

# Office of Research

## colorado school of public health

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# Publication Highlights

## EPIDEMIOLOGY



High Impact Journal Recognition: *Frontiers in Immunology* (Impact Factor 7.561)

***Relationship Between a Vitamin D Genetic Risk Score and Autoantibodies Among First-Degree Relatives of Proband With Rheumatoid Arthritis and Systemic Lupus Erythematosus***

Vanderlinden, LA; Bemis, EA; Seifert, J; Guthridge, JM; Young, KA; Demoruelle, MK; Feser, M; DeJager, W; Macwana, S; Mikuls, TR; O'Dell, JR; Weisman, MH; Buckner, J; Keating, RM; Gaffney, PM; Kelly, JA; Langefeld, CD; Deane, KD; James, JA; Holers, VM; Norris, JM  
*Frontiers in Immunology*

Higher 25-hydroxyvitamin D levels have been associated with reduced risk for autoimmune diseases and are influenced by vitamin D metabolism genes. The authors estimated genetically-determined vitamin D levels by calculating a genetic risk score and investigated whether the vitamin D genetic risk score was associated with the presence of autoantibodies related to rheumatoid arthritis and systemic lupus erythematosus in those at increased risk for developing them. The study found that genes associated with vitamin D levels may play a protective role in the development of rheumatoid arthritis autoantibodies in first degree relatives, perhaps through affecting lifelong vitamin D status. In contrast, these results do not support a similar association in systemic lupus erythematosus first degree relatives, suggesting other mechanisms involved in the relationship between vitamin D and systemic lupus erythematosus autoantibodies not assessed in this study.

## COLORADO INTEGRATED FOOD SAFETY CENTER OF EXCELLENCE

### **Foodborne Illness Outbreaks Reported to National Surveillance, United States, 2009-2018**

White, AE; Tillman, AR; Hedberg, C; Bruce, BB; Batz, M; Seys, SA; Dewey-Mattia, D; Bazaco, MC; Walter, ES  
*Emerging Infectious Diseases*

Foodborne outbreaks reported to national surveillance systems represent a subset of all outbreaks in the United States; not all outbreaks are detected, investigated, and reported. The authors described the structural factors and outbreak characteristics of outbreaks reported during 2009–2018. They categorized states (plus DC) as high (highest quintile), middle (middle 3 quintiles), or low (lowest quintile) reporters on the basis of the number of reported outbreaks per 10 million population. Analysis revealed considerable variation across states in the number and types of foodborne outbreaks reported. High-reporting states reported 4 times more outbreaks than low reporters. Low reporters were more likely than high reporters to report larger outbreaks and less likely to implicate a setting or food vehicle; however, the authors did not observe a significant difference in the types of food vehicles identified. Per capita funding was strongly associated with increased reporting. Investments in public health programming have a measurable effect on outbreak reporting.

## BIostatistics & Informatics

### **MIAMI: mutual information-based analysis of multiplex imaging data**

Seal, S; Ghosh, D  
Bioinformatics

Studying the interaction or co-expression of the proteins or markers in the tumor microenvironment of cancer subjects can be crucial in the assessment of risks, such as death or recurrence. In the conventional approach, the cells need to be declared positive or negative for a marker based on its intensity. For multiple markers, manual thresholds are required for all the markers, which can become cumbersome. The performance of the subsequent analysis relies heavily on this step and thus suffers from subjectivity and lacks robustness. This study presents a new method where different marker intensities are viewed as dependent random variables, and the mutual information between them is considered to be a metric of co-expression. Estimation of the joint density, as required in the traditional form of mutual information, becomes increasingly challenging as the number of markers increases. The authors consider an alternative formulation of mutual information which is conceptually similar but has an efficient estimation technique for which we develop a new generalization. With the proposed method, the authors analyzed a lung cancer dataset finding the co-expression of the markers, HLA-DR and CK to be associated with survival. They also analyzed a triple negative breast cancer dataset finding the co-expression of the immuno-regulatory proteins, PD1, PD-L1, Lag3 and IDO, to be associated with disease recurrence. The study demonstrated the robustness of this method through different simulation studies.

## HEALTH SYSTEMS, MANAGEMENT & POLICY

### **Role of Fibrinogen in Trauma-Induced Coagulopathy**

Meizoso, JP; Moore, EE; Pieracci, FM; Saberi, RA; Ghasabyan, A; Chandler, J; Namias, N; Sauaia, A  
Journal of the American College of Surgeons

Fibrinogen is the first coagulation factor to decrease after massive hemorrhage. European massive transfusion guidelines recommend early repletion of fibrinogen; however, this practice has not been widely adopted in the US. The authors hypothesize that hypofibrinogenemia is common at hospital arrival and is an integral component of trauma-induced coagulopathy. This study entailed review of a prospective observational database of adults meeting the highest-level activation criteria at an urban level 1 trauma center from 2014 through 2020. Resuscitation was initiated with 2:1 red blood cell (RBC) to fresh frozen plasma (FFP) ratios and continued subsequently with goal-directed thrombelastography. Hypofibrinogenemia was defined as fibrinogen below 150 mg/dL. Massive transfusion was defined as more than 10 units RBC or death after receiving at least 1 unit RBC over the first 6 hours of admission. Of 476 trauma activation patients, 70 (15%) were hypofibrinogenemic on admission, median age was 34 years, 78% were male, median New Injury Severity Score (NISS) was 25, and 72 patients died (15%). Admission fibrinogen level was an independent risk factor for massive transfusion (odds ratio [OR] 0.991, 95% CI 0.987–0.996). After controlling for confounders, NISS (OR 1.034, 95% CI 1.017–1.052), systolic blood pressure (OR 0.991, 95% CI 0.983–0.998), thrombelastography angle (OR 0.925, 95% CI 0.896–0.954), and hyperfibrinolysis (OR 2.530, 95% CI 1.160–5.517) were associated with hypofibrinogenemia. Early cryoprecipitate administration resulted in the fastest correction of hypofibrinogenemia. Hypofibrinogenemia is common after severe injury and predicts massive transfusion. Cryoprecipitate transfusion results in the most expeditious correction. Earlier administration of cryoprecipitate should be considered in massive transfusion protocols.

## LIFECOURSE EPIDEMIOLOGY OF ADIPOSITY & DIABETES CENTER

### **Metabolome Alterations Linking Sugar-Sweetened Beverage Intake with Dyslipidemia in Youth: The Exploring Perinatal Outcomes among CHildren (EPOCH) Study**

Cohen, CC; Dabelea, D; Michelotti, G; Tang, L; Shankar, K; Goran, MI; Perng, W  
Metabolites

The objective of this study was to assess intermediary metabolic alterations that link sugar-sweetened beverage intake to cardiometabolic risk factors in youth. A total of 597 participants from the multi-ethnic, longitudinal Exploring Perinatal Outcomes among CHildren (EPOCH) Study were followed in childhood (median 10 yrs) and adolescence (median 16 yrs). A multi-step approach was used: first, mixed models were used to examine the associations of sugar-sweetened beverage intake in childhood with cardiometabolic measures across childhood and adolescence, which revealed a positive association between sugar-sweetened beverage intake and fasting triglycerides for the highest vs. lowest sugar-sweetened beverage quartile: 8.1 (−0.9,17.0); p-trend = 0.057). Second, least absolute shrinkage and selection operator (LASSO) regression was used to select 180 metabolite features (out of 767 features assessed by untargeted metabolomics) that were associated with sugar-sweetened beverage intake in childhood. Finally, 13 of these sugar-sweetened beverage-associated metabolites (from step two) were also prospectively associated with triglycerides across follow-up (from step one) in the same direction as with sugar-sweetened beverage intake (Bonferroni-adj.  $p < 0.0003$ ). All annotated compounds were lipids, particularly dicarboxylated fatty acids, mono- and diacylglycerols, and phospholipids. In this diverse cohort, the authors identified a panel of lipid metabolites that may serve as intermediary biomarkers, linking sugar-sweetened beverage intake to dyslipidemia risk in youth.

## CANCER CENTER

### **Role of Medicaid in Early Detection of Screening-Amenable Cancers**

*Bradley, CJ; Sabik, LM; Entwistle, J; Stevens, JL; Enewold, L; Warren, JL  
Cancer Epidemiology, Biomarkers & Prevention*

This study examines the association between Medicaid enrollment, including through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), and distant stage for three screening-amenable cancers: breast, cervical, and colorectal. The authors use the Surveillance, Epidemiology, and End Results Cancer Registry linked with Medicaid enrollment data to compare patients who were Medicaid insured with patients who were not Medicaid insured. They estimate the likelihood of distant stage at diagnosis using logistic regression. Medicaid enrollment following diagnosis was associated with the highest likelihood of distant stage. Medicaid enrollment through NBCCEDP did not mitigate the likelihood of distant stage disease relative to Medicaid enrollment prior to diagnosis. Non-Hispanic Black patients had a greater likelihood of distant stage breast and colorectal cancer. Residing in higher socioeconomic areas was associated with a lower likelihood of distant stage breast cancer. Medicaid enrollment prior to diagnosis is associated with a lower likelihood of distant stage in screen amenable cancers but does not fully ameliorate disparities. This study highlights the importance of health insurance coverage prior to diagnosis and demonstrates that while targeted programs such as the NBCCEDP provide critical access to screening, they are not a substitute for comprehensive insurance coverage.

## CENTER FOR HEALTH, WORK & ENVIRONMENT

### **Latin American Agricultural Workers' Job Demands and Resources and the Association With Health Behaviors at Work and Overall Health**

*Schwatka, NV; Jaramillo, D; Dally, M; Krisher, L; Dexter, L; Butler-Dawson, J; Clancy, R; Fisher, GG; Newman, LS  
Frontiers in Public Health*

The present study describes the job demands and job resources (JD-R) experienced by agricultural workers in three Latin American countries and their relationship to proactive health behaviors at work and overall health. Following previous research on the JD-R model, the authors hypothesized that job demands (H1) would be negatively related to agricultural workers' self-reported overall health. On the other hand, the authors hypothesized that job resources (H2) would be positively related to agricultural workers' overall health. Furthermore, they hypothesized (H3) that workers' engagement in jobsite health promotion practices via their proactive health behaviors at work would partially mediate the relationship between workers' job resources and job demands and overall health. There was also a research question (R1) about whether there were differences by type of job held. The sample of workers who participated in this study (N = 1,861) worked in Mexico, Guatemala, and Nicaragua for one large agribusiness that produces sugar cane. They worked in two distinct areas: company administration and agricultural operations. The authors administered employee health and safety culture surveys using survey methods tailored to meet the needs of both types of workers. Stratified path analysis models were used to test study hypotheses. In general, the study found support for hypotheses 1 and 2. For example, operations workers reported more physically demanding jobs and administrative workers reported more work-related stress. Regardless, the existence of high job demands was associated with poorer overall health amongst both types of workers. Workers in more health-supportive work environments perform more proactive health behaviors at work, regardless of their role within the organization. However, hypothesis 3 was not supported as proactive health behaviors at work was not associated with overall health. Future research needs in terms of evaluating these hypotheses amongst workers employed by small- and medium-sized agribusinesses as well as those in the informal economy in Latin America are discussed. Important implications for agribusinesses seeking to develop health promotion programs that meet the needs of all workers are also discussed.

## CENTERS FOR AMERICAN INDIAN & ALASKA NATIVE HEALTH

### **Social determinants of obesity in American Indian and Alaska Native peoples aged $\geq$ 50 years**

Goins, RT; Conway, C; Reid, M; Jiang, LH; Chang, J; Huyser, KR; Brega, AG; Steiner, JF; Fyfe-Johnson, AL; Johnson-Jennings, M; Hiratsuka, V; Manson, SM; O'Connell, J  
*Public Health Nutrition*

American Indian and Alaska Native peoples (AI/ANs) have a disproportionately high rate of obesity, but little is known about the social determinants of obesity among older AI/ANs. Thus, this study assessed social determinants of obesity in AI/ANs aged  $\geq$  50 years. A cross-sectional analysis was conducted using multivariate generalized linear mixed models to identify social determinants associated with the risk of being classified as obese (BMI  $\geq$  30.0 kg/m<sup>2</sup>). Analyses were conducted for the total study population and stratified by median county poverty level. Mean BMI was  $29.8 \pm 6.6$  with 43% classified as obese. Women were more likely to be obese than men, and younger ages were associated with higher obesity risk. While having Medicaid coverage was associated with lower odds of obesity, private health insurance was associated with higher odds. Living in areas with lower rates of educational attainment and longer drive times to primary care services were associated with higher odds of obesity. Those who lived in a county where a larger percentage of people had low access to a grocery store were significantly less likely to be obese. The study's findings contribute to the understanding of social determinants of obesity among older AI/ANs and highlight the need to investigate AI/AN obesity, including longitudinal studies with a life course perspective to further examine social determinants of obesity in older AI/ANs.

## CENTER FOR INNOVATIVE DESIGN & ANALYSIS

### **Mechanism-aware imputation: a two-step approach in handling missing values in metabolomics**

Dekermanjian, JP; Shaddox, E; Nandy, D; Ghosh, D; Kechris, K  
*BMC Bioinformatics*

When analyzing large datasets from high-throughput technologies, researchers often encounter missing quantitative measurements, which are particularly frequent in metabolomics datasets. Metabolomics, the comprehensive profiling of metabolite abundances, are typically measured using mass spectrometry technologies that often introduce missingness via multiple mechanisms: (1) the metabolite signal may be smaller than the instrument limit of detection; (2) the conditions under which the data are collected and processed may lead to missing values; (3) missing values can be introduced randomly. Missingness resulting from mechanism (1) would be classified as Missing Not At Random (MNAR), that from mechanism (2) would be Missing At Random (MAR), and that from mechanism (3) would be classified as Missing Completely At Random (MCAR). Two common approaches for handling missing data are the following: (1) omit missing data from the analysis; (2) impute the missing values. Both approaches may introduce bias and reduce statistical power in downstream analyses such as testing metabolite associations with clinical variables. Further, standard imputation methods in metabolomics often ignore the mechanisms causing missingness and inaccurately estimate missing values within a data set. The authors propose a mechanism-aware imputation algorithm that leverages a two-step approach in imputing missing values. First, they use a random forest classifier to classify the missing mechanism for each missing value in the data set. Second, they impute each missing value using imputation algorithms that are specific to the predicted missingness mechanism (i.e., MAR/MCAR or MNAR). Using complete data, they conducted simulations, where they imposed different missingness patterns within the data and tested the performance of combinations of imputation algorithms. The proposed algorithm provided imputations closer to the original data than those using only one imputation algorithm for all the missing values. Consequently, the two-step approach was able to reduce bias for improved downstream analyses.

**Mental health and health behaviors among college student mentors in a randomized controlled trial interrupted by COVID-19**

Miller, RL; Moran, M; Lucas-Thompson, RG; Sanchez, N; Seiter, N; Rayburn, S; Verros, M; Haddock, SA; Zimmerman, TS; Johnson, SA; Shomaker, LB  
*Journal of American College Health*

The benefits of mindfulness-training and mentoring for college students have yet to be investigated. This study aimed to provide an exploratory and descriptive account of their potential benefits during the COVID-19 pandemic. In February 2020, 49 undergraduates (M = 20.51 years-old; 94% female) participated in a randomized trial of 12-week mentoring + mindfulness or mentoring-as-usual. After five weekly mentoring-sessions, programs were interrupted by COVID-19; mentoring continued online. Undergraduates completed questionnaires about mental health, behaviors, and regulatory processes in February and July 2020, with additional COVID-19-related questions at follow-up. Participants reported moderate COVID-19-related perceived stress, but mental health, health behaviors, and regulatory processes did not diminish over time, with no condition differences. Undergraduates described using contemplative practices and social support to cope with COVID-19-stress. Undergraduates showed stable mental health/health behaviors despite moderate COVID-19-related-stress. Future research on mentoring with a mindfulness component among a larger and more heterogeneous sample will be necessary.

**Two-Part Models for Father-Child Relationship Variables: Presence in the Child's Life and Quality of the Relationship Conditional on Some Presence**

Henry, KL; Tran, TP; Agbeke, DV; Lee, HYH; Williford, A; Dziak, JJ  
*Journal of the Society for Social Work and Research*

Parent–child relationship variables are often measured using a two-part approach. For example, when assessing the warmth of the father–child relationship, a child is first asked if they have contact with their father; if so, the level of warmth they feel toward him is ascertained. In this setting, data on the warmth measure is missing for children without contact with their father, and such missing data can pose a significant methodological and substantive challenge when the variable is used as an outcome or antecedent variable in a model. In both cases, it is advantageous to use an analytic method that simultaneously models whether the child has contact with the father, and if they do, the degree to which the father–child relationship is characterized by warmth. This is particularly relevant when the two-part variable is measured over time, as contact status may change. The authors offer a pragmatic tutorial for using two-part variables in regression models, including a brief overview of growth modeling, an explanation of the techniques to handle two-part variables as predictors and outcomes in the context of growth modeling, examples with real data, and syntax in both R and Mplus for fitting all discussed models.

## COMMUNITY & BEHAVIORAL HEALTH

### **Is Household Unemployment Associated With Increased Verbal and Physical Child Abuse During the COVID Pandemic?**

Ma, M; Orsi, R; Brooks-Russell, A  
*Child Maltreatment*

The economic downturn due to the Coronavirus Disease 2019 (COVID-19) pandemic initially led to a large increase in the US unemployment rate. Being laid-off or losing a job could cause financial stress and have an impact on the relationship between parents or other adults in the home and children. This study aimed to assess the effect of household unemployment on child physical and emotional abuse during the early part of the COVID-19 pandemic, with an older population of children. Data were from a sample of 7,555 students from 51 schools that participated in a survey administered from October to December 2020. The authors conducted weighted multivariable logistic regression models and report adjusted odds ratio to estimate associations between recent household unemployment and emotional and physical abuse. Having a parent or other adult in the home with a job loss was associated with higher odds of emotional or physical abuse. The findings are consistent with child maltreatment prevention strategies focused on alleviating economic hardship.

## CENTER FOR GLOBAL HEALTH

### Public Health Practice Feature Article



#### **A prospective cohort study of head circumference and its association with neurodevelopmental outcomes in infants and young children in rural Guatemala**

Connery, AK; Lamb, MM; Colbert, AM; Bauer, D; Olson, D; Paniagua-Avila, A; Calvimontes, M; Bolanos, GA; El Sahly, HM; Munoz, FM; Asturias, EJ  
*Journal of Developmental Origins of Health and Disease*

Microcephaly, an anthropometric marker of reduced brain volume and predictor of developmental disability, is rare in high-income countries. Recent reports show the prevalence of microcephaly to be much higher in lower resource settings. We calculated the prevalence of microcephaly in infants and young children (n = 642; age range = 0.1-35.9 months), examined trends in occipitofrontal circumference growth in the year after birth and evaluated the relationship between occipitofrontal circumference and performance on the Mullen Scales of Early Learning (MSEL) in rural Guatemala. Multivariable regression analyses adjusted for age were performed: (1) a model comparing concurrent MSEL performance and occipitofrontal circumference at all visits per child, (2) concurrent occipitofrontal circumference and MSEL performance by age group, and (3) occipitofrontal circumference at enrollment and MSEL at final visit by age group. Prevalence of microcephaly ranged from 10.1% to 25.0%. Occipitofrontal circumference z-score decreased for most infants throughout the first year after birth. A significant positive association between continuous occipitofrontal circumference measurement and MSEL score suggested that children with smaller occipitofrontal circumference may do worse on ND tests conducted both concurrently and ~1 year later. Results were variable when analyzed by occipitofrontal circumference cutoff scores and stratified by 6-month age groups. Occipitofrontal circumference should be considered for inclusion in developmental screening assessments at the individual and population level, especially when performance-based testing is not feasible.