

Background. The causal attribution of bacterial pathogens to severe acute respiratory infections (SARI) is challenging because many bacteria are frequently detected in the upper respiratory tract of asymptomatic persons. Quantification of pathogen load may help differentiate asymptomatic pathogen carriage from clinically significant infection. We aimed to determine whether real-time PCR (rt-PCR) cycle threshold (Ct) values, as a proxy for bacterial load, differ between adults with SARI and asymptomatic adults.

Methods. Adults with SARI (acute onset of fever and cough, requiring hospitalization) were frequency matched to asymptomatic adults (enrolled from trauma and orthopedic inpatient wards) by age group, catchment area, and enrollment date at three surveillance sites in Guatemala. Nasopharyngeal and oropharyngeal specimens were collected from all participants and tested for pathogens using rt-PCR. Using the Wilcoxon rank sum test, we compared the distributions and median Ct values between ill and asymptomatic adults in whom *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae* were detected.

Results. Between October 2013 and October 2015, 304 adults with SARI and 174 asymptomatic adults were enrolled (Table). *M. catarrhalis*, *S. aureus*, and *S. pneumoniae* were detected with similar frequency in both groups. *H. influenzae* and *K. pneumoniae* were detected more frequently in asymptomatic adults. We found the greatest difference in Ct value distributions between ill (median Ct=30.8) and asymptomatic adults (median Ct=35.6) with *S. pneumoniae* detections ($p < 0.01$) (Figure). Median Ct values of *H. influenzae* (29.3 vs 31.1, $p=0.04$) and *M. catarrhalis* (29.2 vs 31.5, $p=0.05$) were also lower among adults with SARI.

Frequency of select bacterial pathogen detection among adults with SARI and among asymptomatic adults, Guatemala, 2013-2015

Bacteria	Adults with SARI, n (%) (n = 304)	Asymptomatic adults, n (%) (n = 174)
<i>H. influenzae</i> –all types	60 (19.7%)	49 (28.2%)
<i>S. aureus</i>	36 (11.8%)	24 (13.8%)
<i>M. catarrhalis</i>	38 (12.5%)	19 (10.9%)
<i>S. pneumoniae</i>	75 (24.7%)	45 (25.9%)
<i>K. pneumoniae</i>	17 (5.6%)	18 (10.3%)

Distributions of Ct values among adults with SARI and asymptomatic adults in whom a given bacterial pathogen was detected

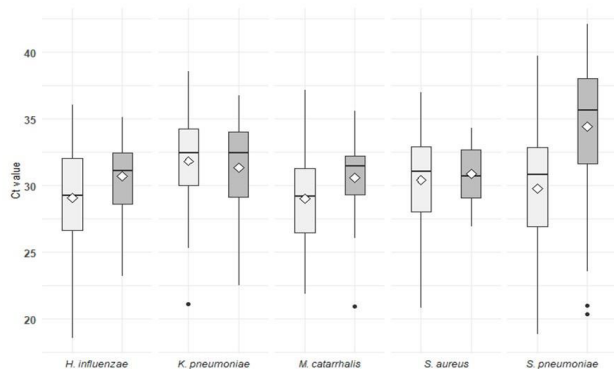


Figure. Distributions of Ct values among adults with SARI (light grey) and asymptomatic adults (dark grey) in whom a given bacterial pathogen was detected. Lower Ct values indicate higher bacterial load. Horizontal lines through boxes indicate group medians and diamonds indicate group means. Boxes show the interquartile range (IQR). Whiskers extend from the hinge to the largest or smallest value at most 1.5xIQR from the hinge. Outlying data points beyond the end of the whiskers are plotted individually.

Conclusion: Pathogen loads of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* were higher among adults with SARI than among asymptomatic adults, suggesting that Ct values may provide insight into SARI etiology for some pathogens, despite the similar frequency of detection among both ill and asymptomatic adults. Future work will normalize Ct values to account for variation in testing and analysis and explore the use of Ct values to estimate population attributable fractions of respiratory infections.

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1468. Culture Conversion and Mortality in Patients With Mycobacterium abscessus (MAB) Lung Disease: A Systematic Literature Review

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Background. Prognosis for patients with MAB lung disease is poor. We sought to examine the potential association between culture conversion and outcomes (progression, mortality) in patients with MAB lung disease.

Methods. English-language MAB lung disease studies with ≥ 10 patients and reporting mortality and/or microbiological outcomes were identified from Embase,

PubMed, relevant congress abstracts, and the Cochrane Library (data cutoff, September 24, 2019) using the National Institute for Health and Clinical Excellence guidance for systematic literature reviews. Two independent reviewers screened 1,551 indexed records; relevant extracted data are expressed as population-weighted means.

Results. Mean all-cause mortality across 17 studies (N=1,291) was 12.1% (range, 3%–33%); mortality attributable to MAB lung disease was 7.6% (range, 0%–27%; N=526, 9 studies). Culture conversion across 44 studies (N=2,237) was 46.7% (range, 0%–98.6%), with higher rates reported for *M. massiliense* subspecies (76.9%; N=507, 15 studies) than *M. abscessus* subspecies (35.8%; N=834, 18 studies). No direct comparisons were made between mortality and culture conversion; in the 13 studies (N=1,202) that reported both outcomes there was a moderate correlation between increased rate of culture conversion and decreased MAB-attributable mortality ($R^2=0.60$). The most common definition of progression (21 studies) was radiographic worsening supported by persistent symptoms and/or positive cultures. Across 8 studies (N=415) 57.8% patients had improvement while 35.2% progressed with treatment. A broad variance in treatment regimen and duration (range, 32 days to > 3 years) was observed. Limitations include a small number of studies, and inconsistency in methods and outcomes definitions.

Conclusion. In this systematic literature review, available data suggest that culture conversion was achieved in less than half of patients and was lower in patients with *M. abscessus* compared with *M. massiliense*. One third of patients had disease progression despite treatment. Some data suggest lower MAB-attributed mortality outcomes in studies with higher culture conversion rates, more evidence is needed to demonstrate a survival benefit associated with culture conversion.

Disclosures. Kevin L Winthrop, MD, MPH, Insmed Incorporated (Consultant, Grant/Research Support) Kevin C Mange, MD, MSCE, Insmed Incorporated (Employee) Zhanna Jumadilova, MD, Insmed Incorporated (Employee) Kristan B Cline, PhD, Insmed Incorporated (Employee) Patrick A Flume, MD, Insmed Incorporated (Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member)

1469. Effect of pneumonia and pneumonia hospitalization episodes on mobility in older adults: results from the Lifestyle Interventions and Independence for Elders (LIFE) Study

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Background. Mobility is a cornerstone of healthy aging. Pneumonia may impact mobility through damage to physiological systems as well as increased inflammation, which has been associated with reduced physical functioning. The objective of this study was to assess the impact of pneumonia on objectively measured physical functioning in a sample of older adults.

Methods. This was a post-hoc analysis of the Lifestyle Interventions and Independence for Elders (LIFE) Study provided by the National Institute on Aging's AgingResearchBiobank. Participants with pre-existing mobility concerns aged 70-89 years were randomized to physical activity or health education interventions. Outcomes included the ability to complete a 400-meter walk and gait speed (meters/second, m/s) and were assessed every 6 months from baseline up to 42 months. New health events were assessed at each visit including overall pneumonia events and pneumonia hospitalizations. Repeated measures regression models evaluated the ability to walk 400-meters and gait speed as separate outcomes controlling for age, sex, race, education, past medical history, the occurrence of other health events, and a cumulative deficit frailty index.

Results. There were 1,635 LIFE Study participants with N=9,872 follow-up measures during the study period. Among these, 174 (10.6%) had a pneumonia event which included 96 hospitalization events. Those with pneumonia events during follow-up were mostly similar to those without pneumonia events at baseline, except for higher prevalence of past hospitalizations and respiratory problems. Any pneumonia event was associated with an adjusted mean gait speed of 0.67 (0.63-0.71) m/s vs. 0.70 (0.66-0.73) m/s in those without pneumonia and 0.60 (0.55-0.64) in those with pneumonia hospitalization. Similarly, pneumonia events were associated with 84% [odds ratio = 1.84 (1.45-2.23)] and pneumonia hospitalizations with 200% [odds ratio = 3.00 (2.48-3.52)] increases in the odds of not being able to walk 400-meters compared to those without pneumonia events.

Conclusion. Pneumonia-related health events were associated with subsequent reduced mobility measured by 400-meter walk tests and gait speed. Preventing pneumonia may be an important component of maintaining physical functioning in older adults.

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1470. Epidemiology of Invasive Pneumococcal Disease (IPD) Following 18 years of Pneumococcal Conjugate Vaccine (PCV) Use in the United States

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Session: P-67. Respiratory Infections - Bacterial

Background. PCVs have been recommended for U.S. children since 2000. A 7-valent vaccine (PCV7) was introduced in 2000. This was replaced by a 13-valent vaccine (PCV13) in 2010. PCV13 was also recommended for adults aged ≥ 65 years in August 2014. We evaluated PCV impact on IPD.

Methods. IPD cases (isolation of pneumococcus from sterile sites) were identified through CDC's Active Bacterial Core surveillance during 1998-2018. Isolates were serotyped by Quellung or whole genome sequencing and classified as PCV13-type and non-vaccine-type (NVT). Incidence rates (cases/100,000) were calculated using U.S. Census Bureau population denominators.

Results. From 1998 through 2018, overall IPD rates among children aged < 5 years decreased by 93% (from 95 to 7 cases/100,000). PCV13-type IPD decreased by 98% (from 88 to 2 cases/100,000). Among adults aged ≥ 65 years, overall IPD rates decreased by 60% (from 61 to 25 cases/100,000). PCV13-type IPD rates declined 86% (from 46 to 7 cases/100,000). Declines were most dramatic in the years following PCV7 introduction, with additional declines after PCV13 introduction in children (Figures 1 and 2). Serotypes 3, 19A, and 19F caused most of the remaining PCV13-type IPD. NVT IPD rates did not change significantly among children. Among adults aged 50-64 years, NVT IPD increased by 83% (from 6 to 12 cases/100,000) ($p < 0.01$). Among adults aged ≥ 65 years, NVT IPD increased by 22% (from 15 to 18 cases/100,000) ($p < 0.01$). The most common NVTs in 2018 were 22F (10% of all IPD), 9N (7%) and 15A (5%). Among children, the proportion of cases with meningitis increased from 5% to 14% ($p < 0.01$), and the proportion with pneumonia/empyema increased from 17% to 31% ($p < 0.01$). Among adults, the proportion of cases with meningitis did not change (3%), while the proportion with pneumonia/empyema increased from 72% to 76% ($p = 0.01$).

Figure 1: Incidence of invasive pneumococcal disease among children aged < 5 years, 1998-2018

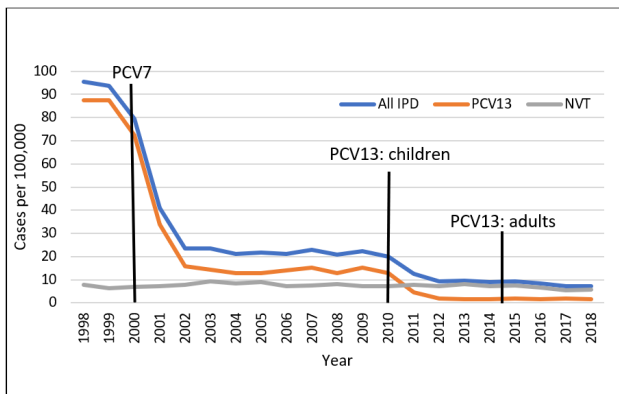
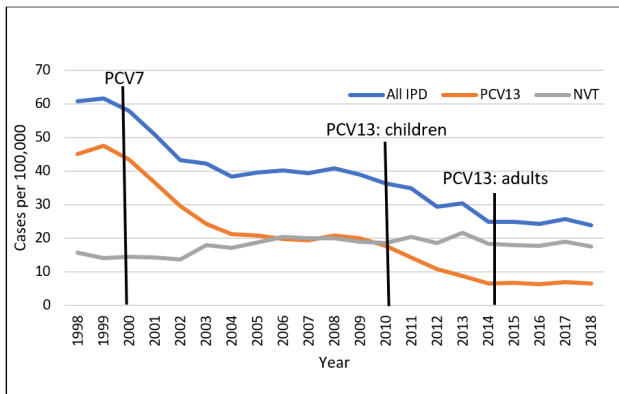


Figure 2: Incidence of invasive pneumococcal disease among adults aged ≥ 65 years, 1998-2018

Conclusion. Overall IPD incidence among children and adults decreased following PCV introduction for children, driven primarily by reductions in PCV-type IPD. NVT IPD increased in older adults, but these increases did not eliminate reductions from PCV13-type IPD.



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1471. Evaluation of Antibiotic De-escalation in Post Cardiac Arrest Patients with Culture-Negative versus Culture-Positive Aspiration Pneumonia

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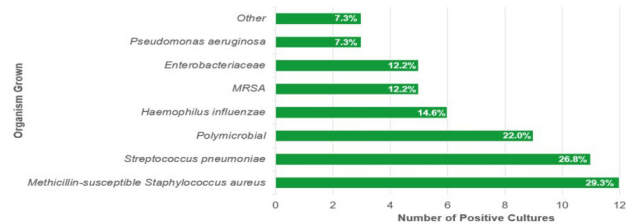
Session: P-67. Respiratory Infections - Bacterial

Background. Cardiac arrest patients are often empirically treated for aspiration pneumonia with broad-spectrum antibiotics. Previous literature has shown no difference in clinical outcomes when discontinuing antimicrobial therapy for suspected aspiration pneumonia with negative respiratory cultures, but the application is limited in this population. This study aimed to assess antibiotic de-escalation practices for suspected aspiration pneumonia in post cardiac arrest patients with respiratory cultures and explore clinical outcomes.

Methods. This retrospective cohort conducted at a level 1 trauma center included adult out-of-hospital cardiac arrest patients who received antimicrobial therapy for suspected aspiration pneumonia. The primary endpoint was incidence of antibiotic de-escalation before day seven comparing culture-negative and culture-positive patients. De-escalation included discontinuation of methicillin-resistant *Staphylococcus aureus* (MRSA) coverage, *Pseudomonas aeruginosa* coverage, atypical coverage or all antibiotics when respective pathogens were not identified from microbiologic or serologic methods. Secondary endpoints included type of de-escalation and clinical outcomes.

Results. Eighty-six patients were included: 45 culture-negative and 41 culture-positive. Figure 1 depicts the breakdown of organisms isolated. Guideline-directed empiric therapy was used in 18.6% of patients, with the remainder receiving excessively broad empiric coverage. Antibiotic de-escalation before day seven occurred in 28 (80%) culture-negative patients and 32 (82%) culture-positive patients ($p = 0.82$), excluding patients who died before day seven. Providers frequently stopped unnecessary MRSA coverage in both groups. In-hospital mortality was higher in the group of patients without antibacterial de-escalation (62% vs. 33%, $p = 0.03$), but hospital length of stay, ICU length of stay, and number of ventilator-free days were not different between groups.

Figure 1: Epidemiology of Pathogens Isolated From Respiratory Cultures in Cardiac Arrest Patients



Conclusion. Culture results were not associated with antibiotic de-escalation in post cardiac arrest patients with suspected aspiration pneumonia. Opportunities exist for further de-escalation in this population, particularly patients with unnecessary pneumococcal coverage.

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1472. Frequency of Occurrence and Antimicrobial Susceptibility of Bacteria Isolated from Patients Hospitalized with Bacterial Pneumonia in the United States, Western Europe, and Eastern Europe: Results from the SENTRY Program (2016-2019)

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Session: P-67. Respiratory Infections - Bacterial

Background. The SENTRY Antimicrobial Surveillance Program monitors the frequency of occurrence and antimicrobial susceptibility of organisms from various infection types worldwide. In this investigation, we evaluate the results for organisms isolated from patients hospitalized with bacterial pneumonia.

Methods. 28,918 bacterial isolates were consecutively collected (1/patient) in 2016-2019 from 121 medical centers located in the United States (US; n=17,770; 82 centers), western Europe (W-EU; n=7,966; 25 centers from 10 nations), and eastern Europe (E-EU; n=3,182; 14 centers from 11 nations). Organisms were tested for susceptibility by reference broth microdilution methods in a central laboratory.

Results. The rank order of organisms varied markedly among geographic regions (Table). Gram-negative bacilli (GNB) represented 69.1%, 76.3%, and 88.6% of organisms in US, W-EU, and E-EU, respectively. Among NF-GNB, *P. aeruginosa* ranked first in W-EU and E-EU and second in the US. *A. baumannii* ranked third in E-EU, and *S. maltophilia* was among the top 8 in all 3 regions (fifth in the US). *P. aeruginosa* susceptibility to piperacillin-tazobactam and meropenem (MEM) were 76.1% and 74.8% in the US, 75.4% and 76.9% in W-EU, and 57.4% and 48.3% in E-EU, respectively. Only 10.4% of *A. baumannii* isolates from E-EU were MEM-susceptible compared to 45.8%