The outer circle sections represent Karius Test detections belonging to different taxonomic groups. The length of each circle section is proportional to the total number of detections of a taxon belonging to that group. The chords connecting a pair of circle sections are proportional to the number of times two taxa from those groups were observed together, weighted by the total number of taxa detected.

**Conclusion.** Plasma mcfDNA NGS offers a rapid, comprehensive non-invasive means of detecting CI-POCI in IC patients with one test. Although rare, co-infections can greatly increase mortality. The KT can provide important insights into means of detecting CI-POCI in IC patients with one test. Although rare, co-infections were observed together, weighted by the total number of taxa detected.

**Disclosures.** Matthew Smollin, PharmD; Karius, Inc. (Employee) Martin S. Lindner, PhD; Karius, Inc. (Consultant) Nicholas R. Degner, MD, MPH; MS; Karius Inc. (Employee, Shareholder) Ricardo Castillo-Galvan, MD MPH; Karius Inc. (Consultant) Jose Alexander, MD; D(ABMM), FCCM, CIC, SM, MB(ASCP), BCMAS; Karius (Employee) Ann MacIntyre, DO; Karius, Inc. (Employee) Bradley Perkins, MD; Karius, Inc. (Employee) Asim A. Ahmed, MD; Karius, Inc. (Employee) Aparna Arum, MD; Karius, Inc. (Employee)

664. Clinical Impact of Cell-Free DNA Metagenomics in Diagnosing Infectious Diseases in Pediatrics: A Single-Center Experience

**Background.** Metagenomic next-generation sequencing (mNGS) of plasma cell-free DNA has significant potential to improve infectious diseases diagnostics through unbiased detection of pathogens. However, the optimal patient population or clinical condition for this testing has not been determined.

**Methods.** We performed a retrospective review of all orders for plasma cell-free DNA mNGS using the Karius test (Karius, Redwood City, CA) from The Children’s Hospital of Philadelphia from 7/1/19-4/30/21. Chart review then determined if the test had a positive, negative, or no clinical impact.

**Results.** 25 mNGS tests were ordered on 24 unique patients. The majority of tests were ordered on immunocompromised patients (Table 1). Most mNGS tests were ordered after completion of routine microbiological testing (17/25, 71%). Three tests were not completed as ordered. Most completed tests (18/22, 82%) had no impact on clinical care as they confirmed the known diagnosis or were not acted upon (Figure 1). mNGS testing had a positive impact in 2 cases. For one patient with congenital heart disease presented with persistent fever and concern for endocarditis despite negative infectious workup, a negative mNGS result allowed for continued monitoring without therapy. Another patient with a lymphomas disorder had mNGS performed due to persistent clinical instability; testing was positive for Candida parapsilosis, allowing for early initiation of antifungal therapy. However, test results had a negative clinical impact in 2 other patients. In a patient with congenital heart disease and fever, identification of two organisms led to prolonged antibiotic therapy for endocarditis without resolution of symptoms. In a patient with leukemia, report of a dematiaceous mold led to further diagnostic testing, including a lumbar puncture, as well as treatment with antifungal therapy despite no clear diagnosis.

**Conclusion.** In this study, the majority of plasma cell-free mNGS tests had no impact on clinical care. mNGS testing did positively impact care in 2 patients, but did not have a negative impact in 2 instances, leading to further testing and unnecessary treatment. Further investigation is needed to determine the ideal population or clinical condition for testing and the ideal time of sending plasma cell-free mNGS tests.

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

665. Clinical and Financial Impact of Next Generation Sequencing (NGS) in Addition to Conventional Microbiology Testing in our Urban Referral Health Center

**Background.** Clinical microbiology traditionally relies on culture methodology and serological testing, that have inherent limitations. Newer diagnostic techniques such as Next Generation Sequencing (NGS) have shown promise to improve microbial identification. In select scenarios, we send clinical specimens to reference laboratories for NGS testing in addition to current standard of care (SOC) diagnostics. We wanted to determine how this diagnostic approach has impacted patient care. We also wanted to review the financial burden through cost-benefit analysis for these ‘send-out’ tests.

**Methods.** We performed a retrospective chart review of all cases over a 3-year period in which NGS was submitted. Data, including demographics, comorbidities, antimicrobial use, and diagnosis (by SOC and NGS) were gathered. We delineated how often there was concordance or discordance between SOC and NGS. We also obtained
Table 1. Pathogens identified by NGS with negative traditional microbiological test results

| Organisms identified by NGS with negative SOC |
|--------------------------------------------|
| *Gordonia spiti* |
| *Bartonella species* |
| *Corynebacterium species* |
| *Streptococcus agalactiae* |

Conclusion. NGS can provide additional diagnostic sensitivity in infectious diseases, which at our institution identified a new pathogen in 20% and a resultant treatment change in 16% of our patients. This testing may also allow physicians to reaffirm the absence of an infection diagnosis. A larger NGS testing population may reveal more significant benefits. While the attributable cost of NGS was substantial, it should be measured against the costs of administration of unnecessary antibiotics, inaccurate diagnosis, and adverse patient outcomes that may result from SOC testing.

Disclosures. All Authors: No reported disclosures

666. Molecular Epidemiology of Methicillin-Resistant *Staphylococcus aureus* in Chile between 1999-2018

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Session: P-30. Diagnostics: Typing/sequencing

Background. The global spread of methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with distinct genetic lineages that predominate in specific geographical regions. Available evidence suggests the Chilean-Cordobes clone (ChC), an ST5-SCCmecI lineage, has largely predominated in Chilean hospitals since its description in the late 1990s. Although the circulation of other MRSA lineages, including community-associated clones, has been well documented, the dynamics of clonal replacement over time has not been explored. Therefore, we aimed to study the molecular epidemiology and dynamics of clonal replacement using a large collection of clinical MRSA strains recovered from Chile during the last two decades.

Methods. We used whole-genome sequencing (WGS) and core-based phylogenomic analysis to identify genetic lineages and explore their relationship in 798 MRSA isolates obtained between 1999-2018 from two tertiary-care Chilean hospitals.

Results. Overall, the most frequently identified clones were the ST5-SCCmecI ChC (n=476, 60%), followed by ST105-SCCmecII (n=119, 15%), ST2-SCCmecIV (n=74, 9%), and ST8-SCCmecII (n=20, 3%). Phylogenomic reconstruction demonstrated 7 major clades: Clade I (CC30); Clade II (CC22); Clade III (CC97); Clade IV (CC8); Clade V (CCST22 and ST105) and Clade VII (CCS/ST5-SCCmecI) (Fig. 1). The ChC clone remained the most frequent MRSA lineage throughout the study period (Fig. 2). However, its relative abundance decreased from >90% of isolates in 1999 to ca. 40% in 2018. This decrease began around 2005 and was associated with a progressive expansion of the ST105-SCCmecII and ST2-SCCmecIV lineages (Fig. 2). A Bayesian molecular clock analysis established the most recent common ancestor in 1964 (95% HPD interval=1961.975-1966.218) and corroborated a CCS expansion event starting in Chile in 1999 (Fig. 3). Interestingly, our analyses revealed two branches within the ST5-SCCmecI lineage: one predominating in 1999-2006, and a more recent branch (related to the ST105-SCCmecII clone) that emerged around 2008.

The seven major clades are represented by colored sections. The Clade I (purple section) was composed of isolates belonging to the CC30. Clade II (cyan section) is composed of isolates of CC22. Clade III (green section) includes isolates of CC97. Clade IV (blue section) grouped isolates of different ST239 and ST8, belonging to the CC8. Clade V (orange section) includes isolates of ST72. Clade VI (yellow section) includes isolates of ST22 and ST105, both belonging to CC3. Clade VII (green section) is mostly composed of isolates of ST5-SCCmecI. The inner ring shows the ST of the isolates; the external ring shows the staphylococcal chromosomal cassette mec (SCCmec) type.