Impact of Respiratory Staphylococcus aureus Abundance on Risk for Ventilator-Associated Pneumonia During Long-Term Care

James J. Harrigan, MD, PharmD¹; Hatem Abdallah¹; Erik L. Clarke, PhD²; Ebbing Lautenbach, MD, MPH, MS^{1,2}; Emily Reesey, MS²; Magda Wernovsky¹; Pam Tolomeo²; Zygmunt Morawski⁴; Jerry Jacob, MD, MS^{1,4}; Michael A. Grippi, MD^{3,4}; Brendan J. Kelly, MD, MS^{1,2}

Objectives

• We sought to evaluate the impact of respiratory Staphylococcus aureus colonization and bacterial community dominance, both diagnosed and undiagnosed, on subsequent S. aureus VAP and VAE during long-term acute care.

Introduction

- Clinically-diagnosed ventilator associated pneumonia (VAP) is common in the long-term acute care hospital (LTACH) setting.^{1,2}
- VAP may contribute to adverse ventilator-associated events (VAE).³
- *S. aureus* is a common causative organism of VAP.^{4,5}
- Healthcare exposure results in significant microbiome disruption, particularly in the setting of critical illness, and may contribute to risk for healthcare-associated infections (HAIs) including VAP.⁶ Bacterial community dominance has been shown to be a useful index of microbiome disruption, which is associated with risk for VAP.⁵

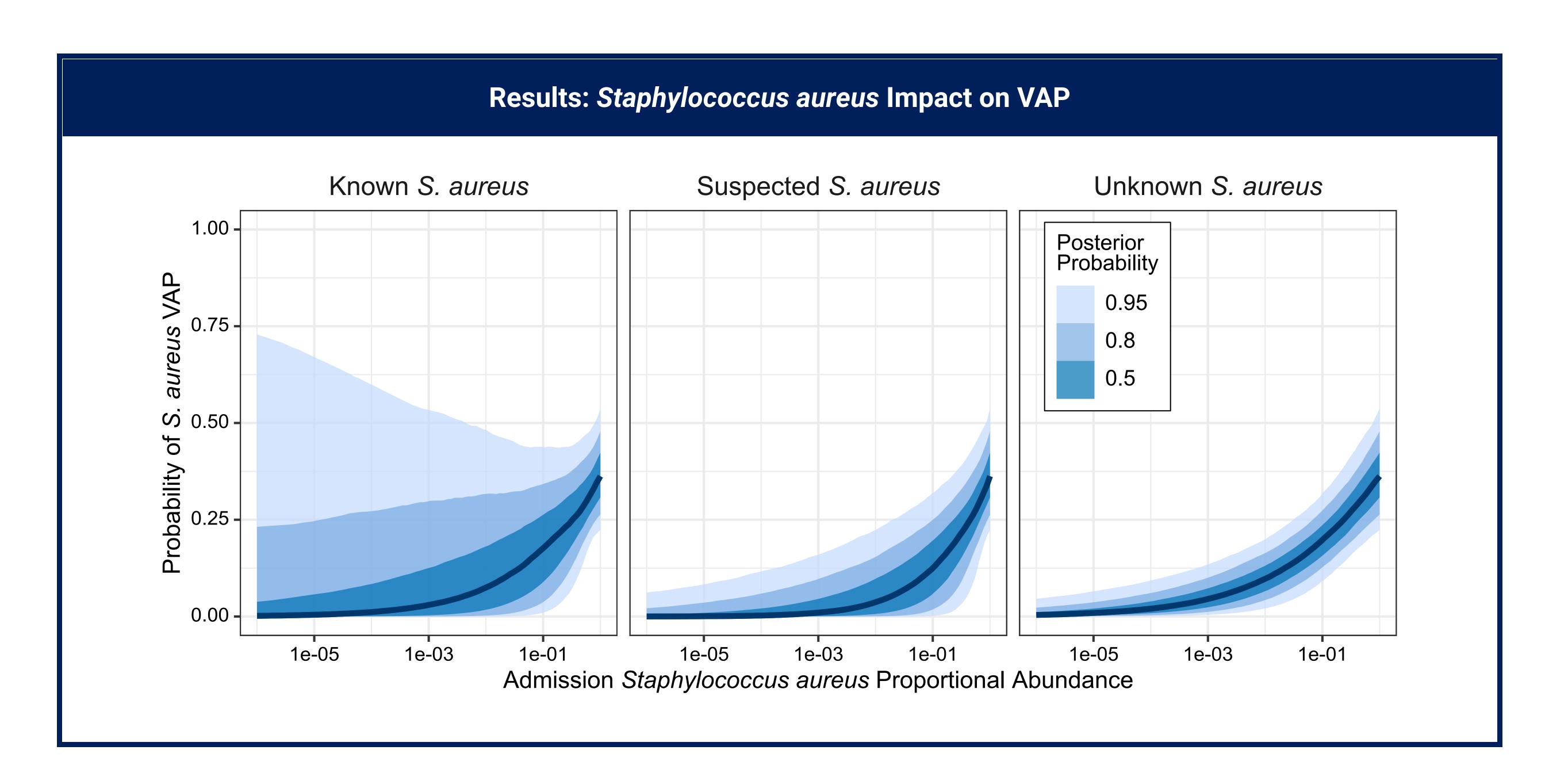
Study Population

• We enrolled 83 subjects on LTACH admission for ventilator weaning: 8 were diagnosed with S. aureus pneumonia during the 14 days prior to admission ("Known S. aureus"), 17 received anti-S. aureus antibiotics within 48 hours of admission ("Suspected S. aureus"), and 58 had neither ("Unknown S. aureus").

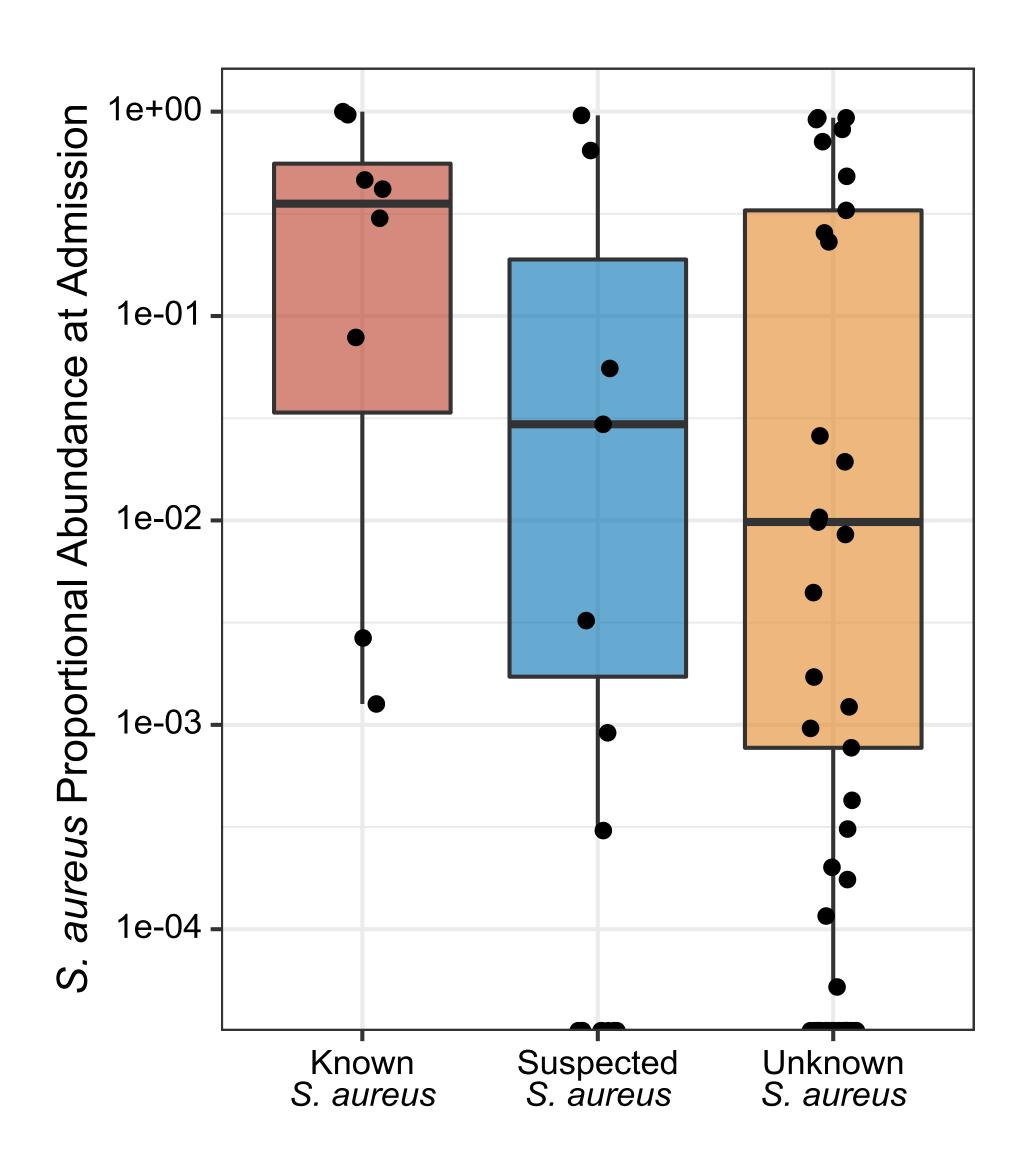
Methods

- We performed longitudinal sampling of endotracheal aspirates, followed by 16S rRNA gene sequencing (Illumina HiSeq).
- Bacterial community profiling was performed to detect error-corrected amplicon sequence variants (ASVs) using QIIME2, and bacterial community diversity was determined from ASV count data.
- 16S rRNA gene quantitative PCR (qPCR) was performed to determine total bacterial abundance.
- Clinically-suspected VAP were defined as a positive endotracheal aspirate culture accompanied by a new or revised antibiotic prescription.
- VAE were defined according to National Healthcare Safety Network (NHSN) surveillance criteria
- Statistical analysis was performed with R and Stan; mixed effects (slope and intercept) models were fit to relate the admission S. aureus abundance to subsequent, clinically-diagnosed S. aureus VAP and VAE.

¹Division of Infectious Diseases; ²Department of Biostatistics, Epidemiology, and Critical Care, University of Pennsylvania; ⁴Good Shepherd Penn Partners, Philadelphia, PA



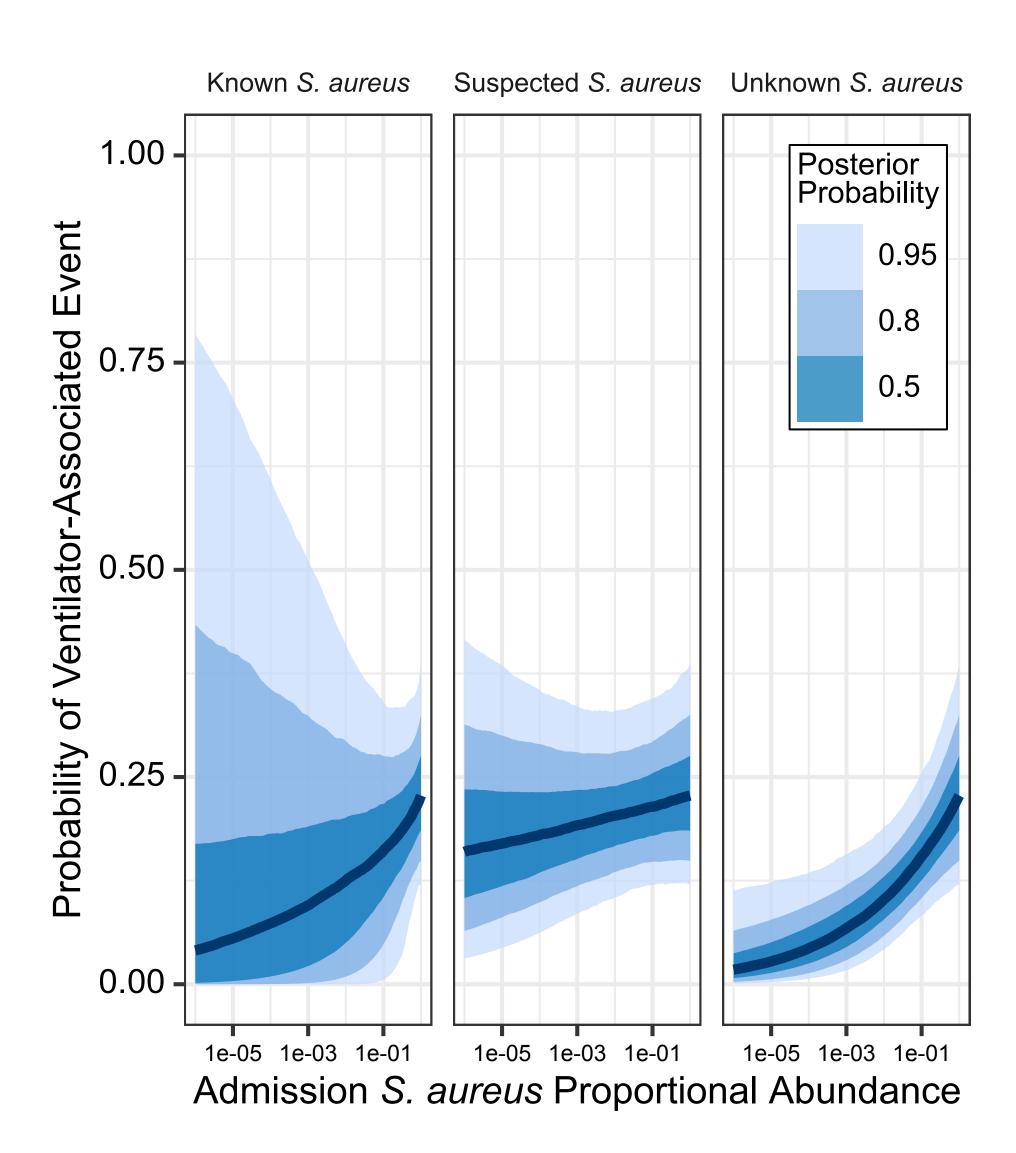
Results: S. *aureus* Colonization Prevalence



• All of the Known S. aureus group 8 had S. aureus detectable by 16S sequencing, with elevated admission S. aureus proportional abundance (median 0.36; range 0.0013 - 1). In the Suspected S. aureus group, only 7 had S. aureus detectable by 16S sequencing, with a wide range of proportional abundance (median 0; range 0 - 0.96). 25 of 58 subjects in the Unknown S. aureus group also had detectable respiratory S. *aureus*, with a wide range (median 0; range 0 - 0.93).

Results: S. *aureus* Impact on VAP & VAE

• Incident S. aureus VAP was observed within 30 days among 2 (25%) of Known S. aureus subjects, 0 (0%) of Suspected S. aureus subjects, and 3 (5.17%) of Unknown S. aureus subjects. VAE was observed within 30 days among 0 (0%) of Known S. aureus subjects, 3 (18%) of Suspected S. aureus subjects, and 1 (1.7%) of Unknown S. aureus subjects. Admission S. aureus abundance was positively associated with 30-day VAP risk in the Suspected (type S error < 0.001) and Unknown (type S error < 0.001) groups, and 30-day VAE risk in the Unknown group (type S error < 0.007).



Conclusions

- We identified a high prevalence of unrecognized respiratory S. aureus colonization among patients admitted to LTACH for weaning from mechanical ventilation.
- The admission S. aureus proportional abundance was associated with increased risk of incident S. aureus VAP among these subjects.
- Of note, the association between admission S. aureus proportional abundance and risk for incident S. aureus VAP was strongest among subjects without recognized S. aureus colonization.
- An association between *S. aureus* proportional abundance and VAE was also observed among subjects without recognized S. aureus colonization.

References

1. Sulis CA, Walkey AJ, Abadi Y, Campbell Reardon C, Joyce-Brady M. Outcomes of a ventilator-associated pneumonia bundle on rates of ventilator-associated pneumonia and other health care-associated infections in a long-term acute care hospital setting. American journal of infection control. 2014 May;42(5):536-538. Available from http://dx.doi.org/10.1016/j.ajic.2014.01.020 PMID: 24773791

2. Walkey AJ, Reardon CC, Sulis CA, Nace RN, Joyce-Brady M. Epidemiology of ventilator-associated pneumonia in a long-term acute care hospital. Infection control and hospital epidemiology: the official journal of the Society of Hospital Epidemiologists of America. [Cambridge University Press, Society for Healthcare Epidemiology of America]; 2009 Apr;30(4):319–324. Available from: http://dx.doi.org/10.1086/596103 PMID: 19245314

3. Klompas M, Anderson D, Trick W, Babcock H, Kerlin MP, Li L, Sinkowitz-Cochran R, Ely EW, Jernigan J, Magill S, Lyles R, O'Neil C, Kitch BT, Arrington E, Balas MC, Kleinman K, Bruce C ankiewicz J, Murphy MV, E Cox C, Lautenbach E, Sexton D, Fraser V, Weinstein RA, Platt R, CDC Prevention Epicenters. The preventability of ventilator-associated events. The CDC prevention epicenters wake up and breathe collaborative. American journal of respiratory and critical care medicine. 2015 Feb;191(3):292–301. Available from: http://dx.doi.org/10.1164/rccm.201407-13940C PMID: 25369558

4. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. American journal of respiratory and critical care medicine. 2005 Feb;171(4):388–416. Available from: http://dx.doi.org/10.1164/rccm.200405-644ST PMID: 15699079 5. Kelly BJ, Imai I, Bittinger K, Laughlin A, Fuchs BD, Bushman FD, Collman RG. Composition and dynamics of the respiratory tract microbiome in intubated patients. Microbiome. 2016 Feb;4(1):7. Available from: http://dx.doi.org/10.1186/s40168-016-0151-8 PMID: 26865050

. Pettigrew MM, Gent JF, Kong Y, Halpin AL, Pineles L, Harris AD, Johnson JK. Gastrointestinal microbiota disruption and risk of colonization with carbapenem-resistant pseudomonas tious diseases: an official publication of the Infectious Diseases Society of America. 2018 Nov;69(4):604–61 nttp://dx.doi.org/10.1093/cid/ciy936 PMID: 303832

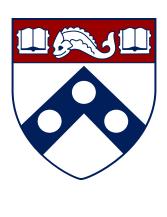
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National Institute of Allergy and Infectious Diseases



Contact Information

- Email: brendank@pennmedicine.upenn.edu
- Code: github.com/bjklab
- Phone: 215.662.6932