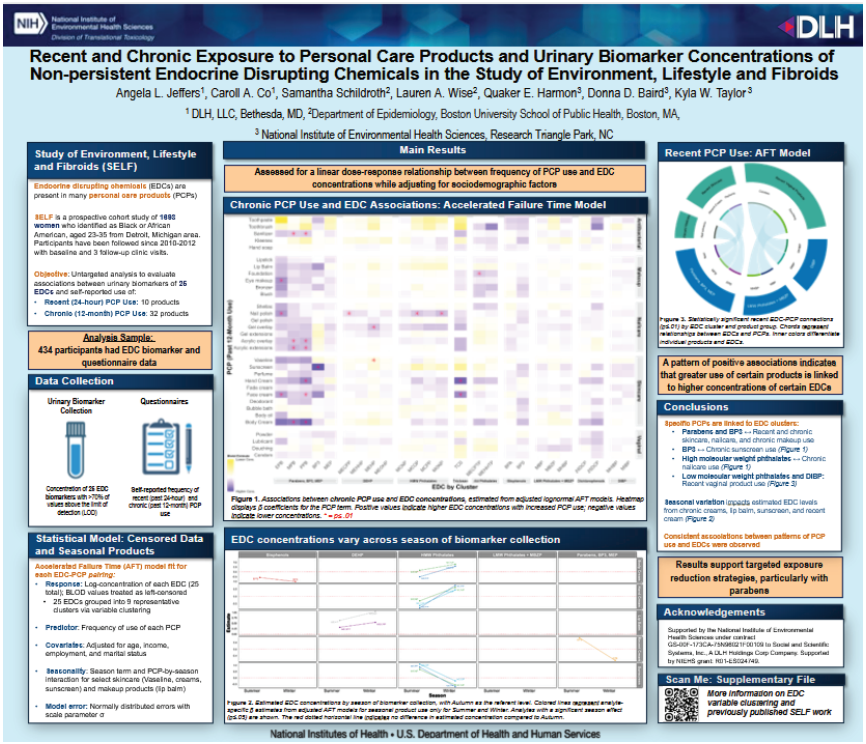
• **Caroll Co** and **Angela Jeffers** were DLH coauthors on, and **Caroll Co** presented, the poster, "Untargeted Screening of Parabens, Phenols, and Phthalates Associated with Chronic Personal Care Product Use," at The Division of Translational Toxicology (DTT, NIEHS) Poster Day 2025.



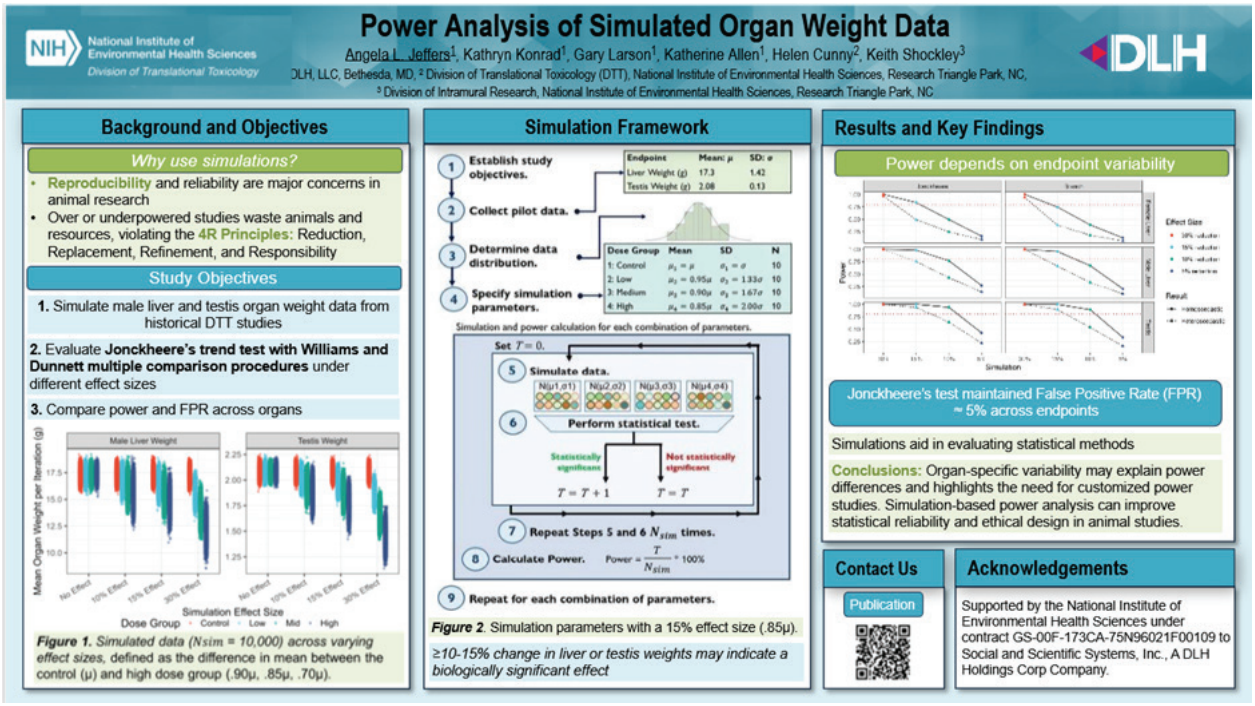
• **Caroll Co**, **Shawn Harris**, and **Guan Xie** were DLH coauthors on, and **Caroll Co** presented, the poster, "Mixed Effects Modeling to Improve Inference in Dose Response Studies with Plate Variability," at the Joint Statistical Meetings (JSM) 2025.



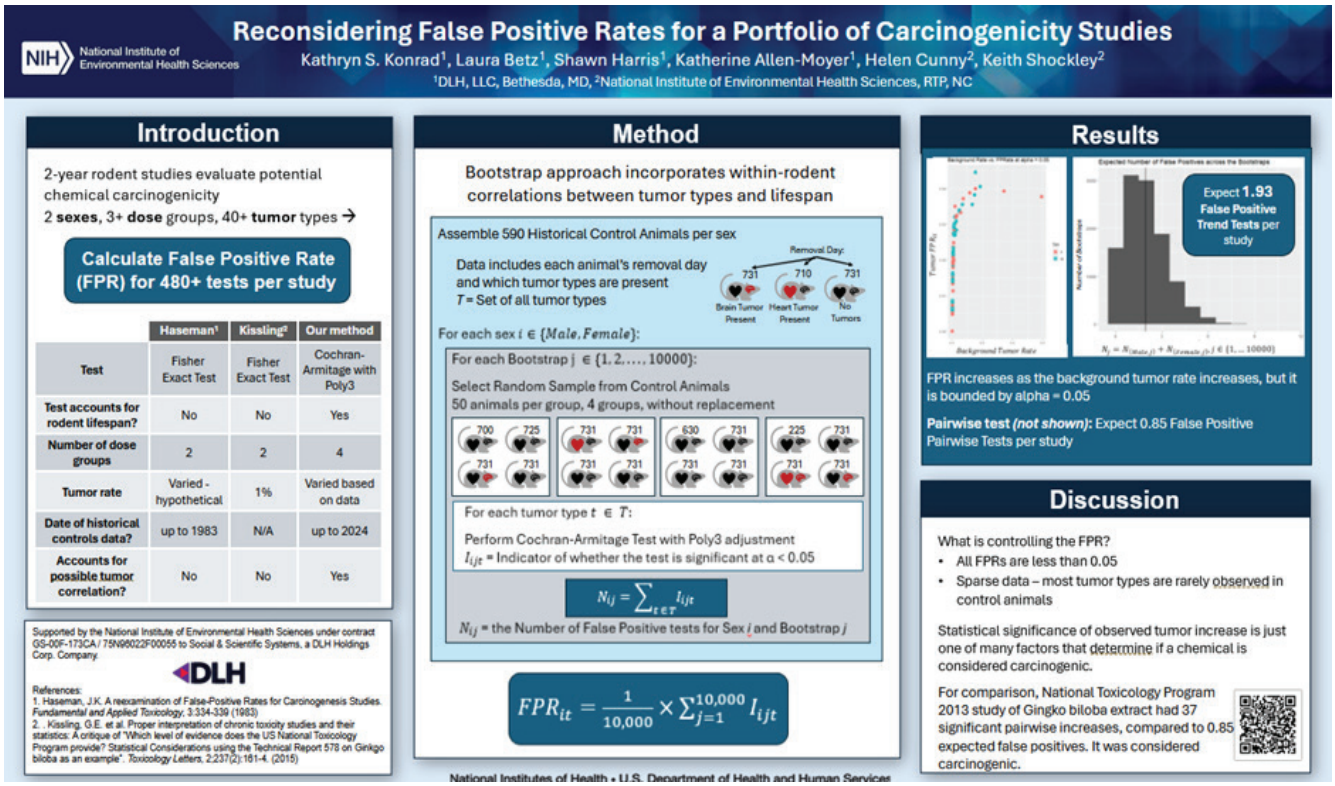
• **Angela Jeffers** and **Caroll Co** were DLH coauthors on, and **Angela Jeffers** presented, the poster, "Recent and Chronic Exposure to Personal Care Products and Urinary Biomarker Concentrations of Non-persistent Endocrine Disrupting Chemicals in the Study of Environment, Lifestyle, and Fibroids," at the Society for Epidemiologic Research (SER) 2025.



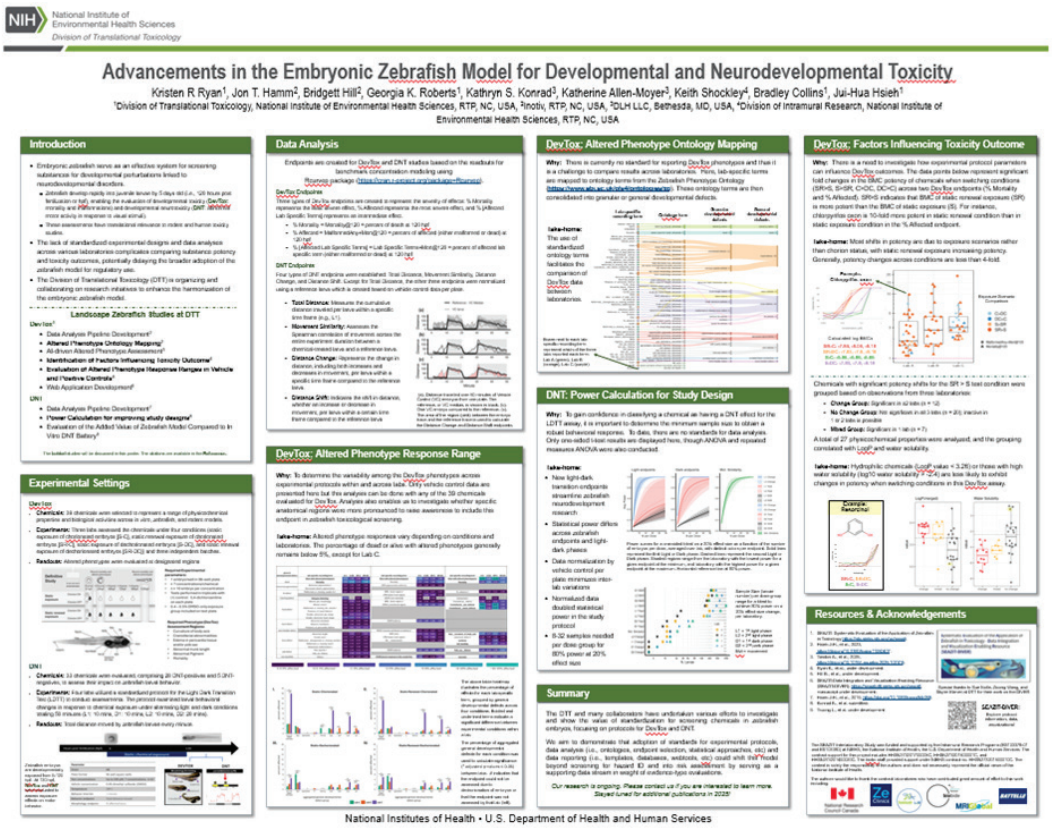
• **Angela Jeffers**, **Kate Konrad**, **Gary Larson**, and **Katherine Allen** were DLH coauthors on, and **Angela Jeffers** presented, the poster, "Power Analysis of Simulated Organ Weight Data," at the Joint Statistical Meetings (JSM) 2025.



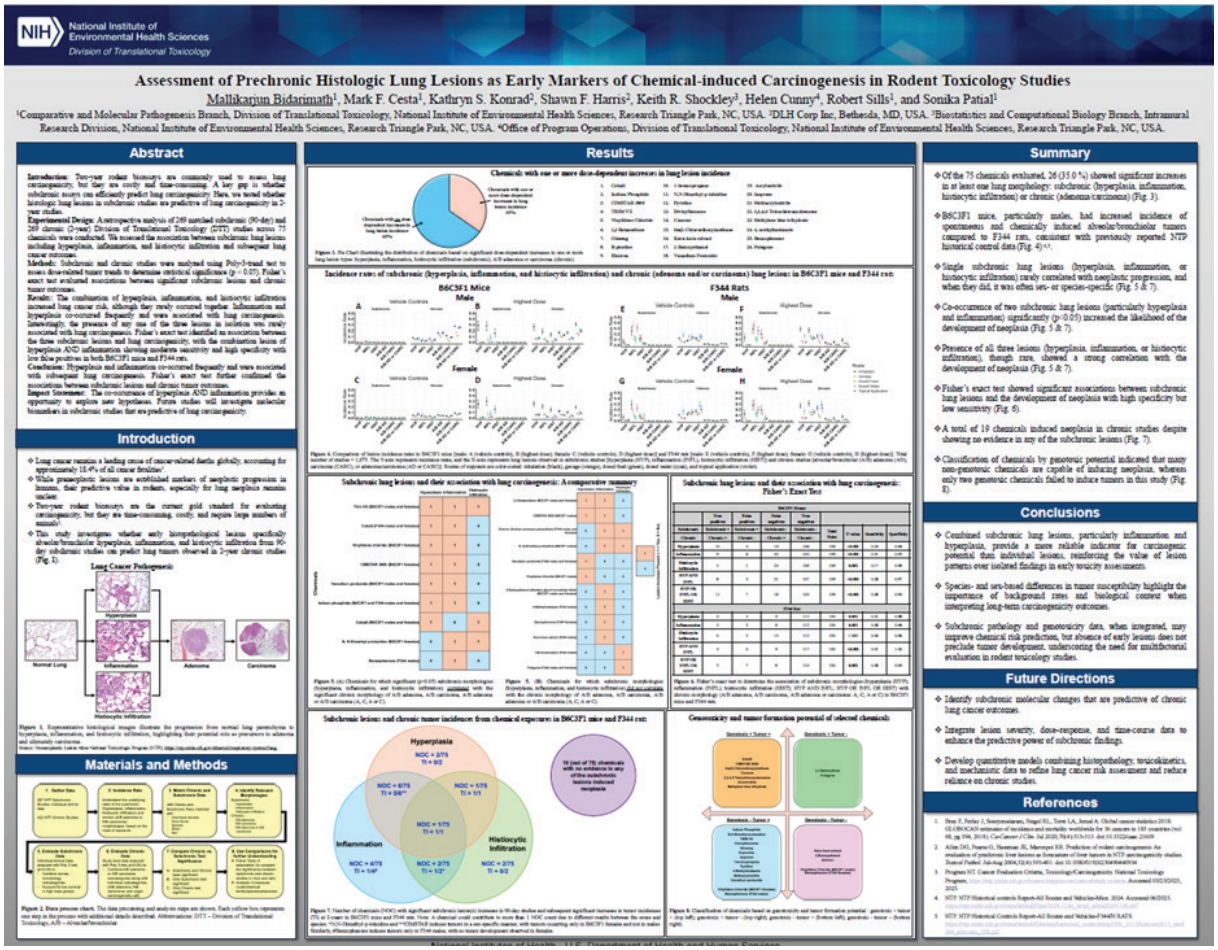
• **Kate Konrad**, **Laura Betz**, **Shawn Harris**, and **Katherine Allen** were DLH coauthors on, and **Kate Konrad** presented, the poster, "Reconsidering False Positive Rates for a Portfolio of Carcinogenicity Studies," at the Joint Statistical Meetings (JSM) 2025.



• **Kate Konrad** and **Katherine Allen** were DLH coauthors on the NIEHS poster, "Advancements in the Embryonic Zebrafish Model for Developmental and Neurodevelopmental Toxicity," presented at the Birth Defects Research/Developmental Neurotoxicity Society combined meeting and the NIEHS Summer Science Day 2025.



• **Kate Konrad** and **Shawn Harris** were DLH coauthors on the NIEHS poster, "Assessment of Prechronic Histologic Lung Lesions as Early Markers of Chemical-Induced Carcinogenesis in Rodent Toxicology Studies," presented at the Society for Toxicologic Pathology Annual Symposium and the NIEHS Summer Science Day 2025.

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