but only if it can be maintained. A family-centered whole foods diet pattern that uses "food as medicine" and considers how individual and family needs/preferences, and SDOHs could be an effective and sustainable multigenerational solution to prevent T2D in families.

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Dysregulated molecular networks in Cib2 knockout mice mimic human age-related macular degeneration*

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OBJECTIVES/GOALS: In mice, it has been shown that loss of Cib2 (calcium and integrin-binding protein 2) results in progressive retinal disease that recapitulates many characteristics of age-related macular degeneration (AMD). This study aims to characterize transcriptional changes in the retinal pigment epithelium (RPE) that underlie this disease process. METHODS/STUDY POPULATION: RPE tissue samples, pooled from 2–3 mice for each biological group, were collected from Cib2-KO and wildtype (WT) mice at two (young) and eight (aged) months of age. Bulk mRNA sequencing was performed using the Illumina HiSeq 4000. Reads were aligned to the UCSC mouse reference genome and quantified using HTSeq. Significant differentially expressed genes (DEGs) between mouse genotype and age groups were assessed using DESeq. CLICK unsupervised clustering followed by gene ontology analysis was performed to identify cellular processes and molecular pathways affected by loss of Cib2 as well as age. RESULTS/ANTICIPATED RESULTS: CLICK analysis revealed several functional pathways that are differentially expressed between sample groups. For example, in both young and aged mice, pathways upregulated in Cib2-KO samples included calcium signaling, RhoA signaling, and integrin signaling. Uniquely downregulated DEGs in young Cib2-KO animals were related to complement and coagulation cascades, LXR/RXR activation (related to lipid synthesis and transport), and phagosomes. Aged Cib2-KO mice displayed the most significant downregulation of genes in the phototransduction pathway, indicating temporal changes in functional pathways that correlate with disease progression. Next steps in analysis include investigating patterns in RPE- and AMD-signature gene sets that may identify molecular pathways more specific to human disease. DISCUSSION/SIGNIFICANCE OF IMPACT: Many current studies investigate the role of complement activation, vesicle trafficking, and ion transport as top contributors to AMD development. We identified DEGs paralleling many of these molecular pathways in Cib2-KO mice, highlighting their potential as a model to study age-related RPE pathologies and evaluate therapeutic interventions.

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Best practices for data management and metadata creation for collaborative biostatistics teams

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OBJECTIVES/GOALS: Our goal is to enhance communication and documentation in collaborative biostatistics by refining data management and metadata processes. We aim to capture critical data collection and generation information, improve transparency and reproducibility, and foster stronger researcher partnerships for more effective collaborations. METHODS/STUDY POPULATION: Traditional statistical analysis plans (SAP) often miss essential contextual knowledge from collaborators, leading to gaps that hinder reproducibility and limit future data use. Biostatistics teams at the University of Kentucky have updated their strategies to better capture important details about data origins and collection processes. By focusing on clear, comprehensive documentation early in the research process, we aim to preserve foundational data insights and improve collaboration efficiency. Our Biostatistics, Epidemiology, and Research Design (BERD) team has established best practices for addressing data management structures with collaborators across medical and healthcare fields – covering all project stages, from initial data collection to metadata creation and dataset finalization. RESULTS/ANTICIPATED RESULTS: We will detail the processes used to improve data management structures and the observed results of these processes. For example, initiating deeper discussions about data origins and collection processes as early as possible in the collaboration has resulted in a more comprehensive project narrative that lays the foundation for effective collaboration. By engaging with project leaders early in the process, we can confirm that critical details about how data were collected and processed are documented, improving both the transparency and reproducibility of research findings. Streamlining the processes of capturing this information makes it more accessible and useful for those with limited statistical backgrounds, which is particularly relevant for faculty and staff in BERD communities and Clinical and Translational Science Awards Programs. DISCUSSION/SIGNIFICANCE OF IMPACT: Nuanced data documentation structures are crucial for transforming raw data into meaningful, reusable datasets. Our initiatives promote clear communication, enhanced efficiency, and streamlined workflows. Translational science researchers can benefit from improving data management and metadata to boost long-term collaborative success.

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Wildfire smoke-driven PM2.5 and its association with persistent respiratory symptoms and repeated asthma exacerbations among adults with asthma

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OBJECTIVES/GOALS: 1) Determine the association between wildfire smoke-driven PM2.5 and risk of persistent respiratory symptoms and repeated asthma exacerbations after the acute wildfire period among adults with asthma. 2) Examine how measures to reduce personal exposure to wildfire smoke, including avoiding outdoor activities, modify this association. METHODS/STUDY POPULATION: This is a retrospective study of adults with asthma in WHAT-NOW, a cohort study of people living in Northern California during the 2018 Camp Fire. Daily smoke-driven PM2.5 was estimated for each participant based on their home address or evacuation location. We examined the association between mean PM2.5 exposure and the presence of respiratory symptoms at both the time of the survey (6–16 months post-wildfire) and at least one other post-wildfire time-period, as well as whether they had a medically attended respiratory

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illness (saw a doctor, visited the ER, or were hospitalized for a respiratory symptom). We examined the interaction of PM2.5 with spending time outdoors during the wildfires. Poisson regression models with robust standard errors were adjusted for age, sex, race, smoking, allergies, and education. RESULTS/ANTICIPATED RESULTS: Among 337 adults with asthma in the WHAT-NOW cohort, one standard deviation higher smoke-driven PM2.5 was associated with higher risk of any persistent respiratory symptom (risk ratio (RR) 1.38, 95% CI 1.07 – 1.78) and having at least one medically attended respiratory illness (RR 1.33, 95% CI 1.07 – 1.65), but not significantly associated with repeated asthma exacerbations (RR 1.30, 95% CI 0.92 – 1.81). However, there was a significant interaction between PM2.5 and outdoor activities during the wildfire on the outcomes of any persistent respiratory symptoms ($p = 0.041$) and repeated asthma exacerbations ($p = 0.028$). The association between PM2.5 and repeated asthma exacerbations was greater among people who spent time outdoors (RR 3.36, 95% CI 1.47 – 10.23) than those who did not (RR 1.00, $p = 0.99$). DISCUSSION/SIGNIFICANCE OF IMPACT: This study provides evidence that exposure to wildfire smoke increases respiratory morbidity among adults with asthma beyond the acute wildfire period. Additionally, it suggests that avoiding outdoor activities on smoky days can significantly decrease the risk of future repeated asthma exacerbations associated with smoke exposure.

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How do you share documents with collaborators external to your institution?

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OBJECTIVES/GOALS: Using secure systems for sharing documents with external collaborators is essential for all researchers. These documents may include protected health information (PHI) or sensitive materials like protocols, study reports, DSMB reports, publications, presentations, abstracts, and statistical analysis plans (SAPs). METHODS/STUDY POPULATION: We surveyed the ACTS Biostatistics, Epidemiology, and Research Design Special Interest Group (BERD-SIG) to gather information about the systems they are currently using or have used in the past for document sharing with external collaborators. The survey focused on the security of these systems, particularly in relation to sharing documents containing PHI. In addition, the survey included questions about various system features of interest. These features included version control, simultaneous editing by multiple users, and access rights management, such as the ability to assign different permissions (e.g., read-only, write, and download) to different individuals. We also invited participants to provide feedback on any additional positive or negative aspects of the systems they use. RESULTS/ANTICIPATED RESULTS: We received 28 completed survey responses. Respondents had an option for choosing more than one system. The top current systems reported were Microsoft Teams (OneDrive, SharePoint) (n = 16), Box (n = 11), Google Docs/Drive (n = 10), and Dropbox (n = 6). Among other systems listed individually were Filelocker, REDCap, Slack, Website, Significant Media Shuttle, and Zulip. Notably, 15 responses indicated the respondents were unsure if their system is secure for sharing documents containing PHI. Respondents also offered feedback on both the positive and negative aspects of these systems. For example, a key advantage of Box was its password-controlled access. However, its incompatibility with office tools and the challenges for external collaborators attempting to access the system were noted as drawbacks. DISCUSSION/SIGNIFICANCE OF IMPACT: Utilizing secure institutional document-sharing systems and understanding their features significantly affects the effectiveness and security of collaborations among researchers, particularly with external partners. This knowledge is especially crucial when sharing documents containing sensitive patient and study data.

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Genome-wide association study of visual memory and spatial organization in a community setting: The Cohorts for Heart and Aging Research in Genomic Epidemiology Consortium*

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OBJECTIVES/GOALS: Poor visual memory and perceptual organization task performance predicts cognitive decline and is sensitive to dementia severity. No genome-wide association study (GWAS) has assessed the genomic basis of cognitive visual-spatial phenotypes. We aimed to identify common genetic variants associated with visual memory and spatial organization. METHODS/STUDY POPULATION: We included dementia- and stroke-free participants aged 45 years or older from up to seven cohorts in the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium, who performed cognitive tasks assessing delayed visual memory (e.g., Benton Visual Retention Test (BVRT, n = 10,934) and visual reproductions (VR, n = 5,527)) or spatial organization (i.e., Hooper Visual Organization Test (HVOT, n = 5,024)). Each cohort used linear regression models to relate common genetic variants imputed to the 1000 Genomes panel to each cognitive phenotype, adjusting for age, sex, population stratification, and education. Summary statistics for the BVRT were meta-analyzed using METAL. Combined GWAS was used for a joint analysis of all traits. RESULTS/ANTICIPATED RESULTS: We identified a genome-wide significant variant related to BVRT performance located near the TSHZ3 gene (rs10425277, $p = 6.76\times10–9$). TSHZ3 is important for the development and function of cortical projecting neurons and may be implicated in Alzheimer's disease progression by repressing CASP4 transcription. Multitrait analyses, including BVRT, VR, and HVOT, identified two additional variants of interest in SMYD3 gene (rs10802275, $p = 5.58\times10–7$) and near ZFPM2 (rs2957459, $p = 2.03\times10–7$), both of which are overexpressed in the brain and have important implications for neurodevelopment. SMYD3 may be directly involved in synaptic dysfunction and has been shown to be upregulated in the prefrontal cortex of Alzheimer's disease patients. DISCUSSION/SIGNIFICANCE OF

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