



PROMOTING ANTIBIOTIC STEWARDSHIP

in Pediatric Outpatient Settings

A Research Brief from the
Center for Pediatric Clinical Effectiveness



Children's Hospital
of Philadelphia

RESEARCH INSTITUTE

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Expanding Antimicrobial Stewardship

Much research has focused on improving how hospitals can judiciously use antibiotics. There have been few studies to guide more selective use of these medicines in outpatient settings, where the vast majority of antibiotic use occurs. In 2016 the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria recommended expanding antibiotic stewardship efforts to outpatient settings. This follows a 2014 recommendation from the Centers for Disease Control and Prevention (CDC) that all acute care hospitals implement antimicrobial stewardship programs.

According to an analysis of the 2010-2011 National Medical Care Survey and National Hospital Ambulatory Care Survey, there was an estimated annual antibiotic prescription rate of 506 per 1,000 people, yet only 353 of these prescriptions were likely appropriate.¹

Inappropriate use of antibiotics contributes to antibiotic resistance, which is when microbes are able to resist the drugs created to destroy them.

Each year in the U.S., at least 2 million people become infected with bacteria that are resistant to antibiotics, and at least 23,000 people die each year as a direct result of these infections, according to the CDC.

This Research Brief summarizes seven years of study by researchers at the Center for Pediatric Clinical Effectiveness (CPCE) at Children's Hospital of Philadelphia (CHOP) who have worked to improve the effectiveness and acceptability of outpatient antimicrobial stewardship. In the process, they have provided health systems and physicians with an evidence-based clinical practice model.

At its core, this model uses the Electronic Health Record (EHR) platform to generate audit data and provide feedback to motivate more judicious use of antibiotics in outpatient settings. This Research Brief demonstrates the promise of programs using EHR platforms to regularly audit prescribing practices, provide personalized and private feedback, and include continuing education.

Antimicrobial stewardship programs can improve patient experience, reduce costs for payers and lead to healthier populations through reduction of antibiotic overuse and resistance.

VARIATION IN PRESCRIBING PRACTICES SUGGESTS ROOM FOR CHANGE



Variability in the Diagnosis and Treatment of Group A Streptococcal Pharyngitis by Primary Care Pediatricians²

This retrospective cohort study of 25 diverse pediatric primary care practices and 222 clinicians found substantial differences in the diagnosis, testing, and treatment of 52,658 cases involving visits for a sore throat. The clinical goal of treating this common bacterial infection is to ensure judicious diagnosis followed by narrow-spectrum antibiotic therapy (penicillin or amoxicillin) when appropriate. According to best practice guidelines, broad-spectrum antibiotics should be reserved for patients with allergies to narrow-spectrum antibiotics. Only 15 to 20 percent of sore throats among 5- to 15-year-olds are from Group A Streptococcal (GAS). Study findings include:

- Half of patients were not tested for GAS.
- Without testing for GAS, physicians prescribed an antibiotic during 841 visits, with 412 patients receiving narrow-spectrum therapy.
- Although receiving negative results for GAS, 13 percent of patients were prescribed antibiotics.
- Only 18 percent of the 222 clinicians accounted for half of all off-guideline antibiotic prescribing.

This variability provides benchmarks for GAS management in pediatric outpatient settings and helps inform interventions to promote antimicrobial stewardship in outpatient settings.

Variation in Antibiotic Prescribing Across a Pediatric Primary Care Network³

This study used one of the nation's largest pediatric healthcare networks, the Pediatric Research Consortium (PeRC), and its shared comprehensive EHR to examine and compare antibiotic prescribing patterns to treat common acute respiratory tract infections (acute otitis media, sinusitis, GAS, and pneumonia) in otherwise healthy children across 25 primary care practices and 222 clinicians. The researchers found substantial variation in antibiotic prescribing across practices during 363,049 visits that could not be explained by patient-specific factors, suggesting the need for outpatient antimicrobial stewardship interventions to address inconsistent and off-guideline antibiotic use:

- 28 percent of visits resulted in antibiotic prescriptions, with antibiotic prescribing by practice ranging from 18 percent to 36 percent.
- A child seen at a high antibiotic use practice is two times as likely to receive antibiotics (and four times as likely to receive a broad-spectrum antibiotic) than a child visiting a low antibiotic use practice.
- Lack of awareness of guidelines or parental pressure to prescribe might contribute to increased rates of inappropriate prescribing of broad spectrum antibiotics.

Variability in Antibiotic Prescribing for Community-Acquired Pneumonia⁴

This retrospective cohort study in an outpatient pediatric primary care network over a four-year period found that antibiotic choice for community-acquired pneumonia (CAP) varied widely across practices: 40.7 percent of patients received the recommended amoxicillin, 42.5 percent received macrolides, and 16.8 percent received broad-spectrum antibiotics. The major drivers of off-guideline prescribing were non-clinical factors, including practice location and private insurance.

The American Academy of Pediatrics supports the treatment of most acute respiratory tract infections (ARTIs) with narrow-spectrum antibiotics.

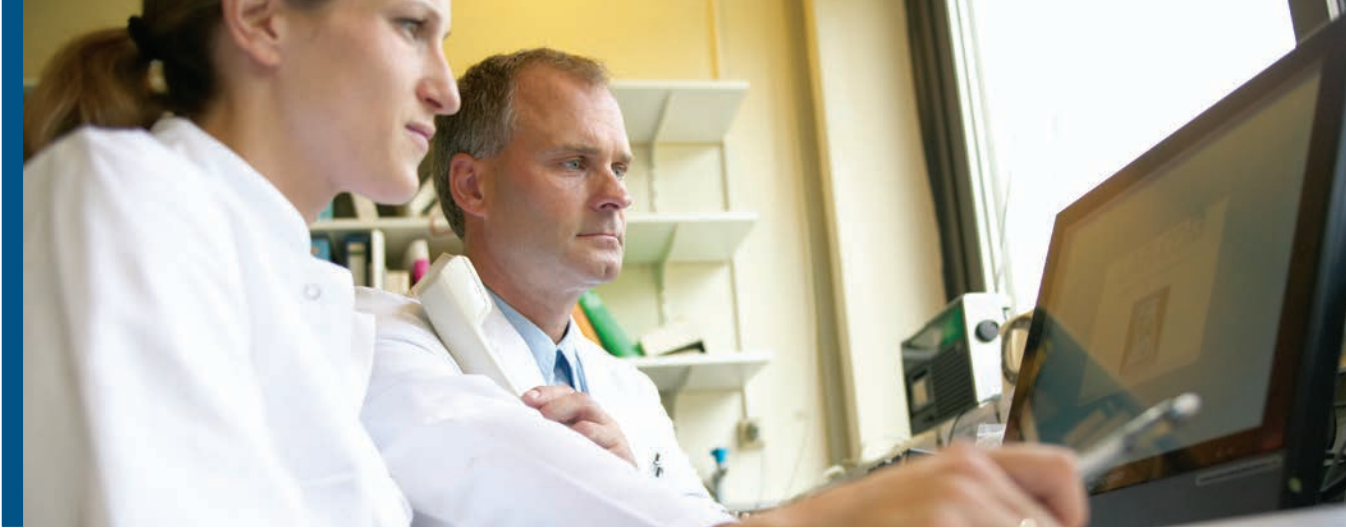


CLINICIAN-DIRECTED INTERVENTION SHOWS POSITIVE EFFECT

In CHOP's large primary care network, CPCE researchers have used a variety of methods, including a cluster randomized trial and qualitative semi-structured interviews to pilot and refine an antimicrobial stewardship intervention. This intervention includes a one-hour clinician education session at the beginning followed by private, personalized audit and feedback reports comparing their rates of guideline-concordant prescribing to others in their practice and network every four months. During the 30-month study period, researchers captured data using a common EHR on 1,259,938 office visits by 185,868 patients to 162 clinicians at 18 practices.

Effect of an Outpatient Antimicrobial Stewardship Intervention on Broad-spectrum Antibiotic Prescribing by Primary Care Pediatricians: A Randomized Trial⁵

To study the effect of the 12-month intervention, researchers randomized the 18 practices into two groups – one receiving the intervention and the other receiving no intervention. Overall, the audit and feedback intervention improved adherence to best practice guidelines for common ARTIs as compared to usual practice. As the chart on page 6 shows, broad-spectrum antibiotic prescribing decreased from 26.8 percent to 14.3 percent among practices receiving the intervention and from 28.4 percent to 22.6 in the control group. The intervention did not reduce off-guideline antibiotic prescribing rates for viral infections, which was already uncommon.

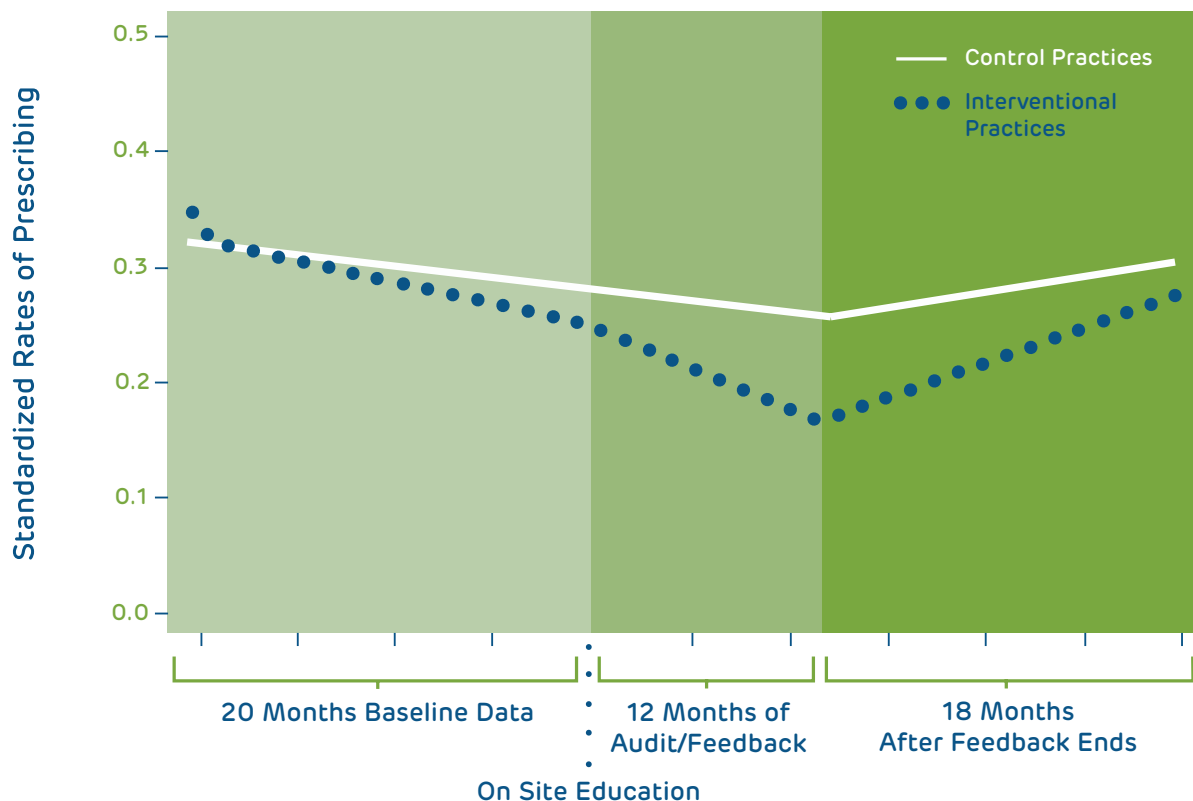


Durability of Benefits of an Outpatient Antimicrobial Stewardship Intervention After Discontinuation of Audit and Feedback⁶

The goal of this study was to assess the durability of the intervention's audit/feedback components. Researchers followed antibiotic prescribing across intervention and control sites for 18 months after termination of audit/feedback and found:

- In the absence of regular audit/feedback, prescribing practices returned to pre-intervention levels: Inappropriate prescribing rose from 16.7 percent to 27.9 percent in the intervention group, and from 25.4 percent to 30.2 percent in the control group.
- Data suggest continued, active audit and feedback are vital to antimicrobial stewardship efforts in outpatient settings.

RATE OF ANTIBIOTIC PRESCRIBING FOR ACUTE VISITS



Pediatrician Perceptions of an Outpatient Antimicrobial Stewardship Intervention⁷

To explore perceptions regarding CHOP's outpatient antimicrobial stewardship intervention and antibiotic overuse for patients with ARTIs, researchers used qualitative, semi-structured interviews with 24 pediatricians that received the intervention.

- Some of the clinicians were deeply skeptical of the audit and feedback reports, with some admitting to ignoring or distrusting them.
- Some of the clinicians do not believe that they play a role in antibiotic overuse despite agreeing that it is a problem.
- Parent pressure for antibiotics was identified by all as a major barrier to more judicious use of this line of medication.

CRITICAL ACTION STEPS TO IMPROVE THE EFFECTIVENESS AND ACCEPTABILITY OF OUTPATIENT ANTIMICROBIAL STEWARDSHIP

- Boost the perceived credibility of audit data
- Engage primary care pediatricians in recognizing that their behavior contributes to antibiotic overuse
- Address perceived parent pressure to prescribe antibiotics
- Determine the appropriate amount and format of audit and feedback needed to sustain consistent judicious use of antibiotics

RESEARCH INTO PRACTICE

CHOP Antibiotic Stewardship in Primary Care

Working with the CHOP Care Network leadership team, CPCE researchers helped adapt the antimicrobial stewardship program into a quality-improvement (QI) project that is now an ongoing, continuous part of the culture of the Network's 30 practices.

CHOP's program includes provider education — championed by informed Network practice leads — to address change management concerns. Decision support tools include point-of-care alerts and family education materials. Recognizing that continuous audit and feedback is critical to success, a real-time data visualization tool is pushed to providers via monthly email feedback reports. Also to address CHOP provider concerns that external providers were prescribing non-recommended antibiotics, an informational mailing packet targeted more than 130+ local urgent care clinics and emergency departments.

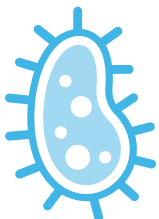
From 2013-2015 appropriate narrow-spectrum antibiotic prescribing for common ARTIs increased by nearly 10 percent during 38,000 visits, and annual costs decreased an estimated \$78,000 for the families and payers tracked during this QI project. Individual families paid on average \$15 to \$24 less for each antibiotic prescription.

CHOP continues to see results of this project, with appropriate first-line antibiotics prescribed by 90 percent of its primary care physicians treating children for routine ARTIs.

INCREASES IN APPROPRIATE PRESCRIBING AFTER INTERVENTION

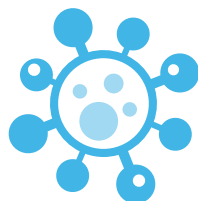
Otitis Media

↑ 9.2%



Sinusitis

↑ 12.5%



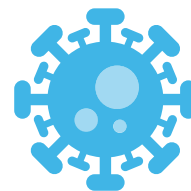
Pharyngitis

↑ 4.2%



Pneumonia

↑ 25.6%



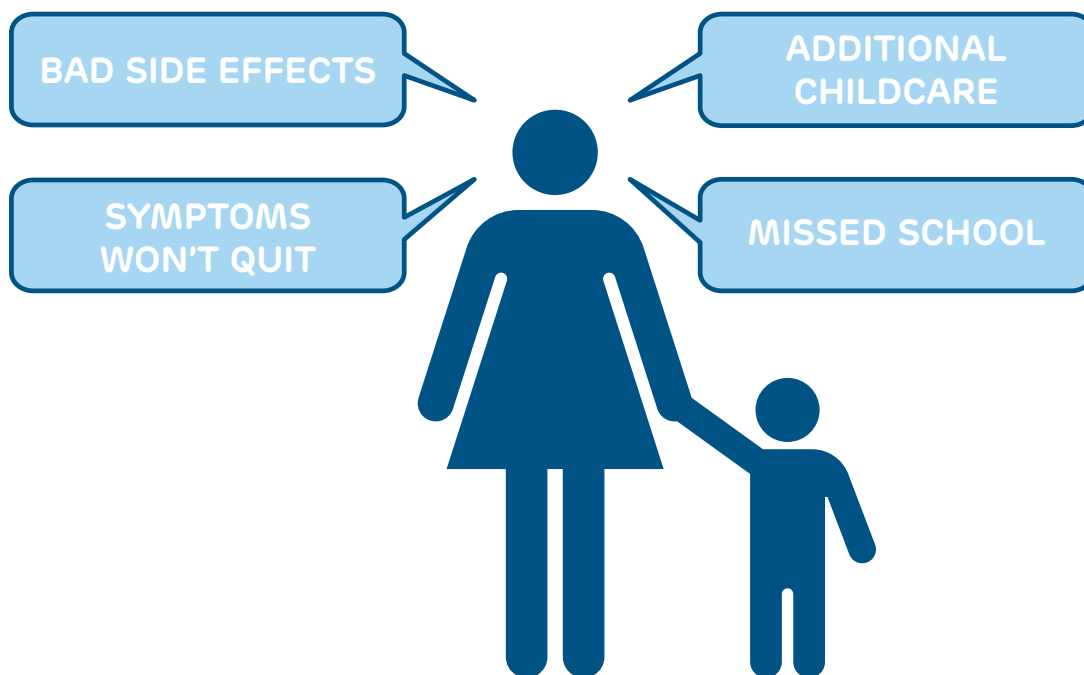


Comparative Effectiveness of Broad Vs. Narrow Spectrum Antibiotics for Acute Respiratory Tract Infections in Children⁸

This qualitative investigation into the thoughts and perceptions of parents and children on their experience with treatment for pediatric ARTIs generated nuanced data that informed the selection of patient- and family-centered outcomes that were then used in a comparative effectiveness study.

The researchers first interviewed more than 100 parents and children who visited primary care pediatric offices with ARTIs (otitis media, GAS, sinusitis) to determine the outcomes related to antibiotics that were most important to them: Parents cited missed school days, additional childcare, adverse side effects, and persistent symptoms as outcomes to avoid.

CAREGIVER CONCERNS ABOUT ARTIs



In a comparative effectiveness trial, researchers then conducted phone interviews with 2,472 caregivers at 10 days and 30 days following antibiotic prescription to measure these patient-centered outcomes, as well as measures provided in the validated PedsQL Survey, where higher scores are associated with better health-related quality of life.

Treatment of ARTIs with narrow-spectrum antibiotics was significantly associated with higher PedsQL scores. Looking at the patient-focused outcomes, the use of broad-spectrum antibiotics was significantly associated with increased risk of adverse drug side effects, something parents want to avoid.

Given these findings and current national prescribing patterns, outpatient antimicrobial stewardship efforts should focus on improving prescribing for the most common childhood ARTIs so that prescribing of narrow-spectrum antibiotics is encouraged.

A background image showing a microscopic view of cells, likely bacteria or viruses, with a blue and purple color scheme. The cells are spherical and have a textured surface.

Beyond CHOP: Replicability and Scalability of Outpatient Antimicrobial Stewardship

In 2016, the CHOP enterprise experienced nearly 1.3 million outpatient visits across its 50-plus-location (and growing) Care Network that provides primary, specialty and urgent care services to a diverse population. CHOP's patient admissions draw mostly from the 19 eastern-most counties in Pennsylvania, as well as from across the state and every county in New Jersey. CHOP has become an incubator for the development of clinical practice models that have potential to scale up and work in other health systems and communities.

CPCE researchers are partnering with colleagues from other children's hospitals and pediatric care networks to increase their capacities for sharing and scaling effective clinical practice models and developing the research tools to test and monitor them.

Dialogue on Acute Respiratory Tract Infections (DART)

CPCE researchers are collaborating with Seattle Children's Hospital researchers, led by Rita Mangione-Smith, MD, MPH, on a clinical trial involving 25 practices in the Pediatric Research in Office Settings (PROS) national network and the North Shore Pediatric network in the state of Illinois. The goal of this study is to develop and test Dialogue on Acute Respiratory Tract Infections (DART), a distance-learning quality improvement program to improve provider communication practices and treatment decisions during ARTI visits. Parent satisfaction and costs of implementation and impact on health care expenditures are also being measured.

In addition to Dr. Mangione-Smith's model for clinician communication training, DART uses the CHOP Outpatient Antimicrobial Stewardship QI model, including its clinician education and audit/feedback components. The clinician toolkit provides webinar training, role play videos, and fact sheets on recommended antibiotic choices for particular ARTI conditions.

If successful in increasing appropriate antibiotic prescribing, DART will provide further validation of the scalability of the outpatient antimicrobial stewardship intervention developed by CHOP's CPCE.

Comparative Effectiveness Research Through a Collaborative Electronic Reporting (CER²) Consortium

CPCE researchers are helping lead an effort through PROS to link data from that EHR-based network with data from independent practices and health systems across the country to develop a platform to promote medication safety and effectiveness for children. Currently, the US lacks a system to use routinely collected EHR clinical data to conduct comparative effectiveness research on pediatric drug therapeutics and other child health topics. CER² involves 222 practice sites in 27 states representing more than 1.2 million people. Multiple studies are currently underway that will detail research methods to improve the analysis of secondary EHR data, supplement routinely collected EHR data with prospective data collection, and use clinical decision support in healthcare decision-making. The long-term goal of this effort is to derive insights from real-world data to broadly improve child health and health care.



RESEARCH INTO POLICY

Key Recommendation 1:

Federal and state agencies should require health care systems to implement antimicrobial stewardship programs in outpatient settings. CHOP research has demonstrated effectiveness, feasibility and scalability of such programs. CDC Core Elements of Outpatient Antibiotic Stewardship provide a framework for antibiotic stewardship for outpatient clinicians and facilities that can guide policy at multiple levels to require:



COMMITMENT

Commit to improving antibiotic prescribing by dedicating the necessary resources



ACTION FOR POLICY AND PRACTICE

Implement at least one policy or practice with demonstrated success at improving antibiotic prescribing



TRACKING AND REPORTING

Track antibiotic prescribing practices and report data back to clinicians



EDUCATION AND EXPERTISE

Offer resources to families on appropriate antibiotic use and provide clinicians access to expertise and training on antibiotic stewardship

Key Recommendation 2:

Encourage EHR vendors to incorporate antimicrobial stewardship for outpatient settings into their suite of clinical effectiveness support modules. The hard work in determining what data elements need to be tracked and provided back to clinical practices has already been completed.

It's Important for Policymakers to Know These Facts

- Antimicrobial stewardship programs ensure that patients get the right antibiotics at the right time for the right duration.
- These programs improve individual patient outcomes, reduce the overall burden of antibiotic resistance, and lower costs for insurers and families that pay for prescriptions.
- A proven effective clinical practice model exists that is scalable and adaptable.
- Clinicians are willing to adopt best practices for quality improvement.
- Parents can be motivated partners to improve antimicrobial stewardship.

RESEARCH FUNDING

- Agency for Healthcare Research and Quality, US Department of Health & Human Services
- Centers for Disease Control and Prevention
- Children's Hospital of Philadelphia
- Eunice Kennedy Shriver National Institute of Child Health and Human Development
- Health Resources and Services Administration Maternal and Child Health Bureau
- National Eye Institute
- National Institutes of Health
- Patient-Centered Outcomes Research Institute (PCORI)

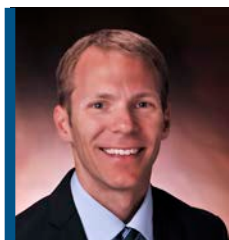
BIBLIOGRAPHY

1. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM Jr, Finkelstein JA, Gerber JS, Hyun DY, Linder JA, Lynfield R, Margolis DJ, May LS, Merenstein D, Metlay JP, Piccirillo JF, Roberts RM, Sanchez GV, Suda KJ, Thomas A. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *JAMA*. 2016 May 3; 315(17):1864-73. PMID: 27139059
2. Fierro JL, Prasad PA, Localio AR, Grundmeier RW, Wasserman RC, Zaoutis TE, Gerber JS. Variability in the Diagnosis and Treatment of Group A Streptococcal Pharyngitis by Primary Care Pediatricians. *Infection Control and Hospital Epidemiology*. 2014 Oct; 35 Suppl 3:S79-85. PMID: 25222902
3. Gerber JS, Prasad PA, Localio RA, Fiks AG, Grundmeier RW, Bell LM, Wasserman RC, Keren R, Zaoutis TE. Variation in Antibiotic Prescribing Across a Pediatric Primary Care Network. *Journal of the Pediatric Infectious Disease Society*. 2015 Dec;4(4):297-304. PMID: 26582868
4. Handy LK, Bryan M, Gerber JS, Zaoutis T, Feemster KA. Variability in Antibiotic Prescribing for Community-Acquired Pneumonia. *Pediatrics*. 2017 Mar 7; e20162331. PMID: 28270546
5. Gerber JS, Prasad PA, Fiks AG, Localio AR, Grundmeier RW, Bell LM, Wasserman RC, Keren R, Zaoutis TE. Effect of an Outpatient Antimicrobial Stewardship Intervention on Broad-spectrum Antibiotic Prescribing by Primary Care Pediatricians: A randomized trial. *JAMA*. 2013 Jun; 309(22):2345-52. PMID: 23757082
6. Gerber JS, Prasad PA, Fiks AG, Localio AR, Bell LM, Keren R, Zaoutis TE. Durability of Benefits of an Outpatient Antimicrobial Stewardship Intervention after Discontinuation of Audit and Feedback. *JAMA*. 2014 Dec; 312(23):2569-70. PMID: 25317759
7. Szymczak JE, Feemster KA, Zaoutis TE, Gerber JS. Pediatrician Perceptions of an Outpatient Antimicrobial Stewardship Intervention. *Infection Control and Hospital Epidemiology*. 2014 Oct; 35 Suppl 3:S69-78. PMID: 25222901
8. Gerber JS, Ross RK, Bryan M, Localio AR, Szymczak JE, Wasserman R, Barkman D, Odeniyi F, Conaboy K, Bell L, Zaoutis TE, Fiks AG. Association of Broad- vs Narrow-Spectrum Antibiotics With Treatment Failure, Adverse Events, and Quality of Life in Children With Acute Respiratory Tract Infections. *JAMA*. 2017 Dec 19;318(23):2325-2336. PMID: 29260224

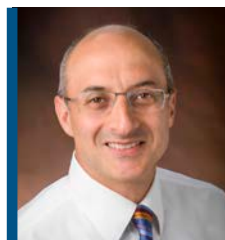
ABOUT

THE

RESEARCHERS



Jeffrey Gerber, MD, PhD, MSCE is the Associate Director for Inpatient Research Activities at the Center for Pediatric Clinical Effectiveness (CPCE) and Director of the Antimicrobial Stewardship Program at Children’s Hospital of Philadelphia (CHOP). Dr. Gerber’s research focuses on the epidemiology and outcomes of antimicrobial use in children with the goal of improving clinical outcomes while limiting the emergence of antimicrobial resistance.



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Theoklis Zaoutis, MD, MSCE is the Director of CPCE. A pediatrician trained in infectious diseases and epidemiology, Dr. Zaoutis’ research interests include the epidemiology, prevention and treatment of healthcare acquired infections, antimicrobial resistance, and antimicrobial use. He is also the Werner and Gertrude Henle Endowed Professor of Pediatrics and Professor of Epidemiology at the Perelman School of Medicine at the University of Pennsylvania and Chief of the Division of Infectious Diseases at CHOP.



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CREDITS

This research brief was produced by the Center for Pediatric Clinical Effectiveness at Children's Hospital of Philadelphia and the Research Communications Department at CHOP.

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