damage and impaired repair mechanisms. Our research evaluates the role of innate immune recognition proteins to provide insights into age-related neurodegeneration and cognitive decline. METHODS/STUDY POPULATION: We will utilize transcriptomic data from the Long-Life Family Study (LLFS), a cohort rich in genetic and phenotypic data related to aging and longevity. Our approach includes assessing a set of innate immune recognition proteins, also known as pattern recognition receptors (PRRs) expression across various age groups, focusing on potential correlations with cognitive performance. By analyzing serum transcriptomic profiles, we aim to map changes in expression and DNA repair genes over time, evaluating their connection to cognitive health and neurodegeneration in aging populations. RESULTS/ANTICIPATED RESULTS: We anticipate that the expression of some PRRs will increase with age and correlate with cognitive decline, suggesting a role in age-related neurodegeneration. We also expect a decrease in DNA repair pathway gene expression in older age groups, contrasting with an increase in genes involved in endogenous DNA detection. These results will reveal how PRRs may function as neuroprotective factors and how their expression changes may relate to the decline in DNA repair processes with age, providing a better understanding of innate immune recognition in cognitive health. DISCUSSION/SIGNIFICANCE OF IMPACT: This study will reveal the role of PRRs in aging and neurodegeneration, potentially establishing them as a key player in neuronal protection. Findings may guide future research into therapeutic strategies targeting them for Alzheimer's and other age-related neurodegenerative diseases.

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Precision education and generative AI in surgery utilization study: A framework for global surgical education

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OBJECTIVES/GOALS: Global surgical education is largely driven by high-income countries (HICs), with curricula not tailored to the needs of low- and middle-income countries (LMICs). This study assessed country-specific needs for global surgical curricula and used generative AI to develop tailored curricula. METHODS/STUDY POPULATION: A curriculum framework was developed using expert opinion. Using a focused needs assessment survey, we evaluated international medical students' and trainees' needs for structured global surgery curricula, covering research, education, data and develop tailored curriculum templates for each country, ensuring alignment with the distinct needs of respective LMIC and HIC respondents. The AI-generated curricula were then compared across countries to identify variations in content and focus areas. RESULTS/ANTICIPATED RESULTS: A total of 145 respondents from 18 countries and 6 continents participated, with 94 from LMICs and 51 from HICs. Four countries [Uganda (n = 31), Nigeria (n = 34), the USA (n = 23), and the UK (n = 23)] had more than 10 respondents, with the creation of a country specific global surgery curriculum. Curricula developed by HIC trainees focused on access to resources and infrastructure, future directions of global surgical research, and the role of medical students and early career development with a decreased focus on the history of global surgery. LMIC country-based curriculum focused on introducing the concepts of global surgery, quantifying the burden and epidemiology of surgical disease and had a greater emphasis on case studies and use cases, with decreased focus on resources and collaboration. DISCUSSION/SIGNIFICANCE OF IMPACT: The research introduces a "precision education" approach that could help close the surgical education access gap globally. Further pilot and qualitative studies are necessary to validate the feasibility of AI-generated needs-based curricula.

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Improving risk stratification in kidney transplant outcomes by modeling antigen processing to inform prediction of T-cell epitopes derived from mismatched HLA proteins

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OBJECTIVES/GOALS: We aim to enhance risk prediction in kidney transplantation outcomes by improving models of peptide antigen presentation of mismatched HLA molecules. HLA-derived peptides presented by HLA Class II to T-cells can activate an immune response, ultimately leading to graft failure. We aim to improve peptide prediction by modeling antigen processing. METHODS/STUDY POPULATION: T-cell epitope models for HLA mismatching struggle to predict which peptides are presented because antigen processing by proteases is not well modeled. We model antigen processing of HLA Class II proteins using 3D HLA structures (crystallography data) to create an HLA-specific antigen processing likelihood (APL) model. APL uses conformational stability measurements such as b-factor, COREX, solvent accessible surface area, and sequence entropy to predict cleavage sites from proteolysis. We will

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integrate APL into a T-cell epitope prediction tool for HLA-derived peptides based on donor and recipient HLA genotypes. Finally, we will associate the risk of graft failure with counts of these peptides derived from APL-integrated prediction models using a historical kidney transplant cohort from 2000 to 2023. RESULTS/ANTICIPATED RESULTS: We expect that applying APL could reduce false-positive peptide binders influencing 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. We expect that merging antigen processing (APL) and peptide-binding (NetMHCIIPan) models into a unified model would enhance risk stratification for graft failure. Current risk stratification still leads to poor outcomes post-transplant, especially for minority population groups. Our model can identify an alternative pool of well-matched donors and has the potential to improve equity for non-White minority candidates. DISCUSSION/SIGNIFICANCE OF IMPACT: Improving the understanding of how HLA matching contributes to kidney transplant outcomes can better stratify risks for kidney transplant recipients, enable personalized treatment, and ultimately improve outcomes for those undergoing kidney transplantation to treat renal diseases.

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Defining and designing a remote monitoring tool for CAR T-cell therapy patients

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OBJECTIVES/GOALS: The research aims to prototype a mobile app for physicians to remotely monitor patients receiving CD19-directed CAR T-cell therapy post-discharge. This app will facilitate standardized data collection across carious CAR-T treatment centers and help harmonize follow-up protocols. METHODS/STUDY POPULATION: A literature review and semi-structured interviews with patients, clinical coordinators, and experts helped identify essential parameters for a mobile app prototype aimed at monitoring adverse effects such as cytokine release syndrome and neurotoxicity. The app was designed through process mapping to combine data from self-reports and wearable devices, such as the Garmin smartwatch. New screens were designed in Figma, drawing from an existing patient monitoring app for allogeneic stem cell transplant follow-up. Finally, a preliminary feasibility study will be conducted to gather feedback on the app prototype from CAR T-cell therapy patients, healthcare providers, and stakeholders, ensuring its effectiveness and usability. RESULTS/ANTICIPATED RESULTS: Semi-structured interviews with people with professional and lived experience with CAR T-cell therapy were conducted to determine what metrics might be monitored and how they could be measured remotely to effectively monitor for side effects. The mobile phone application was then prototyped using process mapping in Visio®, designed in Figma, and preliminary development was completed. The final prototype includes parameters that will be recorded or measured using a combination of self-reporting and devices to monitor body temperature, basic vitals, activity, sleep, and cognitive function, among others. The prototype of the remote monitoring app is the first step in implementing remote monitoring of CAR T patients, standardized data collection, and reduction in the overall cost of CAR T-cell therapy. DISCUSSION/SIGNIFICANCE OF IMPACT: This app will enable physicians to monitor patients for routine follow-ups and adverse effects, such as CRS and ICANS. Future research will validate the digitized ICANS assessment and used to establish best practices for standardizing CAR-T follow-up protocols across Canada.

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Challenges in using real-world data to study opioid use disorder treatment in the hospital

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OBJECTIVES/GOALS: Our research group is focused on care of hospitalized persons with opioid use disorder (OUD) in the era of high-potency synthetic opioids (HPSO). In this work, we describe trends in patient-directed discharge (PDD) and inpatient treatment with medications for opioid use disorder (MOUD). We hypothesized that PDD is associated with MOUD dose and timing. METHODS/STUDY POPULATION: Patient data generated in the routine care of patients was automatically abstracted using a SQL query on Epic Clarity tables in the electronic health record (EHR). We included adult patients admitted to Johns Hopkins Hospital between July 1, 2019 and June 30, 2022, with an ICD-10-CM code for a list of opioid-related disorders (F11.X) consistent with OUD. Demographics, prior medication list, clinical care including hospital service, consultation services, COWS scores, length of time in emergency department, time of triage, time until receipt of methadone or buprenorphine, dosage and timing of MOUD, opioid medications other than methadone or buprenorphine, adjuvant medications; prior methadone or buprenorphine treatment and disposition. Query results were validated by manual abstraction of EHR. RESULTS/ANTICIPATED RESULTS: The SQL identification of the cohort of patients with OUD was found to be accurate. Time of triage, discrete orders completed during hospitalization were well represented in the query. The query was able to identify individual opioid medications but unable to summarize total dose in Morphine Milligram Equivalents. The query did not extract accurate information from patient-controlled analgesia pumps due to the continuous nature of the medication rather than discrete doses reflected in the medication administration record. Finally, the query characterized prior treatment with methadone or buprenorphine as a binary variable – dosage and timing of that prior treatment could not be accurately represented. Finally, stimulant use is not reliably collected in the EHR and was unavailable. DISCUSSION/SIGNIFICANCE OF IMPACT: Given the rise of HPSO, patients may not tolerate delay of MOUD. Improving the granularity of data collected will offer more insight into the inpatient treatment for OUD. Real-world data have promise but requires extensive technical expertise. Future work is needed to improve capture of derived variables such as total dosage of opioids in MME.

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