# Office of Research

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CENTER FOR GLOBAL HEALTH



<u>Early diagnostic indicators of dengue versus other febrile illnesses in Asia and Latin</u>

<u>America (IDAMS study): a multicentre, prospective, observational study</u>

Rosenberger, K; Khanh, LP; Tobian, F; Chanpheaktra, N; Kumar, V; Lum, LCS; Sathar, J; Sandoval, EP; Maron, GM; Laksono, IS; Mahendradhata, Y; Sarker, M; Rahman, R; Caprara, A; Benevides, BS; Marques, ETA; Magalhaes, T; Brasil, P; Calvet, GA; Tami, A; Bethencourt, SE; Hoai, TDT; Thanh, KNT; Van, NT; Tran, NN; Do Chau, V; Yacoub, S; Van, KN; Guzman, MG; Martinez, PA; Ha, QNT; Simmons, CP; Wills, BA; Geskus, RB; Jaenisch, T

Lancet Global Health

Improvements in the early diagnosis of dengue are urgently needed, especially in resource-limited settings where the distinction between dengue and other febrile illnesses is crucial for patient management. This prospective, observational study (IDAMS) included patients aged 5 years and older with undifferentiated fever at presentation from 26 outpatient facilities in eight countries (Bangladesh, Brazil, Cambodia, El Salvador, Indonesia, Malaysia, Venezuela, and Viet Nam). Multivariable logistic regression was used to investigate the association between clinical symptoms and laboratory tests with dengue versus other febrile illnesses. Platelet count, white blood cell count, and the change in these variables from the previous day of illness had a strong association with dengue. Cough and rhinitis had strong associations with other febrile illnesses, whereas bleeding, anorexia, and skin flush were generally associated with dengue. Model performance increased between day 2 and 5 of illness. The results confirm the important role of platelet and white blood cell counts in diagnosing dengue, and the importance of serial measurements over subsequent days. This study successfully quantified the performance of clinical and laboratory markers covering the early period of dengue. These results provide crucial information needed for the update of quidelines, including the Integrated Management of Childhood Illness handbook.

## LIFECOURSE EPIDEMIOLOGY OF ADIPOSITY & DIABETES CENTER

### <u>Comparing the Diagnostic Accuracy of Measures of Maternal Diet During Pregnancy for Offspring Allergy Outcomes: The Healthy Start Study</u>

Venter, C; Palumbo, MP; Glueck, DH; Sauder, KA; Perng, W; O'Mahony, L; Pickett, K; Greenhawt, M; Fleischer, DM; Dabelea, D

Journal of Allergy and Clinical Immunology-In Practice

Allergic diseases in children are increasing. Although maternal diet quality in pregnancy may be protective, it is unclear which measure of maternal diet best predicts offspring diseases. The objective of this study was to examine the associations between multiple diet measures and allergy outcomes, and to compare the diagnostic accuracy of the measures for the prediction of allergy outcomes. Maternal diet during pregnancy was measured using a validated instrument, and scored using 5 measures: the maternal diet index (MDI), Healthy Eating Index, total diet diversity, healthy diet diversity, and unhealthy diet diversity. The study found that better quality and higher diversity of a woman's diet during pregnancy, measured in various ways, is associated with offspring allergy outcomes, with healthy foods associated with decreased risk, and unhealthy foods associated with a higher risk. Of the various measures used to assess maternal diet, the maternal diet index, which appropriately weighted both healthy and unhealthy foods, best predicted childhood allergic disease.

#### ENVIRONMENTAL & OCCUPATIONAL HEALTH

#### Source apportionment of serum PFASs in two highly exposed communities

Wallis, DJ; Barton, KE; Knappe, DRU; Kotlarz, N; McDonough, CA; Higgins, CP; Hoppin, JA; Adgate, JL Science of the Total Environment

Per-and polyfluoroalkyl substances (PFASs) are synthetic chemicals that are ubiquitous in environmental and biolog-ical systems, including human serum. PFASs are used in many products and industrial processes and are tied to numer-ous health effects. Due to multiple sources and exposure pathways, methods are needed to identify PFAS sources in communities to develop targeted interventions. The researchers assessed effectiveness of three source apportionment methods (UNMIX, positive matrix factorization [PMF], and principal component analysis -multiple linear regression [PCA-MLR]) for identifying contributors to human serum PFAS concentrations in two highly exposed populations in Colorado and North Carolina where drinking water was contaminated via upstream sources, including a Space Force base and a fluorochemical manufacturing plant. UNMIX and PMF models extracted three to four potential PFAS exposure sources in the Colorado and North Carolina cohorts while PCA-MLR classified two in each cohort. No sources were characterized in NHANES (National Health and Nutrition Examination Study). Results suggest that these three methods can successfully identify sources in highly exposed populations. Future PFAS exposure research should focus on analyzing serum for an expanded PFAS panel, identifying cohorts with other distinct point source exposures, and combining biological and environmental data to better understand source apportionment results in the context of PFAS toxicokinetic behavior.

#### **EPIDEMIOLOGY**

#### <u>An Oxylipin-Related Nutrient Pattern and Risk of Type 1 Diabetes in the Diabetes</u> <u>Autoimmunity Study in the Young (DAISY)</u>

Buckner, T; Johnson, RK; Vanderlinden, LA; Carry, PM; Romero, A; Onengut-Gumuscu, S; Chen, WM; Fiehn, O; Frohnert, BI; Crume, T; Perng, W; Kechris, K; Rewers, M; Norris, JM
Nutrients

Oxylipins, pro-inflammatory and pro-resolving lipid mediators, are associated with the risk of type 1 diabetes (T1D) and may be influenced by diet. This study aimed to develop a nutrient pattern related to oxylipin profiles and test their associations with the risk of T1D among youth. The nutrient patterns were developed with a reduced rank regression in a nested case-control study within the Diabetes Autoimmunity Study in the Young (DAISY), a longitudinal cohort of children at risk of T1D. The oxylipin profiles (adjusted for genetic predictors) were the response variables. The nutrient patterns were tested in the case-control study, then validated in the DAISY cohort using a joint Cox proportional hazards model. The first nutrient pattern (NP1) was characterized by low beta cryptoxanthin, flavanone, vitamin C, total sugars and iron, and high lycopene, anthocyanidins, linoleic acid and sodium. After adjusting for T1D family history, the HLA genotype, sex and race/ethnicity, NP1 was associated with a lower risk of T1D in the nested case-control study. NP1 was not associated with the risk of T1D in the full DAISY cohort. Future studies are needed to confirm the nested case-control findings and investigate the modifiable factors for oxylipins.

### CENTERS FOR AMERICAN INDIAN & ALASKA NATIVE HEALTH

### <u>American Indian Alaska Native (AIAN) adolescents and obesity: the influence of social determinants of health, mental health, and substance use</u>

Johnson-Jennings, MD; Reid, M; Jiang, LH; Huyser, KR; Brega, AG; Steine, JF; Manson, SM; Chang, JY; Fyfe-Johnson, AL; Hiratsuka, V; Conway, C; O'Connell, J International Journal of Obesity

The objective of this study was to explore the prevalence of obesity among American Indian and Alaska Native (AIAN) adolescents aged 12-19 years in association with social determinants of health (SDOH), and mental health and substance use disorders. Guided by the World Health Organization's Social Determinants of Health Framework, the researchers examined data from the Indian Health Service (IHS) Improving Health Care Delivery Data Project from Fiscal Year 2013, supplemented by county-level data from the U.S. Census and USDA. They observed a prevalence of 32.5% for obesity, 13.8% for mental health disorders, and 5.5% for substance use disorders. Females had lower odds of obesity than males, which decreased with age. Having Medicaid coverage, residing in a county with lower education attainment, and residing in a county with higher rates of poverty were each associated with higher odds of obesity. Residing in a county with high access to a grocery store and residing in a county with a higher proportion of AIANs were each associated with lower odds of obesity. Those with mental health disorders had higher odds of obesity; substance use disorders were associated with decreased odds of obesity. These findings inform future obesity prevention and treatment programs among AIAN youth; in particular, the need to consider mental health, substance use, and SDOH.

#### **COLORADO STATE UNIVERSITY**

### <u>The COVID-19-wildfire smoke paradox: Reduced risk of all-cause mortality due to wildfire smoke in Colorado during the first year of the COVID-19 pandemic</u>

Martenies, SE; Wilson, A; Hoskovec, L; Bol, KA; Burket, TL; Podewils, LJ; Magzamen, S Environmental Research

In 2020, the American West faced two competing challenges: the COVID-19 pandemic and the worst wildfire season on record. Several studies have investigated the impact of wildfire smoke (WFS) on COVID-19 morbidity and mortality, but little is known about how these two public health challenges impact mortality risk for other causes. Using a time-series design, the researchers evaluated how daily risk of mortality due to WFS exposure differed for periods before and during the COVID-19 pandemic. They found that WFS impacted the study area on 10% of county-days. They observed a positive association between the presence of WFS and all-cause mortality risk during the period before the pandemic; however, WFS exposure during the pandemic resulted in decreased risk of all-cause mortality. The researchers hypothesize that mitigation efforts during the first year of the pandemic, e.g., mask mandates, along with high ambient WFS levels encouraged health behaviors that reduced exposure to WFS and reduced risk of all-cause mortality. The results suggest a need to examine how associations between WFS and mortality are impacted by pandemic-related factors and that there may be lessons from the pandemic that could be translated into health-protective policies during future wildfire events.

#### **INJURY & VIOLENCE PREVENTION CENTER**

### <u>Geography, rurality, and community distress: deaths due to suicide, alcohol-use, and drug-use among Colorado Veterans</u>

Spark, TL; Reid, CE; Adams, RS; Schneider, AL; Forster, J; Denneson, LM; Bollinger, M; Brenner, LA Injury Epidemiology

In the USA, deaths due to suicide, alcohol, or drug-related causes (e.g., alcohol-related liver disease, overdose) have doubled since 2002. Veterans appear disproportionately impacted by growing trends. Limited research has been conducted regarding the relationship between community-level factors (e.g., rurality, community distress resulting from economic conditions) and the presence of spatial clustering of suicide, alcohol-related, or drug-related deaths. The authors explored community-level relationships in Colorado Veterans and compared suicide, alcohol-, and drug-related death rates between the Colorado adult population and Veterans. They found that 6.4% of Colorado Veteran deaths were identified as being related to suicide, alcohol, or drugs. Compared to rates in the general population of Colorado adults, Veterans had 1.8 times higher rates of such deaths overall (2.1 times higher for suicide, 1.8 times higher for alcohol-related, 1.3 times higher for drugrelated). Among Veterans, community distress was associated with an increased risk of alcohol-related and drug-related deaths. This same significant association was not identified among those that died by suicide. Rurality was not associated with risk for any of the deaths of interest. There was significant spatial clustering for alcohol-related deaths in southeast Colorado. Upstream prevention efforts, such as community-based interventions targeting alcohol-use and community economic distress, are warranted. More research is also needed to understand how community distress and other social determinants of health impact the community burden of suicide, alcohol-related, and drug-related mortality.

#### **COMMUNITY & BEHAVIORAL HEALTH**

### An artificially intelligent, natural language processing chatbot designed to promote COVID-19 vaccination: A proof-of-concept pilot study

Zhou, S; Silvasstar, J; Clark, C; Salyers, AJ; Chavez, C; Bull, SS Digital Health

The goal of this study was to establish the feasibility of using an artificially intelligent chatbot in diverse healthcare settings to promote COVID-19 vaccination. The researchers designed an artificially intelligent chatbot deployed via short message services and web-based platforms. Guided by communication theories, they developed persuasive messages to respond to users' COVID-19-related questions and encourage vaccination. They implemented the system in healthcare settings in the U.S. between April 2021 and March 2022 and logged the number of users, topics discussed, and information on system accuracy in matching responses to user intents. They regularly reviewed queries and reclassified responses to better match responses to query intents as COVID-19 events evolved. A total of 2479 users engaged with the system, exchanging 3994 COVID-19 relevant messages. The most popular queries to the system were about boosters and where to get a vaccine. The system's accuracy rate in matching responses to user queries ranged from 54% to 91.1%. Accuracy lagged when new information related to COVID emerged, such as that related to the Delta variant. Accuracy increased when new content was added to the system. It is feasible and potentially valuable to create chatbot systems using AI to facilitate access to current, accurate, complete, and persuasive information on infectious diseases. Such a system can be adapted to use with patients and populations needing detailed information and motivation to act in support of their health.

#### **HEALTH SYSTEMS, MANAGEMENT & POLICY**

### <u>Impact of state Medicaid expansion on cross-sector health and social service networks:</u> <u>Evidence from a longitudinal cohort study</u>

Hogg-Graham, R; Mamaril, CB; Benitez, JA; Gatton, K; Mays, GP Health Services Research

The goal of this study was to examine the impact of state Medicaid expansion on the delivery of population health activities in cross-sector health and social services networks. Community networks are multisector, interorganizational networks that provide services ranging from the direct provision of individual social services to the implementation of population-level initiatives addressing community outcomes. The authors used data measuring the composition of cross-sector population health networks 2006-2018 National Longitudinal Survey of Public Health Systems (NALSYS) linked with the Area Health Resource File. Results from the adjusted difference-in-differences estimates indicated that Medicaid expansion was associated with a 2.3 percentage point increase in the density of population health networks. Communities in states that expanded Medicaid experienced significant increases in the participation of local public health, local government, hospital, nonprofit, insurer, and K-12 schools. Of the organizations with significant increases in expansion communities, nonprofits, local public health agencies, hospitals, and local government agencies had the largest gains. The study found increases in cross-sector participation in population health networks in states that expanded Medicaid compared with nonexpansion states, suggesting that additional coverage gains are associated with positive changes in population health network structure.

#### COLORADO STATE UNIVERSITY

### <u>Change in Views of Aging, Physical Activity, and Physical Health Over 8 Weeks: Results From a Randomized Study</u>

Nehrkorn-Bailey, AM; Rodriguez, D; Forsyth, G; Braun, B; Burke, K; Diehl, M Journal of Aging and Physical Activity

The AgingPLUS program targets motivational barriers, including negative views of aging, as mechanisms to increase adult physical activity. A pilot study was conducted to test the efficacy of this new program against a generic successful aging program. Fifty-six participants were randomly assigned to the AgingPLUS group, and 60 participants were assigned to the active control group. Repeated-measures multivariate analyses of variance assessed changes in views of aging, physical activity, blood pressure, and hand-grip strength from pretest (Week 0) to delayed posttest (Week 8). The Condition x Occasion interactions were nonsignificant; however, significant main effects for condition and occasion were found. Follow-up tests showed that views of aging were more positive, and physical activity had significantly increased at Week 8 for all participants. In addition, in the treatment group, elevated blood pressure had significantly decreased and hand-grip strength had significantly increased at Week 8. Despite the nonsignificant multivariate findings, the main effect findings provided partial support for the efficacy of the AgingPLUS program.

#### CENTER FOR HEALTH, WORK & ENVIRONMENT

### <u>Point-of-Care Testing in Chronic Kidney Disease of Non-Traditional Origin: Considerations for Clinical, Epidemiological, and Health Surveillance Research and Practice</u>

Dally, M; Amador, JJ; Butler-dawson, J; Lopez-pilarte, D; Gero, A; Cruz, A; Krisher, L; Pilloni, D; Kupferman, J; Friedman, DJ; Griffin, BR; Newman, LS; Brooks, DR Annals of Global Health

As the prevalence of chronic kidney disease of non-traditional origin (CKDnt) rises in low-resource settings, there is a need for reliable point-of-care creatinine testing. The purpose of this analysis was to assess the accuracy of two commonly used point-of-care creatinine devices, the i-STAT handheld (Abbott, Princeton, NJ, USA) and the StatSensor Creatinine (Nova Biomedical, Waltham, MA, USA) in comparison to venipuncture serum creatinine measures. The affordability, sensitivity, specificity, ease of use, and other considerations for each device are also presented. The i-STAT performed the most accurately, overestimating creatinine by 0.07 mg/ dL with no evidence of proportional bias. The StatSensor Creatinine performed well at low levels of creatinine. Both devices provide acceptable sensitivity and specificity. Although adequate for routine surveillance, StatSensor Creatinine is less accurate as the values of measured creatinine increase, a consideration when using the point-of-care device for screening individuals at risk for CKDnt. Research, clinical, and screening objectives, cost, ease of use, and background prevalence of disease must all be carefully considered when selecting a point-of-care creatinine device. Conclusion: POC testing can be more accessible in resource-limited settings. The selection of the appropriate device will depend on the use-case.

#### CENTER FOR INNOVATIVE DESIGN & ANALYSIS

### <u>RCFGL: Rapid Condition adaptive Fused Graphical Lasso and application to modeling brain</u> <u>region co-expression networks</u>

Seal, S; Li, QH; Basner, EB; Saba, LM; Kechris, K PLOS Computational Biology

Inferring gene co-expression networks can be useful for understanding pathway activity and gene regulation. While jointly estimating co-expression networks of multiple conditions, taking into account condition specificity, such as information about an edge being present only in a specific condition or an edge being present across all the conditions, substantially increases the power. In this paper, a computationally rapid condition adaptive method for jointly estimating gene co-expression networks of multiple conditions is proposed. The novelty of the method is demonstrated through a broad range of simulation studies and a real data analysis with multiple brain regions from a genetically diverse cohort of rats. Inferring gene co-expression networks is a useful process for understanding gene regulation and pathway activity. Condition adaptive fused graphical lasso (CFGL) is an existing method that incorporates condition specificity in a fused graphical lasso (FGL) model for estimating multiple co-expression networks. In this paper, the authors propose a faster alternative of CFGL named rapid condition adaptive fused graphical lasso (RCFGL). In RCFGL, the condition specificity is incorporated into another popular model for joint network estimation, known as fused multiple graphical lasso (FMGL). A more efficient algorithm is used in the iterative steps compared to CFGL, enabling faster computation with complexity of O(p(2)K) and making it easily generalizable for more than three conditions. The authors also present a novel screening rule to determine if the full network estimation problem can be broken down into estimation of smaller disjoint sub-networks, thereby reducing the complexity further. They demonstrate the computational advantage and superior performance of our method compared to two non-condition adaptive methods, FGL and FMGL, and one condition adaptive method, CFGL in both simulation study and real data analysis. They used RCFGL to jointly estimate the gene co-expression networks in different brain regions (conditions) using a cohort of heterogeneous stock rats. They also provide an accommodating C and Python based package that implements RCFGL.