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Public Emotions and Opinions Following the Sudden Cardiac Arrest of a Young Athlete During a Professional Sporting Event: A Twitter-based Sentiment Analysis Nicholas Grubic*

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Introduction: The sudden cardiac arrest (SCA) of an athlete often garners widespread community shock and media attention. During a televised National Football League game between the Buffalo Bills and Cincinnati Bengals on January 2, 2023, 24-year-old athlete Damar Hamlin suffered from a SCA after involvement in a defensive tackle. The objective of this study was to evaluate the public reaction following SCA witnessed during a nationally televised sporting event.

Methods: A database of all English tweets posted on Twitter within 24-hours of Damar Hamlin's collapse (8:55pm local time) was generated using trending search terms and hashtags. Following text mining and cleaning, the National Research Council Canada Word-Emotion Association Lexicon was used to evaluate the textual composition of tweets according to eight emotion categories (anger, fear, anticipation, trust, surprise, sadness, joy, disgust). Hu and Liu's Opinion Lexicon was used to associate unique words with either a "negative" or "positive" opinion.

Results: A total of 377,905 tweets were posted. The most commonly reported emotions were trust (41.0%), anticipation (38.7%), joy (34.4%), and fear (33.4%), followed by surprise (24.8%), sadness (22.9%), anger (21.4%), and disgust (16.7%) (Figure 1A). Among 360,626 words that were cited in Hu and Liu's Opinion Lexicon, 64.0% were associated with a "negative" opinion and 36.0% were associated with a "positive" opinion (Figure 1B). The terms "cardiac", "heart", "arrest", "SCA", "SCD", "CPR", and "AED" constituted 2.0% of all words used in tweets.

Conclusions: The general public expressed mixed emotions in response to a widely publicized SCA of a young, competitive athlete. Incorporating emotions and opinions within training materials and activities for SCA initiatives may improve public interest, engagement, and knowledge retention. The results of this study may also inform best practices to support the public after witnessing these emotionally traumatic events.

Use of omega samples for black box prediction algorithms Hayden L. Smith* Hayden Smith
Jonathan Hurdelbrink

Background: Many machine learning algorithms are considered black boxes – given their use of data partitioning, ensembles, and large weight spaces. These approaches limit an analyst's ability to share manageable sets of model coefficients with users (e.g., clinicians). An option may be to simulate all possible data realizations for a population to create an *omega sample*. This sample can be scored using fitted models and provide a prediction look-up table. Objective: to provide an applied example of an *omega sample*.

Methods: A study was conducted using two years of National Trauma Registry data for the United States. One million records were used to train and test a gradient boosting machine (GBM) and an artificial neural network (NN) model to predict hospital mortality status in trauma patients. Models were compared to the complement probability values for the Trauma Injury Severity Score (TRISS) and used its components as features. An omega sample was then constructed for all possible feature combinations and scored using GBM, NN, and TRISS.

Results: Mortality predictions and model calibration curves for an *omega sample* are presented in Table. Also listed is the amount of data support in the training dataset for each feature combination. The GBM and NN provided better mortality prediction estimates than the traditionally used TRISS model. Of note, the Omega sample was 1,427 KB in size, while the selected GBM model was based on 4,979 trees with max depth three and the NN model included 1,985 trainable weights, respectively.

Conclusions: The presented example demonstrated the utility of an *omega sample* as a user-friendly look-up table. Limitations include if training samples are limited in size compared to the full *omega sample*, which could result in a sizable amount of interpolation and extrapolation. A secondary concern is the multiplicative growth of an *omega sample* (i.e., for every additional unique feature value – the *omega sample* will double in size).

Associations of reproductive factors with expression of CD44, CD24, and ALDH1A1 stem cell markers in benign breast biopsies Lusine Yaghjyan* LUSINE YAGHJYAN Yujing J. Heng Gabrielle M Baker Divya Murthy Matt B. Mahoney Bernard A. Rosner Rulla M. Tamimi

Purpose: Reproductive factors are known to affect breast cancer risk. Whether these factors could influence activity of breast stem cells linked to breast cancer risk is unclear. We examined the associations of reproductive factors with stem cell markers CD44, CD24, and ALDH1A1 in benign breast biopsies.

Methods: This study included cancer-free women with biopsy-confirmed benign breast disease within the Nurses' Health Study (NHS) and NHSII. The data on reproductive and other breast cancer risk factors were obtained from biennial questionnaires. Immunohistochemistry (IHC) was done on tissue microarrays. The study included 393, 405, and 396 women for C44, CD24, and ALDH1A1, respectively. For each core, the IHC expression was assessed using a semi-automated platform, Definiens Tissue Studio, and expressed as % of cells that stain positively for a specific marker out of the total cell count. Generalized linear regression was used to examine the associations of parity, age at 1st birth, breastfeeding, age at menarche, and the time between menarche and age at 1st birth with log-transformed expression of each marker (in epithelium and stroma), adjusted for other breast cancer risk factors.

Results: In multivariate analysis, younger age at menarche was associated with lower CD44 (stroma: β for 12 vs.13 years=-1.49, 95% CI -2.73,-0.25; epithelium: β=-0.88, 95% CI -1.54,-0.22). Time between menarche and age at 1st birth was inversely associated with C44 in epithelium (β per 5-year increase=-0.37, 95% CI -0.69,-0.06). Age at 1st birth and time between menarche and age at 1st birth were inversely associated with ALDH1A1 (stroma: β per 5-year increase=-0.44, 95% CI -0.77,-0.11 and β=-0.47, 95% CI -0.7,-0.15, respectively; epithelium: β=-0.16, 95% CI -0.30,-0.02 and β=-0.17, 95% CI -0.30,-0.03, respectively).

Conclusions: Early-life reproductive factors may be related to CD44 and ALDH1A1 expression in benign breast tissue. Future studies are needed to confirm our findings.

Peritoneal metastasis from early-onset colorectal cancer: Frequency, management, and prognosis Rebecca J. Austin-Datta* Rebecca J. Austin-Datta Carlo La Vecchia Thomas J. George Paolo Boffetta Sean P. Dineen Thanh-Huyen T. Vu Jennifer B. Permuth Hung N. Luu

Background: Incidence of Early-Onset Colorectal Cancer (EOCRC) or those diagnosed before age 50 has increased globally in the past two decades. Peritoneal metastases of colorectal cancer origin (PM-CRC) are relatively frequent in CRC patients and appear more common in EOCRC patients. PM-CRC at any age carries a dismal prognosis; new treatments appear to increase survival time, but studies rarely report treatment by age group. **Objective/Design**: We performed a systematic review to compare variables used by studies on PM-EOCRC, including age chosen when dividing cohorts for analysis, definition of synchronous and metachronous PM, genetics, and treatment regimen. We included studies published in PubMed up to November 2022 if results (e.g., incidence/prognosis, clinical disease course, management of disease) were age-stratified. **Results**: Of 114 screened publications in English, only ten studies met inclusion criteria, and all were retrospective design. Incidence of PM was higher in young vs. old CRC patients (e.g., 23% vs 2% for <25 vs. ≥25 years, $P<0.0001$; and 57% vs. 39% % vs 4% for <20 vs. 20-25 vs. >25 years, $P<0.001$); two studies noted a higher proportion of African-American patients with PM-CRC in younger vs. older age group (e.g., 16% vs. 6% for <50 vs. ≥50 years). There was no consistency in reporting criteria in studies on PM-EOCRC, e.g., race/ethnicity, stage, histology, survival time. Included studies used seven different methods to divide cohorts for analyses, presenting comparison challenges. **Conclusions**: Our review showed a higher proportion of PM in young vs. older CRC patients. This may be due to greater diagnostic attention, lack of organized screening, and presence of more aggressive CRC in the young. The incidence of EOCRC appears to be increasing. To better address this issue, more studies with greater level of detail on key variables, stratified with standard younger/older age groups (e.g., ages <50, ≥50) are needed.

Food Environment Index was Inversely Associated with Gastric Cancer Incidence in the United States Shenghui Wu* Shenghui Wu Yanning Liu

Background— The American Cancer Society estimated that about 26,380 new cases would be diagnosed with gastric cancer (GC) and about 11,090 would die from this type of cancer in 2022. Prior studies have shown that better food access/availability environment was associated with a positive health outcome but did not specifically assess the food environment and risk of GC. Therefore, we conducted the first epidemiologic study prospectively examining the association between the Food Environment Index (FEI) and GC risk in the U.S.

Methods—Surveillance, Epidemiology, and End Results provided information on GC incident cases diagnosed between 2000 and 2015 from 16 population-based cancer registries across the U.S. The county-level food environment was assessed using the FEI, an indicator of access to healthy foods (0 is worst, 10 is best). Poisson regression was used to calculate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for the association between FEI and GC risk adjusting for individual-level and county-level covariates. Restricted cubic spline Poisson regression was used to illustrate the association between logarithmic transformed FEI and IRRs of GC adjusting for potential covariates.

Results— A total of 87,288 GC cases, diagnosed during 2000-2015, were included in the analysis. Higher levels of FEI were associated with a statistically significant reduced risk for GC (multivariable-adjusted IRR for every score increase=0.50, 95% CI 0.35, 0.70; adjusted IRR for the medium vs. low category=0.87, 95% CI 0.81, 0.94; and adjusted IRR for the high vs. low category=0.89, 95% CI 0.82, 0.95). The cubic spline showed statistically significant inverse association between logarithmic transformed FEI and IRRs of GC.

Conclusions—These results suggest that a healthy FE, as measured by FEI, may be a protective factor for GC in the U.S. To reduce the GC incidence, further strategies to improve the food environment at the county level are warranted.

Epigenetic Signatures of WTC-Associated Breast and Prostate Cancers Stephanie Tuminello*
Stephanie Tuminello Nedim Durmus Cecilia Crisanti Matija Snuderl Yu Chen Yian Zhang Yongzhao
Shao Joan Reibman Emanuela Taioli Alan A. Arslan

Introduction: Carcinogens in the WTC dust such as metals, asbestos, and organic pollutants have
been shown to modify epigenetic status. We previously performed epigenome-wide association
studies (EWAS) of breast cancer (blood-based) and prostate cancer (tissue-based) using uniform
Illumina methodology, and identified novel epigenetic signatures of WTC-associated cancer.

Methods: The primary objective of this project was to identify consistent epigenetic signatures of
WTC exposure among cancer cases. Differentially methylated genes (DMGs) identified in our
previous EWAS studies of WTC-associated breast and prostate cancer were compared, with overlap
tested for statistical significance. Gene set enrichment analysis was done to better understand the
functional impact of DMGs. As a secondary objective, we sought to determine whether specific
components of WTC dust were associated with epigenetic changes. DMGs associated with specific
dust components were initially identified in the literature, and then compared against EWAS
results.

Results: WTC exposure was associated with increased global DNA methylation, as well as site-
specific differential DNA methylation in key cancer-related genes. There were 681 consistently
DMGs among both WTC-associated breast (total DMGs=3625) and prostate cancer (total
DMGs=3586; $p_{overlap}$<0.0001). DMGs appeared to be related to cellular organization and mobility.
Moreover, oncogenes and tumor suppressor genes known to be differentially methylated in response
to arsenic, cadmium, beryllium, benzene, PCBs, and dioxin (all previously shown to be present in
WTC dust) were observed to be epigenetically dysregulated among WTC cancer cases. This included
BRCA1, MSH3, and RASSF1, among others.

Conclusion: WTC exposure is associated with long-term epigenetic consequences, which likely
impact cancer-related genes. Epigenetic biomarkers of WTC-associated cancer may prove to be
useful for screening and early detection in WTC-exposed populations.

Heart disease mortality rates disparities across rural and urban counties in Virginia
Priyadarshini Pattath* Priyadarshini Pattath

Background- Rural areas experience higher mortality rates compared with residents of urban areas, particularly from preventable causes such as cardiovascular disease. This study examines county-level differences in mortality due to heart disease by gender, age groups and race/ethnicity across rural and urban counties in Virginia.

Methods- County level population was obtained from the 2019 US Census Bureau. Mortality data was obtained from the Virginia department of health, vital statistics for 2021. Differences in county-level heart disease crude mortality rates, across rural and urban counties, were examined using parametric test and non-parametric tests.

Results- Rural counties had a significantly higher mortality rate (268.97 per 100,000) compared to urban counties (189.54) (p < 0.001). There was a significant difference between mortality of males in urban versus rural counties with a large effect (215.63 versus 301.67 per 100,000) (p < 0.001). Similar results were found when comparing female mortality rate in urban and rural counties. There was a significantly higher rate of mortality in rural counties compared to urban, for the age groups 0- 49 years (32.77 versus 17.0 per 100,000, p < 0.05), 50-59 years (186.77 versus 123.65 per 100,000, p < 0.05) and for 60-69 years (345.75 versus 259.22 per 100,000, p < 0.001). Rural counties had significantly higher heart disease mortality rates across White (273.88 versus 189.69 per 100,000, p < 0.001), Black (252.9 versus 191.21 per 100,000, p < 0.05), and Hispanic groups (610.57 versus 70.58 per 100,000, p < 0.05).

Conclusions- This analysis provides evidence that rural counties had higher rates of heart disease deaths than urban counties. Programs and policies to address heart disease mortality at the intersection of race, ethnicity, age groups, gender and geography may be needed to effectively reduce risks.

Adverse childhood experiences and adult outcomes using a causal framework perspective: challenges and opportunities. Jocelyn Jaen* Jocelyn Jaen Dalia Stern Katherine Keyes Martin Lajous Sharonda M. Lovett

Studies that evaluate the association between adverse childhood experiences (ACEs) on adult outcomes have relied on retrospective assessment and the operationalization of ACEs as the *number of ACEs* exposed (e.g., 0, 1-3, ≥4). We aimed to describe common methodological challenges of investigating ACEs and propose directed acyclic graphs (DAGs) and a causal inference perspective to identify and mitigate potential problems.

Prior studies have included adult variables or factors that post-date childhood (e.g., marital status, disease) as covariates to control for "confounding". By doing so, these investigations are likely blocking mediation pathways that are part of the total causal effect of ACEs on an outcome. In some cases, adult variables can serve as proxies of childhood variables, but only if they are not part of a mediated pathway. However, in other cases, conditioning on adult variables can unintentionally open backdoor pathways and create collider stratification bias.

Exposure to ACEs can also affect the likelihood of reaching adulthood. Depending on 1) the prevalence of ACEs that can affect survival, and 2) their effect on the outcome or variables that we select on, there is a possibility of selection bias. The former affecting generalization of the results to our target population and the latter internal validity (Figure 1).

As for the operationalization of ACEs, using a discrete number or categorization assumes treatment variation irrelevance, which is unlikely. By estimating the effect of ACEs as a cumulative score, we are implying the effect of all ACEs is the same for that outcome and largely linear.

DAGs and a causal inference perspective could be a useful tool to identify and select covariates when studying the impact of ACEs on adult outcomes, offering a comprehensive and transparent approach of the investigators' assumed causal relationships. Researchers should also be explicit about their operationalization of ACEs and how it is to be interpreted.

Joint Exposure to Urban-Rural Status and Medically Underserved Area Residence and Risk of Severe COVID-19 Outcomes in 2020 Andrew Williams* Lakin Mauch Andrew Williams

Purpose: To estimate risk of severe COVID-19 among individuals residing in rural, non-medically underserved counties compared to those living in other counties.

Methods: Individual-level COVID-19 hospitalization and death data and demographic variables were downloaded from the Centers for Disease Control and Prevention. The 2013 National Center for Health Statistics Urban-Rural Classification Scheme was used to classify urban and rural counties. Health Resources and Services Administration's medically underserved area designation was used to identify underserved counties. County-level data were drawn from the 2015-2019 American Community Survey 5-year estimates. Analytic sample included data from Minnesota and Montana in 2020. Urban-rural/MUA joint exposure categories were created: rural/MUA, rural/non-MUA, urban/MUA, urban/non-MUA. Hierarchical logistic regression models estimated associations (odds ratios and 95% confidence intervals) between rurality, MUA status, joint urban-rural/MUA status, and severe COVID-19, overall and stratified by age and state. Models were adjusted for individual- and county-level demographics. We calculated e-values for unmeasured confounders.

Results: Odds of severe outcomes among those living in rural counties were 13% lower (OR:0.87, 95% CI:0.83-0.91) than those in urban counties. Odds of severe outcomes among those living in MUA counties were 24% higher (OR:1.24, 95% CI:1.18-1.30) than those in non-MUA counties. For joint exposure analyses, odds of severe outcomes were highest among those living in urban/MUA counties compared to those in rural/non-MUA counties (OR:1.36, 95% CI:1.27-1.44). An unmeasured confounder would need to have an OR of at least 2.06 to completely explain away the observed association.

Conclusions: In 2020, risk of severe COVID-19 was more pronounced in urban/MUA counties. Results may inform future pandemic preparedness measures by identifying characteristics of counties that are most in need of resources.

A statewide population-based approach to examining Long COVID symptom prevalence and predictors Jana Hirschtick* Jana Hirschtick Yanmei Xie Elizabeth Slocum Robert E. Hirschtick Laura E. Power Michael R. Elliott Robert C. Orellana Nancy L. Fleischer

Background: The current broad definition of Long COVID, as well as an overreliance on clinical cohorts, is leading to a wide array of long COVID estimates with limited generalizability. Our objective was to examine prevalence and predictors of Long COVID symptoms using a statewide population-based probability sample.

Methods: Among 8,000 sampled adults with polymerase-chain-reaction-confirmed SARS-CoV-2 between June 2020 and July 2021 in the Michigan Disease Surveillance System, 2,533 completed our survey (response rate 32.2%). Using modified Poisson regression, we examined sociodemographic, behavioral, and clinical predictors of eight Long COVID symptom clusters, defined as at least one applicable symptom lasting 90 or more days post COVID-19 onset.

Results: Neuropsychiatric Long COVID symptoms were most prevalent (23.7%), followed by systemic (17.1%), musculoskeletal (11.4%), pulmonary (10.4%), dermatologic (6.7%), cardiovascular (6.1%), gastrointestinal (5.4%), and ear, nose, and throat (ENT) symptoms (5.3%). In adjusted analyses, female sex, a pre-existing psychological condition, and intensive care unit admission were strong predictors of most Long COVID symptom clusters. Compared to adults aged 18-24, older adults had a higher prevalence of systemic, pulmonary, musculoskeletal, and ENT symptoms, while middle-aged adults (35-54 years) had a higher prevalence of cardiovascular and dermatologic symptoms. Age was not associated with neuropsychiatric or gastrointestinal symptoms after adjustment. Additionally, there were fewer associations between pre-existing conditions and cardiovascular, neuropsychiatric, and dermatologic symptoms compared to other symptom clusters.

Conclusions: While many predictors of Long COVID symptom clusters were similar, the relationship with age and pre-existing conditions varied across clusters. Cardiovascular, neuropsychiatric, and dermatologic symptoms require further study as potentially distinct from other Long COVID symptoms.

Post-initiation predictors of discontinuation of the sodium-glucose co-transporter-2 inhibitors: A comparative cohort study from the United Kingdom Wajd Alkabbani* Wajd Alkabbani Baiju Shah Arsene Zongo Dean Eurich Mhd. Wasem Alsabbagh John-Michael Gamble

Aim: To estimate time to and assess post-initiation predictors of discontinuation of sodium-glucose co-transporter-2 (SGLT-2) inhibitors compared to dipeptidyl-peptidase-4 (DPP-4) inhibitors in the UK.

Methods: A comparative retrospective cohort using primary care data from the United Kingdom's Clinical Practice Research Datalink. We included new metformin users who initiated SGLT-2 or DPP-4 inhibitors between 1Jan2013 and 31Oct2019. The main outcome was treatment discontinuation (first 90-day gap after treatment end date). We used a Kaplan-Meier estimator, stratified by treatment, to describe time to treatment discontinuation and a series of extended cox models adjusted for baseline characteristics to assess which time-dependent predictors were associated with treatment discontinuation.

Results: The study cohort consisted of 2550 new users of SGLT-2 inhibitors and 8195 new users of DPP-4 inhibitors. The median (95% CI) survival time was 1.51 (1.40-1.60) for SGLT-2 inhibitor users and 1.39 (1.34-1.46) for DPP-4 inhibitor users. The Kaplan–Meier curves were not statistically different between treatments (Log-rank $\times 2 = 1.52$; P=0.218). Diabetic ketoacidosis and fractures after treatment initiation were predictors of discontinuation of SGLT-2 inhibitors only (HR, 95%CI = 2.64,1.37-5.10 and 1.91, 1.28-2.86, respectively) but not DPP-4 inhibitors (HR, 95%CI= 1.14, 0.72-1.82 and 0.90, 0.78-1.04, respectively). Acute kidney injury was a significant predictor of discontinuation for SGLT-2 and DPP-4 inhibitors, albeit significantly higher for SGLT-2 inhibitors (HR 2.60 vs. 1.39). A low eGFR after treatment initiation was associated with a significantly higher rate of discontinuation among SGLT-2 inhibitor users.

Conclusions: Rates of treatment discontinuation among SGLT-2 inhibitors initiators were not different compared to DPP-4 inhibitors. However, specific adverse events after treatment initiation were associated with higher rates of SGLT-2 inhibitor discontinuation.

The Effects of Daily Temperature on Crime Events in Urban Hanoi, Vietnam Using Seven Years of Data (2013-2019) Vu Thuy Huong Le* Vu Thuy Huong Le Bruce H. Alexander Elizabeth V. Wattenberg Jesse D. Berman Quynh Anh Tran

The effects of temperature on behavior change and mental health have previously been explored, but the association between temperature and crime is less well understood, especially in developing countries. Single-city-level data were used to evaluate the association between the short-term effects of temperature on crime events in urban Hanoi, Vietnam. We used quasi-Poisson regression models to investigate the linear effects and distributed lag non-linear models to investigate the non-linear association between daily temperature and daily crime events from 2013 to 2019. There were 3884 crime events, including 1083 violent crimes and 2801 non-violent crimes, during the 7-year study period. For both linear and non-linear effects, there were positive associations between an increase in daily temperature and crime, and the greatest effects were observed on the first day of exposure (lag 0). For linear effects, we estimated that each 5 °C increase in daily mean temperature was associated with a 9.9% (95%CI: 0.2; 20.5), 6.8% (95%CI: 0.6; 13.5), and 7.5% (95%CI: 2.3; 13.2) increase in the risk of violent, non-violent, and total crime, respectively. For non-linear effects, however, the crime risk plateaued at 30 °C and decreased at higher exposures, which presented an inverted U-shape response with a large statistical uncertainty.

Race, age and tuberculosis (TB) epidemic in a low incidence setting, Arkansas, during 2010-2021 Maheen Humayun* Maheen Humayun Wen Ye Joseph H. Bates Zhenhua Yang

Around 10.6 million people fell ill with tuberculosis (TB) and 1.6 million died of TB in 2021, making TB the leading infectious killer only second to COVID-19. While TB incidence has substantially declined in developed countries, it continues to disproportionately aggregate among certain population groups. Hence, we use the TB patient population diagnosed in Arkansas, US during 2010-2021 to characterize the socio-demographic disparities in TB incidence. We used Poisson regression to estimate the 12-year cumulative TB incidence and RR for various socio-demographic groups. While the average statewide TB incidence was 2.58 cases per 100,000 population (95% CI: 2.42, 2.76), the TB incidence was 20.02 (95% CI: 16.60, 24.16) and 131.62 cases per 100,000 (95% CI: 111.39, 155.51) for Asians and Native Hawaiian/Pacific Islanders (NHPI), respectively. After adjusting for sex and age group, the risk of TB was 4.6 times (95% CI: 3.88, 5.45) higher among NH Blacks and 173.58 times higher (95% CI: 140.64, 214.24) among NHPI, compared to NH Whites. NH Whites were at the lowest risk across all age groups while NHPI aged between 0-14 years had 888.70 (95% CI: 402.55, 1961.98) times higher risk of TB compared to similar aged NH Whites. Age disparities were observed within racial/ethnic groups except among NHPI. The risk of TB was highest in the 65 years and over age group for NH Whites, Hispanics and NH Blacks. Among NH Whites, the risk of TB was 95% (RR=0.05, 95% CI: 0.02, 0.11) lower for 0-14 year olds and 50% (RR=0.50, 95% CI: 0.39, 0.64) lower for the 45-64 year old group compared to the 65 years and over group. Aggregated estimates of TB incidence in low burden settings mask the underlying disparities that may fuel the remaining TB epidemic. Increased incidence of TB among young NHPI is indicative of community transmission. For successful and targeted TB interventions, it is important to consider the intersecting effects of race, age and sex.

Polygenic Predisposition, Substance-Free Parenting, Gene x Environment Interaction and Their Associations with Depression Trajectories from Middle to Late Adulthood Ping Chen* Ping Chen Yi Li

Study Objective. Little research has investigated genetic-environment mechanisms of genetic factors and substance-free parenting on health. Besides, new longitudinal studies are needed to assess the interconnection between genetic factors and promotive parenting in relation to health trajectories across the life span. This study applied a life course perspective, using data from a national cohort study, the Health Retirement Study (HRS 1994-2020, n = 7,512), to examine the polygenic risk score (PRS), substance-free parenting and the Gene X Environment (GxE) interaction and their longitudinal associations with depressive symptoms from middle to late adulthood (ages 51-90 years).

Measures and Methods. Two-level mixed models were estimated to assess the additive and interactive associations of PRS (in both continuous construct and binary indicator of high versus low genetic risk) and substance-free parenting with the standardized 8-item Center for Epidemiologic Studies Depression (CES-D) scale. Substance-free parenting was measured by a protective family environment in which parents were not engaged in frequent drinking or drug-use to cause problem in the family before age 18 years old.

Results and Findings. Results show that both polygenic predisposition and substance-free parenting contributed to trajectories of depressive symptoms from middle to older adulthood. Those with a lower polygenic risk experienced higher CES-D levels than those with a higher genetic risk. Additionally, substance-free parenting was associated with mitigated CES-D levels. The significant GxE interaction effect revealed that the protective effect of substance-free parenting for lowered levels of CES-D was greater among individuals with high polygenic risk than those with low polygenic depression-risk. Furthermore, we found that Significant G & E compound processes (When only one conducive G or E condition is present, protective family environment performs better.)

Conclusions and Implications. This study provides a new understanding of how generic factors and promotive parenting operate to influence mental health development from middle to late adulthood. Both polygenic predisposition and substance-free parenting and their interactions contribute to shape health trajectories from middle to late adulthood. Findings have important policy implications to foster substance-free family environments for bettered lifelong psychological development of young children who are susceptible to high genetic depression-risk.

Family Structure and Functionality and its Association with Substance Use and Mental Health among Colombian Adolescents Juan Guillermo Perez-Carreno* Juan Guillermo Perez-Carreno Alyssa M Juan M Catalina

Introduction: Previous studies have shown that family functionality relates to mental health, explaining approximately 25% of the variation in emotional problems among adolescents. To gain a deeper understanding of this association, we aimed to examine whether not having a family is equally as detrimental as having a dysfunctional family.

Methods: We conducted a secondary analysis of the 2015 Colombian National Mental Health Survey to explore the associations between family structure and functionality and history of (i) anxiety disorders, (b) mood disorders, (iii) suicidal behaviors, (iv) substance use and (v) problematic drinking based on the AUDIT, among 1754 adolescents (12-17 years old). Family structure and functionality was assessed based on one item that determined whether study participants had an emotional connection with someone they live with (i.e., having a family) and the family APGAR scale. Associations were explored using logistic regression models that accounted for the complex sample design.

Results: Among adolescents interviewed (mean age of 14.5 years; SD: 1.7), 42.2% reported not having a family, 39.3% reported having a functional family, and 18.5% reported having a dysfunctional family. Compared to those with a functional family, those with a dysfunctional family were more likely to report a history of substance use (aOR=1.69; 95% CI: 1.13-2.51). The odds of having had a history of mood disorders were higher among individuals reporting family dysfunctionality, compared to those reporting family functionality (aOR=2.96; 95% CI: 1.30-6.74). Not having a family or family functionality did not show to be associated with a history of anxiety disorders, suicidal behaviors, or problematic drinking.

Conclusion: These results showed an increased risk for mental health illness and substance use disorder among adolescents living with dysfunctional families. However, reporting not having a family was not associated with mental health problems.

Age and sex differences in the association of insomnia symptoms with all-cause mortality among community-dwelling stroke survivors: a prospective cohort study Wendemi Sawadogo* Wendemi Sawadogo Tilahun Adera

Background: Insomnia is more frequently reported in stroke survivors but the independent role of insomnia in mortality in this vulnerable group is unknown. The purpose of this study was to investigate the association of insomnia symptoms with all-cause mortality among stroke survivors.

Methods: The Health and Retirement Study from 2002 to 2018 was used as the data source. The exposure of interest was insomnia symptoms and was derived from sleep-related factors including difficulty initiating sleep, difficulty maintaining sleep, waking up too early, and nonrestorative sleep. All-cause mortality was assessed by linking the data with the National Death Index. Cox proportional hazards regression models were employed to investigate the association between insomnia symptoms and all-cause mortality.

Results: A total of 3,501 males and females were included in this analysis. Over a mean follow-up of 6 years, 1,782 deaths occurred. Having difficulty initiating sleep and difficulty maintaining sleep most of the time were associated with all-cause mortality only among males aged less than 65 years (HR=2.19, 95% CI=1.31, 3.65 and HR=2.13, 95% CI: 1.27, 3.60, respectively) while waking up too early and nonrestorative sleep were associated with all-cause mortality only among males aged 65 years and over (HR=1.30, 95% CI=1.04, 1.63 and HR=1.28, 95% CI: 1.03, 1.59, respectively). Overall, compared to subjects with no insomnia symptoms, males aged less than 65 years and males aged 65 years and over with insomnia symptoms score ranging from 5 to 8 were respectively associated with increased risk of all-cause mortality (HR=2.24, 95% CI: 1.09, 4.58 and HR=1.26, 95%: 0.97, 1.65).

Conclusion: Our study indicates that insomnia symptoms increased the risk of death among stroke survivors, especially in males and those who are younger than 65 years of age. Increased awareness and management of insomnia symptoms may contribute to the prevention of premature death among these stroke survivors.

Research barriers in under-resourced crisis settings: The impact of a socioeconomic crisis on a maternal and child health cohort in Lebanon Rima Kaddoura* Rima Kaddoura Martine Elbejjani Hani Tamim Lama Charafeddine Ziyad Mahfoud Pascale Salameh Fadi Mirza

Background: Prematurity is a product of a complex interplay of determinants, many of which are closely linked to the social environment. A main consequence of preterm birth is poor developmental outcomes which are exacerbated in contexts of social/socioeconomic adversities, emphasizing the importance of studying birth and developmental outcomes in these contexts.

Objectives: To explore the feasibility of building a prospective mother and child cohort and examine barriers to research in a crisis ridden and low resource setting.

Methods: The project aims to build a prospective Lebanese cohort on developmental outcomes of preterm and full-term babies. It was designed to be conducted at a hospital centre in the capital and to collect data on social determinants and quality of life and assess developmental outcomes at 4-6 months and 9-12 months after birth. As the study is unfolding several barriers have been identified.

Preliminary results: Important challenges concern recruitment, retention and data collection. Only 70 mother-baby pairs completed baseline visits and 50 completed the 4-6 months follow-up. Important barriers include drops in birth and healthcare access (80% drop in bed occupation), migration of healthcare workers, and limited research resources. Over 25% of mothers are unable to disclose their income due to rapid socioeconomic changes. Yet, retention rate is 71%, highlighting the importance of participants' commitment. To address these barriers, we added two medical centres, are scheduling follow ups at paediatrician's visit, and seeking funding to offer transportation and home visits.

Conclusion: Recruitment and data collection challenges are substantial in social determinants of birth and developmental outcomes in the current crisis-ridden Lebanese setting. There is a large need for funds that prioritize hard to reach populations and for integrating design and measurement approaches that can capture a rapidly changing social determinants.

Analytic Approaches to Handling Common Sources of Bias in Placental Histopathology Studies Alexander Layden* Alexander Layden Janet Catov Marnie Bertolet

Background: Placental histopathology is underutilized to study neonatal outcomes due to concerns of bias. We show how to account for confounding, selection bias, and measurement error using the well-studied association between histologic chorioamnionitis (an inflammatory placental lesion) and severe neonatal morbidity.

Methods: Singleton deliveries from the Magee Obstetric Maternal and Infant cohort (n=46,676 deliveries) were analyzed. Chorioamnionitis and severe neonatal morbidity were abstracted from placental histopathology reports and medical records. ORs for chorioamnionitis and odds of severe neonatal morbidity were estimated by logistic regression and stratified by preterm birth (PTB) status (<37 weeks). Bias was accounted for in a step-wise fashion. Confounders were first adjusted for by multivariate regression, propensity weights, inverse probability treatment weights (IPTW), and standardization. Next, selection bias from analyzing only deliveries with histopathology was adjusted for by inverse probability weighting. Lastly, measurement error of the exposure was estimated by simulating 10% misclassification of chorioamnionitis.

Results: Results are depicted in **Figure 1**. Chorioamnionitis was associated with a higher odds of severe neonatal morbidity in PTBs and a non-significant protective effect in term births. Confounders changed the magnitude but not direction of the OR among PTBs. The protective OR in term births reversed to a harmful effect by IPTW. Adjusting for confounders and selection bias did not change the OR among PTBs. In term births, the OR flipped from a protective (OR <1) to a harmful effect (OR >1). Simulating 10% misclassification of chorioamnionitis in PTBs and term births attenuated ORs towards the null, though results remained significant for PTBs.

Conclusions: The OR between chorioamnionitis and severe neonatal morbidity was robust to bias in PTBs, but not term births. Histopathology findings may vary due to bias and analysis strategy.

A prospective study of perceived stress, depressive symptoms, and spontaneous abortion

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Background: Spontaneous abortion (SAB; pregnancy loss <20 weeks' gestation) can lead to stress and depression. However, the extent to which stress and depression cause SAB is understudied. We examined the association of preconception perceived stress and depressive symptoms with rate of SAB in a prospective cohort study.

Methods: Eligible participants self-identified as female, were aged 21-45 years, resided in the U.S. or Canada, and were trying to conceive without the use of fertility treatment. Female participants completed questionnaires at baseline (preconception), every 8 weeks during follow-up, and during early and late pregnancy. Male partners aged ≥21 years completed a baseline questionnaire only. On all questionnaires, participants completed the 10-item version of the Perceived Stress Scale (PSS) and the Major Depression Inventory (MDI). On follow-up and pregnancy questionnaires, female participants self-reported pregnancy outcomes and gestational week at SAB. We restricted analyses to 9,020 female participants who conceived during the study period and 2,515 of their partners. We used Cox regression models to estimate hazard ratios (HRs) and 95% CIs for the association of preconception PSS and MDI scores (on questionnaire closest to conception) with rate of SAB, adjusting for potential confounders. We categorized MDI score as <10, 10-19, 20-29, ≥30 and PSS scores as <15, 15-19, 20-24, ≥25.

Results: High depressive symptoms in either partner were associated with an increased rate of SAB: HRs for MDI score ≥30 vs. <10 were 1.23 [95% CI: 0.96, 1.57] for female partners and 1.26 [95% CI: 0.82, 1.53] for male partners. Results for female MDI score were slightly stronger among nulligravid participants (HR=1.35, 95% CI: 0.90, 2.02). PSS scores were not appreciably associated with SAB for either partner.

Conclusions: More severe depressive symptoms during the preconception period were associated with an increased rate of SAB, whereas perceived stress was not.

Examination of indication creep for CT-P/A use in an Emergency Department setting

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Background: As thrombectomy evaluation has become integrated into Emergency Department (ED) acute stroke assessments, it is possible computed tomography perfusion and angiogram (CT-P/A) indication creep has occurred due to a lack of data to direct its use. Objective: evaluate concordance of provider practices for thrombectomy screening with trial criteria in an ED via CT-P/A.

Methods: A retrospective observational study was conducted for patients >/= 18 years who received a CT-P/A of the head and neck in a United States Midwestern ED between September 2019 through June 2021.

Results: During the study period, 68,403 patients presented to the ED with 718(1%) receiving a CT-P/A. Of these patients, 105(15%) were transferred to a regional facility for potential thrombectomy, with 74(71%) receiving procedure. Of patients receiving CT-P/A, 23 met DAWN criteria for thrombectomy, with 21(91%) transferred for potential thrombectomy and 20(95%) receiving the procedure; in comparison, 81 patients (12%) did not meet all DAWN criteria and were transferred for potential thrombectomy, with 52(64%) receiving procedure. Lastly, 55 patients met DEFUSE-3 criteria for thrombectomy with 49(89%) being transferred for potential thrombectomy; 45(92%) received procedure. In comparison, 53 patients did not meet all DEFUSE-3 criteria and were transferred for potential thrombectomy, with 27(51%) receiving the procedure. During the reviewed period there was a trend of increasing CT-P/A use and decreasing NIHSS, with a proportionally decreasing thrombectomy referral yield (Figure).

Conclusions: This study helps to understand CT-P/A usage, especially in patients outside of treatment criteria per current thrombectomy literature. There was an appearance of indication creep, CT-P/A use beyond thrombectomy trial criteria, which appears to have some, albeit less, yield in capturing interventional candidates. This progressive trend requires more clarity on the ideal criteria for CT-P/A use.

Identifying associated factors with breast cancer screening among U.S. women by disability type Amarachukwu Orji* Amarachukwu Orji Tarang Parekh, PhD, MBBS

Identifying associated factors with breast cancer screening among vulnerable populations, including women with disabilities can be used to target and improve screening efforts. The study identified associated factors with less-than-optimal breast cancer screening in women by disability type. Women aged 50-74 (n=219,534) from Behavioral Risk Factor Surveillance System data (2018 and 2020) were analyzed. The primary outcome measure was breast cancer screening in the last 2 years. Disability type was self-identified based on affirmative response to having a sensory disability only, cognitive disability only, physical disability only, and multiple disability only. Modified Poisson regression was used to obtain prevalence ratios for the association between disability type and breast cancer screening adjusted for demographics, socioeconomic factors, and healthcare access. Among women with disability,74% had breast cancer screening within the last two years compared to women without disabilities (80.8%). By disability type, the prevalence of breast cancer screening was higher among women with a physical disability (77.3%) and lower among those with multiple disabilities (72%). In the adjusted Poisson models, women with any disability reported lower likelihood of breast cancer screening compared to those without any disability. By disability types, women with multiple (aPR: 0.90, 95%CI 0.89, 0.90) and sensory disabilities (aPR: 0.93, 95% CI 0.92, 0.94) had the lowest likelihood of receiving routine breast cancer screening. Furthermore, women who identified as younger, bisexual, and racial/ethnic minority were less likely to receive routine breast cancer screening across disability type. The study found a substantially low prevalence of breast cancer screening in women with a disability regardless of disability type. Across age, sexual orientation, and race/ethnicity, ensuring inclusivity of breast cancer screening programs may be pathways to improve breast cancer screening in women with disabilities.

Heterogeneity across outcomes reported in randomized controlled trials for older adults with major depressive disorder: findings from a systematic survey Myanca Rodrigues*
Myanca Rodrigues Zuhayr Syed Pegah Ghiassi Alexander Dufort Nitika Sanger Stephanie Sanger Balpreet Panesar Alessia D'Elia Sameer Parpia Zainab Samaan Lehana Thabane

Background:

Heterogeneity in the use of outcomes across clinical trials creates challenges for the interpretation of results regarding intervention effectiveness. Core outcome sets (COS), a minimum set of outcomes that must be reported in trials, have been proposed as a viable solution to address inconsistency in the selection of outcomes. We conducted a methodological review to synthesize the definitions and measurement of outcomes reported in trials for older adults with depression, which represents the first step towards the development of a COS.

Methods:

We searched four databases to identify trials assessing any intervention for major depressive disorder among older adults published between 2011 and 2021. We grouped reported outcomes thematically and mapped them onto core outcome areas (physiological/clinical, life impact, resource use, adverse events, and death), and used descriptive analysis to summarize outcome heterogeneity.

Results:

There were 434 total outcomes reported by 49 included trials, which were measured using 135 different outcome measurement instruments and grouped into 100 unique outcome terms. Most outcome terms mapped to the physiological/clinical core area (47%), followed by life impact (42%). Over half of all terms (52%) were reported by only a single study. The majority of trials (n=31/49) reported a single, discernable primary outcome. The most commonly reported outcome, "depressive symptom severity" was assessed by 40 studies using 16 different outcome measurement instruments.

Conclusions:

There is substantial heterogeneity in the outcomes and outcome measurement instruments used in geriatric depression trials. A standard set of outcomes and accompanying measurement tools is necessary to facilitate comparison and synthesis of trial findings.

Cross-sectional associations of depressive symptoms and suicidality with substance use over time Miranda Delawalla* Miranda Delawalla Isaac Rhew Yolanda Evans Daniel Enquobahrie

Purpose: Given high prevalence of adolescent depressive symptoms and substance use, as well as changing trends in their associations, we investigated change over time of cross-sectional associations of depressive symptoms and suicidality with substance use in nationally representative samples of high school students.

Methods: We utilized Youth Risk Behavior Survey (YRBS) for high school students from 1991 to 2019 (n=217,340) to assess cross-sectional associations of past 12-month depressive symptoms, serious consideration of suicide, having made a suicide plan, suicide attempts, and injurious suicide attempts with any past 30-day use of alcohol, cannabis, and electronic vapor products; any past 30-day binge drinking; and any lifetime prescription pain medicine misuse. Using survey-weighted logistic regression, we estimated aORs, 95% CIs, and p-values.

Results: Associations of depressive symptoms with alcohol use remained relatively stable over time, after an increase from 1999 (aOR: 1.66; 95% CI: 1.37, 2.00; p<0.001) to 2001 (aOR: 2.10; 95% CI: 1.89, 2.33; p<0.001; Figure 1). For cannabis, the association increased from 2009 (aOR: 1.95; 95% CI: 1.68, 2.27; p<0.001) to 2017 (aOR: 2.65; 95% CI: 2.26, 3.12; p<0.001), then decreased in 2019 (aOR: 2.16; 95%: 1.89, 2.47; p<0.001). Findings for associations of suicidality indicators with alcohol and cannabis use were similar to associations of depressive symptoms. Analyses for binge drinking, electronic vapor products, and prescription pain medicine misuse were limited by recent introduction of or changes to YRBS question content.

Conclusions: Broadly, all associations of past 12-month depressive symptom and suicidality indicators with past 30-day ever use of alcohol and cannabis increased slightly over time. Our findings may inform efforts to identify adolescents at high risk for substance use. Further research is needed to monitor recent trends comprehensively.

Medications for Opioid Use Disorder in the US: Barriers to Treatment and Psychosocial Impact Tahmid Khan* Tahmid Khan Silvia S. Martins Megan E. Marziali

Background: Quarantine guidelines implemented during the COVID-19 pandemic has created barriers in access to Medications for Opioid Use Disorder (MOUD). Our study aimed to examine MOUD utilization among patients with OUD based on insurance coverage and psychosocial impacts which resulted from negative mental health outcomes due to inadequate treatment access.

Methods: Data was obtained from SAMHSA's 2020 National Survey of Drug Use and Health. Multivariable logistic regression analysis was performed to determine associations of insured vs. uninsured people with OUD. Multivariable logistic regression was then performed to see unadjusted and adjusted models for MOUD and each of the psychosocial impact categories.

Findings: When controlled for covariates the odds of MOUD for respondents who are insured is almost three times those who are uninsured (OR: 2.82, 95% CI: 1.09, 8.86). For respondents with MOUD there was minimal impact in their in social activities (OR: 0.09, 95% CI: 0.02, 0.26) and household activities by age (OR: 1.18, 95% CI: 1.04, 1.33) compared to those without.

Conclusions: The study revealed an increase in the non-white uninsured population and a clear difference in people's ability to take part in social, work or educational and household activities depending on the use of MOUD. The results suggest a broader investigation into MOUD access for vulnerable populations.

Adolescent Alcohol Use: A Comparison of Rural and Urban Prevalence Josiane Kabayundo*

Josiane Kabayundo Shinobu Watanabe-Galloway David W. Palm Jennie Hill

Background: While there is evidence of a higher prevalence of alcohol use among adults, little is known about adolescents' alcohol use in rural communities. Objectives: 1) To examine the time trend of excessive alcohol use between 2012 and 2018; 2) to compare excessive alcohol use and examine the factors associated with excessive alcohol use among rural and urban adolescents. Methods: The 2010-2018 Nebraska Risk and Protective Factor Student Survey data were analyzed. The sample comprised 24,419 students in the 8th, 10th, and 12th grades of all public and non-public schools. The primary exposure variable was the school location (urban vs. rural). A chi-square test and a two-sample t-test were used to compare alcohol use between rural and urban students. Multiple logistic regression was performed to identify potential factors associated with excessive alcohol use. A trend analysis was conducted using the Cochran-Armitage Trend Test. Results: From 2010 to 2018, alcohol use decreased significantly in both rural and urban students. Binge alcohol use decreased from 14.2% to 7.9% in rural adolescents, and from 12.7% to 6.3% among urban students. The rural-urban status was significantly associated with binge drinking and lifetime alcohol use for some grades. For example, the odds of binge drinking were higher among rural adolescents compared to urban adolescents of 8th and 10th graders (POR=2.04; 95% CI: 1.30, 3.21; POR=1.71; 95% CI: 1.33, 2.20) respectively. Despite the significant decline of alcohol use in rural and urban adolescents, the prevalence of alcohol use was consistently higher among rural youths than urban youths. Alcohol accessibility, alcohol-related perceptions, social and environmental factors were significant predictors of alcohol use among respondents. Conclusion: To address the unique challenges facing rural adolescents, targeted public health programs and policies should be developed.

Comparison of Symptom Networks in Male vs. Female Adults with Past 12-Month Non-Medical Use of Prescription Pain Relievers Alyssa Falise* Alyssa Falise Juan Guillermo Perez Carreno Melissa Fenton Catherine W Striley Catalina Lopez Quintero

Overdose rates have increased among males and females with non-medical use of prescription pain relievers (NMUPPR) since 1999. Females reported a six-fold increase; males a four-fold increase. Higher rates of comorbid psychiatric conditions among females may influence opioid use disorder (OUD)-related symptoms. We aimed to observe variations in the inter-relationships between OUD symptoms by sex. Data from 744 males and 835 females aged 18 years and older with past 12-month NMUPPR surveyed in the National Epidemiological Survey on Alcohol and Related Conditions III were analyzed. Responses to the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) OUD diagnostic criteria were utilized for three network analyses (all, males, females), which observed the interrelationships between diagnostic criteria while stratifying by sex. A total of 391 (25%) participants met criteria for OUD (190 males, 201 females). Each of the criteria were positively correlated for males. Females had one negative correlation between failing to participate in obligations and using in physically hazardous conditions (range – male: 0.00-0.30, female: -0.07-0.31). The most central criteria included using longer/larger doses, spending long periods of time getting/using/recovering from use, and cravings. Among males, use despite knowledge of physical/psychological ailments was also central. For females, use despite interpersonal complications was central. Males' highest betweenness was seen with getting/using/recovering for longer periods of time and withdrawal, whereas females had the highest betweenness with cravings. These findings provide evidence to support there are variations in the most central DSM-5 OUD criteria and their associations with other criteria when stratifying by sex. Future research should identify whether variations in network topology are associated with differences in prescription availability and the increased comorbid psychiatric conditions noted in females.