20th Freeman-Seage Symposium

On Infectious Disease Epidemiology

Tuesday April 29, 2025

Open to the Harvard Longwood Community

ORAL PRESENTATIONS: Kresge G3 | 1:30 - 4:30PM

POSTER RECEPTION: FXB Atrium | 4:45 - 6:30PM

In memory of Dr. Jonathan Freeman and Dr. George R. Seage III and their contributions to the Infectious Disease Epidemiology Program, we present ongoing research by current and former students, postdocs, and research associates.

CENTER *for* COMMUNICABLE DISEASE DYNAMICS | HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

Table of Contents

About the Honorees

Jonathan Freeman (1939-2000)
Jonathan Freeman was a faculty member at the Harvard Chan School of Public Health from 1990 until May 2000. He was instrumental in creating and leading the Interdisciplinary Program in Infectious Disease Epidemiology (IPIDE). Freeman designed and taught courses on the investigation and transmission dynamics of infectious disease outbreaks, promoting an active interest in infectious disease epidemiology at a time when it was not widely popular. As a faculty member at Harvard Medical School, he practiced infectious disease medicine at Boston City Hospital (now Boston Medical Center), Brigham and Women's Hospital, and the West Roxbury Veterans Affairs. Freeman was also an active member of the Society for Healthcare Epidemiology of America, where he taught a famously rigorous course on epidemiology principles for hospital epidemiologists. His research interests included hospital-acquired infections, tuberculosis, and malaria.

George R. Seage III (1957-2021)
George R. Seage III was a faculty member at Harvard Chan School of Public Health from 1999 until his passing in 2021. He was a valued member of the Department Epidemiology and a leader in the field of human immunodeficiency virus (HIV) research. He played a key role in the earliest efforts to understand HIV and acquired immunodeficiency syndrome (AIDS), bringing epidemiologic skills and expertise to the the field.

Seage was passionate about and dedicated to mentoring the next generation of infectious disease epidemiologists. He contributed to establishing program to mentor early career investigators in the Pediatric HIV/AIDS Cohort Study (PHACS). He was also the co-principal investigator of a T32 graduate training program in infectious disease epidemiology and biodefense and served as the director of the IPIDE.

Oral Presentations

KRESGE G3 | 1:30 - 4:30PM

1:30 PM	Welcome and Introduction **Marc Lipsitch,** DPhil, Professor of Epidemiology
1:35 PM	Transmission or Importation? Using SARS-CoV-2 Genomics to Guide Infection Control protocols **Mui Pham,** Postdoctoral Research Fellow, Epidemiology
1:50 PM	Biological drivers of frequency dependent selection in post-vaccine pneumococcal populations **Indra Gonzalez Ojeda,** PhD Student, Physics
2:05 PM	Alcohol use, alcohol outlets, and spatial HIV epidemic burden in South Africa **Domonique Reed,** Postdoctoral Research Fellow, Epidemiology
2:20 PM	Quantifying the impact of antibiotic use and genetic determinants of resistance on Neisseria gonorrhoeae lineage dynamics **David Helekal,** Postdoctoral Research Fellow, Epidemiology
2:35 PM	**Q&A Session** Moderated by **Bill Hanage**, Professor, Epidemiology

2:50 PM BREAK

Oral Presentations

KRESGE G3 | 1:30 - 4:30PM

3:10 PM	Evolutionary and host demographic factors shaping the diversity of a multilocus antigen in Neisseria gonorrhoeae **QinQin Yu**, Postdoctoral Research Fellow, Immunology and Infectious Dis.
3:25 PM	Equity considerations in COVID-19 vaccine allocation modelling: a methodological study **Eva Rumpler,** PhD Candidate, Epidemiology
3:40 PM	Comparing strategies to introduce two new antibiotics that minimize drug resistance in gonorrhea: a modeling study **Madeleine Kline,** MD-PhD Candidate, Population Health Sciences
3:55 PM	**Q&A Session** Moderated by **Bill Hanage,** Professor, Epidemiology
4:20 PM	Closing Remarks **Megan Murray,** Professor in the Department of Epidemiology

Poster Presentations

FXB ATRIUM | 4:45 - 6:30PM

1 Spatiotemporal variability of malaria transmission in the Brazilian Amazon driven by weather and climate patterns
Nicholas J. Arisco, Postoctoral Research Fellow, Global Health and Population

2 Can Group B Streptococcus (GBS) strain diversity in carriage be recovered from low-abundance metagenomic samples? A simulation study
Ruchita Balasubramanian, PhD Candidate, Epidemiology

3 Surveillance for TB drug resistance using routine rapid diagnostic testing data: Methodological development and application in Brazil
Sarah Baum, PhD Student, Global Health and Population

4 Focusing a Viral Risk Ranking Tool on Prediction
Katherine Budeski, PhD Student, Epidemiology

5 Exploring SARS-CoV-2 Intrahost Evolution and Transmission with Deep Sequencing Genomic Surveillance Data
Léa Cavalli, PhD Candidate, Epidemiology

6 Why should we study indirect effects of antimicrobial treatment strategies?
Juan Gago, Postdoctoral Research Fellow, Epidemiology

7 Linking Genetic Distance to Invasiveness in Streptococcus pneumoniae
Sophia Lerebours (Undergraduate student at Harvard College)**, Indra Gonzalez Ojeda** (PhD Student, Physics)**, Marc Lipsitch**, DPhil (Professor, Epidemiology)

Poster Presentations

FXB ATRIUM | 4:45 - 6:30PM

8 Prevalence of Chronic Pulmonary Aspergillosis in Tuberculosis Populations: A Systematic Review and Meta-Analysis
Alicia Madden, Research Assistant, Global Health and Social Medicine

9 Mining and Malaria: Addressing Mobility and Access in the Guyana Shield
Andrea Parra Salazar, PhD Student, Global Health and Population

10 Heterogeneous constraint and adaptation across the malaria parasite life cycle
Sarah Perkins, PhD Candidate, Biology

11 Low-Cost Approaches for Detecting Antimicrobial Resistance in Bacterial Infections in Resource-Limited Settings: A Scoping Review
David Roach, Instructor in Medicine

12 Seasonal forcing and waning immunity drive the sub-annual periodicity of the COVID-19 epidemic
Ilan N. Rubin, Postdoctoral Research Fellow, Epidemiology

13 Target trial emulation with test restricted sampling to estimate COVID-19 booster vaccine efficacy: a cohort study
Beau Schaeffer, PhD Student, Epidemiology

14 Isoniazid Preventive Therapy (IPT) and TB infection in intrahousehold contacts
Oscar Zazueta Fierro, PhD Student, Population Health Sciences

Abstracts

ORAL PRESENTATIONS

Transmission or Importation? Using SARS-CoV-2 Genomics to Guide Infection Control protocols

Mui Pham, Postdoctoral Research Fellow, Epidemiology

Effective outbreak management relies on the timely and accurate identification of infection sources. In this ongoing project, we integrate epidemiological and genomic data to distinguish between transmission and importation events during real-time SARS-CoV-2 outbreak investigations. We leverage the Bayesian inference tool phybreak, which uniquely facilitates the modeling of multiple introductions, to analyze surveillance and whole-genome sequencing data from the National Basketball Association Occupational Health Program spanning November 28, 2020, to September 13, 2022. Our approach quantifies the probability that each case represents either an importation from the community or a transmission within the NBA. In addition, we assess how the accuracy of these esimtates vary depending on the prevalence and genetic diversity of circulating SARS-CoV-2 variants. These insights are critical for informing and optimizing infection control protocols by identifying cases where additional data collection is needed to accurately determine the source of infection. Results presented in this talk are preliminary and are not suitable for broader dissemination.

Biological drivers of frequency dependent selection in post-vaccine pneumococcal populations

Indra Gonzalez Ojeda, PhD Student, Physics

Streptococcus pneumoniae often colonizes the human nasopharynx asymptomatically, but can sometimes cause invasive diseases such as pneumonia, meningitis, and sepsis. In the early 2000s, the pneumococcal conjugate vaccine (PCV) was introduced. This vaccine targets a subset of pneumococcal serotypes, distinguished by differences in their capsular polysaccharides. The selective removal of these invasive-associated serotypes by the PCV provides a unique opportunity to study the evolution of S. pneumoniae populations following vaccination. Interestingly, although strains with vaccine-targeted capsules decrease in frequency (as expected), the frequencies of accessory genes initially become perturbed but subsequently bounce back to their original values. This pattern is thought to be driven by negative frequency-dependent selection (NFDS) acting on the accessory genome. NFDS is a type of balancing selection in which the fitness of a variant is inversely correlated with its frequency; rare variants gain an advantage, whereas common variants are selected against, thus driving traits toward intermediate frequencies. Despite evidence supporting the role of NFDS in shaping pneumococcal populations, the biological mechanisms underlying this phenomenon remain unclear. In this talk, I will discuss our progress toward identifying the specific biological functions subject to NFDS, aiming to better understand the evolutionary forces structuring S. pneumoniae populations. By combining genomic data and predictive modeling, we are working toward uncovering the forces driving this intriguing phenomenon.

Abstracts

ORAL PRESENTATIONS

Alcohol use, alcohol outlets, and spatial HIV epidemic burden in South Africa

Domonique Reed, Postdoctoral Research Fellow, Epidemiology

While alcohol use is associated with HIV acquisition and transmission in South Africa, actionable and effective approaches to intervening against alcohol use are less clear. Reaching individuals through alcohol outlets may be an efficient strategy to reach persons with disproportionate risk. The objectives of this study are to examine the association between individual-level alcohol use and HIV prevalence across South Africa and to assess the association between alcohol outlet density and HIV prevalence in the Western Cape, South Africa. We analyzed data from the 2017 South African HIV Biobehavioral, Serostatus, and Media Impact Survey (SABSSM V), supplemented by the 2011 South African National Census and the 2017 Western Cape Liquor Authority Licensing Database. First, logistic regression was used to estimate the association between individual-level alcohol use and HIV status among the full national survey sample. Second, restricted to data from Western Cape province, we used spatial binomial regression to estimate the association between alcohol outlet density (number of licensed outlets per 1,000 people) and HIV prevalence across small area layers. Both analyses were adjusted for demographic covariates and weighted to account for the SABSSM V survey design. In the national sample (n = 42,756 individuals), HIV prevalence was higher among lifetime abstainers (19.6%) compared to those who had ever consumed alcohol (15.7%). However, among ever drinkers, HIV prevalence was higher among those reporting hazardous alcohol use (16.6%) than among those who abstained in the past 12 months (13.6%). Low-risk, harmful, and potential alcohol dependence use in the past 12 months was associated with a 45% (95% CI: 1.12-1.93), 32% (95% CI: 0.95-1.82), and 33% (95% CI: 0.89-1.98) higher odds of HIV, respectively, compared to recent abstainers. In the spatial analysis of the Western Cape province (n=8,408 small area layers), areas with medium alcohol outlet density (>0 to 2 alcohol outlets per 1,000 people) and high alcohol outlet density (>2 alcohol outlets per 1,000 people) were associated with a 41% (95% CI: 0.99-1.97) and 5% (95% CI: 0.73-1.47) higher odds of HIV compared to areas with low alcohol outlet density (0 alcohol outlets per 1,000 people). Additionally, areas where over 50% of outlets were on-site consumption venues had a 21% (95% CI: 0.90-1.61) higher odds of HIV compared to areas with a higher proportion of off-site consumption venues. These findings highlight the complex relationship between alcohol use, alcohol availability, and HIV, underscoring the importance of addressing both individual and structural drivers of HIV when developing prevention interventions.

Abstracts

ORAL PRESENTATIONS

Quantifying the impact of antibiotic use and genetic determinants of resistance on Neisseria gonorrhoeae lineage dynamics

David Helekal, Postdoctoral Research Fellow, Epidemiology

The dynamics of antimicrobial resistance in bacterial populations are informed by the fitness impact of genetic determinants of resistance and antibiotic pressure. However, estimates of real-world fitness impact have been lacking. To address this gap, we developed a hierarchical Bayesian phylodynamic model to quantify contributions of resistance determinants to strain success in a 20-year collection of Neisseria gonorrhoeae isolates. Fitness contributions varied with antibiotic use, and genetic pathways to phenotypically identical resistance conferred distinct fitness effects. These findings were supported by in vitro and experimental infection competition. Quantifying these fitness contributions to lineage dynamics reveals opportunities for investigation into other genetic and environmental drivers of fitness. This work thus establishes a method for linking pathogen genomics and antibiotic use to define factors shaping ecological trends.

Evolutionary and host demographic factors shaping the diversity of a multilocus antigen in Neisseria gonorrhoeae

QinQin Yu, Postdoctoral Research Fellow, Immunology and Infectious Diseases

The rise in antibiotic resistant gonorrhea has underscored the importance of developing a vaccine and understanding the basis of immune evasion in Neisseria gonorrhoeae. Opacity proteins (Opa) are one of the most abundant, diverse, and immunogenic antigens in N. gonorrhoeae. Opa are encoded by up to 11 opa loci per genome and diversity is generated via gene conversion, recombination between strains, and phase variation via frameshift mutations. Standard short-read sequencing platforms are unable to capture multilocus genes, limiting our understanding of opa diversity and evolution. We used 86 publicly available complete genomes of N. gonorrhoeae, generated 87 additional complete genomes from representative isolates across the N. gonorrhoeae phylogeny using Oxford Nanopore long-read sequencing, developed new computational tools to analyze the highly diverse opa sequences, and identified the genetic processes and host pressures shaping opa diversity and evolution. Our results support a model of Opa variation where phase variation modulates the expression of highly diverse opa alleles within strains on short timescales, and opa gene duplication followed by recombination and mutation and lead to diversification of the opa repertoire on long timescales. Our results also suggest that opa evolutionary pressures vary with genetic locus and sexual network.

Abstracts

ORAL PRESENTATIONS

Equity considerations in COVID-19 vaccine allocation modelling: a methodological study

Eva Rumpler, PhD Candidate, Epidemiology

We conducted a methodological study of COVID-19 vaccine allocation modelling papers, specifically looking for publications that considered equity. We found that most models did not take equity into account, with the vast majority of publications presenting aggregated results and no results by any subgroup (e.g. age, race, geography, etc). We then give examples of how modelling can be useful to answer equity questions, and highlight some of the findings from the publications that did. Lastly, we describe eight considerations that seem important to consider when including equity in future vaccine allocation models.

Comparing strategies to introduce two new antibiotics that minimize drug resistance in gonorrhea: a modeling study

Madeleine Kline, MD-PhD Candidate, Population Health Sciences

Drug resistance is a major threat to the ongoing treatability of gonorrhea. As of 2020, intramuscularly injected ceftriaxone is the only remaining first-line therapy. Reduced susceptibility to ceftriaxone has already been detected worldwide, further emphasizing the need for more treatment options. Two first-in-class oral antibiotics showed successful phase III trial results and will likely be approved to treatment gonorrhea soon. Prior modeling showed that holding a new treatment in reserve until there is high resistance to the current medication is a consistently worse drug introduction strategy than the random allocation or combination strategies. However, there are many more ways to introduce two new medications with one existing treatment, and there is a lack of research to indicate which of these strategies would reduce overall drug resistance best. We utilize a deterministic, compartmental model to simulate two implementation strategies: a) sequential and b) equal allocation. Preliminary results suggest that balancing selective pressures at a population level rather than reserving new drugs reduces overall gonorrhea drug resistance, which aligns with prior modeling but contradicts classical antibiotic stewardship dogma.

Abstracts

POSTER PRESENTATIONS

1 Spatiotemporal variability of malaria transmission in the Brazilian Amazon driven by weather and climate patterns

Nicholas J. Arisco, Postoctoral Research Fellow, Global Health and Population

Since the 1950s, the Amazon has experienced increasingly atypical climatological patterns, often driven by El Niño or La Niña (ENSO) events, which, alongside deforestation, have exacerbated climatic changes and affected malaria transmission. In 2023 and 2024, the region faced some of its most severe droughts on record, linking these weather patterns more closely to malaria prevalence. This study aimed to estimate the impact of lagged weather and ENSO events on malaria transmission in the Brazilian Amazon from 2003 to 2022, utilizing daily individual-level data from the Brazilian Malaria Epidemiological Surveillance Information System (Sivep-Malaria). A case-crossover approach was employed to analyze these effects at the Amazon-wide and state levels, using generalized additive quasipoisson models to assess the influence of ENSO events. Results showed that above-median weather conditions in the week prior to infection increased malaria risk, while protective effects were noted with two- and three-week lags. Additionally, ENSO events, such as El Niño and La Niña, were associated with a net decrease in malaria cases, though their effects varied significantly. This study emphasizes the need for proactive, fine-scale malaria control using weather forecasting and early warning systems, highlighting the heterogeneity of weather impacts across different regions.

Abstracts

POSTER PRESENTATIONS

2 Can Group B Streptococcus (GBS) strain diversity in carriage be recovered from low-abundance metagenomic samples? A simulation study"

Ruchita Balasubramanian, PhD Candidate, Epidemiology

Group B Streptococcus (GBS) is a gut commensal and cause of neonatal invasive disease, potentially following vaginal dysbiosis[1]. While maternal colonization is linked to neonatal disease, understanding GBS colonization dynamics across body sites remains critical. One hypothesis suggests vaginal colonization is seeded from the gut, given its gastrointestinal carriage[2]. Without whole genome sequences from either niche, metagenomic samples offer an alternative to explore GBS strain diversity. However, low GBS abundance in the gut complicates strain typing.

We conducted a simulation study to assess GBS strain typing at low abundance. Using Seq2mgs, we created 78 synthetic metagenomes by spiking GBS reads into a background metagenome (Accession: SRR12344432) at relative abundances of 0.01X, 0.005X, 0.001X[3]. For each clonal complex (CC), we used 2-3 publicly available GBS genomes from the CDC ABC's surveillance system to generate synthetic metagenomes. Using k-mer based tool StrainGE, we tested these synthetic metagenomes against 130 RefSeq reference genomes[4].

The GBS CC's were accurately identified for all synthetic metagenomes except CC12 and CC452. CC12 samples were identified as a mix of ST7 and ST283, while 3/9 CC452 samples were identified as a mix of ST23 and ST452. ST mismatches are likely based on limitations of ST typing (based only on 7 housekeeping genes), and the particular heterogeneity of CC12[5,6]. We are in the process of generating a phylogeny containing the 500 publicly available CDC genomes and the Refseq genomes to see if the reference genome identified clusters closes with the genome used for creating the spiked metagenomic sample for CC12.

Ultimately, our simulation shows the ability to accurately recapitulate GBS strain types despite low abundance in complex microbial backgrounds. This confirms the potential of using this approach on empirical metagenomic samples to investigate GBS dynamics across carriage niches.

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3. Van Camp P-J, Porollo A. SEQ2MGS: an effective tool for generating realistic artificial metagenomes from the existing sequencing data. NAR Genomics and Bioinformatics 2022; 4: lqac050.
4. StrainGE: a toolkit to track and characterize low-abundance strains in complex microbial communities | Genome Biology | Full Text. https://genomebiology.biomedcentral.com/articles/10.1186/s13059-022-02630-0#Sec12 (accessed Jan 24, 2025).
5. Jones N, Bohnsack JF, Takahashi S, et al. Multilocus sequence typing system for group B streptococcus. J Clin Microbiol 2003; 41: 2530–6.
6. Hsu J-F, Chen Y-N, Chu S-M, et al. Clonal Complex 12 Serotype Ib Streptococcus agalactiae Strain Causing Complicated Sepsis in Neonates: Clinical Features and Genetic Characteristics. Microbiol Spectr; 11: e03778-22.

Abstracts

POSTER PRESENTATIONS

3 Surveillance for TB drug resistance using routine rapid diagnostic testing data: Methodological development and application in Brazil

Sarah Baum, PhD Student, Global Health and Population

While data on drug-resistant tuberculosis (DR-TB) may be routinely collected by National TB Control Programs using rapid diagnostic tests (RDTs), these data streams may not be fully utilized for DR-TB surveillance where low testing coverage may bias inferences due to systematic differences in RDT access. Here, we develop a method to correct for potential biases in routine RDT data to estimate trends in the prevalence of TB drug resistance among notified TB cases.
We developed a method that attempts to correct for non-random use of RDT testing in the context of routine TB diagnosis to recover unbiased estimates of resistance among new and previously treated TB cases. Applying this approach to recent national case-level data from Brazil, we find that modeled estimates were higher than naïve estimates, and with narrower uncertainty intervals compared to estimates produced by the World Health Organization. We highlight the value of this approach to settings where testing coverage is low or variable, as well as settings where coverage may surpass existing coverage thresholds, but that could nonetheless benefit from additional statistical correction.

4 Focusing a Viral Risk Ranking Tool on Prediction

Katherine Budeski, PhD Student, Epidemiology

Preparing to rapidly respond to emerging infectious diseases is critical. SpillOver: Viral Risk Ranking is an open-source tool developed to assess the risk of novel wildlife-origin viruses spilling over from animals to humans and spreading in human populations. Several risk factors used by the tool depend on evidence of previous zoonotic spillover itself or sustained transmission in humans. Therefore, we reanalyzed the Ranking Comparison after removing eight of the thirty-one risk factors that require post-spillover knowledge and compared the adjusted risk rankings to the originals. The area under the receiver operating characteristic curve deteriorated from 0.94 for the original risk scores to 0.73 for the adjusted ones for predicting the classification as a human virus. We also compared the mean and standard deviation of the risk scores for the human and non-human viruses at the risk factor level. Most excluded spillover-dependent risk factors had dissimilar means between the human and non-human virus classifications, but non-spillover dependent risk factors frequently showed similar means between the two classifications. The original formulation of the tool depended on the inclusion of spillover-dependent risk factors to quantitatively assess the risk of zoonotic spillover for a novel virus. Future iterations of the tool should omit such risk factors and consider other non-spillover dependent risk factors to ensure the tool is fit for risk prediction of novel viruses.

Abstracts

POSTER PRESENTATIONS

5 Exploring SARS-CoV-2 Intrahost Evolution and Transmission with Deep Sequencing Genomic Surveillance Data

Léa Cavalli, PhD Candidate, Epidemiology

Studying within-host variation reveals the evolutionary trajectory of new mutations during infections and their potential persistence at the population level through transmission. In this study, we used deep sequencing data from Boston University's COVID-19 testing initiative to analyze SARS-CoV-2 within-host variation. Given the absence of experimental controls, we developed data filtering methods to distinguish true intrahost single nucleotide variants (iSNVs) from sequencing errors and contamination, addressing a major challenge in sub-consensus variation studies. We observed shared intrahost variation among closely related samples as a marker of transmission and found that new mutations are infrequently transmitted. Among de novo iSNVs that emerged during transmission, purifying selection predominated, indicating that most non-synonymous mutations are quickly eliminated. Some recurring synonymous and missense iSNVs appeared, likely representing mutational hotspots rather than genuine sites of positive selection. These findings suggest that new VoCs, characterized by largely divergent genotypes, are unlikely to emerge from the gradual transmission of mutations between acutely infected individuals, prompting the exploration of alternative hypotheses.

6 Why should we study indirect effects of antimicrobial treatment strategies?

Juan Gago, Postdoctoral Research Fellow, Epidemiology

Causal inference provides powerful tools for estimating the impact of interventions, but traditional methods often focus solely on direct treatment effects. In the context of infectious diseases, where pathogens are inherently contagious, this approach is insufficient. An intervention applied to one individual can influence the health outcomes of their contacts—creating indirect or spillover effects that must be accounted for in any comprehensive analysis.

Antimicrobial resistance represents a critical domain where these indirect effects have substantial public health implications. When new therapeutic regimes are introduced, we must evaluate not only the benefits and risks to treated individuals but also the broader consequences for the community. Enhancing our causal inference methods to accommodate these complex interference patterns is therefore essential for accurate estimation of treatment impacts.

In this study, we explore key clinical scenarios where capturing indirect effects significantly influences decision-making around antimicrobial use. By properly accounting for these spillover mechanisms, we demonstrate how causal inference can optimize antimicrobial stewardship and ultimately improve community health outcomes in the face of increasing resistance challenges.

Abstracts

POSTER PRESENTATIONS

7 Linking Genetic Distance to Invasiveness in Streptococcus pneumoniae

Sophia Lerebours (Undergraduate student at Harvard College)**, Indra Gonzalez Ojeda** (PhD Student, Physics)**, Marc Lipsitch**, DPhil (Professor, Epidemiology)

Understanding how bacterial genomic variation relates to pathogenicity is essential for predicting and controlling infectious disease. One important trait, invasiveness, reflects a strain's likelihood of causing disease after colonization. In Streptococcus pneumoniae, invasiveness varies across serotypes and strains and is influenced by features like the polysaccharide capsule. However, calculating invasiveness typically requires large-scale surveillance efforts that collect both carriage and invasive disease data, which are resource-intensive. The relationship between genetic distance and invasiveness remains poorly characterized. Here, we preliminarily show that more invasive pneumococcal strains tend to form genetically tighter clusters, suggesting an inverse relationship between invasiveness and within-strain genetic diversity. Using CDC Active Bacterial Core surveillance data and MASH-estimated distances, we applied a nearest-neighbor chaining approach to summarize the genetic relatedness of isolates within serotypes. We observed that strains with higher invasiveness often exhibit lower average genetic distance between isolates. This finding suggests that more invasive strains may appear genetically tighter, not because of recent transmission, but because they are more often sampled from disease cases, leading to less observed variation. In contrast, less invasive strains may accumulate greater observed diversity due to broader and more prolonged circulation. These differences in sampling patterns may create a detectable genomic signature associated with invasiveness. Further research is necessary to confirm these results and characterize the relationship between invasiveness and genetic distance. As genomic surveillance expands, methods linking genetic distance to clinical outcomes could support faster risk assessments for emerging pathogens. Our framework may extend to other bacteria where disease outcomes are harder to measure but genomic data are abundant.

Abstracts

POSTER PRESENTATIONS

8 Prevalence of Chronic Pulmonary Aspergillosis in Tuberculosis Populations: A Systematic Review and Meta-Analysis

Alicia Madden, Research Assistant, Global Health and Social Medicine

Tuberculosis (TB) is a major global health concern, with long-term complications persisting even after successful treatment. One such complication is chronic pulmonary aspergillosis (CPA), a progressive fungal disease that frequently develops in TB survivors and contributes significantly to post-TB lung disease (PTLD). CPA is underrecognized and often misdiagnosed as TB due to similar clinical presentations. Several recent studies of TB patient cohorts have conducted screening for CPA, but the true burden of this disease among TB patients remains unclear. Through a systematic review and meta-analysis, we aimed to estimate the prevalence of CPA among patients currently or previously treated for TB. We conducted a systematic search inPubMed, Cochrane Library, Web of Science, and Science Direct for cohort and cross-sectional studies that estimated CPA prevalence in TB patients according to current diagnostic criteria. After screening 1,575 unique studies and reviewing 118 full texts, we included 22 studies with a total of 2,884 patients in our review. We used a random-effects meta-analysis to estimate pooled CPA prevalence, with subgroup and meta-regression analyses exploring factors influencing CPA burden.

Our meta-analysis revealed a high burden of CPA in tuberculosis patient populations. Among all TB patients, CPA prevalence was 9% (95% CI: 6%, 12%) during treatment and 13% (95% CI: 6%, 27%) post-treatment. Among patients with persistent respiratory symptoms, CPA prevalence was 20% during treatment and 48% (95% CI: 36%, 61%) post-treatment. A mixed-effects meta-regression identified symptom status and timing of CPA assessment as predictors of CPA prevalence, with no significant variation by world region. The considerable CPA burden among TB survivors, particularly in those with persistent symptoms following TB treatment, underscores the need for routine CPA screening in TB programs. Since TB is often diagnosed even when sputum smear and culture are negative, it is possible that some individuals given TB treatment may instead have CPA. Accurate diagnosis and access to appropriate therapies could improve patient outcomes for both CPA and TB.

Abstracts

POSTER PRESENTATIONS

9 Mining and Malaria: Addressing Mobility and Access in the Guyana Shield

Andrea Parra Salazar, PhD Student, Global Health and Population

The Guyana Shield region faces unique public health challenges for the control and elimination of malaria that differ from traditional deforestation-driven disease patterns seen elsewhere. Gold mining has been proven to be closely linked with malaria transmission, and land-use change has traditionally been described as the main driver behind increased malaria incidence in mining communities. While environmental conditions remain necessary for malaria transmission to occur, we contend that the failure of current control strategies stems primarily from overlooking crucial social dynamics: the exceptional remoteness of mining operations and the highly mobile workforce that circulates through these sites. Together, these elements create complex transmission networks that current approaches struggle to address.

We present evidence showing that proximity to mining operations is a critical determinant of malaria transmission patterns, with significant differences in travel distances and connectivity patterns between mining and non-mining populations. Using network analysis metrics including fadeout effects and outdegree centrality, we quantify how these mobility patterns influence disease spread. Our findings highlight the need for malaria control strategies specifically tailored to address the unique challenges of healthcare delivery in remote mining communities of the Guyana Shield region. Although the introduction of Rapid Diagnostic Tests (RDTs) has shown promising impacts, including decreased travel distances for diagnosis and treatment, strategic placement of these diagnostic resources remains crucial. This research provides insights into centering social dynamics in diagnostic and treatment distribution to maximize coverage of high-risk populations while accounting for the unstable and shifting nature of settlements in mining areas.

Abstracts

POSTER PRESENTATIONS

10 Heterogeneous constraint and adaptation across the malaria parasite life cycle

Sarah Perkins, PhD Candidate, Biology

Evolutionary forces vary across genomes, creating disparities in how traits evolve. In organisms with complex life cycles, it is unclear how intrinsic differences among discrete life stages impact evolution. We looked for life history-driven changes in patterns of adaptation in Plasmodium falciparum, a malaria-causing parasite with a multi-stage life cycle. Categorizing genes based on their expression in different life stages, we compared patterns of between- and within- species polymorphism across stages by estimating nonsynonymous to synonymous substitution rate ratios (dN/dS) and mean pairwise nucleotide diversity (πNS/πS). Considering these alongside estimates of Tajima's D, fixation probability, adaptive divergence proportion and rate, and FST, we looked for changes in the drift-selection balance in life stages subject to transmission bottlenecks and changes in ploidy. We observed signals of reduced selection efficacy in genes exclusively expressed in sporozoites, the parasite form transmitted from mosquitoes to humans and often targeted by vaccines and monoclonal antibodies. We discuss implications for how parasites evolve to resist therapeutics and consider functional, molecular, and population genetic factors that could contribute to these patterns.

11 Low-Cost Approaches for Detecting Antimicrobial Resistance in Bacterial Infections in Resource-Limited Settings: A Scoping Review

David Roach, Instructor in Medicine

Antimicrobial resistance (AMR) poses a major global health threat, with disproportionate impacts in low- and middle-income countries (LMICs) where access to diagnostic infrastructure is limited. Timely detection of resistance is critical to guide appropriate therapy and prevent the spread of resistant infections, yet most current diagnostic platforms remain expensive, infrastructure-dependent, and poorly suited to resource-limited settings. In this scoping review, we systematically identified and characterized low-cost and low-resource diagnostic approaches for detecting AMR in both sexually transmitted and common bacterial infections, applying the WHO REASSURED criteria to assess their feasibility for implementation in LMICs. A wide array of emerging technologies were identified—including genotypic, phenotypic, and process-oriented approaches—that show promise for use in decentralized or near-point-of-care settings. However, we found limited evidence of clinical integration, impact on antibiotic prescribing, or health outcomes, and none of the identified diagnostics fully met all REASSURED criteria. These findings highlight a critical gap between diagnostic innovation and real-world implementation, underscoring the need for expanded field validation, implementation research, and targeted investment to accelerate the adoption of AMR diagnostics in high-burden but low-resource settings.

Abstracts

POSTER PRESENTATIONS

12 Seasonal forcing and waning immunity drive the sub-annual periodicity of the COVID-19 epidemic

Ilan N. Rubin, Postdoctoral Research Fellow, Epidemiology

Seasonal trends in infectious diseases are shaped by climatic and social factors, with many respiratory viruses peaking in winter. However, the seasonality of COVID-19 remains in dispute, with significant waves of cases across the United States occurring in both winter and summer. Using wavelet analysis of COVID-19 cases, we find that the periodicity of epidemic COVID-19 varies markedly across the U.S. and correlates with winter temperatures, indicating seasonal forcing. However, the pattern of multiple waves per year that has been so disruptive and unique to COVID-19 cannot be explained by seasonal forcing. Using a modified SIRS model that allows specification of the tempo of waning immunity, we show that specific forms of non-durable immunity can sufficiently explain the sub-annual waves characteristic of the COVID-19 epidemic. Extending the wavelet analyses to more recent wastewater viral surveillance data shows a possible stabilization of the epidemic dynamics to a biannual cycle in California and Massachusetts.

13 Target trial emulation with test restricted sampling to estimate COVID-19 booster vaccine efficacy: a cohort study

Beau Schaeffer, PhD Student, Epidemiology

Observational studies play a critical role in the generation of evidence for vaccine safety and efficacy in the post-market period. The target trial emulation (TTE) framework has been developed to overcome design-induced biases common to cohort studies, however, it is not robust to unmeasured confounding caused by differential health seeking behavior. The test negative design (TND) is a common alternative approach used in these settings but not without compromises. We emulated a target trial evaluating COVID-19 bivalent booster efficacy using electronic health records from the Kaiser Permanente of Northern California network that incorporates key sampling features of the TND. We use negative control exposures and outcomes to show that fine-matching is not sufficient to eliminate unmeasured confounding and we compare results from a standard TTE design to those from our "test restricted" sampling. This study is one of the first implementations of recent theoretical developments to the causal framework underlying widely used study designs for evaluating infectious disease interventions.

Abstracts

POSTER PRESENTATIONS

14 Isoniazid Preventive Therapy (IPT) and TB infection in intrahousehold contacts

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Preventive therapy is known to prevent progression to TB disease in individuals with latent infection, however, uncertainty exists regarding whether preventive therapy prevents initial TB infection (conversion from negative to positive TST).
The goal of this study is to evaluate the effectiveness of Isoniazid Preventive Therapy (IPT) in preventing tuberculosis (TB) infection among tuberculin skin test (TST)-negative household contacts of TB-positive patients within a prospective cohort in Perú.

RETURN TO THE FIRST PAGE