genotypes. To measure risk stratification of APL-informed peptide predictions, we will use a historical kidney transplant cohort from 2000 to 2023. RESULTS/ANTICIPATED RESULTS: We expect the application of APL could reduce false- positive peptide binders that influence risk prediction scores. We anticipate improved peptide prediction accuracy compared to existing tools such as NetMHCIIPan which assumes all possible peptides are equally likely to emerge from antigen processing. NetMHCIIPan is currently used by PIRCHE-II HLA mismatch risk algorithm. Out of 12 donor–recipient transplant pairs, NetMHCIIPan has found an average of 41 peptides per pairing and APL found an average of 62 peptides per pairing. These peptides are unique to each prediction, so a combined prediction could reduce the peptide list. We expect that merging antigen processing (APL) and peptide binding (NetMHCIIPan) models into a unified model would enhance risk stratification for graft failure compared to PIRCHE-II. DISCUSSION/SIGNIFICANCE OF IMPACT: More holistic modeling of immune pathways can lead to more realistic numbers of peptides found from mismatched HLA proteins. Understanding how HLA matching contributes to kidney transplant outcomes can better stratify risks for recipients, enabling personalized treatment to induce immune tolerance and ultimately improving outcomes.

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The role of signup recency in volunteer registries: Evidence from the All IN For Health database

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OBJECTIVES/GOALS: To evaluate whether signup recency in the Indiana CTSI All IN For Health Volunteer Registry influences responsiveness to outreach for clinical trial recruitment, testing the hypothesis that newer records are more likely to yield referrals. METHODS/STUDY POPULATION: Outreach data from the TrialX Connect registry were analyzed. Each outreach was coded as referral versus no response. Volunteers were grouped by time since signup: <6 months (n=386), 6–12 months (n=282), 1–2 years (n=659), 2–3 years (n=760), and >3 years (n=13,592). Conversion rate was defined as referrals per unique volunteers outreached. Statistical comparisons were made across categories. RESULTS/ANTICIPATED RESULTS: Conversion rates were stable across categories (2.14–3.36%). The 6–12 month cohort had the highest rate (3.36%), while 2–3 years had the lowest (2.14%). Newer (<6 months) volunteers converted at 2.28%. Most referrals (n=345) came from >3 year signups, reflecting their numerical dominance (13,592 signups, ~90% of registry). DISCUSSION/SIGNIFICANCE OF IMPACT: Signup recency showed little impact on responsiveness (steady at ~2–3%). Older records produced most referrals due to larger volume, emphasizing the lasting value of long-term participants. Results suggest focusing on sustained engagement and retention over simply expanding the registry.

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Mapping common and distinct neurocircuitry: Information-theoretic integration of asymmetric CBMA datasets

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OBJECTIVES/GOALS: To develop an information-theoretic alternative to ALE that integrates uneven datasets using log-likelihood ratios (LLRs) under noise versus signal world models. This approach aims to improve reproducibility, signal-to-noise ratio, and computational scalability in neuroimaging meta-analysis. METHODS/STUDY POPULATION: We used both real and simulated coordinate-based datasets to build an information-theoretic meta-analysis framework. The method models each study's activations under noise versus signal expectations and computes voxelwise LLRs to combine information asymmetrically across uneven datasets. Implemented in Python with NumPy and custom modules, it integrates watershed segmentation for cluster detection and simulation-based calibration. Validation compares results to ALE, testing robustness to injected noise and recovery from highly imbalanced datasets. RESULTS/ANTICIPATED RESULTS: Studies are ongoing. We anticipate improved SNR and recovery robustness compared to ALE, as our approach avoids pre-thresholding before combining information across datasets. Simulation evidence suggests far greater computational efficiency (e.g., reducing 45-min–20-hour ALE runs to under two minutes locally). Conceptually, the framework parallels modern AI training strategies – modeling signal and noise distributions to calibrate evidence rather than relying on fixed significance thresholds. These innovations leverage information theory, watershed algorithms, and simulation calibration to yield interpretable, high-resolution evidence maps. DISCUSSION/SIGNIFICANCE OF IMPACT: This framework advances coordinate-based meta-analysis by modeling evidence directly rather than inferring it through p-values. It improves reproducibility, interpretability, and cross-disorder comparability, supporting more robust and scalable neurocircuit mapping for researchers and clinicians.

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Beyond proteinopathies: Direct RNA sequencing illuminates epitranscriptomic alterations in Alzheimer's disease-related genes

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OBJECTIVES/GOALS: To date, no study has jointly profiled RNA isoforms and modifications associated with Alzheimer's disease neuropathological changes (ADNC) in a human cohort. Therefore, the overall objective of this study is to identify and characterize RNA isoforms and modifications that associate with ADNC by leveraging long-read direct RNA sequencing. METHODS/STUDY POPULATION: This translational study will analyze human prefrontal cortex tissue from a well-defined cohort of 12 individuals. The cohort consists of six individuals with severe Alzheimer's disease neuropathological changes and six age- and sex-matched non-demented controls. Leveraging long-read direct RNA sequencing, which uniquely quantifies both RNA isoform and modifications simultaneously, can provide novel insights into how severe Alzheimer's disease neuropathological changes drive changes in RNA isoform expression patterns and alter RNA modifications contributing to isoform dysregulation. RESULTS/ANTICIPATED RESULTS: My preliminary data from human prefrontal cortex (n=2) revealed pseudouridine sites, 1 of ~170 known RNA modifications, in Alzheimer's disease-risk genes (APP, CLU, SORT1, and BIN1), supporting the need to map RNA modifications across Alzheimer's disease-relevant isoforms. My central hypothesis is that severe Alzheimer's disease neuropathological changes (ADNCs) drive transcriptomic and epitranscriptomic dysregulation by altering RNA isoforms. Thus, my two working hypotheses are 1) severe ADNC drives transcriptomic dysregulation of RNA isoforms and 2) severe ADNC drives epitranscriptomic dysregulation of RNA modifications. DISCUSSION/SIGNIFICANCE OF IMPACT: This project will be the first to jointly profile RNA isoforms and modifications accounting for Alzheimer's disease neuropathological changes, offering candidate regulatory targets for therapeutic development. Importantly, this research will equip me with an expertise in RNA biology, neurodegenerative diseases, and bioinformatics.

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When clinical decision support falls short: Lessons from piloting a patient-centered prescribing tool for post-operative opioids at discharge

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OBJECTIVES/GOALS: A clinical decision support tool (CDS) with an individualized prescribing approach was piloted to determine impact on opioid overprescribing rates for surgical patients at discharge. As a follow-up, clinicians were interviewed to determine current challenges to opioid prescribing and required components of an effective CDS for discharge opioids. METHODS/STUDY POPULATION: In the EHR-based randomized control trial, patients admitted to a qualifying surgical service for 24+ hours postoperatively were randomized to the individualized CDS tool with a taper based on inpatient opioid use or the standard discharge order set. Performance of the CDS tool was assessed by rate of opioid mismatch, that is, the difference between median inpatient and daily discharge dose in morphine milligram equivalents (MMEs). Pilot results were further investigated using a sequential explanatory design. Semi-structured interviews were held with discharging clinicians. A purposive sampling strategy with snowball sampling was used to identify providers. Data saturation was used to determine sample sufficiency. Interview transcripts were coded and thematically analyzed, with 40% group coded. RESULTS/ANTICIPATED RESULTS: Among 61 randomized patients, median discharge MME (30 [IQR 22.5, 45] remained four times the median inpatient MME (7.5 [IQR 0, 30]) after the pilot period. Nine nurse practitioners and six general surgery residents were interviewed (n=15). Perceived challenges to opioid prescribing centered on three themes: limited protocolization for standard cases; lack of workflow efficiency; and systemic barriers (patient insurance and pharmacy). Clinicians identified at least one useful component of the tool for their current practice. Crucial CDS tool components identified by prescribing clinicians included seamless integration with the electronic health record, adequate clinician training, effective communication of treatment plan with the patient, and clinician buy-in to overcome current prescribing culture. DISCUSSION/SIGNIFICANCE OF IMPACT: Multiple patient- and system-related factors impede standardization of opioid prescribing for postoperative patients. CDS tools in this area are a well-received idea, and the tool is now being redesigned to promote effective integration into clinician workflow with multiple stages of intervention, prior to resuming the randomized control trial.

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Frontiers Trial Finder: Implementing a mobile platform integrated with a Clinical Trial Management System to enhance accessibility and engagement

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OBJECTIVES/GOALS: A key barrier to clinical trial (CT) access is knowing which trials are enrolling. Frontiers has developed a Trial Finder mobile app that displays streamlined, up-to-date trial availability that can be integrated to other institutions. We're gathering usability feedback and exploring interest from other institutions in adopting the tool. METHODS/STUDY POPULATION: The Frontiers Trial Finder app is a unique tool that extracts trial data and status directly from a Clinical Trial Management System (CTMS). It includes helpful links to ClinicalTrials.gov and provides ways to connect with the study team. The app updates automatically every night, storing the extracted data in a separate stream that can be accessed through the app or online. Its interface is custom-designed in-house and fully customizable, allowing the integration of additional resources such as FAQs, links to partner affiliates, and more. During onboarding, we identified two key efforts: first, organizing the trial directory by defining parent groups and subgroups; and