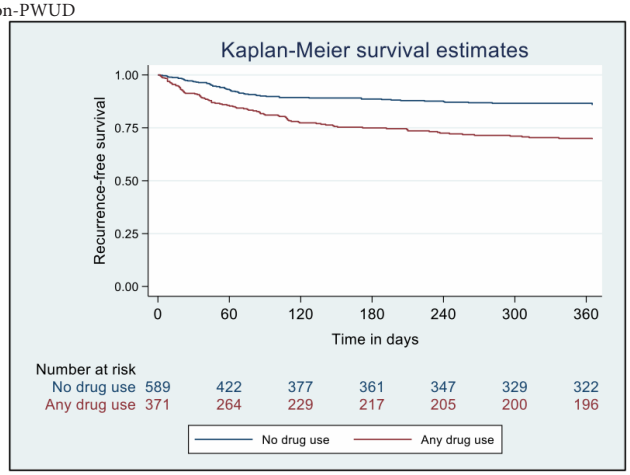
Figure 1: One-year Infection-free survival in persons who use drugs (PWUD) vs. non-PWUD



Conclusion. PWUD had higher proportions of *S. aureus* vertebral osteomyelitis, epidural abscess, and endocarditis than non-PWUD, lower odds of treatment completion, and greater risk of infection persistence/recurrence at one year. Among PWUD, opioid and stimulant use were common and undertreated. New patient centered models of care that deliver synchronized *S. aureus* infection and substance use disorder therapy are urgently needed.

Disclosures. **All Authors**: No reported disclosures

40. The Impact of Medically Assisted Therapy for Opiate Use Disorder in staphylococcus Aureus Bacteremia Patients Within a Large Hospital System - A Retrospective Cohort Study

Brooks A. Keene, MD, MS[1]; Shadi Saboori, MD, MPH[1]; Jacqueline Meredith, PharmD, BCPS, BCIDP[2]; Deanna King, MD, MS[1]; Christopher Polk, MD[3]; Michael Leonard, MD[3]; [1]Atrium Health Carolinas Medical Center, Charlotte, North Carolina [2]Atrium Health, Carolinas Medical Center, Charlotte, North Carolina [3]Atrium Health, Charlotte, North Carolina

Session: O-8. Bacteremia and Endocardits

Background. Intravenous drug use (IVDU) is a risk factor for development of *S. aureus* bacteremia (SAB) and prevalent in opiate use disorder (OUD). While the standard of care involves treating the underlying OUD with medically assisted therapy (MAT), it is unknown how much impact this has on clinical endpoints.

Methods. We conducted a retrospective cohort study of patients with IVDU with hospitalizations for SAB during a 28-month period from 9/2016 through 12/2018 in 10 urban and rural North Carolina hospitals in a single large health system. We compared outcomes for patients receiving prescription for MAT at discharge versus no MAT at discharge. MAT was defined as receiving methadone, buprenorphine, or naltrexone. Patients who expired inpatient were excluded from analysis. Clinical endpoints were 30- and 90-day mortality and 30-day SAB-related readmissions.

Results. Of the 174 patients, 28% received a prescription for MAT at discharge. The majority of the patients were Caucasian (88%), female (57%), with mean age of 37 years. Factors that significantly increased likelihood of MAT at discharge were female gender (34% vs 20%, p=0.04), having a complicated SAB (33% vs 28%, p=0.01), presence of a spinal/epidural abscess (57% vs 43%, p=0.002), and increased length of stay (LOS) (37 days vs 24 days, p=< 0.001). No difference in 30- and 90-day mortality was observed; only one patient in each group died within 90 days. Prescription for any MAT at discharge was associated with a significant decrease in the risk of SAB-related 30-day readmission (0% vs 17%, p=0.002).

Table 1: Baseline Characteristics

Table 1: Baseline Characteristics

	MAT at Discharge	No MAT at Discharge	P Value
	no. of patients (%)	*no. of patients (%)*	
All participants	**(n=49)**	**(n=125)**	
Mean Age (yrs)	36	38	0.16
Female Gender	34 (.34)	65 (.66)	0.04
Race			0.32
White/Caucasian	45 (.29)	108 (.71)	
Other Race or Unknown	4 (.19)	17 (.81)	
Hospital with Available Addiction Medicine Consultant	28 (.33)	56 (.67)	0.14
Admitting Service			0.22
Hospitalist	37 (.26)	103 (.74)	
Critical Care	6 (.27)	16 (.73)	
Other	6 (.50)	6 (.50)	
Blood culture with MRSA	24 (.25)	71 (.75)	0.35
Complicated Blood Stream Infection	43 (.33)	88 (.67)	0.01
Staph Bacteremia Complications			
Endocarditis	24 (.32)	52 (.68)	0.38
Suspected septic emboli	28 (.29)	68 (.71)	0.74
Soft tissue abscess	9 (.24)	29 (.76)	0.49
Spinal / epidural abscess	12 (.57)	9 (.43)	0.002
Osteomyelitis	3 (.15)	17 (.85)	0.16
Length of Stay (days)	37	24	<0.001

Table 2: MAT & Clinical Outcomes in S. aureus Bacteremia

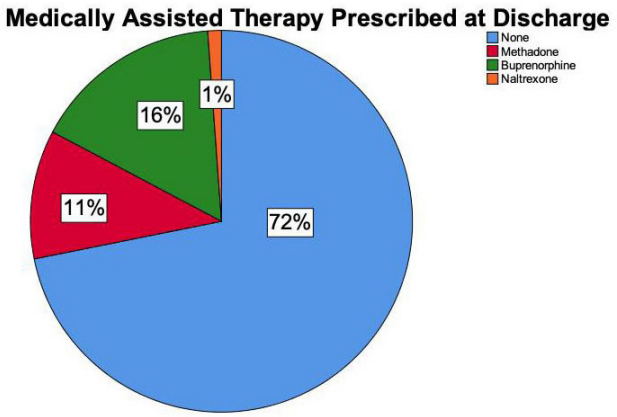
Table 2: MAT & Clinical Outcomes in S. aureus Bacteremia

	MAT at Discharge	No MAT at Discharge	P Value
	no. of patients (%)	*no. of patients (%)*	
All participants	**(n=49)**	**(n=125)**	
30-day mortality (inpatient deaths excluded)	0	0	–
90 day mortality (inpatient deaths exluded)	1 (.5)	1 (.5)	0.49
SAB-associated 30 day readmission*	0 (0)	21 (.17)	0.002

*SAB-associated readmission defined as including progressive worsening of original infectious foci(s), disseminated bacterial seeding from original foci(s), issues with outpatient parenteral antimicrobial therapy, or adverse drug reaction

Figure 1: Medically Assisted Therapy Prescribed at Discharge

Conclusion. Gender, more complicated infections, and prolonged LOS may increase the likelihood of receiving a prescription for MAT at discharge. MAT prescription at discharge may decrease the risk of 30-day SAB related re-admission (NNT 5.9). The results suggest that provision of MAT to patients with SAB and history of IVDU should be incorporated into standardized treatment guidelines.



Disclosures. **All Authors**: No reported disclosures

41. Impact of Gut Microbiome Changes on Hematopoietic Stem Cell Transplantation Outcomes in Children.

Mehgan Teherani, MD, MS[1]; Zoe Pratte, PhD[2]; Samridhi Banskota, n/a[1]; Dalia Gulick, BS, DC[2]; Naima Djeddar, MA, MS[2]; Scott Gillespie, MS, MSPH[1]; Gregory Gibson, PhD, BSc[2]; Muna Qayed, MD, MSCE[1]; [1]Emory University, Atlanta, Georgia; [2]Georgia Institute of Technology, Atlanta, Georgia

Session: O-9. Basic and Translational Science

Background. In adults undergoing allogeneic hematopoietic cell transplantation (HCT), higher gut microbiome diversity is associated with reduced bloodstream infections (BSI) and improved overall survival (OS). Rifaximin prophylaxis in adult HCT helps to maintain microbiome diversity. We examine changes in microbiome in a cohort of pediatric patients undergoing HCT.

Methods. Patients were enrolled in an institutional biorepository (n=82) with a subset enrolled in an ongoing trial using rifaximin (n=21) between 2013–2020. All patients had HCT for a hematologic malignancy, using myeloablative conditioning. Patients in the rifaximin trial received rifaximin starting 7 days before HCT (D-7) through D+28, otherwise, no prophylactic antibiotics were used. Systemic antibiotic timing was categorized as none, early (≤ Day 0, day of HCT), and late (> D0). We performed 16s rRNA sequencing from stool for 73 subjects, at baseline (D-7), and weekly through D+28 (engraftment). Microbiome diversity was assessed by Shannon index.

Results. Median age was 9 years (range 1–20), 59% male, 41% Caucasian and 29% Black. There were no differences in BSI or mortality by age, sex, or race.

Microbiome diversity changed significantly over time (p=0.008). Drop in diversity was most notable in patients who had early antibiotics (Mean=1.4, CI -0.15, 2.94, p=0.077). Higher diversity was seen when patients received none or late versus early antibiotics, but this was not statistically significant (Figure 1, p=0.23). Piperacillin-tazobactam was used empirically in 91% of patients. OS at 1 year was 88.5% (CI 68.4%, 96.1%) for patients with high (≥ median) D+28 diversity compared to 60% (CI 38.4%, 76.1%) for patients with low diversity (Figure 2, p=0.018) Only 1 of 21 (4.8%) in the rifaximin group developed a BSI with a gut bacterium compared to 8 of 61 (13.1%) not on rifaximin within the first 30 days (trial enrollment ongoing).

Figure 1. Effect of systemic antibiotic timing on microbiome diversity over time.

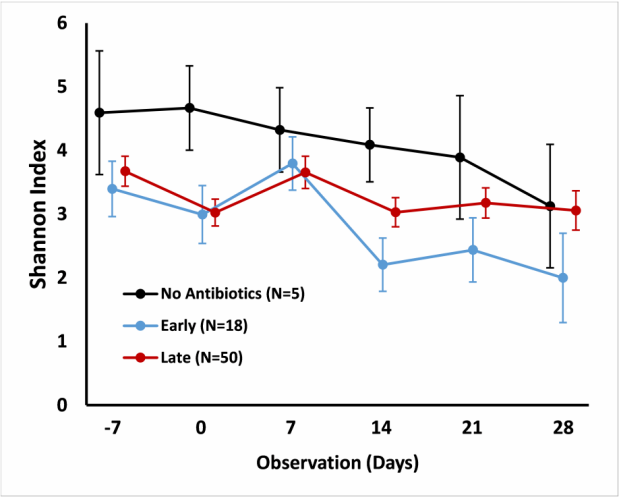
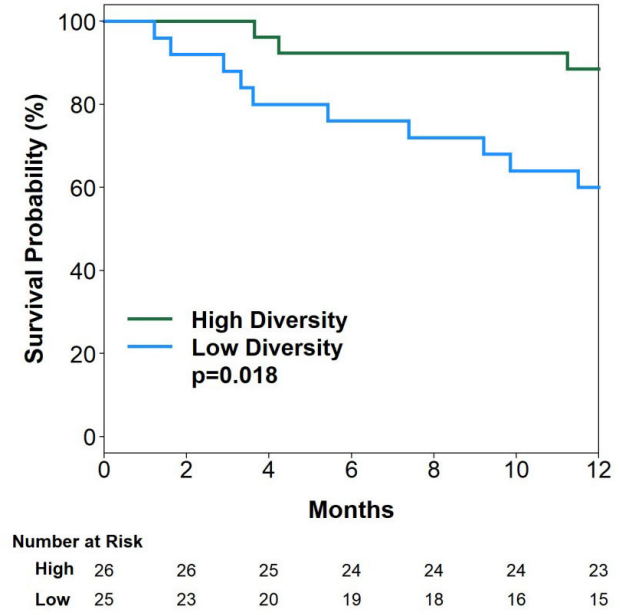


Figure 2. One-year overall survival of patients with high (>2.77) versus low (<2.77) diversity defined by median Shannon-Index.

Conclusion. We have shown a significant correlation between engraftment microbiome diversity and 1-year OS. Early antibiotic exposure was detrimental to microbiome diversity. Approaches to preserve microbiome diversity and prevent BSI are likely to improve HCT outcomes. Our ongoing trial using rifaximin will provide preliminary data regarding this approach.



Disclosures. **All Authors**: No reported disclosures

42. Common Population Variants Cause Susceptibility to Disseminated Coccidioidomycosis

Amy P. Hsu, n/a[1]; Joie Davis, AGN-BC[2]; Alexandria L. Chaput, MS[3]; Daniel A. Powell, PhD[3]; Nima Pouladi, MD, PhD[3]; Yves Lussier, MD, FCAMI[3]; Joshua Fierer, MD[4]; Jeffrey A. Frelinger, PhD[5]; John N. Galgiani, MD[3]; Michail Lionakis, MD, ScD[6]; Steven M. Holland, MD[7]; [1]NIAID / NIH; University of Maryland, College Park, Bethesda, Maryland; [2]Laboratory of Clinical Immunology and Microbiology, Bethesda, Maryland; [3]The University of Arizona, Tucson, Arizona; [4]UC San Diego School of Medicine, La Jolla, California; [5]University of Arizona, Tucson, Arizona; [6]National Institute of Allergy and Infectious Diseases, Bethesda, Maryland; [7]Laboratory of Clinical Immunology and Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

Session: O-9. Basic and Translational Science

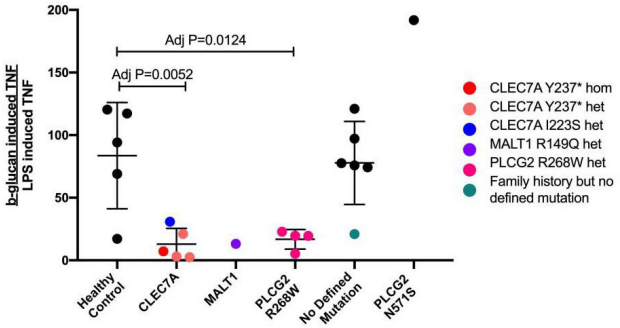
Background. *Coccidioides* are endemic, dimorphic fungi found in soils of southwestern United States, Mexico and Central America. Infection occurs via inhalation of arthroconidia which swell, differentiate into spherules and rupture releasing endospores. While the majority of infected individuals will never report illness, roughly 1/3 seek medical attention for fungal pneumonia and ~1% of those present with disseminated coccidioidomycosis (DCM). IL12-IFNγ pathway mutations have been reported in DCM but are exceedingly rare and cannot account for the ~500–600 cases of DCM/year.

Methods. We performed whole exome sequencing on 66 individuals with DCM, retaining variants predicted damaging (CADD >15) with a population frequency < 10%.

Results. Homozygous *CLEC7A* c.714T >G; p.Y238* causing a truncated Dectin-1 receptor was overrepresented (OR=9.8449, 95% CI 3.0841 to 31.4260, P=0.0001). Dectin-1 signaling pathway variants included 3 homozygous and 11 heterozygous *CLEC7A* p.Y238* individuals, one each *CLEC7A* p.I223S and *MALT1* p.R149Q and five *PLCG2* p.R268W. Since Dectin-1 is the receptor for b-glucan, a major *Coccidioides* cell-wall component, we hypothesized that Dectin-1 pathway variants could affect fungal recognition and cellular response. Healthy control PBMCs stimulated with purified β-glucan or heat-killed *Candida albicans* induced 6-fold more TNFα than patients with homozygous or heterozygous *CLEC7A*, *PLCG2* or *MALT1* variants (P=0.0022, Ordinary one-way ANOVA). Additionally, one patient with a family history of DCM but lacking a defined mutation also failed to up-regulate TNFα after stimulation.

Normalized TNF production from healthy control and DCM patient's peripheral blood mononuclear cells

Conclusion.



These data are consonant with increased dissemination in *Clec7a*$^{-/-}$ mice as well as in patients receiving anti-TNF biologics. These gene variants accounted for 31% of our DCM cohort (21/66 patients). This is the first demonstration of variants outside the IL12-IFNg pathway impairing fungal recognition and cellular response in coccidioidomycosis. Common heterozygous variants may be sufficient for disease susceptibility to highly pathogenic organisms.

Disclosures. **Michail Lionakis, MD, ScD**, **Matinas BioPharma** (Research Grant or Support)

43. The Capsule and Beyond: Genetic Determinants of Pediatric streptococcus Pneumoniae empyema

Nicole L. Pershing, MD PhD[1]; Aurelie Kapusta, PhD[2]; Shannon Nielsen, BS[1]; Hillary Crandall, MD, PhD[1]; Kent Korgenski, MS[1]; Carrie L. Byington, MD[3]; Krow Ampofo, MBChB[1]; Anne Blascke, MD PHD[1]; [1]University of Utah, Salt Lake City, Utah; [2]University of Utah, IDbyDNA, Salt Lake City, Utah; [3]University of California Health, Oakland, California

Session: O-9. Basic and Translational Science

Background. *Streptococcus pneumoniae* is the most common cause of pneumonia in children, including empyema, a severe complication with increasing incidence in the post-pneumococcal vaccine era. Only a subset of > 90 serotypes cause empyema. Virulence determinants of empyema remain largely unknown.

Methods. We performed Illumina sequencing of invasive Pneumococcal isolates from pediatric patients at Primary Children's Hospital (Salt Lake City, UT) isolated between 1996–2018, *de novo* genome assembly (SPADES), annotation (PROKKA), serotyping (Quelling and SeroBA), and pan-genome assembly (ROARY). SCOARY and pyseer were used for microbial GWAS. Maximum likelihood phylogeny was calculated using RAxML/Gubbins.

Results. 366 pneumococcal isolates were analyzed from 39 serotypes and multiple phenotypes including pneumonia (n=76), empyema (n=63), CNS infection (n=54), and isolated bacteremia (n=79). Serotypes and empyema phenotype clustered roughly by phylogeny. Most analyzed empyema isolates after 2010 were serotype 3 (19/25); prior to PCV-13 introduction serotypes 1 (8/38), 7F (7/38), and 19A (11/38) were more highly represented. Genes implicated in capsule synthesis, transposases, and metabolism were statistically correlated with the empyema phenotype.

Conclusion. Specific capsular or metabolic genes may confer optimal fitness for pleural disease. Further characterization of these genetic associations is needed and will inform future treatment and prevention.

Disclosures. **Carrie L. Byington, MD**, **BioFire** (Other Financial or Material Support, Royalties for Intellectual Property)**IDbyDNA** (Advisor or Review Panel member) **Krow Ampofo, MBChB**, **Merck** (Grant/Research Support)

44. In-host Infection Dynamics Of Pseudomonas Aeruginosa Pneumonia

Kelly E. R. Bachta, MD PhD[1]; Jonathan P. Allen, PhD[2]; Alan R. Hauser, MD PhD[1]; [1]Northwestern University, Chicago, Illinois; [2]Loyola University Chicago, Maywood, Illinois