with 82 AERD patients. Taste sensitivity to denatonium (DB), serving as a proxy for tuft cell T2R functionality, will be assessed using a validated 13-point scale, and correlations with clinical outcomes – SNOT-22, histopathologic, CT, and endoscopic scores – will be analyzed using linear regression. Aim 2: Sinonasal epithelial cells will be collected from AERD patients either hyper- or hyposensitive to DB and from healthy controls. We will establish ALI cultures and expose them to varying DB concentrations. Secretions will be analyzed for antimicrobial peptide release via bacterial kill assays and for IL-25 and β-defensin 2 via ELISA. Tuft cell frequency and baseline IL-25 mRNA expression will be assessed using immunofluorescence and quantitative real-time polymerase chain reaction, respectively. RESULTS/ANTICIPATED RESULTS: We expect that higher DB taste sensitivity in AERD patients will correlate with worse clinical outcomes, reflected by elevated 6-month postoperative SNOT-22 scores, indicating increased symptoms. Additionally, we anticipate that preoperative Lund-MacKay and Lund-Kennedy scores, along with histopathological metrics, will be worse in DB-hypersensitive patients, establishing a link between taste sensitivity and disease burden. In vitro, we predict that AERD patients with DB hypersensitivity will demonstrate significantly higher IL-25 and β-defensin 2 secretion and reduced bacterial colonies in kill assays. We also expect increased tuft-cell frequency and baseline IL-25 mRNA in AERD-derived cultures compared to healthy controls, highlighting T2R functionality's role in AERD pathogenesis. DISCUSSION/SIGNIFICANCE OF IMPACT: This project aims to investigate a putative new role for Tuft cells in AERD pathogenesis by correlating Tuft cell T2R functionality with outcomes in AERD patients and with inflammatory response in vitro. Findings could lead to predictive clinical taste tests and future genotyping studies to identify T2R polymorphisms correlated with AERD severity.

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The Effect of Pesticide Exposure on Immunological Responses in Children Against SARS-CoV-2

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OBJECTIVES/GOALS: To assess the effect on the immune response to COVID-19 in children exposed to pesticides. The hypothesis is that increased pesticide exposure results in different immunological response to COVID-19. The goal of the proposal is to improve scientific knowledge on factors affecting COVID-19 and identify a modifiable factor to reduce these disparities. METHODS/STUDY POPULATION: A cross-sectional analysis of children (aged 5–17 years) with asthma to assess pesticide exposure and immune markers of SARS-CoV-2. SARS-CoV-2 infection or vaccination was determined with blood exposome RNA analyses assessed from blood samples taken at baseline. Immunological response was measured using neutralizing, phagocytizing, and NK-activating antibody responses biomarkers using plasma antibody isotyping, effector functions, T-cell activation-induced marker (AIM), and recall cytokine secretion assays on lysed, whole blood. Pesticide exposure was assessed as concentration of four urinary metabolites in a spot urine sample adjusted for creatinine. Unadjusted regression models were created to assess the effect of 3-phenoxy benzoic acid, a common pyrethroid pesticide, on immune markers. RESULTS/ANTICIPATED RESULTS: Children's (N = 30) average age was 10 years (interquartile range: 8–11) A majority of children were male (63%) and Non-Hispanic Black (73%). The majority of children had markers of SARS-CoV-2 infection (77%). Of the 4 pesticide metabolites assessed, only 3-PBA was commonly found (77% of samples > LOQ). Higher urinary concentrations of 3-PBA are associated with a significant (p DISCUSSION/SIGNIFICANCE OF IMPACT: Significant associations in cytokine and inflammatory marker may indicate a Th2-skewed response, and dysregulated cytokine responses can lead to severe disease. A suggested increase in T-cell activation markers (e.g., CD4, CD8) may indicate potential exhaustion if excessively activated.

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Prevalence of heteroresistance in urinary *Escherichia coli* in Metropolitan Atlanta, Georgia

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OBJECTIVES/GOALS: Urinary tract infections (UTIs) cause significant morbidity, and many patients require multiple courses of antibiotics increasing the risk of antibiotic resistance. We determined the prevalence of urinary antibiotic heteroresistance (HR), which has been associated with treatment failures in vivo, to three first-line antibiotics for UTIs. METHODS/STUDY POPULATION: Clinical urine *Escherichia coli* isolates from patients in metropolitan Atlanta, Georgia in August 2023 were collected as part of public health surveillance performed by the CDC-funded, Georgia Emerging Infections Program (EIP). Only the first *E. coli* isolate collected for each patient was included in this study. Antibiotic susceptibility was determined through medical record review. HR to nitrofurantoin, trimethoprim-sulfamethoxazole, and fosfomycin was determined by population analysis profiling (PAP), where broth dilutions of *E. coli* were plated on increasing concentrations of the antibiotic. HR was defined as survival of >1 in 106 cfu but fewer than 50% survival at 1X antibiotic breakpoint (bp), resistant as > 50% survival at 1X bp and susceptible as survival of RESULTS/ANTICIPATED RESULTS: Among 355 patients, 21 (5.9%) were resistant or intermediate to nitrofurantoin and 92 (26%) were resistant to trimethoprim-sulfamethoxazole. Antibiotic susceptibility data were missing from 5(1.4%) and 11(3%) of isolates for nitrofurantoin and trimethoprim-sulfamethoxazole, respectively. Susceptibility testing was not routinely performed nor reported for fosfomycin, thus excluded. PAP revealed that of the total 355 isolates, 3(0.84%) were heteroresistant to nitrofurantoin, 17(4.8%) were heteroresistant to trimethoprim-sulfamethoxazole, and 27(7.6%) were

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heteroresistant to fosfomycin. Of the isolates found to be susceptible by standard testing, 1(0.3%) and 9(3.6%) were heteroresistant to nitrofurantoin and trimethoprim-sulfamethoxazole by PAP, respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: Despite low rates of HR to nitrofurantoin and trimethoprim-sulfamethoxazole (0.84%, 4.8%), HR to fosfomycin was more frequent (7.6%). Given that susceptibility is not generally performed for fosfomycin, this could have implications for including fosfomycin as a first-line treatment for *E. coli* UTIs.

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Assessing genetic diversity of the Pfs25 vaccine candidate: Implications for malaria transmission-blocking vaccine in Africa

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OBJECTIVES/GOALS: Transmission-blocking vaccines hold promise for malaria elimination by reducing community transmission. But a major challenge that limits the development of efficacious vaccines is the vast parasite's genetic diversity. This work aims to assess the genetic diversity of the Pfs25 vaccine candidate in complex infections across African countries. METHODS/STUDY POPULATION: We employed next-generation amplicon deep sequencing to identify nonsynonymous single nucleotide polymorphisms (SNPs) in 194 *Plasmodium falciparum* samples from four endemic African countries: Senegal, Tanzania, Ghana, and Burkina Faso. The individuals aged between 1 and 74 years, but most of them ranged from 1 to 19 years, and all presented symptomatic *P. falciparum* infection. The genome amplicon sequencing was analyzed using Geneious software and *P. falciparum* 3D7 as a reference. The SPNs were called with a minimum coverage of 500bp, and for this work, we used a very sensitive threshold of 1% variant frequency to determine the frequency of SNPs. The identified SNPs were threaded to the crystal structure of the Pfs25 protein, which allowed us to predict the impact of the novel SNP in the protein or antibody binding. RESULTS/ANTICIPATED RESULTS: We identified 26 SNPs including 24 novel variants, and assessed their population prevalence and variant frequency in complex infections. Notably, five variants were detected in multiple samples (L63V, V143I, S39G, L63P, and E59G), while the remaining 21 were rare variants found in individual samples. Analysis of country-specific prevalence showed varying proportions of mutant alleles, with Ghana exhibiting the highest prevalence (44.6%), followed by Tanzania (12%), Senegal (11.8%), and Burkina Faso (2.7%). Moreover, we categorized SNPs based on their frequency, identifying dominant variants (>25%), and rare variants (DISCUSSION/SIGNIFICANCE OF IMPACT: We identified additional SNPs in the Pfs25 gene beyond those previously reported. However, the majority of these newly discovered display low variant frequency and population prevalence. Further research exploring the functional implications of these variations will be important to elucidate their role in malaria transmission.

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Disparities in healthcare discrimination among sexual minority groups: Insights from the NIH All of Us Program

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OBJECTIVES/GOALS: Discriminatory experiences within healthcare settings significantly hinder equitable health access for sexual minority groups (SMPs) in the USA. These discriminatory experiences can manifest in various forms (e.g., refusal of care). We aimed to explore different types of discrimination encountered by SMPs in the healthcare settings. METHODS/STUDY POPULATION: This study utilized secondary data from the NIH All of Us Research Program. For this analysis, we selected cohorts self-identifying as gay (n = 9,454), bisexual (n = 15,284), lesbian (n = 5,267), and straight (n = 349,748), enabling robust comparisons across SMPs and straight individuals. We employed analysis of variance and Chi-square analyses to assess group differences in healthcare discrimination, using key indicators from the Discrimination in Medical Settings Scale. These indicators captured experiences such as being treated with less respect or courtesy and feeling ignored by healthcare providers, providing a comprehensive view of discriminatory encounters in healthcare settings for SMPs. RESULTS/ANTICIPATED RESULTS: Our analyses revealed that bisexual individuals reported the highest levels of healthcare discrimination (mean = 3.64, SD = 2.45), followed by lesbians (mean = 3.37, SD = 2.47), other SMPs (mean = 3.36, SD = 2.53), gay (mean = 2.69, SD = 2.47), and straight participants (mean = 2.60, SD = 2.42). Among the seven discrimination indicators, the most reported experience was feeling like a doctor or nurse was not listening, with 76.8% of bisexual participants, 72.3% of lesbians, 68.8% of other SMPs, and 56.9% of gay participants reporting this experience. This was followed by reports of being treated with less respect and being treated with less courtesy in healthcare settings. These findings highlight the pervasive nature of healthcare discrimination among SMPs, particularly bisexual individuals. DISCUSSION/SIGNIFICANCE OF IMPACT: SMPs experience higher levels of

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