IMPACT: Our findings suggest that variants related to visual memory and spatial organization are involved in neurodevelopmental and degenerative pathways. This GWAS adds to the growing body of GWAS literature on the genetic basis of cognitive function. Additional analyses are underway to replicate these findings and extend functional annotation.

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Fixing or mixing? Improving small sample size longitudinal microbiome models*

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OBJECTIVES/GOALS: Longitudinal studies capture dynamic host–environment interactions crucial to microbiome research. Commonly used mixed-effects models can struggle with small clinical samples, like many endometrial cancer studies. We will compare them to simpler fixed-effects models, aiming to develop a new fixed-effects differential abundance alternative. METHODS/STUDY POPULATION: Starting with simulated data for linear models with a single treatment effect, we will incrementally increase complexity to reflect real-world microbiome data. To observe conditions of misspecification, simulated data of repeated measures will be generated using different distributions, while varying parameters and interclass correlation. In each condition, linear fixed- and mixed-effects models will be fitted 1000 times to empirically determine p-value, type 1 error rate, and power. We will increase the verisimilitude of our approach by using endometrial cancer data from our lab as a real background, while adding simulated signals. This data will be used to assess extant differential abundance models against our novel fixed-effects model. RESULTS/ANTICIPATED RESULTS: Our initial findings indicate that fixed-effects models maintain control over type 1 error rates in small samples, while mixed-effects models do not perform as reliably. We are now exploring the effects of confounders on type 1 error rates and power in linear models, while our next step will evaluate generalized linear models in a differential abundance context. We expect that the fixed-effects models will continue to be as reliable as mixed-effects models, while being less computationally complex. After establishing our theoretical basis, our novel model should perform comparably to mixed-effects models on pseudo-simulated endometrial cancer data and better at small sample sizes. We will finally apply our model to real endometrial cancer data to identify microbial markers of disease predisposition. DISCUSSION/SIGNIFICANCE OF IMPACT: By characterizing and improving these statistical tools, we seek to increase the robustness and power of microbiome study results (especially at small sample sizes), ultimately supporting better-informed translational research decisions. This work underscores the importance of statistical methods in advancing microbiome research.

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Leveraging the biodesign process to create impactful medical technologies: A study in neurosurgery

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OBJECTIVES/GOALS: This study demonstrates the utility of the CBID biodesign process for identifying and prioritizing high-impact neurosurgical needs. The research emphasizes the process's role in developing innovative medical technologies that align with the healthcare ecosystem's demands and stakeholder priorities. METHODS/STUDY POPULATION: The CBID Spiral Innovation Model, integrating clinical, technical, business, and strategic considerations across clinical challenges in neurosurgery was employed over a 15-week period at a tertiary care center. The process involved three phases: (1) needs identification through 8 weeks of clinical immersion, (2) 7–8 weeks of stakeholder engagement via informational interviews, surveys, and conferences, and (3) iterative refinement based on evidence generation and market value. Stakeholders included over 70 clinicians (neurosurgeons, neurocritical care specialists, neurologists, etc.) across 15 institutions as well as more than 10 payers and hospital administrators. Data collection encompassed direct observation, structured interviews, and comprehensive literature review. RESULTS/ANTICIPATED RESULTS: The initial list of 300+ identified neurosurgical needs was reduced to 271 after clinician and market input. High-level market and clinical evidence assessments further reduced this to 74 needs. Finally, through iterative evaluation of evidence generation, market opportunity, and stakeholder feedback, five critical unmet needs in stroke, traumatic brain injury, hydrocephalus, and epilepsy were identified for technological innovation. These needs met the criteria for clinical importance, economic viability, and market accessibility. The findings highlight the effectiveness of the biodesign process in creating a roadmap for innovation that is both clinically relevant and commercially viable. DISCUSSION/SIGNIFICANCE OF IMPACT: This study underscores the effectiveness of structured need-finding and prioritization within neurosurgery. Integrating stakeholder perspectives and rigorous analysis, it provides a replicable framework for medical innovation to accelerate the development of impactful solutions across medicine.

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Geographic landscape of US broadband availability from 2017 to 2020

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OBJECTIVES/GOALS: Telehealth is a key solution to improving access to healthcare and disease detection, especially in rural areas. Telehealth access relies on the presence of broadband in an area, which has shifted with the growing importance of internet. We aim to assess the distribution of US county-level broadband availability from 2017 to 2020 overall and by rurality. METHODS/STUDY POPULATION: We employed an ecologic study design to examine the distributions of two measures of broadband availability across all US counties from 2017 to 2020. Broadband presence was defined as counties meeting the Federal Communications Commission (FCC) definition of broadband with at least one high-speed internet provider and an average download/upload speed of at least 25/3 megabits per second using 2017–2020 FCC Broadband Deployment Data. Broadband access, or county-year proportion of households with broadband, was defined using 2017–2020 data from the American Community Survey. We used log-binomial and linear regression models and a difference-in-difference analytical approach to estimate the difference in the change in broadband presence and access from 2017 to 2020 between rural and urban counties. RESULTS/ANTICIPATED RESULTS: Overall, broadband presence increased

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