IMPACT: This work will provide evidence on a possible role of amyloid in the pathophysiology of LS in a subset of patients. Our results will guide more robust quantitative analyses, including proteomics and transcriptomics, and for the first time, may support trial of anti-amyloid medical therapies to slow the progression of this primarily surgical disorder.

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## Prevalence of hearing loss and hearing aid use among US older adults: Health and retirement study

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OBJECTIVES/GOALS: Emerging studies demonstrate association of hearing loss with adverse mental and cognitive outcomes, warranting the need for reliable measures of hearing in epidemiological research. This study compared the prevalence of hearing loss among US adults based on objective and self-reported measures, as well as hearing aid use from the HRS. METHODS/STUDY POPULATION: This is a cross-sectional study utilizing data from the 2016/18 Health and Retirement Study (HRS), a nationally representative cohort of US adults aged ≥50 years. Participants who completed both the objective hearing screening using the HearCheck device and hearing-related questionnaires were included (n=13,087). Survey weights were applied to account for the complex sampling design to estimate the prevalence of hearing loss as well as hearing aid use among those with objective hearing loss. Agreement between objective and self-reported hearing status was assessed using Cohen's κ. Multivariable regression analyses examined demographic factors (age, sex, race/ethnicity, income, and education) associated with under-reporting of hearing loss and hearing aid use. RESULTS/ANTICIPATED RESULTS: In this nationally representative sample of US adults aged ≥50 years, the prevalence of objective hearing loss was 52.6% [95% CI: 51.5-53.7] and self-reported hearing loss was 26.9% [25.9-27.9%]. Hearing aid use rate was 9.7% [8.9-10.5] among those with any objective hearing loss (score<6) and 44.9% [41.1-48.9] among those with moderate or worse hearing loss (score<3). Agreement between objective and self-reported hearing was low (Cohen's κ=0.2), with 61.6% [60.1-63.0] under-reporting their hearing loss. In a multivariable model accounting for demographic factors, under-reporting was more likely among females (OR: 1.8 [1.6-2.1]) and individuals with higher education (OR: 2.0 [1.6-2.6]). Hearing aid use was associated with higher education (OR: 2.9 [2.0-4.2]) and higher income (OR: 2.8 [1.9-4.0]). DISCUSSION/SIGNIFICANCE OF IMPACT: Hearing loss is common in older US adults, yet hearing aid use remains low. Frequent under-reporting of hearing loss highlights the need for objective measures in epidemiology studies to elucidate the impact of hearing loss on health outcomes. Addressing costs and awareness may improve access and lessen negative health effects related to hearing loss.

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## The impact of BT2-modulated BCAA reduction as a novel therapeutic for Alzheimer's disease

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OBJECTIVES/GOALS: This study evaluates whether BT2-mediated reduction of branched-chain amino acids enhances cognitive performance and alters cortical gene expression in transgenic Alzheimer's disease mouse models, clarifying BCAA's role in AD pathology and assessing BT2's potential as a disease-modifying therapy. METHODS/STUDY POPULATION: Four groups of mice were used: wild-type vehicle, wild-type with 20 mg BT2, AD vehicle, and AD with 20 mg BT2(3,6-dichlorobenzobthiophene2-carboxylic acid). BT2, an inhibitor of branched-chain aminotransferase 2, was administered intraperitoneally to reduce BCAA accumulation implicated in mTOR overactivation and tau hyperphosphorylation. Cortical tissue samples were collected for RT-qPCR analysis of 17 genes linked to neurodegeneration. Y-Maze behavioral assays assessed spatial memory and cognition. ANOVA with post-hoc Tukey's tests ($\alpha = 0.05$) assessed intergroup significance between behavioral and transcriptional outcomes. Additionally, a Random Forest Regressor Model was utilized in order to identify gene expression patterns predictive of cognitive improvement following BT2 treatment. RESULTS/ANTICIPATED RESULTS: BT2 (3,6-dichlorobenzo[b]thiophene-2-carboxylic acid) treatment restored Beclin-1, VPS-26, NRF2, and NF-κB expression to near wild-type levels, correlating with improved Y-Maze performance. These changes enhanced autophagy, reduced inflammation, and improved mitochondrial resilience. Partial recovery of BACE1, MFN2, and PSD-95 indicated moderate restoration of amyloid processing and synaptic plasticity. Enrichr analysis highlighted pathways in autophagy, mitochondrial biogenesis, and miRNA regulation, suggesting BT2 exerts neuroprotective effects by modulating metabolic and inflammatory homeostasis. The Random Forest Regressor Model's Feature importance mapping further revealed that changes in Beclin-1, NRF2, and NF-κB expression most strongly correlated with behavioral recovery. DISCUSSION/SIGNIFICANCE OF IMPACT: BT2 shows strong potential in mitigating Alzheimer's pathology through branched-chain amino acid modulation. It normalizes NRF2, Beclin-1, and NF-κB, promoting neuroprotection and cognitive improvement. This supports BT2 as a promising metabolic therapy warranting further long-term studies.

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## Using machine learning models to predict COVID-19 vaccine hesitancy in rural populations during the pandemic: A cross-sectional study

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OBJECTIVES/GOALS: Widespread COVID-19 vaccine hesitancy was a critical barrier to managing the pandemic. Rural populations represent a key demographic in this challenge, yet the specific drivers of their hesitancy remain underexplored. To address this gap, we

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analyzed a survey of 454 participants in rural Mississippi to identify key predictors of vaccine hesitancy. METHODS/STUDY POPULATION: We employed six machine learning models and a logistic regression model, using feature importance and partial dependence analyses to understand the influence of demographic, behavioral, and belief-based factors. RESULTS/ANTICIPATED RESULTS: Among participants, 98 (21.6%) reported vaccine hesitancy. The Bayesian Additive Regression Trees (BART) model identified vaccine safety as the most critical predictor, with hesitancy probabilities dropping from 0.4 to below 0.1 among those who agreed that vaccines are safe. Different from some other studies, factors such as vaccine accessibility and healthcare provider support had limited influence. Belief in vaccine safety and education level were the primary drivers of vaccine hesitancy in the rural population. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings suggest that public health interventions targeting rural communities must better communicate vaccine safety to effectively combat hesitancy.

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## Integrating BERD and biomedical informatics data services to accelerate translational science

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OBJECTIVES/GOALS: The objectives of this project aim to (1) feature strengthened areas of integration between Biostatistics, Epidemiology & Research Design (BERD) and Biomedical Informatics (BMI) Cores, (2) exemplify an inter-core approach to maximize CTSA data service resources, and (3) discuss opportunities to adapt this approach in other CTSA hubs. METHODS/STUDY POPULATION: BERD and BMI Cores are partnered disciplines integral to the mission of CTSA hubs but often operate independently of each other which can result in unfulfilled data resource linkages. In 2023, the University of Kentucky Center for Clinical and Translational Science integrated joint operations between the two cores to maximize research data support services. This project defines three areas of inter-core collaboration between BERD and BMI in CTSA hubs in academic medical centers: (1) collaborative needs assessment for research data support services, (2) joint consultations for study design, analysis, and data extraction, and (3) partnered joint data resource navigation. Process comparisons of previous and current workflows are presented to show the advantages of utilizing collaborative core efforts. RESULTS/ANTICIPATED RESULTS: When operations are integrated, BERD and BMI Cores leverage CTSA resources to a higher capacity, with data-intensive research support becoming more effective and expedited for project timelines and workflows across the CTSA, especially in support of translational science and research. Early evaluation results support improved operation performance metrics and inter-core teamwork satisfaction. With this partnership, BERD and BMI cores strengthen CTSA data research support services including functional datasets, higher-level service, and leveraging institutional resources. Common service issues including cycles of data re-extractions and limited data support are now avoided when BERD and BMI cores address investigator needs with a joint approach. DISCUSSION/SIGNIFICANCE OF IMPACT: CTSAs aiming to improve research navigation efficiency might approach joint BERD and BMI core collaborations and adapt these strategies to fit institutional infrastructure. This collaboration can serve as a case study in translational science innovation, addressing persistent CTSA workflow, hiring, and resource allocation.

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## Exploring the link between the gut microbiome in babies and later development of autism spectrum disorder

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OBJECTIVES/GOALS: Autism spectrum disorder (ASD) is a complex neurodevelopmental condition with unclear biological causes, potentially influenced by the gut-brain axis. This study sought to explore the infant gut microbiome to identify whether specific changes in the microbiota during early infancy are associated with later diagnosis of ASD. METHODS/STUDY POPULATION: Study participants included a subset of children from MARBLES (Markers of Autism Risk in Babies – Learning Early Signs), an ASD enriched-risk cohort study. Infant stool samples were collected from these children between 0 and 7 months of age. At 36 months of age, children were clinically classified as having ASD (n=42), or non-typically developing without ASD (Non-TD, n=16), or typically developing (TD, n=79). The fecal microbiome was investigated using 16S rRNA gene sequencing to evaluate whether the gut microbial composition during early infancy was associated with later neurodevelopmental diagnoses. RESULTS/ANTICIPATED RESULTS: Overall, no significant differences in alpha diversity or beta diversity, or bacterial abundance, were found between groups of infants who developed ASD or Non-TD compared to those who went on to have TD. However, our findings highlight some early alterations in gut microbial composition during infancy that may relate to later neurodevelopmental outcomes. For example, infants who developed ASD showed slightly lower Veillonella and Flavonifractor levels, suggesting minor early microbial distinctions potentially linked to neurodevelopment. These differences are less pronounced than the effects of delivery mode or diet on the infant gut microbiome. DISCUSSION/SIGNIFICANCE OF IMPACT: Although we found no significant differences in bacterial abundance in early infancy linked to later

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